

**PYRIDINE CARBOXAMIDE DERIVATIVES FOR USE
AS ANTICANCER AGENTS**

The invention relates to chemical compounds, or pharmaceutically acceptable salts thereof, which possess B-Raf inhibitory activity and are accordingly useful for their anti-cancer activity and thus in methods of treatment of the human or animal body. The invention also relates to processes for the manufacture of said chemical compounds, to pharmaceutical compositions containing them and to their use in the manufacture of medicaments of use in the production of an anti-cancer effect in a warm-blooded animal such as man.

The classical Ras, Raf, MAP protein kinase/extracellular signal –regulated kinase kinase (MEK), extracellular signal –regulated kinase (ERK) pathway plays a central role in the regulation of a variety of cellular functions dependent upon cellular context, including cellular proliferation, differentiation, survival, immortalization and angiogenesis (reviewed in Peyssonnaud and Eychene, *Biology of the Cell*, 2001, 93, 3-62). In this pathway, Raf family members are recruited to the plasma membrane upon-binding to guanosine triphosphate (GTP) loaded Ras resulting in the phosphorylation and activation of Raf proteins. Activated Rafs then phosphorylate and activate MEKs, which in turn phosphorylate and activate ERKs. Upon activation, ERKs translocate from the cytoplasm to the nucleus resulting in the phosphorylation and regulation of activity of transcription factors such as Elk-1 and Myc.

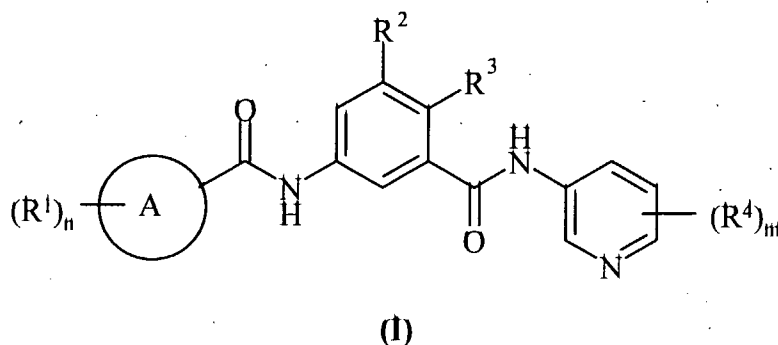
The Ras/Raf/MEK/ERK pathway has been reported to contribute to the tumorigenic phenotype by inducing immortalisation, growth factor-independent growth, insensitivity to growth-inhibitory signals, ability to invade and metastasis, stimulating angiogenesis and inhibition of apoptosis (reviewed in Kolch et al., *Exp.Rev. Mol. Med.*, 2002, 25 April, <http://www.expertreviews.org/02004386h.htm>). In fact, ERK phosphorylation is enhanced in approximately 30% of all human tumours (Hoshino et al., *Oncogene*, 1999, 18, 813-822). This may be a result of overexpression and/or mutation of key members of the pathway.

Three Raf serine/threonine protein kinase isoforms have been reported Raf-1 /c-Raf, B-Raf and A-Raf (reviewed in Mercer and Pritchard, *Biochim. Biophys. Acta*, 2003, 1653, 25-40), the genes for which are thought to have arisen from gene duplication. All three Raf genes are expressed in most tissues with high-level expression of B-Raf in neuronal tissue and A-Raf in urogenital tissue. The highly homologous Raf family members have overlapping but distinct biochemical activities and biological functions (Hagemann and Rapp, *Expt. Cell Res.* 1999, 253, 34-46). Expression of all three Raf genes is required for normal murine

development however both c-Raf and B-Raf are required to complete gestation. B-Raf Δ - mice die at E12.5 due to vascular haemorrhaging caused by increased apoptosis of endothelial cells (Wojnowski et al., Nature Genet., 1997, 16, 293-297). B-Raf is reportedly the major isoform involved in cell proliferation and the primary target of oncogenic Ras. Activating somatic missense mutations have been identified exclusively for B-Raf, occurring with a frequency of 66% in malignant cutaneous melanomas (Davies et al., Nature, 2002, 417, 949-954) and also present in a wide range of human cancers, including but not limited to papillary thyroid tumours (Cohen et al., J. Natl. Cancer Inst., 2003, 95, 625-627), cholangiocarcinomas (Tannapfel et al., Gut, 2003, 52, 706-712), colon and ovarian cancers (Davies et al., Nature, 2002, 417, 949-954). The most frequent mutation in B-Raf (80%) is a glutamic acid for valine substitution at position 600. These mutations increase the basal kinase activity of B-Raf and are thought to uncouple Raf/MEK/ERK signalling from upstream proliferation drives including Ras and growth factor receptor activation resulting in constitutive activation of ERK. Mutated B-Raf proteins are transforming in NIH3T3 cells (Davies et al., Nature, 2002, 417, 949-954) and melanocytes (Wellbrock et al., Cancer Res., 2004, 64, 2338-2342) and have also been shown to be essential for melanoma cell viability and transformation (Hingorani et al., Cancer Res., 2003, 63, 5198-5202). As a key driver of the Raf/MEK/ERK signalling cascade, B-Raf represents a likely point of intervention in tumours dependent on this pathway.

AstraZeneca application WO 00/55120 discloses certain amide derivatives which are inhibitors of the production of cytokines such as TNF, in particular of TNF α , and various interleukins, in particular IL-1. The present inventors have surprisingly found that certain other, novel, amide derivatives are potent B-Raf inhibitors and are accordingly expected to be useful in the treatment of neoplastic disease.

Accordingly, the present invention provides a compound of formula (I):



wherein:

Ring A is phenyl or a monocyclic 5 or 6 membered fully-unsaturated heterocyclic ring; wherein said phenyl or heterocyclic ring may be optionally fused to a five or six membered carbocyclyl or heterocyclyl forming a bicyclic ring; and wherein if said heterocyclyl or heterocyclic ring contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R⁵;

R¹ is a substituent on carbon and is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino, N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, N-(C₁₋₆alkyl)-N-(C₁₋₆alkoxy)sulphamoyl, N,N'-(C₁₋₆alkyl)₂ureido, N',N'-(C₁₋₆alkyl)₂ureido, N-(C₁₋₆alkyl)-N',N'-(C₁₋₆alkyl)₂ureido, C₁₋₆alkylsulphonylamino, carbocyclyl-R⁶- or heterocyclyl-R⁷-; wherein R¹ may be optionally substituted on carbon by one or more R⁸; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R⁹;

n is selected from 0-4; wherein the values of R¹ may be the same or different;

R² is selected from hydrogen, halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁰- or heterocyclyl-R¹¹-; wherein R² may be optionally substituted on carbon by one or more R¹²; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R¹³;

R³ is selected from halo, hydroxy, cyano, methyl, methoxy or hydroxymethyl;

R⁴ is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁴- or heterocyclyl-R¹⁵-;

wherein R^4 may be optionally substituted on carbon by one or more R^{16} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{17} ;

m is selected from 0-4; wherein the values of R^4 may be the same or different;

- 5 R^8 and R^{12} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, N -(C_{1-6} alkyl)- N -(C_{1-6} alkoxy)amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl)₂carbamoyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2,
- 10 C_{1-6} alkoxycarbonyl, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^{18} - or heterocyclyl- R^{19} -; wherein R^8 and R^{12} independently of each other may be optionally substituted on carbon by one or more R^{20} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{21} ;
- 15 R^{16} is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl)₂carbamoyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2, C_{1-6} alkoxycarbonyl, N -(C_{1-6} alkyl)sulphamoyl,
- 20 N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^{22} - or heterocyclyl- R^{23} -; wherein R^{16} may be optionally substituted on carbon by one or more R^{24} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{25} ;

- R^6 , R^7 , R^{10} , R^{11} , R^{14} , R^{15} , R^{18} , R^{19} , R^{22} and R^{23} are independently selected from a
- 25 direct bond, -O-, -N(R^{26})-, -C(O)-, -N(R^{27})C(O)-, -C(O)N(R^{28})-, -S(O)_s-, -SO₂N(R^{29})- or -N(R^{30})SO₂-; wherein R^{26} , R^{27} , R^{28} , R^{29} and R^{30} are independently selected from hydrogen or C_{1-6} alkyl and s is 0-2;

- R^5 , R^9 , R^{13} , R^{17} , R^{21} and R^{25} are independently selected from C_{1-6} alkyl, C_{1-6} alkanoyl, C_{1-6} alkylsulphonyl, C_{1-6} alkoxycarbonyl, carbamoyl, N -(C_{1-6} alkyl)carbamoyl,
- 30 N,N -(C_{1-6} alkyl)carbamoyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl;

R^{20} and R^{24} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxymethyl, methylamino, ethylamino, dimethylamino,

diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, phenyl, methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulphamoyl, *N*-ethylsulphamoyl,

- 5 *N,N*-dimethylsulphamoyl, *N,N*-diethylsulphamoyl or *N*-methyl-*N*-ethylsulphamoyl; or a pharmaceutically acceptable salt thereof;

with the proviso that said compound is not:

N-[4-chloro-3-({[6-(4-methylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

- 10 *N*-[4-chloro-3-({[6-(4-ethylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

N-{4-chloro-3-[(3-(dimethylamino)propyl)(methylamino)pyridin-3-yl]amino}carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide;

N-{4-chloro-3-[(2-(dimethylamino)ethyl)(methylamino)pyridin-3-yl]amino}carbonyl]

- 15 phenyl}-2-morpholin-4-ylisonicotinamide; or

N-[4-chloro-3-({[6-(4-methyl-1,4-diazepan-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide.

According to a further feature of the present invention there is provided a compound of formula (I) wherein:

- 20 **Ring A** is carbocyclyl or heterocyclyl; wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R⁵;

R¹ is a substituent on carbon and is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino,

- 25 *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl,

N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl,

N-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino,

carbocyclyl-R⁶- or heterocyclyl-R⁷-; wherein R¹ may be optionally substituted on carbon by one or more R⁸; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may

- 30 be optionally substituted by a group selected from R⁹;

n is selected from 0-4; wherein the values of R¹ may be the same or different;

R² is selected from hydrogen, halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy,

C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁰- or heterocyclyl-R¹¹-;

5 wherein R² may be optionally substituted on carbon by one or more R¹²; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R¹³;

R³ is selected from halo, hydroxy, cyano, methyl, methoxy or hydroxymethyl;

R⁴ is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy,

10 carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁴- or heterocyclyl-R¹⁵-;

15 wherein R⁴ may be optionally substituted on carbon by one or more R¹⁶; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R¹⁷;

m is selected from 0-4; wherein the values of R⁴ may be the same or different;

R⁸ and R¹² are independently selected from halo, nitro, cyano, hydroxy,

20 trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino,

25 carbocyclyl-R¹⁸- or heterocyclyl-R¹⁹-; wherein R⁸ and R¹² independently of each other may be optionally substituted on carbon by one or more R²⁰; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R²¹;

R¹⁶ is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy,

30 C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R²²- or heterocyclyl-R²³-;

wherein R^{16} may be optionally substituted on carbon by one or more R^{24} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{25} ;

$R^6, R^7, R^{10}, R^{11}, R^{14}, R^{15}, R^{18}, R^{19}, R^{22}$ and R^{23} are independently selected from a
 5 direct bond, -O-, -N(R^{26})-, -C(O)-, -N(R^{27})C(O)-, -C(O)N(R^{28})-, -S(O)_s-, -SO₂N(R^{29})- or -N(R^{30})SO₂-; wherein $R^{26}, R^{27}, R^{28}, R^{29}$ and R^{30} are independently selected from hydrogen or C₁₋₆alkyl and s is 0-2;

$R^5, R^9, R^{13}, R^{17}, R^{21}$ and R^{25} are independently selected from C₁₋₆alkyl, C₁₋₆alkanoyl, C₁₋₆alkylsulphonyl, C₁₋₆alkoxycarbonyl, carbamoyl, N-(C₁₋₆alkyl)carbamoyl,
 10 N,N-(C₁₋₆alkyl)carbamoyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl;
 R^{20} and R^{24} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxymethyl, methylamino, ethylamino, dimethylamino, diethylamino, N-methyl-N-ethylamino, acetylaminomethyl, N-methylcarbamoyl, N-ethylcarbamoyl,
 15 N,N-dimethylcarbamoyl, N,N-diethylcarbamoyl, N-methyl-N-ethylcarbamoyl, methylthio, ethylthio, methylsulphonyl, ethylsulphonyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, N-methylsulphamoyl, N-ethylsulphamoyl, N,N-dimethylsulphamoyl, N,N-diethylsulphamoyl or N-methyl-N-ethylsulphamoyl;
 or a pharmaceutically acceptable salt thereof;

20 with the proviso that said compound is not:

N-[4-chloro-3-({[6-(4-methylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

N-[4-chloro-3-({[6-(4-ethylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

25 N-{4-chloro-3-[(6-[[3-(dimethylamino)propyl](methylamino)pyridin-3-yl]amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide;

N-{4-chloro-3-[(6-[[2-(dimethylamino)ethyl](methylamino)pyridin-3-yl]amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide; or

30 N-[4-chloro-3-({[6-(4-methyl-1,4-diazepan-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide.

In this specification the term "alkyl" includes both straight and branched chain alkyl groups. References to individual alkyl groups such as "propyl" are specific for the straight chain version only and references to individual branched chain alkyl groups such as

'isopropyl' are specific for the branched chain version only. For example, "C₁₋₆alkyl" includes C₁₋₄alkyl, C₁₋₃alkyl, propyl, isopropyl and *t*-butyl. A similar convention applies to other radicals, for example "phenylC₁₋₆alkyl" includes phenylC₁₋₄alkyl, benzyl, 1-phenylethyl and 2-phenylethyl. The term "halo" refers to fluoro, chloro, bromo and iodo.

- 5 Where optional substituents are chosen from "one or more" groups it is to be understood that this definition includes all substituents being chosen from one of the specified groups or the substituents being chosen from two or more of the specified groups.

Ring A may be a "monocyclic 5 or 6 membered fully unsaturated heterocyclic ring".

- A "monocyclic 5 or 6 membered fully unsaturated heterocyclic ring" is fully unsaturated,
 10 monocyclic ring containing 5 or 6 atoms of which at least one atom is chosen from nitrogen, sulphur or oxygen, which may, unless otherwise specified, be carbon or nitrogen linked, wherein a -CH₂- group can optionally be replaced by a -C(O)- and a ring sulphur atom may be optionally oxidised to form the S-oxides. Examples of a "monocyclic 5 or 6 membered fully unsaturated heterocyclic ring" are pyridyl, pyrazolyl, thienyl, isoxazolyl, furanyl,
 15 1,3-thiazolyl, pyrimidinyl and pyrrolyl.

- Ring A may also be phenyl or a monocyclic 5 or 6 membered fully unsaturated heterocyclic ring; "wherein said phenyl or heterocyclic ring may be optionally fused to a five or six membered carbocyclyl or heterocyclyl forming a bicyclic ring". Here said bicyclic ring is a bicyclic ring containing 8, 9 or 10 atoms of which at least one atom is chosen from
 20 nitrogen, sulphur or oxygen, which may, unless otherwise specified, be carbon or nitrogen linked, wherein a -CH₂- group can optionally be replaced by a -C(O)- and a ring sulphur atom may be optionally oxidised to form the S-oxides. Examples of such a bicyclic ring include indolyl, 2,3-dihydrobenzofuranyl, imidazo[1,2-a]pyridinyl, benzimidazolyl and 2-oxoindolinyl.

- 25 A "heterocyclyl" is a saturated, partially saturated or unsaturated, mono or bicyclic ring containing 4-12 atoms of which at least one atom is chosen from nitrogen, sulphur or oxygen, which may, unless otherwise specified, be carbon or nitrogen linked, wherein a -CH₂- group can optionally be replaced by a -C(O)- and a ring sulphur atom may be optionally oxidised to form the S-oxides. Examples and suitable values of the term "heterocyclyl" are
 30 morpholino, piperidyl, pyridyl, pyranyl, pyrrolyl, pyrazolyl, isothiazolyl, indolyl, quinolyl, thienyl, 1,3-benzodioxolyl, thiadiazolyl, piperazinyl, thiazolidinyl, pyrrolidinyl, thiomorpholino, pyrrolinyl, homopiperazinyl, 3,5-dioxapiperidinyl, tetrahydropyranyl, imidazolyl, pyrimidyl, pyrazinyl, pyridazinyl, isoxazolyl, *N*-methylpyrrolyl, 4-pyridone,

1-isoquinolone, 2-pyrrolidone, 4-thiazolidone, pyridine-*N*-oxide and quinoline-*N*-oxide. A particular example of the term "heterocyclyl" is pyrazolyl. In one aspect of the invention a "heterocyclyl" is a saturated, partially saturated or unsaturated, monocyclic ring containing 5 or 6 atoms of which at least one atom is chosen from nitrogen, sulphur or oxygen, it may, unless otherwise specified, be carbon or nitrogen linked, a -CH₂- group can optionally be replaced by a -C(O)- and a ring sulphur atom may be optionally oxidised to form the S-oxides.

A "carbocyclyl" is a saturated, partially saturated or unsaturated, mono or bicyclic carbon ring that contains 3-12 atoms; wherein a -CH₂- group can optionally be replaced by a -C(O)-. Particularly "carbocyclyl" is a monocyclic ring containing 5 or 6 atoms or a bicyclic ring containing 9 or 10 atoms. Suitable values for "carbocyclyl" include cyclopropyl, cyclobutyl, 1-oxocyclopentyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, phenyl, naphthyl, tetralinyl, indanyl or 1-oxoindanyl. A particular example of "carbocyclyl" is phenyl.

An example of "C₁₋₆alkanoyloxy" is acetoxy. Examples of "C₁₋₆alkoxycarbonyl" include methoxycarbonyl, ethoxycarbonyl, *n*- and *t*-butoxycarbonyl. Examples of "C₁₋₆alkoxy" include methoxy, ethoxy and propoxy. Examples of "C₁₋₆alkanoylamino" include formamido, acetamido and propionylamino. Examples of "C₁₋₆alkylS(O)_a wherein a is 0 to 2" include methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl and ethylsulphonyl. Examples of "C₁₋₆alkanoyl" include propionyl and acetyl. Examples of "*N*-(C₁₋₆alkyl)amino" include methylamino and ethylamino. Examples of "*N,N*-(C₁₋₆alkyl)₂amino" include di-*N*-methylamino, di-(*N*-ethyl)amino and *N*-ethyl-*N*-methylamino. Examples of "C₂₋₆alkenyl" are vinyl, allyl and 1-propenyl. Examples of "C₂₋₆alkynyl" are ethynyl, 1-propynyl and 2-propynyl. Examples of "*N*-(C₁₋₆alkyl)sulphamoyl" are *N*-(methyl)sulphamoyl and *N*-(ethyl)sulphamoyl. Examples of "*N*-(C₁₋₆alkyl)₂sulphamoyl" are *N,N*-(dimethyl)sulphamoyl and *N*-(methyl)-*N*-(ethyl)sulphamoyl. Examples of "*N*-(C₁₋₆alkyl)carbamoyl" are *N*-(C₁₋₄alkyl)carbamoyl, methylaminocarbonyl and ethylaminocarbonyl. Examples of "*N,N*-(C₁₋₆alkyl)₂carbamoyl" are *N,N*-(C₁₋₄alkyl)₂carbamoyl, dimethylaminocarbonyl and methylethylaminocarbonyl. Examples of "C₁₋₆alkylsulphonyl" are mesyl, ethylsulphonyl and isopropylsulphonyl. Examples of "C₁₋₆alkylsulphonylamino" are mesylamino, ethylsulphonylamino and isopropylsulphonylamino. Examples of "C₁₋₆alkoxycarbonylamino" are methoxycarbonylamino and *t*-butoxycarbonylamino. Examples of "*N*-(C₁₋₆alkyl)-*N*-(C₁₋₆alkoxy)sulphamoyl" are *N*-(methyl)-*N*-(methoxy)sulphamoyl and *N*-(ethyl)-*N*-(propoxy)sulphamoyl. Example of "*N,N'*-(C₁₋₆alkyl)₂ureido" are

N,N'-dimethylureido and *N*-methyl-*N'*-propylureido. Examples of "*N,N'*-(C₁₋₆alkyl)₂ureido" are *N,N'*-diethylureido and *N'*-methyl-*N'*-propylureido. Example of "*N*-(C₁₋₆alkyl)-*N,N'*-(C₁₋₆alkyl)₂ureido" are *N*-(methyl)-*N'*-ethyl-*N'*-isopropylureido and *N*-ethyl-*N,N'*-diethylureido. Examples of "*N*-(C₁₋₆alkyl)-*N*-(C₁₋₆alkoxy)amino" are

5 *N*-(methyl)-*N*-(propoxy)amino and *N*-methyl-*N*-methoxyamino.

A suitable pharmaceutically acceptable salt of a compound of the invention is, for example, an acid-addition salt of a compound of the invention which is sufficiently basic, for example, an acid-addition salt with, for example, an inorganic or organic acid, for example hydrochloric, hydrobromic, sulphuric, phosphoric, trifluoroacetic, citric or maleic acid. In

10 addition a suitable pharmaceutically acceptable salt of a compound of the invention which is sufficiently acidic is an alkali metal salt, for example a sodium or potassium salt, an alkaline earth metal salt, for example a calcium or magnesium salt, an ammonium salt or a salt with an organic base which affords a physiologically-acceptable cation, for example a salt with methylamine, dimethylamine, trimethylamine, piperidine, morpholine or

15 tris-(2-hydroxyethyl)amine.

Some compounds of the formula (I) may have chiral centres and/or geometric isomeric centres (*E*- and *Z*- isomers), and it is to be understood that the invention encompasses all such optical, diastereoisomers and geometric isomers that possess B-Raf inhibitory activity. The invention further relates to any and all tautomeric forms of the

20 compounds of the formula (I) that possess B-Raf inhibitory activity.

It is also to be understood that certain compounds of the formula (I) can exist in solvated as well as unsolvated forms such as, for example, hydrated forms. It is to be understood that the invention encompasses all such solvated forms which possess B-Raf inhibitory activity.

25 Particular values of variable groups are as follows. Such values may be used where appropriate with any of the definitions, claims or embodiments defined hereinbefore or hereinafter.

Ring A is a monocyclic 5 or 6 membered fully-unsaturated heterocyclic ring; wherein if heterocyclic ring contains an -NH- moiety that nitrogen may be optionally substituted by a

30 group selected from R⁵.

Ring A is phenyl fused to a five or six membered carbocyclyl or heterocyclyl forming a bicyclic ring; wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R⁵.

Ring A is a heterocyclic ring fused to a five or six membered carbocyclyl or heterocyclyl forming a bicyclic ring; wherein if said heterocyclyl or heterocyclic ring contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R⁵.

Ring A is carbocyclyl.

5 Ring A is phenyl.

Ring A is heterocyclyl; wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R⁵.

Ring A is pyridyl.

10 Ring A is pyrazolyl; wherein said pyrazolyl may be optionally substituted on nitrogen by a group selected from R⁵.

Ring A is thienyl.

Ring A is imidazo[1,2-a]pyridinyl.

Ring A is indolyl.

Ring A is 2,3-dihydrobenzofuranyl.

15 Ring A is isoxazolyl.

Ring A is benzimidazolyl.

Ring A is 2-oxoindolinyl.

Ring A is furanyl.

Ring A is 1,3-thiazolyl.

20 Ring A is pyrimidinyl.

Ring A is pyrrolyl.

Ring A is phenyl, pyridyl, pyrazolyl, thienyl, indolyl, 2,3-dihydrobenzofuranyl, imidazo[1,2-a]pyridinyl, isoxazolyl, benzimidazolyl, 2-oxoindolinyl, furanyl, 1,3-thiazolyl, pyrimidinyl and pyrrolyl; wherein said pyrazolyl, indolyl, pyrrolyl may be optionally
25 substituted on nitrogen by a group selected from R⁵; wherein

R⁵ is selected from C₁₋₆alkyl.

Ring A is phenyl, pyridyl, pyrazolyl, thienyl, indolyl, 2,3-dihydrobenzofuranyl and imidazo[1,2-a]pyridinyl; wherein said pyrazolyl may be optionally substituted on nitrogen by a group selected from R⁵; wherein

30 R⁵ is C₁₋₆alkyl.

Ring A is phenyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1-methylpyrazol-5-yl, 1-*r*-butylpyrazol-5-yl, thien-2-yl, thien-3-yl, indol-2-yl, 1-methylindol-2-yl, indol-4-yl, indol-5-yl, indol-6-yl, indol-7-yl, 2,3-dihydrobenzofuran-7-yl, imidazo[1,2-a]pyridin-2-yl, isoxazol-3-yl,

pyrrol-2-yl, benzimidazol-6-yl, 1-methyl-2-oxoindolin-5-yl, furan-2-yl, 1,3-thiazol-5-yl, pyrimidin-4-yl and 1-methylpyrrol-2-yl.

Ring A is phenyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1-methylpyrazol-5-yl, thien-2-yl, thien-3-yl, indol-5-yl, indol-6-yl, 2,3-dihydrobenzofuran-7-yl or imidazo[1,2-a]pyridinyl.

5 Ring A is not pyridyl.

Ring A is not pyrid-4-yl.

R^1 is a substituent on carbon and is selected from halo, cyano, hydroxy, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkoxy, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylS(O)_a wherein a is 0 to 2, C_{1-6} alkoxycarbonylamino, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl)₂sulphamoyl,
10 N -(C_{1-6} alkyl)- N -(C_{1-6} alkoxy)sulphamoyl, N',N' -(C_{1-6} alkyl)₂ureido, C_{1-6} alkylsulphonylamino, carbocyclyl- R^6 - or heterocyclyl- R^7 -; wherein R^1 may be optionally substituted on carbon by one or more R^8 ;

R^8 is selected from halo, cyano, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, N,N -(C_{1-6} alkyl)₂amino, N,N -(C_{1-6} alkyl)₂carbamoyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2,
15 N,N -(C_{1-6} alkyl)₂sulphamoyl, N -(C_{1-6} alkyl)- N -(C_{1-6} alkoxy)amino, carbocyclyl- R^{18} - or heterocyclyl- R^{19} -; wherein R^8 may be optionally substituted on carbon by one or more R^{20} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{21} ;

R^6 , R^7 , R^{18} and R^{19} are independently selected from a direct bond, -O-, -S(O)_s- or
20 -N(R^{30})SO₂-; wherein R^{30} is selected from hydrogen and s is 2;

R^{21} is selected from C_{1-6} alkyl;

R^{20} is selected from cyano or hydroxy.

R^1 is a substituent on carbon and is selected from halo, cyano, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkoxy, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylS(O)_a wherein a is 0 to 2,
25 N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^6 - or heterocyclyl- R^7 -; wherein R^1 may be optionally substituted on carbon by one or more R^8 ;

R^8 is selected from halo, cyano, hydroxy, N,N -(C_{1-6} alkyl)₂amino or heterocyclyl- R^{19} -; wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{21} ;

30 R^6 , R^7 and R^{19} are independently selected from a direct bond, -S(O)_s- or -N(R^{30})SO₂-; wherein R^{30} is hydrogen and s is 0-2;

R^{21} is C_{1-6} alkyl.

R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano, hydroxy, sulphamoyl, methyl, ethyl, isopropyl, sec-butyl, *t*-butyl, 2-methylbut-2-yl, 3-methylbut-2-yl, 1,1-dimethylprop-2-yn-1-yl, 1,1-dimethylbut-2-yn-1-yl, 3,3-dimethylbut-1-yn-1-yl, 3-methylbut-1-yn-1-yl, methoxy, ethoxy, propoxy, isopropoxy, isobutoxy, 5 *N,N*-dimethylamino, *N,N*-diethylamino, methylthio, mesyl, *t*-butoxycarbonylamino, *N*-methylsulphamoyl, *N*-methyl-*N*-propylsulphamoyl, *N,N*-dimethylsulphamoyl, *N*-(methyl)-*N*-(methoxy)sulphamoyl, *N,N'*-dimethylureido, mesylamino, cyclopropyl- R^6 -, phenyl- R^6 -, morpholino- R^7 -, imidazolyl- R^7 -, 1,3-thiazolyl- R^7 -, pyridyl- R^7 -, piperidiny- R^7 - or azetidiny- R^7 -; wherein R^1 may be optionally substituted on carbon by one or more R^8 ;

10 R^8 is selected from fluoro, cyano, hydroxy, methyl, methoxy, *N,N*-dimethylamino, *N,N*-dimethylcarbamoyl, methylthio, mesyl, *N,N*-dimethylsulphamoyl, *N*-(methyl)-*N*-(methoxy)sulphamoyl, cyclopropyl- R^{18} -, piperazinyl- R^{19} -, pyrrolyl- R^{19} - or tetrahydrofuryl- R^{19} -; wherein R^8 may be optionally substituted on carbon by one or more R^{20} ; and wherein said piperazinyl may be optionally substituted on nitrogen by a group selected 15 from R^{21} ;

R^6 , R^7 , R^{18} and R^{19} are independently selected from a direct bond, -O-, -S(O)_s- or -N(R^{30})SO₂-; wherein R^{30} is selected from hydrogen and s is 2;

R^{21} is selected from methyl or ethyl;

R^{20} is selected from cyano or hydroxy.

20 R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano, methyl, isopropyl, *t*-butyl, 3-methylbut-1-yn-1-yl, 3,3-dimethylbut-1-yn-1-yl, methoxy, propoxy, isopropoxy, isobutoxy, dimethylamino, methylthio, mesyl, *N,N*-dimethylsulphamoyl, mesylamino, cyclopropyl- R^6 - or azetidin-1-yl- R^7 -; wherein R^1 may be optionally substituted on carbon by one or more R^8 ;

25 R^8 is selected from fluoro, cyano, hydroxy, dimethylamino or piperazin-1-yl- R^{19} -; wherein said piperazinyl may be optionally substituted on nitrogen by a group selected from R^{21} ;

R^6 , R^7 and R^{19} are independently selected from a direct bond, -S(O)_s- or -N(R^{30})SO₂-; wherein R^{30} is hydrogen and s is 2;

30 R^{21} is methyl or ethyl.

R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano, hydroxy, sulphamoyl, methyl, trifluoromethyl, 1-cyano-1-methylethyl, methoxy, ethoxy, propoxy, isopropoxy, isobutoxy, *N,N*-dimethylamino, difluoromethylthio,

N,N-dimethylsulphamoyl, *t*-butyl, mesyl, cyclopropylaminosulphonyl, azetidin-1-ylsulphonyl, tetrahydrofuran-2-ylmethylaminosulphonyl, *N*-methyl-*N*-(2,3-dihydroxypropyl)sulphamoyl, mesylamino, morpholinosulphonyl, 1-methylpiperazin-4-ylmethyl, 1-ethylpiperazin-4-ylmethyl, 3,3-dimethylbut-1-yn-1-yl, morpholino, *N,N*-dimethylaminomethyl, 3-methyl-3-hydroxybut-1-yn-1-yl, methylthiomethyl, mesylmethyl, *N*-(methyl)-*N*-(methoxy)sulphamoyl, 2-hydroxymethylpiperidin-1-ylsulphonyl, 3-hydroxymethylpiperidin-1-ylsulphonyl, 4-hydroxymethylpiperidin-1-ylsulphonyl, 1,1-difluoroethyl, piperidin-1-yl, *N,N*-diethylamino, *N,N'*-dimethylureido, cyclopropyl, *t*-butoxycarbonylamino, pyrid-2-yl, phenoxy, 2-methoxy-1,1-dimethylethyl, mesylmethyl, 1,3-thiazol-2-yl, 2-methyl-1,3-thiazol-5-yl, 1-methylcyclopropyl, 1,1-dimethylprop-2-yn-1-yl, 1-(*N,N*-dimethylsulphamoyl)-1-methylethyl, 1,1-dimethylbut-2-yn-1-yl, *N*-(methyl)-*N*-(methoxy)aminomethyl, 1-(*N,N*-dimethylcarbamoyl)-1-methylethyl, 4-methylimidazol-1-yl, 1-(cyclopropyl)-1-methylethyl, 2-methyl-3,4-dihydroxybut-2-yl, 2-methylbut-2-yl, 1-hydroxy-1-cyclopropylethyl, 1-cyanoethyl, 2-cyano-3-methylbut-2-yl, 2-cyanobut-2-yl, 1-hydroxy-2-cyanoprop-2-yl and 2-cyanopyrrol-1-ylmethyl.

R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano, methyl, *t*-butyl, trifluoromethyl, dimethylaminomethyl, 1-methyl-1-cyanoethyl, 4-methylpiperazin-1-ylmethyl, 4-ethylpiperazin-1-ylmethyl, 3-hydroxy-3-methylbut-1-yn-1-yl, 3,3-dimethylbut-1-yn-1-yl, methoxy, propoxy, isopropoxy, isobutoxy, dimethylamino, difluoromethylthio, *N,N*-dimethylsulphamoyl, mesyl, cyclopropylaminosulphonyl, azetidin-1-ylsulphonyl or mesylamino.

R^1 is a substituent on carbon and is selected from 1-methyl-1-cyanoethyl.

R^1 is a substituent on carbon and is selected from trifluoromethyl.

n is selected from 0-2; wherein the values of R^1 may be the same or different.

25 n is 0.

n is 1.

n is 2; wherein the values of R^1 may be the same or different.

R^2 is hydrogen.

R^3 is selected from halo, methyl or methoxy.

30 R^3 is selected from halo or methyl.

R^3 is selected from fluoro, chloro, methyl or methoxy.

R^3 is selected from fluoro, chloro or methyl.

R^3 is fluoro.

- 15 -

R³ is chloro.

R³ is methyl.

R³ is methoxy.

R³ is not chloro.

- 5 R⁴ is selected from halo, cyano, hydroxy, amino, carbamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, C₁₋₆alkoxycarbonyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁴- or heterocyclyl-R¹⁵-; wherein R⁴ may be optionally substituted on carbon by one or more R¹⁶; and wherein if said heterocyclyl contains
- 10 an -NH- moiety that nitrogen may be optionally substituted by a group selected from R¹⁷;

R¹⁶ is selected from halo, hydroxy, amino, C₁₋₆alkoxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, carbocyclyl-R²²- or heterocyclyl-R²³-; wherein R¹⁶ may be optionally substituted on carbon by one or more R²⁴; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R²⁵;

- 15 R¹⁴, R¹⁵, R²² and R²³ are independently selected from a direct bond, -N(R²⁶)- or -C(O)N(R²⁸)-; wherein R²⁶ and R²⁸ are hydrogen;

R¹⁷ and R²⁵ are independently selected from C₁₋₆alkyl and C₁₋₆alkoxycarbonyl;

R²⁴ is methyl or phenyl.

- R⁴ is selected from halo, cyano, amino, C₁₋₆alkyl, C₁₋₆alkoxy, *N*-(C₁₋₆alkyl)amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl or heterocyclyl-R¹⁵-; wherein
- 20 R¹⁵ is a direct bond.

- R⁴ is selected from fluoro, chloro, bromo, cyano, hydroxy, amino, carbamoyl, ureido, methyl, ethyl, propyl, prop-1-ynyl, methoxy, ethoxy, propoxy, isopropoxy, acetyl, methylamino, ethylamino, propylamino, isopropylamino, butylamino, dimethylamino, *N*-methyl-*N*-ethylamino, *N*-methyl-*N*-propylamino, formylamino, acetylamino, propanoylamino, 2,2-dimethylpropanoylamino, *N*-methylcarbamoyl, methoxycarbonyl, *N,N*-dimethylsulphamoyl, mesylamino, cyclopropyl-R¹⁴-, cyclobutyl-R¹⁴-, piperazinyl-R¹⁵-, pyrrolyl-R¹⁵-, pyrrolidinyl-R¹⁵-, pyrazolyl-R¹⁵- or morpholino-R¹⁵-; wherein R⁴ may be optionally substituted on carbon by one or more R¹⁶; and wherein said piperazinyl or
- 25 pyrrolidinyl may be optionally substituted on nitrogen by a group selected from R¹⁷;
- 30

R¹⁶ is selected from fluoro, hydroxy, amino, methoxy, methylamino, *N,N*-dimethylamino, cyclopropyl-R²²-, 1,3-dioxolanyl-R²³-, imidazolyl-R²³-, morpholino-R²³-, piperazinyl-R²³-, piperidinyl-R²³- or pyrrolidinyl-R²³-; wherein R¹⁶ may be

optionally substituted on carbon by one or more R^{24} ; and wherein said piperazinyl or pyrrolidinyl may be optionally substituted on nitrogen by a group selected from R^{25} ;

R^{14} , R^{15} , R^{22} and R^{23} are independently selected from a direct bond, $-N(R^{26})-$ or $-C(O)N(R^{28})-$; wherein R^{26} and R^{28} are hydrogen;

5 R^{17} and R^{25} are independently selected from methyl and *t*-butoxycarbonyl;

R^{24} is methyl or phenyl.

R^4 is selected from fluoro, chloro, bromo, cyano, amino, methyl, methoxy, methylamino, acetylamino, *N*-methylcarbamoyl or morpholino.

R^4 is selected from fluoro, chloro, bromo, cyano, hydroxy, amino, carbamoyl, ureido,
 10 methyl, ethyl, methoxy, methylamino, isopropylamino, morpholino, 2-(dimethylamino)ethylamino, 2-(hydroxy)ethylamino, 2-(amino)ethylamino, 3-(pyrrolidin-1-yl)propylamino, *N*-methylcarbamoyl, acetylamino, 2-hydroxyacetylamino, trifluoromethyl, mesylamino, 2,2-dimethylpropanoylamino, 3-methoxypropanoylamino, cyclobutylcarbonylamino, cyclopropylamino, 2,3-dihydroxypropylamino, 1,3-dihydroxyprop-
 15 2-ylamino, 1-methylpiperazin-4-yl, 1-methylpiperazin-4-ylmethyl, acetyl, *N*-methyl-*N*-(3-dimethylaminopropyl)amino, *N*-methyl-*N*-(2-methoxyethyl)amino, dimethylamino, hydroxymethyl, 1,2-dihydroxyethyl, pyrazol-5-ylamino, 3-aminoprop-1-yn-1-yl, 3-hydroxyprop-1-yn-1-yl, 3-methylaminoprop-1-yn-1-yl, 3-dimethylaminoprop-1-yn-1-yl, 4-aminobutylamino, pyrrolidin-2-ylamino, 3-methylaminopropyl, 3-dimethylaminopropyl, 3-
 20 hydroxypropyl, 3-dimethylaminopropylamino, aminomethyl, piperazin-1-yl, 1-methylpiperazin-4-yl, 2,2-dimethyl-1,3-dioxolan-4-ylmethylamino, pyrrolidin-3-ylmethylamino, piperidin-4-ylmethylamino, imidazol-2-ylmethylamino, methoxymethyl, *N,N*-dimethylsulphamoyl, formylamino, morpholinomethyl, aminomethyl, 2-(dimethylamino)ethylamino, pyrrol-1-yl, pyrrol-2-yl, pyrrolidin-2-yl, imidazol-4-yl,
 25 cyclobutylamino, *N*-methyl-*N*-(2-dimethylaminoethyl)amino, 2-dimethylaminoethoxy, dimethylaminomethyl, cyclopropylaminomethyl, piperidin-1-ylmethyl, methylaminomethyl, pyrrolidin-2-ylmethoxy, 3-dimethylaminopropoxy, methoxycarbonyl, 1-(*t*-butoxycarbonyl)pyrrolidin-2-ylmethylamino, 1-(*t*-butoxycarbonyl)pyrrolidin-2-ylmethoxy, 2-phenoxyacetylamino and 1-(*t*-butoxycarbonyl)pyrrolidin-2-yl.

30 m is selected from 0-2; wherein the values of R^4 may be the same or different.

m is 0.

m is 1.

m is 2; wherein the values of R^4 may be the same or different.

Therefore in a further aspect of the invention there is provided a compound of formula (I) (as depicted above) wherein:

Ring A is phenyl, pyridyl, pyrazolyl, thienyl, indolyl, 2,3-dihydrobenzofuranyl, imidazo[1,2-a]pyridinyl, isoxazolyl, benzimidazolyl, 2-oxoindolinyl, furanyl, 1,3-thiazolyl, 5 pyrimidinyl and pyrrolyl; wherein said pyrazolyl, indolyl, pyrrolyl may be optionally substituted on nitrogen by a group selected from R⁵;

R¹ is a substituent on carbon and is selected from halo, cyano, hydroxy, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkoxy, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonylamino, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, 10 *N*-(C₁₋₆alkyl)-*N*-(C₁₋₆alkoxy)sulphamoyl, *N',N'*-(C₁₋₆alkyl)₂ureido, C₁₋₆alkylsulphonylamino, carbocyclyl-R⁶- or heterocyclyl-R⁷-; wherein R¹ may be optionally substituted on carbon by one or more R⁸;

n is selected from 0-2; wherein the values of R¹ may be the same or different;

R² is hydrogen;

15 R³ is selected from halo, methyl or methoxy;

R⁴ is selected from halo, cyano, hydroxy, amino, carbamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, C₁₋₆alkoxycarbonyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁴- or heterocyclyl-R¹⁵-; wherein R⁴ may be 20 optionally substituted on carbon by one or more R¹⁶; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R¹⁷;

R⁵ is selected from C₁₋₆alkyl;

m is selected from 0-2; wherein the values of R⁴ may be the same or different;

R⁶, R⁷, R¹⁸ and R¹⁹ are independently selected from a direct bond, -O-, -S(O)_s- or 25 -N(R³⁰)SO₂-; wherein R³⁰ is selected from hydrogen and s is 2;

R⁸ is selected from halo, cyano, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, *N,N*-(C₁₋₆alkyl)₂amino, *N,N*-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, *N*-(C₁₋₆alkyl)-*N*-(C₁₋₆alkoxy)amino, carbocyclyl-R¹⁸- or heterocyclyl-R¹⁹-; wherein R⁸ may be optionally substituted on carbon by one or more R²⁰; 30 and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R²¹;

R¹⁴, R¹⁵, R²² and R²³ are independently selected from a direct bond, -N(R²⁶)- or -C(O)N(R²⁸)-; wherein R²⁶ and R²⁸ are hydrogen;

R^{16} is selected from halo, hydroxy, amino, C_{1-6} alkoxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, carbocyclyl- R^{22} - or heterocyclyl- R^{23} -; wherein R^{16} may be optionally substituted on carbon by one or more R^{24} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{25} ;

5 R^{17} and R^{25} are independently selected from C_{1-6} alkyl and C_{1-6} alkoxycarbonyl;

R^{21} is selected from C_{1-6} alkyl;

R^{20} is selected from cyano or hydroxy;

R^{24} is methyl or phenyl;

or a pharmaceutically acceptable salt thereof;

10 with the proviso that said compound is not:

N -[4-chloro-3-({[6-(4-methylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

N -[4-chloro-3-({[6-(4-ethylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

15 N -{4-chloro-3-[(6-[[3-(dimethylamino)propyl](methyl)amino]pyridin-3-yl]amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide;

N -{4-chloro-3-[(6-[[2-(dimethylamino)ethyl](methyl)amino]pyridin-3-yl]amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide; or

N -[4-chloro-3-({[6-(4-methyl-1,4-diazepan-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-

20 morpholin-4-ylisonicotinamide.

Therefore in a further aspect of the invention there is provided a compound of formula (I) (as depicted above) wherein:

Ring A is phenyl, pyridyl, pyrazolyl, thienyl, indolyl, 2,3-dihydrobenzofuranyl and imidazo[1,2-a]pyridinyl; wherein said pyrazolyl may be optionally substituted on nitrogen by

25 a group selected from R^5 ;

R^1 is a substituent on carbon and is selected from halo, cyano, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkoxy, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylS(O)_a wherein a is 0 to 2,

N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^6 - or heterocyclyl- R^7 -; wherein R^1 may be optionally substituted on carbon by one or more R^8 ;

30 n is selected from 0-2; wherein the values of R^1 may be the same or different;

R^2 is hydrogen;

R^3 is selected from halo or methyl;

R^4 is selected from halo, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxy, N -(C_{1-6} alkyl)amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl or heterocyclyl- R^{15} ;

m is selected from 0-2; wherein the values of R^4 may be the same or different;

R^5 is C_{1-6} alkyl;

5 R^6 , R^7 and R^{19} are independently selected from a direct bond, $-S(O)_s-$ or $-N(R^{30})SO_2-$; wherein R^{30} is hydrogen and s is 0-2;

R^8 is selected from halo, cyano, hydroxy, N,N -(C_{1-6} alkyl)₂amino or heterocyclyl- R^{19} ; wherein if said heterocyclyl contains an $-NH-$ moiety that nitrogen may be optionally substituted by a group selected from R^{21} ;

10 R^{15} is a direct bond;

R^{21} is C_{1-6} alkyl;

or a pharmaceutically acceptable salt thereof;

with the proviso that said compound is not:

N -{4-chloro-3-[(6-[[3-(dimethylamino)propyl](methyl)amino]pyridin-3-yl)amino]carbonyl}phenyl}-2-morpholin-4-ylisonicotinamide; or
 15 N -{4-chloro-3-[(6-[[2-(dimethylamino)ethyl](methyl)amino]pyridin-3-yl)amino]carbonyl}phenyl}-2-morpholin-4-ylisonicotinamide.

Therefore in a further aspect of the invention there is provided a compound of formula (I) (as depicted above) wherein:

20 Ring A is phenyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1-methylpyrazol-5-yl, 1-*t*-butylpyrazol-5-yl, thien-2-yl, thien-3-yl, indol-2-yl, 1-methylindol-2-yl, indol-4-yl, indol-5-yl, indol-6-yl, indol-7-yl, 2,3-dihydrobenzofuran-7-yl, imidazo[1,2-*a*]pyridin-2-yl, isoxazol-3-yl, pyrrol-2-yl, benzimidazol-6-yl, 1-methyl-2-oxoindolin-5-yl, furan-2-yl, 1,3-thiazol-5-yl, pyrimidin-4-yl and 1-methylpyrrol-2-yl;

25 R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano, hydroxy, sulphamoyl, methyl, trifluoromethyl, 1-cyano-1-methylethyl, methoxy, ethoxy, propoxy, isopropoxy, isobutoxy, N,N -dimethylamino, difluoromethylthio, N,N -dimethylsulphamoyl, *t*-butyl, mesyl, cyclopropylaminosulphonyl, azetidin-1-ylsulphonyl, tetrahydrofuran-2-ylmethylaminosulphonyl, N -methyl- N -(2,3-dihydroxypropyl)sulphamoyl, mesylamino, morpholinosulphonyl, 1-methylpiperazin-4-ylmethyl, 1-ethylpiperazin-4-ylmethyl, 3,3-dimethylbut-1-yn-1-yl, morpholino, N,N -dimethylaminomethyl, 3-methyl-3-hydroxybut-1-yn-1-yl, methylthiomethyl, mesylmethyl, N -(methyl)- N -(methoxy)sulphamoyl, 30 2-hydroxymethylpiperidin-1-ylsulphonyl, 3-hydroxymethylpiperidin-1-ylsulphonyl, 4-

hydroxymethylpiperidin-1-ylsulphonyl, 1,1-difluoroethyl, piperidin-1-yl, *N,N*-diethylamino, *N',N'*-dimethylureido, cyclopropyl, *t*-butoxycarbonylamino, pyrid-2-yl, phenoxy, 2-methoxy-1,1-dimethylethyl, mesylmethyl, 1,3-thiazol-2-yl, 2-methyl-1,3-thiazol-5-yl, 1-methylcyclopropyl, 1,1-dimethylprop-2-yn-1-yl, 1-(*N,N*-dimethylsulphamoyl)-1-methylethyl, 1,1-dimethylbut-2-yn-1-yl, *N*-(methyl)-*N*-(methoxy)aminomethyl, 1-(*N,N*-dimethylcarbamoyl)-1-methylethyl, 4-methylimidazol-1-yl, 1-(cyclopropyl)-1-methylethyl, 2-methyl-3,4-dihydroxybut-2-yl, 2-methylbut-2-yl, 1-hydroxy-1-cyclopropylethyl, 1-cyanoethyl, 2-cyano-3-methylbut-2-yl, 2-cyanobut-2-yl, 1-hydroxy-2-cyanoprop-2-yl and 2-cyanopyrrol-1-ylmethyl;

10 n is selected from 0-2; wherein the values of R^1 may be the same or different;

R^2 is hydrogen;

R^3 is selected from fluoro, chloro, methyl or methoxy;

R^4 is selected from fluoro, chloro, bromo, cyano, hydroxy, amino, carbamoyl, ureido, methyl, ethyl, methoxy, methylamino, isopropylamino, morpholino, 2-

15 (dimethylamino)ethylamino, 2-(hydroxy)ethylamino, 2-(amino)ethylamino, 3-(pyrrolidin-1-yl)propylamino, *N*-methylcarbamoyl, acetylamino, 2-hydroxyacetylamino, trifluoromethyl, mesylamino, 2,2-dimethylpropanoylamino, 3-methoxypropanoylamino, cyclobutylcarbonylamino, cyclopropylamino, 2,3-dihydroxypropylamino, 1,3-dihydroxyprop-2-ylamino, 1-methylpiperazin-4-yl, 1-methylpiperazin-4-ylmethyl, acetyl, *N*-methyl-*N*-(3-dimethylaminopropyl)amino, *N*-methyl-*N*-(2-methoxyethyl)amino, dimethylamino, hydroxymethyl, 1,2-dihydroxyethyl, pyrazol-5-ylamino, 3-aminoprop-1-yn-1-yl, 3-hydroxyprop-1-yn-1-yl, 3-methylaminoprop-1-yn-1-yl, 3-dimethylaminoprop-1-yn-1-yl, 4-aminobutylamino, pyrrolidin-2-ylamino, 3-methylaminopropyl, 3-dimethylaminopropyl, 3-hydroxypropyl, 3-dimethylaminopropylamino, aminomethyl, piperazin-1-yl, 1-

25 methylpiperazin-4-yl, 2,2-dimethyl-1,3-dioxolan-4-ylmethylamino, pyrrolidin-3-ylmethylamino, piperidin-4-ylmethylamino, imidazol-2-ylmethylamino, methoxymethyl, *N,N*-dimethylsulphamoyl, formylamino, morpholinomethyl, aminomethyl, 2-(dimethylamino)ethylamino, pyrrol-1-yl, pyrrol-2-yl, pyrrolidin-2-yl, imidazol-4-yl, cyclobutylamino, *N*-methyl-*N*-(2-dimethylaminoethyl)amino, 2-dimethylaminoethoxy, 30 dimethylaminomethyl, cyclopropylaminomethyl, piperidin-1-ylmethyl, methylaminomethyl, pyrrolidin-2-ylmethoxy, 3-dimethylaminopropoxy, methoxycarbonyl, 1-(*t*-butoxycarbonyl)pyrrolidin-2-ylmethylamino, 1-(*t*-butoxycarbonyl)pyrrolidin-2-ylmethoxy, 2-phenoxyacetylamino and 1-(*t*-butoxycarbonyl)pyrrolidin-2-yl;

m is selected from 0-2; wherein the values of R^4 may be the same or different;
or a pharmaceutically acceptable salt thereof;
with the proviso that said compound is not:

N-[4-chloro-3-({[6-(4-methylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-

5 morpholin-4-ylisonicotinamide;

N-{4-chloro-3-[(6-[[3-(dimethylamino)propyl](methyl)amino]pyridin-3-yl}amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide; or

N-{4-chloro-3-[(6-[[2-(dimethylamino)ethyl](methyl)amino]pyridin-3-yl}amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide.

10 Therefore in a further aspect of the invention there is provided a compound of formula (I) (as depicted above) wherein:

Ring A is phenyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1-methylpyrazol-5-yl, thien-2-yl, thien-3-yl, indol-5-yl, indol-6-yl, 2,3-dihydrobenzofuran-7-yl or imidazo[1,2-a]pyridinyl;

R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano,
15 methyl, *t*-butyl, trifluoromethyl, dimethylaminomethyl, 1-methyl-1-cyanoethyl, 4-methylpiperazin-1-ylmethyl, 4-ethylpiperazin-1-ylmethyl, 3-hydroxy-3-methylbut-1-yn-1-yl, 3,3-dimethylbut-1-yn-1-yl, methoxy, propoxy, isopropoxy, isobutoxy, dimethylamino, difluoromethylthio, *N,N*-dimethylsulphamoyl, mesyl, cyclopropylaminosulphonyl, azetidin-1-ylsulphonyl or mesylamino;

20 n is selected from 0-2; wherein the values of R^1 may be the same or different;

R^2 is hydrogen;

R^3 is selected from fluoro, chloro or methyl;

R^4 is selected from fluoro, chloro, bromo, cyano, amino, methyl, methoxy, methylamino, acetylamino, *N*-methylcarbamoyl or morpholino;

25 m is selected from 0-2; wherein the values of R^4 may be the same or different.
or a pharmaceutically acceptable salt thereof.

