

Novel thiochromeno[2,3-c]quinolin-12-one derivatives, preparation
method and application thereof

BACKGROUND OF THE INVENTION

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1. FIELD OF THE INVENTION

The invention relates to development of cancer drug, especially
relates to the development of novel
thiochromeno[2,3-c]quinolin-12-one derivatives, preparation method
10 and application thereof.

2. DESCRIPTION OF THE PRIOR ART

Telomerase is the enzyme that synthesizes telomeric DNA, the
terminal DNA at chromosome ends which, together with
telomere-binding proteins, confers stability to chromosomes. In most
15 of organism, the replication and maintenance of the length of
telomere has to rely on telomerase. The telomerase is composed of
RNA and protein subunits. At present, part of important telomerase
subunits had been identified. The composition of human telomerase
comprising: human telomerase reverse transcriptase (hTERT) having
20 reverse transcriptase activity, human telomerase RNA component
used as a template, and some telomere-binding proteins such as
human telomerase-associated protein, p23, hsp90, hsp40, hsp70 and
the like.

Many research studies had indicated that the activity of human
25 telomerase can only be detected in cells having high proliferation
ability, for example, germ cells, hemopoietic cells, part of stem cells,

most of immortalized cells and most of tumor cells. In the somatic cell, the telomere will be shorten gradually as the number of cell division increased, which may be considered as the mitotic clock for counting the number of cell division. When a telomere is shortened to a certain extent, cell will stop division and entering aging stage, stay at this stage for a period of time, and then goes to death. This period of time is called mortality stage 1 (M1 stage). When a tumor suppressor gene such as p53 or Rb is mutated within M1 stage, the cell might escape from aging stage and keeps on cell division in this period of time which is called mortality stage 2 (M2 stage). If a cell lacks of telomerase activity during this period, the length of a telomere will be reduced still, the telomere will not be able to protect the the terminal end of the chromosome, and this might result into the instability of the chromosome, as well as the cell can not transfer genetic information completely and enters apoptosis in the end. Therefore, M2 stage is also called a crisis satge. Most of cells will die in M2 stage, except small part of cells with telomerase activity will survive. This small part of cells will continue to divide without limitation and become an immortalized cell (or a cancer cell).

In view of the foregoing, it is thought generally that the activation of telomerase can maintain the length of a telomere so as to prevent a cell from entering the ageing stage; or the inhibition of telomerase activity can be used to limit the division of a cancer cell. Both thought may become the key factors in the development of a cell toward immortalization or cancerization. In summary, using the telomerase inhibitors to treat the cancer have been considered as a

novel cancer-specific therapy, as most tumor cells have high expression of telomerase, whereas most normal somatic cells express low or undetectable levels of telomerase and is therefore an attractive target for the design of anticancer agents.

5 Cancers arise from abnormal proliferation of DNA. Therefore, selectively destroy the DNA of cancer cells without damaging the DNA of normal cells is highly desired. However, it is difficult to differentiate the DNAs between normal cells and cancer cells. Consequently, specific 'targeted therapy' was developed following
10 identification of the differences between normal cells and cancer cells, and when combined with other chemotherapies or radiation therapies, targeted therapy can significantly reduce side effects and provide better treatment outcomes. Thus, targeted therapy currently is a popular field in studying cancer treatments. Because topoisomerases
15 have been found to play an indispensable role in DNA replication, they have become the objects of targeted therapy for anticancer treatments. The anticancer drug camptothecin discovered by M.E. Wall and M.C. Wani in 1966 through systematic screening of natural substances is an inhibitor for type I topoisomerases.

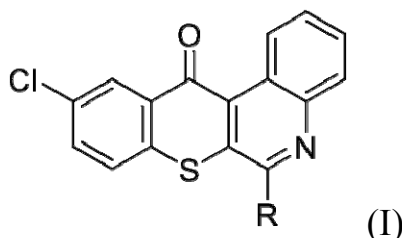
20 Unfortunately, camptothecin has numerous disadvantages and thus cannot be used for clinical treatment. For example, the lactone ring can be easily hydrolyzed to hydroxycarboxylate *in vivo* at the normal pH and then binds to serum albumin and lose its effect of inhibiting the function of type I topoisomerases. In addition, the
25 structure of the tricomplex of camptothecin-Top I-DNA is not stable

because the complex is not maintained by covalent bonds and water solubility of camptothecin is poor which causes lower bioavailability. The p-glycoprotein (MDR1, ABCB1) efflux transporter proteins in the cell membrane transported the drugs out of the cells and more
 5 important is that some tumor cells have slowly developed resistance and adverse drug side effects against camptothecin. As a result, a number of water-soluble semi-synthetic drugs were developed even after commercialization of camptothecin such as Topotecan (HYCAMTIN[®]) which is used for treating ovarian cancer and
 10 Irinotecan (CAMPTO[®]) which is used for treating colon cancer and both have issues when used for clinical treatment.

Hence, based on the importance of topoisomerase inhibitors in development of anticancer drugs, the inventor of this application developed a series of novel thiochromeno[2,3-c]quinolin-12-one
 15 derivatives and disclosed the preparation methods as well as relevant applications herein after a number of innovative improvements.

SUMMARY OF THE INVENTION

In one aspect, present invention provides a compound as shown
 20 in formulation (I):



wherein the R is selected from the groups consisting of:

- i) halo, amino, hydroxyl and thiol groups;

- ii) linear alkyl chains of $N(CH_2)_nH$, alkyl groups with substituted side chains, alkyl side chains with a substituted amino group and alkyl side chains with a substituted hydroxyl group, wherein $1 \leq n \leq 10$;
- 5 iii) $O(CH_2)_nH$, $N(CH_3)_2$, $NH(CH_2)_nNH(CH_2)_nOH$, wherein $1 \leq n \leq 10$;
- iv) nitrogen-containing cycloalkyl groups and heterocyclic compounds of C_{3-12} which contain 1 to 3 heteroatoms selected from O, S and N, wherein the ortho-, para- and meta- position
 10 can be further selected independently from one of the groups consisting of: hydrogen group, $(CH_2)_n$ alkyl groups, $(CH_2)_n$ hydroxyl groups, $(CH_2)_nC_{3-12}$ cycloalkyl groups, $(CH_2)_nC_{3-12}$ nitrogen-containing cycloalkyl groups, $(CH_2)_n$ benzene rings, formyl group and $(CH_2)_nCOC_{3-12}$ nitrogen-containing
 15 cycloalkyl groups, wherein $0 \leq n \leq 10$;
- v) $NH(CH_2)_nR_1$, $0 \leq n \leq 10$, wherein R_1 is selected from the groups consisting of: $N(CH_3)_2$, $C(NH_2)_2$, linear alkyl chains of $NH(CH_2)_nH$, alkyl groups with substituted side chains, alkyl side chains with a substituted amino group and alkyl
 20 side chains with a substituted hydroxyl group;
- vi) $NH(CH_2)_nR_2$, $0 \leq n \leq 10$, wherein R_2 is selected from the groups consisting of: benzene rings, C_{3-12} cycloalkyl groups and heterocyclic groups of which contain 1 to 3 heteroatoms selected from O, S and N, wherein the ortho-, para- and meta-
 25 position can be further selected independently from one of the groups consisting of: Methoxyl group, amino group, benzene rings, alkyl, amino, nitro, hydroxyl groups with

substituted C1-C3 side chains and C₃₋₁₂ heterocyclic groups;
 wherein the C₃₋₁₂ heterocyclic groups which contain 1 to 3
 heteroatoms selected from O, S and N;

and their pharmaceutically acceptable salts, stereoisomers and
 5 enantimers.

According to the invention, wherein the R group consisting of i)
 ~ vi) are selected from the group consisting of chlorine, hydroxyl,
 methoxyl, dimethylamino, piperazin-1-yl, 4-methylpiperazin-1-yl,
 4-ethylpiperazin-1-yl, 4-(2-hydroxyethyl)piperazin-1-yl,
 10 4-Benzylpiperazin-1-yl, 4-phenylpiperazin-1-yl, morpholino,
 thiomorpholino, piperidin-1-yl, 4-hydroxypiperidin-1-yl,
 4-Benzylpiperidin-1-yl, (1,4'-Bipiperidin)-1'-yl,
 4-(3-(piperidin-4-yl)propyl)piperidin-1-yl, pyrrolidin-1-yl,
 2-oxopiperidin-1-yl, methylamino, ethylamino, propylamino,
 15 butylamino, isobutylamino, pentan-3-ylamino,
 (2-(dimethylamino)ethyl)amino, (2-(diethylamino)ethyl)amino,
 2-ethanolamino, 3-propanolamino, 5-pentanolamino,
 (1-hydroxybutan-2-yl)amino, (4-methylpentan-2-yl)amino,
 (2-Aminoethyl)amino, (2-((2-hydroxyethyl)amino)ethyl)amino,
 20 (2-morpholinoethyl)amino, (3-(dimethylamino)propyl)amino,
 (3-(diethylamino)propyl)amino,
 (3-((2-hydroxyethyl)amino)propyl)amino,
 (2,3-dihydro-1H-inden-2-yl)amino, cyclohexylamino,
 (1-Benzylpiperidin-4-yl)amino, (thiophen-2-ylmethyl)amino,
 25 (cyclohexylmethyl)amino, benzylamino, (pyridin-2-ylmethyl)amino,
 (Benzo[d][1,3]dioxol-5-ylmethyl)amino, (2-methoxybenzyl)amino,
 (3,4-dimethoxybenzyl)amino, phenethylamino,

(4-methoxyphenethyl)amino, (4-aminophenethyl)amino, guanidine and piperidin-1-ylamino.

According to the invention, wherein the compound is selected from the group consisting of:

- 5 3-((4-Chlorophenyl)thio)-2-hydroxyquinoline-4-carboxylic acid,
- 6,9-Dichloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-hydroxy-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-methoxy-12H-thiochromeno[2,3-c]quinolin-12-one
- 10-Chloro-6-dimethylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10 10-Chloro-6-(piperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(4-methylpiperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(4-ethylpiperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 15 10-Chloro-6-(4-(2-hydroxyethyl)piperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 6-(4-Benzylpiperazin-1-yl)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 20 10-Chloro-6-(4-phenylpiperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-morpholino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-thiomorpholino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 25 10-Chloro-6-(piperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(4-hydroxypiperidin-1-yl)-12H-thiochromeno[2,3-c]quin

- olin-12-one,
 6-(4-Benzylpiperidin-1-yl)-10-chloro-12H-thiochromeno[2,3-c]quinol
 in-12-one,
 6-([1,4'-Bipiperidin]-1'-yl)-10-chloro-12H-thiochromeno[2,3-c]quinoli
 5 n-12-one,
 10-Chloro-6-(4-(3-(piperidin-4-yl)propyl)piperidin-1-yl)-12H-thiochr
 omeno[2,3-c]quinolin-12-one,
 10-Chloro-6-(pyrrolidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-o
 ne,
 10 10-Chloro-6-(2-oxopiperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-
 12-one,
 10-Chloro-6-methylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-ethylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-propylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
 15 6-(Butylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-isobutylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-(pentan-3-ylamino)-12H-thiochromeno[2,3-c]quinolin-1
 2-one,
 10-Chloro-6-((2-(dimethylamino)ethyl)amino)-12H-thiochromeno[2,3
 20 -c]quinolin-12-one,
 10-Chloro-6-((2-(diethylamino)ethyl)amino)-12H-thiochromeno[2,3-c
]quinolin-12-one,
 10-Chloro-6-(2-ethanolamino)-12H-thiochromeno[2,3-c]quinolin-12-
 one,
 25 10-Chloro-6-(3-propanolamino)-12H-thiochromeno[2,3-c]quinolin-12
 -one,
 10-Chloro-6-(5-pentanolamino)-12H-thiochromeno[2,3-c]quinolin-12