In another aspect of the invention, preferred compounds of the invention are any one of the Examples or a pharmaceutically acceptable salt thereof.

In another aspect of the invention, preferred compounds of the invention are any one
30 of:

N-(6-amino-5-chloropyridin-3-yl)-5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide;

N-(6-amino-5-chloropyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)-5-fluorobenzoyl]amino}-2-methylbenzamide;

5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}-*N*-(5-methoxypyridin-3-yl)-2-methylbenzamide;

5 *N*-(6-amino-5-chloropyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide;

5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}-*N*-(5,6-dimethylpyridin-3-yl)-2-methylbenzamide;

N-(3-{[(6-amino-5-chloropyridin-3-yl)amino]carbonyl}-4-methylphenyl)-2-(1-cyano-1-methylethyl)isonicotinamide;

10

N-(6-amino-5-chloropyridin-3-yl)-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide;

N-(6-acetylaminopyridin-3-yl)-5-[3-(cyano-dimethyl-methyl)-benzoylamino]-2-methylbenzamide;

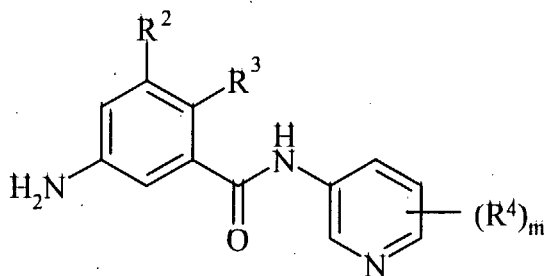
15 *N*-[6-(acetylaminopyridin-3-yl)]-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide; and

N-(6-amino-5-methylpyridin-3-yl)-2-chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}benzamide;

or a pharmaceutically acceptable salt thereof.

20 Another aspect of the present invention provides a process for preparing a compound of formula (I) or a pharmaceutically acceptable salt thereof which process (wherein variable groups are, unless otherwise specified, as defined in formula (I)) comprises of:

Process a) reacting an amine of the formula (II)

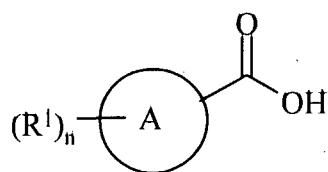


(II)

25

with an acid of formula (III):

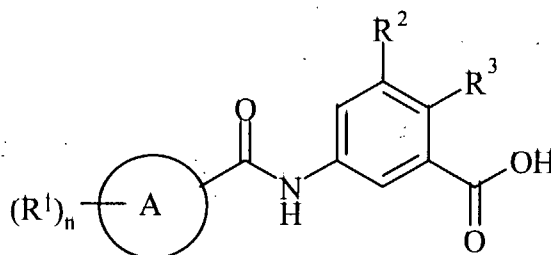
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(III)

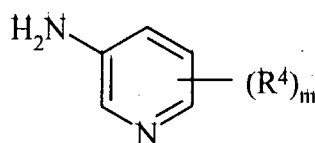
or an activated acid derivative thereof;

Process b) reacting an acid of formula (IV):



(IV)

with an amine of formula (V):



(V)

10 or an activated acid derivative thereof;

and thereafter if necessary:

i) converting a compound of the formula (I) into another compound of the formula (I);

ii) removing any protecting groups;

iii) forming a pharmaceutically acceptable salt.

15 Specific reaction conditions for the above reactions are as follows.

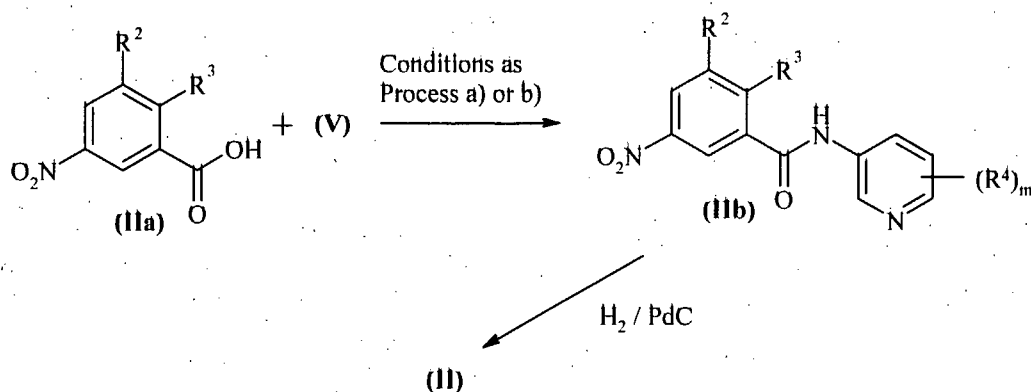
Process a) and *Process b)* Amines and acids may be coupled together in the presence of a suitable coupling reagent. Standard peptide coupling reagents known in the art can be employed as suitable coupling reagents, or for Example carbonyldiimidazole and dicyclohexyl-carbodiimide, optionally in the presence of a catalyst such as

20 dimethylaminopyridine or 4-pyrrolidinopyridine, optionally in the presence of a base for Example triethylamine, pyridine, or 2,6-di-*alkyl*-pyridines such as 2,6-lutidine or 2,6-di-*tert*-butylpyridine. Suitable solvents include dimethylacetamide, dichloromethane, benzene, tetrahydrofuran and dimethylformamide. The coupling reaction may conveniently be performed at a temperature in the range of -40 to 40 °C.

25 Suitable activated acid derivatives include acid halides, for Example acid chlorides,

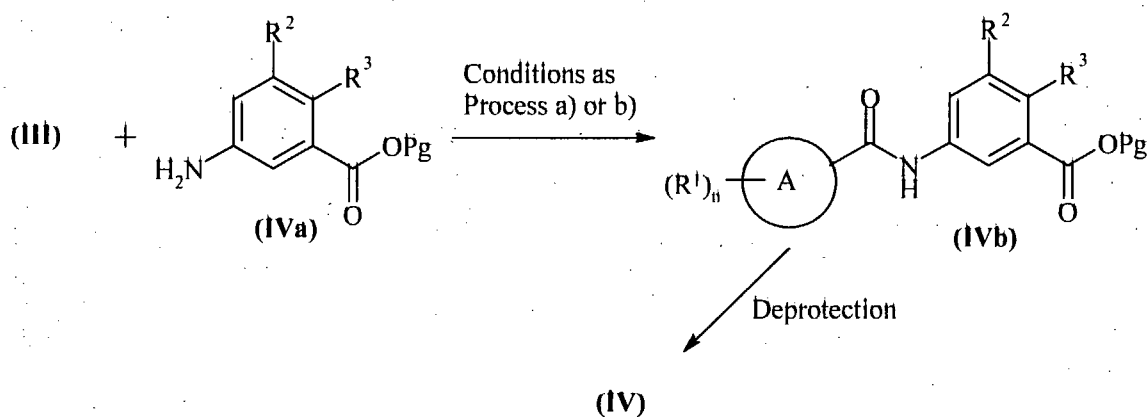
and active esters, for Example pentafluorophenyl esters. The reaction of these types of compounds with amines is well known in the art, for Example they may be reacted in the presence of a base, such as those described above, and in a suitable solvent, such as those described above. The reaction may conveniently be performed at a temperature in the range of 5 -40 to 40 °C.

Amines of formula (II) may be prepared according to *Scheme 1*:



Scheme 1

Acids of formula (IV) may be prepared according to *Scheme 2*:



Scheme 2

Wherein Pg is an acid protecting group, for example such as those described herein below.

Compounds of formula (III), (V), (IIa) and (IVa) are commercially available compounds, or they are known in the literature or they may be prepared by standard processes known in the art.

It will be appreciated that certain of the various ring substituents in the compounds of the present invention may be introduced by standard aromatic substitution reactions or generated by conventional functional group modifications either prior to or immediately following the processes mentioned above, and as such are included in the process aspect of

the invention. Such reactions and modifications include, for example, introduction of a substituent by means of an aromatic substitution reaction, reduction of substituents, alkylation of substituents and oxidation of substituents. The reagents and reaction conditions for such procedures are well known in the chemical art. Particular examples of aromatic substitution reactions include the introduction of a nitro group using concentrated nitric acid, the introduction of an acyl group using, for example, an acyl halide and Lewis acid (such as aluminium trichloride) under Friedel Crafts conditions; the introduction of an alkyl group using an alkyl halide and Lewis acid (such as aluminium trichloride) under Friedel Crafts conditions; and the introduction of a halogeno group. Particular examples of modifications include the reduction of a nitro group to an amino group by for example, catalytic hydrogenation with a nickel catalyst or treatment with iron in the presence of hydrochloric acid with heating; oxidation of alkylthio to alkylsulphinyl or alkylsulphonyl.

It will also be appreciated that in some of the reactions mentioned herein it may be necessary/desirable to protect any sensitive groups in the compounds. The instances where protection is necessary or desirable and suitable methods for protection are known to those skilled in the art. Conventional protecting groups may be used in accordance with standard practice (for illustration see T.W. Green, *Protective Groups in Organic Synthesis*, John Wiley and Sons, 1991). Thus, if reactants include groups such as amino, carboxy or hydroxy it may be desirable to protect the group in some of the reactions mentioned herein.

A suitable protecting group for an amino or alkylamino group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an alkoxycarbonyl group, for example a methoxycarbonyl, ethoxycarbonyl or *t*-butoxycarbonyl group, an arylmethoxycarbonyl group, for example benzyloxycarbonyl, or an aroyl group, for example benzoyl. The deprotection conditions for the above protecting groups necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or alkoxycarbonyl group or an aroyl group may be removed for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an acyl group such as a *t*-butoxycarbonyl group may be removed, for example, by treatment with a suitable acid as hydrochloric, sulphuric or phosphoric acid or trifluoroacetic acid and an arylmethoxycarbonyl group such as a benzyloxycarbonyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon, or by treatment with a Lewis acid for example boron tris(trifluoroacetate). A suitable alternative protecting group

for a primary amino group is, for example, a phthaloyl group which may be removed by treatment with an alkylamine, for example dimethylaminopropylamine, or with hydrazine.

A suitable protecting group for a hydroxy group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an aroyl group, for example benzoyl, or an arylmethyl group, for example benzyl. The deprotection conditions for the above protecting groups will necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or an aroyl group may be removed, for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an arylmethyl group such as a benzyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

A suitable protecting group for a carboxy group is, for example, an esterifying group, for example a methyl or an ethyl group which may be removed, for example, by hydrolysis with a base such as sodium hydroxide, or for example a *t*-butyl group which may be removed, for example, by treatment with an acid, for example an organic acid such as trifluoroacetic acid, or for example a benzyl group which may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

The protecting groups may be removed at any convenient stage in the synthesis using conventional techniques well known in the chemical art.

As stated hereinbefore the compounds defined in the present invention possess anti-cancer activity which is believed to arise from the B-Raf inhibitory activity of the compounds. These properties may be assessed, for example, using the procedure set out below.

B-Raf in vitro ELISA assay

Activity of human recombinant, purified wild type His-B-Raf protein kinase was determined in vitro using an enzyme-linked immunosorbent assay (ELISA) assay format, which measures phosphorylation of the B-Raf substrate, human recombinant, purified His-derived (detagged) MEK1. The reaction utilized 2.5 nM B-Raf, 0.15 μ M MEK1 and 10 μ M adenosine triphosphate (ATP) in 40 mM *N*-(2-hydroxyethyl)piperazine-*N'*-(2-ethanesulfonic acid hemisodium salt (HEPES), 5 mM 1,4-dithio-DL-threitol (DTT), 10 mM MgCl_2 , 1 mM ethylenediaminetetraacetic acid (EDTA) and 0.2 M NaCl (1x HEPES buffer), with or without compound at various concentrations, in a total reaction volume of 25 μ l in 384 well plates. B-Raf and compound were preincubated in 1x HEPES buffer for 1 hour at 25 °C. Reactions were initiated with addition of MEK1 and ATP in 1x HEPES buffer and incubated

at 25 °C for 50 minutes and reactions stopped by addition of 10 µl 175 mM EDTA (final concentration 50 mM) in 1x HEPES buffer. 5 µl of the assay mix was then diluted 1:20 into 50 mM EDTA in 1x HEPES buffer, transferred to 384 well black high protein binding plates and incubated overnight at 4 °C. Plates were washed in tris buffered saline containing 0.1% Tween20 (TBST), blocked with 50 µl Superblock (Pierce) for 1 hour at 25 °C, washed in TBST, incubated with 50 µl rabbit polyclonal anti-phospho-MEK antibody (Cell Signaling) diluted 1:1000 in TBS for 2 hours at 25 °C, washed with TBST, incubated with 50 µl goat anti-rabbit horseradish peroxidase -linked antibody (Cell Signaling) diluted 1:2000 in TBS for 1 hour at 25 °C and washed with TBST. 50 µl of fluorogenic peroxidase substrate (Quantiablu - Pierce) was added and following incubation for 45-60 minutes, 50 µl QuantiabluSTOP (Pierce) was added. Blue fluorescent product was detected at excitation 325 and emission 420 using a TECAN Ultra plate reader. Data was graphed and IC₅₀s calculated using Excel Fit (Microsoft).

When tested in the above *in vitro* assay, the compounds of the present invention exhibited activity less than 30 µM. For example the following results were obtained:

Example No	IC ₅₀ (µM)
Example 44	0.057
Example 5	0.505
Example 9	1.08

According to a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore, in association with a pharmaceutically-acceptable diluent or carrier.

The composition may be in a form suitable for oral administration, for example as a tablet or capsule, for parenteral injection (including intravenous, subcutaneous, intramuscular, intravascular or infusion) as a sterile solution, suspension or emulsion, for topical administration as an ointment or cream or for rectal administration as a suppository.

In general the above compositions may be prepared in a conventional manner using conventional excipients.

The compound of formula (I) will normally be administered to a warm-blooded animal at a unit dose within the range 1-1000 mg/kg, and this normally provides a therapeutically-effective dose. Preferably a daily dose in the range of 10-100 mg/kg is employed. However the daily dose will necessarily be varied depending upon the host treated,

the particular route of administration, and the severity of the illness being treated.

Accordingly the optimum dosage may be determined by the practitioner who is treating any particular patient.

According to a further aspect of the present invention there is provided a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore for use in a method of treatment of the human or animal body by therapy.

We have found that the compounds defined in the present invention, or a pharmaceutically acceptable salt thereof, are effective anti-cancer agents which property is believed to arise from their B-Raf inhibitory properties. Accordingly the compounds of the present invention are expected to be useful in the treatment of diseases or medical conditions mediated alone or in part by B-Raf, i.e. the compounds may be used to produce a B-Raf inhibitory effect in a warm-blooded animal in need of such treatment.

Thus the compounds of the present invention provide a method for treating cancer characterised by inhibition of B-Raf, i.e. the compounds may be used to produce an anti-cancer effect mediated alone or in part by the inhibition of B-Raf.

Such a compound of the invention is expected to possess a wide range of anti-cancer properties as activating mutations in B-Raf have been observed in many human cancers, including but not limited to, melanoma, papillary thyroid tumors, cholangiocarcinomas, colon, ovarian and lung cancers. Thus it is expected that a compound of the invention will possess anti-cancer activity against these cancers. It is in addition expected that a compound of the present invention will possess activity against a range of leukaemias, lymphoid malignancies and solid tumours such as carcinomas and sarcomas in tissues such as the liver, kidney, bladder, prostate, breast and pancreas. In particular such compounds of the invention are expected to slow advantageously the growth of primary and recurrent solid tumours of, for example, the skin, colon, thyroid, lungs and ovaries. More particularly such compounds of the invention, or a pharmaceutically acceptable salt thereof, are expected to inhibit the growth of those primary and recurrent solid tumours which are associated with B-Raf, especially those tumours which are significantly dependent on B-Raf for their growth and spread, including for example, certain tumours of the skin, colon, thyroid, lungs and ovaries. Particularly the compounds of the present invention are useful in the treatment of melanomas.

Thus according to this aspect of the invention there is provided a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore for use as a medicament.

According to a further aspect of the invention there is provided the use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore in the manufacture of a medicament for use in the production of a B-Raf inhibitory effect in a warm-blooded animal such as man.

- 5 According to this aspect of the invention there is provided the use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore in the manufacture of a medicament for use in the production of an anti-cancer effect in a warm-blooded animal such as man.

- According to a further feature of the invention, there is provided the use of a
10 compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined herein before in the manufacture of a medicament for use in the treatment of melanoma, papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer, leukaemias, lymphoid malignancies, carcinomas and sarcomas in the liver, kidney, bladder, prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon, thyroid, lungs
15 and ovaries.

 According to a further feature of this aspect of the invention there is provided a method for producing a B-Raf inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as defined above.

- 20 According to a further feature of this aspect of the invention there is provided a method for producing an anti-cancer effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as defined above.

- According to an additional feature of this aspect of the invention there is provided a
25 method of treating melanoma, papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer, leukaemias, lymphoid malignancies, carcinomas and sarcomas in the liver, kidney, bladder, prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon, thyroid, lungs and ovaries, in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective
30 amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined herein before.

According to a further aspect of the invention there is provided the use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore for use in the production of a B-Raf inhibitory effect in a warm-blooded animal such as man.

According to this aspect of the invention there is provided the use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore for use in the production of an anti-cancer effect in a warm-blooded animal such as man.

According to a further feature of the invention, there is provided the use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined hereinbefore for use in the treatment of melanoma, papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer, leukaemias, lymphoid malignancies, carcinomas and sarcomas in the liver, kidney, bladder, prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon, thyroid, lungs and ovaries.

In a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined herein before in association with a pharmaceutically-acceptable diluent or carrier for use in the production of a B-Raf inhibitory effect in a warm-blooded animal such as man.

In a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined herein before in association with a pharmaceutically-acceptable diluent or carrier for use in the production of an anti-cancer effect in a warm-blooded animal such as man.

In a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as defined herein before in association with a pharmaceutically-acceptable diluent or carrier for use in the treatment of melanoma, papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer, leukaemias, lymphoid malignancies, carcinomas and sarcomas in the liver, kidney, bladder, prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon, thyroid, lungs and ovaries in a warm-blooded animal such as man.

The B-Raf inhibitory treatment defined hereinbefore may be applied as a sole therapy or may involve, in addition to the compound of the invention, conventional surgery or radiotherapy or chemotherapy. Such chemotherapy may include one or more of the following categories of anti-tumour agents :-

- (i) antiproliferative/antineoplastic drugs and combinations thereof, as used in medical oncology, such as alkylating agents (for example cis-platin, carboplatin, cyclophosphamide, nitrogen mustard, melphalan, chlorambucil, busulphan and nitrosoureas); antimetabolites (for example antifolates such as fluoropyrimidines like 5-fluorouracil and tegafur, raltitrexed, 5 methotrexate, cytosine arabinoside and hydroxyurea; antitumour antibiotics (for example anthracyclines like adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin and mithramycin); antimitotic agents (for example vinca alkaloids like vincristine, vinblastine, vindesine and vinorelbine and taxoids like taxol and taxotere); and topoisomerase inhibitors (for example epipodophyllotoxins like etoposide and 10 teniposide, amsacrine, topotecan and camptothecin);
- (ii) cytostatic agents such as antioestrogens (for example tamoxifen, toremifene, raloxifene, droloxifene and idoxifene), oestrogen receptor down regulators (for example fulvestrant), antiandrogens (for example bicalutamide, flutamide, nilutamide and cyproterone acetate), LHRH antagonists or LHRH agonists (for example goserelin, leuprorelin and 15 buserelin), progestogens (for example megestrol acetate), aromatase inhibitors (for example as anastrozole, letrozole, vorazole and exemestane) and inhibitors of 5 α -reductase such as finasteride;
- (iii) Agents which inhibit cancer cell invasion (for example metalloproteinase inhibitors like marimastat and inhibitors of urokinase plasminogen activator receptor function);
- 20 (iv) inhibitors of growth factor function, for example such inhibitors include growth factor antibodies, growth factor receptor antibodies (for example the anti-erb2 antibody trastuzumab [Herceptin™] and the anti-erb1 antibody cetuximab [C225]), farnesyl transferase inhibitors, MEK inhibitors, tyrosine kinase inhibitors and serine/threonine kinase inhibitors, for example inhibitors of the epidermal growth factor family (for example EGFR 25 family tyrosine kinase inhibitors such as *N*-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (gefitinib, AZD1839), *N*-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine (erlotinib, OSI-774) and 6-acrylamido-*N*-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)quinazolin-4-amine (CI 1033)), for example inhibitors of the platelet-derived growth factor family and for example inhibitors of the 30 hepatocyte growth factor family;
- (v) antiangiogenic agents such as those which inhibit the effects of vascular endothelial growth factor, (for example the anti-vascular endothelial cell growth factor antibody bevacizumab [Avastin™], compounds such as those disclosed in International Patent

Applications WO 97/22596, WO 97/30035, WO 97/32856 and WO 98/13354) and compounds that work by other mechanisms (for example linomide, inhibitors of integrin $\alpha v \beta 3$ function and angiostatin);

(vi) vascular damaging agents such as Combretastatin A4 and compounds disclosed in

5 International Patent Applications WO 99/02166, WO00/40529, WO 00/41669, WO01/92224, WO02/04434 and WO02/08213;

(vii) antisense therapies, for example those which are directed to the targets listed above, such as ISIS 2503, an anti-ras antisense;

(viii) gene therapy approaches, including for example approaches to replace aberrant genes
10 such as aberrant p53 or aberrant BRCA1 or BRCA2, GDEPT (gene-directed enzyme pro-drug therapy) approaches such as those using cytosine deaminase, thymidine kinase or a bacterial nitroreductase enzyme and approaches to increase patient tolerance to chemotherapy or radiotherapy such as multi-drug resistance gene therapy;

(ix) immunotherapy approaches, including for example ex-vivo and in-vivo approaches to
15 increase the immunogenicity of patient tumour cells, such as transfection with cytokines such as interleukin 2, interleukin 4 or granulocyte-macrophage colony stimulating factor, approaches to decrease T-cell anergy, approaches using transfected immune cells such as cytokine-transfected dendritic cells, approaches using cytokine-transfected tumour cell lines and approaches using anti-idiotypic antibodies;

20 (x) Cell cycle inhibitors including for example CDK inhibitors (eg flavopiridol) and other inhibitors of cell cycle checkpoints (eg checkpoint kinase); inhibitors of aurora kinase and other kinases involved in mitosis and cytokinesis regulation (eg mitotic kinesins); and histone deacetylase inhibitors; and

(xi) endothelin antagonists, including endothelin A antagonists, endothelin B antagonists and
25 endothelin A and B antagonists; for example ZD4054 and ZD1611 (WO 96 40681), atrasentan and YM598.

Such conjoint treatment may be achieved by way of the simultaneous, sequential or separate dosing of the individual components of the treatment. Such combination products employ the compounds of this invention within the dosage range described hereinbefore and
30 the other pharmaceutically-active agent within its approved dosage range.

In addition to their use in therapeutic medicine, the compounds of formula (I) and their pharmaceutically acceptable salts are also useful as pharmacological tools in the development and standardisation of *in vitro* and *in vivo* test systems for the evaluation of the

effects of inhibitors of B-Raf in laboratory animals such as cats, dogs, rabbits, monkeys, rats and mice, as part of the search for new therapeutic agents.

In the above other pharmaceutical composition, process, method, use and medicament manufacture features, the alternative and preferred embodiments of the compounds of the invention described herein also apply.

Examples

The invention will now be illustrated by the following non limiting examples in which, unless stated otherwise:

- (i) temperatures are given in degrees Celsius ($^{\circ}\text{C}$); operations were carried out at room or ambient temperature, that is, at a temperature in the range of $18\text{-}25^{\circ}\text{C}$;
- (ii) organic solutions were dried over anhydrous sodium sulphate; evaporation of solvent was carried out using a rotary evaporator under reduced pressure (600-4000 Pascals; 4.5-30 mmHg) with a bath temperature of up to 60°C ;
- (iii) in general, the course of reactions was followed by TLC and reaction times are given for illustration only;
- (iv) final products had satisfactory proton nuclear magnetic resonance (NMR) spectra and/or mass spectral data;
- (v) yields are given for illustration only and are not necessarily those which can be obtained by diligent process development; preparations were repeated if more material was required;
- (vi) when given, NMR data is in the form of delta values for major diagnostic protons, given in parts per million (ppm) relative to tetramethylsilane (TMS) as an internal standard, determined at 400 MHz using perdeuterio dimethyl sulphoxide (DMSO-d_6) as solvent unless otherwise indicated;
- (vii) chemical symbols have their usual meanings; SI units and symbols are used;
- (viii) solvent ratios are given in volume:volume (v/v) terms; and
- (ix) mass spectra were run with an electron energy of 70 electron volts in the chemical ionization (CI) mode using a direct exposure probe; where indicated ionization was effected by electron impact (EI), fast atom bombardment (FAB) or electrospray (ESP); values for m/z are given; generally, only ions which indicate the parent mass are reported; and unless otherwise stated, the mass ion quoted is $(\text{MH})^{+}$;
- (x) where a synthesis is described as being analogous to that described in a previous example the amounts used are the millimolar ratio equivalents to those used in the previous example;
- (xi) the following abbreviations have been used:

	HATU	<i>O</i> -(7-Azabenzotriazol-1-yl)- <i>N,N,N',N'</i> -tetramethyluronium hexafluorophosphate;
	THF	tetrahydrofuran;
	DMF	<i>N,N</i> -dimethylformamide;
5	EtOAc	ethyl acetate;
	DIEA	<i>N,N</i> -diisopropylethylamine;
	DCM	dichloromethane;
	DMSO	dimethylsulphoxide;
	MeCN	acetonitrile;
10	NBS	<i>N</i> -bromosuccinimide; and
	MeOH	methanol;

(xii) "ISCO" refers to normal phase flash column chromatography using 12 g and 40 g pre-packed silica gel cartridges used according to the manufacturers instruction obtained from ISCO, Inc, 4700 superior street Lincoln, NE, USA.; and

15 (xiii) "Gilson HPLC" refers to a YMC-AQC18 reverse phase HPLC Column with dimension 20 mm/100 and 50 mm/250 in water/MeCN with 0.1% TFA as mobile phase, obtained

(xiv) Parr Hydrogenator or Parr shaker type hydrogenators are systems for treating chemicals with hydrogen in the presence of a catalyst at pressures up to 5 atmospheres (60 psig) and temperatures to 80 °C.

20

Example 1

5-[(3-Fluorobenzoyl)amino]-2-methyl-*N*-pyridin-3-ylbenzamide

A solution of 5-amino-2-methyl-*N*-pyridin-3-ylbenzamide (Method 68; 60 mg, 0.264 mmol), 3-fluorobenzoic acid (41 mg, 0.290 mmol) and DIEA (115 µL, 0.66 mmol) in DMF
 25 (1.5 ml) was treated with HATU (120 mg, 0.3168 mmol). The reaction mixture was shaken overnight at 25 °C. Water (10 ml) was added slowly to precipitate the product. The resulting precipitate was washed with water (10 ml), isolated and dried overnight in a vacuum oven at 70 °C to give the title compound 61.2 mg, (66%) as a solid. NMR (300 MHz): 10.59 (s, 1H), 10.43 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.92 (s, 1H), 7.75-7.84 (m, 3H), 7.55-
 30 7.63 (m, 1H), 7.37-7.48 (m, 2H), 7.31 (d, 1H), 2.35 (s, 3H); *m/z* 349.

Examples 2-120

The following compounds were prepared by the procedure in Example 1 using 5-amino-2-methyl-*N*-pyridin-3-ylbenzamide (Method 68) or 5-amino-2-chloro-*N*-(5-fluoropyridin-3-yl)benzamide for (Method 79) Example 55 and the appropriate SM. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex.	Compound	NMR	m/z	SM
2	4-Chloro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}pyridine-2-carboxamide	10.83 (s, 1H), 10.62 (s, 1H), 8.90 (s, 1H), 8.72 (d, 1H), 8.30 (d, 1H), 8.14-8.21 (m, 2H), 8.09 (s, 1H), 7.83-7.95 (m, 2H), 7.29-7.41 (m, 2H), 2.35 (s, 3H)	367	4-Chloropyridine-2-carboxylic acid
3	2-Methyl-5-{[4-methyl-3-(trifluoromethyl)benzoyl]amino}- <i>N</i> -pyridin-3-ylbenzamide	10.59 (s, 1H), 10.52 (s, 1H), 8.88 (s, 1H), 8.25-8.32 (m, 2H), 8.17 (d, 2H), 7.83-7.94 (m, 2H), 7.63 (d, 1H), 7.30-7.41 (m, 2H), 2.52 (s, 3H), 2.35 (s, 3H)	414	4-Methyl-3-(trifluoromethyl)benzoic acid
4	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1H-indole-6-carboxamide	11.48 (s, 1H), 10.58 (s, 1H), 10.28 (s, 1H), 8.89 (s, 1H), 8.31 (d, 1H), 8.19 (d, 1H), 8.08 (s, 1H), 7.98 (s, 1H), 7.87 (d, 1H), 7.65 (s, 2H), 7.55 (t, 1H), 7.39 (dd, 1H), 7.29 (d, 1H), 6.52 (s, 1H), 2.35 (s, 3H)	371	1H-Indole-6-carboxylic acid
5	5-[(3-Cyanobenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.58 (d, 2H), 8.88 (s, 1H), 8.42 (s, 1H), 8.24-8.32 (m, 2H), 8.18 (d, 1H), 8.07 (d, 1H), 7.91 (s, 1H), 7.73-7.85 (m, 2H), 7.30-7.42 (m, 2H), 2.36 (s, 3H)	357	3-Cyanobenzoic acid

Ex.	Compound	NMR	m/z	SM
6	1,3-Dimethyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1H-pyrazole-5-carboxamide	10.55 (s, 1H), 10.05 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 8.00 (s, 1H), 7.83 (d, 1H), 7.39 (dd, 1H), 7.24 (d, 1H), 6.55 (s, 1H), 3.82 (s, 3H), 2.31 (d, 6H)	350	1,3-Dimethyl-1H-pyrazole-5-carboxylic acid
7	5-[(4-Fluoro-3-methylbenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.59 (s, 1H), 10.35 (s, 1H), 8.89 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.81-7.95 (m, 4H), 7.26-7.41 (m, 3H), 2.33 (d, 6H)	364	4-Fluoro-3-methylbenzoic acid
8	5-[(4-Methoxy-3-methylbenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.57 (s, 1H), 10.14 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.91 (s, 1H), 7.80-7.88 (m, 3H), 7.39 (dd, 1H), 7.28 (d, 1H), 7.06 (d, 1H), 3.79-3.88 (m, 3H), 2.34 (s, 3H), 2.21 (s, 3H)	376	4-Methoxy-3-methylbenzoic acid
9	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2,3-dihydro-1-benzofuran-7-carboxamide	10.58 (s, 1H), 9.84 (s, 1H), 8.89 (s, 1H), 8.31 (d, 1H), 8.18 (d, 1H), 7.86 (s, 1H), 7.77 (d, 1H), 7.60 (d, 1H), 7.37-7.46 (m, 2H), 7.29 (d, 1H), 6.98 (t, 1H), 4.74 (t, 2H), 3.27 (t, 2H), 2.34 (s, 3H)	374	2,3-Dihydro-1-benzofuran-7-carboxylic acid
10	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1H-indole-5-carboxamide	11.45 (s, 1H), 10.59 (s, 1H), 10.25 (s, 1H), 8.90 (s, 1H), 8.26-8.32 (m, 2H), 8.20 (d, 1H), 8.00 (s, 1H), 7.87 (d, 1H), 7.75 (d, 1H), 7.37-7.50 (m, 3H), 7.28 (d, 1H), 6.58 (s, 1H), 2.35 (s, 3H)	371	1H-Indole-5-carboxylic acid

Ex.	Compound	NMR	m/z	SM
11	8-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}imidazo[1,2- <i>a</i>]pyridine-2-carboxamide	10.58 (s, 1H), 10.14 (s, 1H), 8.89 (s, 1H), 8.44-8.52 (m, 2H), 8.31 (d, 1H), 8.19 (d, 1H), 8.07 (s, 1H), 7.94 (d, 1H), 7.39 (dd, 1H), 7.30 (d, 1H), 7.17 (d, 1H), 6.91 (t, 1H), 2.57 (s, 3H), 2.35 (s, 3H)	386	8-Methyl-imidazo[1,2- <i>a</i>]pyridine-2-carboxylic acid
12	5-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}nicotinamide	10.53 (s, 1H), 10.46 (s, 1H), 8.86, (d, 1H), 8.23 (d, 1H), 8.55, (s, 1H), 8.24 (d, 1H), 8.12 (d, 1H), 8.06 (s, 1H), 7.85 (d, 1H), 7.75 (m, 1H), 7.33 (m, 1H), 7.25 (m, 1H), 2.33 (s, 3H), 2.30 (s, 3H)	346	5-Methylnicotinic acid
13	6-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}pyridine-2-carboxamide	10.46 (s, 1H), 10.39 (s, 1H), 8.74 (d, 1H), 8.14 (d, 1H), 8.02 (s, 1H), 7.90 (d, 1H), 7.7-7.8 (m, 3H), 7.37 (m, 1H), 7.23 (m, 1H), 7.15 (d, 1H), 2.46 (s, 3H), 2.20 (s, 3H)	346	6-Methylpyridine-2-carboxylic acid
14	5-{[4-Methoxy-3-(trifluoromethyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.59 (s, 1H), 9.00 (s, 1H), 8.39 (s, 3H), 8.26 (s, 1H), 8.02 (s, 1H), 7.93 (s, 1H), 7.49 (s, 2H), 7.37 (s, 1H), 4.06 (s, 3H), 2.43 (s, 3H)	429	4-Methoxy-3-(trifluoromethyl)-benzoic acid
15	2-Methyl-5-{[2-methyl-5-(trifluoromethyl)benzoyl]amino}- <i>N</i> -pyridin-3-ylbenzamide	10.61 (s, 2H), 8.89 (s, 1H), 8.32 (d, 1H), 8.19 (d, 1H), 7.88 (s, 1H), 7.77 (m, 3H), 7.58 (d, 1H), 7.40 (m, 1H), 7.32 (d, 1H), 3.39 (m, 1H), 2.47 (s, 3H), 2.36 (s, 3H)	413	2-Methyl-5-(trifluoromethyl)-benzoic acid

Ex.	Compound	NMR	m/z	SM
16	2-Chloro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-5-(trifluoromethyl)benzamide	10.73 (s, 1H), 10.57 (s, 1H), 8.83 (s, 1H), 8.26 (d, 1H), 8.13 (d, 1H), 7.97 (s, 1H), 7.74-7.89 (m, 3H), 7.68 (d, 1H), 7.24-7.39 (m, 2H), 3.29 (s, 4H), 2.45 (s, 3H), 2.31 (s, 3H)	434	2-Chloro-5-(trifluoromethyl)-benzoic acid
17	2-Fluoro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-5-(trifluoromethyl)benzamide	10.95 (s, 1H), 10.84 (s, 1H), 9.10 (s, 1H), 8.53 (d, 1H), 8.41 (d, 1H), 8.28 (d, 1H), 8.23 (dd, 1H), 8.06 (s, 1H), 7.97 (d, 1H), 7.85 (t, 1H), 7.63 (dd, 1H), 7.55 (d, 1H), 2.58 (s, 3H)	417	2-Fluoro-5-(trifluoromethyl)-benzoic acid
18	5-{[3-Fluoro-5-(trifluoromethyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.60 (s, 2H), 10.58 (s, 2H), 8.85 (s, 1H), 8.27 (d, 1H), 8.14 (s, 2H), 8.09 (d, 1H), 7.93 (d, 1H), 7.85 (s, 1H), 7.80 (d, 1H), 7.37 (dd, 1H), 7.29 (d, 1H), 2.31 (s, 3H),	417	3-Fluoro-5-(trifluoromethyl)-benzoic acid
19	5-{[4-Fluoro-3-(trifluoromethyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.53 (s, 2H), 8.80 (s, 1H), 8.21-8.36 (m, 3H), 8.10 (d, 1H), 7.81 (s, 1H), 7.76 (d, 1H), 7.64 (t, 1H), 7.32 (dd, 1H), 7.24 (d, 1H), 2.28 (s, 3H)	417	4-Fluoro-3-(trifluoromethyl)-benzoic acid
20	1-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide	10.61 (s, 1H), 10.54 (s, 1H), 8.88 (s, 1H), 8.32 (s, 1H), 8.18 (s, 1H), 7.88 (s, 1H), 7.78 (s, 1H), 7.58 (s, 1H), 7.37 (s, 2H), 4.18 (s, 3H), 2.36 (s, 3H)	403	1-Methyl-3-(trifluoromethyl)-1H-pyrazole-5-carboxylic acid

Ex.	Compound	NMR	m/z	SM
21	2-Methyl-5-({3-[(methylsulfonyl)amino]benzoyl}amino)- <i>N</i> -pyridin-3-ylbenzamide	10.61 (s, 1H), 10.43 (s, 1H), 10.02 (s, 1H), 8.91 (s, 1H), 8.32 (d, 1H), 8.20 (d, 1H), 7.90-7.99 (m, 1H), 7.70-7.85 (m, 3H), 7.38-7.54 (m, 3H), 7.32 (d, 1H), 3.05 (s, 3H), 2.37 (s, 3H)	424	3-[(Methylsulfonyl)amino]benzoic acid
22	5-(1-Cyano-1-methylethyl)- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}thiophene-3-carboxamide	11.09 (s, 1H), 10.29 (s, 1H), 9.21 (s, 1H), 8.55 (d, 1H), 8.47 (d, 1H), 8.37 (s, 1H), 7.97 (d, 1H), 7.84 (m, 2H), 7.72 (d, 1H), 7.33 (d, 1H), 2.36 (s, 3H), 1.79 (s, 6H)	405	Method 110
23	5-(1-Cyano-1-methylethyl)- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}thiophene-2-carboxamide	11.01 (s, 1H), 10.46 (s, 1H), 9.16 (s, 1H), 8.51 (d, 1H), 8.46 (d, 1H), 7.96 (dd, 2H), 7.78 (dd, 2H), 7.34-7.30 (m, 2H), 2.36 (s, 3H), 1.78 (s, 6H)	404	Method 109
24	5-{{4-Chloro-3-(1-cyano-1-methylethyl)benzoyl}amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	11.04 (s, 1H), 10.58 (s, 1H), 9.17 (d, 1H), 8.53 (d, 1H), 8.45 (d, 1H), 8.03-7.94 (m, 3H), 7.82-7.73 (m, 3H), 7.35 (d, 1H), 2.37 (s, 3H), 1.86 (s, 6H)	433	Method 26
25	2-(1-Cyano-1-methylethyl)- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}isonicotinamide	11.21 (s, 1H), 10.81 (s, 1H), 9.28 (s, 1H), 8.81 (d, 1H), 8.62-8.53 (m, 2H), 8.03 (d, 2H), 7.99-7.82 (m, 3H), 7.37 (d, 1H), 2.39 (s, 3H), 1.76 (s, 6H)	400	Method 112

Ex.	Compound	NMR	m/z	SM
26	5-[(3-tert-Butyl benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.97 (s, 1H), 10.36 (s, 1H), 9.15 (s, 1H), 8.50 (d, 1H), 8.42 (d, 1H), 8.00 (d, 1H), 7.94 (s, 1H), 7.84-7.73 (m, 3H), 7.62 (d, 1H), 7.45 (t, 1H), 7.32 (d, 1H), 2.37 (s, 3H), 1.33 (s, 9H)	388	Method 113
27	5-{[3-(Azetidin-1-ylsulfonyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.66 (s, 1H), 10.58 (s, 1H), 8.87 (d, 1H), 8.35 (m, 2H), 8.30 (dd, 1H), 8.17 (m, 1H), 8.02 (m, 1H), 7.88 (m, 3H), 7.39 (dd, 1H), 7.33 (d, 1H), 3.71 (t, 2H), 2.68 (s, 3H), 2.36 (bs, 2H), 2.00 (m, 2H)	451	Method 121
28	2-Methyl-5-{[3-(methylsulfonyl)benzoyl]amino}- <i>N</i> -pyridin-3-ylbenzamide	11.19 (s, 1H), 10.80 (s, 1H), 9.25 (s, 1H), 8.56 (m, 3H), 8.31 (m, 1H), 8.13 (m, 1H), 8.03 (d, 1H), 7.86 (m, 3H), 7.35 (d, 1H), 2.49 (s, 3H), 2.38 (s, 3H)	409	3-(Methylsulfonyl)-benzoic acid
29	5-({3-[(Cyclopropylamino)sulfonyl]benzoyl}amino)-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	11.16 (s, 1H), 10.74 (s, 1H), 9.24 (s, 1H), 8.58 (d, 1H), 8.53 (d, 1H), 8.42 (bs, 1H), 8.27 (d, 1H), 8.08 (d, 1H), 8.03 (d, 1H), 8.01 (d, 1H), 7.86 (m, 2H), 7.79 (t, 1H), 7.35 (d, 1H), 2.38 (s, 3H), 2.12 (m, 1H), 0.47 (m, 2H), 0.37 (m, 2H)	450	Method 122
30	5-{[4-[(Dimethylamino)methyl]-3-(trifluoromethyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	11.25 (s, 1H), 10.82 (s, 1H), 9.20-9.35 (m, 1H), 8.52-8.65 (m, 2H), 8.37-8.48 (m, 2H), 8.05 (s, 1H), 7.83-7.98 (m, 2H), 7.31-7.45 (m, 2H), 4.58 (s, 2H), 2.73-2.85 (m, 6H), 2.40 (s, 3H)	456	Method 23

Ex.	Compound	NMR	m/z	SM
31	5-{{[4-[(4-Ethyl piperazin-1-yl)methyl]-3-(trifluoromethyl)benzoyl]amino}-2-methyl-N-pyridin-3-ylbenzamide	11.33 (s, 1H), 10.78 (s, 1H), 9.32 (s, 1H), 8.58-8.72 (m, 2H), 8.29-8.43 (m, 2H), 8.06 (s, 2H), 8.00 (dd, 1H), 7.88 (d, 1H), 7.37 (d, 1H), 3.99 (s, 2H), 3.43-3.58 (m, 3H), 3.12 (d, 5H), 2.85 (s, 1H), 2.40 (s, 3H)	525	Method 22
32	5-({3-(1-Cyano-1-methylethyl)-5-[(dimethylamino)methyl]benzoyl}amino)-2-methyl-N-pyridin-3-ylbenzamide	11.12 (s, 1H), 10.70 (s, 1H), 9.20 (s, 1H), 8.45-8.60 (m, 2H), 8.18 (d, 2H), 8.04 (d, 2H), 7.78-7.92 (m, 2H), 7.37 (d, 1H), 4.43 (s, 2H), 2.74 (s, 6H), 2.32-2.44 (m, 3H), 1.79 (s, 6H)	455	Method 28
33	5-{{[3-(3-Hydroxy-3-methylbut-1-yn-1-yl)benzoyl]amino}-2-methyl-N-pyridin-3-ylbenzamide	10.38 (s, 1H), 10.25 (s, 1H), 8.68 (s, 1H), 8.11 (d, 1H), 7.98 (d, 1H), 7.80 (s, 1H), 7.73 (s, 2H), 7.64 (d, 1H), 7.29-7.42 (m, 2H), 7.19 (dd, 1H), 7.11 (d, 1H), 2.16 (s, 3H), 1.28 (s, 6H)	413	Method 25
34	5-{{[3-(3,3-Dimethylbut-1-yn-1-yl)benzoyl]amino}-2-methyl-N-pyridin-3-ylbenzamide	11.07 (s, 1H), 10.47 (s, 1H), 9.20 (s, 1H), 8.55 (d, 1H), 8.47 (d, 1H), 8.02 (d, 1H), 7.95 (s, 1H), 7.89 (d, 1H), 7.84-7.80 (m, 2H), 7.58-7.47 (m, 2H), 7.33 (d, 1H), 2.36 (s, 3H), 1.30 (s, 9H)	411	Method 24

Ex.	Compound	NMR	m/z	SM
35	5-({3-(1-Cyano-1-methylethyl)-5-[(4-methylpiperazin-1-yl)methyl]benzoyl} amino)-2-methyl-N-pyridin-3-ylbenzamide	10.92 (s, 1H), 10.60 (s, 1H), 9.09 (s, 1H), 8.34-8.49 (m, 2H), 8.09 (s, 2H), 7.99 (s, 1H), 7.89 (d, 2H), 7.67 (dd, 1H), 7.35 (d, 1H), 4.15 (br. s, 2H), 3.2- 3.6 (br. m, 8H), 2.78 (s, 3H), 2.39 (s, 3H), 1.69-1.82 (m, 6H)	510	Method 27
36	5-[(3,5-Dimethylbenzoyl) amino]-2-methyl-N-pyridin-3-ylbenzamide	10.58 (s, 1H), 10.26 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.91 (s, 1H), 7.83 (d, 1H), 7.56 (s, 2H), 7.39 (dd, 1H), 7.29 (d, 1H), 7.22 (s, 1H), 2.34 (s, 9H)	359	3,5-Dimethylbenzoic acid
37	5-[(3,5-Difluorobenzoyl) amino]-2-methyl-N-pyridin-3-ylbenzamide	10.60 (s, 1H), 10.47 (s, 1H), 8.88 (s, 1H), 8.31 (d, 1H), 8.18 (d, 1H), 7.90 (s, 1H), 7.81 (d, 1H), 7.69 (d, 2H), 7.55 (s, 1H), 7.30-7.42 (m, 2H), 2.36 (s, 3H)	367	3,5-Difluorobenzoic acid
38	5-[(3-Iodobenzoyl)amino]-2-methyl-N-pyridin-3-ylbenzamide	10.59 (s, 1H), 10.42 (s, 1H), 8.88 (s, 1H), 8.31 (s, 2H), 8.18 (d, 1H), 7.89-7.98 (m, 3H), 7.83 (d, 1H), 7.29-7.41 (m, 3H), 2.35 (s, 3H)	457	3-Iodobenzoic acid
39	5-[(3,5-Dimethoxybenzoyl) amino]-2-methyl-N-pyridin-3-ylbenzamide	10.58 (s, 1H), 10.28 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.17 (d, 1H), 7.90 (s, 1H), 7.83 (d, 1H), 7.39 (dd, 1H), 7.30 (d, 1H), 7.10 (s, 2H), 6.71 (s, 1H), 3.80-3.83 (m, 6H), 2.35 (s, 3H)	391	3,5-Dimethoxybenzoic acid
40	2-Methyl-5-[(3-methylbenzoyl) amino]-N-pyridin-3-ylbenzamide	10.58 (s, 1H), 10.31 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.92 (s, 1H), 7.83 (d, 1H), 7.73-7.79 (m, 2H), 7.36-7.43 (m, 3H), 7.29 (d, 1H), 2.39 (s, 3H), 2.34 (s, 3H)	345	3-Methylbenzoic acid

Ex.	Compound	NMR	m/z	SM
41	5-[(3-Isopropoxy benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.58 (s, 1H), 10.29 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.93 (s, 1H), 7.83 (d, 1H), 7.37-7.50 (m, 4H), 7.29 (d, 1H), 7.14 (d, 1H), 4.67-4.74 (m, 1H), 2.35 (s, 3H), 1.28 (d, 6H)	389	3-Isopropoxybenzoic acid
42	5-{[3-(Dimethylamino) benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.57 (s, 1H), 10.23 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 7.91 (s, 1H), 7.83 (d, 1H), 7.27-7.41 (m, 3H), 7.21-7.24 (m, 2H), 6.92 (d, 1H), 2.95 (s, 6H), 2.34 (s, 3H)	374	3-(Dimethylamino)benzoic acid
43	5-({3-[(Difluoromethyl) thio]benzoyl}amino)-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.29 (s, 1H), 10.23 (s, 1H), 8.88 (s, 1H), 8.31 (d, 1H), 8.10-8.18 (m, 2H), 8.07 (d, 1H), 7.89 (s, 1H), 7.75-7.84 (m, 2H), 7.62 (t, 1H), 7.34-7.38 (m, 1H), 7.30 (d, 1H), 3.77 (d, 1H), 2.38 (s, 3H)	413	3-[(Difluoromethyl)thio]benzoic acid
44	5-[(3-Chloro benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.29 (s, 1H), 10.22 (s, 1H), 8.88 (s, 1H), 8.30 (s, 1H), 8.14 (d, 1H), 8.02 (s, 1H), 7.93 (d, 1H), 7.89 (s, 1H), 7.80 (d, 1H), 7.61-7.65 (m, 1H), 7.55 (t, 1H), 7.36 (dd, 1H), 7.29 (d, 1H), 2.38 (s, 3H)	365	3-Chlorobenzoic acid
45	2-Methyl-5-[(3-propoxybenzoyl) amino]- <i>N</i> -pyridin-3-ylbenzamide	10.58 (s, 1H), 10.31 (s, 1H), 8.88 (s, 1H), 8.31 (d, 1H), 8.18 (d, 1H), 7.93 (s, 1H), 7.84 (d, 1H), 7.48-7.55 (m, 2H), 7.37-7.46 (m, 2H), 7.30 (d, 1H), 7.15 (d, 1H), 4.00 (t, 2H), 2.35 (s, 3H), 1.75 (q, 2H), 0.99 (t, 3H)	389	3-Propoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
46	5-[(3-Methoxybenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.28 (s, 1H), 10.07 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.14 (d, 1H), 7.91 (s, 1H), 7.81 (d, 1H), 7.56 (d, 1H), 7.51 (s, 1H), 7.43 (t, 1H), 7.36 (dd, 1H), 7.28 (d, 1H), 7.14 (d, 1H), 3.85 (s, 3H), 2.38 (s, 3H)	361	3-Methoxybenzoic acid
47	5-[(3-Bromobenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.29 (s, 1H), 10.22 (s, 1H), 8.88 (s, 1H), 8.31 (d, 1H), 8.12-8.22 (m, 2H), 7.97 (d, 1H), 7.89 (s, 1H), 7.75-7.83 (m, 2H), 7.49 (t, 1H), 7.34-7.39 (m, 1H), 7.29 (d, 1H), 2.38 (s, 3H)	410	3-Bromobenzoic acid
48	5-[(3-Isobutoxybenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.57 (s, 1H), 10.30 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.17 (d, 1H), 7.91 (s, 1H), 7.83 (d, 1H), 7.48-7.54 (m, 2H), 7.36-7.45 (m, 2H), 7.29 (d, 1H), 7.15 (d, 1H), 3.81 (d, 2H), 2.34 (s, 3H), 1.96-2.10 (m, 1H), 0.94-1.00 (m, 6H)	403	3-Isobutoxybenzoic acid
49	5-[[3-(1-Cyano-1-methylethyl)benzoyl]amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.59 (s, 1H), 10.43 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 8.05 (s, 1H), 7.88-7.97 (m, 2H), 7.84 (d, 1H), 7.75 (d, 1H), 7.60 (t, 1H), 7.39 (dd, 1H), 7.32 (d, 1H), 2.36 (s, 3H), 1.71-1.76 (m, 6H)	398	3-(1-Cyano-1-methylethyl)-benzoic acid
50	2-Methyl- <i>N</i> -pyridin-3-yl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.44 (s, 1H), 10.42 (s, 1H), 8.72 (d, $J=2.2\text{Hz}$, 1H), 8.10-8.15 (m, 3H), 8.04 (d, $J=8.3\text{Hz}$, 1H), 7.61-7.83 (m, 4H), 7.15-7.25 (m, 2H), 2.18 (s, 1H)	400	3-Trifluorobenzoic acid