-one,

10-Chloro-6-((1-hydroxybutan-2-yl)amino)-12H-thiochromeno[2,3-c]
quinolin-12-one,

10-Chloro-6-((4-methylpentan-2-yl)amino)-12H-thiochromeno[2,3-c]

5 quinolin-12-one,

6-((2-Aminoethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinoli
n-12-one,

10-Chloro-6-((2-((2-hydroxyethyl)amino)ethyl)amino)-12H-thiochro
meno[2,3-c]quinolin-12-one,

10 10-Chloro-6-((2-morpholinoethyl)amino)-12H-thiochromeno[2,3-c]qu
inolin-12-one,

10-Chloro-6-((3-(dimethylamino)propyl)amino)-12H-thiochromeno[2,
3-c]quinolin-12-one,

10-Chloro-6-((3-(diethylamino)propyl)amino)-12H-thiochromeno[2,3

15 -c]quinolin-12-one,

10-Chloro-6-((3-((2-hydroxyethyl)amino)propyl)amino)-12H-thiochro
meno[2,3-c]quinolin-12-one,

10-Chloro-6-((2,3-dihydro-1H-inden-2-yl)amino)-12H-thiochromeno[
2,3-c]quinolin-12-one,

20 10-Chloro-6-(cyclohexylamino)-12H-thiochromeno[2,3-c]quinolin-12
-one,

6-((1-Benzylpiperidin-4-yl)amino)-10-chloro-12H-thiochromeno[2,3-
c]quinolin-12-one,

10-Chloro-6-((thiophen-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]

25 quinolin-12-one,

10-Chloro-6-((cyclohexylmethyl)amino)-12H-thiochromeno[2,3-c]qui
nolin-12-one,

6-(Benzylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one

,

10-Chloro-6-((pyridin-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,

5 6-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,

10-Chloro-6-((2-methoxybenzyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,

10-Chloro-6-((3,4-dimethoxybenzyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,

10-Chloro-6-(phenethylamino)-12H-thiochromeno[2,3-c]quinolin-12-one,

10-Chloro-6-((4-methoxyphenethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,

15 6-((4-Aminophenethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,

2-(10-Chloro-12-oxo-12H-thiochromeno[2,3-c]quinolin-6-yl)guanidine,

10-Chloro-6-(piperidin-1-ylamino)-12H-thiochromeno[2,3-c]quinolin-12-one,

and their salts.

In another aspect, the invention provides a pharmaceutical composition comprising an effective amount of the abovementioned compound and at least one pharmaceutically acceptable vehicle, diluent or excipient.

In another aspect, the invention provides a method for inhibiting Topoisomerase I activity which comprises administering an effective

amount of the abovementioned compound.

In another aspect, the invention provides a method for inhibiting Topoisomerase II activity which comprises administering an effective amount of the compound according to claim 1.

5 In another aspect, the invention provides a method for the treatment of cancer which comprises administering an effective amount of the compound according to claim 1.

According to the invention,, wherein the cancer is selected from the groups consisting of leukemia, non-small cell lung cancer, 10 colorectal cancer, central nervous system (CNS) cancer, melanoma, ovarian cancer, renal cancer, prostate cancer and breast cancer.

In another aspect, the invention provides a method for preparation of thiochromeno[2,3-*c*]quinolin-12-one derivatives, wherein the method comprising:

- 15 (1) mix isatin, 2-((4-chlorophenyl)thio)acetic acid and sodium acetate was heated at 150 °C for 1 h, after cooling the mixture was added acetic acid, the precipitate was collected, washed with acetic acid, water and n-hexane, and obtained compound 2 (3-((4-Chlorophenyl)thio)-2-hydroxyquinoline-4-carboxylic acid); 20
- (2) a solution of compound 2 (3-((4-Chlorophenyl)thio)-2-hydroxyquinoline-4-carboxylic acid) in phosphoryl trichloride was heated at 150 °C for 48 h, after cooling the mixture was poured into water 0 °C, the precipitate was 25 collected by filtration, then added into 10% NaHCO₃ with vigorous stirring for 1 h, the resulting precipitate was collected and washed with H₂O, the crude solid was

recrystallized by dichloromethane to give compound 3

(6,9-Dichloro-12H-thiochromeno[2,3-c] quinolin-12-one);

(3) a solution of compound 3 (6,9-Dichloro-12H-thiochromeno
[2,3-c]quinolin-12-one) in DMF was added conc. HCl and
5 refluxed, after 6 hours, the conc. HCl was added dropwise
and refluxed for another 12 hours, the mixture was
evaporated in vacuo and treated with H₂O, after filtered the
crude solid was washed with EtOH to give compound 4
(10-Chloro-6-hydroxy-12H-thiochromeno[2,3-c]quinolin-12-
10 one);

(4) a suspension of compound 3 (6,9-Dichloro-12H-
thiochromeno[2,3-c]quinolin-12-one) and sodium methoxide
in methanol was refluxed for 16 h, after cooled the solvent
was removed, filtrated and washed with ethanol and n-hexane
15 to collect compound 5 (10-Chloro-6-methoxy-12H-
thiochromeno[2,3-c]quinolin-12-one);

(5) a solution of compound 3 (6,9-Dichloro-12H-
thiochromeno[2,3-c]quinolin-12-one), appropriate secondary
amines and sodium carbonate in DMSO was refluxed for 10
20 hours, then the reaction was added ice-water, the precipitate
was filtered, washed with water/methanol and collected to get
compound 6-21:

10-Chloro-6-dimethylamino-12H-thiochromeno[2,3-c]quinoli
n-12-one,

25 10-Chloro-6-(piperazin-1-yl)-12H-thiochromeno[2,3-c]quinol
in-12-one,

10-Chloro-6-(4-methylpiperazin-1-yl)-12H-thiochromeno[2,3

- c]quinolin-12-one,
 10-Chloro-6-(4-ethylpiperazin-1-yl)-12H-thiochromeno[2,3-c]
]quinolin-12-one,
 10-Chloro-6-(4-(2-hydroxyethyl)piperazin-1-yl)-12H-thiochr
 5 omeno[2,3-c]quinolin-12one,
 6-(4-Benzylpiperazin-1-yl)-10-chloro-12H-thiochromeno[2,3-
 c]quinolin-12-one,
 10-Chloro-6-(4-phenylpiperazin-1-yl)-12H-thiochromeno[2,3
 -c]quinolin-12-one,
 10 10-Chloro-6-morpholino-12H-thiochromeno[2,3-c]quinolin-1
 2-one,
 10-Chloro-6-thiomorpholino-12H-thiochromeno[2,3-c]quino
 lin-12-one,
 10-Chloro-6-(piperidin-1-yl)-12H-thiochromeno[2,3-c]quino
 15 lin-12-one,
 10-Chloro-6-(4-hydroxypiperidin-1-yl)-12H-thiochromeno[2,
 3-c]quinolin-12-one,
 6-(4-Benzylpiperidin-1-yl)-10-chloro-12H-thiochromeno[2,3-
 c]quinolin-12-one,
 20 6-([1,4'-Bipiperidin]-1'-yl)-10-chloro-12H-thiochromeno[2,3-
 c]quinolin-12-one,
 10-Chloro-6-(4-(3-(piperidin-4-yl)propyl)piperidin-1-yl)-12H
 -thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-(pyrrolidin-1-yl)-12H-thiochromeno[2,3-c]quino
 25 lin-12-one, and
 10-Chloro-6-(2-oxopiperidin-1-yl)-12H-thiochromeno[2,3-c]
 quinolin-12-one respectively;

- (6) a solution of compound 3 (6,9-Dichloro-12H-thiochromeno[2,3-c]quinolin-12-one) in DMSO was added appropriate primary amines and refluxed for 8 hours, after cooled the reaction was added water, the precipitate was filtered and washed with water and methanol to collect compound N1~N34:
- 10-Chloro-6-methylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-ethylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-propylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 6-(Butylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-isobutylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(pentan-3-ylamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-(dimethylamino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-(diethylamino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(2-ethanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(3-propanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(5-pentanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one,

- nolin-12-one,
 10-Chloro-6-((1-hydroxybutan-2-yl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 10-Chloro-6-((4-methylpentan-2-yl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 5 6-((2-Aminoethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]
]quinolin-12-one,
 10-Chloro-6-((2-((2-hydroxyethyl)amino)ethyl)amino)-12H-t
 hiochromeno[2,3-c]quinolin-12-one,
 10 10-Chloro-6-((2-morpholinoethyl)amino)-12H-thiochromeno[
 2,3-c]quinolin-12-one,
 10-Chloro-6-((3-(dimethylamino)propyl)amino)-12H-thiochr
 omeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((3-(diethylamino)propyl)amino)-12H-thiochro
 15 meno[2,3-c]quinolin-12-one,
 10-Chloro-6-((3-((2-hydroxyethyl)amino)propyl)amino)-12H
 -thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((2,3-dihydro-1H-inden-2-yl)amino)-12H-thioch
 romeno[2,3-c]quinolin-12-one,
 20 10-Chloro-6-(cyclohexylamino)-12H-thiochromeno[2,3-c]qui
 nolin-12-one,
 6-((1-Benzylpiperidin-4-yl)amino)-10-chloro-12H-thiochrom
 eno[2,3-c]quinolin-12-one,
 10-Chloro-6-((thiophen-2-ylmethyl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 25 10-Chloro-6-((cyclohexylmethyl)amino)-12H-thiochromeno[
 2,3-c]quinolin-12-one,

6-(Benzylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((pyridin-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
 5 6-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((2-methoxybenzyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((3,4-dimethoxybenzyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-(phenethylamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((4-methoxyphenethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
 15 6-((4-Aminophenethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
 2-(10-Chloro-12-oxo-12H-thiochromeno[2,3-c]quinolin-6-yl)guanidine, and
 10-Chloro-6-(piperidin-1-ylamino)-12H-thiochromeno[2,3-c]quinolin-12-one respectively.

These features and advantages of the present invention will be fully understood and appreciated from the following detailed description of the accompanying Drawings.

25 BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 depicts the general scheme for a series of thiochromeno[2,3-c]quinolin-12-one derivatives.

Fig. 2 is the effect of compounds **5, 7, 8, 16, 19** and CPT on DNA relaxation catalyzed by TOP I at a concentration of 25 μ M and 50 μ M.

Fig. 3 is the effect of compounds **N2, N7, N8, N9, N14-N19, N25**, and CPT on DNA relaxation catalyzed by TOP I at a concentration of 50 μ M.

Fig. 4a-d are the effects of compounds **7, N7, N14, N15, N18, N19** and **N25** on TOP I mediated supercoiled DNA relaxation.

Fig. 5 is the effect of compounds **5, 7, 8, 16, 19** and VP-16 on DNA relaxation catalyzed by TOP II at a concentration of 25 μ M and 50 μ M.

Fig. 6 is the effect of compounds **N2, N7, N8, N9, N14-N19, N25**, and VP-16 on DNA relaxation catalyzed by TOP II at a concentration of 50 μ M.

Fig. 7a-d are the effects of compounds **7, N7, N8, N14, N15, N18**, and **N19** on TOP II mediated supercoiled DNA relaxation.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

20

Unless defined otherwise, all technical and scientific terms used herein have the meaning commonly understood by a person skilled in the art to which this invention belongs. As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

25 The present invention will now be described more specifically with reference to the following embodiments, which are provided for the

purpose of demonstration rather than limitation.

The term "**treatment**", "**under treatment**" and similar terms refer to the methods which ameliorate, improve, reduce or reverse the patient's disease or any relevant symptoms caused by the disease, or
5 methods which can prevent onset of such diseases or any resulting symptoms.