Ex.	Compound	NMR	m/z	SM
51	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-5-piperidin-1-yl nicotinamide	10.58 (s, 1H), 10.40 (s, 1H), 8.87 (d, 1H), 8.46 (s, 2H), 8.30 (d, 1H), 8.17 (d, 1H), 7.90 (d, 1H), 7.82 (dd, 1H), 7.70 (s, 1H), 7.40 (dd, 1H), 7.32 (d, 1H), 3.30-3.26 (m, 4H), 2.35 (s, 3H), 1.69-1.59 (m, 6H)	416	Method 30
52	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-5-morpholin-4-yl nicotinamide	11.00 (s, 1H), 10.65 (s, 1H), 9.14 (s, 1H), 8.60 (s, 1H), 8.54-8.50 (m, 2H), 8.32 (d, 1H), 8.00-7.97 (m, 2H), 7.83-7.77 (m, 2H), 7.36 (d, 1H), 3.77 (t, 4H), 3.33 (t, 4H), 2.37 (s, 3H)	418	Method 31
53	5-(Diethylamino)- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl} nicotinamide	11.18 (s, 1H), 11.05 (s, 1H), 9.23 (s, 1H), 8.59-8.51 (m, 3H), 8.32 (d, 1H), 8.07 (s, 1H), 8.03 (s, 1H), 7.90-7.85 (m, 2H), 7.36 (d, 1H), 3.53 (q, 4H), 2.38 (s, 3H), 1.14 (t, 6H)	404	Method 32
54	5-(1-Cyano-1-methylethyl)- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl} nicotinamide	11.23 (s, 1H), 10.78 (s, 1H), 9.29 (d, 1H), 9.12 (d, 1H), 8.96 (d, 1H), 8.62 (d, 1H), 8.56 (d, 1H), 8.44 (t, 1H), 8.03 (d, 1H), 7.95 (dd, 1H), 7.84 (dd, 1H), 7.37 (d, 1H), 2.39 (s, 3H), 1.80 (s, 6H)	400	Method 33
55	2-Chloro-5-[(3-cyclopropylbenzoyl)amino]- <i>N</i> -(5-fluoropyridin-3-yl)benzamide	11.06 (s, 1H), 10.45 (s, 1H), 8.68 (s, 1H), 8.36 (d, 1H), 8.16 (dt, 1H), 8.05 (d, 1H), 7.95 (dd, 1H), 7.71 (d, 1H), 7.55 - 7.65 (m, 2H), 7.40 (t, 1H), 7.27 - 7.36 (m, 1H), 2.01 (ddd, 1H), 0.95 - 1.04 (m, 2H), 0.76 (ddd, 2H)	410	Method 34

Ex.	Compound	NMR	m/z	SM
56	5-[(3-Cyclopropyl-5-fluorobenzoyl) amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	11.15 (s, 1H), 10.44 (s, 1H), 9.25 (s, 1H), 8.58 (d, 1H), 8.52 (d, 1H), 8.01 (d, 1H), 7.78 - 7.93 (m, 2H), 7.46 - 7.56 (m, 2H), 7.34 (d, 1H), 7.16 (d, 1H), 2.37 (s, 3H); 2.04 (td, 1H), 0.95 - 1.07 (m, 2H), 0.81 (dt, 2H)	391	Method 226
57	5-Chloro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl] phenyl}-1 <i>H</i> -indole-2-carboxamide	11.95 (s, 1H), 10.60 (s, 1H), 10.40 (s, 1H), 8.88 (s, 1H), 8.31 (d, 1H), 8.17 (d, 1H), 7.93 (s, 1H), 7.87 (d, 1H), 7.78 (s, 1H), 7.45 (d, 1H), 7.42 (s, 1H), 7.39 (m, 1H), 7.32 (d, 1H), 7.24 (d, 1H), 2.36 (s, 3H)	405	5-chloro-1 <i>H</i> -indole-2-carboxylic acid
58	4,6-Difluoro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl] phenyl}-1 <i>H</i> -indole-2-carboxamide	12.20 (s, 1H), 10.62 (s, 1H), 10.39 (s, 1H), 8.89 (s, 1H), 8.32 (d, 1H), 8.18 (d, 1H), 7.93 (s, 1H), 7.86 (d, 1H), 7.56 (s, 1H), 7.40 (m, 1H), 7.34 (d, 1H), 7.08 (d, 1H), 6.95 (m, 1H), 2.37 (s, 3H)	407	4,6-difluoro-1 <i>H</i> -indole-2-carboxylic acid
59	2-Chloro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl] phenyl} isonicotinamide	10.17 (s, 1H), 9.98 (s, 1H), 9.56 (s, 1H), 8.80 (s, 1H), 8.19 (s, 1H), 8.11 (s, 1H), 7.80 (s, 1H), 7.72 (s, 1H), 7.14 (s, 2H), 6.99 (s, 1H), 3.66 (s, 3H), 2.15 (s, 3H)	367	2-chloroisonicotinic acid
60	5-{[4-Chloro-3-(trifluoromethyl) benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 2H), 8.92 (s, 1H), 8.40 (s, 1H), 8.34 (s, 1H), 8.24 (s, 2H), 7.92 (s, 2H), 7.83 (s, 1H), 7.44 (s, 1H), 7.33 (s, 1H), 2.37 (s, 3H)	434	4-chloro-3-(trifluoromethyl)benzoic acid

Ex.	Compound	NMR	m/z	SM
61	5-Methoxy- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -indole-2-carboxamide	11.58 (s, 1H), 10.59 (s, 1H), 10.26 (s, 1H), 8.90 (s, 1H), 8.31 (s, 1H), 8.19 (s, 1H), 7.91 (s, 2H), 7.35 (s, 3H), 7.13 (s, 1H), 6.87 (s, 1H), 3.78 (s, 3H), 2.34 (s, 3H)	401	5-methoxy-1 <i>H</i> -indole-2-carboxylic acid
62	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -indole-2-carboxamide	11.75 (s, 1H), 10.60 (s, 1H), 10.32 (s, 1H), 8.89 (s, 1H), 8.31 (s, 1H), 8.19 (s, 1H), 7.95 (s, 1H), 7.87 (s, 1H), 7.67 (s, 1H), 7.43 (s, 3H), 7.32 (s, 1H), 7.21 (s, 1H), 7.05 (s, 1H), 2.36 (s, 3H)	371	1 <i>H</i> -indole-2-carboxylic acid
63	5-Chloro-2-methoxy- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}benzamide	10.59 (s, 1H), 10.30 (s, 1H), 8.89 (s, 1H), 8.33 (s, 1H), 8.19 (s, 1H), 7.88 (s, 1H), 7.76 (s, 1H), 7.58 (s, 2H), 7.40 (s, 1H), 7.31 (s, 1H), 7.22 (s, 1H), 3.91 (s, 3H), 2.35 (s, 3H)	396	5-chloro-2-methoxybenzoic acid
64	5-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -indole-2-carboxamide	11.60 (s, 1H), 10.59 (s, 1H), 10.26 (s, 1H), 8.89 (s, 1H), 8.31 (s, 1H), 8.19 (s, 1H), 7.94 (s, 1H), 7.87 (s, 1H), 7.44 (s, 1H), 7.35 (s, 3H), 7.05 (s, 1H), 3.31 (s, 3H), 2.36 (s, 3H)	385	5-methyl-1 <i>H</i> -indole-2-carboxylic acid
65	5-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}isoxazole-3-carboxamide	10.75 (s, 1H), 10.57 (s, 1H), 8.87 (s, 1H), 8.31 (s, 1H), 8.18 (s, 1H), 7.95 (s, 1H), 7.81 (s, 1H), 7.39 (s, 1H), 7.30 (s, 1H), 6.66 (s, 1H), 3.30 (s, 3H), 2.34 (s, 3H)	337	5-methylisoxazole-3-carboxylic acid
66	2-Chloro-6-methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}isonicotinamide	10.76 (s, 2H), 8.97 (s, 1H), 8.37 (s, 1H), 8.27 (s, 1H), 7.95 (s, 1H), 7.82 (s, 3H), 7.52 (s, 1H), 7.33 (s, 1H), 2.55 (s, 3H), 2.36 (s, 3H)	381	2-chloro-6-methylisonicotinic acid

Ex.	Compound	NMR	m/z	SM
67	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide	10.59 (s, 1H), 10.44 (s, 1H), 8.90 (s, 1H), 8.32 (s, 2H), 8.19 (s, 1H), 7.91 (s, 1H), 7.83 (s, 1H), 7.41 (s, 1H), 7.34 (s, 1H), 7.27 (s, 1H), 7.15 (s, 1H), 3.73 (s, 4H), 3.54 (s, 4H), 2.36 (s, 3H)	416	2-morpholin-4-ylisonicotinic acid
68	1- <i>tert</i> -Butyl-3-methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -pyrazole-5-carboxamide	10.66 (s, 1H), 10.56 (s, 1H), 8.86 (s, 1H), 8.31 (s, 1H), 8.17 (s, 1H), 7.84 (s, 1H), 7.70 (s, 1H), 7.40 (s, 1H), 7.28 (s, 1H), 6.38 (s, 1H), 2.33 (s, 3H), 2.18 (s, 3H), 1.57 (s, 9H)	392	1- <i>tert</i> -butyl-3-methyl-1 <i>H</i> -pyrazole-5-carboxylic acid
69	5-[(3-Cyclopropylbenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.57 (s, 1H), 10.29 (s, 1H), 8.88 (s, 1H), 8.31 (s, 1H), 8.18 (s, 1H), 7.93 (s, 1H), 7.84 (s, 1H), 7.71 (s, 1H), 7.63 (s, 1H), 7.40 (s, 2H), 7.30 (s, 2H), 4.09 (s, 1H), 2.35 (s, 3H), 1.00 (s, 2H), 0.76 (s, 2H)	372	Method 34
70	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -indole-7-carboxamide	11.29 (s, 1H), 10.62 (s, 1H), 10.40 (s, 1H), 8.91 (s, 1H), 8.33 (s, 1H), 8.19 (s, 1H), 8.11 (s, 1H), 7.84 (s, 3H), 7.36 (s, 3H), 7.12 (s, 1H), 6.55 (s, 1H), 2.37 (s, 3H)	371	1 <i>H</i> -indole-7-carboxylic acid
71	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -indole-4-carboxamide	11.38 (s, 1H), 10.59 (s, 1H), 10.29 (s, 1H), 8.91 (s, 1H), 8.32 (s, 1H), 8.20 (s, 1H), 8.02 (s, 1H), 7.85 (s, 1H), 7.59 (s, 2H), 7.48 (s, 1H), 7.40 (s, 1H), 7.30 (s, 1H), 7.21 (s, 1H), 6.86 (s, 1H), 2.36 (s, 3H)	371	1 <i>H</i> -indole-4-carboxylic acid

Ex.	Compound	NMR	m/z	SM
72	<i>tert</i> -Butyl {3-[(4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}amino)carbonyl]phenyl} carbamate	10.62 (s, 1H), 10.35 (s, 1H), 9.58 (s, 1H), 8.90 (s, 1H), 8.33 (s, 1H), 8.20 (s, 1H), 8.04 (s, 1H), 7.93 (s, 1H), 7.81 (s, 1H), 7.56 (s, 2H), 7.41 (s, 2H), 7.29 (s, 1H), 2.35 (s, 3H), 1.49 (s, 9H)	446	3-[(<i>tert</i> -butoxycarbonyl)amino]benzoic acid
73	2,2-Dimethyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2,3-dihydro-1-benzofuran-7-carboxamide	10.60 (s, 1H), 9.78 (s, 1H), 8.89 (s, 1H), 8.31 (s, 1H), 8.19 (s, 1H), 7.87 (s, 1H), 7.68 (s, 2H), 7.36 (s, 3H), 6.97 (s, 1H), 3.10 (s, 2H), 2.35 (s, 3H), 1.53 (s, 6H)	402	2,2-dimethyl-2,3-dihydro-1-benzofuran-7-carboxylic acid
74	5-Bromo- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2-furamide	10.59 (s, 1H), 10.42 (s, 1H), 8.88 (s, 1H), 8.31 (s, 1H), 8.17 (s, 1H), 7.84 (s, 2H), 7.47 (s, 1H), 7.39 (s, 1H), 7.29 (s, 1H), 6.83 (s, 1H), 2.34 (s, 3H)	401	5-bromo-2-furoic acid
75	2,4-Dimethyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1,3-thiazole-5-carboxamide	10.57 (s, 1H), 10.18 (s, 1H), 8.88 (s, 1H), 8.30 (s, 1H), 8.18 (s, 1H), 7.80 (s, 1H), 7.70 (s, 1H), 7.39 (s, 1H), 7.28 (s, 1H), 2.65 (s, 3H), 2.53 (s, 3H), 2.33 (s, 3H)	367	2,4-dimethyl-1,3-thiazole-5-carboxylic acid
76	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-5-pyridin-2-ylthiophene-2-carboxamide	10.59 (s, 1H), 10.39 (s, 1H), 8.88 (s, 1H), 8.57 (s, 1H), 8.31 (s, 1H), 8.19 (s, 1H), 8.01 (s, 2H), 7.85 (s, 4H), 7.36 (s, 3H), 2.35 (s, 3H)	414	5-pyridin-2-ylthiophene-2-carboxylic acid

Ex.	Compound	NMR	m/z	SM
77	1-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -indole-2-carboxamide	10.61 (s, 1H), 10.43 (s, 1H), 8.90 (s, 1H), 8.32 (s, 1H), 8.20 (s, 1H), 7.97 (s, 1H), 7.80 (s, 1H), 7.71 (s, 1H), 7.58 (s, 1H), 7.35 (s, 4H), 7.15 (s, 1H), 4.01 (s, 3H), 2.35 (s, 3H)	385	1-methyl-1 <i>H</i> -indole-2-carboxylic acid
78	2-Methyl- <i>N</i> -pyridin-3-yl-5-{{2-(trifluoromethyl)benzoyl}amino}benzamide	10.66 (s, 1H), 10.59 (s, 1H), 8.87 (s, 1H), 8.30 (s, 1H), 8.17 (s, 1H), 7.82 (s, 3H), 7.70 (s, 3H), 7.38 (s, 1H), 7.30 (s, 1H), 2.34 (s, 3H)	400	2-(trifluoromethyl)benzoic acid
79	2-Methyl-5-[(3-phenoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.57 (s, 1H), 10.39 (s, 1H), 8.89 (s, 1H), 8.31 (s, 1H), 8.19 (s, 1H), 7.92 (s, 1H), 7.79 (s, 2H), 7.57 (s, 2H), 7.41 (s, 3H), 7.30 (s, 1H), 7.20 (s, 2H), 7.07 (s, 2H), 2.35 (s, 3H)	424	3-phenoxybenzoic acid
80	5-({3-(1-Cyano-1-methylethyl)-5-[(methylthio)methyl]benzoyl}amino)-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.93 (s, 1H), 10.49 (s, 1H), 9.14 (s, 1H), 8.49 (d, 1H), 8.36 (d, 1H), 7.92 - 8.03 (m, 2H), 7.80 - 7.92 (m, 2H), 7.64 - 7.75 (m, 2H), 7.38 (d, 1H), 3.84 (s, 2H), 2.38 (s, 3H), 2.01 (s, 3H), 1.77 (s, 6H)	458	Method 37
81	{3-(1-Cyano-1-methylethyl)-5-[(4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl)amino]carbonyl}phenyl}methanesulfonic acid	10.94 (s, 1H), 10.43 (s, 1H), 9.13 (s, 1H), 8.44 (dd, 2H), 7.99 (s, 1H), 7.88 - 7.95 (m, 2H), 7.84 (dd, 1H), 7.68 - 7.76 (m, 1H), 7.65 (s, 1H), 7.34 (d, 1H), 3.81 (s, 2H), 2.39 (s, 3H), 1.75 (s, 6H)	492	Method 38

Ex.	Compound	NMR	m/z	SM
82	5-[(3-{1-[(Dimethylamino)sulfonyl]-1-methylethyl}benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.85 (s, 1H), 10.44 (s, 1H), 9.06 (s, 1H), 8.45 (d, 1H), 8.35 (d, 1H), 8.15 (s, 1H), 7.96 - 8.01 (m, 2H), 7.80 - 7.88 (m, 2H), 7.65 (dd, 1H), 7.57 (t, 1H), 7.33 (d, 1H), 2.60 (s, 6H), 2.37 (s, 3H), 1.79 (s, 6H)	480	Method 40
83	5-{[3-(1,1-Dimethylprop-2-yn-1-yl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.85 (s, 1H), 10.38 (s, 1H), 9.07 (s, 1H), 8.45 (d, 1H), 8.36 (d, 1H), 8.08 (s, 1H), 7.96 (s, 1H), 7.74 - 7.86 (m, 3H), 7.65 (q, 1H), 7.50 (t, 1H), 7.32 (d, 1H), 2.35 (s, 3H), 1.57 (s, 6H)	397	Method 41
84	5-{[3-(1,1-Dimethylbut-2-yn-1-yl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.59 (s, 1H), 10.38 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.18 (d, 1H), 8.08 (s, 1H), 7.92 (s, 1H), 7.80 - 7.87 (m, 2H), 7.77 (d, 1H), 7.50 (t, 1H), 7.40 (dd, 1H), 7.31 (d, 1H), 2.36 (s, 3H), 1.85 (s, 3H), 1.55 (s, 6H)	411	Method 42
85	5-[(3-{[(Dimethylamino)carbonyl]amino}benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.45 (s, 1H), 9.90 (s, 1H), 8.66 (s, 1H), 8.08 (s, 1H), 8.02 (d, 1H), 7.93 (d, 1H), 7.56 (d, 2H), 7.36 (dd, 1H), 7.20 - 7.28 (m, 2H), 7.07 (d, 1H), 6.84 - 6.97 (m, 2H), 2.05 (s, 7H), 1.90 (s, 3H)	417	Method 45
86	5-{[3-(1,1-Difluoroethyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.92 (s, 1H), 10.50 (s, 1H), 9.11 (s, 1H), 8.48 (d, 2H), 8.37 (d, 1H), 8.12 (s, 2H), 8.06 (d, 1H), 7.96 (s, 1H), 7.79 (dd, 3H), 7.60 - 7.72 (m, 2H), 7.32 (d, 1H), 2.35 (s, 3H), 1.98 (t, 3H)	395	Method 47

Ex.	Compound	NMR	m/z	SM
87	2-Methyl-5-{{[3-(1-methylcyclopropyl)benzoyl]amino}-N-pyridin-3-ylbenzamide	10.85 (s, 1H), 10.36 (s, 1H), 9.08 (s, 1H), 8.44 (d, 1H), 8.34 (d, 1H), 7.98 (s, 1H), 7.72 - 7.85 (m, 3H), 7.64 (q, 1H), 7.44 (s, 2H), 7.33 (d, 1H), 2.37 (s, 3H), 1.43 (s, 3H), 0.89 - 0.95 (m, 2H), 0.78 - 0.87 (m, 2H)	385	Method 49
88	5-[(3-(1-Cyano-1-methylethyl)-5-{{[methoxy(methyl)amino]methyl}benzoyl}amino)-2-methyl-N-pyridin-3-ylbenzamide	10.61 (s, 1H), 10.44 (s, 1H), 8.90 (s, 1H), 8.31 (d, 1H), 8.19 (d, 1H), 7.83 - 7.99 (m, 4H), 7.76 (s, 1H), 7.40 (dd, 1H), 7.33 (d, 1H), 3.88 (s, 2H), 3.27 (s, 3H), 2.62 (s, 3H), 2.38 (s, 3H), 1.76 (s, 6H)	471	Method 50
89	5-({3-(1-Cyano-1-methylethyl)-5-[(methylsulfonyl)methyl]benzoyl}amino)-2-methyl-N-pyridin-3-ylbenzamide	10.93 (s, 1H), 10.52 (s, 1H), 9.13 (s, 1H), 8.48 (s, 1H), 8.39 (d, 1H), 8.07 (s, 1H), 7.95 (d, 2H), 7.78 - 7.89 (m, 2H), 7.64 - 7.77 (m, 1H), 7.37 (d, 1H), 4.67 (s, 2H), 3.00 (s, 3H), 2.39 (s, 3H), 1.78 (s, 6H)	490	Method 175
90	2-Methyl-N-pyridin-3-yl-5-{{[3-(1,3-thiazol-2-yl)benzoyl]amino}benzamide	11.03 (s, 1H), 10.62 (s, 1H), 9.20 (s, 1H), 8.49 - 8.56 (m, 2H), 8.45 (d, 1H), 8.16 (d, 1H), 8.02 - 8.08 (m, 2H), 7.99 (d, 1H), 7.76 - 7.88 (m, 3H), 7.68 (t, 1H), 7.35 (d, 1H), 2.37 (s, 3H)	414	Method 51
91	5-[(3-Fluoro-5-methylbenzoyl)amino]-2-methyl-N-pyridin-3-ylbenzamide	10.56 (s, 1H), 10.35 (s, 1H), 8.88 (s, 1H), 8.30 (d, 1H), 8.17 (d, 1H), 7.91 (s, 1H), 7.82 (dd, 1H), 7.65 (s, 1H), 7.56 (d, 1H), 7.40 (dd, 1H), 7.31 (d, 1H), 7.28 (d, 1H), 2.41 (s, 3H), 2.36 (s, 3H)	364	3-fluoro-5-methylbenzoic acid

Ex.	Compound	NMR	m/z	SM
92	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2-(trifluoromethyl)-1 <i>H</i> -benzimidazole-6-carboxamide	9.72 (s, 1H), 9.62 (s, 1H), 8.78 (d, 1H), 8.85 (s, 1H), 8.83 (s, 1H), 8.27 (dd, 1H), 8.00 – 8.03 (m, 2H), 7.75 (dd, 2H), 7.27 (dd, 1H), 7.22 (d, 1H), 2.42 (s, 3H)	440	2-(trifluoromethyl)-1 <i>H</i> -benzimidazole-6-carboxylic acid
93	1-Methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -pyrrole-2-carboxamide	10.55 (s, 1H), 9.83 (s, 1H), 8.87 (d, 1H), 8.29 (dd, 1H), 8.17 (dd, 1H), 7.87 (d, 1H), 7.75 (dd, 1H), 7.38 (dd, 1H), 7.25 (d, 1H), 7.04 (dd, 1H), 7.00 (s, 1H), 6.09 (dd, 1H), 3.86 (s, 3H), 2.83 (s, 3H)	335	1-methyl-1 <i>H</i> -pyrrole-2-carboxylic acid
94	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-1 <i>H</i> -pyrrole-2-carboxamide	8.86 (d, 1H), 8.30 (s, 1H), 8.26 (d, 1H), 7.89 (d, 1H), 7.59 (dd, 1H), 7.45 (dd, 1H), 7.28 (d, 1H), 7.01 (dd, 1H), 7.96 – 7.99 (m, 1H), 3.25 (s, 3H)	321	1 <i>H</i> -pyrrole-2-carboxylic acid
95	5-[(4-Bromo-3-methylbenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	9.64 (s, 2H), 8.94 (d, 1H), 8.80 – 8.83 (m, 2H), 7.99 (d, 1H), 7.94 (s, 1H), 7.79 (dd, 1H), 7.68 – 7.73 (m, 2H), 7.86 (dd, 1H), 7.27 (d, 1H), 2.45 (s, 3H), 2.42 (ss, 3H)	424	3-methyl-4-bromobenzoic acid
96	5-[(3,5-Dichlorobenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	9.77 (s, 1H), 9.67 (s, 1H), 8.95 (s, 1H), 8.28 – 8.34 (m, 2H), 7.99 (d, 1H), 7.96 (d, 2H), 7.79 (dd, 1H), 7.71 (t, 1H), 7.37 (dd, 1H), 7.28 (d, 1H), 2.42 (s, 3H)	400	3,5-dichlorobenzoic acid

Ex.	Compound	NMR	m/z	SM
97	5-[(4-Methoxy benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	9.63 (s, 1H), 9.46 (s, 1H), 8.95 (d, 1H), 8.80 – 8.83 (m, 2H), 7.97 – 8.01 (m, 3H), 7.80 (dd, 1H), 7.37 (dd, 1H), 7.25 (d, 1H), 7.03 (s, 2H), 3.87 (s, 3H), 2.41 (s, 3H)	362	4-methoxybenzoic acid
98	2,5-Dichloro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}benzamide	9.63 (s, 1H), 9.46 (s, 1H), 8.95 (d, 1H), 8.30 – 8.33 (m, 2H), 7.95 – 8.02 (m, 3H), 7.80 (dd, 1H), 7.86 (dd, 1H), 7.25 (dd, 1H), 7.00 – 7.03 (m, 2H), 4.12 (dd, 2H), 2.41 (s, 3H), 1.88 (t, 3H)	400	2,5-dichlorobenzoic acid
99	5-[(2,5-Dimethyl benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	9.83 (s, 1H), 8.71 (s, 1H), 8.48 (d, 1H), 8.21 (s, 1H), 8.17 (d, 1H), 7.90 (s, 1H), 7.50 (d, 1H), 7.85 (dd, 1H), 7.17 (s, 1H), 7.02 – 7.09 (m, 3H), 2.37 (s, 3H), 2.32 (s, 3H), 2.24 (s, 3H)	360	2,5-dimethylbenzoic acid
100	5-Chloro-2-fluoro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}benzamide	9.67 (s, 1H), 9.57 (s, 1H), 8.94 (s, 1H), 8.80 – 8.83 (m, 2H), 7.96 (s, 1H), 7.75 – 7.81 (m, 2H), 7.58 – 7.63 (m, 1H), 7.29 – 7.37 (m, 3H), 2.43 (s, 3H)	384	2-fluoro-5-chlorobenzoic acid
101	5-[(3,4-Dimethyl benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 9.65 (s, 1H), 9.10 (d, 1H), 8.83 (s, 1H), 8.19 (s, 1H), 8.11 (s, 1H), 7.64 – 7.70 (m, 3H), 7.52 (d, 1H), 7.01 (d, 1H), 6.70 (d, 1H), 2.25 (s, 3H), 2.17 (s, 3H), 2.12 (s, 3H)	360	3,4-dimethylbenzoic acid
102	5-[(4-Ethoxy benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	9.74 (s, 2H), 8.94 (s, 1H), 8.28 – 8.32 (m, 2H), 7.93 – 7.97 (m, 2H), 7.73 (d, 1H), 7.64 (s, 1H), 7.52 (s, 2H), 7.86 (dd, 1H), 7.30 (d, 1H), 2.42 (s, 3H)	376	4-ethoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
103	4-Methoxy-2-methyl- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}benzamide	10.56 (s, 1H), 10.26 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.17 (d, 1H), 7.90 (s, 1H), 7.71 (d, 1H), 7.36 – 7.45 (m, 2H), 7.26 (d, 1H), 6.83 – 6.86 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H)	376	2-methyl-4-methoxybenzoic acid
104	5-[(3,4-Dimethoxybenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.56 (s, 1H), 10.16 (s, 1H), 8.87 (s, 1H), 8.30 (d, 1H), 8.16 (d, 1H), 7.89 (d, 1H), 7.83 (dd, 1H), 7.62 (dd, 1H), 7.53 (d, 1H), 7.38 (dd, 1H), 7.28 (d, 1H), 7.07 (d, 1H), 3.83 (s, 6H), 2.34 (s, 3H)	392	3,4-dimethoxybenzoic acid
105	5-[(3-Chloro-5-fluorobenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.59 (s, 1H), 10.50 (s, 1H), 8.87 (d, 1H), 8.30 (dd, 1H), 8.17 (d, 1H), 7.89 – 7.91 (m, 2H), 7.75 – 7.83 (m, 2H), 7.71 (ddd, 1H), 7.38 (dd, 1H), 7.80 (d, 1H), 2.36 (s, 3H)	384	3-fluoro-5-chlorobenzoic acid
106	2-Methyl-5-[(4-propoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.57 (s, 1H), 10.19 (s, 1H), 8.88 (d, 1H), 8.80 (dd, 1H), 8.18 (d, 1H), 7.97 (s, 1H), 7.92 – 7.94 (m, 2H), 7.83 (dd, 1H), 7.39 (dd, 1H), 7.28 (d, 1H), 7.06 (d, 2H), 4.01 (t, 2H), 2.35 (s, 3H), 1.75 (m, 2H), 0.99 (t, 3H)	390	4-propoxybenzoic acid
107	5-[(3,4-Dichlorobenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.58 (s, 1H), 10.46 (s, 1H), 8.88 (s, 1H), 8.80 (d, 1H), 8.17 (d, 1H), 8.02 (t, 1H), 7.91 – 7.93 (m, 1H), 7.82 (dd, 1H), 7.67 (d, 1H), 7.55 – 7.60 (m, 1H), 7.40 (dd, 1H), 7.32 (d, 1H), 2.83 (s, 3H)	400	3,4-dichlorobenzoic acid

Ex.	Compound	NMR	m/z	SM
108	5-{[3-(Aminosulfonyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.83 (s, 1H), 10.63 (s, 1H), 9.04 (s, 1H), 8.38 - 8.44 (m, 2H), 8.32 (d, 1H), 8.18 (d, 1H), 8.02 (d, 1H), 7.96 (s, 1H), 7.83 (d, 1H), 7.75 (t, 1H), 7.62 (dd, 1H), 7.50 (s, 2H), 7.34 (d, 1H), 2.36 (s, 3H)	411	Method 130
109	5-[(3-{[4-(Hydroxymethyl)piperidin-1-yl]sulfonyl}benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.86 (s, 1H), 10.64 (s, 1H), 9.07 (s, 1H), 8.45 (d, 1H), 8.32 - 8.40 (m, 2H), 8.23 (d, 1H), 8.04 (d, 1H), 7.97 (s, 1H), 7.79 (ddd, 2H), 7.65 (dd, 1H), 7.34 (d, 1H), 3.84 - 3.98 (m, 1H), 3.63 - 3.72 (m, 1H), 3.50 - 3.57 (m, 1H), 3.37 (dd, 1H), 2.94 - 3.07 (m, 1H), 2.36 - 2.42 (m, 2H), 1.72 (d, 1H), 1.34 - 1.49 (m, 3H), 1.05 - 1.21 (m, 2H)	509	Method 131
110	5-[(3-{[3-(Hydroxymethyl)piperidin-1-yl]sulfonyl}benzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	11.07 (s, 1H), 10.71 (s, 1H), 9.19 (s, 1H), 8.41 - 8.56 (m, 2H), 8.21 - 8.34 (m, 2H), 8.00 (s, 1H), 7.89 - 7.96 (m, 1H), 7.82 (t, 3H), 7.35 (d, 1H), 3.68 (d, 1H), 3.56 (d, 1H), 3.30 (dd, 1H), 3.01 - 3.17 (m, 3H), 2.34 - 2.42 (m, 3H), 2.23 (t, 1H), 1.98 (t, 1H), 1.60 - 1.72 (m, 1H), 1.44 - 1.59 (m, 2H), 1.18 (t, 2H), 0.87 (m, 1H)	509	Method 123

Ex.	Compound	NMR	m/z	SM
111	5-[(3-{[2-(Hydroxymethyl)piperidin-1-yl]sulfonyl}benzoyl)amino]-2-methyl-N-pyridin-3-ylbenzamide	11.23 (s, 1H), 10.74 (s, 1H), 9.27 (s, 1H), 8.51 - 8.63 (m, 2H), 8.23 - 8.35 (m, 2H), 8.02 (s, 1H), 7.89 - 7.96 (m, 2H), 7.76 - 7.89 (m, 2H), 7.35 (d, 1H), 3.68 (d, 2H), 3.18 (d, 2H), 3.00 - 3.09 (m, 1H), 2.38 (s, 3H), 2.23 (t, 2H), 1.70 (d, 2H), 1.33 (s, 1H), 1.10 - 1.22 (m, 3H)	509	Method 124
112	5-[(3-{[Methoxy(methyl)amino]sulfonyl}benzoyl)amino]-2-methyl-N-pyridin-3-ylbenzamide	10.80 (s, 1H), 10.69 (s, 1H), 9.02 (s, 1H), 8.36 - 8.43 (m, 3H), 8.30 (d, 1H), 8.02 - 8.06 (m, 1H), 7.94 (s, 1H), 7.81 - 7.90 (m, 2H), 7.59 (dd, 1H), 7.34 (d, 1H), 3.74 (s, 3H), 2.77 (s, 3H), 2.37 (s, 3H)	455	Method 125
113	5-[(3-{[(2,3-Dihydroxypropyl)(methyl)amino]sulfonyl}benzoyl)amino]-2-methyl-N-pyridin-3-ylbenzamide	10.60 (m, 2H), 8.88 (d, 1H), 8.29 - 8.35 (m, 2H), 8.28 (d, 1H), 8.18 (d, 1H), 7.97 (d, 1H), 7.91 (d, 1H), 7.78 - 7.89 (m, 2H), 7.39 (dd, 1H), 7.33 (d, 1H), 4.88 (d, 1H), 4.63 (t, 1H), 3.58 - 3.68 (m, 1H), 3.30 (m, 5.12, 2H), 3.12 (dd, 1H), 2.85 (dd, 1H), 2.78 (s, 3H), 2.36 (s, 3H)	536	Method 126
114	2-Methyl-N-pyridin-3-yl-5-[(3-{[(tetrahydrofuran-2-ylmethyl)amino]sulfonyl}benzoyl)amino]benzamide	11.19 (s, 1H), 10.75 (s, 1H), 9.23 (m, 1H), 8.50 - 8.60 (m, 2H), 8.41 (t, 1H), 8.24 (d, 1H), 8.03 (d, 1H), 7.92 - 8.00 (m, 2H), 7.85 - 7.90 (m, 2H), 7.75 (t, 1H), 7.34 (d, 1H), 3.79 (m, 1H), 3.64 (m, 1H), 3.50 - 3.58 (m, 1H), 2.79 (t, 2H), 2.37 (s, 2H), 1.78 - 1.85 (m, 1H), 1.69 - 1.77 (m, 2H), 1.47 - 1.58 (m, 1H)	495	Method 127

Ex.	Compound	NMR	m/z	SM
115	2-Methyl-5-{[3-(morpholin-4-ylsulfonyl)benzoyl]amino}- <i>N</i> -pyridin-3-ylbenzamide	11.19 (s, 1H), 10.75 (s, 1H), 9.26 (d, 1H), 8.51 - 8.62 (m, 2H), 8.33 - 8.40 (m, 1H), 8.29 (t, 1H), 8.02 (d, 1H), 7.89 - 7.97 (m, 2H), 7.83 - 7.87 (m, 2H), 7.36 (d, 1H), 3.60 - 3.66 (m, 4H), 2.87 - 2.94 (m, 4H), 2.39 (s, 3H)	481	Method 128
116	<i>N</i> -{4-Methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2-(trifluoromethyl)pyrimidine-4-carboxamide	10.79 (s, 1H), 10.59 (s, 1H), 9.35 (d, 1H), 8.88 (d, 1H), 8.37 (d, 1H), 8.31 (dd, 1H), 8.18 (d, 1H), 8.01 (d, 1H), 7.95 (dd, 1H), 7.33 - 7.43 (m, 2H), 2.38 (s, 3H)	402	Method 177
117	3-(1-Cyano-1-methylethyl)-2-fluoro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}benzamide	10.91 (s, 1H), 10.63 (s, 1H), 9.11 (m, 1H), 8.48 (m, 1H), 8.39 (d, 1H), 7.90 (s, 1H), 7.72 (s, 2H), 7.64 (m, 2H), 7.36 (m, 2H), 2.36 (s, 3H), 1.77 (s, 6H)	417	Method 114
118	5-{[3-(2-Methoxy-1,1-dimethylethyl)benzoyl]amino}-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.56 (s, 1H), 10.30 (s, 1H), 8.88 (s, 1H), 8.26 - 8.36 (m, 1H), 8.18 (d, 1H), 7.91 (m, 2H), 7.84 (dd, 1H), 7.79 (d, 1H), 7.59 (d, 1H), 7.36 - 7.48 (m, 2H), 7.30 (d, 1H), 3.41 (s, 2H), 3.21 (s, 3H), 2.36 (s, 3H), 1.28 (s, 6H)	418	Method 178
119	5-(1-Cyano-1-methylethyl)-2-fluoro- <i>N</i> -{4-methyl-3-[(pyridin-3-ylamino)carbonyl]phenyl}benzamide	11.14 (s, 1H), 10.67 (s, 1H), 9.23 (m, 1H), 8.57 (d, 1H), 8.51 (d, 1H), 7.96 (m, 1H), 7.87 (m, 1H), 7.74 (m, 3H), 7.43 (t, 1H), 7.34 (d, 1H), 2.37 (s, 3H), 1.72 (s, 6H)	417	Method 53

Ex.	Compound	NMR	m/z	SM
120	5-[(3-Chloro-4-fluorobenzoyl)amino]-2-methyl- <i>N</i> -pyridin-3-ylbenzamide	10.59 (s, 1H), 10.46 (s, 1H), 8.88 (d, 1H), 8.82 (dd, 1H), 8.17 – 8.24 (m, 2H), 7.99 – 8.04 (m, 1H), 7.90 (s, 1H), 7.82 (dd, 1H), 7.61 (t, 1H), 7.40 (dd, 1H), 7.32 (d, 1H), 2.36 (s, 3H)	384	3-chloro-4-fluorobenzoic acid

Example 121**2-Chloro-5-[(3-fluorobenzoyl)amino]-*N*-pyridin-3-ylbenzamide**

A solution of 5-amino-2-chloro-*N*-pyridin-3-ylbenzamide (Method 76; 65 mg, 0.264 mmol), 3-fluorobenzoic acid (41 mg, 0.290 mmol), and DIEA (115 μ l, 0.66 mmol) in DMF (1.5 ml) was treated with HATU (120 mg, 0.3168 mmol). The reaction mixture was shaken overnight at 25 °C. Water (10 ml) was added slowly to precipitate the product. The resulting precipitate was washed with water (10 ml), isolated and dried overnight in a vacuum oven at 70 °C to give the title compound 46.9 mg, (48%) as a solid. NMR (300 MHz): 10.81 (s, 1H), 10.59 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.03 (s, 1H), 7.93 (dd, 1H), 7.74-7.84 (m, 2H), 7.54-7.65 (m, 2H), 7.37-7.51 (m, 2H); *m/z* 369.

Examples 122-157

The following compounds were prepared by the procedure in Example 121 using 5-amino-2-chloro-*N*-pyridin-3-ylbenzamide (Method 76) and the appropriate SM with the exception of Example 157 which was prepared from 2-chloro-5-[[3-(trifluoromethyl)benzoyl]amino]benzoic acid (Method 224) and *N*-(5-aminopyridin-2-yl)acetamide. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex.	Compound	NMR	m/z	SM
122	2-Chloro-5-[(3,5-dimethylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.44 (s, 1H), 8.86 (s, 1H), 8.33 (s, 1H), 8.16 (d, 1H), 8.04 (s, 1H), 7.90-7.99 (m, 1H), 7.52-7.60 (m, 3H), 7.41 (dd, 1H), 7.23 (s, 1H), 2.30-2.37 (m, 6H)	379	3,5-Dimethylbenzoic acid
123	2-Chloro-5-[(3,5-difluorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.82 (s, 1H), 10.63 (s, 1H), 8.85 (s, 1H), 8.33 (s, 1H), 8.16 (d, 1H), 8.01 (s, 1H), 7.87-7.95 (m, 1H), 7.69 (d, 2H), 7.51-7.63 (m, 2H), 7.41 (dd, 1H)	387	3,5-Difluorobenzoic acid
124	2-Chloro-5-[(3-iodobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.59 (s, 1H), 8.85 (s, 1H), 8.31 (s, 2H), 8.16 (d, 1H), 7.90-8.03 (m, 4H), 7.58 (d, 1H), 7.31-7.45 (m, 2H)	477	3-Iodobenzoic acid
125	2-Chloro-5-[(3,5-dimethoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.80 (s, 1H), 10.44 (s, 1H), 8.85 (s, 1H), 8.33 (s, 1H), 8.16 (d, 1H), 8.02 (s, 1H), 7.91-7.98 (m, 1H), 7.57 (d, 1H), 7.41 (dd, 1H), 7.10 (s, 2H), 6.73 (s, 1H), 3.79-3.86 (m, 6H)	411	3,5-Dimethoxybenzoic acid
126	2-Chloro-5-[(3-methylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.80 (s, 1H), 10.49 (s, 1H), 8.86 (s, 1H), 8.33 (s, 1H), 8.16 (d, 1H), 8.04 (s, 1H), 7.90-7.98 (m, 1H), 7.72-7.79 (m, 2H), 7.57 (d, 1H), 7.36-7.44 (m, 3H), 2.39 (s, 3H)	365	3-Methylbenzoic acid

Ex.	Compound	NMR	m/z	SM
127	2-Chloro-5-[(3-isopropoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.46 (s, 1H), 8.86 (s, 1H), 8.33 (s, 1H), 8.16 (d, 1H), 8.05 (s, 1H), 7.90-7.98 (m, 1H), 7.38-7.52 (m, 5H), 7.15 (d, 1H), 4.61-4.74 (m, 1H), 1.28 (d, 6H)	409	3-Isopropoxybenzoic acid
128	2-Chloro-5-[(3-(dimethylamino)benzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.80 (s, 1H), 10.40 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.03 (s, 1H), 7.95 (d, 1H), 7.56 (d, 1H), 7.41 (dd, 1H), 7.32 (t, 1H), 7.19-7.25 (m, 2H), 6.93 (d, 1H), 2.90-2.98 (m, 6H)	394	3-(Dimethylamino)benzoic acid
129	2-Chloro-5-[(3-[(difluoromethyl)thio]benzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.65 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.17 (s, 2H), 8.08 (d, 1H), 8.03 (s, 1H), 7.91-7.98 (m, 1H), 7.73-7.88 (m, 1H), 7.54-7.69 (m, 2H), 7.31-7.45 (m, 2H)	433	3-[(Difluoromethyl)-thio]benzoic acid
130	2-Chloro-5-[(3-chlorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.61 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.02 (s, 2H), 7.88-7.96 (m, 2H), 7.65-7.73 (m, 1H), 7.59 (dd, 2H), 7.41 (dd, 1H)	386	3-Chlorobenzoic acid
131	2-Chloro-5-[(3-propoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.80 (s, 1H), 10.47 (s, 1H), 8.86 (s, 1H), 8.33 (s, 1H), 8.16 (d, 1H), 8.04 (s, 1H), 7.95 (d, 1H), 7.46-7.55 (m, 3H), 7.39-7.44 (m, 2H), 7.16 (d, 1H), 4.00 (t, 2H), 1.74 (m, 2H), 0.99 (t, 3H)	409	3-Propoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
132	2-Chloro-5-[(3-methoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.80 (s, 1H), 10.49 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.03 (s, 1H), 7.91-7.98 (m, 1H), 7.52-7.59 (m, 2H), 7.38-7.50 (m, 3H), 7.18 (d, 1H), 3.83 (s, 3H)	381	3-Methoxybenzoic acid
133	5-[(3-Bromobenzoyl)amino]-2-chloro- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.61 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (s, 2H), 8.02 (s, 1H), 7.95 (t, 2H), 7.82 (d, 1H), 7.54 (m, 2H), 7.41 (dd, 1H)	430	3-Bromobenzoic acid
134	2-Chloro-5-[(3-isobutoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.80 (s, 1H), 10.47 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.04 (s, 1H), 7.91-7.98 (m, 1H), 7.54 (dd, 3H), 7.38-7.48 (m, 2H), 7.17 (d, 1H), 3.82 (d, 2H), 2.04 (ddd, 1H), 0.99 (d, 6H)	423	3-Isobutoxybenzoic acid
135	2-Chloro- <i>N</i> -pyridin-3-yl-5-[(3-(trifluoromethyl)benzoyl)amino]benzamide	10.82 (s, 1H), 10.73 (s, 1H), 8.85 (s, 1H), 8.24-8.38 (m, 3H), 8.17 (d, 1H), 8.02 (s, 1H), 7.98 (t, 2H), 7.80 (t, 1H), 7.60 (d, 1H), 7.41 (dd, 1H)	419	3-(Trifluoromethyl)-benzoic acid
136	2-Chloro-5-[(3-(1-cyano-1-methylethyl)benzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.81 (s, 1H), 10.58 (s, 1H), 8.85 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.03 (d, 2H), 7.95 (d, 2H), 7.77 (d, 1H), 7.55-7.66 (m, 2H), 7.41 (dd, 1H), 1.74 (s, 6H)	418	3-(1-Cyano-1-methylethyl)-benzoic acid
137	2-Chloro-5-[(3-[(dimethylamino)sulfonyl]benzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.79 (d, 2H), 8.85 (d, 1H), 8.29-8.35 (m, 3H), 8.16 (d, 1H), 8.02 (s, 1H), 7.94-7.99 (m, 2H), 7.84 (t, 1H), 7.60 (d, 1H), 7.41 (dd, 1H), 2.65 (s, 6H)	458	Method 120

Ex.	Compound	NMR	m/z	SM
138	2-Chloro-5-[(3-cyclopropyl-5-fluorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	11.33 (s, 1H), 10.65 (s, 1H), 9.16 (d, 1H), 8.56 (d, 1H), 8.45 (d, 1H), 8.06 - 8.16 (m, 1H), 7.95 (dd, 1H), 7.82 (dd, 1H), 7.50 - 7.63 (m, 3H), 7.17 (d, 1H), 2.04 (ddd, 1H), 0.96 - 1.07 (m, 2H), 0.81 (ddd, 2H)	410	Method 226
139	<i>N</i> -{4-Chloro-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2-methylisonicotinamide	11.11 (s, 1H), 10.85 (s, 1H), 9.03 (s, 1H), 8.71 (d, 1H), 8.45 (s, 1H), 8.30 (d, 1H), 8.03 (d, 1H), 7.75 - 7.89 (m, 3H), 7.54 - 7.69 (m, 2H), 2.58 (s, 3H)	367	2-methylisonicotinic acid
140	<i>N</i> -{4-Chloro-3-[(pyridin-3-ylamino)carbonyl]phenyl}-2-cyanoisonicotinamide	11.10 (s, 1H), 10.95 (s, 1H), 9.03 (s, 1H), 8.98 (d, 1H), 8.52 (s, 1H), 8.47 (d, 1H), 8.31 (d, 1H), 8.19 (dd, 1H), 8.06 (d, 1H), 7.91 (dd, 1H), 7.63 - 7.68 (m, 1H), 7.63 (s, 1H)	378	2-cyanoisonicotinic acid
141	2-Chloro-5-[(5-chloro-2-fluorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	9.57 (s, 1H), 9.45 (s, 1H), 8.80 (s, 1H), 8.16 - 8.23 (m, 2H), .84 (s, 1H), 7.63 - 7.70 (m, 2H), 7.45 - 7.52 (m, 1H), 7.16 - 7.27 (m, 3H)	405	2-fluoro-5-chlorobenzoic acid
142	2-Chloro-5-[(3-fluoro-5-methylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	9.77 (s, 2H), 9.92 (d, 1H), 8.35 (d, 1H), 8.30 d, 1H), 8.10 - 8.12 (m, 1H), 7.94 - 7.98 (m, 1H), 7.67 (s, 1H), 7.54 (d 1H), 7.51 (d, 1H), 7.88 (dd, 1H), 7.21 (d, 1H), 2.42 (s, 3H)	384	3-fluoro-5-methylbenzoic acid

Ex.	Compound	NMR	m/z	SM
143	<i>N</i> -{4-Chloro-3-[(pyridin-3-ylamino)carbonyl]phenyl}-4-methoxy-2-methylbenzamide	10.74 (s, 1H), 10.38 (s, 1H), 9.00 (d, 1H), 8.88 (d, 1H), 8.29 – 8.33 (m, 1H), 8.16 (d, 1H), 8.02 (s, 1H), 7.99 (dd, 1H), 7.67 (dd, 1H), 7.45 (dd, 1H), 6.86 – 6.91 (m, 2H), 3.86 (s, 3H), 2.47 (s, 3H)	396	2-methyl-4-methoxybenzoic acid
144	2-Chloro-5-{[3-fluoro-5-(trifluoromethyl)benzoyl]amino}- <i>N</i> -pyridin-3-ylbenzamide	10.88 (s, 1H), 10.76 (s, 1H), 9.01 (d, 1H), 8.38 – 8.40 (m, 1H), 8.29 – 8.34 (m, 1H), 8.28 (s, 1H), 8.18 – 8.22 (m, 2H), 8.03 (dd, 1H), 7.97 – 8.00 (d, 1H), 8.62 (d, 1H), 8.46 (dd, 1H),	438	3-fluoro-5-trifluoromethylbenzoic acid
145	2-Chloro-5-[(2,5-dimethylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.76 (s, 1H), 10.50 (s, 1H), 9.02 (d, 1H), 8.39 (d, 1H), 8.32 (d, 1H), 8.18 (d, 1H), 7.99 – 8.03 (m, 2H), 8.59 (d, 1H), 7.22 (s, 1H), 7.46 (dd, 1H), 2.41 (s, 3H), 2.33 (s, 3H)	380	2,5-dimethylbenzoic acid
146	5-[(4-Bromo-3-methylbenzoyl)amino]-2-chloro- <i>N</i> -pyridin-3-ylbenzamide	10.75 (s, 1H), 10.62 (s, 1H), 9.02 (d, 1H), 8.40 (dd, 1H), 8.30 – 8.34 (m, 1H), 8.20 (d, 1H), 8.03 – 8.07 (m, 2H), 8.71 – 8.86 (m, 2H), 7.60 (d, 1H), 7.46 (dd, 1H), 2.47 (s, 3H)	446	3-methyl-4-bromobenzoic acid
147	2-Chloro-5-[(3,4-dimethoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.72 (s, 1H), 10.41 (s, 1H), 9.00 (d, 1H), 8.88 (dd, 1H), 8.29 – 8.33 (m, 1H), 8.18 (d, 1H), 8.06 (d, 1H), 7.76 (d, 1H), 7.68 (d, 1H), 7.56 (d, 1H), 7.47 (dd, 1H), 7.16 (d, 1H), 3.92 (s, 3H), 6.99 (s, 3H)	412	3,4-dimethoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
148	2-Chloro-5-[(3-chloro-5-fluorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.22 (s, 1H), 10.11 (s, 1H), 8.65 (d, 1H), 8.02 – 8.04 (m, 1H), 7.98 (d, 1H), 7.87 (d, 1H), 7.69 – 7.75 (m, 2H), 7.56 (d, 1H), 7.48 (dd, 1H), 7.21 (dd, 1H), 6.99 (d, 1H)	404	3-fluoro-5-chlorobenzoic acid
149	2-Chloro-5-[(3,4-dimethylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.74 (s, 1H), 10.45 (s, 1H), 9.02 (s, 1H), 8.39 (dd, 1H), 8.30 – 8.34 (m, 1H), 8.22 (d, 1H), 8.07 (dd, 1H), 7.85 (s, 1H), 7.82 (dd, 1H), 7.46 (dd, 1H), 7.81 (d, 1H), 2.32 (s, 6H)	380	3,4-dimethylbenzoic acid
150	2-Chloro-5-[(4-methoxy-3-methylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.72 (s, 1H), 10.37 (s, 1H), 9.00 (d, 1H), 8.88 (dd, 1H), 8.29 – 8.33 (m, 1H), 8.28 (d, 1H), 8.04 – 8.08 (m, 1H), 7.96 – 7.99 (m, 1H), 7.91 (s, 1H), 7.65 (d, 1H), 7.46 (dd, 1H), 7.42 (d, 1H), 3.94 (s, 3H), 2.23 (s, 3H)	396	3-methyl-4-methoxybenzoic acid
151	2-Chloro-5-[(4-methoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.73 (s, 1H), 10.43 (s, 1H), 9.03 (d, 1H), 8.39 (dd, 1H), 8.30 – 8.34 (m, 1H), 8.21 (d, 1H), 8.04 – 8.11 (m, 3H), 7.56 (d, 1H), 7.46 (dd, 1H), 7.12 (d, 1H), 3.90 (s, 3H)	382	4-methoxybenzoic acid
152	2-Chloro-5-[(3,5-dichlorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.75 (s, 1H), 9.00 (d, 1H), 8.39 (dd, 1H), 8.29 – 8.34 (m, 1H), 8.17 (d, 1H), 8.08 (s, 1H), 8.01 – 8.05 (m, 2H), 7.86 – 7.89 (m, 1H), 7.62 (d, 1H), 7.46 (dd, 1H)	421	3,5-dichlorobenzoic acid

Ex.	Compound	NMR	m/z	SM
153	2-Chloro-5-[(4-ethoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.73 (s, 1H), 10.42 (s, 1H), 9.03 (s, 1H), 8.39 (d, 1H), 8.30 – 8.35 (m, 1H), 8.23 (d, 1H), 8.02 – 8.10 (m, 3H), 7.56 (d, 1H), 7.45 (dd, 1H), 7.09 (d, 2H), 4.15 (dd, 2H), 1.39 (t, 3H)	396	4-ethoxybenzoic acid
154	2-Chloro-5-[[3-morpholin-4-yl-5-(trifluoromethyl)benzoyl]amino]- <i>N</i> -pyridin-3-ylbenzamide	10.83 (s, 1H), 10.60 (s, 1H), 8.86 (d, 1H), 8.34 (d, 1H), 8.17 (ddd, 1H), 7.94 – 8.00 (m, 2H), 7.71 (s, 1H), 7.66 (s, 1H), 7.58 (d, 1H), 7.40 – 7.45 (m, 2H), 3.75 – 3.78 (m, 4H), 3.27 – 3.31 (m, 4H)	506	3-trifluoromethyl-5-morpholinobenzoic acid
155	2-Chloro-5-[(3-cyclopropylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	11.24 (s, 1H), 10.51 (d, 1H), 9.14 (s, 1H), 8.54 (s, 1H), 8.35 – 8.48 (m, 1H), 8.06 – 8.16 (m, 1H), 7.93 (dd, 1H), 7.70 (d, 2H), 7.56 – 7.66 (m, 2H), 7.28 – 7.43 (m, 2H), 1.97 – 2.06 (m, 1H), 0.95 – 1.04 (m, 2H), 0.70 – 0.79 (m, 2H)	393	Method 34
156	2-Chloro-5-[(3,4-dichlorobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.93 (s, 1H), 10.92 (s, 1H), 9.20 (d, 1H), 8.57 (dd, 1H), 8.61 (dd, 1H), 8.47 (d, 1H), 8.36 (d, 1H), 8.20 – 8.24 (m, 2H), 8.05 (d, 1H), 7.78 (d, 1H), 7.65 (dd, 1H)	400	3,4-dichlorobenzoic acid
157	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-2-chloro-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	¹ H NMR (300 MHz) 10.72 (d, 2H), 10.51 (s, 1H), 8.67 (s, 1H), 8.17 – 8.34 (m, 3H), 7.92 – 8.10 (m, 5H), 7.76 – 7.86 (m, 1H), 7.60 (d, 1H), 2.09 (s, 3H)	477	Method 224 and <i>N</i> -(5-aminopyridin-2-yl)acetamide

Example 158*N*-(6-Acetylpyridin-3-yl)-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a solution of *N*-(6-bromopyridin-3-yl)-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 215; 100 mg) in NMP (3 ml) were added tributyl[(1*E*)-2-methoxyprop-1-en-1-yl]stannane (0.4 ml), Pd(PPh₃)₄ (50 mg) under argon. The resulting mixture was heated to 80°C for 10 hours. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine, saturated aqueous NaF solution and dried with MgSO₄. Evaporation of the solvent gave a solid, which was dissolved in 2 N HCl and stirred for 3 hours at room temperature. Extraction of the aqueous layer with EtOAc (3x 25 ml) and the organic layer was washed with brine and dried with MgSO₄. Evaporation gave a brown solid, which was purified by Reverse phase HPLC (5-95% MeCN/H₂O, 15 min). The title compound (2 mg) was collected by evaporation. NMR (300 MHz) 11.26 (s, 1H), 10.82 (s, 1H), 9.03 (d, 1H), 8.6 – 8.63 (m, 3H), 7.8 – 8.23 (m, 4H), 7.88 (t, 1H), 7.69 (d, 1H), 2.68 (s, 3H), m/z 461.