The term "**pharmaceutically acceptable**" is used to describe substances to be used in the composition must be compatible with other ingredients in the formulation and be harmless to the subject.

10 The inventive composition can be prepared into a dosage form for suitable application of the inventive composition by using technology commonly understood by a person skilled in the art through formulating the abovementioned *Lactobacillus* isolated strain(s) with a pharmaceutically acceptable vehicle, wherein the
15 excipients include, but are not limited to, solution, emulsion, suspension, powder, tablet, pill, lozenge, troche, chewing gum, slurry, and other suitable forms.

The pharmaceutically acceptable vehicle may contain one or several reagents selecting from the following list: solvents, emulsifiers,
20 suspending agents, decomposers, binding agents, excipients, stabilizing agents, chelating agents, diluents, gelling agents, preservatives, lubricants, surfactants and other agents suitable for use in the invention.

In the abovementioned compositions, one or more dissolving aids,
25 buffers, preservatives, colorants, fragrances, flavoring agents and the

like, which are commonly used for formulation can be added as desired.

The term "**pharmaceutically acceptable excipients**", as used herein, refers to substances known by persons skilled in the art, which
5 are physiologically inert, pharmacologically inactive and are compatible with the physical as well as chemical characteristics of sorafenib or GW5074. Pharmaceutically acceptable excipients include, but are not limited to, polymers, resins, plasticizers, fillers, lubricants, diluents, binders, disintegrants, solvents, co-solvents, surfactants,
10 preservatives, sweetening agents, flavoring agents, pharmaceutical grade dyes or pigments, and viscosity agents.

The term "**pharmaceutical composition**" is used to describe solid or liquid compositions in a form, concentration and purity that are suitable for administration in patients (e.g. humans or animals) and
15 can induce desired physiological changes following administration. Pharmaceutical compositions are typically sterile and non-pyrogenic.

The present invention will now be described more specifically with reference to the following embodiments, which are provided for the purpose of demonstration rather than limitation. The drugs as well
20 as biomaterials used in the invention are all commercially available materials and the sources disclosed below are merely examples.

All reactions were monitored by thin-layer chromatography (TLC) coated with silica gel 60 F₂₅₄. Melting points of all synthetic compounds were measured with Büchi B-545 melting point apparatus.
25 ¹H NMR: Varian GEMINI-300 (300 MHz) or Agilent 400 MR DD2

(400 MHz); δ values are in ppm relative to tetramethylsilane (TMS) as an internal standard (0 ppm). Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintuplet), sext (sextet), sep (septet), m (multiplet), dd (doublet of doublet), dt (doublet of triplet),
5 td (triplet of doublet), qd (quartet of doublet) and br (broadened).
Mass spectra: High resolution electrospray ionization (HRESI): Finnigan MAT 95S (Instrumentation Center, National Taiwan University, Taipei, Taiwan). X-ray Single Crystal Diffraction: Bruker Enraf-Nonius APEX II diffractometer (Department of Chemistry,
10 National Taiwan Normal University). Typical experiments illustrating the general procedures for the preparation of the thiochromenoquinolones are described below (Fig. 1).

General procedures for chemical synthesis

General procedure A : Preparation of compound 2

15 A mixture of isatin (1) (0.44 g, 2.99 mmol), 2-((4-chlorophenyl)thio)acetic acid (0.70 g, 3.47 mmol), and sodium acetate (0.05 g) was heated at 150 °C in miniclave for 1 h (TLC monitored). After cooling, the mixture was added acetic acid 10 mL, and the gray precipitate was collected, washed with acetic acid, water
20 and n-hexane, and obtained light purple compound.

General procedure B : Preparation of compound 3

A solution of compound 2 (0.55 g, 2.1 mmol) in phosphoryl trichloride (5 mL) was heated at 150 °C for 48 h. After cooling, the mixture was poured into ice (50 mL) at 0 °C. The resulting green
25 precipitate that separated was collected by filtration. The filtered cake

was suspended in 10% NaHCO₃ solution (50 mL) with vigorous stirring for 1 h. The resulting precipitate was collected and washed with H₂O. The crude solid was recrystallized from dichloromethane to give yellow product.

5 General procedure C : Preparation of compound 4

To a solution of compound 3 (0.32 g, 0.96 mmol) in DMF (20 mL) was added conc. HCl (3 mL) and refluxed. After 6 h, the conc. HCl (6 mL) was added dropwise and refluxed for another 12 h. The mixture was evaporated in vacuo and treated with H₂O (20 mL), after
10 filtered the crude solid was washed with EtOH to give yellow solid.

General procedure D : Preparation of compound 5

A suspension of compound 3 (0.33 g, 1.0 mmol) and sodium methoxide (0.55g, 10 mmol) in methanol (20 mL) was refluxed for 16 h. After cooled, the solvent was removed by rotarvapor vacuum,
15 filtrated and washed with ethanol and n-hexane to collect the white solid.

General procedure E : Preparation of compounds 6-21

Compound 3 (0.33 g, 1.0 mmol), appropriate secondary amines (1.1 mmol) and sodium carbonate (5 mmol) in DMSO (20 mL) was
20 refluxed for 10 h (TLC monitored). After 30 min, the reaction was added ice-water (100 mL). The precipitate was filtered, washed with water/methanol and collected to get the yellow solid.

General procedure F : Preparation of compounds N1-N32

To a solution of compound 3 (0.33 g, 1.0 mmol) in DMSO (30
25 mL) was added appropriate primary amines (1.1 mmol) and refluxed for 8 h (TLC monitored). After cooled, the reaction was added water

(100 mL). The precipitate was filtered and washed with water and hot methanol to collect the yellow solid.