Example 159*N*-{6-[(2-Hydroxyethyl)amino]pyridin-3-yl}-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a solution of *N*-{6-[(2-{[tert-butyl(dimethyl)silyl]oxy}ethyl)amino]pyridine-3-yl}-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Method 99; 125 mg) in THF was added tertbutylammonium fluoride (3 ml, 1.0M in THF) and the resulting dark red solution was stirred at room temperature for 2 hours. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. Evaporation of the solvent gave a pale purple oil, which was purified by Reverse phase HPLC (5-95% ACN/ H₂O, 20 min). The title compound (43 mg) was collected by evaporation as a pale purple solid. NMR (300 MHz): 10.59 (s, 2H), 8.47 (s, 1H), 8.23 – 8.35 (m, 2H), 7.88 – 8.03 (m, 3H), 7.75 – 7.86 (m, 2H), 7.34 (d, 1H), 7.06 (s, 1H), 3.58 – 3.67 (m, 4H), 2.36 (s, 3H); m/z 459.

Example 160

5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-[6-(glycoloylamino)-5-methylpyridin-3-yl]-2-methylbenzamide

To a solution of *N*-(6-{[(benzyloxy)acetyl]amino}-5-methylpyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide (Example 316; 30 mg) in MeOH (3 ml) were added HCO₂NH₄ and HCO₂H (5 ml, 1:10 v/v) and the resulting mixture was refluxed for 12 hours. The mixture was partitioned between EtOAc and H₂O and the organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. Evaporation of the solvent gave a solid, which was purified by Reverse phase HPLC (5-95% ACN/H₂O, 15 min). The title compound (5 mg) was collected by evaporation. NMR (300 MHz): 10.55 (s, 1H), 10.43 (s, 1H), 9.62 (s, 1H), 8.55 (d, 1H), 8.03 - 8.10 (m, 2H), 7.96 (d, 1H), 7.89 (d, 1H), 7.85 (dd, 1H), 7.75 (d, 1H), 7.61 (t, 1H), 7.33 (d, 1H), 4.08 - 4.18 (m, 2H), 2.37 (s, 3H), 2.19 (s, 3H), 1.76 (s, 6H); m/z 486.

Example 161

N-[6-(Aminomethyl)pyridin-3-yl]-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide

To a solution of 5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-*N*-(6-cyanopyridin-3-yl)-2-methylbenzamide (Example 321; 100 mg) in THF (3ml) was added slowly LiAlH₄ (3 ml, 1.0M in THF) and the resulting mixture was stirred at ambient temperature for 5 minutes. The mixture was cooled with an ice bath and a saturated solution of tartaric acid was added slowly until evolution of gas ceased. The mixture was filtered to remove the aluminium salts and the filtrate was partitioned between EtOAc and H₂O. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. Evaporation of the solvent gave a solid, which was purified by reverse phase HPLC (5-95% ACN/H₂O, 15 min). The title compound (50 mg) was collected by evaporation. NMR (300 MHz): 10.72 (s, 1H), 10.52 (s, 1H), 8.96 (s, 1H), 8.33 - 8.41 (bs, 2H), 8.22 (d, 1H), 8.08 (s, 1H), 7.95 - 8.03 (m, 2H), 7.82 (d, 1H), 7.77 (d, 1H), 7.61 (t, 1H), 7.54 (d, 1H), 7.28 - 7.41 (m, 2H), 4.11 - 4.20 (m, 2H), 2.38 (s, 3H), 1.79 (s, 6H); m/z 429.

Example 162

The following compound was prepared by the procedure of Example 161, using the appropriate starting material.

Ex	Compound	NMR	M/z	SM
162	<i>N</i> -[5-(Aminomethyl)pyridin-3-yl]-2-chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}benzamide	10.99 (s, 1H), 10.60 (s, 1H), 8.71 (s, 1H), 8.42 (s, 1H), 8.17 - 8.28 (m, 2H), 8.01 - 8.11 (m, 2H), 7.88 - 8.01 (m, 2H), 7.78 (d, 1H), 7.53 - 7.68 (m, 2H), 4.13 (dd, 2H) 1.74 (s, 6H)	449	Example 313

Example 1635-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-*N*-[5-(methoxymethyl)pyridin-3-yl]-2-methylbenzamide

5 To a solution of 5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-*N*-[5-(hydroxymethyl)pyridin-3-yl]-2-methylbenzamide (Example 299; 24 mg) in THF (2 ml) was added slowly at 0°C NaH (5 mg) and the mixture was stirred at this temperature for 30 minutes. MeI (0.05 ml) was added and the mixture was stirred at room temperature for 4 hours. The mixture was cooled with an ice bath and H₂O was added until evolution of gas

10 ceased. The mixture was partitioned between EtOAc and H₂O. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. Evaporation of the solvent gave a solid, which was purified by reverse phase HPLC (5-95% MeCN/H₂O, 15 min). The title compound (5.7 mg) was collected by evaporation. NMR (300 MHz): 10.89 (s, 1H), 10.41 (s, 1H), 8.45 (s, 1H), 8.30 (s, 1H), 8.20 (d, 1H), 8.05 (s, 1H), 7.90 - 8.00 (m, 2H), 7.86 (d, 1H), 7.76 (d, 1H),

15 7.65(t, 1H), 7.32 (d, 1H), 4.50 (s, 2H) 3.35(s, 3H) 2.10 (s, 3H), 1.76 (s, 6H); m/z 443.

Example 1642-Chloro-*N*-(5-fluoropyridin-3-yl)-5-{[3-fluoro-5-(trifluoromethyl)benzoyl]amino}-benzamide

20 A solution of 5-amino-2-chloro-*N*-(5-fluoropyridin-3-yl)benzamide (Method 79; 124 mg, 0.466 mmol) and DIEA (405 µL, 2.33 mmol, 5.0 equiv) in THF (2.0 ml) was treated with 3-fluoro-5-(trifluoromethyl)benzoyl chloride (131 mg, 0.582 mmol, 1.25 equiv). The reaction mixture was stirred for 12 h at 25 °C. The reaction was quenched with 10% NaOH and extracted with EtOAc. The organics were dried with NaCl_(sat) and then Na₂SO_{4(s)} and removed

25 under reduced pressure. The residue was purified directly by Gilson reverse phase preparatory HPLC (5-95% MeCN/H₂O) to give 75 mg of product (35%). NMR: 11.11 (s, 1H), 10.80 (s, 1H), 8.68 (s, 1H), 8.37 (s, 1H), 8.18-8.12 (m, 3H), 8.03-7.93 (m, 3H), 7.63 (d, 1H); m/z 456.

Example 165**2-Chloro-*N*-[6-(1,2-dihydroxyethyl)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide**

To a solution of *N*-(6-bromopyridin-3-yl)-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 215; 100 mg) in NMP (3 ml) were added tributyl vinyl tin (0.4 ml), Pd(PPh₃)₄ (50 mg) under argon. The resulting mixture was heated to 80°C for 10 hours. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine, saturated aqueous NaF solution and dried with MgSO₄. Evaporation of the solvent gave a solid, which was dissolved in a mixture of acetone/H₂O (1:1 v/v, 2 ml). *N*-methyl morpholine oxide (60 mg) was added followed by a solution of OsO₄ in *t*-BuOH (0.04 ml, 2.5 w/v) and the resulting mixture was stirred at ambient temperature for 12 hours. A solution of sodium thiosulphate (1N, 10 ml) was added and the resulting solution was stirred for 3 hours at room temperature. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. Evaporation of the solvent gave a solid, which was purified by reverse phase HPLC (5-95% MeCN/H₂O, 15 min). The title compound (11 mg) was collected by evaporation. NMR (300 MHz): 10.54 (s, 1H), 10.34 (s, 1H), 8.00-8.55 (m, 4H), 7.80 - 7.95 (m, 3H), 7.08-7.55 (m, 3H), 3.23-3.51 (m, 3H); *m/z* 480.

Example 166**2-Fluoro-5-[(3-fluorobenzoyl)amino]-*N*-pyridin-3-ylbenzamide**

A solution of 5-amino-2-fluoro-*N*-pyridin-3-ylbenzamide (Method 75; 30.5 mg, 0.132 mmol), 3-fluorobenzoic acid (20.5 mg, 0.145 mmol) and DIEA (60 µL, 0.35 mmol) in DMF (1.5 ml) was treated with HATU (60 mg, 0.1584 mmol). The reaction mixture was shaken overnight at 25 °C. Water (10 ml) was added slowly to precipitate the product. The resulting precipitate was washed with water (10 ml), isolated and dried overnight in a vacuum oven at 70 °C to give the title compound 32 mg, (68%) as a solid. NMR: 10.65 (s, 1H), 10.52 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.15 (d, 1H), 8.09 (d, 1H), 7.93-8.02 (m, 1H), 7.75-7.84 (m, 2H), 7.56-7.66 (m, 1H), 7.37-7.48 (m, 3H); *m/z* 353.

Examples 167-182

The following compounds were prepared by the procedure in Example 166 using 5-amino-2-fluoro-*N*-pyridin-3-ylbenzamide (Method 75) and the appropriate SM. In some

cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex.	Compound	NMR	m/z	SM
167	5-[(3,5-Dimethyl benzoyl)amino]-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.37 (s, 1H), 8.87 (s, 1H), 8.33 (d, 1H), 8.07-8.18 (m, 2H), 7.93-8.01 (m, 1H), 7.57 (s, 2H), 7.34-7.43 (m, 2H), 7.23 (s, 1H), 2.35 (s, 6H)	363	3,5-Dimethylbenzoic acid
168	5-[(3,5-Difluoro benzoyl)amino]-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.66 (s, 1H), 10.57 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.15 (d, 1H), 8.08 (d, 1H), 7.97 (d, 1H), 7.69 (d, 2H), 7.55 (t, 1H), 7.36-7.44 (m, 2H)	371	3,5-Difluorobenzoic acid
169	2-Fluoro-5-[(3-iodobenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.52 (s, 1H), 8.86 (s, 1H), 8.32 (s, 2H), 8.15 (d, 1H), 8.07 (d, 1H), 7.97 (d, 3H), 7.32-7.43 (m, 3H)	461	3-Iodobenzoic acid
170	5-[(3,5-Dimethoxy benzoyl)amino]-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.38 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.15 (d, 1H), 8.08 (d, 1H), 7.94-8.03 (m, 1H), 7.34-7.43 (m, 2H), 7.11 (s, 2H), 6.72 (s, 1H), 3.82 (s, 6H)	395	3,5-Dimethoxybenzoic acid
171	2-Fluoro-5-[(3-methylbenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.74 (s, 1H), 10.51 (s, 1H), 8.96 (s, 1H), 8.42 (d, 1H), 8.17-8.28 (m, 2H), 8.07 (d, 1H), 7.81-7.89 (m, 2H), 7.44-7.54 (m, 4H), 2.58 (s, 3H)	349	3-Methylbenzoic acid
172	2-Fluoro-5-[(3-isopropoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.67 (s, 1H), 10.39 (s, 1H), 8.88 (s, 1H), 8.34 (d, 1H), 8.17 (d, 1H), 8.11 (s, 1H), 7.92-8.02 (m, 1H), 7.47-7.53 (m, 2H), 7.38-7.45 (m, 3H), 7.15 (d, 1H), 4.70 (dt, 1H), 1.29 (d, 6H)	393	3-Isopropoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
173	5-{[3-(Dimethylamino)benzoyl]amino}-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.33 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.09 (d, 1H), 7.97 (d, 1H), 7.36-7.42 (m, 2H), 7.31 (d, 1H), 7.22-7.24 (m, 2H), 6.93 (d, 1H), 2.96 (s, 6H)	378	3-(Dimethylamino)benzoic acid
174	5-({3-[(Difluoromethyl)thio]benzoyl}amino)-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.57 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.14-8.18 (m, 2H), 8.08 (m, 2H), 7.96-8.01 (m, 1H), 7.81 (d, 1H), 7.55-7.71 (m, 2H), 7.40 (m, 2H)	417	3-[(Difluoromethyl)thio]benzoic acid
175	5-[(3-Chlorobenzoyl)amino]-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.67 (s, 1H), 10.56 (s, 1H), 8.87 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.09 (d, 1H), 8.03 (s, 1H), 7.95-8.00 (m, 1H), 7.93 (d, 1H), 7.68 (d, 1H), 7.58 (t, 1H), 7.35-7.44 (m, 2H)	369	3-Chlorobenzoic acid
176	2-Fluoro-5-[(3-propoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.41 (s, 1H), 8.87 (s, 1H), 8.33 (d, 1H), 8.08-8.18 (m, 2H), 7.94-8.01 (m, 1H), 7.49-7.55 (m, 2H), 7.35-7.46 (m, 3H), 7.16 (d, 1H), 4.00 (t, 2H), 1.71-1.80 (m, 2H), 1.00 (t, 3H)	393	3-Propoxybenzoic acid
177	2-Fluoro-5-[(3-methoxybenzoyl)amino]- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.43 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.09 (s, 1H), 7.98 (d, 1H), 7.57-7.35 (m, 5H), 7.17 (d, 1H), 3.83 (s, 3H)	365	3-Methoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
178	5-[(3-Bromo benzoyl)amino]-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.65 (s, 1H), 10.55 (s, 1H), 8.86 (s, 1H), 8.33 (d, 1H), 8.16 (s, 2H), 8.08 (d, 1H), 7.97 (d, 2H), 7.81 (d, 1H), 7.51 (t, 1H), 7.39 (t, 2H)	414	3-Bromobenzoic acid
179	2-Fluoro-5-[(3-isobutoxybenzoyl) amino]- <i>N</i> -pyridin-3-ylbenzamide	10.66 (s, 1H), 10.41 (s, 1H), 8.87 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.10 (d, 1H), 7.94-8.02 (m, 1H), 7.49-7.55 (m, 2H), 7.36-7.46 (m, 3H), 7.16 (d, 1H), 3.82 (d, 2H), 1.99-2.08 (m, 1H), 1.00 (d, 6H)	407	3-Isobutoxybenzoic acid
180	2-Fluoro- <i>N</i> -pyridin-3-yl-5-{[3-(trifluoromethyl) benzoyl]amino} benzamide	10.67 (s, 2H), 8.86 (s, 1H), 8.25-8.35 (m, 3H), 8.16 (d, 1H), 8.09 (d, 1H), 7.99 (d, 2H), 7.80 (t, 1H), 7.36-7.45 (m, 2H)	403	3-(Trifluoromethyl)-benzoic acid
181	5-{[3-(1-Cyano-1-methylethyl) benzoyl]amino}-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.64 (s, 1H), 10.57 (s, 1H), 8.78 (s, 1H), 8.19-8.27 (m, 3H), 8.07 (d, 1H), 7.99 (d, 1H), 7.85-7.95 (m, 2H), 7.75 (t, 1H), 7.28-7.36 (m, 2H), 2.56 (s, 6H)	402	Method 19
182	5-({3-[(Dimethylamino) sulfonyl]benzoyl} amino)-2-fluoro- <i>N</i> -pyridin-3-ylbenzamide	10.66 (s, 1H), 10.52 (s, 1H), 8.87 (s, 1H), 8.33 (d, 1H), 8.16 (d, 1H), 8.03-8.09 (m, 2H), 7.93-8.03 (m, 2H), 7.76 (d, 1H), 7.61 (t, 1H), 7.40 (t, 2H), 1.75 (s, 6H)	442	Method 120

Example 183**5-[[3-(1-Cyano-1-methylethyl)benzoyl]amino]-2-methyl-*N*-(6-methylpyridin-3-yl)benzamide**

A solution of 5-[3-(cyano-dimethyl-methyl)-benzoylamino]-2-methyl-benzoic acid (Method 20; 200 mg, 0.620 mmol), 6-methylpyridin-3-amine (65 mg, 0.602 mmol) and DIEA (0.32 ml, 1.86 mmol) in DMF (1.3 ml) was treated with HATU (354 mg, 0.930 mmol). The

reaction was stirred at 25 °C for 12 h. The reaction was then quenched with H₂O (5 ml) and extracted with EtOAc (20 ml). The organics were washed with NaCl_(sat) (50 ml) and dried with MgSO₄. The solvents were removed under reduced pressure to give a yellow solid (208 mg), which was purified by Gilson reverse phase preparatory HPLC (5-95% MeCN/H₂O, 20 min). The solvents were removed under reduced pressure to give a white solid (116mg) of the title compound. NMR: 11.01-11.30 (s, 1H), 10.37-10.68 (s, 1H), 9.01-9.32 (s, 1H), 8.48 (d, 1H), 7.93-8.13 (m, 3H), 7.68-7.88 (m, 3H), 7.59 (t, 1H), 7.28 (d, 1H), 2.56-2.76 (s, 3H), 2.23-2.43 (s, 3H), 1.45-1.92 (s, 6H); m/z 413.

10 Examples 184-317

The following compounds were prepared by the procedure in Example 183 using the appropriate SMs. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex.	Compound	NMR	m/z	SM
184	5-{[3-(1-Cyano-1-methylethyl) benzoyl]amino}- <i>N</i> -(6-methoxy pyridin-3-yl)-2-methylbenzamide	10.29-10.49 (s, 1H), 9.53-9.71 (s, 1H), 8.20 (d, 1H), 8.02-8.11 (s, 1H), 7.97 (dd, 2H), 7.84-7.92 (s, 2H), 7.83 (d, 1H), 7.75 (d, 1H), 7.60 (t, 1H), 7.29 (d, 1H), 7.03 (d, 1H), 3.82-4.03 (s, 3H), 2.29-2.43 (s, 3H), 1.63-1.84 (s, 6H)	429	6-Methoxy-pyridin-3-amine and Method 20
185	5-{[3-(1-Cyano-1-methylethyl) benzoyl]amino}-2-methyl- <i>N</i> -(4-methylpyridin-3-yl)benzamide	10.28-10.64 (s, 2H), 9.00-9.18 (s, 1H), 8.61 (d, 1H), 8.03-8.18 (s, 2H), 7.98 (d, 1H), 7.90 (d, 1H), 7.80-7.87 (s, 1H), 7.72-7.78 (s, 1H), 7.62 (t, 1H), 7.34 (d, 1H), 2.51-2.58 (s, 3H), 2.36-2.47 (s, 3H), 1.72-1.85 (s, 6H)	413	4-Methylpyridin-3-amine and Method 20

Ex.	Compound	NMR	m/z	SM
186	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}- <i>N</i> -(4-methoxy pyridin-3-yl)-2-methylbenzamide	10.48-10.50 (s, 1H), 10.37-10.41 (s, 1H), 9.35-9.37 (s, 1H), 8.75 (s, 1H), 8.06-8.13 (s, 1H), 7.90-8.04 (m, 2H), 7.68-7.90 (m, 3H), 7.62 (t, 1H), 7.33 (d, 1H), 4.14-4.16 (s, 3H), 2.36-2.45 (s, 3H), 1.74-1.79 (s, 6H)	429	4-Methoxy-pyridin-3-amine and Method 20
187	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl- <i>N</i> -(6-morpholin-4-ylpyridin-3-yl)benzamide	10.40-10.45 (s, 1H), 10.31-10.38 (s, 1H), 8.41-8.55 (s, 1H), 8.03-8.07 (s, 1H), 7.84-8.03 (m, 3H), 7.71-7.84 (m, 2H), 7.61 (t, 1H), 7.32 (d, 1H), 7.03 (d, 1H), 3.74 (t, 4H), 3.42 (t, 4H), 2.28-2.43 (s, 3H), 1.71-1.80 (s, 6H)	484	Method 84 and Method 20
188	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl- <i>N</i> -(5-methylpyridin-3-yl)benzamide	10.36-10.42 (s, 1H), 8.71-8.92 (s, 2H), 8.02-8.07 (s, 1H), 7.95 (d, 1H), 7.82-7.87 (s, 2H), 7.74 (d, 3H), 7.60 (t, 1H), 7.32 (d, 2H), 4.17-4.29 (s, 2H), 1.71-1.79 (s, 6H)	413	Method 100 and Method 20
189	<i>N</i> -(5-Chloro pyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.81-10.87 (s, 1H), 10.61-10.63 (s, 1H), 8.80-8.83 (s, 1H), 8.36-8.41 (s, 2H), 8.22-8.35 (m, 2H), 7.92-8.02 (m, 2H), 7.71-7.90 (m, 2H), 7.35 (d, 1H), 2.35-2.41 (s, 3H)	434	5-Chloropyridin-3-amine and Method 21
190	<i>N</i> -(5-Methoxy pyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.79-10.83 (s, 1H), 10.59-10.63 (s, 1H), 8.63-8.69 (s, 1H), 8.25-8.38 (m, 2H), 8.15-8.22 (s, 1H), 7.91-8.07 (m, 3H), 7.77-7.90 (m, 2H), 7.35 (d, 1H), 3.85-3.92 (s, 3H), 2.35-2.41 (s, 3H)	430	Method 118 and Method 21

Ex.	Compound	NMR	m/z	SM
191	<i>N</i> -(6-Amino-5-bromopyridin-3-yl)-2-methyl-5- {[3-(trifluoromethyl)benzoyl]amino} benzamide	10.54-10.63 (s, 1H), 10.32-10.42 (s, 1H), 8.18-8.45 (m, 4H), 8.00 (d, 1H), 7.92-7.94 (s, 1H), 7.76-7.85 (m, 2H), 7.31 (d, 2H), 2.31-2.40 (s, 3H)	494	Method 77 and Method 21
192	<i>N</i> -(5-Bromopyridin-3-yl)-5- {[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide	10.76-10.85 (s, 1H), 10.40-10.48 (s, 1H), 8.80-8.88 (s, 1H), 8.48-8.59 (s, 1H), 8.41-8.47 (s, 1H), 8.04-8.09 (s, 1H), 7.89-8.00 (m, 2H), 7.85 (d, 1H), 7.76 (d, 1H), 7.60 (t, 1H), 7.33 (d, 1H), 2.33-2.42 (s, 3H), 1.69-1.81 (s, 6H)	477	Method 119 and Method 20
193	<i>N</i> -(5-Bromopyridin-3-yl)-2-methyl-5- {[3-(trifluoromethyl)benzoyl]amino} benzamide	10.77-10.87 (s, 1H), 10.60-10.62 (s, 1H), 8.82-8.86 (s, 1H), 8.53-8.55 (s, 1H), 8.47-8.48 (s, 1H), 8.24-8.36 (m, 2H), 7.72-8.04 (m, 4H), 7.35 (d, 2H), 2.36-2.39 (s, 3H)	478	Method 119 and Method 21
194	2-Methyl- <i>N</i> -(5-methylpyridin-3-yl)-5- {[3-(trifluoromethyl)benzoyl]amino} benzamide	10.99-11.08 (s, 1H), 10.56-10.69 (s, 1H), 8.96-9.08 (s, 1H), 8.43-8.47 (s, 1H), 8.21-8.42 (m, 3H), 7.92-8.09 (m, 2H), 7.70-7.89 (m, 2H), 7.35 (d, 1H), 2.42-2.49 (s, 3H), 2.33-2.41 (s, 3H)	413	Method 100 and Method 21

Ex.	Compound	NMR	m/z	SM
195	<i>N</i> -(6-Chloro-5-methylpyridin-3-yl)-5-[[3-(1-cyano-1-methylethyl)benzoyl]amino]-2-methylbenzamide	10.65-10.70 (s, 1H), 10.41-10.46 (s, 1H), 8.53-8.58 (s, 1H), 8.19-8.26 (s, 1H), 8.02-8.09 (s, 1H), 7.89-8.02 (m, 2H), 7.85 (d, 1H), 7.74 (d, 1H), 7.61 (t, 1H), 7.33 (d, 1H), 2.30-2.42 (m, 6H), 1.67-1.81 (s, 6H)	446	Method 85 and Method 20
196	5-[3-(Cyano-dimethyl-methyl)-benzoylamino]- <i>N</i> -(6-fluoro-5-methyl-pyridin-3-yl)-2-methylbenzamide	10.60 (s, 1H), 10.42 (s, 1H), 8.33 (s, 1H), 8.14-8.27 (m, 1H), 8.02-8.11 (m, 1H), 7.96 (d, 1H), 7.89-7.93 (m, 1H), 7.84 (dd, 1H), 7.74-7.80 (m, 1H), 7.61 (t, 1H), 7.33 (d, 1H), 2.33-2.41 (m, 3H), 2.27 (s, 3H), 1.76 (s, 6H)	431	6-Fluoro-5-methylpyridin-3-amine and Method 20
197	<i>N</i> -(6-Amino-5-bromopyridin-3-yl)-5-[[3-(1-cyano-1-methylethyl)benzoyl]amino]-2-methylbenzamide	10.26-10.53 (m, 2H), 8.36-8.46 (s, 1H), 8.23-8.33 (s, 1H), 8.04-8.12 (s, 1H), 7.70-7.99 (m, 4H), 7.52-7.69 (s, 1H), 7.22-7.41 (s, 1H), 2.34-2.39 (s, 3H), 1.71-1.81 (s, 6H)	492	Method 77 and Method 20
198	5-[3-(Cyano-dimethyl-methyl)-benzoylamino]- <i>N</i> -(6-fluoro-pyridin-3-yl)-2-methylbenzamide	10.67 (s, 1H), 10.43 (s, 1H), 8.57 (s, 1H), 8.25-8.35 (m, 1H), 8.03-8.13 (m, 1H), 7.89-8.00 (m, 2H), 7.84 (dd, 1H), 7.74-7.79 (m, 1H), 7.61 (t, 1H), 7.33 (d, 1H), 7.22 (dd, 1H), 2.30-2.35 (m, 3H), 1.76 (s, 6H)	417	6-Fluoropyridin-3-amine and Method 20

Ex.	Compound	NMR	m/z	SM
199	5-{{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-[6-(methylamino)pyridin-3-yl]benzamide	10.57-10.61 (s, 1H), 10.43-10.48 (s, 1H), 8.48-8.56 (s, 1H), 8.04-8.09 (s, 1H), 7.90-8.01 (m, 3H), 7.70-7.85 (m, 2H), 7.61 (t, 1H), 7.33 (d, 1H), 7.04 (d, 1H), 2.90-2.97 (s, 3H), 2.36-2.39 (s, 3H), 1.72-1.77 (s, 6H)	427	Method 93 and Method 20
200	2-Methyl-N-[6-(methylamino)pyridin-3-yl]-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.48-10.74 (m, 2H), 8.61-8.86 (s, 1H), 8.47-8.57 (s, 1H), 8.20-8.39 (m, 2H), 7.91-8.12 (m, 3H), 7.80 (dd, 2H), 7.34 (d, 1H), 7.09 (d, 1H), 2.86-3.01 (s, 3H), 2.32-2.41 (s, 3H)	428	Method 93 and Method 21
201	N-(6-Acetylamino-pyridin-3-yl)-5-[3-(cyano-dimethylmethyl)-benzoylamino]-2-methyl-benzamide	10.65 (s, 1H), 10.55 (s, 1H), 10.43 (s, 1H), 8.73 (d, 1H), 7.89-8.30 (m, 5H), 7.83 (dd, 1H), 7.73-7.79 (m, 1H), 7.61 (t, 3H), 7.32 (d, 1H), 2.37 (s, 3H), 2.04-2.21 (m, 3H), 1.56-1.91 (m, 6H)	455	N-(5-Aminopyridin-2-yl)acetamide and Method 20
202	N-(6-Amino-pyridin-3-yl)-5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide	10.60-10.65 (s, 1H), 10.45-10.49 (s, 1H), 8.54-8.61 (s, 1H), 7.91-8.16 (m, 6H), 7.77 (dd, 2H), 7.60 (t, 1H), 7.33 (d, 1H), 7.03 (d, 1H), 2.33-2.39 (s, 3H), 1.69-1.78 (s, 6H)	413	Pyridine-2,5-diamine and Method 20

Ex.	Compound	NMR	m/z	SM
203	<i>N</i> -Methyl-5-[(2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzoyl)amino]nicotinamide	10.76-10.83 (s, 1H), 10.59-10.63 (s, 1H), 8.99-9.00 (s, 1H), 8.75 (d, 2H), 8.63-8.66 (s, 1H), 8.16-8.37 (m, 2H), 7.90-8.08 (m, 2H), 7.74-7.90 (m, 2H), 7.35 (d, 1H), 2.71-2.75 (q, 3H), 2.37-2.39 (m, 3H)	456	Method 133 and Method 21
204	<i>N</i> -(6-Amino-5-methylpyridin-3-yl)-5-[[3-(1-cyano-1-methylethyl)benzoyl]amino]-2-methylbenzamide	10.58-10.60 (s, 1H), 10.43-10.46 (s, 1H), 8.40-8.47 (s, 1H), 8.03-8.10 (m, 1H), 7.86-8.01 (m, 3H), 7.71-7.87 (m, 4H), 7.63 (t, 1H), 7.33 (d, 1H), 2.34-2.39 (s, 3H), 2.19-2.23 (s, 3H), 1.72-1.79 (s, 6H)	427	Method 94 and Method 20
205	<i>N</i> -(5-Amino pyridin-3-yl)-5-[[3-(1-cyano-1-methylethyl)benzoyl]amino]-2-methylbenzamide	10.97-11.07 (s, 1H), 10.50-10.53 (s, 1H), 8.38-8.41 (s, 1H), 8.05-8.08 (s, 1H), 7.93-8.00 (m, 2H), 7.73-7.90 (m, 2H), 7.62 (t, 1H), 7.38 (d, 1H), 2.35-2.39 (s, 3H), 1.74-1.79 (s, 6H)	413	Method 95 and Method 20
206	2-Methyl- <i>N</i> -(6-morpholin-4-ylpyridin-3-yl)-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.55-10.65 (s, 1H), 10.32-10.45 (s, 1H), 8.37-8.45 (s, 1H), 8.24-8.36 (m, 2H), 7.90-8.09 (m, 3H), 7.76-7.86 (m, 2H), 7.36 (d, 1H), 7.16 (d, 1H), 3.75 (t, 4H), 3.49 (t, 4H), 2.32-2.40 (s, 3H)	484	Method 84 and Method 21

Ex.	Compound	NMR	m/z	SM
207	5-[(5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]- <i>N</i> -methyl nicotinamide	10.76-10.83 (s, 1H), 10.59-10.63 (s, 1H), 8.99-9.00 (s, 1H), 8.75 (d, 2H), 8.63-8.66 (s, 1H), 8.16-8.37 (m, 2H), 7.90-8.08 (m, 2H), 7.74-7.90 (m, 2H), 7.35 (d, 1H), 2.71-2.75 (q, 3H), 2.37-2.39 (m, 3H)	456	Method 133 and Method 20
208	<i>N</i> -(3-{[(5-Bromopyridin-3-yl)amino]carbonyl}-4-methylphenyl)-2-(1-cyano-1-methylethyl)isonicotinamide	10.80-10.86 (s, 1H), 10.65-10.73 (s, 1H), 8.79-8.87 (s, 2H), 8.50-8.55 (s, 1H), 8.46-8.49 (s, 1H), 8.00-8.05 (s, 1H), 7.80-7.94 (m, 3H), 7.36 (d, 1H), 2.36-2.43 (s, 3H), 1.75-1.79 (s, 6H)	478	Method 119 and Method 29
209	<i>N</i> -(5-Chloropyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide	10.80-10.85 (s, 1H), 10.44-10.49 (s, 1H), 8.78-8.82 (s, 1H), 8.38-8.40 (s, 2H), 8.04-8.10 (s, 1H), 7.90-8.00 (m, 2H), 7.85 (d, 1H), 7.76 (d, 1H), 7.61 (t, 1H), 7.34 (d, 1H), 2.35-2.41 (s, 3H), 1.72-1.78 (s, 6H)	432	5-Chloropyridin-3-amine and Method 20
210	<i>N</i> -[6-(Cyclopropylamino)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.62 (d, 2H), 8.57 (d, 1H), 8.30 (s, 1H), 8.27 (d, 1H), 7.99 - 8.05 (m, 1H), 7.96 (d, 2H), 7.78 - 7.83 (m, 1H), 7.77 (s, 1H), 7.33 (d, 1H), 7.05 (d, 1H), 2.64-2.60 (m, 1H), 2.35 (s, 3H), 0.89 (s, 2H), 0.56 - 0.65 (m, 2H)	455	Method 243 and Method 21

Ex.	Compound	NMR	m/z	SM
211	2-Chloro- <i>N</i> -[6-(cyclobutylamino)pyridin-3-yl]-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.84 (d, 2H), 8.48 (d, 1H), 8.24 - 8.34 (m, 2H), 8.07 (d, 1H), 7.90 - 8.02 (m, 3H), 7.80 (t, 1H), 7.60 (d, 1H), 7.05 (d, 1H), 4.13 - 4.28 (m, 1H), 2.38 - 2.47 (m, 2H), 1.92 - 2.06 (m, 2H), 1.67 - 1.82 (m, 2H)	490	Method 244 and Method 224
212	<i>N</i> -[6-(Cyclobutylamino)pyridin-3-yl]-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.43 (s, 2H), 8.31 (d, 1H), 8.12 (s, 1H), 8.09 (d, 1H), 7.74 - 7.84 (m, 3H), 7.61 (t, 2H), 7.14 (d, 1H), 6.83 (d, 1H), 3.95 - 4.09 (m, 1H), 2.20 - 2.29 (m, 2H), 2.16 (s, 3H), 1.73 - 1.87 (m, 2H), 1.48 - 1.63 (m, 2H)	469	Method 244 and Method 21
213	2-Chloro- <i>N</i> -[6-(isopropylamino)pyridin-3-yl]-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.80 (d, 2H), 8.47 (d, 1H), 8.31 (s, 1H), 8.27 (d, 1H), 8.07 (d, 1H), 7.88 - 8.02 (m, 3H), 7.80 (t, 1H), 7.60 (d, 1H), 7.03 (d, 1H), 3.92 - 3.88 (m, 1H), 1.22 (d, 6H)	477	Method 245 and Method 224
214	<i>N</i> -[6-(Isopropylamino)pyridin-3-yl]-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.54 (s, 1H), 10.01 (s, 1H), 8.22 - 8.32 (m, 3H), 7.97 (d, 1H), 7.76 - 7.85 (m, 3H), 7.68 (dd, 1H), 7.28 (d, 1H), 6.43 (d, 1H), 6.21 (d, 1H), 3.86 - 4.01 (m, 1H), 2.34 (s, 3H), 1.12 (d, 6H)	466	Method 245 and Method 21

Ex.	Compound	NMR	m/z	SM
215	<i>N</i> -(6-Bromo pyridin-3-yl)-2-chloro-5-{[3-(trifluoromethyl) benzoyl]amino} benzamide	10.99 (s, 1H), 10.81 (s, 1H), 8.72 (d, 1H), 8.25 - 8.38 (m, 2H), 8.17 - 8.25 (m, 1H), 8.04 - 8.14 (m, 1H), 7.93 - 8.01 (m, 1H), 7.71 - 7.86 (m, 2H), 7.63 (dd, 2H)	499	6-bromopyridin-3-amine and Method 224
216	2-Chloro- <i>N</i> -(5-fluoropyridin-3-yl)-5-{[3-(trifluoromethyl) benzoyl]amino} benzamide	11.11 (s, 1H), 10.78 (s, 1H), 8.69 (s, 1H), 8.25 - 8.40 (m, 3H), 8.17 (d, 1H), 8.06 (s, 1H), 7.98 (s, 2H), 7.80 (t, 1H), 7.61 (d, 1H)	439	Method 252 and Method 224
217	<i>N</i> -(5-Fluoro pyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl) benzoyl]amino} benzamide	10.84 (s, 1H), 10.58 (s, 1H), 8.70 (s, 1H), 8.24 - 8.35 (m, 3H), 8.15 - 8.21 (m, 1H), 7.91 - 7.99 (m, 2H), 7.76 - 7.89 (m, 2H), 7.34 (d, 1H), 2.36 (s, 3H)	418	Method 252 and Method 21
218	2-Chloro-5-[(3,5-dimethylbenzoyl) amino]- <i>N</i> -(5-fluoropyridin-3-yl)benzamide	11.06 (s, 1H), 10.44 (s, 1H), 8.68 (s, 1H), 8.36 (d, 1H), 8.11 - 8.22 (m, 1H), 8.06 (d, 1H), 7.95 (dd, 1H), 7.54 - 7.61 (m, 3H), 7.24 (s, 1H), 2.35 (s, 6H)	398	Method 79 and 3,5-dimethylbenzoic acid
219	<i>N</i> -(5-Bromo pyridin-3-yl)-2-chloro-5-[(3,5-dimethylbenzoyl) amino]benzamide	11.00 (s, 1H), 10.43 (s, 1H), 8.79 (d, 1H), 8.42 - 8.51 (m, 2H), 8.05 (d, 1H), 7.94 (dd, 1H), 7.51 - 7.61 (m, 3H), 7.23 (s, 1H), 2.35 (s, 6H)	460	Method 80 and 3,5-dimethylbenzoic acid

Ex.	Compound	NMR	m/z	SM
220	5-[(3-Cyclopropyl benzoyl)amino]- <i>N</i> -(5-methoxy pyridin-3-yl)-2-methylbenzamide	10.69 (s, 1H), 10.28 (s, 1H), 8.59 (s, 1H), 8.14 (s, 1H), 7.94 (d, 2H), 7.81 (dd, 1H), 7.60 – 7.73 (m, 2H), 7.27 – 7.42 (m, 3H), 3.80 – 3.88 (m, 3H), 2.35 (s, 3H), 1.93 – 2.06 (m, 1H), 0.92 – 1.03 (m, 2H), 0.69 – 0.79 (m, 2H)	402	Method 69 and Method 34
221	2-Chloro-5-[(3-cyclopropyl benzoyl)amino]- <i>N</i> -(5-methoxy pyridin-3-yl)benzamide	10.91 (s, 1H), 10.46 (s, 1H), 8.54 (d, 1H), 8.16 (d, 1H), 8.05 (d, 1H), 7.89 – 7.96 (m, 2H), 7.62 – 7.74 (m, 2H), 7.57 (d, 1H), 7.40 (t, 1H), 7.28 – 7.34 (m, 1H), 3.84 – 3.88 (m, 3H), 1.98 – 2.06 (m, 1H), 1.00 (ddd, 2H), 0.72 – 0.83 (m, 2H)	422	Method 78 and Method 34
222	5-[(3-Cyclopropyl-5-fluorobenzoyl) amino]- <i>N</i> -(5-methoxypyridin-3-yl)-2-methyl benzamide	10.93 – 11.07 (m, 1H), 10.42 (d, 1H), 8.69 – 8.82 (m, 1H), 8.32 (dd, 1H), 8.10 (d, 1H), 7.98 (d, 1H), 7.76 – 7.87 (m, 1H), 7.46 – 7.56 (m, 2H), 7.33 (d, 1H), 7.16 (d, 1H), 3.91 (s, 3H), 2.36 (s, 3H), 2.04 (ddd, 1H), 0.97 – 1.07 (m, 2H), 0.76 – 0.87 (m, 2H)	420	Method 69 and Method 226
223	<i>N</i> -[6-(Acetyl amino) pyridine-3-yl]-2-methyl-5-[[4-[(4-methylpiperazin-1-yl)methyl]-3-(trifluoromethyl) benzoyl]amino] benzamide hydrochloride	10.50 (s, 1H), 10.45 (s, 2H), 9.50 (s, br, 1H), 8.70 (s, 1H), 8.30 (m, 2H), 7.85-8.05 (m, 5H), 7.30 (d, 1H), 3.75 (s, 2H), 3.40 (m, 2H), 3.05 (m, 2H), 2.90 (m, 2H), 2.80 (s, 3H), 2.40 (m, 2H), 2.35 (s, 3H), 2.10 (s, 3H)	568	Method 35 and Method 70

Ex.	Compound	NMR	m/z	SM
224	<i>N</i> -[6-(Acetylamino)pyridine-3-yl]-5-{[4-[(dimethylamino)methyl]-3-(trifluoromethyl)benzoyl]amino}-2-methylbenzamide hydrochloride	10.70 (s, 1H), 10.50 (m, 2H), 9.90 (brs, 1H), 8.75 (s, 1H), 8.40 (m, 2H), 7.90-8.10 (m, 5H), 7.40 (m, 1H), 4.60 (s, 2H), 2.90 (s, 6H), 2.42 (s, 3H), 2.19 (s, 3H)	513	Method 23 and Method 70
225	<i>N</i> -[3-({[6-(Acetylamino)pyridine-3-yl]amino}carbonyl)-4-methylphenyl]-2-[(dimethylamino)methyl]-5-(trifluoromethyl)benzamide hydrochloride	11.02 (s, 1H), 10.60 (m, 2H), 9.70 (brs, 1H), 8.78 (s, 1H), 8.00-8.29 (m, 6H), 7.80 (d, 1H), 7.40 (d, 1H), 4.56 (s, 2H), 2.86 (s, 6H), 2.45 (s, 3H), 2.15 (s, 3H)	513	Method 36 and Method 70
226	<i>N</i> -[3-({[6-(Acetylamino)pyridin-3-yl]amino}carbonyl)-4-methylphenyl]-1,3,3-trimethyl-2-oxoindoline-5-carboxamide	10.53 (s, 1H), 10.48 (s, 1H), 10.16 (s, 1H), 8.68 (s, 1H), 8.00 – 8.10 (m, 2H), 7.95 – 8.00 (m, 2H), 7.89 (s, 1H), 7.84 (d, 1H), 7.29 (d, 1H), 7.15 (d, 1H), 3.18 (s, 3H), 2.34 (s, 3H), 2.07 (s, 3H), 1.31 (s, 6H)	485	Method 39 and Method 70

Ex.	Compound	NMR	m/z	SM
227	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-2-methyl-5-{{3-(4-methyl-1 <i>H</i> -imidazol-1-yl)-5-(trifluoromethyl)benzoyl}amino}benzamide	10.66 (s, 1H), 10.43 – 10.50 (m, 2H), 9.52 (s, 1H), 8.67 (s, 1H), 8.58 (s, 1H), 8.43 (d, 2H), 8.12 (s, 1H), 8.04 (s, 2H), 7.82 – 7.88 (m, 2H), 7.36 (d, 1H), 2.38 (s, 3H), 2.33 (s, 3H), 2.07 (s, 3H)	536	Method 201 and Method 70
228	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-5-{{3-(2,3-dihydroxy-1,1-dimethylpropyl)benzoyl}amino}-2-methylbenzamide	8.65 (s, 1H), 8.10 (s, 2H), 7.97 (s, 1H), 7.89 (s, 1H), 7.78 (d, 1H), 7.67 (t, 2H), 7.47 (t, 1H), 7.33 (d, 1H), 3.80 (d, 1H), 3.24 (d, 2H), 2.46 (s, 3H), 2.19 (s, 3H), 1.40 (d, 6H)	490	Method 43 and Method 70
229	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-5-{{3-(1-cyclopropyl-1-methylethyl)benzoyl}amino}-2-methylbenzamide	10.47 (s, 2H), 10.29 (s, 1H), 8.68 (s, 1H), 8.06 (s, 2H), 8.00 (s, 1H), 7.91 (s, 1H), 7.81 (t, 2H), 7.69 (d, 1H), 7.46 (dd, 1H), 7.30 (d, 1H), 2.36 (s, 3H), 2.09 (s, 3H), 1.21 (s, 6H), 0.99 – 1.12 (m, 1H), 0.40 (d, 2H), 0.30 (d, 2H)	470	Method 44 and Method 70
230	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-5-{{3-(1,1-dimethylpropyl)benzoyl}amino}-2-methylbenzamide	10.56 (s, 1H), 10.50 (s, 1H), 10.32 (s, 1H), 8.71 (s, 1H), 8.00 – 8.13 (m, 2H), 7.86 – 7.94 (m, 2H), 7.81 (dd, 2H), 7.56 (d, 1H), 7.46 (t, 1H), 7.31 (d, 1H), 2.37 (s, 3H), 2.09 (s, 3H), 1.67 (q, 2H), 1.31 (s, 6H), 0.64 (t, 3H)	458	Method 167 and Method 70

Ex.	Compound	NMR	m/z	SM
231	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-5-{{[3-(1-cyclopropyl-1-hydroxyethyl)benzoyl]amino}-2-methylbenzamide	8.55 (s, 1H), 8.03 (s, 1H), 7.98 (s, 1H), 7.81 (s, 1H), 7.63 – 7.73 (m, 2H), 7.58 (d, 1H), 7.37 (t, 1H), 7.21 (d, 1H), 2.35 (s, 3H), 2.09 (s, 3H), 1.42 (s, 3H), 1.14 – 1.24 (m, 2H), 0.28 – 0.43 (m, 4H)	472	Method 46 and Method 70
232	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-5-({3-[cyclopropyl(hydroxy)methyl]benzoyl}amino)-2-methylbenzamide	10.56 (s, 1H), 10.51 (s, 1H), 10.34 (s, 1H), 8.69 (s, 1H), 8.00 – 8.11 (m, 2H), 7.97 (s, 1H), 7.92 (s, 1H), 7.78 – 7.86 (m, 2H), 7.58 (d, 1H), 7.47 (t, 1H), 7.29 (d, 1H), 4.04 (d, 1H), 2.34 (s, 3H), 2.07 (s, 3H), 1.00 – 1.13 (m, 1H), 0.34 – 0.49 (m, 4H)	458	Method 48 and Method 70
233	5-[(3-Chlorobenzoyl)amino]- <i>N</i> -(5-methoxypyridin-3-yl)-2-methylbenzamide	10.56 (s, 1H), 10.49 (s, 1H), 8.64 (d, 1H), 8.00 – 8.12 (m, 5H), 7.92 (dd, 2.17 Hz, 1H), 7.58 – 7.71 (m, 2H), 7.34 (d, Hz, 1H), 3.92 (s, 3H), 2.43 (s, 3H)	396	Method 69 and 3-chlorobenzoic acid
234	5-[(3,5-Dimethylbenzoyl)amino]- <i>N</i> -(5-methoxypyridin-3-yl)-2-methylbenzamide	10.51 (s, 1H), 10.24 (s, 1H), 8.61 (d, 1H), 8.06 (d, 2H), 7.99 (d, 2H), 7.89 (dd, 1H), 7.63 (s, 2H), 7.27 (d, 1H), 7.19 (s, 1H), 3.87 (s, 3H), 2.38 (s, 3H), 2.32 (s, 6H)	390	Method 69 and 3,5-dimethylbenzoic acid

Ex.	Compound	NMR	m/z	SM
235	5-[(3,4-Dimethylbenzoyl) amino]-N-(5-methoxypyridin-3-yl)-2-methylbenzamide	10.55 (s, 1H), 8.65 (d, 1H), 8.11 (s, 1H), 8.10 (s, 1H), 8.05 (t, 1H), 7.94 (dd, 1H), 7.86 (s, 1H), 7.82 (d, 1H), 7.81 (dd, 2H), 3.92 (s, 3H), 2.42 (s, 3H), 2.32 (s, 6H)	390	Method 69 and 3,4-dimethoxybenzoic acid
236	5-[(3,4-Dichlorobenzoyl) amino]-N-(5-methoxypyridin-3-yl)-2-methylbenzamide	10.55 (s, 1H), 10.75 (s, 1H), 8.82 (d, 1H), 8.49 (d, 1H), 8.21-8.80 (m, 4H), 8.10 (dd, 1H), 8.03 (d, 1H), 7.62 (d, 1H), 4.10 (s, 3H), 2.61 (s, 3H)	430	Method 69 and 3,4-dichlorobenzoic acid
237	5-[(3,5-Dichlorobenzoyl) amino]-N-(5-methoxypyridin-3-yl)-2-methylbenzamide	10.56 (s, 2H), 8.63 (d, 1H), 8.10 (d, 1H), 8.06 – 8.07 (m, 2H), 8.02 – 8.04 (m, 2H), 7.90 (dd, 1H), 7.84 (t, 1H), 7.83 (d, 1H), 3.92 (s, 3H), 2.43 (s, 3H)	430	Method 69 and 3,5-dichlorobenzoic acid
238	5-[(3-Chloro-5-fluorobenzoyl) amino]-N-(5-methoxypyridin-3-yl)-2-methylbenzamide	10.57 (s, 1H), 10.55 (s, 1H), 8.65 (d, 1H), 8.10 (dd, 2H), 8.03 (d, 1H), 7.99 (s, 1H), 7.83 – 7.92 (m, 2H), 7.64 – 7.69 (m, 1H), 7.34 (d, 1H), 7.34 (d, 1H), 3.92 (s, 3H), 2.44 (s, 3H)	414	Method 69 and 3-chloro-5-fluorobenzoic acid
239	5-[(4-Methoxy-3-methylbenzoyl) amino]-N-(5-methoxypyridin-3-yl)-2-methylbenzamide	10.55 (s, 1H), 10.15 (s, 1H), 8.62 (d, 1H), 8.02 – 8.10 (m, 3H), 7.86 (dd, 1H), 7.65 (d, 1H), 7.81 (d, 1H), 6.82 – 6.90 (m, 2H), 3.91 (s, 3H), 3.86 (s, 3H), 2.45 (s, 3H), 2.41 (s, 3H)	406	Method 69 and 3-methyl-4-methoxybenzoic acid

Ex.	Compound	NMR	m/z	SM
240	5-{{[3-Fluoro-5-(trifluoromethyl)benzoyl]amino}- <i>N</i> -(5-methoxy pyridin-3-yl)-2-methylbenzamide	10.70 (s, 1H), 10.57 (s, 1H), 8.63 (s, 1H), 8.29 (s, 1H), 8.20 (d, 1H), 8.11 (d, 1H), 8.06 (d, 1H), 8.02 – 8.04 (m, 1H), 7.95 (d, 1H), 7.90 (dd, 1H), 7.35 (d, 1H), 3.92 (s, 3H), 2.44 (s, 3H)	448	Method 69 and 3-methyl-5-trifluoromethylbenzoic acid
241	<i>N</i> -(5-Methoxy pyridin-3-yl)-2-methyl-5-{{[3-methylbenzoyl]amino}benzamide	10.55 (s, 1H), 10.33 (s, 1H), 8.65 (s, 1H), 8.11 (s, 2H), 8.04 (s, 1H), 7.94 (dd, 1H), 7.86 – 7.89 (m, 2H), 7.43 (d, 2H), 7.32 (d, 1H), 3.92 (s, 3H), 2.43 (s, 3H), 2.41 (s, 3H)	376	Method 69 and 3-methylbenzoic acid
242	2-Methoxy- <i>N</i> -pyridin-3-yl-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.52 (s, 1H), 10.35 (s, 1H), 8.87 (d, 1H), 8.26 – 8.31 (m, 3H), 8.20 (d, 1H), 8.06 (d, 1H), 7.96 – 8.00 (m, 2H), 7.78 (t, 1H), 7.39 (dd, 1H), 7.23 (d, 1H), 3.92 (s, 3H)	416	Method 71 and 3-trifluoromethylbenzoic acid
243	<i>N</i> -(5-Amino pyridin-3-yl)-2-chloro-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.70 (s, 1H), 10.48 (s, 1H), 8.31 (s, 2H), 7.92 – 8.02 (m, 4H), 7.76 – 7.84 (m, 1H), 7.68 (d, 1H), 7.55 – 7.62 (m, 1H), 7.49 (t, 1H), 5.40 (s, 2H)	435	Method 95 and Method 224
244	<i>N</i> -(5-Aminopyridin-3-yl)-2-methyl-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.98 (s, 1H), 10.61 (s, 1H), 8.37 (s, 1H), 8.28 (s, 2H), 7.89 – 8.01 (m, 3H), 7.76 – 7.89 (m, 4H), 7.35 (d, 1H), 6.59 (s, 1H), 1.98 (s, 3H)	415	Method 95 and Method 21

Ex.	Compound	NMR	m/z	SM
245	2-Chloro- <i>N</i> -[6-(cyclopropylamino)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.88 (s, 1H), 10.76 (s, 1H), 8.55 (s, 1H), 8.24 – 8.32 (m, 2H), 8.09 (d, 1H), 7.88 – 8.02 (m, 3H), 7.81 (t, 1H), 7.61 (d, 1H), 7.06 (d, 1H), 2.60 – 2.69 (m, 1H), 0.91 (d, 2H), 0.56 – 0.70 (m, 2H)	476	Method 243 and Method 224
246	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-5-({3-[(2-cyano-1 <i>H</i> -pyrrol-1-yl)methyl]benzoyl}amino)-2-methylbenzamide	10.38 (s, 1H), 10.26 (s, 1H), 8.24 (d, 1H), 8.04 (d, 1H), 7.91 (d, 1H), 7.85 (s, 1H), 7.72 – 7.81 (m, 2H), 7.55 (t, 1H), 7.42 (dd, 2H), 7.36 (d, 1H), 7.29 (d, 1H), 7.01 (dd, 1H), 6.28 (dd, 1H), 5.32 (s, 2H), 2.34 (s, 3H)	487	Method 81 and Method 228
247	2-Methyl-5-{[3-(trifluoromethyl)benzoyl]amino}- <i>N</i> -[6-(trifluoromethyl)pyridin-3-yl]benzamide	10.70 (s, 1H), 10.61 (s, 1H), 8.21 – 8.45 (m, 3H), 7.90 – 8.11 (m, 4H), 7.80 (t, 1H), 7.58 (d, 1H), 7.37 – 7.43 (m, 1H)	468	6-(trifluoromethyl)pyridin-3-amine and Method 21
248	5-[(3-Chloro-4-methoxybenzoyl)amino]-2-methoxy- <i>N</i> -pyridin-3-ylbenzamide	10.34 (s, 1H), 10.24 (s, 1H), 8.87 (d, 1H), 8.30 (dd, 1H), 8.20 (d, 1H), 8.10 (d, 1H), 8.04 (d, 1H), 7.96 (ddd, 2H), 7.39 (dd, 1H), 7.29 (d, 1H), 7.20 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H)	412	3-chloro-4-methoxybenzoic acid and Method 71

Ex.	Compound	NMR	m/z	SM
249	2-Chloro-5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}-N-(6-hydroxypyridin-3-yl)benzamide	10.56 (s, 1H), 10.34 (s, 1H), 8.06 (s, 1H), 7.89 – 8.02 (m, 4H), 7.77 (d, 1H), 7.64 (d, 1H), 7.52 – 7.61 (m, 2H), 6.40 (d, 1H), 1.75 (s, 6H)	437	Method 214 and Method 223
250	N-(6-Amino-5-chloropyridin-3-yl)-5-{{[3-(1-cyano-1-methylethyl)-5-fluorobenzoyl]amino}-2-methylbenzamide	10.55 (s, 1H), 10.49 (s, 1H), 8.38 (d, 1H), 8.17 (d, 1H), 7.96 (s, 1H), 7.88 (s, 1H), 7.76 – 7.86 (m, 2H), 7.64 (d, 1H), 7.33 (d, 1H), 2.36 (s, 3H), 1.76 (s, 6H)	468	Method 229 and Method 81
251	5-{{[3-(1-Cyano-1-methylethyl)-5-fluorobenzoyl]amino}-N-(5-isopropoxy-pyridin-3-yl)-2-methylbenzamide	10.77 (s, 1H), 10.51 (s, 1H), 8.63 (s, 1H), 8.12 (s, 1H), 7.91 – 7.99 (m, 3H), 7.78 – 7.84 (m, 2H), 7.65 (d, 1H), 7.35 (d, 1H), 4.56 – 4.78 (m, 1H), 2.37 (s, 3H), 1.72 (s, 6H), 1.32 (d, 6H)	476	Method 72 and Method 229
252	2-Chloro-5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}-N-(6-methylpyridin-3-yl)benzamide	10.68 (s, 1H), 10.55 (s, 1H), 8.72 (d, 1H), 7.99 – 8.05 (m, 3H), 7.93 – 7.96 (m, 2H), 7.75 – 7.78 (m, 1H), 7.56 – 7.64 (m, 2H), 7.25 (d, 1H), 2.43 (s, 3H), 1.74 (s, 6H)	433	3-Amino-6-picoline and Method 223

Ex.	Compound	NMR	m/z	SM
253	<i>N</i> -{5-[(Dimethylamino)sulfonyl]pyridin-3-yl}-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.95 (s, 1H), 10.58 (s, 1H), 9.14 (d, 1H), 8.57 – 8.64 (m, 2H), 8.23 – 8.32 (m, 2H), 7.96 – 7.99 (m, 2H), 7.76 – 7.86 (m, 2H), 7.35 (d, 1H), 2.70 (s, 6H), 2.38 (s, 3H)	507	Method 185 and Method 21
254	2-Chloro- <i>N</i> -(5-chloro-6-methylpyridin-3-yl)-5-[[3-(1-cyano-1-methylethyl)benzoyl]amino]benzamide	10.97 (s, 1H), 10.61 (s, 1H), 8.69 (d, 1H), 8.32 (d, 1H), 8.02 – 8.10 (m, 2H), 7.90 – 8.01 (m, 2H), 7.78 (d, 1H), 7.57 – 7.69 (m, 2H), 2.53 (s, 3H), 1.75 (s, 6H)	469	Method 212 and Method 223
255	5-[[3-(1-Cyano-1-methylethyl)benzoyl]amino]- <i>N</i> -(6-[[2-(dimethylamino)ethyl]amino]pyridin-3-yl)-2-methylbenzamide	10.40 (s, 1H), 10.12 (s, 1H), 8.40 (s, 1H), 8.06 (s, 1H), 7.89 – 7.98 (m, 2H), 7.72 – 7.79 (m, 2H), 7.52-7.75 (m, 2H), 7.30 (d, 1H), 7.14 (t, 1H), 6.70 – 6.81 (bs, 1H), 6.59 (d, 1H), 3.56 – 3.61 (m, 2H), 3.24 (t, 2H), 2.84 (s, 6H), 2.35 (s, 3H), 1.75 (s, 6H)	485	Method 189 and Method 20
256	<i>N</i> -(3-[[6-Amino-5-chloropyridin-3-yl]amino]carbonyl)-4-methylphenyl)-2-(1-cyano-1-methylethyl)isonicotinamide	10.67 (s, 1H), 10.37 (s, 1H), 8.82 (s, 1H), 8.30 (s, 1H), 8.09 (s, 1H), 8.02 (s, 1H), 7.84 – 7.93 (m, 2H), 7.81 (d, 1H), 7.34 (d, 1H), 2.32 (s, 3H), 1.77 (s, 6H)	451	Method 186 and Method 29

Ex.	Compound	NMR	m/z	SM
257	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-5-{{[3-(1-cyanoethyl)benzoyl]amino}-2-methylbenzamide	10.42 (s, 1H), 10.36 (s, 1H), 8.27 (s, 1H), 8.04 (s, 1H), 7.99 (s, 1H), 7.95 (d, 1H), 7.88 (s, 1H), 7.81 (d, 1H), 7.49 – 7.72 (m, 3H), 7.31 (d, 1H), 4.07 – 4.21 (q, 1H), 2.35 (s, 3H), 1.61 (d, 3H)	436	Method 81 and 3-(1-cyanoethyl)benzoic acid
258	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-2-methyl-5-{{[3-(2-methyl-1,3-thiazol-5-yl)benzoyl]amino}benzamide	10.50 (s, 1H), 10.48 (s, 1H), 8.51 (s, 1H), 8.36 (s, 1H), 8.11 – 8.20 (m, 2H), 8.08 (s, 1H), 7.95 (s, 1H), 7.90 (d, 1H), 7.83 (d, 1H), 7.65 – 7.75 (m, 2H), 7.61 (t, 1H), 7.32 (d, 1H), 2.75 (s, 3H), 2.36 (s, 3H)	480	Method 81 and 3-(2-methyl-1,3-thiazol-5-yl)benzoic acid
259	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-5-{{[3-(1-cyano-1,2-dimethylpropyl)benzoyl]amino}-2-methylbenzamide	10.39 (s, 1H), 10.28 (s, 1H), 8.24 (s, 1H), 8.04 (s, 1H), 8.01 (s, 1H), 7.96 (d, 1H), 7.86 (s, 1H), 7.82 (d, 1H), 7.70 (d, 1H), 7.62 (t, 1H), 7.31 (d, 1H), 2.35 (s, 3H), 2.23 – 2.33 (m, 1H), 1.72 (s, 3H), 1.08 (d, 3H), 0.77 (d, 3H)	478	Method 81 and Method 203
260	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-5-{{[3-(1-cyano-1-methylpropyl)benzoyl]amino}-2-methylbenzamide	10.40 (s, 1H), 10.28 (s, 1H), 8.25 (s, 1H), 8.04 (s, 1H), 8.02 (s, 1H), 7.96 (d, 1H), 7.91 (s, 1H), 7.82 (d, 1H), 7.71 (d, 1H), 7.61 (t, 1H), 7.31 (d, 1H), 2.35 (s, 3H), 2.04 (q, 2H), 1.73 (s, 3H), 0.88 (t, 3H)	464	Method 81 and Method 204

Ex.	Compound	NMR	m/z	SM
261	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-5-{{3-(1-cyano-2-hydroxy-1-methylethyl)benzoyl}amino}-2-methylbenzamide	10.43 (s, 1H), 10.39 (s, 1H), 8.29 (s, 1H), 8.09 (s, 1H), 8.00 (s, 1H), 7.96 (d, 1H), 7.93 (s, 1H), 7.81 (dd, 1H), 7.72 (d, 1H), 7.60 (t, 1H), 7.31 (d, 1H), 4.14 (d, 2H), 2.36 (s, 3H), 1.70 (s, 3H)	466	Method 81 and Method 205
262	<i>N</i> -(6-Amino-5-methylpyridin-3-yl)-2-chloro-5-{{3-(1-cyano-1-methylethyl)benzoyl}amino}benzamide	10.76 (s, 1H), 10.60 (s, 1H), 8.42 (s, 1H), 8.02 – 8.09 (m, 2H), 7.96 (d, 1H), 7.89 (dd, 1H), 7.83 (s, 1H), 7.77 (d, 1H), 7.56 – 7.68 (m, 3H), 2.20 (s, 3H), 1.75 (s, 6H)	450	Method 192 and Method 223
263	<i>N</i> -(5-Bromo-6-chloropyridin-3-yl)-2-chloro-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	11.17 (s, 1H), 10.79 (s, 1H), 8.69 (dd, 2H), 8.19 – 8.47 (m, 2H), 7.91 – 8.20 (m, 3H), 7.84 (t, 1H), 7.65 (d, 1H)	534	5-bromo-6-chloropyridin-3-amine and Method 224
264	2-Chloro- <i>N</i> -(2,6-dimethylpyridin-3-yl)-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.61 (s, 1H), 10.57 (s, 1H), 8.50 (d, 1H), 8.30 – 8.39 (m, 1H), 7.80 – 8.11 (m, 5H), 7.64 (d, 1H), 7.10 (s, 1H), 2.51 (s, 3H), 2.48 (s, 3H)	448	2,6-dimethylpyridin-3-amine and Method 224
265	<i>N</i> -(6-Amino-4-methylpyridin-3-yl)-2-chloro-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.78 (s, 1H), 10.54 (s, 1H), 8.40-8.49 (m, 2H), 7.83 – 7.77 (m, 5H), 7.65-7.71 (m, 2H), 7.10 (s, 1H), 2.81 (s, 3H)	449	4-methylpyridin-2,5-diamine and Method 224

Ex.	Compound	NMR	m/z	SM
266	2-Chloro- <i>N</i> -(4-methylpyridin-3-yl)-5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	10.65 (s, 1H), 10.46 (s, 1H), 8.42-8.54 (m, 3H), 7.41 – 7.79 (m, 5H), 7.12-7.31 (m, 2H), 7.10 (s, 1H), 2.84 (s, 3H)	434	4-methylpyridin-5-diamine and Method 224
267	2-Chloro- <i>N</i> -(2-fluoropyridin-3-yl)-5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	10.73 (s, 1H), 10.61 – 10.69 (m, 1H), 8.21 – 8.45 (m, 3H), 7.90 – 8.11 (m, 4H), 7.82 (t, 1H), 7.59 (d, 1H), 7.37 – 7.50 (m, 1H)	438	6-fluoropyridin-5-diamine and Method 224
268	(<i>R</i>)-2-Chloro- <i>N</i> - $\{6-[(2,3$ -dihydroxypropyl)amino]pyridin-3-yl $\}$ -5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	10.01 (s, 2H), 9.72 (s, 1H), 8.43 (s, 1H), 7.64 - 8.01 (m, 6H), 7.21 - 7.47 (m, 3H), 3.88 (m, 1H), 3.79 - 3.85 (m, 4H)	509	Method 246 and Method 224
269	2-Chloro- <i>N</i> -(6- $\{[2$ -hydroxy-1-(hydroxymethyl)ethyl]amino $\}$ pyridin-3-yl)-5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	9.98 (s, 2H), 9.64 (s, 1H), 8.50 (s, 1H), 7.84 - 8.01 (m, 4H), 7.62 - 7.89 (m, 3H), 7.56 (t, 1H), 7.41 (d, 1H), 3.88 (1H, m) 3.54-3.87 (4H, m)	509	Method 247 and Method 224

Ex.	Compound	NMR	m/z	SM
270	<i>N</i> -[6-(Acetylamino)-4-methylpyridin-3-yl]-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.01 (s, 2H), 9.70 (s, 1H), 9.32 (s, 1H), 8.55 (s, 1H), 7.67 - 8.00 (m, 6H), 7.31-7.49 (m, 2H), 2.83 (s, 3H), 2.01 (s, 6H)	490	<i>N</i> -(5-amino-4-methylpyridin-2-yl)acetamide and Method 224
271	2-Chloro- <i>N</i> -(2-fluoro-6-methylpyridin-3-yl)-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	¹ H NMR (300 MHz) 10.79 (s, 1H), 10.58 (s, 1H), 8.55 (d, 1H), 8.31 - 8.41 (m, 1H), 7.83 - 8.16 (m, 5H), 7.65 (d, 1H), 7.10 (s, 1H), 2.87 (s, 3H)	451	2-fluoro-6-methylpyridin-3-amine and Method 224
272	2-Chloro- <i>N</i> -[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.50 (s, 2H), 9.41 (s, 1H), 8.59 (s, 1H), 7.91 - 8.17 (m, 4H), 7.70 - 7.82 (m, 2H), 7.58 (t, 1H), 7.11 - 7.32 (m, 2H), 3.76 - 3.88 (m, 4H), 3.11 - 3.30 (m, 4H), 2.22 (s, 3H), 1.76 (s, 6H)	517	Method 190 and Method 224
273	<i>N</i> -[5-(Hydroxymethyl)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide		430	Method 21 and Method 242

Ex.	Compound	NMR	m/z	SM
274	2-Chloro- <i>N</i> -[6-(1H-pyrazol-5-ylamino)pyridin-3-yl]-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.85 (s, 1H), 10.50 (s, 1H), 8.52 (s, 1H), 8.24 (s, 1H), 8.13 (s, 1H), 7.96 - 8.10 (m, 3H), 7.77 - 7.91 (m, 3H), 7.60 - 7.73 (m, 2H), 7.40 (d, 1H),	501	Method 191 and Method 224
275	<i>N</i> -{6-[(4-Aminobutyl)amino]pyridin-3-yl}-2-chloro-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.70 (s, 1H), 10.60 (s, 1H), 8.48 (s, 1H), 8.00 - 8.10 (m, 2H), 7.86 - 7.97 (m, 3H), 7.77 (d, 1H), 7.50 - 7.67 (m, 2H), 7.01 (d, 1H), 3.27 - 3.56 (m, 2H), 3.10 - 3.21 (m, 2H), 1.74 - 2.04 (m, 4H), 1.76 (s, 6H)	505	Method 248 and Method 224
276	5-{{3-(1-Cyano-1-methylethyl)benzoyl}amino}-2-methyl- <i>N</i> -(6-piperazin-1-ylpyridin-3-yl)benzamide	10.52 (s, 2H), 9.42 (s, 1H), 8.60 (s, 1H), 7.91 - 8.22 (m, 4H), 7.70 - 7.85 (m, 2H), 7.61 (t, 1H), 7.09 - 7.47 (m, 2H), 3.77 - 3.88 (m, 4H), 3.11 - 3.34 (m, 4H), 2.36 (s, 3H), 1.76 (s, 6H)	483	Method 249 and Method 20
277	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-2-methyl-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.49 (d, 3H), 8.64 (d, 1H), 8.17 - 8.30 (m, 2H), 7.88 - 8.09 (m, 3H), 7.85 (d, 1H), 7.68 - 7.81 (m, 2H), 7.26 (d, 1H), 2.30 (s, 3H), 2.03 (s, 3H)	457	<i>N</i> -(5-aminopyridin-2-yl)acetamide and Method 21

Ex.	Compound	NMR	m/z	SM
278	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-2-chloro-5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}benzamide	10.72 (s, 1H), 10.58 (s, 1H), 10.53 (s, 1H), 8.67 (s, 1H), 8.06 (d, 3H), 8.02 (d, 1H), 7.92 - 7.99 (m, 2H), 7.77 (d, 1H), 7.56 - 7.67 (m, 2H), 2.07 - 2.11 (m, 3H), 1.76 (s, 6H)	476	<i>N</i> -(5-aminopyridin-2-yl)acetamide and Method 223
279	2-Chloro- <i>N</i> -[5-(1 <i>H</i> -pyrrol-1-yl)pyridin-3-yl]-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	11.00 (s, 1H), 10.76 (s, 1H), 8.26 - 8.39 (m, 3H), 8.08 (d, 1H), 7.94 - 8.03 (m, 2H), 7.82 (t, 1H), 7.63 (d, 1H), 7.39 - 7.42 (m, 2H), 6.35 (t, 2H)	485	Method 202 and Method 224
280	<i>N</i> -(5,6-Diaminopyridin-3-yl)-2-methyl-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.59 (s, 1H), 10.47 (s, 1H), 8.24 - 8.35 (m, 2H), 8.00 (d, 1H), 7.88 (s, 2H), 7.74 - 7.85 (m, 2H), 7.47 (s, 2H), 7.33 (d, 1H), 7.29 (s, 1H), 2.34 (s, 3H)	430	Method 196 and Method 21
281	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-2-chloro-5-{{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.44 (s, 1H), 10.41 (s, 1H), 8.33 (s, 1H), 8.11 (s, 1H), 8.05 (s, 1H), 7.96 (d, 1H), 7.90 (s, 1H), 7.74 - 7.82 (m, 2H), 7.61 (t, 1H), 7.31 (d, 1H),	469	Method 186 and Method 224

Ex.	Compound	NMR	m/z	SM
282	<i>N</i> -(6-Amino-5-bromopyridin-3-yl)-2-chloro-5-([3-(trifluoromethyl)benzoyl]amino)benzamide	10.74 (s, 1H), 10.51 (s, 1H), 8.25 - 8.33 (m, 3H), 8.16 (s, 1H), 7.91 - 8.03 (m, 3H), 7.81 (t, 1H), 7.59 (d, 1H)	515	Method 187 and Method 224
283	2-Chloro- <i>N</i> -(5-chloropyridin-3-yl)-5-([3-(1-cyano-1-methylethyl)benzoyl]amino)benzamide	11.06 (s, 1H), 10.60 (s, 1H), 8.77 (s, 1H), 8.42 (s, 1H), 8.36 (s, 1H), 8.03 - 8.07 (m, 2H), 7.94 - 8.01 (m, 2H), 7.78 (d, 1H), 7.56 - 7.68 (m, 2H), 1.76 (s, 6H)	455	Method 215 and Method 223
284	5-([3-(1-Cyano-1-methylethyl)benzoyl]amino)- <i>N</i> -(5,6-dimethylpyridin-3-yl)-2-methylbenzamide	11.00 (s, 1H), 10.47 (s, 1H), 8.96 (s, 1H), 8.30 (s, 1H), 8.06 (s, 1H), 8.02 (s, 1H), 7.96 (d, 1H), 7.74 - 7.82 (m, 2H), 7.62 (t, 1H), 7.34 (d, 1H), 2.58 (s, 6H), 2.39 (s, 3H), 2.36 (s, 3H), 1.76 (s, 6H)	427	Method 211 and Method 20
285	2-Chloro-5-([3-(1-cyano-1-methylethyl)benzoyl]amino)- <i>N</i> -(5-methoxypyridin-3-yl)benzamide	11.00 (s, 1H), 10.60 (s, 1H), 8.59 (s, 1H), 8.23 (s, 1H), 7.84-8.09 (m, 5H), 7.78 (d, 1H), 7.58 - 7.67 (m, 2H), 3.89 (s, 3H), 1.74 (s, 6H)	451	Method 118 and Method 223
286	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-5-([3-(1-cyano-1-methylethyl)benzoyl]amino)-2-methylbenzamide	10.44 (s, 1H), 10.40 (s, 1H), 8.34 (s, 1H), 8.11 (s, 1H), 8.06 (s, 1H), 7.96 (d, 1H), 7.90 (s, 1H), 7.74 - 7.84 (m, 2H), 7.61 (t, 1H), 7.32 (d, 1H), 2.34 (s, 3H), 1.72 (s, 6H)	450	Method 186 and Method 20

Ex.	Compound	NMR	m/z	SM
287	2-Chloro- <i>N</i> -(5-chloropyridin-3-yl)-5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	11.07 (s, 1H), 10.76 (s, 1H), 8.78 (s, 1H), 8.23 - 8.50 (m, 4H), 8.06 (s, 1H), 7.93 - 8.02 (m, 2H), 7.81 (t, 1H), 7.63 (d, 1H)	456	Method 215 and Method 224
288	5- $\{[3$ -(1-Cyano-1-methylethyl)benzoyl]amino $\}$ - <i>N</i> -(6-hydroxy-5-methylpyridin-3-yl)-2-methylbenzamide	10.39 (s, 1H), 10.04 (s, 1H), 8.06 (s, 1H), 7.95 (d, 1H), 7.73 - 7.87 (m, 4H), 7.61 (t, 1H), 7.48 (d, 1H), 7.29 (d, 1H), 2.34 (s, 3H), 1.99 (s, 3H), 1.76 (s, 6H)	429	Method 216 and Method 20
289	2-Chloro- <i>N</i> -[5-methoxy-6-(methylamino)pyridin-3-yl]-5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	10.76 (s, 1H), 10.67 (s, 1H), 8.30 (s, 1H), 8.27 (d, 1H), 8.06 - 8.13 (m, 2H), 8.01 (d, 1H), 7.90 (d, 1H), 7.81 (t, 1H), 7.61 (d, 1H), 7.41 (s, 1H), 3.92 (s, 3H), 2.95 (s, 3H)	481	Method 195 and Method 224
290	2-Chloro- <i>N</i> -[5-chloro-6-(methylamino)pyridin-3-yl]-5- $\{[3$ -(trifluoromethyl)benzoyl]amino $\}$ benzamide	10.73 (s, 1H), 10.49 (s, 1H), 8.24 - 8.36 (m, 3H), 7.89 - 8.06 (m, 4H), 7.80 (t, 1H), 7.58 (d, 1H), 2.83 (s, 3H)	485	Method 194 and Method 224

Ex.	Compound	NMR	m/z	SM
291	<i>N</i> -[6-(Acetylamino)-5-chloropyridin-3-yl]-2-chloro-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.70 (s, 1H), 8.21 - 8.33 (m, 2H), 7.97 - 8.02 (m, 2H), 7.67 - 7.89 (m, 6H), 7.44 (d, 1H), 2.08 (s, 3H)	513	Method 209 and Method 224
292	<i>N</i> -[6-(Acetylamino)-5-bromopyridin-3-yl]-2-methyl-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.66 (s, 1H), 8.22 - 8.33 (m, 2H), 7.97 - 8.00 (m, 2H), 7.67 - 7.89 (m, 6H), 7.43 (d, 1H), 2.16 (s, 3H), 2.07 (s, 3H)	536	Method 208 and Method 21
293	2-Chloro- <i>N</i> -[5-chloro-6-(methylamino)pyridin-3-yl]-5-{{3-(1-cyano-1-methylethyl)benzoyl}amino}benzamide	10.87 (s, 1H), 10.58 (s, 1H), 8.23 (s, 1H), 8.04 (s, 1H), 7.92 - 8.02 (m, 3H), 7.75 - 7.85 (m, 2H), 7.52 - 7.65 (m, 3H), 2.09 (s, 3H), 1.75 (s, 6H)	484	Method 194 and Method 223
294	2-Chloro-5-{{3-(1-cyano-1-methylethyl)benzoyl}amino}- <i>N</i> -{6-[(3-pyrrolidin-1-ylpropyl)amino]pyridin-3-yl}benzamide	10.75 (s, 1H), 10.63 (s, 1H), 9.75 (bs, 1H), 8.49 (s, 1H), 8.03 - 8.10 (m, 2H), 7.86 - 7.99 (m, 3H), 7.78 (d, 1H), 7.52 - 7.67 (m, 2H), 7.01 (d, 1H), 3.28 - 3.52 (m, 4H), 3.08 - 3.28 (m, 4H), 1.84 - 2.06 (m, 6H), 1.76 (s, 6H)	547	Method 250 and Method 223

Ex.	Compound	NMR	m/z	SM
295	2-Chloro-5-{{[3-(1-cyano-1-methyl ethyl)benzoyl] amino}-N-[5-(hydroxymethyl) pyridin-3-yl]benzamide	10.95 (s, 1H), 10.60 (s, 1H), 8.81 (s, 1H), 8.35 (s, 1H), 8.25 (s, 1H), 8.03 - 8.09 (m, 2H), 7.91 - 7.98 (m, 2H), 7.79 (d, 1H), 7.55 - 7.67 (m, 2H), 4.60 (s, 2H), 1.75 (s, 6H)	451	Method 242 and Method 223
296	N-[3-{{[6-(Acetylamino) pyridin-3-yl] amino} carbonyl)-4-chlorophenyl]-2-(1-cyano-1-methyl ethyl) isonicotinamide	10.84 (s, 1H), 10.72 (s, 1H), 10.50 (s, 1H), 8.84 (d, 1H), 8.66 (s, 1H), 7.98 - 8.10 (m, 4H), 7.95 (d, 1H), 7.88 (d, 1H), 7.60 (d, 1H), 2.01 (s, 3H), 1.78 (s, 6H)	479	N-(5-aminopyridin-2-yl)acetamide and Method 29
297	N-[6-(Acetylamino)-5-methoxypyridin-3-yl]-2-chloro-5-{{[3-(trifluoromethyl) benzoyl] amino} benzamide	10.86 (s, 1H), 10.76 (s, 1H), 9.75 (bs, 1H), 8.23 - 8.35 (m, 3H), 7.90 - 8.09 (m, 4H), 7.82 (t, 1H), 7.63 (d, 1H), 3.83 (s, 3H), 2.04 (s, 3H)	509	Method 210 and Method 224
298	2-Chloro-5-{{[3-(1-cyano-1-methyl ethyl)benzoyl] amino}-N-(6-ethylpyridin-3-yl)benzamide	11.16 (s, 1H), 10.67 (s, 1H), 9.02 (s, 1H), 8.34 (d, 1H), 8.11 (s, 1H), 8.06 (s, 1H), 7.96 (dd, 2H), 7.78 (d, 1H), 7.57 - 7.72 (m, 3H), 2.88 (q, 2H), 1.76 (s, 6H), 1.27 (t, 3H)	449	Method 213 and Method 223

Ex.	Compound	NMR	m/z	SM
299	5-{{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-[5-(hydroxymethyl)pyridin-3-yl]-2-methylbenzamide		457	Method 20 and Method 242
300	5-{{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-(5-fluoropyridin-3-yl)-2-methylbenzamide	10.87 (s, 1H), 10.43 (s, 1H), 8.70 (s, 1H), 8.34 (s, 1H), 8.20 (d, 1H), 8.05 (s, 1H), 7.90 - 8.00 (m, 2H), 7.86 (d, 1H), 7.76 (d, 1H), 7.62 (t, 1H), 7.35 (d, 1H), 2.35 (s, 3H), 1.76 (s, 6H)	417	Method 252 and Method 20
301	5-{{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-(6-{{[3-(dimethylamino)propyl]amino}pyridin-3-yl)-2-methylbenzamide	10.42 (s, 1H), 10.01 (s, 1H), 8.24 (s, 1H), 8.07 (s, 1H), 7.96 (d, 1H), 7.66 - 7.87 (m, 4H), 7.62 (t, 1H), 7.28 (d, 1H), 6.48 (d, 1H), 6.39 (bs, 1H), 3.17 - 3.25 (m, 2H), 2.34 (s, 3H), 2.27 (t, 2H), 2.13 (s, 6H), 1.75 (s, 6H), 1.68 (m, 2H)	500	Method 193 and Method 20
302	5-[(2-Chloro-5-{{[3-(1-cyano-1-methylethyl)benzoyl]amino}benzoyl]amino]nicotinamide	11.02 (s, 1H), 10.59 (s, 1H), 8.93 (s, 1H), 8.80 (s, 1H), 8.61 (s, 1H), 8.22 (s, 1H), 8.05 - 8.06 (m, 2H), 7.93 - 7.99 (m, 2H), 7.79 (d, 1H), 7.52 - 7.70 (m, 3H), 1.73 (s, 6H)	464	Method 134 and Method 223

Ex.	Compound	NMR	m/z	SM
303	<i>N</i> -(6-Chloro pyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl) benzoyl]amino}-2-methylbenzamide	10.75 (s, 1H), 10.44 (s, 1H), 8.77 (s, 1H), 8.23 (d, 1H), 8.03 (s, 1H), 7.96 (d, 1H), 7.95 (s, 1H), 7.85 (d, 1H), 7.77 (d, 1H), 7.61 (t, 1H), 7.54 (d, 1H), 7.34 (d, 1H), 2.37 (s, 3H), 1.84 (s, 6H)	435	2-chloropyridine-5-amine and Method 20
304	2-Chloro- <i>N</i> -[5-(hydroxymethyl) pyridin-3-yl]-5-{[3-(trifluoromethyl) benzoyl]amino} benzamide	10.81 (s, 1 H) 10.73 (s, 1 H) 8.70 (d, 1 H) 8.24 - 8.33 (m, 3 H) 8.18 (s, 1 H) 7.92 - 8.03 (m, 3 H) 7.80 (t, 1 H) 7.60 (d, 1 H) 5.39 (t, 1 H) 4.54 (d, 2 H)	451	Method 242 and Method 224
305	Methyl 5-[(5-{[3-(1-cyano-1-methyl ethyl)benzoyl] amino}-2-methyl benzoyl)amino] pyridine-2-carboxylate		457	Method 20 and Method 90
306	<i>N</i> -{5-[2-(Dimethylamino) ethoxy]pyridin-3-yl}-2-methyl-5-{[3-(trifluoromethyl) benzoyl]amino} benzamide	10.73 (s, 1H), 10.61 (s, 1H), 9.69 (s, 1H), 8.48 (s, 1H), 8.14 (s, 1H), 8.10 (s, 1H), 7.93 - 8.03 (m, 2H), 7.76 - 7.85 (m, 2H), 7.35 (d, 1H), 4.43 (t, 2H), 3.41 - 3.52 (m, 2H), 2.79 - 2.95 (m, 6H), 2.37 (s, 3H), 2.17 (s 6H)	488	Method 221 and Method 21

Ex.	Compound	NMR	m/z	SM
307	<i>N</i> -(6-Amino-5-chloropyridin-3-yl)-2-methyl-5- {[3-(trifluoromethyl)benzoyl]amino} benzamide	10.59 (s, 1H), 10.41 (s, 1H), 8.22 - 8.46 (m, 3H), 8.13 (s, 1H), 7.99 (d, 1H), 7.90 (s, 1H), 7.74 - 7.86 (m, 2H), 7.34 (d, 1H), 2.25 (s, 3H)	451	Method 186 and Method 21
308	5- {[3-(1-Cyano-1-methylethyl)benzoyl]amino}- <i>N</i> -(5-methoxy pyridin-3-yl)-2-methylbenzamide	10.84 (s, 1H), 10.46 (s, 1H), 8.68 (s, 1H), 8.15 (s, 1H), 8.06 (s, 1H), 8.02 (s, 1H), 7.92 - 7.99 (m, 2H), 7.83 (d, 1H), 7.77 (d, 1H), 7.63 (t, 1H), 7.35 (d, 1H), 3.89 (s, 3H), 2.38 (s, 3H), 1.75 (s, 6H)	430	Method 118 and Method 20
309	5- {[3-(1-Cyano-1-methylethyl)benzoyl]amino}- <i>N</i> -(5-isopropoxy pyridin-3-yl)-2-methylbenzamide	10.56 (s, 1H), 10.43 (s, 1H), 8.47 (s, 1H), 8.04 (s, 1H), 8.02 (d, 1H), 7.96 (d, 1H), 7.92 (s, 1H), 7.80 - 7.88 (m, 2H), 7.76 (d, 1H), 7.61 (t, 1H), 7.33 (d, 1H), 4.56 - 4.76 (m, 1H), 2.37 (s, 3H), 1.76 (s, 6H), 1.31 (d, 6H)	458	Method 219 and Method 20
310	3-(1-Cyano-1-methylethyl)-2-fluoro- <i>N</i> -(3- {[(5-methoxypyridin-3-yl)amino] carbonyl}-4-methylphenyl) benzamide	10.89 (s, 1H), 10.68 (s, 1H), 8.72 (s, 1H), 8.26 (s, 1H), 8.04 (s, 1H), 7.88 (s, 1H), 7.73 (d, 1H), 7.60 - 7.70 (m, 2H), 7.35 - 7.41 (m, 2H), 3.90 (s, 3H), 2.37 (s, 3H), 1.79 (s, 6H)	448	Method 69 and Method 114

Ex.	Compound	NMR	m/z	SM
311	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-{5-[3-(dimethylamino)propoxy]pyridin-3-yl}-2-methylbenzamide	10.79 (s, 1H), 10.49 (s, 1H), 9.94 - 10.13 (bs, 1H), 8.55 (s, 1H), 8.16 (s, 1H), 8.04 - 8.11 (m, 2H), 7.93 - 8.01 (m, 2H), 7.82 (d, 1H), 7.77 (d, 1H), 7.67 - 7.72 (d, 1H), 7.61 (t, 1H), 7.34 (d, 1H), 4.19 (t, 2H), 3.18 - 3.27 (m, 2H), 2.80 (d, 3H), 2.37 (s, 3H), 2.13 - 2.22 (m, 2H), 1.72 (s, 6H)	501	Method 222 and Method 20

Ex	Compound	M/z	SM
312	N-(5-Amino-6-methylpyridin-3-yl)-2-chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino} benzamide	449	Method 74 and Method 223
313	2-Chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-N-(5-cyanopyridin-3-yl)benzamide	444	Method 223 and Method 232
314	tert-Butyl 2-[(5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]pyridine-2-yl}amino)methyl]pyrrolidine-1-carboxylate	598	Method 82 and Method 20
315	tert-Butyl 2-[(5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]pyridin-3-yl}oxy)methyl]pyrrolidine-1-carboxylate	599	Method 220 and Method 20
316	N-(6-{[(Benzyloxy)acetyl]amino}-5-methylpyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide	576	Method 233 and Method 20
317	2-Chloro-N-{6-amino-pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide	435	pyridine-2,5-diamine and Method 224

Example 318

N-{6-[(Aminocarbonyl)amino]pyridin-3-yl}-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide

To a solution of *N*-(6-aminopyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide (Example 202; 314 mg, 0.760 mmol) in THF (5ml), sodium hydride (145 mg, 3.04 mmol) and trichloroacetyl isocyanate (0.14 ml, 1.14 mmol) were added and the reaction mixture was stirred overnight at 25°C. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄.

Evaporation of the solvent gave a white solid that was dissolved in MeOH (10 ml) and purged with ammonia gas. Evaporation of the solvent gave a tan solid, which was purified by reverse phase HPLC (5-55% MeCN/H₂O, 15 min). The title compound (65 mg) was collected by evaporation as a white solid. NMR (300 MHz): 10.41 (s, 2H), 9.20 (s, 1H), 8.58 (s, 1H), 7.99 - 8.08 (m, 2H), 7.96 (d, 1H), 7.89 (s, 1H), 7.83 (dd, 1H), 7.75 (d, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 7.32 (d, 1H), 6.85 (s, 1H), 2.36 (s, 3H), 1.76 (s, 6H); m/z 457.

Example 319

2-Chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-*N*-[5-(dimethylamino)-6-methylpyridin-3-yl]benzamide

To a solution of *N*-(5-amino-6-methylpyridin-3-yl)-2-chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}benzamide (Example 312; 145 mg) in DMF (2 ml) was added at 0°C Cs₂CO₃ (317 mg) and the mixture was stirred at this temperature for 30 minutes. MeI (0.81 ml) was added and the mixture was stirred at room temperature for 4 hours. The mixture was cooled with an ice bath and H₂O was added. The mixture was partitioned between EtOAc and H₂O. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. Evaporation of the solvent gave a solid, which was purified by reverse phase HPLC (5-95% MeCN/H₂O, 15 min using hexyl benzene column). The title compound (3.4 mg) was collected by evaporation. NMR (300 MHz): 10.79 (s, 1H), 10.23 (s, 1H), 8.04 (s, 1H), 8.01 (d, 1H), 7.98-7.95 (m, 2H), 7.84 (d, 1H), 7.78 (d, 1H), 7.52 - 7.66 (m, 3H), 2.83(s, 6H) 2.41 (s, 3H), 1.65 (s, 6H); m/z 478.

Example 3205-[(5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]-N-methylpyridine-2-carboxamide

A solution of methyl 5-[(5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]pyridine-2-carboxylate (Example 305; 100 mg) in THF (1 ml) was cooled to -78°C and treated with a solution of $\text{Me}_3\text{Al}-\text{MeNH}_2$ (the solution was made by adding slowly Me_3Al (0.35 ml, 1M in THF) to a solution of MeNH_2 (0.35 ml, 1M in THF) at -78°C and allowing the solution to stir for 30 minutes at this temperature). The reaction mixture was stirred overnight at 25°C . The mixture was partitioned between EtOAc and H_2O . The organics were washed with $\text{NaCl}_{(\text{sat})}$ and then dried with $\text{Na}_2\text{SO}_{4(\text{s})}$. Evaporation of the solvent gave a solid, which was purified by reverse phase HPLC (5-95% MeCN/ H_2O , 15 min). The title compound (2 mg) was collected by evaporation. NMR (300 MHz): 10.85 (s, 1H), 10.44 (s, 1H), 8.95 (s, 1H), 8.20 - 8.50 (m, 2H), 7.70 - 8.18 (m, 6H), 7.51 - 7.66 (m, 1H), 7.19 - 7.51 (m, 1H), 2.87 (s, 3H), 2.30 (s, 3H) 1.70 (s, 6H); m/z 456

Example 3215-[3-(Cyano-dimethyl-methyl)-benzoylamino]-N-(6-cyano-pyridin-3-yl)-2-methyl-benzamide

A solution of 5-[3-(cyanodimethyl-methyl)-benzoylamino]-2-methyl-benzoic acid (Method 20; 300 mg, 0.928 mmol) in SOCl_2 (5 ml) was refluxed at 80°C for 2 h. Then a solution of 5-aminopyridine-2-carbonitrile (221 mg, 1.86 mmol) in THF (5 ml) was treated with NaH (50% in mineral oil) (111 mg, 2.32 mmol). This reaction was stirred at 25°C for 1 h. After removing the SOCl_2 from the first reaction, the resulting product was dissolved in THF and added to the second reaction and stirred at 25°C for 30 min. The reaction was then quenched with H_2O (10 ml), extracted with EtOAc (25 ml), washed with brine (50 ml) and dried with MgSO_4 . The solvents were removed under reduced pressure to give an orange solid (637 mg) which was purified by Gilson reverse phase preparatory HPLC (5-95% MeCN/ H_2O , 20 min) to yield a yellow solid (10 mg). NMR (300 MHz): 11.07 (s, 1H), 10.61 (s, 1H), 9.02 (d, 1H), 8.42 (dd, 1H), 8.22-8.36 (m, 2H), 7.95-8.08 (m, 3H), 7.73-7.92 (m, 2H), 7.36 (d, 1H), 2.48-2.51 (m, 6H), 2.38 (s, 3H); m/z 424.

Example 322

5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-[5-(1*H*-pyrazol-4-yl)pyridin-3-yl]benzamide

N-(5-Bromopyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide (Example 192; 256mg, 0.54mmol), 1*H*-pyrazol-4-ylboronic acid (125mg, 0.64mmol), Cs₂CO₃ (352mg 1.08mmol) and Pd(PPh₃)₄ (62mg, 0.054mmol) were put in a microwave tube, dioxane (4ml) and water (1ml) were added. The tube was heated in microwave (Smith, Personal Chemistry™) and heated at 180°C for 2000 seconds. The solution was filtered, and separated between EtOAc and water. Organic layer was dried and evaporated under reduced pressure. The crude product was purified by reverse phase HPLC (5-75% MeCN/H₂O, 15 min) and the title compound (75.6 mg, 30%) was collected by evaporation. NMR (300 MHz) 10.88 (s, 1H), 10.52 (s, 1H), 8.54 (s, 1H), 8.26 (s, 1H), 8.13 (s, 1H), 7.96 - 8.09 (m, 3H), 7.80 - 7.93 (m, 3H), 7.63 - 7.73 (m, 2H), 7.42 (d, 1H), 2.20 (s 3H), 1.82 (s, 6H); m/z 466.

Examples 323-324

The following compounds were prepared by the procedure of Example 322, using the appropriate starting material

Ex	Compound	NMR	M/z	SM
323	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-[5-(1 <i>H</i> -pyrrol-2-yl)pyridin-3-yl]benzamide	11.70 (s, 1H), 10.87 (s, 1H), 10.47 (s, 1H), 8.79 (s, 1H), 8.72 (s, 1H), 8.55 (s, 1H), 8.06 (s, 1H), 8.00 (s, 1H), 7.95 (d, 1H), 7.81 (d, 1H), 7.75 (d, 1H), 7.63 (t, 1H), 7.35 (d, 1H), 7.02 (s, 1H), 6.68 (s, 1H), 6.22 (s, 1H), 2.40 (s, 3H), 1.75 (s, 6H)	465	1 <i>H</i> -pyrrol-2-ylboronic acid

Ex	Compound	NMR	M/z	SM
324	tert-Butyl 2-{5-[(5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]pyridin-3-yl}pyrrolidine-1-carboxylate		569	1-(tert-butoxycarbonyl)pyrrolidine-2-yl]boronic acid

Example 325**2-Methyl-N-[5-(4-methylpiperazin-1-yl)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide**

- 5 To a 10 ml round bottom flask equipped with a magnetic stirring bar was added Pd₂(dba)₃ (34 mg, 0.038 mmol), BINAP (47 mg, 0.075 mmol), and sodium *tert*-butoxide (72 mg, 0.752 mmol). Toluene (2 ml) was added followed by 1-methylpiperazine (56 mg, 0.564 mmol) and the reaction was allowed to stir at room temperature for 10 min before the addition of *N*-(5-bromopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide
- 10 (Example 193; 180 mg, 0.376 mmol). The resulting reaction mixture was warmed to 80 °C and was allowed to stir for 12 h before being cooled and diluted with EtOAc (~ 100 ml). The organic phase was poured into a separator funnel and washed with saturated aqueous NaHCO₃ (~ 100 ml). The organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified on a 40 g SiO₂ column using MeOH/EtOAc
- 15 (1:10) as eluent giving 144 mg (77%) of the title compound as a white solid. NMR (300 MHz): 10.91 (s, 1H), 10.65 (s, 1H), 8.57 (s, 1H), 8.32-8.26 (m, 3H), 8.10 (s, 1H), 8.02 (d, 1H), 7.99 (d, 1H), 7.82-7.78 (m, 2H), 7.35 (d, 1H), 3.99-3.93 (m, 2H), 3.55-3.50 (m, 2H), 3.32-3.12 (m, 4H), 2.82 (s, 3H), 2.37 (s, 3H); *m/z* 499.

20 Examples 326-336

The following compounds were prepared by the procedure in Example 325 using *N*-(5-bromopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 193), *N*-(5-bromopyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide (Example 192), *N*-(5-bromopyridin-3-yl)-2-chloro-5-[(3,5-

dimethylbenzoyl)amino]benzamide (Example 219) and the appropriate SM. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
326	2-Methyl- <i>N</i> -(5-morpholin-4-ylpyridin-3-yl)-5-([3-(trifluoromethyl)benzoyl]amino)benzamide	11.06 (s, 1H), 10.67 (s, 1H), 8.66 (s, 1H), 8.33-8.27 (m, 3H), 8.10 (s, 1H), 8.04 (d, 1H), 7.97 (d, 1H), 7.82-7.77 (m, 2H), 7.36 (d, 1H), 3.77 (t, 4H), 3.30 (t, 4H), 2.37 (s, 3H)	485	Morpholine
327	<i>N</i> -{5-[[3-(Dimethylamino)propyl](methyl)amino]pyridin-3-yl}-2-methyl-5-([3-(trifluoromethyl)benzoyl]amino)benzamide	11.01 (s, 1H), 10.66 (s, 1H), 8.54 (s, 1H), 8.32-8.27 (m, 2H), 8.14 (d, 1H), 8.05 (d, 1H), 7.98 (d, 1H), 7.89 (s, 1H), 7.82-7.77 (m, 2H), 7.36 (d, 1H), 3.56-3.51 (m, 2H), 3.10-3.03 (m, 2H), 3.02 (s, 3H), 2.74 (s, 3H), 2.72 (s, 3H), 2.37 (s, 3H), 1.97-1.89 (m, 2H)	514	<i>N,N,N'</i> -trimethylpropane-1,3-diamine
328	<i>N</i> -[5-(Dimethylamino)pyridin-3-yl]-2-methyl-5-([3-(trifluoromethyl)benzoyl]amino)benzamide	11.02 (s, 1H), 10.65 (s, 1H), 8.58 (s, 1H), 8.31-8.27 (m, 2H), 8.04 (dd, 2H), 7.98 (d, 1H), 7.83-7.77 (m, 3H), 7.35 (d, 1H), 3.04 (s, 6H), 2.37 (s, 3H)	443	<i>N,N</i> -dimethylamine
329	<i>N</i> -(5-([3-(Dimethylamino)propyl]amino)pyridin-3-yl)-2-methyl-5-([3-(trifluoromethyl)benzoyl]amino)benzamide	11.06 (s, 1H), 10.69 (s, 1H), 8.41 (s, 1H), 8.31-8.28 (m, 2H), 8.02-7.92 (m, 4H), 7.82 (t, 2H), 7.33 (d, 1H), 3.29-3.20 (m, 2H), 3.18-3.05 (m, 2H), 2.74 (s, 3H), 2.73 (s, 3H), 2.36 (s, 3H), 1.96-1.89 (m, 2H)	501	<i>N,N</i> -dimethylpropane-1,3-diamine

Ex	Compound	NMR	M/z	SM
330	<i>N</i> -{5-[(2-Methoxyethyl)(methyl)amino]pyridin-3-yl}-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	11.02 (s, 1H), 10.67 (s, 1H), 8.58 (s, 1H), 8.31-8.28 (m, 2H), 8.09 (d, 1H), 8.04-7.96 (m, 2H), 7.84-7.77 (m, 3H), 7.35 (d, 1H), 3.65-3.59 (m, 2H), 3.55-3.49 (m, 2H), 3.24 (s, 3H), 3.04 (s, 3H), 2.37 (s, 3H)	487	2-methoxy- <i>N</i> -methylethanamine
331	<i>N</i> -(5-[[2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]amino]pyridin-3-yl)-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	11.04 (s, 1H), 10.66 (s, 1H), 8.60 (s, 1H), 8.32-8.29 (m, 2H), 8.02 (dd, 2H), 7.99 (d, 1H), 7.83-7.78 (m, 3H), 7.34 (d, 1H), 4.26-4.22 (m, 1H), 3.79-3.55 (m, 2H), 3.12-3.05 (m, 2H), 2.37 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H)	530	1-(2,2-dimethyl-1,3-dioxolan-4-yl)methanamine
332	<i>N</i> -(5-[[2-(Dimethylamino)ethyl]amino]pyridin-3-yl)-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.72 (s, 1H), 10.59 (s, 1H), 8.30-8.24 (m, 3H), 7.99-7.96 (m, 2H), 7.87-7.76 (m, 4H), 7.34 (d, 1H), 3.49 (t, 2H), 3.29-3.26 (m, 2H), 2.84 (s, 6H), 2.36 (s, 3H)	486	<i>N,N</i> -dimethylethane-1,2-diamine
333	<i>N</i> -{5-[[2-(Dimethylamino)ethyl](methyl)amino]pyridin-3-yl}-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.72 (s, 1H), 10.59 (s, 1H), 8.30-8.24 (m, 3H), 7.99-7.96 (m, 2H), 7.87-7.76 (m, 4H), 7.34 (d, 1H), 3.49 (t, 2H), 3.29-3.26 (m, 2H), 2.84 (s, 6H), 2.36 (s, 3H)	501	<i>N,N,N'</i> -trimethylethane-1,2-diamine

Ex	Compound	NMR	M/z	SM
334	5-{{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-[5-(4-methylpiperazin-1-yl)pyridin-3-yl]benzamide	11.06 (s, 1H), 10.77 (s, 1H), 8.55 (s, 1H), 8.34-8.29 (m, 3H), 8.12 (s, 1H), 8.03 (d, 1H), 7.98 (d, 1H), 7.84-7.78 (m, 2H), 7.34 (d, 1H), 4.00-3.93 (m, 2H), 3.56-3.50 (m, 2H), 3.33-3.11 (m, 4H), 2.82 (s, 3H), 2.37 (s, 3H), 1.59 (s, 6H)	498	1-methylpiperazine
335	2-Chloro-5-[(3,5-dimethylbenzoyl)amino]-N-(5-morpholin-4-ylpyridin-3-yl)benzamide	10.99 (s, 1H), 10.45 (s, 1H), 8.50 (d, 1H), 8.23 (d, 1H), 8.10 (d, 1H), 7.94-7.88 (m, 2H), 7.59 (s, 1H), 7.56 (s, 2H), 7.24 (s, 1H), 3.76 (t, 4H), 3.25 (t, 4H), 2.35 (s, 6H)	466	Morpholine
336	2-Chloro-N-{5-[[2-(dimethylamino)ethyl](methyl)amino]pyridin-3-yl}-5-[(3,5-dimethylbenzoyl)amino]benzamide	10.88 (s, 1H), 10.48 (s, 1H), 8.35 (s, 1H), 8.11 (d, 1H), 8.08 (s, 1H), 7.87 (dd, 1H), 7.73 (s, 1H), 7.58 (s, 1H), 7.56 (s, 2H), 7.24 (s, 1H), 3.76 (t, 2H), 3.29-3.26 (m, 2H), 2.98 (s, 3H), 2.85 (s, 3H), 2.83 (s, 3H), 2.35 (s, 6H)	481	N,N,N'-trimethylethane-1,2-diamine

Example 337

N-[5-(3-Aminoprop-1-yn-1-yl)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

- 5 To a 10 ml round bottom flask equipped with a magnetic stirring bar was added N-(5-bromopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 193; 200 mg, 0.418 mmol) and MeCN (1.75 ml). Et₃N (0.293 ml, 2.10 mmol) was added followed by prop-2-yn-1-amine (58 mg, 1.05 mmol), CuI (25 mg, 0.125 mmol), and Pd(PPh₃)₄ (96 mg, 0.084 mmol). The reaction was warmed to 50 °C with stirring for 12 h
- 10 before being cooled to room temperature, diluted with 50 ml of EtOAc, and filtered through a pad of SiO₂. The SiO₂ was rinsed with an additional 50 ml of EtOAc and the combined filtrate

was concentrated *in vacuo* to yield the crude product, which was purified on a 40 g SiO₂ column using MeOH/EtOAc (1:10) as eluent giving 102 mg (55%) of the title compound as an off-white solid. NMR (300 MHz): 10.82 (s, 1H), 10.62 (s, 1H), 8.46-8.40 (m, 2H), 8.31-8.27 (m, 3H), 7.98-7.95 (m, 2H), 7.84-7.77 (m, 2H), 7.34 (d, 1H), 4.08-4.02 (m, 2H), 2.36 (s, 3H); *m/z* 453.