Example 1

3-((4-Chlorophenyl)thio)-2-hydroxyquinoline-4-carboxylic acid

5 **(TC-SCI) (2)**

The pure compound was obtained as a gray solid (yield 86%). (R_f = 0.5 at EA: AcOH = 20: 1). Mp 306-308 °C. ^1H NMR (300 MHz, DMSO- d_6): δ (ppm) 7.26 (3H, t, J = 7.6 Hz, Ar-H), 7.34 (2H, d, J = 6.0 Hz, Ar-H), 7.39 (1H, d, J = 8.0 Hz, Ar-H), 7.46 (1H, d, J = 8.0 Hz, Ar-H), 7.62 (1H, t, J = 8.0 Hz, Ar-H), 12.22 (1H, s, -COOH). ^{13}C NMR (100 MHz, DMSO- d_6): δ (ppm) 115.58, 116.26, 120.36, 123.21, 126.21, 129.33, 130.30, 131.47, 132.54, 134.36, 140.11, 151.69, 159.37, 166.80 (C=O). HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{10}\text{NO}_3\text{SCl}$ $[\text{M}]^+$ 331.0070; found $[\text{M}+\text{H}]^+$ 332.0147 (100), $[\text{M}+\text{H}+2]^+$ 334.0122 (33);
15 found $[\text{M}-\text{H}]^-$ 330.0002.

Example 2

6,9-Dichloro-12H-thiochromeno[2,3-c]quinolin-12-one (3)

The yellow solid material was isolated in 90% yield (R_f = 0.50 at CH_2Cl_2 : n-hexane = 1: 1). Mp 259-261°C (CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.71 (2H, m, Ar-H), 7.77-7.85 (2H, m, Ar-H), 8.10-8.13 (m, 1H, Ar-H), 8.60 (t, 1H, J = 1.2 Hz, Ar-H), 9.67-9.71 (1H, m, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 124.87, 126.28, 127.85, 129.17, 129.39, 129.93, 130.31, 131.20, 131.90, 133.01, 133.09, 133.38, 134.43, 145.27, 146.61, 180.64 (C=O). HRMS (ESI) calcd for $\text{C}_{16}\text{H}_7\text{NOSCl}_2$ $[\text{M}]^+$ 330.9625; found $[\text{M}+\text{H}]^+$ 331.9699 (100),
25 $[\text{M}+\text{H}+2]^+$ 333.9672 (67), $[\text{M}+\text{H}+4]^+$ 335.9645 (11).

Example 3

**10-Chloro-6-hydroxy-12H-thiochromeno[2,3-c]quinolin-12-one
(4)**

The yellow solid material was isolated in 95% yield ($R_f = 0.40$ at
 5 EA). Mp > 410 °C. ^1H NMR (400 MHz, DMSO- d_6): δ ppm 7.35 (1H,
 td, $J = 7.2, 1.2$ Hz, Ar-H), 7.47 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H), 7.59
 (1H, td, $J = 7.2$ Hz, 1.6 Hz, Ar-H), 7.89 (1H, dd, $J = 8.4$ Hz, 2.4 Hz,
 Ar-H), 8.10 (1H, d, $J = 8.8$ Hz, Ar-H), 8.38 (1H, d, $J = 2.4$ Hz, Ar-H),
 9.35 (1H, dd, $J = 8.4, 2.4$ Hz, Ar-H), 12.73 (br, 1H, -OH). ^{13}C NMR
 10 (75 MHz, CDCl_3): δ (ppm) 116.61, 117.52, 123.65, 126.82, 128.44,
 130.22, 130.49, 130.54, 132.52, 133.00, 133.42, 135.09, 136.27,
 138.90, 158.70, 180.38 (C=O). HRMS (ESI) m/z calcd for
 $\text{C}_{16}\text{H}_8\text{NO}_2\text{SCl}$ $[\text{M}]^+$: 312.9964, found, 314.0051.

Example 4

**10-Chloro-6-methoxy-12H-thiochromeno[2,3-c]quinolin-12-one
(5)**

The gray solid material was isolated in 91% yield ($R_f = 0.52$ at
 CH_2Cl_2 : n-hexane = 1: 1). Mp 227-228 °C. ^1H NMR (400 MHz,
 CDCl_3): δ (ppm) 4.27 (3H, s, $-\text{OCH}_3$), 7.60 (1H, td, $J = 7.6, 1.2$ Hz,
 20 Ar-H), 7.37 (1H, d, $J = 2.0$ Hz, Ar-H), 7.70 (1H, td, $J = 7.6$ Hz, 1.6 Hz,
 Ar-H), 7.94 (1H, dd, $J = 8.0$ Hz, 1.2 Hz, Ar-H), 8.60 (1H, d, $J = 1.6$
 Hz, Ar-H), 9.64 (1H, dd, $J = 8.8$ Hz, 1.2 Hz, Ar-H). ^{13}C NMR (100
 MHz, CDCl_3): δ (ppm) 54.83 (OCH_3), 122.91, 126.23, 126.54, 126.76,
 127.66, 127.95, 129.23, 129.50, 130.54, 132.49, 133.48, 133.85,
 25 143.82, 156.06, 180.47 (C=O). HRMS (ESI) m/z calcd for
 $\text{C}_{17}\text{H}_{10}\text{NO}_2\text{SCl}$ $[\text{M}]^+$ 327.0121; found $[\text{M}+\text{H}]^+$ 328.0203, $[\text{M}+\text{H}+2]^+$
 330.0172.

Example 5

10-Chloro-6-dimethylamino-12H-thiochromeno[2,3-c]quinolin-12-one (6)

Product **6** was prepared from **3** and dimethylamine. The
 5 light-yellow solid material was isolated in 85% yield ($R_f = 0.45$ at
 CH_2Cl_2 : n-hexane = 1: 1). Mp 194-195 °C. ^1H NMR (400 MHz,
 CDCl_3): δ (ppm) 3.06 (6H, s, $-\text{CH}_3$), 7.59-7.67 (3H, m, Ar-H), 7.71
 (1H, t, $J = 7.2$ Hz, Ar-H), 8.00 (1H, d, $J = 8.4$ Hz, Ar-H), 8.59 (1H, d, J
 $= 1.2$ Hz, Ar-H), 9.60 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz,
 10 CDCl_3): δ (ppm) 43.00, 123.44, 125.71, 127.22, 127.78 128.47,
 129.07, 129.37, 130.59, 130.67, 132.23, 132.46, 133.61, 134.36,
 144.84, 158.32, 181.52 ($\underline{\text{CO}}$). HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{OSCl}$
 $[\text{M}]^+$ 340.0437; found $[\text{M}+\text{H}]^+$ 341.0517 (100), $[\text{M}+\text{H}+2]^+$ 343.0501
 (33).

15 Example 6

10-Chloro-6-(piperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (7)

Product **7** was prepared from **3** and piperazine. The dark-yellow
 solid material was isolated in 69% yield ($R_f = 0.12$ at EA: MeOH:
 20 ammonia water = 20: 5: 1). Mp 211-213 °C. ^1H NMR (400 MHz,
 CDCl_3): δ (ppm) 3.20 (4H, t, $J = 4.8$ Hz, $-\text{CH}_2-$), 3.36 (4H, t, $J = 4.8$
 Hz, $-\text{CH}_2-$), 7.60-7.66 (3H, m, Ar-H), 7.70 (1H, td, $J = 8.0, 1.2$ Hz,
 Ar-H), 7.99 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H), 8.56 (1H, d, $J = 2.0$ Hz,
 Ar-H), 9.60 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz,
 25 CDCl_3): δ (ppm) 45.95, 52.31, 123.62, 125.81, 127.58, 127.86, 128.72,
 129.10, 129.37, 130.65, 130.99, 132.17, 132.47, 133.63, 134.33,
 144.94, 157.61, 181.45 ($\underline{\text{CO}}$). HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{N}_3\text{OSCl}$

$[M]^+$ 381.0703; found $[M+H]^+$ 382.0783.

Example 7

10-Chloro-6-(4-methylpiperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (8)

Product **8** was prepared from **3** and 1-methylpiperazine. The green-yellow solid material was isolated in 80% yield ($R_f = 0.24$ at EA: methanol = 5: 1). Mp 212-214 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 2.51 (3H, s, $-\text{CH}_3$), 2.84 (4H, br, $-\text{CH}_2-$), 3.50 (4H, t, $J = 4.5$ Hz, $-\text{CH}_2-$), 7.60-7.66 (3H, m, Ar-H), 7.68-7.72 (1H, td, $J = 8.1, 1.5$ Hz, Ar-H), 8.01 (1H, dd, $J = 8.1, 1.5$ Hz, Ar-H), 8.56 (1H, d, $J = 1.5$ Hz, Ar-H), 9.60 (1H, dd, $J = 8.4, 1.5$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 45.73, 50.31, 54.65, 123.70, 125.90, 127.60, 127.80, 128.82, 129.20, 129.39, 130.62, 130.84, 132.36, 132.47, 133.78, 134.24, 145.08, 157.18, 181.42 (C=O). HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{OSCl}$ $[M]^+$ 395.0859; found $[M+H]^+$ 396.0926.

Example 8

10-Chloro-6-(4-ethylpiperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (9)

Product **9** was prepared from **3** and 1-ethylpiperazine. The yellow solid material was isolated in 74% yield ($R_f = 0.48$ at EA: MeOH = 10: 1). Mp 196-198 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.19 (3H, t, $J = 7.2$ Hz, $-\text{CH}_3$), 2.58 (2H, q, $J = 7.2$ Hz, $-\text{CH}_2-$), 2.78 (4H, br, $-\text{CH}_2-$), 3.46 (4H, t, $J = 4.4$ Hz, $-\text{CH}_2-$), 7.61-7.66 (3H, m, Ar-H), 7.68-7.73 (1H, td, $J = 8.4, 1.6$ Hz, Ar-H), 8.01 (1H, dd, $J = 8.0, 1.2$ Hz, Ar-H), 8.59 (1H, d, $J = 4.0$ Hz, Ar-H), 9.62 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 12.07, 50.88, 52.46, 52.67, 123.55, 125.77, 127.48, 127.83, 128.78, 129.12, 129.36, 130.62,

130.76, 132.21, 132.47, 133.62, 134.34, 144.97, 157.34, 181.50 ($\underline{\text{CO}}$). HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{OSCl}$ $[\text{M}]^+$ 409.1016; found $[\text{M}+\text{H}]^+$ 410.1069.

Example 9

5 ***10-Chloro-6-(4-(2-hydroxyethyl)piperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12one (10)***

Product **10** was prepared from **3** and 2-(piperazin-1-yl)ethanol. The green-yellow solid material was isolated in 60% yield ($R_f = 0.37$ at EA: MeOH= 2: 1). Mp 211-213 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 2.74 (2H, t, $J = 5.2$ Hz, $-\text{CH}_2-$), 2.87 (4H, t, $J = 3.6$ Hz, $-\text{CH}_2-$), 3.45 (4H, t, $J = 3.6$ Hz, $-\text{CH}_2-$), 3.72 (2H, t, $J = 5.2$ Hz, $-\text{CH}_2\text{O}-$), 7.62-7.67 (3H, m, Ar-H), 7.72 (1H, td, $J = 7.2, 1.6$ Hz, Ar-H), 8.01 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H), 8.59 (1H, d, $J = 0.6$ Hz, Ar-H), 9.62 (1H, dd, $J = 4.8, 1.2$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 50.85, 52.72, 57.74, 59.35, 123.65, 125.81, 127.66, 127.82, 128.73, 129.14, 129.44, 130.68, 130.77, 132.19, 132.51, 133.69, 134.21, 144.90, 157.26, 181.43 ($\underline{\text{CO}}$). HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}_2\text{SCl}$ $[\text{M}]^+$ 425.0965; found $[\text{M}+\text{H}]^+$ 426.1024.