Examples 338-340

The following compounds were prepared by the procedure in LD29 using *N*-(5-bromopyridin-3-yl)-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide (Example 193) and the appropriate SM. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
338	<i>N</i> -[5-(3-Hydroxyprop-1-yn-1-yl)pyridin-3-yl]-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.73 (s, 1H), 10.59 (s, 1H), 8.83 (s, 1H), 8.34-8.26 (m, 4H), 7.97 (d, 1H), 7.92 (d, 1H), 7.87-7.79 (m, 2H), 7.33 (d, 1H), 4.33 (s, 2H), 2.36 (s, 3H)	454	prop-2-yn-1-ol
339	2-Methyl- <i>N</i> -{5-[3-(methylamino)prop-1-yn-1-yl]pyridin-3-yl}-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.83 (s, 1H), 10.64 (s, 1H), 8.46 (s, 1H), 8.31-8.26 (m, 3H), 7.98-7.95 (m, 3H), 7.85-7.77 (m, 2H), 7.33 (d, 1H), 4.19 (t, 2H), 3.05 (t, 2H), 2.36 (s, 3H)	467	<i>N</i> -methylprop-2-yn-1-amine
340	<i>N</i> -{5-[3-(Dimethylamino)prop-1-yn-1-yl]pyridin-3-yl}-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide	10.82 (s, 1H), 10.63 (s, 1H), 8.48 (s, 1H), 8.31-8.26 (m, 3H), 7.99-7.96 (m, 2H), 7.85-7.77 (m, 3H), 7.34 (d, 1H), 4.39 (s, 2H), 2.88 (s, 6H), 2.36 (s, 3H)	481	<i>N,N</i> -dimethylprop-2-yn-1-amine

Example 341**N-[5-(3-Hydroxypropyl)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide**

To a 25 ml round bottom charged with a magnetic stirring bar and N-[5-(3-hydroxyprop-1-yn-1-yl)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 338; 45 mg, 0.100 mmol) was added MeOH (10 ml). 10% Pd/C (15 mg) was carefully added and the reaction was placed under 1 atm of H₂ using a balloon. The reaction was allowed to stir for 12 h at room temperature before being purged with argon, diluted with ~15 ml of EtOAc, and filtered through a pad of SiO₂. The SiO₂ pad was rinsed with an additional 25 ml of EtOAc and the combined filtrate was concentrated *in vacuo* to yield the crude product, which was purified on a 40 g SiO₂ column using EtOAc as eluent giving 44 mg (98%) of the title compound as an off-white solid. NMR (300 MHz): 10.85 (s, 1H), 10.60 (s, 1H), 8.32-8.26 (m, 5H), 7.99-7.97 (m, 2H), 7.84-7.76 (m, 2H), 7.34 (d, 1H), 3.43 (t, 2H), 2.75-2.69 (m, 2H), 2.37 (s, 3H), 1.78-1.71 (m, 2H); *m/z* 459.

Examples 342-343

The following compounds were prepared by the procedure in Example 341 and the appropriate SM. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
342	2-Methyl-N-{5-[3-(methylamino)propyl]pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.89 (s, 1H), 10.64 (s, 1H), 8.34-8.25 (m, 5H), 8.00-7.97 (m, 2H), 7.85-7.76 (m, 2H), 7.33 (d, 1H), 2.64-2.59 (m, 2H), 2.49 (s, 3H), 2.37 (s, 3H), 2.30-2.26 (m, 2H), 1.78-1.75 (m, 2H)	472	Example 339
343	N-{5-[3-(Dimethylamino)propyl]pyridin-3-yl}-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.67 (s, 1H), 10.60 (s, 1H), 8.30-8.22 (m, 5H), 8.05-7.97 (m, 2H), 7.80 (t, 2H), 7.34 (d, 1H), 3.15-3.09 (m, 2H), 2.79 (s, 3H), 2.77 (s, 3H), 2.65-2.59 (m, 2H), 2.36 (s, 3H), 1.98-1.88 (m, 2H)	486	Example 340

Example 344

2-Chloro-*N*-{5-[(4-methylpiperazin-1-yl)methyl]pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a 10 ml round bottom flask charged with a magnetic stir bar and 2-chloro-*N*-[5-(hydroxymethyl)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 304; 0.200 g, 0.444 mmol) was added Et₃N (0.19 ml, 1.34 mmol). The reaction was cooled to 0 °C in an ice bath and methanesulfonyl chloride (0.05 ml, 0.578 mmol) was added dropwise via syringe. The reaction was allowed to stir at this temperature for 15 min before 1-methylpiperazine (0.500 ml, 4.44 mmol) was added via syringe. The reaction was allowed to stir to room temperature over 3 h before being poured over ~50 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~50 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified by semi-preparative reverse phase HPLC giving 0.190 g (80%) of the title compound as a pale yellow solid NMR (300 MHz): 10.95 (s, 1H), 10.78 (s, 1H), 8.75 (d, 1H), 8.33-8.26 (m, 4H), 8.10 (d, 1H), 7.99 (d, 1H), 7.88 (dd, 1H), 7.80 (t, 1H), 7.60 (d, 1H), 3.74 (s, 2H), 3.42-3.32 (m, 4H), 3.11-3.00 (m, 4H), 2.78 (s, 3H), *m/z* 533.

Examples 345-351

The following compounds were prepared by the procedure in Example 344 using the appropriate SMs. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
345	2-Methyl- <i>N</i> -[5-(morpholin-4-ylmethyl)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	10.80 (s, 1H), 10.59 (s, 1H), 8.78 (d, 1H), 8.60 (s, 1H), 8.42 (d, 1H), 8.30-8.24 (m, 2H), 8.01-7.97 (m, 2H), 7.82-7.75 (m, 2H), 7.34 (d, 1H), 3.76 (t, 4H), 3.25 (t, 4H), 3.22 (s, 2H), 2.36 (s, 3H)	500	Morpholine and Example 273

Ex	Compound	NMR	M/z	SM
346	2-Chloro- <i>N</i> -{5-[(dimethylamino)methyl]pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide	11.04 (s, 1H), 10.79 (s, 1H), 8.77 (d, 1H), 8.55 (s, 1H), 8.44 (s, 1H), 8.31-8.26 (m, 2H), 8.11 (d, 1H), 8.00 (d, 1H), 7.92 (dd, 1H), 7.80 (t, 1H), 7.62 (d, 1H), 4.39 (s, 2H), 2.77 (s, 6H)	477	<i>N</i> , <i>N</i> -dimethylamine and Example 304
347	2-Chloro- <i>N</i> -{5-[(cyclopropylamino)methyl]pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide	11.00 (s, 1H), 10.77 (s, 1H), 8.71 (s, 1H), 8.55 (s, 1H), 8.45 (s, 1H), 8.31-8.26 (m, 2H), 8.10 (d, 1H), 8.00 (d, 1H), 7.91 (dd, 1H), 7.81 (t, 1H), 7.62 (d, 1H), 4.34 (s, 2H), 2.80-2.75 (m, 1H), 0.85-0.76 (m, 4H)	490	Cyclopropylamine and Example 304
348	2-Chloro- <i>N</i> -[5-(piperidin-1-ylmethyl)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide	11.03 (s, 1H), 10.78 (s, 1H), 8.76 (d, 1H), 8.55 (s, 1H), 8.44 (d, 1H), 8.30-8.26 (m, 2H), 8.12 (d, 1H), 8.00 (d, 1H), 7.90 (dd, 1H), 7.81 (t, 1H), 7.61 (d, 1H), 4.39 (d, 2H), 3.36 (d, 2H), 2.95-2.90 (m, 2H), 1.85-1.62 (m, 6H)	518	Piperidine and Example 304
349	2-Chloro- <i>N</i> -(5-{[(2-methoxyethyl)(methyl)amino]methyl}pyridin-3-yl)-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide	11.03 (s, 1H), 10.78 (s, 1H), 8.77 (d, 1H), 8.57 (s, 1H), 8.45 (s, 1H), 8.30-8.26 (m, 2H), 8.11 (d, 1H), 8.00 (d, 1H), 7.89 (dd, 1H), 7.81 (t, 1H), 7.61 (d, 1H), 4.50-4.30 (m, 2H), 3.68 (s, 2H), 3.32-3.25 (m, 5H), 2.75 (s, 3H)	522	2-methoxy- <i>N</i> -methylethanamine and Example 304

Ex	Compound	NMR	M/z	SM
350	2-Chloro- <i>N</i> -(5-{[[2-(dimethylamino)ethyl](methyl)amino]methyl}pyridin-3-yl)-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	11.01 (s, 1H), 10.80 (s, 1H), 8.77 (d, 1H), 8.44 (s, 2H), 8.30-8.26 (m, 2H), 8.11 (d, 1H), 8.00 (d, 1H), 7.88 (dd, 1H), 7.80 (t, 1H), 7.62 (d, 1H), 3.38 (s, 2H), 2.82 (s, 6H), 2.54-2.40 (m, 4H), 2.44 (s, 3H)	534	N,N,N'-trimethylethane-1,2-diamine and Example 304
351	2-Chloro- <i>N</i> -(5-{[(methylamino)methyl]pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide	11.01 (s, 1H), 10.80 (s, 1H), 8.77 (d, 1H), 8.44 (s, 2H), 8.30-8.26 (m, 2H), 8.11 (d, 1H), 8.00 (d, 1H), 7.88 (dd, 1H), 7.80 (t, 1H), 7.62 (d, 1H), 3.38 (s, 2H), 2.82 (s, 6H), 2.54-2.40 (m, 4H), 2.44 (s, 3H)	463	Methylamine and Example 304

Example 352

2-Methyl-*N*-(5-{[(pyrrolidin-3-yl)methyl]amino}pyridin-3-yl)-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

- 5 To a 25 ml round bottom flask charged with a magnetic stir bar and *tert*-butyl 3-formylpyrrolidine-1-carboxylate (0.121 g, 0.603 mmol) was added MeOH (3 ml) and glacial acetic acid (0.3 ml). To the reaction mixture was added *N*-(5-aminopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 244; 0.25 g, 0.603 mmol) and the reaction was allowed to stir at room temperature for 10 min. To the resulting mixture was
- 10 added a 1M solution of NaBH₃CN in THF (1.21 ml), and the reaction was allowed to stir for 4 h at room temperature before being quenched with ~ 5 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~50 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was dissolved in MeOH (5 ml). A 4N solution of HCl in
- 15 dioxane was added until a pH of 3 (~ 0.5 ml) was achieved. The reaction was allowed to stir at room temperature for 12 h before being concentrated *in vacuo* which was purified by semi-preparative reverse phase HPLC giving 0.09 g (30%) of the title compound as a white solid. NMR (300 MHz): 10.97 (s, 1H), 10.67 (s, 1H), 8.42 (s, 1H), 8.33 (s, 1H), 8.29 (d, 1H), 7.91 -

8.05 (m, 4H), 7.76 - 7.89 (m, 2H), 7.36 (d, 1H), 3.27 - 3.38 (m, 2H), 3.20 (d, 2H), 2.86 - 2.99 (m, 3H), 2.48 - 2.64 (m, 2H), 2.05 - 2.18 (m, 2H), 1.61 - 1.76 (m, 1H); m/z 499.

Examples 353-356

- 5 The following compounds were prepared by the procedure in Example 352, using *N*-(5-aminopyridin-3-yl)-2-methyl-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide (Example 244), and the appropriate SM. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
353	2-Methyl- <i>N</i> -{5-[(piperidin-4-ylmethyl)amino]pyridin-3-yl}-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.82 (s, 1H), 10.61 (s, 1H), 8.58 (s, 1H), 8.31 (d, 2H), 8.27 (d, 1H), 7.95 - 8.03 (m, 2H), 7.76 - 7.89 (m, 3H), 7.34 (d, 1H), 3.30-3.25 (m, 2H), 3.03 (d, 2H), 2.86 (d, 2H), 2.36 (s, 3H), 1.90-1.86 (m, 4H), 1.36-1.30 (m, 1H)	512	tert-butyl 4-formylpiperidine-1-carboxylate
354	<i>N</i> -{5-[(1H-Imidazol-2-ylmethyl)amino]pyridin-3-yl}-2-methyl-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.78 (s, 1H), 10.60 (s, 1H), 8.40 (d, 1H), 8.30 (s, 1H), 8.27 (d, 1H), 7.89 - 8.00 (m, 3H), 7.74 - 7.83 (m, 3H), 7.63 (s, 2H), 7.33 (d, 1H), 4.76 (s, 2H), 2.34 (s, 3H)	496	1H-imidazole-2-carbaldehyde
355	<i>N</i> -{5-[(2-Hydroxyethyl)amino]pyridin-3-yl}-2-methyl-5-{{3-(trifluoromethyl)benzoyl}amino}benzamide	10.92 (s, 1H), 10.61 (s, 1H), 8.41 (d, 1H), 8.31 (s, 1H), 8.27 (d, 1H), 7.88 - 8.00 (m, 3H), 7.76 - 7.84 (m, 3H), 7.35 (d, 1H), 3.59 (t, 2H), 3.19 (t, 2H), 2.36 (s, 3H)	459	{{tert-butyl(dimethyl)silyl}oxy}acetaldehyde

Ex	Compound	NMR	M/z	SM
356	<i>N</i> -{5-[(2-Aminoethyl)amino]pyridin-3-yl}-2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino}benzamide	10.91 (s, 1H), 10.65 (s, 1H), 8.40 (d, 1H), 8.30 (s, 1H), 8.27 (d, 1H), 7.88 - 8.01 (m, 3H), 7.76 - 7.84 (m, 3H), 7.35 (d, 1H), 3.26 (t, 2H), 3.19 (t, 2H), 2.36 (s, 3H)	458	tert-butyl (2-oxoethyl)carbamate

Example 357

2-Chloro-*N*-{5-[(methanesulfonyl)amino]pyridin-3-yl}-5-[[3-(trifluoromethyl)benzoyl]amino}benzamide

To a 10 ml round bottom flask equipped with a magnetic stir bar was added *N*-(5-aminopyridin-3-yl)-2-chloro-5-[[3-(trifluoromethyl)benzoyl]amino]benzamide (Example 243; 80 mg, 0.184 mmol). Pyridine (2.0 ml) was added followed by methanesulfonyl chloride (0.018 ml, 0.23 mmol). The reaction was warmed to 50 °C and allowed to stir for 12 h before being poured over ~50 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~50 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified on a 40 g SiO₂ column using EtOAc as eluent giving 50 mg (53%) of the title compound as an off-white solid. NMR (300 MHz): 10.90 (s, 1H), 10.74 (s, 1H), 10.14 (s, 1H), 8.66 (s, 1H), 8.26 (s, 3H), 8.15 (s, 1H), 7.98 (s, 3H), 7.81 (s, 1H), 7.60 (s, 1H), 3.08 (s, 3H); *m/z* 514.

Example 358

The following compound was prepared by the procedure in Example 357, using *N*-(6-aminopyridin-3-yl)-5-[[3-(1-cyano-1-methylethyl)benzoyl]amino]-2-methylbenzamide (Example 202) and the appropriate SM. Further purification was required (column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
358	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-{6-[(methylsulfonyl)amino]pyridin-3-yl}benzamide	10.46 (d, 2H), 8.60 (s, 1H), 8.06 (s, 2H), 7.94 (s, 2H), 7.85 (s, 1H), 7.76 (s, 2H), 7.61 (d, 1H), 7.31 (d, 1H), 7.00 (d, 1H), 3.27 (s, 3H), 2.35 (s, 3H), 1.74 (s, 6H)	493	Methanesulfonyl chloride

Example 359*N*-[5-(Acetylamino)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a 10 ml round bottom flask equipped with a magnetic stir bar was added *N*-(5-aminopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 244; 200 mg, 0.482 mmol). Pyridine (5.0 ml) was added followed acetyl chloride (0.044 ml, 0.603 mmol). The reaction was allowed to stir to for 12 h at room temperature before being poured over ~50 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~50 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified by on a 40 g SiO₂ column using EtOAc as eluent giving 160 mg (73%) of the title compound as an off-white solid. NMR (300 MHz): 10.74 (s, 1H), 10.57 (s, 1H), 10.34 (s, 1H), 8.63 (d, 2H), 8.59 (s, 1H), 8.31 (s, 1H), 8.27 (d, 1H), 7.90 - 8.00 (m, 2H), 7.76 - 7.86 (m, 2H), 7.33 (d, 1H), 2.36 (s, 3H), 2.09 (s, 3H); *m/z* 457.

Examples 360-361

The following compound was prepared by the procedure in Example 359, using *N*-(6-aminopyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide (Example 202) and the appropriate SM. In some cases, further purification was required (supercritical fluid, Gilson reverse phase preparatory HPLC or column chromatography utilizing an ISCO system).

Ex	Compound	NMR	M/z	SM
360	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-{6-[(2,2-dimethylpropanoyl)amino]pyridin-3-yl}-2-methylbenzamide	10.50 (s, 1H), 10.41 (s, 1H), 9.79 (s, 1H), 8.72 (d, 1H), 8.00 - 8.09 (m, 3H), 7.88 - 7.97 (m, 2H), 7.83 (dd, 1H), 7.75 (d, 1H), 7.60 (t, 1H), 7.31 (d, 1H), 2.36 (s, 3H), 1.74 (s, 6H), 1.10 (m, 9H)	499	2,2-dimethylpropanoyl chloride
361	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-{6-[(cyclobutylcarbonyl)amino]pyridin-3-yl}-2-methylbenzamide	10.48 (s, 1H), 10.40 (s, 1H), 10.29 (s, 1H), 8.67 (d, 1H), 8.02 - 8.13 (m, 3H), 7.94 (d, 1H), 7.80 - 7.90 (m, 2H), 7.73 - 7.78 (m, 1H), 7.60 (t, 1H), 7.31 (d, 1H), 2.36 (s, 3H), 2.21 (d, 3H), 2.03 - 2.19 (m, 3H), 1.86 - 1.96 (m, 1H), 1.81 (s, 1H), 1.74 (s, 6H)	496	cyclobutanecarbonyl chloride

Example 362

N-{5-[(Aminocarbonyl)amino]pyridin-3-yl}-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

- 5 To a 25 ml round bottom flask equipped with a magnetic stir bar was added N-(5-aminopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 244; 0.25 g, 0.603 mmol). Anhydrous THF (3.0 ml) was added followed trichloroacetyl isocyanate (0.286 ml, 2.40 mmol). The reaction was allowed to stir to for 1 h at room temperature before concentrated *in vacuo*. The resulting residue was dissolved in a 2N
- 10 solution of NH₃ in MeOH (10 ml) and allowed to stir for 3 h at room temperature. The reaction mixture was concentrated *in vacuo* to yield the crude product, which was purified by semi-preparative reverse phase HPLC giving 0.132 g (49%) of the title compound as a white solid NMR (300 MHz): 10.75 (s, 1H), 10.57 (s, 1H), 9.10 (s, 1H), 8.56 (s, 2H), 8.43 (s, 1H), 8.25 - 8.32 (m, 2H), 7.92 - 8.00 (m, 2H), 7.76 - 7.85 (m, 2H), 7.33 (d, 1H), 6.13 (s, 2H), 2.36
- 15 (s, 3H); *m/z* 458.

Example 363

N-[5-(Formylamino)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a 25 ml round bottom flask equipped with a magnetic stir bar was added *N*-(5-aminopyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 244; 0.30 g, 0.723 mmol). Anhydrous DCM (3.0 ml) was added followed Et₃N (0.507 ml, 3.62 mmol), and acetic-formic anhydride (0.159 g, 1.80 mmol). The reaction was allowed to stir to for 4 h at room temperature before being poured over ~50 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~50 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified on a 40 g SiO₂ column using EtOAc as eluent giving 171 mg (53%) of the title compound as a white solid. NMR (300 MHz): 10.73 (s, 1H), 10.57 (s, 2H), 8.58 - 8.69 (m, 3H), 8.33 (d, 2H), 8.27 (d, 1H), 7.90 - 8.00 (m, 2H), 7.76 - 7.87 (m, 2H), 7.33 (d, 1H), 2.36 (s, 3H); *m/z* 443.

Example 364

2-Methyl-*N*-[5-(methylamino)pyridin-3-yl]-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a 25 ml round bottom flask equipped with a magnetic stir bar was added *N*-[5-(formylamino)pyridin-3-yl]-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 363; 0.12 g, 0.271 mmol). Anhydrous THF (3 ml) was added and the reaction mixture was cooled to 0 °C with an ice bath. Lithium aluminium hydride (15 mg, 0.394 mmol) was added and the reaction was allowed to warm to room temperature with stirring over 3 h. The reaction was carefully quenched with ~ 10 ml of H₂O and the resulting mixture was poured into a separator funnel and extracted with ~50 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified on a 40 g SiO₂ column using EtOAc as eluent giving 68 mg (59%) of the title compound as a white solid. NMR (300 MHz): 10.86 (s, 1H), 10.59 (s, 1H), 8.38 (d, 1H), 8.24 - 8.34 (m, 2H), 7.95 - 8.01 (m, 2H), 7.73 - 7.86 (m, 4H), 7.34 (d, 1H), 2.76 (s, 3H), 2.36 (s, 3H); *m/z* 430.

Example 365

N-{5-[(2,3-Dihydroxypropyl)amino]pyridin-3-yl}-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a 25 ml round bottom flask charged with a magnetic stir bar and *N*-(5-{[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]amino}pyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 331; 0.50 mg, 0.094 mmol) was added 3 ml of a 2 N HCl solution in Et₂O. Water (0.05 ml) was added and the reaction was allowed to stir for 2 h at room temperature before being concentrated *in vacuo* to yield the crude product which was purified by semi-preparative reverse phase HPLC giving 0.037 g (80%) of the title compound as a white solid. NMR (300 MHz): 11.00 (s, 1H), 10.65 (s, 1H), 8.59 (s, 1H), 8.32-8.29 (m, 2H), 8.02 (dd, 2H), 7.99 (d, 1H), 7.83- 7.78 (m, 3H), 7.34 (d, 1H), 4.26-4.22 (m, 1H), 3.79-3.54 (m, 2H), 3.12-3.05 (m, 2H), 2.37 (s, 3H); *m/z* 489.

Example 366

15 2-Chloro-*N*-{6-[(3-methoxypropanoyl)amino]pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide

To a solution of 2-chloro-*N*-{6-amino-pyridin-3-yl}-5-{[3-(trifluoromethyl)benzoyl]amino}benzamide (Example 317; 40mg) in DCM (0.5 ml) at 0°C was added 3-methoxy propanoyl chloride (0.100 ml) followed by Et₃N (0.80 ml) and the resulting mixture was stirred at room temperature for 3 hours. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. Evaporation of the solvent gave a solid, which was purified by reverse phase HPLC (5-95% MeCN/H₂O, 15 min). The title compound (4 mg) was collected by evaporation. NMR (300 MHz): 10.64 (s, 1H), 10.02 (s, 1H), 8.18-8.47 (m, 3H), 7.82 - 7.96 (m, 3H), 7.43-7.66 (m, 3H), 7.07 (d, 1H), 3.69 - 3.72 (m, 2H), 3.33 (s, 3H), 2.11-2.21 (m, 2H); *m/z* 520.

Example 367

5-{[3-[2-(Dimethylamino)-1,1-dimethyl-2-oxoethyl]benzoyl]amino}-2-methyl-*N*-(6-methylpyridin-3-yl)benzamide

30 A solution of 5-{[3-[2-(dimethylamino)-1,1-dimethyl-2-oxoethyl]benzoyl]amino}-2-methylbenzoic acid (Method 54, 71 mg, 0.193 mmol), 3-amino-6-picoline (21 mg, 0.193 mmol) and DIEA (0.10 ml, 0.58 mmol, 3.0 equiv) in DMF (2 ml) was treated with HATU (88 mg, 0.232 mmol, 1.2 equiv). The reaction mixture was stirred for 12 h at 40 °C. The reaction

was quenched with 10% NaOH and extracted with EtOAc. The organics were dried with NaCl_(sat) and then Na₂SO_{4(s)} and removed under reduced pressure. The residue was purified directly by column chromatography (5% MeOH in EtOAc) to give 70 mg of product (73%). NMR: 11.16 (s, 1H), 10.46 (s, 1H), 9.15 (m, 1H), 8.48 (d, 1H), 8.02 (s, 1H), 7.84 (m, 4H), 7.51 (t, 1H), 7.34 (m, 2H), 2.78 (bs, 3H), 2.68 (s, 1H), 2.46 (s, 3H), 2.37 (s, 3H), 1.48 (s, 6H); *m/z* 459.

Example 368

5 5-[(Dimethylamino)sulfonyl]-N-(4-methyl-3-[(6-methylpyridin-3-yl)amino]carbonyl}phenyl)nicotinamide

A solution of 5-[(5-[(dimethylamino)sulfonyl]pyridin-3-yl)carbonyl]amino]-2-methylbenzoic acid (Method 55; 77 mg, 0.212 mmol), 3-amino-6-picoline (23 mg, 0.212 mmol) and DIEA (0.12 ml, 0.64 mmol, 3.0 equiv) in DMF (2 ml) was treated with HATU (97 mg, 0.254 mmol, 1.2 equiv). The reaction mixture was stirred for 12 h at 40 °C. The reaction was quenched with 10% NaOH and extracted with EtOAc. The organics were dried with NaCl_(sat) and then Na₂SO_{4(s)} and removed under reduced pressure. The residue was purified directly by Gilson reverse phase preparatory HPLC (5-95% MeCN/H₂O) to give 18 mg of product (13%). NMR: 10.89 (s, 2H), 10.80 (s, 1H), 9.39 (d, 1H), 9.11 (d, 1H), 9.02 (s, 1H), 8.64 (t, 1H), 8.29 (dd, 1H), 7.96 (d, 1H), 7.82 (dd, 1H), 7.62 (d, 1H), 7.37 (d, 1H), 2.71 (s, 6H), 2.57 (s, 3H), 2.38 (s, 3H); *m/z* 454.

Example 369

N-{6-[(2-Aminoethyl)amino]pyridin-3-yl}-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide

25 Tert-butyl {2-[(5-aminopyridin-2-yl)amino]ethyl} carbamate (Method 73; 331 mg, 1.24 mmol) was combined with 5-[3-(cyanodimethyl-methyl)-benzoylamino]-2-methylbenzoic acid (Method 20; 400 mg, 1.24 mmol), HATU (708 mg, 1.86 mmol) and DIEA (0.65 ml, 3.72 mmol) in 2.48 ml of DMF and the reaction mixture was stirred overnight at 25°C. LC/MS confirmed the formation of tert-butyl [2-({5-[(5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]pyridin-2-yl}amino)ethyl]carbamate, and the reaction was quenched with H₂O. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. Evaporation of the solvent gave a light brown solid (*m/z* 557), which was redissolved in 10 ml of HCl in 1,4-

dioxane and stirred overnight at 25°C. Evaporation of the solvent gave a brown gummy solid, which was purified by reverse phase HPLC (5-95% MeCN/H₂O, 20 min). The title compound (44 mg) was collected by evaporation as a brown solid. NMR (300 MHz): 10.41 (s, 1H), 10.18 (s, 1H), 10.00 (s, 1H), 8.28 - 8.50 (m, 1H), 8.01 - 8.12 (m, 1H), 7.88 - 8.00 (m, 2H), 7.70 - 7.87 (m, 4H), 7.61 (t, 1H), 7.32 (d, 1H), 6.65 (s, 2H), 2.94 - 3.13 (m, 1H), 2.85 - 2.96 (m, 1H), 2.68 - 2.80 (m, 1H), 2.35 (s, 3H), 2.23 - 2.33 (m, 1H), 1.76 (s, 6H); m/z 457.

Example 370

5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-N-[5-(isopropylamino)pyridin-3-yl]-2-methylbenzamide

N-(5-Aminopyridin-3-yl)-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzamide (Example 205; 164 mg, 0.398 mmol) was combined with acetone and sodium triacetoxyborohydride (337 mg, 1.59 mmol) in 0.80 ml of THF and heated at 30°C in a sealed tube overnight. LC/MS confirmed the formation of the product and the mixture was partitioned between H₂O and EtOAc. The organic layer was washed with brine and dried with MgSO₄. Evaporation of the solvent gave a yellow solid, which was purified by reverse phase HPLC (5-95% MeCN/H₂O, 20 min). The title compound (40 mg) was collected by evaporation as a white solid. NMR (300 MHz): 10.91 (s, 1H), 10.47 (s, 1H), 8.39 (s, 1H), 8.06 (t, 1H), 7.93 - 8.01 (m, 2H), 7.74 - 7.85 (m, 5H), 7.63 (t, 1H), 7.36 (d, 1H), 2.37 (s, 3H), 1.76 (s, 6H), 1.18 (m, 7H); m/z 456.

Example 371

5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-(5-pyrrolidin-2-ylpyridin-3-yl)benzamide

tert-Butyl 2-{5-[(5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoyl)amino]pyridin-3-yl}pyrrolidine-1-carboxylate (Example 324; 50 mg) was dissolved in MeOH (3 ml) and 4N HCl in 1,4-dioxane (2.5 ml) was added at 0°C and the resulting mixture was stirred for 2 hours at room temperature. Evaporation of the solvents afforded the title compound as an off-white solid (32 mg). NMR (300 MHz): 10.72 (s, 1H), 10.46 (s, 1H), 8.85 (s, 1H), 8.43 - 8.54 (m, 1H), 8.25 (s, 1H), 8.06 (s, 1H), 8.01 (t, 1H), 7.96 (d, 1H), 7.3 - 7.81 (m, 2H), 7.61 (t, 1H), 7.34 (d, 1H), 4.23 (m, 1H), 3.73 (m, 2H), 2.27 (s, 3H), 1.93-2.22 (m, 4H), 1.78 (s, 6H), m/z 469.

Examples 372-373

The following examples were made by the procedure of Example 371 using the appropriate starting materials.

Ex	Compound	NMR	M/z	SM
372	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-{6-[(pyrrolidin-2-ylmethyl)amino]pyridin-3-yl}benzamide	10.69 (s, 1H), 10.54 (s, 1H), 9.42 (bs, 1H), 9.32 (bs, 1H), 8.58 (s, 1H), 8.-2 - 8.15 (m, 2H), 7.-1 - 8.01 (m, 2H), 7.84 (d, 1H), 7.75 (d, 1H), 7.61 (t, 1H), 7.31 (d, 1H), 7.23 (d, 1H), 3.-5 - 3.85 (m, 4H), 3.-3 - 3.26 (m, 1H), 2.36 (s, 3H), 2.-9 - 2.22 (m, 2H), 1.-3 - 2.01 (m, 2H), 1.76 (s, 6H)	498	Example 314
373	5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-methyl-N-[5-(pyrrolidin-2-ylmethoxy)pyridin-3-yl]benzamide	10.35 (s, 1H), 8.04 (s, 1H), 7.-8 - 8.00 (m, 2H), 7.76 (d, 1H), 7.-5 - 7.73 (m, 2H), 7.-5 - 7.65 (m, 2H), 7.27 (d, 1H), 7.21 (s, 1H), 4.-0 - 4.56 (m, 1H), 4.33 (t, 1H), 3.-9 - 3.24 (m, 2H), 2.15 (s, 3H), 1.-6 - 2.04 (m, 4H), 1.75 (s, 6H)	499	Example 315

5 Preparation of Starting Materials**Method 1****3-Cyanomethyl-benzoic acid methyl ester**

A suspension of methyl-3-(bromomethyl)benzoate (13.5 g, 58.9 mmol) and sodium cyanide (4.33 g, 88.4 mmol) in DMF (25 ml) and water (1 ml) was stirred at 75 °C for 5 h. The reaction mixture was quenched with water (50 ml) and extracted with EtOAc (100 ml × 3). The combined organics were dried and concentrated under reduced pressure. The resulting residue was purified by column chromatography utilizing an ISCO system (hexane-EtOAc) to give 7.2 g (70%) of colourless oil. NMR: 7.90 (s, 1H), 7.86 (d, 1H), 7.60 (d, 1H), 7.50 (m, 1H), 4.10 (s, 2H), 3.80 (s, 3H); *m/z* 175.

Methods 2-7

The following compounds were prepared by the procedure of Method 1, using the appropriate starting material.

Meth	Compound	m/z	SM
2	Methyl 4-chloro-3-(cyanomethyl)benzoate	210	Method 136
3	[4-({[tert-Butyl(diphenyl)silyl]oxy}methyl)-2-thienyl]acetonitrile	393	Method 106
4	Methyl 3-(cyanomethyl)-5-methylbenzoate	189	Method 137
5	Methyl 5-(cyanomethyl)nicotinate	177	Method 140
6	(2-Fluoro-3-methylphenyl)acetonitrile	150	1-(Bromo methyl)-2-fluoro-3-methylbenzene
7	Methyl 5-(cyanomethyl)-2-fluorobenzoate	195	Method 141

5 Method 8**3-(1-Cyano-1-methylethyl)benzoic acid methyl ester**

A solution of 3-cyanomethyl-benzoic acid methyl ester (Method 1; 7.2 g, 41.1 mmol) in anhydrous DMSO (80 ml) was treated with NaH (60% in mineral oil, 4.9 g, 123.3 mmol). Methyl iodide was added dropwise at 0 °C. The reaction mixture was stirred at 25 °C for 12 h.

- 10 The reaction mixture was quenched with water (200 ml) and extracted with EtOAc. The combined organics were dried and concentrated under reduced pressure. The crude product was purified by column chromatography utilizing an ISCO system (hexane-EtOAc) to give 5.5 g (66%) of a colourless oil. NMR: 8.05 (s, 1H), 7.90 (d, 1H), 7.75 (d, 1H), 7.55 (m, 1H), 3.80 (s, 3H), 1.62 (s, 6H); *m/z* 203.

15

Methods 9-18

The following compounds were prepared by the procedure of Method 8, using the appropriate starting material.

Meth	Compound	m/z	SM
9	2-Methyl-2-(2-thienyl)propanenitrile	152	2-Thienyl acetonitrile
10	Methyl 4-chloro-3-(1-cyano-1-methylethyl)benzoate	238	Method 2

Meth	Compound	m/z	SM
11	2-[4-({[tert-Butyl(diphenyl)silyl]oxy}methyl)-2-thienyl]-2-methylpropanenitrile	421	Method 3
12	Methyl 3-(1-cyano-1-methylethyl)-5-methylbenzoate	217	Method 4
13	Methyl 5-(1-cyano-1-methylethyl)nicotinate	205	Method 5
14	Methyl 5-(1-cyano-1-methylethyl)-2-fluorobenzoate	222	Method 7
15	2-(2-Fluoro-3-methylphenyl)-2-methylpropanenitrile	178	Method 6
16	Methyl 2-(3-bromophenyl)-2-methylpropanoate	258	Method 89
17	2-(3-Bromophenyl)-2-methylpropyl methyl ether	244	Method 179
18	2-(3-Bromo-5-fluorophenyl)-2-methylpropanenitrile	298	Method 199 and Methyl iodide

Method 19

3-(1-Cyano-1-methylethyl)benzoic acid

A solution of 3-(1-cyano-1-methylethyl)benzoic acid methyl ester (Method 8; 5.5 g, 27.1 mmol) in 100 ml of THF/MeOH/H₂O (3:1:1) was treated with lithium hydroxide (1.95 g) in 20 ml water. The mixture was stirred at 25 °C for 12 h. The solvent was removed under reduced pressure and the resulting solution was diluted with water, then acidified with 10% HCl to pH = 1-3. The resulting white solid (4.83 g, 94%) was filtered, washed with water and dried. NMR: 13.00 (s, 1H), 7.95 (s, 1H), 7.80 (d, 1H), 7.65 (d, 1H), 7.45 (m, 1H), 1.60 (s, 6H); m/z 189.

Methods 20-55

The following compounds were prepared by the procedure of Method 19, using the appropriate starting material.

Meth	Compound	m/z	SM
20	5-[3-(Cyanodimethyl-methyl)-benzoylamino]-2-methylbenzoic acid	336	Method 96
21	2-Methyl-5-{[3-(trifluoromethyl)benzoyl]-amino}benzoic acid	323	Method 97
22	4-[(4-Ethylpiperazin-1-yl)methyl]-3-(trifluoromethyl)benzoic acid	316	Method 143

Meth	Compound	m/z	SM
23	4-[(Dimethylamino)methyl]-3-(trifluoromethyl)benzoic acid	247	Method 144
24	3-(3,3-Dimethylbut-1-yn-1-yl)benzoic acid	203	Method 115
25	3-(3-Hydroxy-3-methylbut-1-yn-1-yl)benzoic acid	204	Method 116
26	4-Chloro-3-(1-cyano-1-methylethyl)benzoic acid	224	Method 10
27	3-(1-Cyano-1-methylethyl)-5-[(4-methylpiperazin-1-yl)methyl]benzoic acid	301	Method 145
28	3-(1-Cyano-1-methylethyl)-5-[(dimethylamino)methyl]benzoic acid	246	Method 146
29	5-[[2-(1-Cyano-1-methylethyl)isonicotinoyl]amino]-2-methylbenzoic acid	323	Method 98
30	5-Piperidin-1-yl nicotinic acid	207	Method 234
31	5-Morpholin-4-yl nicotinic acid	209	Method 235
32	5-(Diethylamino)nicotinic acid	195	Method 236
33	5-(1-Cyano-1-methylethyl)nicotinic acid	191	Method 13
34	3-Cyclopropylbenzoic acid	163	Method 237
35	4-[(4-Methylpiperazin-1-yl)methyl]-3-(trifluoromethyl)benzoic acid	303	Method 147
36	2-[(Dimethylamino)methyl]-5-(trifluoromethyl)benzoic acid	248	Method 148
37	3-(1-Cyano-1-methylethyl)-5-[(methylthio)methyl]benzoic acid	250	Method 253
38	Sodium [3-carboxy-5-(1-cyano-1-methylethyl)phenyl]methanesulfonate	283	Method 254
39	1,3,3-Trimethyl-2-oxoindoline-5-carboxylic acid	219	Method 218
40	3-{1-[(Dimethylamino)sulfonyl]-1-methylethyl}benzoic acid	271	Method 160
41	3-(1,1-Dimethylprop-2-yn-1-yl)benzoic acid	188	Method 161
42	3-(1,1-Dimethylbut-2-yn-1-yl)benzoic acid	202	Method 164
43	3-(2,3-Dihydroxy-1,1-dimethylpropyl)benzoic acid	224	Method 166
44	3-(1-Cyclopropyl-1-methylethyl)benzoic acid	205	Method 238
45	3-[[[(Dimethylamino)carbonyl]amino]benzoic acid	209	Method 168
46	3-(1-Cyclopropyl-1-hydroxyethyl)benzoic acid	206	Method 170
47	3-(1,1-Difluoroethyl)benzoic acid	186	Method 171

Meth	Compound	m/z	SM
48	3-[Cyclopropyl(hydroxy)methyl]benzoic acid	193	Method 172
49	3-(1-Methylcyclopropyl)benzoic acid	177	Method 239
50	3-(1-Cyano-1-methylethyl)-5-{{methoxy(methyl)amino}methyl}benzoic acid	262	Method 174
51	3-(1,3-Thiazol-2-yl)benzoic acid	205	Method 176
52	2-(3-Bromophenyl)-2-methylpropanoic acid	244	Method 16
53	5-(1-Cyano-1-methylethyl)-2-fluorobenzoic acid	208	Method 14
54	5-({3-[2-(Dimethylamino)-1,1-dimethyl-2-oxoethyl]benzoyl}amino)-2-methylbenzoic acid	369	Method 182
55	5-[(5-[(Dimethylamino)sulfonyl]pyridin-3-yl}carbonyl)amino]-2-methylbenzoic acid	364	Method 183

Method 564-Methyl-3-trifluoromethyl-benzoic acid methyl ester

A solution of KOH (84 mg, 1.5 mmol) in DMSO (5 ml) was stirred for 30 min at 25 °C. The above slurry was then treated with 4-methyl-3-trifluoromethyl-benzoic acid (306 mg, 1.5 mmol) in DMSO (5 ml) and the resulting mixture was stirred for 15 min, and iodomethane (426 mg, 3 mmol) was then added to the mixture. The reaction was stirred for 2 h at 25 °C and then quenched with water. The resulting solution was extracted with EtOAc. The organic layer was washed with NaCl_(sat) and dried with Na₂SO_{4(s)}. The organics were removed under reduced pressure to give the title compound as an oil 327 mg (100%). NMR: 8.10 (m, 2H), 7.60 (s, 1H), 3.86 (s, 3H), 2.45 (s, 3H); *m/z* 218.

Method 572-Methyl-5-nitro-*N*-pyridin-3-ylbenzamide

A solution of 2-methyl-5-nitrobenzoic acid (1.4 grams, 7.7 mmol) and 3-aminoaniline (0.73 g, 7.7 mmol) in DMF (10 ml) was treated with HATU (2.2 grams, 7.7 mmol) and pyridine (5 equiv). The resulting solution was stirred at 25 °C for 48 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography utilizing an ISCO system to afford 1.65 grams (84% yield) of the title compound as a white, crystalline solid. NMR (300 MHz): 10.82 (s, 1H), 8.91 (d, 1H), 8.35-8.39 (m, 2H), 8.26-8.29 (m, 1H), 8.20 (d, 1H), 7.95 (s, 1H), 7.64 (d, 1H), 7.43-7.48 (m, 1H), 2.68 (s, 3H); *m/z* 258.

Methods 58-67

The following compound was prepared by the procedure of Method 57, using the appropriate starting material.

Meth	Compound	m/z	SM
58	2-Fluoro-5-nitro- <i>N</i> -pyridin-3-ylbenzamide	261	2-Fluoro-5-nitrobenzoic acid
59	2-Chloro-5-nitro- <i>N</i> -pyridin-3-ylbenzamide	278	2-Chloro-5-nitrobenzoic acid
60	2-Methyl-5-nitro- <i>N</i> -(6-amino-5-chloropyridin-3-yl)benzamide	308	2-Methyl-5-nitrobenzoic acid and Method 186
61	<i>N</i> -(5-Methoxypyridin-3-yl)-2-methyl-5-nitrobenzamide	288	2-Methyl-5-nitrobenzoic acid and Method 118
62	2-Chloro- <i>N</i> -(5-methoxypyridin-3-yl)-5-nitrobenzamide	309	2-Chloro-5-nitrobenzoic acid and Method 118
63	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-2-methyl-5-nitrobenzamide	315	2-Methyl-5-nitrobenzoic acid and <i>N</i> -(5-amino pyridin-2-yl)acetamide
64	2-Methoxy-5-nitro- <i>N</i> -pyridin-3-ylbenzamide	273	2-Methoxy-5-nitrobenzoic acid and 3-aminopyridine
65	2-Chloro- <i>N</i> -(5-fluoropyridin-3-yl)-5-nitrobenzamide	296	2-Chloro-5-nitrobenzoic acid and Method 252
66	<i>N</i> -(5-Bromopyridin-3-yl)-2-chloro-5-nitrobenzamide	357	2-Chloro-5-nitrobenzoic acid and Method 119
67	<i>N</i> -(5-Isopropoxypyridin-3-yl)-2-methyl-5-nitrobenzamide	316	Method 219 and 2-methyl-5-nitrobenzoic acid

5 Method 68**5-Amino-2-methyl-*N*-pyridin-3-ylbenzamide**

A solution of 2-methyl-5-nitro-*N*-pyridin-3-ylbenzamide (Method 57; 1.65 grams, 6.4 mmol) in MeOH was treated with 10% Pd/C and hydrogenated for 45 min at 10 psi using a Parr Hydrogenator. The catalyst was removed by filtration and the solvent evaporated. The crude product was purified by column chromatography utilizing an ISCO system to provide 975 mgs (67% yield) of white solid. NMR (300 MHz): 10.25 (s, 1H), 8.71-8.72 (m, 1H),

8.11-8.14 (m, 1H), 8.01 (d, 1H), 8.18-8.23 (m, 1H), 6.79 (d, 1H), 6.63-6.64 (m, 1H), 6.42-6.46 (m, 1H), 4.96 (bs, 2H), 2.04 (s, 3H); m/z 228.

Methods 69-74

- 5 The following compounds were prepared by the procedure of Method 68, using the appropriate starting material.

Method	Compound	M/z	SM
69	5-Amino- <i>N</i> -(5-methoxypyridin-3-yl)-2-methylbenzamide	258	Method 61
70	<i>N</i> -[6-(Acetylamino)pyridin-3-yl]-5-amino-2-methylbenzamide	285	Method 63
71	5-Amino-2-methoxy- <i>N</i> -pyridin-3-ylbenzamide	244	Method 64
72	5-Amino- <i>N</i> -(5-isopropoxypyridin-3-yl)-2-methylbenzamide	286	Method 67
73	Tert-Butyl {2-[(5-aminopyridin-2-yl)amino]ethyl}carbamate	253	Method 207
74	2-Methylpyridine-3,5-diamine	124	Method 200

Method 75

5-Amino-2-fluoro-*N*-pyridin-3-ylbenzamide

- 10 A solution of 2-fluoro-5-nitro-*N*-pyridin-3-ylbenzamide (Method 58; 127 mg, 0.487 mmol) in MeOH (2 ml) was treated with an excess of zinc metal and acetic acid (150 μ l, 2.5 mmol). The reaction was heated to reflux for 30 min then cooled to 25 °C. The solids were removed by filtration through a pad of diatomaceous earth and the solvents were removed under reduced pressure. The crude product was purified by column chromatography utilizing
15 an ISCO system to provide the title compound (35 mgs, 31% yield); m/z 231.

Methods 76-82

The following compounds were prepared by the procedure of Method 75, using the appropriate starting material.

Meth	Compound	m/z	SM
76	5-Amino-2-chloro- <i>N</i> -pyridin-3-ylbenzamide	248	Method 59
77	3-Bromopyridine-2,5-diamine	188	3-Bromo-5-nitro pyridin-2-amine

Meth	Compound	m/z	SM
78	5-Amino-2-chloro- <i>N</i> -(5-methoxypyridin-3-yl)benzamide	278	Method 62
79	5-Amino-2-chloro- <i>N</i> -(5-fluoropyridin-3-yl)benzamide	267	Method 65
80	5-Amino- <i>N</i> -(5-bromopyridin-3-yl)-2-chlorobenzamide	327	Method 66
81	5-Amino- <i>N</i> -(6-amino-5-chloropyridin-3-yl)-2-methylbenzamide	278	Method 60
82	<i>tert</i> -Butyl 2-{[(5-aminopyridin-2-yl)amino]methyl}pyrrolidine-1-carboxylate	294	Method 157

Method 834-(5-Nitropyridin-2-yl)morpholine

A solution of 2-chloro-5-nitropyridine (400 mg, 1.52 mmol) and DIEA (440 μ L, 1.52 mmol) in EtOH (10 ml) was treated with morpholine (660 μ L, 4.56 mmol). The solution was heated up at 70 °C for 12 h. The solvents were removed under reduced pressure. *M/z* 211.

Method 846-Morpholin-4-ylpyridin-3-amine

A solution of 4-(5-nitropyridin-2-yl)morpholine (Method 83; 418 mg, 2 mmol) in MeOH (5 ml) was treated with a solution of ammonium chloride (540 mg, 10 mmol) and iron powder in water (5 ml). The resulting solution was heated to 78 °C for 2 h. The solution was then filtered at 50 °C and the solvents were removed under reduced pressure. The crude product was dissolved in acetone and filtered to remove any inorganic salts. The organic phase was then concentrated in vacuo to give the title compound material. *M/z* 179.

Method 85

The following compound was prepared by the procedure of Method 84, using the appropriate starting material.

Meth	Compound	m/z	SM
85	6-Chloro-5-methylpyridin-3-amine	337	2-Chloro-3-methyl-5-nitropyridine

Method 86**Methyl 2-methyl-5-nitrobenzoate**

- A solution of 2-methyl-5-nitrobenzoic acid (3.9 g, 21.5 mmol) in MeOH (20 ml) was treated with $\text{HCl}_{(\text{g})}$ for 10 min. The reaction was then refluxed in a sealed tube at 65 °C for 24 h. The solvent was evaporated giving a cream coloured solid (4.8 g) which was dissolved in EtOAc (200 ml), washed with H_2O (200 ml) and brine (200 ml), and dried with MgSO_4 . The solvents were removed under reduced pressure to give a white solid (3.4 g). *M/z*: 179.

Methods 87-91

- The following compounds were prepared by the procedure of Method 86, using the appropriate starting material.

Ex	Compound	M/z	SM
87	Methyl 3-acetylbenzoate	179	3-acetylbenzoic acid
88	Methyl 2-fluoro-5-methylbenzoate	169	2-Fluoro-5-methyl benzoic acid
89	Methyl (3-bromophenyl)acetate	230	(3-Bromophenyl)-acetic acid
90	Methyl 5-aminopyridine-2-carboxylate	153	5-aminopyridine-2-carboxylic acid
91	Methyl 2-chloro-5-nitrobenzoate	216	2-chloro-5-nitrobenzoic acid

Method 92**Methyl 5-amino-2-methylbenzoate**

- A solution of methyl 2-methyl-5-nitrobenzoate (Method 86; 3.4 g) and 10% palladium on carbon (672 mg) in MeOH (20 ml) was treated with H_2 for 48 h. The reaction mixture was then filtered through diatomaceous earth and washed with MeOH (20 ml) and EtOAc (10 ml). The solvents were removed under reduced pressure to give a brown oil (2.7 g). *M/z* 165.

20 Methods 93-95

The following compounds were prepared by the procedure of Method 92, using the appropriate starting material.

Meth	Compound	m/z	SM
93	N^2 -Methylpyridine-2,5-diamine	123	Method 132

Meth	Compound	m/z	SM
94	3-Methylpyridine-2,5-diamine	123	3-Methyl-5-nitropyridin-2-amine
95	Pyridine-3,5-diamine	109	2-Chloro-3,5-dinitropyridine

Method 96Methyl 5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-methylbenzoate

A solution of methyl 5-amino-2-methylbenzoate (Method 92; 2.7 g, 16.4 mmol), 3-
 5 (cyano-dimethyl-methyl)-benzoic acid (3.133 g, 16.6 mmol) and DIEA (8.67 ml, 49.8 mmol)
 in DMF (33 ml) at 0 °C was treated with HATU (9.466 g, 24.9 mmol). The reaction was
 stirred at 25 °C for 24 h. The reaction mixture was quenched with H₂O (30 ml) and then
 extracted with EtOAc (100 ml). The organics were washed with NaCl_(sat) (200 ml) and dried
 with MgSO₄. The solvents were removed under reduced pressure to give a reddish brown oil
 10 (5.58 g) of the title compound. *M/z* 336.

Methods 97-99

The following compounds were prepared by the procedure of Method 96, using the
 appropriate starting material.

Meth	Compound	m/z	SM
97	Methyl 2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino} benzoate	337	3-(Trifluoromethyl)-benzoic acid
98	Methyl 5-{[2-(1-cyano-1-methylethyl)isonicotinoyl]amino}-2-methylbenzoate	337	Method 112
99	<i>N</i> -{6-[(2-{[tert-Butyl(dimethyl)silyl]oxy}ethyl)amino]pyridine-3-yl}-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide	573	Method 188 and Method 21

Method 1005-Methylpyridin-3-amine

A solution of 6-chloro-5-methylpyridin-3-amine (Method 85; 2 mmol) and 10% Pd on
 carbon (20% w/w) in MeOH (10 ml) was treated with H₂. The solution was stirred at 25 °C
 20 for 12 h. The reaction mixture was filtered through a pad of diatomaceous earth and the
 solvents were removed under reduced pressure to yield the title compound which was used
 without further purification. *M/z* 108.

Method 101**tert-Butyl(diphenyl)(3-thienylmethoxy)silane**

To 3-thienylmethanol (5.0 g, 43.8 mmol) was added 86 ml of DMF followed by imidazole (8.94 g, 131.4 mmol). The reaction mixture was cooled to 0 °C and treated with 5 *tert*-butylchlorodiphenylsilane (15.0 g, 54.7 mmol) and was allowed to stir 6 h to 25 °C before being quenched by the addition of 250 ml saturated aqueous NH₄Cl. The resulting mixture was extracted with EtOAc (3 x 125 ml). The combined organic phase was washed 1x with brine (100 ml), dried with MgSO₄, and concentrated *in vacuo*. The crude reaction product was purified on 120 g SiO₂ using hexanes/EtOAc 10:1 as eluent giving 14.8 g of the title 10 compound as a colourless oil (96 %). *M/z* 353.

Method 102

The following compound was prepared by the procedure of Method 101, using the appropriate starting material.

Meth	Compound	m/z	SM
102	3-Bromo-5-({[<i>tert</i> -butyl(diphenyl)silyl]oxy}methyl)pyridine	427	Method 240

Method 103**2-(5-Formyl-2-thienyl)-2-methylpropanenitrile**

THF (5.8 ml) was added to 2-methyl-2-(2-thienyl)propanenitrile (Method 9; 0.260 g, 1.71 mmol) and the reaction mixture was cooled to -78 °C. To the cooled reaction was added 20 1.26 ml of *tert*-butyl lithium (1.7 M solution in pentanes) dropwise via syringe. The resulting bright yellow mixture was allowed to stir for 1 h before DMF (0.330 ml, 4.27 mmol) was added via syringe. The reaction was stirred for 6 h at -78 °C before being quenched by the addition of 25 ml of saturated aqueous NH₄Cl. The resulting mixture was extracted with EtOAc (3 x 25 ml). The combined organic phase was washed 1x with brine (50 ml), dried 25 with MgSO₄, and concentrated *in vacuo* giving 0.271 g of the title compound (88 %) as a colourless oil. *M/z* 180.

Method 104

The following compound was prepared by the procedure of Method 103, using the 30 appropriate starting material.

Meth	Compound	m/z	SM
104	4-([<i>tert</i> -Butyl(diphenyl)silyl]oxy)methyl)thiophene-2-carbaldehyde	381	Method 101

Method 1054-([*tert*-Butyl(diphenyl)silyl]oxy)methyl)-2-thienyl]methanol

4-([*tert*-Butyl(diphenyl)silyl]oxy)methyl)thiophene-2-carbaldehyde (Method 104; 3.99 g, 10.48 mmol) was dissolved in MeOH (50 ml). With stirring, NaBH₄ (0.792 g, 20.96 mmol) was added in one portion. After 1 h, the reaction was carefully quenched with a solution of NH₄Cl_(sat) (~250 ml). The resulting mixture was extracted with EtOAc (3 x 125 ml). The combined organic phase was washed with brine (250 ml), dried with MgSO₄, and concentrated *in vacuo* giving the crude reaction product which was purified on 120 g SiO₂ using hexanes/EtOAc 5:2 as eluent giving 3.99 g of the title compound as a colourless oil (98 %) m/z 384.

Method 106{[5-(Bromomethyl)-3-thienyl]methoxy}(*tert*-butyl)diphenylsilane

Anhydrous THF (45 ml) was added to 4-([*tert*-butyl(diphenyl)silyl]oxy)methyl)-2-thienyl]methanol (Method 105; 4.2 g, 10.98 mmol). Phosphorous tribromide (3.56 g, 13.17 mmol) was added dropwise via syringe and the reaction was allowed to stir for 1 h. at 25 °C before being quenched by NaHCO_{3(sat)} (250 ml). The reaction mixture was extracted with EtOAc (2 x 250 ml) and the combined organic phase was dried with MgSO₄ and concentrated *in vacuo* to yield the crude reaction product which was purified on 120 g SiO₂ using hexanes/EtOAc 10:1 as eluent giving 3.70 g of the title compound as a yellow oil (76 %) m/z 447.

Method 1072-[4-(Hydroxymethyl)-2-thienyl]-2-methylpropanenitrile

Anhydrous THF (25 ml) was added to 2-[4-([*tert*-butyl(diphenyl)silyl]oxy)methyl)-2-thienyl]-2-methylpropanenitrile (Method 11; 0.880 g, 2.10 mmol). A 1 M solution of tetrabutylammonium fluoride in THF (5.25 mmol) was added dropwise via syringe and the reaction was allowed to stir for 12 h at 25 °C before being quenched with NH₄Cl_(sat) (50 ml). The reaction mixture was extracted with EtOAc (2 x 50 ml) and the combined organic phase

was dried with MgSO_4 and concentrated *in vacuo* to yield the crude reaction product which was purified on 40 g SiO_2 using hexanes/EtOAc 2:1 as eluent giving 0.270 g of the title compound as a colourless oil (71 %) m/z 182.

5 Method 108

2-(4-Formyl-2-thienyl)-2-methylpropanenitrile

To DMSO (0.277 g, 3.55 mmol) was added 10 ml of anhydrous DCM. The reaction was cooled to -78°C and oxalyl chloride (0.225 g, 1.78 mmol) was added dropwise via syringe and the reaction was allowed to stir for 30 min. at this temperature. A 1 M solution of 10 2-[4-(hydroxymethyl)-2-thienyl]-2-methylpropanenitrile (Method 107; 0.270 g, 1.48 mmol) in DCM was then added dropwise via syringe and the reaction was allowed to stir for 30 min. at this temperature. Triethylamine (0.718 g, 7.40 mmol) was then added and the reaction was allowed to warm to 25°C with stirring over 1 h before being quenched with $\text{NaHCO}_{3(\text{sat})}$ (250 ml). The reaction mixture was then extracted with EtOAc (2 x 50 ml) and the combined 15 organic phase was dried with MgSO_4 and concentrated *in vacuo* to yield the crude reaction product which was purified on 40 g SiO_2 using hexanes/EtOAc 10:1 as eluent giving 0.262 g of the title compound as a colourless oil (99 %) m/z 180.

Method 109

20 5-(1-Cyano-1-methylethyl)thiophene-2-carboxylic acid

To 2-(5-formyl-2-thienyl)-2-methylpropanenitrile (Method 103; 0.271 g, 1.51 mmol) was added 7.5 ml of tertiary butyl alcohol and 4.5 ml of 2-methyl-2-butene. The reaction mixture was treated dropwise with an aqueous pre-mixed solution of NaClO_2 (1.22 g, 13.60 mmol) and NaH_2PO_4 (1.45 g, 10.57 mmol) in 7 ml of H_2O . The reaction mixture was stirred 25 for 30 min. at 25°C before the volatiles were removed on a rotary evaporator. The resulting crude product was washed with $\text{NaHCO}_{3(\text{sat})}$ (1 x 50 ml) and extracted was extracted with EtOAc (3 x 25 ml). The combined organic phase was washed 1x with brine (50 ml), dried with MgSO_4 , and conc. *in vacuo* giving 0.265 g of the title compound (90 %) as a white solid. M/z 196.

30

Method 110

The following compound was prepared by the procedure of Method 109, using the appropriate starting material.

Meth	Compound	m/z	SM
110	5-(1-Cyano-1-methylethyl)thiophene-3-carboxylic acid	196	Method 108

Method 111**2-Methyl-2-(4-methylpyridin-2-yl)propanenitrile**

2-Fluoro-4-methylpyridine (1.00 g, 9.00 mmol), 2-methylpropanenitrile (2.48 g, 36 mmol), and anhydrous toluene (30 ml) were stirred. Potassium hexamethyldisilazide (13.5 mmol) was added and the reaction was refluxed for 1 h. before being cooled to 25 °C. The reaction was quenched with $\text{NH}_4\text{Cl}_{(\text{sat})}$ (50 ml) and the mixture was extracted with EtOAc (2 x 50 ml). The combined organic phase was dried with MgSO_4 and concentrated *in vacuo* to yield the crude reaction product which was purified on 40 g SiO_2 using hexanes/EtOAc 5:1 as eluent giving 0.870 g of the title compound as a colourless oil (60 %). *M/z* 161.

Method 112**2-(1-Cyano-1-methylethyl)isonicotinic acid**

Water (15 ml) was added to 2-methyl-2-(4-methylpyridin-2-yl)propanenitrile (Method 111; 0.870 g, 5.43 mmol). The reaction mixture was heated to 60 °C and KMnO_4 (4.3 g, 27 mmol) was added. The reaction was heated to reflux for 2 h, and was then filtered through a bed of diatomaceous earth. The pH was adjusted to 4 by the careful addition of 1 N HCl and the aqueous phase was extracted with EtOAc (4 x 25 ml). The organic phase was dried with MgSO_4 and concentrated *in vacuo* to yield the crude reaction product which was purified on 40 g SiO_2 using EtOAc/MeOH 10:1 as eluent giving 0.700 g of the title compound as a white solid (68 %); *m/z* 191.

Methods 113-114

The following compounds were prepared by the procedure of Method 112, using the appropriate starting material.

Meth	Compound	m/z	SM
113	3-tert-Butylbenzoic acid	179	1-tert-Butyl-3-methylbenzene
114	3-(1-Cyano-1-methylethyl)-2-fluorobenzoic acid	208	Method 15

Method 115Ethyl 3-(3,3-dimethylbut-1-yn-1-yl)benzoate

MeCN (8.70 ml) was added to ethyl 3-bromobenzoate (0.500 g, 2.18 mmol). Triethylamine (1.53 ml, 10.9 mmol) was added followed by 3,3-dimethylbut-1-yne (0.27 g, 3.27 mmol). With stirring Pd(PPh₃)₄ (0.25 g, 0.21 mmol) and CuI (0.083 g, 0.436 mmol) were added and the reaction was warmed to 60 °C for 4 h. The reaction was then diluted with EtOAc (~ 50 ml) and filtered through a pad of SiO₂, and concentrated *in vacuo*. The crude product was purified on 40 g SiO₂ using hexanes/EtOAc 10:1 as eluent giving 0.45 g of the title compound as a colourless oil (91 %); m/z 231.

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Method 116

The following compound was prepared by the procedure of Method 115, using the appropriate starting material.

Meth	Compound	m/z	SM
116	Methyl 3-(3-hydroxy-3-methylbut-1-yn-1-yl)benzoate	218	Methyl 3-bromobenzoate and 2-methylbut-3-yn-2-ol

15 **Method 117**5-Methoxynicotinic acid

A solution of methyl 5-hydroxynicotinate (633 mg, 4.1 mmol) in DMSO (7 ml) was treated with potassium hydroxide (918 mg, 16.4 mmol). The solution was stirred at 25 °C for 1 h. Methyl iodide (2.0 M in THF, 2.25 ml, 4.5 mmol) was then added. The solution was stirred an additional 1 h. The reaction was quenched with H₂O and extracted with EtOAc. The water layer was concentrated under reduced pressure to give 494 mg of crude product, 78.8%. M/z 153.

Method 11825 5-Methoxypyridin-3-amine hydrochloride:

A solution of 5-methoxynicotinic acid (Method 117; 494 mg, 3.24 mmol) and DIEA (1.1 ml, 6.5 mmol) in tert-BuOH (16 ml) was treated with diphenylphosphoryl azide (1.4 ml, 6.5 mmol). The resulting solution was heated at 85 °C for 5 h. The solution was then concentrated under reduced pressure and the crude product was dissolved in 4.0 M HCl in dioxane (20 ml). The solution was stirred at 25 °C for 12 h. The solvents were removed under

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reduced pressure to give 392 mg, 75.4% of the title compound as its hydrochloride salt. *M/z* 124.

Method 119

- 5 The following compounds were prepared by the procedure of Method 118, using the appropriate starting material.

Meth	Compound	m/z	SM
119	5-Bromopyridin-3-amine	173	5-Bromonicotinic acid

Method 120

3-[(Dimethylamino)sulfonyl]benzoic acid

- 10 A solution of 3-(chlorosulfonyl) benzoic acid (2.60 g, 12 mmol) in DCM (20 ml) was treated with dimethylamine (2.0 M in THF, 20 ml, 40 mmol, 3.3 equiv). After 30 min, the reaction was quenched with 10% HCl and extracted with EtOAc. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. The organics were then removed under reduced pressure to give 1.80 g, 65%; *m/z* 229.

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Methods 121-131

The following compounds were prepared by the procedure of Method 120, using the appropriate starting material.

Meth	Compound	m/z	SM
121	3-(Azetidin-1-ylsulfonyl)-benzoic acid	241	Azetidine
122	3-[(Cyclopropylamino)sulfonyl]benzoic acid	241	Cyclopropylamine
123	3-[[3-(Hydroxymethyl)piperidin-1-yl]sulfonyl]benzoic acid	300	Piperidin-3-ylmethanol
124	3-[[2-(Hydroxymethyl)piperidin-1-yl]sulfonyl]benzoic acid	300	Piperidin-2-ylmethanol
125	3-[[Methoxy(methyl)amino]sulfonyl]benzoic acid	246	(Methoxyamino)-methane
126	3-[[2,3-Dihydroxypropyl](methyl)amino]sulfonyl]benzoic acid	304	3-(Methylamino)propane-1,2-diol

Meth	Compound	m/z	SM
127	3-{[(Tetrahydrofuran-2-ylmethyl)amino]sulfonyl} benzoic acid	286	(Tetrahydrofuran-2-ylmethyl)amine
128	3-(Morpholin-4-ylsulfonyl)benzoic acid	272	Morpholine
129	<i>N,N</i> -Dimethylpyridine-3-sulfonamide	187	3-Pyridine sulfonyl chloride hydrochloride and dimethylamine
130	3-(Aminosulfonyl)benzoic acid	202	Ammonia
131	3-{[4-(Hydroxymethyl)piperidin-1-yl]sulfonyl}benzoic acid	300	Piperidin-4-ylmethanol

Method 132*N*-Methyl-5-nitropyridin-2-amine

A solution of 2-chloro-5-nitropyridine (400 mg, 1.52 mmol) was dissolved in 2.0 M methyl amine in MeOH (5 ml). The solution was heated up at 70 °C for 12 h. The solvents were removed under reduced pressure; *m/z* 153.

Method 1335-Amino-*N*-methylnicotinamide

A solution of 5-aminonicotinic acid (414 mg, 3 mmol), DIEA (1.57 ml, 9 mmol) and methyl amine (2.0 M in THF, 4.5 ml, 9 mmol) in DMF (10 ml) was treated with HATU (1.71 g, 4.5 mmol). The reaction was stirred for 5 h and then quenched with H₂O (30 ml). The reaction mixture was extracted with EtOAc (50 ml), washed with NaCl_(sat) (20 ml) and dried with MgSO₄. The organics were removed under reduced pressure; *m/z* 151.

Method 134

The following intermediate were prepared according to the procedure of Method 133 using the appropriate starting materials.

Method	Compound	m/z	SM
134	5-Aminonicotinamide	138	ammonia

Method 135**4-Bromomethyl-3-trifluoromethyl-benzoic acid methyl ester**

A suspension of 4-methyl-3-trifluoromethyl-benzoic acid methyl ester (Method 56; 327 mg, 1.5 mmol), NBS (267 mg, 1.5 mmol) and catalytic amount of benzoyl peroxide in 5 CCl₄ (10 ml) was heated to reflux for 3 h. The reaction mixture was cooled to 25 °C, filtered through a pad of silica gel, and washed with DCM. The organics were removed under reduced pressure and the crude product was purified by column chromatography utilizing an ISCO system (hexane-EtOAc) to give 252 mg (56.5%). NMR: 7.70-8.25 (m, 3H), 4.85 (s, 2H), 3.91 (s, 3H); *m/z* 297.

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Methods 136-142

The following compounds were prepared by the procedure of Method 135, using the appropriate starting material.

Meth	Compound	<i>m/z</i>	SM
136	Methyl 3-(bromomethyl)-4-chlorobenzoate	264	Methyl 4-chloro-3-methylbenzoate
137	Methyl 3-(bromomethyl)-5-methylbenzoate	243	Methyl 3,5-dimethylbenzoate
138	Methyl 3-(bromomethyl)-5-(1-cyano-1-methylethyl)benzoate	296	Method 12
139	Methyl 2-(bromomethyl)-5-(trifluoromethyl)benzoate	298	Methyl 2-methyl-5-(trifluoromethyl)benzoate
140	Methyl 5-(bromomethyl)nicotinate	231	Methyl 5-methylnicotinate
141	Methyl 5-(bromomethyl)-2-fluorobenzoate	248	Method 88
142	Methyl 4-(bromomethyl)-3-(trifluoromethyl)benzoate	298	Methyl 4-methyl-3-(trifluoromethyl)benzoate

15 **Method 143****Methyl 4-[(4-ethylpiperazin-1-yl)methyl]-3-(trifluoromethyl)benzoate**

A mixture of 4-bromomethyl-3-trifluoromethyl-benzoic acid methyl ester (Method 135; 252 mg, 0.85 mmol), *N*-ethyl piperazine (193 mg, 1.70 mmol) and potassium carbonate (235 mg, 1.70 mmol) in MeCN (10 ml) was stirred at 80 °C for 4 h. The reaction mixture was

then loaded on silica gel and purified by column chromatography utilizing an ISCO system (hexane-EtOAc) to give 172 mg, (61.5%). NMR: 8.20 (d, 1H), 8.15 (s, 1H), 7.94 (d, 1H), 3.89 (s, 3H), 3.68 (s, 2H), 2.40 (bs, 8H), 2.30 (q, 2H), 0.98 (t, 3H); m/z 330.

5 Methods 144-145

The following compounds were prepared by the procedure of Method 143, using the appropriate starting material.

Meth	Compound	m/z	SM
144	Methyl 4-[(dimethylamino)methyl]-3-(trifluoromethyl)benzoate	261	Dimethylamine and Method 135
145	Methyl 3-(1-cyano-1-methylethyl)-5-[(4-methylpiperazin-1-yl)methyl]benzoate	315	Methyl piperazine and Method 138
146	Methyl 3-(1-cyano-1-methylethyl)-5-[(dimethylamino)methyl]benzoate	260	Dimethylamine and Method 138
147	Methyl 4-[(4-methylpiperazin-1-yl)methyl]-3-(trifluoromethyl)benzoate	317	Methyl piperazine and Method 142
148	Methyl 2-[(dimethylamino)methyl]-5-(trifluoromethyl)benzoate	262	Dimethylamine and Method 139

Method 149

10 N-Cyclopropyl-5-nitropyridin-2-amine

To a 100 ml round bottom flask charged with a magnetic stir bar and 2-bromo-5-nitropyridine (1.00 g, 4.92 mmol) was added EtOH (20 ml). Et₃N (2.80 ml, 20 mmol) was added followed by cyclopropyl amine (0.86 g, 15 mmol) and the reaction was warmed to 70 °C with stirring for 4 h before being cooled to room temperature. The crude reaction mixture was then quenched with ~150 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~150 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the title compound as a yellow solid 0.850 g (96%), which was used without further purification; m/z 180.

Methods 150-158

The following compounds were prepared by the procedure of Method 149, using the appropriate starting material.

Meth	Compound	m/z	SM
150	<i>N</i> -Isopropyl-5-nitropyridin-2-amine	182	isopropylamine
151	(2 <i>R</i>)-3-[(5-Nitropyridin-2-yl)amino]propane-1,2-diol	214	(2 <i>R</i>)-3-aminopropane-1,2-diol
152	2-[(5-Nitropyridin-2-yl)amino]propane-1,3-diol	214	2-aminopropane-1,3-diol
153	1-(5-Nitropyridin-2-yl)piperazine	209	piperazine
154	5-Nitro- <i>N</i> -(3-pyrrolidin-1-ylpropyl)pyridin-2-amine	251	(3-pyrrolidin-1-ylpropyl)amine
155	<i>N</i> -(5-Nitropyridin-2-yl)butane-1,4-diamine	211	butane-1,4-diamine
156	<i>N</i> -(2-{[tert-Butyl(dimethyl)silyl]oxy}ethyl)-5-nitropyridin-2-amine	298	2-((tert-butyl(dimethyl)silyl)oxy)ethyl amine
157	<i>tert</i> -Butyl 2-[[[(5-nitropyridin-2-yl)amino]methyl]pyrrolidine-1-carboxylate	323	<i>tert</i> -butyl 2-(aminomethyl)pyrrolidine-1-carboxylate
158	<i>N</i> -Cyclobutyl-5-nitropyridin-2-amine	194	cyclobutylamine

5 Method 159**Methyl 3-[[[(dimethylamino)sulfonyl]methyl]benzoate**

To a solution of sodium [3-(methoxycarbonyl)phenyl]methanesulfonate (Method 225; 3.3 g, 13.0 mmol) in DCM at -40 °C was added PCl₅. The reaction was allowed to warm to room temperature with stirring over 4 hours. The crude reaction was filtered, and concentrated *in vacuo* to yield the crude product that was subjected to ISCO purification using EtOAc/hexanes (3:1) as the eluent produced 372 mg of the sulfonyl chloride intermediate. The intermediate was then diluted in a solution of K₂CO₃, HNMe₂ and DCM. After allowing the reaction mixture to stir for 10 minutes, the mixture was concentrated *in vacuo* to yield the crude product that was purified on an ISCO using EtOAc/hexanes (1:4) which yielded 165 mg (5 %) of the title compound as a yellow solid. ¹H NMR (300 MHz): 7.95 - 8.03 (m, 2H), 7.58 (d, 1H), 7.42 (t, 1H), 4.21 (s, 2H), 3.87 (s, 3H), 2.71 (s, 6H).

Method 160Methyl 3-{1-[(dimethylamino)sulfonyl]-1-methylethyl}benzoate

A solution of methyl 3-{[(dimethylamino)sulfonyl]methyl}benzoate (Method 159; 165 mg, 0.642 mmol) in anhydrous THF (5 ml) was treated with NaHMDS (1.4 ml, 1.41 mmol) at -78 °C. Immediately, iodomethane (0.1 ml, 1.61 mmol) was added and the reaction mixture was allowed to gradually warm to room temperature while stirring for an additional 2 h. The reaction mixture was then quenched with aqueous NH₄Cl and extracted with EtOAc. The combined organic extracts were dried with MgSO₄ and concentrated *in vacuo* to yield the crude product. The crude product was purified by column chromatography utilizing an ISCO system EtOAc/hexanes (1:5) to give 85 mg (47%) of title compound. ¹H NMR (300 MHz): 8.26 (s, 1H), 7.97 - 8.09 (m, 1H), 7.89 (d, 1H), 7.47 (t, 1H), 3.95 (s, 3H), 2.55 - 2.67 (m, 6H), 1.86 (s, 6H).

Method 161

The following compounds were prepared by the procedure of Method 160, using the appropriate starting material.

Meth	Compound	M/z	SM
161	Methyl 3-[1,1-dimethyl-3-(trimethylsilyl)prop-2-yn-1-yl]benzoate	276	Method 162

Method 162Methyl 3-[3-(trimethylsilyl)prop-2-yn-1-yl]benzoate

Trimethylsilyl acetylene (2.4 ml, 17.0 mmol) was added to a solution of methyl 3-(bromomethyl)benzoate (3.0 g, 13.1 mmol), Pd₂dba₃ (300 mg, 0.3 mmol), triphenylphosphine (343 mg, 1.3 mmol), Cs₂CO₃ (6.0 g, 18.3 mmol), and CuI (187 mg, 1.0 mmol) in THF (50 ml). The reaction mixture was stirred overnight at 50 °C. After allowing the mixture to cool to room temperature, it was then diluted with EtOAc (~ 100 ml) and washed with brine. The mixture was then filtered through a pad of diatomaceous earth, dried over Na₂SO₄ and concentrated *in vacuo*. The crude product was purified on SiO₂ using hexanes/EtOAc 4:1 as eluent giving 2.2 g (67 %) of the title compound. ¹H NMR (300 MHz): 8.03 (s, 1H), 7.92 (d, 1H), 7.57 (d, 1H), 7.40 (t, 1H), 3.93 (s, 3H), 3.71 (s, 2H), 0.21 (s, 9H).

Method 163**Methyl 3-(1,1-dimethylprop-2-yn-1-yl)benzoate**

To a solution of methyl 3-[1,1-dimethyl-3-(trimethylsilyl)prop-2-yn-1-yl]benzoate (Method 161; 170 mg, 0.62 mmol) in anhydrous MeOH (5 ml) was added potassium carbonate (1.2 g, 9.3 mmol). The reaction was stirred overnight at room temperature, filtered, and concentrated *in vacuo*. The crude product was subjected to ISCO purification using EtOAc/Hexanes (1:5) as eluent to yield 180 mg (70 %) of the title compound as a colourless oil. ¹H NMR (300 MHz): 8.20 (s, 1H), 7.91 (d, 1H), 7.79 (d, 1H), 7.39 (t, 1H), 3.91 (s, 3H), 2.37 (s, 1H), 1.61 (s, 6H).

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Method 164**Methyl 3-(1,1-dimethylbut-2-yn-1-yl)benzoate**

A solution of methyl 3-(1,1-dimethylprop-2-yn-1-yl)benzoate (Method 163; 100 mg, 0.495 mmol) in 1 ml of THF was cooled to -78 °C. A 1M solution of LiHMDS in THF (0.55 ml, 0.55 mmol) was added, followed by methyl iodide (46 µL, 0.743 mmol). The reaction mixture was then allowed to warm to room temperature over 2 h and was then quenched with brine. The mixture was extracted with EtOAc, and the combined organic extract was dried over MgSO₄, filtered, and concentrated *in vacuo* to yield 100 mg (93%) of the title compound which was used without further purification. ¹H NMR (300 MHz): 8.19 (s, 1H), 7.89 (d, 1H), 7.79 (d, 1H), 7.39 (t, 1H), 3.91 (s, 3H), 1.83 - 1.88 (m, 3H), 1.56 (s, 6H).

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Method 165**Methyl 3-(1,1-dimethylprop-2-en-1-yl)benzoate**

To a solution of methyl 3-[1,1-dimethyl-3-(trimethylsilyl)prop-2-yn-1-yl]benzoate (Method 161; 300 mg, 1.49 mmol) and quinoline (4 drops) in anhydrous toluene (5 ml) was added Lindlar's catalyst (50 mg) under an atmosphere of H₂. The reaction mixture was allowed to stir for 5 h at room temperature before being filtered through diatomaceous earth. The filtrate was concentrated *in vacuo* which yielded 170 mg (56 %) of the title compound which was used without further purification. ¹H NMR (300 MHz): 8.03 (s, 1H), 7.86 (d, 2H), 7.52 (d, 2H), 7.36 (t, 2H), 6.01 (dd, 1H), 5.08 (s, 1H), 5.03 (d, 1H), 3.90 (s, 3H), 1.41 (s, 6H).

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Method 166**Methyl 3-(2,3-dihydroxy-1,1-dimethylpropyl)benzoate**

A solution of methyl 3-(1,1-dimethylprop-2-en-1-yl)benzoate (Method 165; 0.273 g, 1.33 mmol) in 2 ml of *tert*-BuOH and 2 ml of H₂O was added NMO and K₂OsO₄(H₂O)₂. The reaction mixture was allowed to stir at room temperature overnight before being quenched with 30 mg of Na₂SO₃. The mixture was extracted with EtOAc and the combined extract was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo* to yield 240 mg (75 %) of the title compound crude was used without further purification. ¹H NMR (300 MHz): 8.06 (s, 1H), 7.90 (d, 1H), 7.59 (d, 1H), 7.40 (t, 1H), 3.82 (d, 1H), 3.53 (d, 1H), 3.37 (t, 1H), 1.38 (d, 6H).

Method 167**3-(1,1-Dimethylpropyl)benzoic acid**

A solution of 3-(1,1-dimethylprop-2-yn-1-yl)benzoic acid (Method 41; 170 mg, 0.90 mmol) in anhydrous MeOH (5 ml) was treated with Pd/C (17 mg). The reaction mixture was placed under an atmosphere of H₂ with a balloon and allowed to stir for 12 h at room temperature. The reaction mixture was then filtered through a pad of diatomaceous earth, and the filtrate was concentrated *in vacuo* which yielded 150 mg (86%) of the title compound which was used without further purification. *M/z* 192.

Method 168**Methyl 3-([(dimethylamino)carbonyl]amino)benzoate**

To a solution of methyl 3-isocyanatobenzoate (1.0 g, 5.64 mmol) in dichloroethane was added triethylamine (2.36 ml, 16.9 mmol) and dimethylamine hydrochloride (550 mg, 6.74 mmol). After allowing the reaction mixture to stir for 10 minutes, the solvent was removed *in vacuo*. The crude product was subjected to ISCO purification using EtOAc/hexanes (1:1) to yield 670 mg (54 %) of the title compound as a white crystalline solid. *M/z* 222.

Method 169**Ethyl 3-(cyclopropylcarbonyl)benzoate**

To a solution of ethyl 3-iodobenzoate (1.8 ml, 10.0 mmol) in THF (40 ml) at -78 °C was added isopropyl magnesium chloride (2.0M, 7.0 ml, 14.0 mmol). After 30 min. of

stirring, CuCN (1.1 g, 12.0 mmol) and LiCl (1.0 g, 24.0 mmol) were added simultaneously. After 20 minutes when reaction mixture colour changed to a orange colour, cyclopropane carbonyl chloride (3.0 ml, 33.0 mmol) was added, and then the reaction mixture was allowed to reach to room temperature over 1 hour with stirring. The mixture was diluted with EtOAc and added to aqueous solution of NH₄Cl. The organic extract was dried over Na₂SO₄, filtered, and concentrated *in vacuo* to yield the crude product which was chromatographed with a ISCO system using EtOAc/hexanes (1:1) as eluent to yield 1.2 g (50%) of the title compound. ¹H NMR (300 MHz): 8.66 (s, 1H), 8.22 (d, 1H), 8.17 (d, 1H), 7.55 (t, 1H), 4.40 (q, 2H), 2.76 - 2.67 (m, 1H), 1.40 (t, 3H), 1.29 - 1.21 (m, 2H), 1.12 - 1.01 (m, 2H).

Method 170

Ethyl 3-(1-cyclopropyl-1-hydroxyethyl)benzoate

A solution of ethyl 3-(cyclopropylcarbonyl)benzoate (Method 169; 363 mg, 1.66 mmol) in THF (6 ml) was cooled to -78 °C. To the reaction mixture was added methyl magnesium bromide (3.0M, 0.73 ml, 2.16 mmol). The reaction was allowed to stir for 3 h at this temperature before being quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc and poured into a separator funnel. The organic extract was collected, dried over Na₂SO₄, and concentrated *in vacuo* to yield the crude product which was purified with an ISCO system using EtOAc/hexanes (1:1) as eluent to yield 1.2 g (50%) of the title compound. ¹H NMR (300 MHz): 8.19 (s, 1H), 7.92 (d, 1H), 7.72 (d, 1H), 7.40 (t, 1H), 4.37 (q, 2H), 1.78 (s, 1H), 1.51 (s, 3H), 1.38 (t, 3H), 1.32 - 1.21 (m, 1H), 0.46-0.37 (m, 4H).

Method 171

Methyl 3-(1,1-difluoroethyl)benzoate

A solution of methyl 3-acetylbenzoate (Method 87; 700 mg, 3.9 mmol) in 5 ml of DeoxoFluorTM was stirred overnight at 85 °C. The reaction was allowed to cool to room temperature and quenched with brine. The mixture was poured into a separator funnel and extracted with EtOAc. The organic extract was dried over Na₂SO₄, filtered, and concentrated *in vacuo* to yield the crude product. The crude oil was then subjected to ISCO purification using EtOAc/hexanes (1:4) as eluent to yield 396 mg (50%) of the title compound as a colourless oil. ¹H NMR (300 MHz): 7.96 (s, 1H), 7.86 (d, 1H), 7.50 (d, 1H), 7.31 - 7.22 (m, 1H), 3.73 (s, 3H), 1.74 (t, 3H).

Method 172**Ethyl 3-[cyclopropyl(hydroxy)methyl]benzoate**

To a solution of ethyl 3-(cyclopropylcarbonyl)benzoate (Method 169; 363 mg, 1.66 mmol) in anhydrous EtOH (5 ml) was added sodium borohydride (70 mg, 1.86 mmol). The reaction was allowed to stir for 3 h at room temperature before being quenched by the addition of saturated aqueous NH₄Cl. The mixture was diluted with EtOAc and poured into a separator funnel. The organic extract was dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was purified with an ISCO system using EtOAc/hexanes (1:1) as eluent which yielded 210 mg (77 %) of the title compound. ¹H NMR (300 MHz): 8.07 (s, 1H), 7.95 (d, 1H), 7.61 (d, 1H), 7.41 (t, 1H), 4.36 (q, 2H), 4.04 (d, 1H), 2.16 (s, 1H), 1.38 (t, 3H), 1.27 - 1.15 (m, 1H), 0.66 - 0.54 (m, 2H), 0.52 - 0.36 (m, 2H).

Method 173**Methyl 3-isopropenylbenzoate**

A solution of methyl triphenylphosphonium iodide in THF (5 ml) was cooled to 0 °C. To the cooled mixture was added *n*-BuLi (2.5 M, 1.0 ml, 2.52 mmol) and the reaction was allowed to stir for 30 min at this temperature. To the mixture was added a solution of methyl 3-acetylbenzoate (Method 87; 375 mg, 2.10 mmol) in THF (15 ml). After stirring at 0 °C for one hour, the reaction was allowed to warm to room temperature and was stirred for an additional 2 h. The mixture was then quenched with water and diluted with EtOAc and poured into a separator funnel. The organic extract was dried over Na₂SO₄, filtered and concentrated *in vacuo* giving the crude product which was purified using an ISCO system with EtOAc/hexanes (1:9) as eluent to yield 108 mg (29%) of the title compound as a colourless oil. ¹H NMR (300 MHz): 8.15 (s, 1H), 7.96 (d, 1H), 7.67 (d, 1H), 7.41 (t, 1H), 5.45 (s, 1H), 5.16 (s, 1H), 3.94 (s, 3H), 2.19 (s, 3H).

Method 174**Methyl 3-(1-cyano-1-methylethyl)-5-{[methoxy(methyl)amino]methyl}benzoate**

To a solution of methyl 3-(bromomethyl)-5-(1-cyano-1-methylethyl)benzoate (Method 138; 176 mg, 0.595 mmol) in 5 ml of DMF was added K₂CO₃ (206 mg, 1.49 mmol) and NHMeOMe·HCl (65 mg, 0.666 mmol). The reaction was warmed to 85 °C and stirred at this temperature for 12 h. The reaction was then cooled to room temperature and quenched with water. The mixture was poured into a separator funnel and extracted with EtOAc. The organic

extract were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude residue was purified on an ISCO using EtOAc/hexanes (1:1) as the eluent giving 88 mg (54%) of the title compound as a colourless oil. ^1H NMR (300 MHz): 8.02 (s, 1H), 7.98 (s, 1H), 7.74 (s, 1H), 3.93 (s, 3H), 3.82 (s, 2H), 3.35 (s, 3H), 2.65 (s, 3H), 1.77 (s, 6H).

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Method 1753-(1-Cyano-1-methylethyl)-5-[(methylsulfonyl)methyl]benzoic acid

To a solution of 3-(1-cyano-1-methylethyl)-5-[(methylthio)methyl]benzoic acid (Method 37; 58 mg, 0.23 mmol) in MeCN (5 ml) and H_2O (3 ml) was added potassium peroxymonosulfate (358 mg, 0.582 mmol). The resulting reaction mixture was allowed to stir at room temperature overnight before being quenched with water. The mixture was poured into a separator funnel and extracted with EtOAc. The organic extract was dried over Na_2SO_4 , filtered, and concentrated *in vacuo* which yielded 60 mg (92%) of the title compound as a colourless oil which was used without further purification. M/z 281.

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Method 176Methyl 3-(1,3-thiazol-2-yl)benzoate

To a round bottom flask equipped with a magnetic stir bar was added a solution of thiazole (461 μl , 6.51 mmol) in 15 ml of THF. The resulting mixture was cooled to -78°C and *n*-BuLi (3.80 ml, 6.0 mmol) was added to the solution. The reaction was allowed to stir at this temperature for 10 min. and ZnCl_2 (1.9 g, 13.95 mmol) was then added. The resulting mixture was allowed to stir for an additional 30 min. at this temperature followed by the addition of $\text{Pd}(\text{PPh}_3)_4$ (269 mg, 0.233 mmol) and methyl 3-bromobenzoate (1.0 g, 4.65 mmol). The reaction was allowed to warm to room temperature, was fitted with a reflux condenser, and was heated to 80°C for 2 h. The mixture was then cooled to room temperature and quenched with saturated aqueous NH_4Cl . The reaction was poured into a separator funnel and with EtOAc. The organic extract was dried over Na_2SO_4 , filtered, and concentrated *in vacuo* which provided 282 mg (28%) of the title compound as a colourless oil which was used without further purification. M/z 219.

30

Method 177**2-(Trifluoromethyl)pyrimidine-4-carboxylic acid**

A solution of methyl 2-(trifluoromethyl)pyrimidine-4-carboxylic acid (1.00 g, 4.85 mmol) in THF/H₂O (3:1, 8 ml) was treated with 2 N LiOH (2.5 ml, 4.85 mmol). After stirring the solution for 12 h, the solvents were removed under reduced pressure to give the desired product; *m/z* 193.

Method 178**3-(2-Methoxy-1,1-dimethylethyl)benzoic acid**

2-(3-Bromophenyl)-2-methylpropyl methyl ether (Method 17; 281 mg, 1.16 mmol) in THF (10 ml) at -78 °C under Ar was treated with *tert*-BuLi (1.7 M in pentane, 1.4 ml, 2.31 mmol, 2.0 equiv). The reaction stirred for 15 min and then CO_{2(g)} was bubbled through the reaction mixture. After 10 min, the reaction was quenched with 10% NaOH and extracted with EtOAc. The aqueous layer was acidified with 10% HCl and extracted with EtOAc. The organics were dried with NaCl_(sat) and Na₂SO_{4(s)} and then removed under reduced pressure; *m/z* 209.

Method 179**2-(3-Bromophenyl)-2-methylpropan-1-ol**

A solution of 2-(3-bromophenyl)-2-methylpropanoic acid (Method 52, 300 mg, 1.23 mmol) in anhydrous THF (10 ml) was treated with BH₃ (1.0 M in THF, 2.49 ml, 2.49 mmol, 1.5 equiv) drop wise under argon at 0 °C. The ice bath was removed and the reaction was stirred for 12 h. The reaction was quenched with 10% HCl and extracted with EtOAc. The organics were washed with NaCl_(sat) and the dried with Na₂SO_{4(s)}. The solvents were removed under reduced pressure to give 265 mg (94%); *m/z* 230.

Method 180**2-(3-Bromophenyl)-2-methylpropanoyl chloride**

A solution of 2-(3-bromophenyl)-2-methylpropanoic acid (Method 52, 564 mg, 2.32 mmol) in DCM (5 ml) was treated with oxalyl chloride (0.31 ml, 3.48 mmol, 1.5 equiv) and DMF (0.10 ml) under argon at 25 °C. The reaction stirred for 4 h, and then the solvents were removed under reduced pressure to give 265 mg (94%); *m/z* 262.

Method 181**2-(3-Bromophenyl)-N,N,2-trimethylpropanamide**

2-(3-Bromophenyl)-2-methylpropanoyl chloride (Method 180, 607 mg, 2.32 mmol) was treated with dimethylamine (2.0 M in THF, 5 ml, 10 mmol, 4.3 equiv). The reaction stirred for 30 min. The reaction was quenched with 10% HCl and extracted with EtOAc. The organics were washed with NaCl_(sat) and the dried with Na₂SO_{4(s)}. The solvents were removed under reduced pressure to give 539 mg (86%); *m/z* 271.

Method 182

10 **Methyl 5-({3-[2-(dimethylamino)-1,1-dimethyl-2-oxoethyl]benzoyl}amino)-2-methylbenzoate**

2-(3-Bromophenyl)-N,N,2-trimethylpropanamide (Method 181; 200 mg, 0.740 mmol), methyl 5-amino-2-methylbenzoate (Method 92; 122 mg, 0.740 mmol, 1.0 equiv), Pd(OAc)₂ (17 mg, 0.075 mmol, 10 mol%), Mo(CO)₆ (293 mg, 1.11 mmol, 1.5 equiv), Cs₂CO₃ (362 mg, 1.11 mmol, 1.5 equiv) and BINAP (46 mg, 0.074 mmol, 10 mol%) in toluene-MeCN 1:1 (2 ml) was heated at 90 °C under Ar for 12 h. The reaction was quenched with 10% NaOH and extracted with EtOAc. The organics were dried with NaCl_(sat) and Na₂SO_{4(s)} and then removed under reduced pressure. The residue was then purified by column chromatography utilizing an ISCO system (EtOAc-hexane) to give 75 mg (27%) of the desired product; *m/z* 383.

Method 183

The following compound was prepared by the procedure of Method 182, using the appropriate starting materials.

Meth	Compound	<i>m/z</i>	SM
183	Methyl 5-[(5-[(dimethylamino)sulfonyl]pyridin-3-yl)carbonyl]amino]-2-methylbenzoate	378	Method 230 and Method 92

25 **Method 184****5-[(Diphenylmethylene)amino]-N,N-dimethylpyridine-3-sulfonamide**

A stirred mixture of 5-bromo-N,N-dimethylpyridine-3-sulfonamide (Method 230; 170 mg, 0.641 mmol), benzophenone imine (0.13 ml, 0.769 mmol, 1.2 equiv), Cs₂CO₃ (313 mg, 0.962 mmol, 1.5 equiv), BINAP (40 mg, 0.064 mmol, 10 mol%) in dioxane (3 ml) was treated with Pd₂(dba)₃ (30 mg, 0.032 mmol, 5 mol%). The reaction mixture was heated to 100 °C for

12 hours. The reaction was then quenched with 10% NaOH(aq) and extracted with EtOAc. The organics were dried with NaCl_(sat) and then Na₂SO_{4(s)} and removed under reduced pressure. The resulting solid was purified by column chromatography utilizing an ISCO system (hexanes-EtOAc) to give 234 mg (99%); *m/z* 366.

5

Method 185**5-Amino-*N,N*-dimethylpyridine-3-sulfonamide**

A solution of 5-[(diphenylmethylene)amino]-*N,N*-dimethylpyridine-3-sulfonamide (Method 184; 234 mg, 0.640 mmol) in THF (3 ml) was treated with 10% HCl (5 ml). The reaction mixture was stirred for 10 min. The reaction was quenched with 10% HCl(aq) and extracted with EtOAc. The aqueous layer was saturated with K₂CO₃ and extracted with EtOAc and the solvents were removed under reduced pressure to give 129 mg (99%); *m/z* 202.

15 **Method 186****3-Chloropyridine-2,5-diamine**

Into a 300ml three-neck flask, 13.9g (0.1mol) of 2-amino-5-nitropyridine, (14.7g, 0.11mol) of *N*-chlorosuccinimide and 150ml of toluene were added. The resulting reaction mixture was stirred at 80 °C for one hour. During the reaction, formation of 2-chloroamino-5-nitropyridine was confirmed. After completion of the reaction by LCMS, the reaction mixture was cooled to room temperature and 100 ml of H₂O were added. The solution was filtered and the isolated solid was washed with H₂O and toluene (50ml each). 2-amino-3-chloro-5-nitropyridine was obtained (10.8 g, 62%) and it was used in the next step without further purification. *M/z* 175.

25 Into a 500ml three-neck flask, 2-amino-3-chloro-5-nitropyridine (8.72g, 50mmol) was dissolved in MeOH (125 ml). A solution of ammonium chloride (13.5 g, 250mmol) in H₂O (125 ml) were added, followed by 14g of iron powder. The solution was stirred with mechanic stirring at 78 °C for 2 hours. The solution was filtered at 50 °C and the isolated solid was washed by hot MeOH. The solvent was evaporated by vacuum and the crude product was
30 extracted by acetone and filtered. The acetone solution was evaporated and dissolved in 50ml MeOH whereupon 50ml of a solution of 4N hydrogen chloride in dioxane was added slowly. The resulting solution was sonicated for 10 minutes, and then filtered. The solid was washed

by acetone and dried in a vacuum oven. 3-chloropyridine-2, 5-diamine (7.5 g, HCl salt) was isolated as an off-white powder. *M/z* 145.

Method 187

- 5 The following compound was prepared by the procedure of Method 186, using the appropriate starting material.

Method	Compound	m/z	SM
187	3-Bromo-pyridine-2,5-diamine	189	2-amino-5-nitropyridine and NBS

Method 188

N²-(2-{{tert-butyl(dimethyl)silyl}oxy}ethyl)pyridine-2,5-diamine

- 10 To a solution of 2-chloro-5-nitro pyridine (400 mg, 2.5 mmol) in EtOH (5ml) was added 2-((tert-butyl(dimethyl)silyl)oxy)ethyl amine (3 ml) and the resulting mixture was heated to reflux for 3 hours. Evaporation of the solvent under reduced pressure afforded 5-nitro-2-[2-hydroxy)ethylamino]pyridine (680 mg) that was used in the next step without any further purification.
- 15 *N*-(2-{{tert-butyl(dimethyl)silyl}oxy}ethyl)-5-nitropyridin-2-amine (Method 156; 1.29 g, 4.34 mmol) was dissolved in 20 ml of MeOH and 260 mg of palladium (10 wt. % on activated carbon-Degussa®) was added. The reaction was subjected to 1 atmosphere of hydrogen overnight. LC/MS confirmed the formation of the product. The reaction mixture was filtered through diatomaceous earth and washed with MeOH and EtOAc. The title
- 20 compound (970 mg) was collected by evaporation as a thick red oil. *M/z* 268.

Methods 189-199

The following compounds were prepared by the procedure of Method 188, using the appropriate starting material.

Meth	Compound	m/z	SM
189	<i>N</i> -2-[2-(Dimethylamino)ethyl]pyridine-2,5-diamine	181	2,2-dimethylamino-ethylamine
190	6-(4-Methylpiperazin-1-yl)pyridin-3-amine	193	4-methyl piperazine

Meth	Compound	m/z	SM
191	<i>N</i> -2-1H-Pyrazol-5-ylpyridine-2,5-diamine	176	3-amino-1H-pyrazole
192	3-Methylpyridine-2,5-diamine	124	2-chloro-3-methyl-5-nitropyridine
193	<i>N</i> -2-[3-(Dimethylamino)propyl]pyridine-2,5-diamine	195	2,2-dimethylamino-propylamine
194	<i>N</i> -2-Methylamine-3-chloro-pyridine-5-amine	158	2,3-dichloro-5-nitro amine and methylamine
195	<i>N</i> -2-Methylamine-3-methoxy-pyridine-5-amine	154	2-chloro-3-methoxy-5-nitro pyridine
196	Pyridine 2,3,5-triamine	125	2-chloro-3,5-dinitropyridine And ammonia

Method 197**(3-Bromo-5-fluorophenyl)methanol**

A solution of 3-bromo-5-fluorobenzoic acid (1.14 g, 5.21 mmol) in anhydrous THF (10 ml) was treated with BH₃ (1.0 M in THF, 8.0 ml, 8.0 mmol, 1.5 equiv) dropwise under nitrogen at 0 °C. The mixture was stirred at 0 °C for 30 min then allowed to warm to 25 °C and stirred for 12 h. The reaction was quenched with 10% HCl and extracted with EtOAc. The organic layer was washed with 10% NaOH and then dried with NaCl_(sat) and Na₂SO_{4(s)}. The solvents were removed under reduced pressure. The resulting product was carried directly to the next step; *m/z* 284.

Method 198**3-Bromo-5-fluorobenzyl methanesulfonate**

A solution of (3-bromo-5-fluorophenyl)methanol (Method 197; 1.07 g, 5.22 mmol) in anhydrous DCM (20 ml) was cooled to 0 °C. To this solution, DIEA (1.4 ml, 7.83 mmol, 1.5 equiv) and methane sulfonyl chloride (0.5 ml, 6.26 mmol, 1.2 equiv) were added respectively. The mixture was stirred at 25 °C for 2 h. The reaction was quenched with 10% HCl and extracted with EtOAc. The organic layer was washed with NaHCO_{3(sat)} and then dried with NaCl_(sat) and Na₂SO_{4(s)}. The solvents were removed under reduced pressure. The resulting product was carried directly to the next step; *m/z* 208.

Method 199**(3-Bromo-5-fluorophenyl)acetonitrile**

A suspension of 3-bromo-5-fluorobenzyl methanesulfonate (Method 198; 1.27 g, 4.49 mmol) and sodium cyanide (0.264 g, 5.38 mmol, 1.2 equiv) in DMF (9 ml) and water (1 ml) was stirred at 40 °C for 5 h. The reaction mixture was quenched with water and extracted with EtOAc. The organic layer was dried with NaCl_(sat) and Na₂SO_{4(s)}. The solvents were removed under reduced pressure. The resulting product was purified by chromatography using 5% EtOAc in Hexane to give the desired product; *m/z* 215.

10 Method 200**2-Methyl-3,5-dinitropyridine**

Diethyl malonate (1.52 mL, 10 mmol) was dissolved in 50 mL THF, sodium hydride (400 mg, 10 mmol) was added to the solution in portions. The solution was stirred until gas evolution ceased. 2-chloro-3,5-dinitropyridine (2.03 g, 10 mmol) was added and the resulting solution was stirred an additional 10 minutes. The solvent was evaporated *in vacuo*. Sulfuric acid (20 mL, 6 N) was added to the crude intermediate and the resulting solution was heated to 100 °C over night. The solution was cooled to room temperature and neutralized by the addition of 2N sodium hydroxide_(aq). The solution was extracted with ethyl acetate and the combined organic layer was washed with water and dried with sodium sulfate. The solution was filtered and concentrated *in vacuo*, yielding 680 mg of the title compound that was used without further purification (37.2 %).

Method 201**3-(4-Methyl-1*H*-imidazol-1-yl)-5-(trifluoromethyl)benzoic acid**

To a solution of 3-(4-methyl-1*H*-imidazol-1-yl)-5-(trifluoromethyl)benzonitrile (Method 206; 180 mg, 0.717 mmol) in 5 ml of dioxane was added 7 ml of a 1M NaOH solution. The reaction mixture was allowed to stir overnight at 100 °C. The reaction mixture was cooled to room temperature and quenched by the careful addition of concentrated HCl until a pH of 3 was obtained. The aqueous phase was extracted with EtOAc, dried over Na₂SO₄, filtered and concentrated *in vacuo* to yield 816 mg (74 %) of the title compound as a yellow solid which was used without further purification. *M/z* 271.

Method 202**5-(1*H*-Pyrrol-1-yl)pyridin-3-amine**

To a solution of 5-(1*H*-pyrrol-1-yl)nicotinic acid (3.0 g, 15.9 mmol) in 80 ml of *t*-butanol, DPPA (6.89 ml, 31.9 mmol) and DIEA (5.56 ml, 31.9 mmol) were added and the reaction mixture was heated at 80°C in a sealed tube overnight. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and sodium bicarbonate and dried with MgSO₄. Evaporation of the solvent gave a brown solid *m/z* 260. This material was dissolved in MeOH (30 ml) and 4*N* HCl in 1,4-dioxane (25 ml) was added at 0°C and the resulting mixture stirred for 2 hours at room temperature. Ether was then added to the mixture and 5-(1*H*-pyrrol-1-yl)pyridin-3-amine (3.356g), a mustard yellow precipitate, was collected by filtration. *M/z* 160.

Method 203**3-(1-Cyano-1,2-dimethylpropyl)benzoic acid**

To a solution of 3-(1-cyanoethyl)benzoic acid (500 mg) in THF (50ml) at -78°C was added slowly a solution of LiHMDS (60ml, 1.0*M* in THF) and the resulting red solution was allowed to stir at this temperature for 30 minutes. Isopropyl iodide (10 ml) was added slowly and the resulting mixture was warmed up to room temperature and stirred for 10 hours. The mixture was partitioned between EtOAc and H₂O and the aqueous layer was acidified with 1*N* HCl until pH 3. The aqueous layer was extracted with EtOAc (3x) and dried with MgSO₄. Evaporation of the solvent under pressure afforded the desired compound as a white solid (300 mg). ¹H NMR (300 MHz) 8.03 (s, 1H), 7.92 (d, 2H), 7.71 (d, 2H), 7.56 (t, 1H), 2.20 (h, 1H), 1.67 (s, 3H), 1.05 (d, 3H), 0.72 (d, 3H).

25 Methods 204-205

The following compounds were prepared by the procedure of Method 203, using the appropriate starting material.

Method	Compound	<i>m/z</i>	SM
204	3-(1-Cyano-1-methylpropyl)benzoic acid	¹ H NMR (300 MHz) 8.07 (s, 1H), 7.91 (d, 1H), 7.73 (d, 1H), 7.57 (t, 1H), 1.98 (q, 2H), 1.69 (s, 3H), 0.82 (t, 3H)	iodoethane

Method	Compound	m/z	SM
205	3-(1-Cyano-2-hydroxy-1-methylethyl)benzoic acid	¹ H NMR (300 MHz) 8.01 (s, 1H), 7.90 (d, 1H), 7.72 (d, 1H), 7.54 (t, 1H), 4.20 (d, 1H), 4.01 (d, 1H), 1.69 (s, 3H), 0.82 (t, 3H)	paraformaldehyde

Method 2063-(4-Methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)benzonitrile

To a solution of 3-fluoro-5-(trifluoromethyl)benzonitrile (5.0 g, 26.4 mmol) in 25 ml of DMA was added 2-methyl imidazole (6.5 g, 79.3 mmol). The reaction mixture was stirred at 145 °C overnight. The reaction mixture was allowed to cool to room temperature and was quenched with ~50 ml of brine and then extracted three times with EtOAc. The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo* to yield the crude product. The crude sample was subjected to ISCO purification using EtOAc as eluent to yield 4.0 g (61%) of the title compound as a white solid. *M/z* 251.

Method 207tert-Butyl {2-[(5-nitropyridin-2-yl)amino]ethyl} carbamate

To a solution of *N*-(5-nitropyridin-2-yl)ethane-1,2-diamine (1.0 g, 5.49 mmol) in THF (20 ml) at 0°C, sodium hydride (395 mg, 8.22 mmol) and di-tert-butyl dicarbonate (1.20g, 5.49 mmol) were added. The reaction mixture was stirred overnight at 25°C. LC/MS confirmed the formation of the product so the reaction was quenched with H₂O. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. The title compound (1.11 g) was collected by evaporation as a yellow oily solid. *M/z* 284

Method 208*N*-(5-Amino-3-bromopyridin-2-yl)acetamide

To a solution of 2-amino-3-bromo-5-nitro pyridine (3.0g, 13.8 mmol) in pyridine (20 ml) at 0°C was added slowly acetyl chloride (2.5 ml) and the resulting mixture was stirred for 1 hour at ambient temperature. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. Evaporation under reduced

pressure afforded the acetyl derivative, which was used in the next step without further purification.

Into a three-neck flask, 2-acetylamino-3-bromo-5-nitropyridine (2.0g) was dissolved in MeOH (25 ml). A solution of ammonium chloride (1.3 g, 250mmol) in H₂O (25 ml) was added, followed by 1.4g of iron powder. The solution was stirred by at 78 °C for 2 hours. The solution was filtered at 50 °C and the isolated solid was washed by hot MeOH. The solvent was evaporated under reduced pressure and the product was extracted by acetone and filtered. The acetone solution was evaporated to give the title compound (900 mg) as solid. *M/z* 231.

10 Methods 209-210

The following compounds were prepared by the procedure of Method 208, using the appropriate starting material.

Method	Compound	m/z	SM
209	<i>N</i> -(5-Amino-3-chloropyridin-2-yl)acetamide	186	Method 186 (1 st part)
210	<i>N</i> -(5-Amino-3-methoxypyridin-2-yl)acetamide	182	2-amino-3-methoxy-5-nitro pyridine

Method 211

15 2,3-Dimethyl-pyridine-5-amine

To a solution of NaH (80 mg, 60% w/w) in ether (4 ml) at 0 °C was added slowly diethyl malonate (0.3 ml). After the evolution of gas had ceased, 2-bromo-3-methyl-5-nitro pyridine (434 mg) was added portion-wise. After 30 min, the reaction was quenched with 10% HCl and extracted with EtOAc. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. The organics were then removed under reduced pressure to give the malonate adduct. The crude product was dissolved in 30 ml of 6N H₂SO₄ and heated to 110°C for 5 hours. The mixture was cooled in an ice bath and a solution of 2N NaOH was added until pH neutral. The desired product was collected by filtration (100 mg). *M/z* 154.

The 2,3-dimethyl-5-nitro-pyridine (100 mg) was dissolved in 10 ml of MeOH and 100 mg of palladium (10 wt. % on activated carbon-Degussa®) was added. The reaction mixture was subjected to 1 atmosphere of hydrogen overnight. LC/MS confirmed the formation of the product and the reaction mixture was filtered through diatomaceous earth and washed with MeOH and EtOAc. The product (60 mg) was collected by evaporation. *M/z* 123.

Methods 212-213

The following compounds were prepared by the procedure of Method 211, using the appropriate starting material.

Method	Compound	m/z	SM
212	2-Methyl-3-chloro-pyridine-5-amine	143	Method 227
213	6-Ethylpyridin-3-amine	123	2-chloro-5-nitro-pyridine and diethyl methyl malonate

5

Method 2142-Hydroxypyridine-5-amine

5-Nitropyrid-2-one (420 mg, 3 mmol) was dissolved in MeOH (7 ml) and a solution of ammonium chloride (810 mg) in H₂O (7 ml) was added, followed by 840 mg of iron powder.

- 10 The solution was stirred at 78 °C for 2 hours. The solution was filtered at 50 °C and the isolated solid was washed by hot MeOH. The solvent was evaporated under reduced pressure and the desired product was isolated by filtration (170 mg). *M/z* 111.

Methods 215-217

- 15 The following compounds were prepared by the procedure of Method 214, using the appropriate starting material.

Method	Compound	m/z	SM
215	3-Chloropyridine-5-amine	129	3-chloro-5-nitro pyridine
216	2-Hydroxy-picoline-5-amine	125	2-hydroxy-5-nitro-3-picoline
217	Methyl 2-chloro-5-amino benzoate	186	Method 91

Method 218Methyl 1,3,3-trimethyl-2-oxoindoline-5-carboxylate

- 20 To a solution of methyl 2-oxoindoline-5-carboxylate (400 mg, 2.09 mmol) in THF (10 ml) at -78 °C was added LiHMDS (1.0 M, 16.7 ml, 16.75 mmol) and MeI (1.3 ml, 20.9 mmol). The reaction was allowed to stir overnight to room temperature. The reaction was then quenched with ~25 ml aqueous NH₄Cl. After dilution with EtOAc, the mixture was washed with brine, and then dried over Na₂SO₄ and concentrated *in vacuo* to yield the crude product

that was purified on SiO₂ using EtOAc/hexanes as eluent which yielded 81 mg (17%) the title compound as a yellow solid. *M/z* 233.

Method 219

5-Isopropoxy-pyridin-3-amine

5-Bromopyridin-3-ol (1g, 5.75mmol) was dissolved in 20ml DMF, isopropyl bromide (1.65ml, 17.2mmol) and Cs₂CO₃ (8.6gram, 25.9mmol) were added. The solution was stirred at room temperature overnight. The solution was filtered and separated between EtOAc and water. The organic layer was dried and evaporated under reduced pressure to afford the title compound (1.2 g).

Methods 220-222

The following compounds were prepared by the procedure of Method 219, using the appropriate starting material.

Method	Compound	m/z	SM
220	tert-Butyl 2-{[(5-aminopyridin-3-yl)oxy]methyl}pyrrolidine-1-carboxylate	293	tert-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate
221	5-[2-(Dimethylamino)ethoxy]pyridin-3-amine	181	(2-chloroethyl) dimethylamine
222	5-[3-(Dimethylamino)propoxy]pyridin-3-amine	196	(3-chloropropyl) dimethylpropylamine

Method 223

5-{[3-(1-Cyano-1-methylethyl)benzoyl]amino}-2-chlorobenzoic acid

3-(1-Cyano-1-methylethyl)benzoic acid (Method 19, 150 mg) was combined with methyl 5-amino-2-chlorobenzoate (Method 217, 120 mg), HATU (400 mg) and DIEA (0.6 ml) in DMF (3 ml) and stirred overnight at 25°C. LC/MS confirmed the formation of the product, methyl 5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-chlorobenzoate. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. Methyl 5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-chlorobenzoate was collected by evaporation as a reddish-brown oil.

Methyl 5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-2-chlorobenzoate (120 mg) was dissolved in a 3:1:1 (v/v/v) solution of THF/MeOH/H₂O and lithium hydroxide (50 mg) was added slowly. The reaction was then stirred overnight at 25°C. LC/MS confirmed the formation of the product. The organic solvents were evaporated and the remaining material was separated between EtOAc and H₂O. The aqueous layer was collected and acidified to a pH of between 3 and 4 with 2N HCl. The mixture was partitioned between H₂O and EtOAc, and the organic layer was washed with brine and dried with MgSO₄. The title compound (85 mg) was collected by evaporation as a white solid.

10 Method 224

The following compound was prepared by the procedure of Method 223, using the appropriate starting material.

Method	Compound	M/z	SM
224	2-Chloro-5-{[3-(trifluoromethyl)benzoyl]amino}benzoic acid	344	Methyl 2-chloro-5-amino benzoate (Method 217) and 3-trifluorobenzoic acid

Method 225

15 Sodium [3-(methoxycarbonyl)phenyl]methanesulfonate

To a solution of methyl 3-(bromomethyl)benzoate (2.5 g, 19.0 mmol) in 25 ml of acetone and 25 ml of H₂O, was added sodium sulfite (1.5 g, 12.0 mmol) and tertabutylammonium iodide (4.4 g, 12.0 mmol). The reaction warmed to 75 °C and was allowed to stir for 12 h at this temperature. The reaction mixture was cooled to room temperature and concentrated *in vacuo* to yield the title compound as a yellow solid 2.5 g (99%). M/z 230.

Method 226

3-Cyclopropyl-5-fluorobenzoic acid

25 To a 50 ml round bottom flask charged with a magnetic stir bar was added 3-bromo-5-fluorobenzoic acid (0.500 g, 4.56 mmol) and cyclopropylboronic acid (0.590 g, 6.84 mmol). Toluene (15 ml) and H₂O (0.75 ml) were added followed by K₃PO₄ (3.86 g, 18.24 mmol) and Pd(PPh₃)₄ (1.05 g, 0.912 mmol). The resulting reaction mixture was heated to 100 °C for 12 h, was cooled to room temperature, and quenched with 10% aqueous NaOH (~100 ml). The

reaction mixture was poured into a separator funnel and extracted with EtOAc (~100 ml). The resulting aqueous phase was isolated and brought to a pH of ~ 2 by the careful addition of 3N HCl at which time the desired product precipitated. The precipitate was collected via vacuum filtration, washed with an additional portion of H₂O (~100 ml), collected, and dried under vacuum for 24 h which yielded 0.310 g of the title compound (37%) as an off white solid. *M/z* 181.

Method 227

2,3-Dichloro-5-nitro-pyridine

10 To a solution of 5-nitro-2-hydroxypyridine (700 mg, 5 mmol) in concentrated HCl (3.3 ml) was heated to 50°C to facilitate dissolution. A solution of KClO₃ (214 mg) in H₂O (3ml) was added drop-wise to the above solution in such a way the internal temperature did not exceed 60°C. The resulting mixture was stirred at ambient temperature for 15 minutes, cooled to 0 °C and the product 3-chloro-5-nitro-2-hydroxypyridine was collected by filtration
15 (600 mg, 68%). The pyridine (600 mg) was dissolved in quinoline (0.4 ml) and POCl₃ (0.35 ml). The resulting mixture was heated to 120°C for 2 hours. The mixture was partitioned between EtOAc and H₂O. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. The organics were then removed under reduced pressure to give the title compound (358 mg, 55%) as a brown solid. *M/z* 194.

20

Method 228

3-[(2-Cyano-1*H*-pyrrol-1-yl)methyl]benzoic acid

To a solution of methyl 3-(bromomethyl)benzoate (500 mg) in DMF (10 ml) was added a solution of 2-cyano pyrrole (350 mg) in DMF (5 ml) which had been previously
25 treated with NaH (100 mg). The resulting mixture was stirred at ambient temperature for 3 hours. The mixture was partitioned between EtOAc and H₂O. The organics were washed with NaCl_(sat) and then dried with Na₂SO_{4(s)}. Evaporation of the solvent gave methyl 3-[(2-cyano-1*H*-pyrrol-1-yl)methyl]benzoate (300 mg). *M/z* 241.

Methyl 3-[(2-cyano-1*H*-pyrrol-1-yl)methyl]benzoate (300 mg) was dissolved in
30 MeOH/H₂O (10 ml, 3:1 v/v) and LiOH (60 mg) was added. The resulting mixture was stirred at room temperature for 10 hours. The aqueous phase was filtered and washed with EtOAc. The basic aqueous layer was acidified by the addition of 1N HCl until pH 3. The aqueous

layer was extracted with EtOAc (3x) and then dried with Na₂SO_{4(s)}. Evaporation of the solvent afforded the title compound as a white solid (210 mg); *m/z* 226.

Method 229

3-(1-Cyano-1-methylethyl)-5-fluorobenzoic acid

- 2-(3-Bromo-5-fluorophenyl)-2-methylpropanenitrile (Method 18; 258 mg, 1.07 mmol) in THF (10 ml) at -78 °C under Ar was treated with *t*BuLi (1.7 M in pentane, 2.13 mmol, 2.0 equiv). The reaction was stirred for 15 min and then CO_{2(g)} was bubbled through the reaction mixture. After 10 min, the reaction was quenched with 10% NaOH and extracted with EtOAc.
- 10 The aqueous layer was acidified with 10% HCl and extracted with EtOAc. The organics were dried with NaCl_(sat) and Na₂SO_{4(s)} and then removed under reduced pressure; *m/z* 208.

Method 230

5-Bromo-*N,N*-dimethylpyridine-3-sulfonamide

- 15 A solution of *N,N*-dimethylpyridine-3-sulfonamide (Method 129, 1.30 g, 6.98 mmol) and NaOAc (1.72 g, 20.9 mmol, 3.0 equiv) in HOAc (10 ml) was treated with Br₂ (0.72 ml, 14.0 mmol, 2.0 equiv). The reaction was stirred for 12 h at 50 °C. The reaction was quenched with H₂O and extracted with EtOAc. The organics were dried with NaCl_(sat) and Na₂SO_{4(s)} and then removed under reduced pressure. The residue was then purified by column
- 20 chromatography utilizing an ISCO system (EtOAc-hexane) to give 340 mg (18%) of the desired product; *m/z* 266.

Method 231

5-Fluoronicotinic acid

- 25 To a 1L round bottom flask charged with a magnetic stir bar and 2,6-dichloro-5-fluoronicotinic acid (5.00 g, 23.8 mmol) was added MeOH (240 ml) and DIEA (8.30 ml, 48.0 mmol). To this solution was carefully added 500 mg of palladium on carbon (10 wt %). The resulting reaction mixture was purged with H₂ and placed under an atmosphere of H₂ (1 atm) using a balloon. The reaction was allowed to stir at ambient temperature for 12 h before being
- 30 filtered through a bed of diatomaceous earth. The filtrate was concentrated *in vacuo* to a volume of ~ 25 ml and diluted with ~250 ml of Et₂O. A precipitate formed (DIPEA/HCl salt) which was filtered off using a Buchner funnel. The filtrate was concentrated *in vacuo* to yield

3.2 g (98%) the title compound as a yellow oil which was used without further purification; m/z 141.

Method 232

5 5-Aminonicotinonitrile

5-Bromonicotinonitrile (1.26g, 6.8mmol), Cs_2CO_3 (3.74g, 11.5mmol), BINAP (716mg, 1.15mmol), $\text{Pd}_2(\text{dba})_3$ (526mg, 0.575mmol) were put in a round bottle, toluene 25mL and 1,1-diphenylmethanimine (1.43ml, 8.6mmol) were added and the mixture was degassed for 5 minutes. The solution was heated at 100 °C over night. The crude product was filtered and evaporated, and dissolved in dioxane (10ml) followed by the addition of 4N HCl in dioxane 10ml. The solution was stirred at room temperature for 30 minutes. The residue left after evaporation was separated between water and ethyl acetate. Evaporation of the solvent gave the title compound (800 mg). M/z 120.

15 Method 233

N-(5-Amino-3-methylpyridin-2-yl)-2-(benzyloxy)acetamide

To a solution of 2-amino-3-methyl-5-nitropyridine (1.0g) in pyridine (20 ml) at 0°C was added slowly (benzyloxy)acetyl chloride (2.5 ml) and the resulting mixture was stirred for 1 hour at ambient temperature. The mixture was partitioned between H_2O and EtOAc, and the organic layer was washed with brine and dried with MgSO_4 . Evaporation under reduced pressure afforded the acetyl derivative which was used in the next step without further purification. (m/z 302)

Into a three-neck flask, the residue (500 mg) was dissolved in MeOH (25 ml). A solution of ammonium chloride (1.3 g, 250mmol) in H_2O (25 ml) was added, followed by 1.4g of iron powder. The solution was stirred by at 78°C for 2 hours. The solution was filtered at 50°C and the isolated solid was washed by hot methanol. The solvent was evaporated under reduced pressure and the product was extracted by acetone and filtered. The acetone solution was evaporated to give the title compound (100 mg) as solid. M/z 272.

30 Method 234

Methyl 5-piperidin-1-yl nicotinate

A 25 ml round bottom flask was charged with a magnetic stir bar, methyl 5-bromonicotinate (0.500 g, 2.31 mmol), piperidine (0.305 g, 3.46 mmol), and toluene (5 ml).

Caesium carbonate (2.25 g, 6.93 mmol), palladium (II) acetate (52 mg, 0.23 mmol), and BINAP (0.287 g, 0.46 mmol) were then added. The reaction was heated to 80 °C for 8 h before being diluted with EtOAc (~ 50 ml), filtered through a pad of SiO₂, and concentrated *in vacuo*. The crude product was purified on 40 g SiO₂ using EtOAc as eluent giving 0.376 g of the title compound as a colourless oil (74 %). M/z 221.

Methods 235-236

The following compounds were prepared by the procedure of Method 234, using the appropriate starting material.

Meth	Compound	m/z	SM
235	Methyl 5-morpholin-4-yl nicotinate	223	morpholine
236	Methyl 5-(diethylamino)nicotinate	209	diethylamine

Method 237

Methyl 3-cyclopropylbenzoate

To a 100 ml round bottom flask charged with a magnetic stir bar and DCM (20 ml) was added 12.3 ml of diethyl zinc (1M in hexanes). The reaction mixture was cooled to 0 °C and trifluoroacetic acid (1.40 g, 12.3 mmol) was added dropwise via syringe. The reaction was stirred at this temperature for 20 mins. followed by the addition of CH₂I₂ (3.30 g, 12.3 mmol). The reaction mixture was stirred for 20 mins. before methyl 3-vinylbenzoate (1.00 g, 6.16 mmol) was added. The reaction was then allowed to warm to room temperature with stirring for 3 h. before being quenched by the addition of ~50 ml of saturated aqueous NH₄Cl. The mixture was poured into a separator funnel and the aqueous phase was further extracted with DCM (3 x 50 ml). The combined organic extract was dried with MgSO₄ and concentrated *in vacuo* to yield the crude reaction product which was purified on 120 g SiO₂ using hexanes/EtOAc 10:1 as eluent giving 1.01 g of the title compound as a colourless oil (94 %) m/z 177.

Methods 238-239

The following compounds were prepared by the procedure of Method 237, using the appropriate starting material.

Meth	Compound	m/z	SM
238	Methyl 3-(1-cyclopropyl-1-methylethyl)benzoate	219	Method 165

Meth	Compound	m/z	SM
239	Methyl 3-(1-methylcyclopropyl)benzoate	191	Method 173

Method 240**(5-Bromopyridin-3-yl)methanol**

To a 500 ml three neck flask fitted with a reflux condenser was added with a magnetic stir bar and MeOH (65 ml). NaBH₄ (12.2 g, 324 mmol) was carefully added followed by methyl 5-bromonicotinate (7.0 g, 32.4 mmol). The reaction mixture was heated to reflux with stirring for 5 h before being cooled to room temperature and the reaction mixture was quenched by the slow addition of ~ 250 ml of H₂O. The MeOH was removed under reduced pressure and the resulting aqueous phase was extracted with ~250 ml of EtOAc. The organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified on a 120 g SiO₂ column using MeOH/EtOAc (1:10) as eluent giving 2.3 g (37%) of the title compound as a white solid *m/z* 189.

Method 24115 **5-([*tert*-Butyl(diphenyl)silyl]oxy)methyl)-*N*-(diphenylmethylene)pyridin-3-amine**

To a 200 ml round bottom flask charged with a magnetic stir bar was added 3-bromo-5-([*tert*-butyl(diphenyl)silyl]oxy)methylpyridine (Method 102; 5.2 g, 12.2 mmol). Toluene (60 ml) was added followed by benzophenone imine (2.55 ml, 15.25 mmol), sodium *tert*-butoxide (2.00 g, 21.35 mmol), Pd₂(dba)₃ (0.558 g, 0.61 mmol), and BINAP (1.13 g, 1.83 mmol). The reaction was heated to 80 °C with stirring for 5 h before being cooled to room temperature and quenched with ~200 ml saturated aqueous NaHCO₃. The mixture was poured into a separator funnel and extracted with ~200 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the crude product, which was purified on a 120 g SiO₂ column using hexanes/EtOAc (9:1) as eluent giving 5.26 g (82%) of the title compound as a white solid *m/z* 527.

Method 242**(5-Aminopyridin-3-yl)methanol hydrochloride**

To a 500 ml round bottom flask charged with a magnetic stir bar was added 5-([*tert*-butyl(diphenyl)silyl]oxy)methyl)-*N*-(diphenylmethylene)pyridin-3-amine (Method 241; 5.2 g, 9.87 mmol). MeOH (200 ml) was added followed by the addition of 50 ml of 3N HCl with

stirring. The reaction was allowed to stir for 12 h at room temperature before being concentrated *in vacuo*. The crude oil diluted with EtOAc (~100 ml) and a precipitate formed. The solid was collected on a Buchner funnel to provide 1.24 g (79 %) of the title compound as an off white solid *m/z* 125.

5

Method 243

N²-Cyclopropylpyridine-2,5-diamine

To a 100 ml round bottom flask charged with a magnetic stir bar and *N*-cyclopropyl-5-nitropyridin-2-amine (Method 149; 0.800 g, 4.46 mmol) was added EtOH (15 ml). Tin (II) chloride dihydrate (4.03 g, 17.84 mmol) was added and the reaction was warmed to 70 °C with stirring for 4 h before being cooled to room temperature. The crude reaction mixture was then quenched with ~150 ml of saturated aqueous NaHCO₃. The resulting mixture was poured into a separator funnel and extracted with ~150 ml of EtOAc. The combined organic extract was dried with MgSO₄, filtered, and concentrated *in vacuo* to yield the title compound as a yellow solid 0.551 g (83%), which was used without further purification; *m/z* 150.

15

Methods 244-250

The following compounds were prepared by the procedure of Method 243, using the appropriate starting material.

Meth	Compound	m/z	SM
244	<i>N</i> ² -Cyclobutylpyridine-2,5-diamine	164	Method 158
245	<i>N</i> ² -Isopropylpyridine-2,5-diamine	152	Method 150
246	(2 <i>R</i>)-3-[(5-Aminopyridin-2-yl)amino]propane-1,2-diol	184	Method 151
247	2-[(5-Aminopyridin-2-yl)amino]propane-1,3-diol	184	Method 152
248	<i>N</i> ² -(4-Aminobutyl)pyridine-2,5-diamine	180	Method 155
249	6-Piperazin-1-ylpyridin-3-amine	178	Method 153
250	<i>N</i> ² -(3-Pyrrolidin-1-ylpropyl)pyridine-2,5-diamine	220	Method 154

20

Method 251

***tert*-Butyl (5-fluoropyridin-3-yl)carbamate**

To a 100 ml round bottom flask charged with a magnetic stir bar was added 5-fluoronicotinic acid (Method 231; 1.00 g, 7.09 mmol). *Tert*-butyl alcohol was added (20 ml) followed by DIEA (3.08 ml, 17.7 mmol). Diphenyl phosphoryl azide (3.83 ml, 17.72 mmol)

25

was added and the flask was fitted with a reflux condenser. The reaction was heated to reflux for 12 h, cooled, and the crude reaction mixture was concentrated *in vacuo*. The resulting oil was dissolved in EtOAc (~ 200 ml) and the organic phase was washed 3 x 200 ml saturated aqueous NaHCO₃. The organic phase was dried with MgSO₄, filtered, and concentrated *in vacuo* yielding the crude product which was purified on SiO₂ (120 g) using EtOAc/hexanes (1:5) as eluent to yield 0.83 g (55%) of the title compound; *m/z* 213.

Method 252

5-Fluoropyridin-3-amine hydrochloride

10 To a 100 ml round bottom flask charged with a magnetic stir bar and *tert*-butyl (5-fluoropyridin-3-yl)carbamate (Method 251; 0.800 g, 3.77 mmol) was added MeOH (100 ml). A 4N solution of HCl in dioxane was then added until the reaction mixture reached a pH of ~ 3. The reaction was allowed to stir for 12 h before being concentrated *in vacuo*. The crude product was suspended in ~250 ml of Et₂O. A white precipitate formed which was collected
15 via vacuum filtration. The filter cake was washed with an additional 250 ml of Et₂O and dried on a vacuum to yield 0.510 g (91%) of the title compound as a white solid; *m/z* 113.

Method 253

Methyl 3-(1-cyano-1-methylethyl)-5-[(methylthio)methyl]benzoate

20 A solution of methyl 3-(bromomethyl)-5-(1-cyano-1-methylethyl)benzoate (Method 138; 80 mg, 0.27 mmol) in 1 ml of EtOH was added sodium thiomethoxide. The mixture was stirred over open atmosphere at reflux. Evaporation the residual solvents yielded the product which was used without any further purification *m/z* 263.

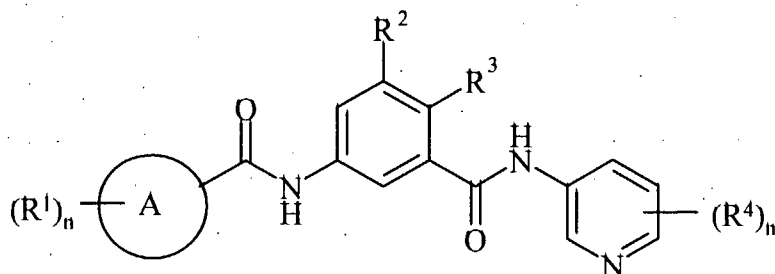
Method 254

Sodium [3-(1-cyano-1-methylethyl)-5-(methoxycarbonyl)phenyl]methanesulfonate

To a solution of methyl 3-(bromomethyl)-5-(1-cyano-1-methylethyl)benzoate (Method 138; 230 mg, 0.777 mmol) in 5 ml of acetone and 5 ml of water was added sodium sulfite. The mixture was stirred over open atmosphere at reflux. The reaction was cooled to room
30 temperature and the solvents were removed *in vacuo* to yield the title compound which was used without any further purification. *M/z* 297.

Claim

1. A compound of formula (I):



(I)

wherein:

Ring A is phenyl or a monocyclic 5 or 6 membered fully-unsaturated heterocyclic ring; wherein said phenyl or heterocyclic ring may be optionally fused to a five or six membered carbocyclyl or heterocyclyl forming a bicyclic ring; and wherein if said heterocyclyl or heterocyclic ring contains an $-NH-$ moiety that nitrogen may be optionally substituted by a group selected from R^5 ;

R^1 is a substituent on carbon and is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, $N-(C_{1-6}alkyl)amino$, $N,N-(C_{1-6}alkyl)_2amino$, $C_{1-6}alkanoylamino$, $N-(C_{1-6}alkyl)carbamoyl$, $N,N-(C_{1-6}alkyl)_2carbamoyl$, $C_{1-6}alkylS(O)_a$ wherein a is 0 to 2, $C_{1-6}alkoxycarbonyl$, $C_{1-6}alkoxycarbonylamino$, $N-(C_{1-6}alkyl)sulphamoyl$, $N,N-(C_{1-6}alkyl)_2sulphamoyl$, $N-(C_{1-6}alkyl)-N-(C_{1-6}alkoxy)sulphamoyl$, $N,N'-(C_{1-6}alkyl)_2ureido$, $N',N'-(C_{1-6}alkyl)_2ureido$, $N-(C_{1-6}alkyl)-N',N'-(C_{1-6}alkyl)_2ureido$, $C_{1-6}alkylsulphonylamino$, carbocyclyl- R^6 - or heterocyclyl- R^7 -; wherein R^1 may be optionally substituted on carbon by one or more R^8 ; and wherein if said heterocyclyl contains an $-NH-$ moiety that nitrogen may be optionally substituted by a group selected from R^9 ;

n is selected from 0-4; wherein the values of R^1 may be the same or different;

R^2 is selected from hydrogen, halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $C_{1-6}alkanoyl$, $C_{1-6}alkanoyloxy$, $N-(C_{1-6}alkyl)amino$, $N,N-(C_{1-6}alkyl)_2amino$, $C_{1-6}alkanoylamino$, $N-(C_{1-6}alkyl)carbamoyl$, $N,N-(C_{1-6}alkyl)_2carbamoyl$, $C_{1-6}alkylS(O)_a$ wherein a is 0 to 2, $C_{1-6}alkoxycarbonyl$, $N-(C_{1-6}alkyl)sulphamoyl$, $N,N-(C_{1-6}alkyl)_2sulphamoyl$, $C_{1-6}alkylsulphonylamino$, carbocyclyl- R^{10} - or heterocyclyl- R^{11} -;

wherein R^2 may be optionally substituted on carbon by one or more R^{12} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{13} ;

R^3 is selected from halo, hydroxy, cyano, methyl, methoxy or hydroxymethyl;

- 5 R^4 is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl)₂carbamoyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2, C_{1-6} alkoxycarbonyl, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^{14} - or heterocyclyl- R^{15} -; wherein R^4 may be optionally substituted on carbon by one or more R^{16} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{17} ;

m is selected from 0-4; wherein the values of R^4 may be the same or different;

- 15 R^8 and R^{12} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, N -(C_{1-6} alkyl)- N -(C_{1-6} alkoxy)amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl)₂carbamoyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2, C_{1-6} alkoxycarbonyl, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^{18} - or heterocyclyl- R^{19} -; wherein R^8 and R^{12} independently of each other may be optionally substituted on carbon by one or more R^{20} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{21} ;

- 25 R^{16} is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl)₂carbamoyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2, C_{1-6} alkoxycarbonyl, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl)₂sulphamoyl, C_{1-6} alkylsulphonylamino, carbocyclyl- R^{22} - or heterocyclyl- R^{23} -; wherein R^{16} may be optionally substituted on carbon by one or more R^{24} ; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{25} ;
- 30

$R^6, R^7, R^{10}, R^{11}, R^{14}, R^{15}, R^{18}, R^{19}, R^{22}$ and R^{23} are independently selected from a direct bond, -O-, -N(R^{26})-, -C(O)-, -N(R^{27})C(O)-, -C(O)N(R^{28})-, -S(O)_s-, -SO₂N(R^{29})- or -N(R^{30})SO₂-; wherein $R^{26}, R^{27}, R^{28}, R^{29}$ and R^{30} are independently selected from hydrogen or C₁₋₆alkyl and s is 0-2;

5 $R^5, R^9, R^{13}, R^{17}, R^{21}$ and R^{25} are independently selected from C₁₋₆alkyl, C₁₋₆alkanoyl, C₁₋₆alkylsulphonyl, C₁₋₆alkoxycarbonyl, carbamoyl, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)carbamoyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl;

R^{20} and R^{24} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxymethyl, methylamino, ethylamino, dimethylamino, diethylamino, N-methyl-N-ethylamino, acetylaminomethyl, N-methylcarbamoyl, N-ethylcarbamoyl, N,N-dimethylcarbamoyl, N,N-diethylcarbamoyl, N-methyl-N-ethylcarbamoyl, phenyl, methylthio, ethylthio, methylsulphonyl, ethylsulphonyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, N-methylsulphamoyl, N-ethylsulphamoyl, N,N-dimethylsulphamoyl, N,N-diethylsulphamoyl or N-methyl-N-ethylsulphamoyl;

or a pharmaceutically acceptable salt thereof;

with the proviso that said compound is not:

N-[4-chloro-3-({[6-(4-methylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

20 N-[4-chloro-3-({[6-(4-ethylpiperazin-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide;

N-{4-chloro-3-[(6-[[3-(dimethylamino)propyl](methyl)amino]pyridin-3-yl)amino]carbonyl}phenyl]-2-morpholin-4-ylisonicotinamide;

25 N-{4-chloro-3-[(6-[[2-(dimethylamino)ethyl](methyl)amino]pyridin-3-yl)amino]carbonyl}phenyl]-2-morpholin-4-ylisonicotinamide; or

N-[4-chloro-3-({[6-(4-methyl-1,4-diazepan-1-yl)pyridin-3-yl]amino}carbonyl)phenyl]-2-morpholin-4-ylisonicotinamide.

2. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in claim 1 wherein Ring A is phenyl, pyridyl, pyrazolyl, thienyl, indolyl, 2,3-dihydrobenzofuranyl, imidazo[1,2-a]pyridinyl, isoxazolyl, benzimidazolyl, 2-oxoindolinyl, furanyl, 1,3-thiazolyl, pyrimidinyl and pyrrolyl; wherein said pyrazolyl, indolyl, pyrrolyl may

be optionally substituted on nitrogen by a group selected from R^5 ; wherein R^5 is selected from C_{1-6} alkyl.

3. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed
 5 in either claim 1 or claim 2 wherein R^1 is a substituent on carbon and is selected from halo, cyano, hydroxy, sulphonyl, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkoxy, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylS(O)_a wherein a is 0 to 2, C_{1-6} alkoxycarbonylamino, N -(C_{1-6} alkyl)sulphonyl, N,N -(C_{1-6} alkyl)₂sulphonyl, N -(C_{1-6} alkyl)- N -(C_{1-6} alkoxy)sulphonyl, N',N' -(C_{1-6} alkyl)₂ureido, C_{1-6} alkylsulphonylamino, carbocyclyl- R^6 - or heterocyclyl- R^7 ;
 10 wherein R^1 may be optionally substituted on carbon by one or more R^8 ; wherein R^8 is selected from halo, cyano, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, N,N -(C_{1-6} alkyl)₂amino, N,N -(C_{1-6} alkyl)₂carbonyl, C_{1-6} alkylS(O)_a wherein a is 0 to 2, N,N -(C_{1-6} alkyl)₂sulphonyl, N -(C_{1-6} alkyl)- N -(C_{1-6} alkoxy)amino, carbocyclyl- R^{18} - or heterocyclyl- R^{19} -; wherein R^8 may be optionally substituted on carbon by one or more R^{20} ;
 15 and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{21} ;
 R^6 , R^7 , R^{18} and R^{19} are independently selected from a direct bond, -O-, -S(O)_s- or -N(R^{30})SO₂-; wherein R^{30} is selected from hydrogen and s is 2;
 R^{21} is selected from C_{1-6} alkyl; and
 20 R^{20} is selected from cyano or hydroxy.

4. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed
 in any one of claims 1-3 wherein n is selected from 0-2; wherein the values of R^1 may be the
 same or different.

25

5. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed
 in any one of claims 1-4 wherein R^2 is hydrogen.
6. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed
 30 in any one of claims 1-5 wherein R^3 is selected from halo, methyl or methoxy.
7. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed
 in any one of claims 1-6 wherein R^4 is selected from halo, cyano, hydroxy, amino, carbonyl,

ureido, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, C₁₋₆alkoxycarbonyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, carbocyclyl-R¹⁴- or heterocyclyl-R¹⁵-; wherein R⁴ may be optionally substituted on carbon by one or more R¹⁶; and wherein if said
 5 heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R¹⁷; wherein

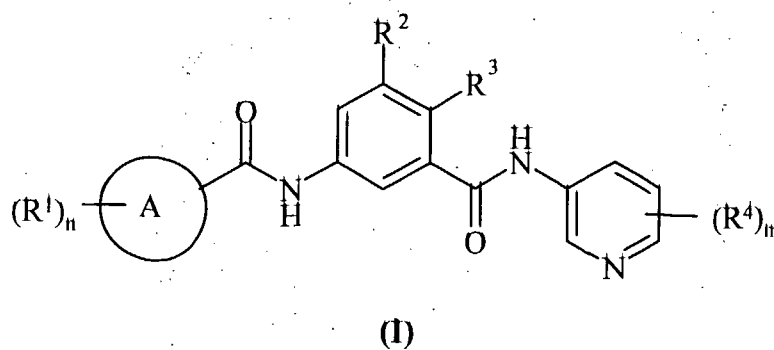
R¹⁶ is selected from halo, hydroxy, amino, C₁₋₆alkoxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, carbocyclyl-R²²- or heterocyclyl-R²³-; wherein R¹⁶ may be optionally substituted on carbon by one or more R²⁴; and wherein if said heterocyclyl contains an -NH-
 10 moiety that nitrogen may be optionally substituted by a group selected from R²⁵;

R¹⁴, R¹⁵, R²² and R²³ are independently selected from a direct bond, -N(R²⁶)- or -C(O)N(R²⁸)-; wherein R²⁶ and R²⁸ are hydrogen;

R¹⁷ and R²⁵ are independently selected from C₁₋₆alkyl and C₁₋₆alkoxycarbonyl; and R²⁴ is methyl or phenyl.

15 8. A compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-7 wherein m is selected from 0-2; wherein the values of R⁴ may be the same or different.

20 9. A compound of formula (I):



wherein:

Ring A is phenyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1-methylpyrazol-5-yl, 1-*t*-butylpyrazol-5-yl, thien-2-yl, thien-3-yl, indol-2-yl, 1-methylindol-2-yl, indol-4-yl, indol-5-yl, indol-6-yl, indol-7-yl, 2,3-dihydrobenzofuran-7-yl, imidazo[1,2-*a*]pyridin-2-yl, isoxazol-3-yl, pyrrol-2-yl, benzimidazol-6-yl, 1-methyl-2-oxoindolin-5-yl, furan-2-yl, 1,3-thiazol-5-yl, pyrimidin-4-yl or 1-methylpyrrol-2-yl;

25

- R^1 is a substituent on carbon and is selected from fluoro, chloro, bromo, iodo, cyano, hydroxy, sulphamoyl, methyl, trifluoromethyl, 1-cyano-1-methylethyl, methoxy, ethoxy, propoxy, isopropoxy, isobutoxy, *N,N*-dimethylamino, difluoromethylthio, *N,N*-dimethylsulphamoyl, *t*-butyl, mesyl, cyclopropylaminosulphonyl, azetidin-1-ylsulphonyl, 5 tetrahydrofuran-2-ylmethylaminosulphonyl, *N*-methyl-*N*-(2,3-dihydroxypropyl)sulphamoyl, mesylamino, morpholinosulphonyl, 1-methylpiperazin-4-ylmethyl, 1-ethylpiperazin-4-ylmethyl, 3,3-dimethylbut-1-yn-1-yl, morpholino, *N,N*-dimethylaminomethyl, 3-methyl-3-hydroxybut-1-yn-1-yl, methylthiomethyl, mesylmethyl, *N*-(methyl)-*N*-(methoxy)sulphamoyl, 2-hydroxymethylpiperidin-1-ylsulphonyl, 3-hydroxymethylpiperidin-1-ylsulphonyl, 4- 10 hydroxymethylpiperidin-1-ylsulphonyl, 1,1-difluoroethyl, piperidin-1-yl, *N,N*-diethylamino, *N',N'*-dimethylureido, cyclopropyl, *t*-butoxycarbonylamino, pyrid-2-yl, phenoxy, 2-methoxy-1,1-dimethylethyl, mesylmethyl, 1,3-thiazol-2-yl, 2-methyl-1,3-thiazol-5-yl, 1-methylcyclopropyl, 1,1-dimethylprop-2-yn-1-yl, 1-(*N,N*-dimethylsulphamoyl)-1-methylethyl, 1,1-dimethylbut-2-yn-1-yl, *N*-(methyl)-*N*-(methoxy)aminomethyl, 1- 15 (*N,N*-dimethylcarbamoyl)-1-methylethyl, 4-methylimidazol-1-yl, 1-(cyclopropyl)-1-methylethyl, 2-methyl-3,4-dihydroxybut-2-yl, 2-methylbut-2-yl, 1-hydroxy-1-cyclopropylethyl, 1-cyanoethyl, 2-cyano-3-methylbut-2-yl, 2-cyanobut-2-yl, 1-hydroxy-2-cyanoprop-2-yl and 2-cyanopyrrol-1-ylmethyl;
- n is selected from 0-2; wherein the values of R^1 may be the same or different;
- 20 R^2 is hydrogen;
- R^3 is selected from fluoro, chloro, methyl or methoxy;
- R^4 is selected from fluoro, chloro, bromo, cyano, hydroxy, amino, carbamoyl, ureido, methyl, ethyl, methoxy, methylamino, isopropylamino, morpholino, 2-(dimethylamino)ethylamino, 2-(hydroxy)ethylamino, 2-(amino)ethylamino, 3-(pyrrolidin-1-yl)propylamino, *N*-methylcarbamoyl, acetylamino, 2-hydroxyacetylamino, trifluoromethyl, mesylamino, 2,2-dimethylpropanoylamino, 3-methoxypropanoylamino, cyclobutylcarbonylamino, cyclopropylamino, 2,3-dihydroxypropylamino, 1,3-dihydroxyprop-2-ylamino, 1-methylpiperazin-4-yl, 1-methylpiperazin-4-ylmethyl, acetyl, *N*-methyl-*N*-(3-dimethylaminopropyl)amino, *N*-methyl-*N*-(2-methoxyethyl)amino, dimethylamino, 25 hydroxymethyl, 1,2-dihydroxyethyl, pyrazol-5-ylamino, 3-aminoprop-1-yn-1-yl, 3-hydroxyprop-1-yn-1-yl, 3-methylaminoprop-1-yn-1-yl, 3-dimethylaminoprop-1-yn-1-yl, 4-aminobutylamino, pyrrolidin-2-ylamino, 3-methylaminopropyl, 3-dimethylaminopropyl, 3-hydroxypropyl, 3-dimethylaminopropylamino, aminomethyl, piperazin-1-yl, 1-

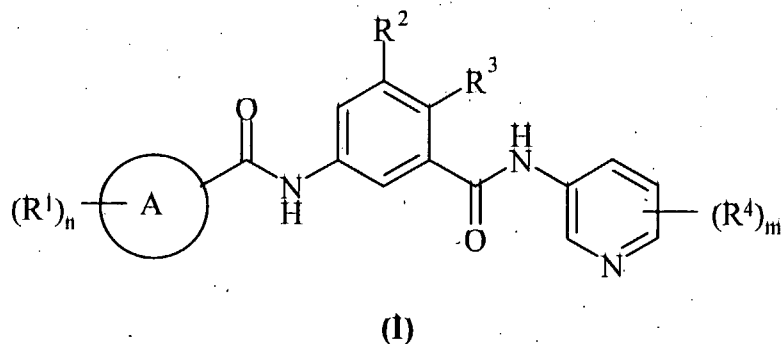
methylpiperazin-4-yl, 2,2-dimethyl-1,3-dioxolan-4-ylmethylamino, pyrrolidin-3-ylmethylamino, piperidin-4-ylmethylamino, imidazol-2-ylmethylamino, methoxymethyl, *N,N*-dimethylsulphamoyl, formylamino, morpholinomethyl, aminomethyl, 2-(dimethylamino)ethylamino, pyrrol-1-yl, pyrrol-2-yl, pyrrolidin-2-yl, imidazol-4-yl, cyclobutylamino, *N*-methyl-*N*-(2-dimethylaminoethyl)amino, 2-dimethylaminoethoxy, dimethylaminomethyl, cyclopropylaminomethyl, piperidin-1-ylmethyl, methylaminomethyl, pyrrolidin-2-ylmethoxy, 3-dimethylaminopropoxy, methoxycarbonyl, 1-(*t*-butoxycarbonyl)pyrrolidin-2-ylmethylamino, 1-(*t*-butoxycarbonyl)pyrrolidin-2-ylmethoxy, 2-phenoxyacetylamino and 1-(*t*-butoxycarbonyl)pyrrolidin-2-yl;

- 10 m is selected from 0-2; wherein the values of R^4 may be the same or different; or a pharmaceutically acceptable salt thereof; with the proviso that said compound is not:

N-[4-chloro-3-({6-(4-methylpiperazin-1-yl)pyridin-3-yl}amino)carbonyl]phenyl]-2-morpholin-4-ylisonicotinamide;

- 15 *N*-{4-chloro-3-[(6-[3-(dimethylamino)propyl](methyl)amino)pyridin-3-yl]amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide; or
N-{4-chloro-3-[(6-[2-(dimethylamino)ethyl](methyl)amino)pyridin-3-yl]amino)carbonyl]phenyl}-2-morpholin-4-ylisonicotinamide.

- 20 10. A compound of formula (I):



selected from:

- N*-(6-amino-5-chloropyridin-3-yl)-5-{{3-(1-cyano-1-methylethyl)benzoyl}amino}-2-methylbenzamide;
- 25 *N*-(6-amino-5-chloropyridin-3-yl)-5-{{3-(1-cyano-1-methylethyl)-5-fluorobenzoyl}amino}-2-methylbenzamide;
- 5-{{3-(1-cyano-1-methylethyl)benzoyl}amino}-*N*-(5-methoxypyridin-3-yl)-2-methylbenzamide;

N-(6-amino-5-chloropyridin-3-yl)-2-methyl-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide;

5-{[3-(1-cyano-1-methylethyl)benzoyl]amino}-*N*-(5,6-dimethylpyridin-3-yl)-2-methylbenzamide;

5 *N*-(3-{[(6-amino-5-chloropyridin-3-yl)amino]carbonyl}-4-methylphenyl)-2-(1-cyano-1-methylethyl)isonicotinamide;

N-(6-amino-5-chloropyridin-3-yl)-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide;

10 *N*-(6-acetylamino-pyridin-3-yl)-5-[3-(cyano-dimethyl-methyl)-benzoylamino]-2-methylbenzamide;

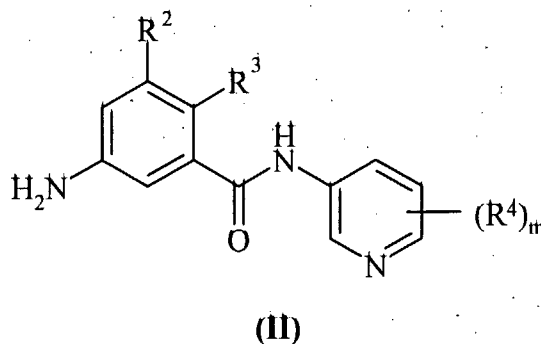
N-[6-(acetylamino)pyridin-3-yl]-2-chloro-5-{[3-(trifluoromethyl)benzoyl]amino} benzamide; and

N-(6-amino-5-methylpyridin-3-yl)-2-chloro-5-{[3-(1-cyano-1-methylethyl)benzoyl]amino} benzamide;

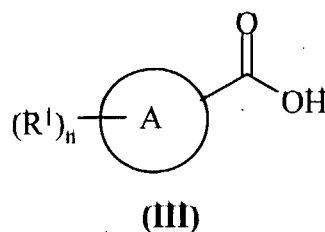
15 or a pharmaceutically acceptable salt thereof.

11. A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt thereof which process, wherein variable groups are, unless otherwise specified, as defined in claim 1, comprises of:

20 *Process a)* reacting an amine of the formula (II)

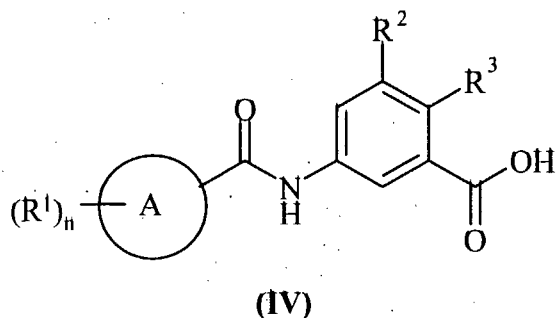


with an acid of formula (III):

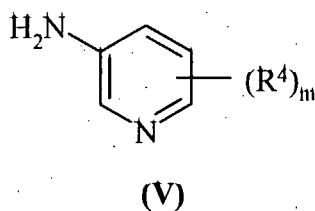


25 or an activated acid derivative thereof;

Process b) reacting an acid of formula (IV):



with an amine of formula (V):



or an activated acid derivative thereof;

and thereafter if necessary:

- i) converting a compound of the formula (I) into another compound of the formula (I);
- 10 ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt.

12. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10, in association
15 with a pharmaceutically-acceptable diluent or carrier.

13. A compound of the formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10 for use as a medicament.

20 14. The use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10, in the manufacture of a medicament for use in the production of a B-Raf inhibitory effect in a warm-blooded animal such as man.

15. The use of a compound of the formula (I), or a pharmaceutically acceptable salt
25 thereof, as claimed in any one of claims 1-10, in the manufacture of a medicament for use in the production of an anti-cancer effect in a warm-blooded animal such as man.

16. The use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10, in the manufacture of a medicament for use in the treatment of melanoma, papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer, leukaemias, lymphoid malignancies, carcinomas and sarcomas in
5 the liver, kidney, bladder, prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon, thyroid, lungs and ovaries.

17. A method for producing a B-Raf inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective
10 amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10.

18. A method for producing an anti-cancer effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount
15 of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10.

19. A method of treating melanoma, papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer, leukaemias, lymphoid malignancies, carcinomas
20 and sarcomas in the liver, kidney, bladder, prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon, thyroid, lungs and ovaries, in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10.

25

20. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10, in association with a pharmaceutically-acceptable diluent or carrier for use in the production of a B-Raf inhibitory effect in a warm-blooded animal such as man.

30

21. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10, in association

with a pharmaceutically-acceptable diluent or carrier for use in the production of an anti-cancer effect in a warm-blooded animal such as man.

22. A pharmaceutical composition which comprises a compound of the formula (I), or a
5 pharmaceutically acceptable salt thereof, as claimed in any one of claims 1-10, in association
with a pharmaceutically-acceptable diluent or carrier for use in the treatment of melanoma,
papillary thyroid tumours, cholangiocarcinomas, colon cancer, ovarian cancer, lung cancer,
leukaemias, lymphoid malignancies, carcinomas and sarcomas in the liver, kidney, bladder,
prostate, breast and pancreas, and primary and recurrent solid tumours of the skin, colon,
10 thyroid, lungs and ovaries in a warm-blooded animal such as man.