Example 10

20 ***6-(4-Benzylpiperazin-1-yl)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (11)***

Product **11** was prepared from **3** and 4-benzylpiperazine. The yellow solid material was isolated in 81% yield ($R_f = 0.43$ at EA: n-hexane = 1: 4). Mp 191-193 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 2.78 (4H, br, $-\text{CH}_2\text{N}-$), 3.43 (4H, t, $J = 4.85$ Hz, $-\text{NCH}_2-$), 3.68 (2H, s, $-\text{CH}_2-$), 7.27-7.42 (5H, m, Ar'-H), 7.61-7.67 (3H, m, Ar-H), 7.71 (1H, td, $J = 7.6, 1.6$ Hz, Ar-H), 8.00 (1H, dd, $J = 8.4, 1.2$ Hz,

Ar-H), 8.58 (1H, d, $J = 2.0$ Hz, Ar-H), 9.61 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 50.94, 52.96, 63.08, 123.57, 125.78, 127.18, 127.48, 127.83, 128.33, 128.73, 129.09, 129.17, 129.34, 130.58, 130.90, 132.18, 132.44, 133.60, 134.36, 138.11, 144.95, 157.48, 181.47 (C=O). HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{22}\text{N}_3\text{OSCl}$ $[\text{M}]^+$ 471.1172; found $[\text{M}+\text{H}]^+$ 472.1241.

Example 11

10-Chloro-6-(4-phenylpiperazin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (12)

Product **12** was prepared from **3** and 1-phenylpiperazine. The yellow solid material was isolated in 77% yield ($R_f = 0.73$ at EA: n-hexane = 1: 4). Mp 236-237 °C. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 3.50-3.60 (8H, m, $-\text{CH}_2-$), 6.94 (1H, t, $J = 7.2$ Hz, $\text{Ar}'\text{-H}$), 7.04 (2H, d, $J = 8.4$ Hz, $\text{Ar}'\text{-H}$), 7.33 (2H, t, $J = 7.5$ Hz, $\text{Ar}'\text{-H}$), 7.63-7.67 (3H, m, Ar-H), 7.71 (1H, t, $J = 7.2$ Hz, Ar-H), 8.02 (1H, d, $J = 7.2$ Hz, Ar-H), 8.58 (1H, s, Ar-H), 9.63 (1H, d, $J = 8.1$ Hz, Ar-H). ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) 48.60, 50.33, 115.77, 119.51, 123.21, 125.38, 127.14, 127.30, 128.27, 128.65, 128.71, 128.88, 130.23, 131.77, 131.97, 133.22, 133.70, 144.52, 150.90, 156.83, 159.91, 180.91 (C=O). HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{20}\text{N}_3\text{OSCl}$ $[\text{M}]^+$ 457.1016; found $[\text{M}+\text{H}]^+$ 458.1095.

Example 12

10-Chloro-6-morpholino-12H-thiochromeno[2,3-c]quinolin-12-one (13)

Product **13** was prepared from **3** and morpholine. The yellow solid material was isolated in 70% yield ($R_f = 0.42$ at CH_2Cl_2). Mp 217-218 °C. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 3.41 (4H, t, $J = 4.5$

Hz, -NCH₂-), 4.02 (4H, t, *J* = 4.5 Hz, -CH₂O-), 7.62-7.70 (3H, m, Ar-H), 7.73 (1H, td, *J* = 7.5, 1.5 Hz, Ar-H), 8.03 (1H, dd, *J* = 8.4, 1.5 Hz, Ar-H), 8.59 (1H, dd, *J* = 2.1, 0.6 Hz, Ar-H), 9.35 (1H, dd, *J* = 8.7, 1.8 Hz, Ar-H). ¹³C NMR (75 MHz, CDCl₃): δ (ppm) 51.36, 66.88, 123.92, 126.06, 127.85, 127.91, 128.94, 129.34, 129.52, 130.71, 131.05, 132.50, 132.61, 133.95, 134.29, 145.23, 157.29, 181.51 (C=O). HRMS (ESI) calcd for C₂₀H₁₅N₂O₂SCl [M]⁺ 382.8633; found [M+H]⁺ 383.0620.

Example 13

10 **10-Chloro-6-thiomorpholino-12H-thiochromeno[2,3-c]quinolin-12-one (14)**

Product **14** was prepared from **3** and thiomorpholine. The yellow solid material was isolated in 86% yield (*R*_f = 0.77 at EA: n-hexane = 1: 4). Mp 219-220 °C. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 2.98 (4H, t, *J* = 4.8 Hz, -NCH₂-), 3.64 (4H, t, *J* = 5.1 Hz, -SCH₂-), 7.62-7.84 (3H, m, Ar-H), 7.73 (1H, td, *J* = 8.4, 1.8 Hz, Ar-H), 8.06 (1H, dd, *J* = 8.1, 1.5 Hz, Ar-H), 8.57 (1H, dd, *J* = 1.8, 0.6 Hz, Ar-H), 9.61 (1H, dd, *J* = 7.8, 1.2 Hz, Ar-H). ¹³C NMR (75 MHz, CDCl₃): δ (ppm) 27.06, 52.64, 114.95, 123.23, 125.40, 127.27, 127.31, 128.30, 128.68, 128.87, 130.55, 131.81, 131.96, 133.29, 133.70, 144.93, 157.43, 180.86 (C=O). HRMS (ESI) *m/z* calcd for C₂₀H₁₅N₂S₂OC⁺ [M]⁺ 398.0314, found [M+H]⁺ 399.0420, [M+H+2]⁺ 401.0394.

Example 14

25 **10-Chloro-6-(piperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (15)**

Product **15** was prepared from **3** and piperidine. The yellow solid material was isolated in 86% yield (*R*_f = 0.75 at EA). Mp 187-188 °C.

¹H NMR (400 MHz, CDCl₃): δ (ppm) 1.71-1.74 (2H, m, -CH₂-), 1.88 (4H, p, *J* = 4.5 Hz, -CH₂-), 3.31 (4H, t, *J* = 4.2 Hz, -NCH₂-), 7.60-7.64 (2H, m, Ar-H), 7.61 (1H, d, *J* = 6.3 Hz, Ar-H), 7.69 (1H, td, *J* = 5.1, 1.2 Hz, Ar-H), 7.99 (1H, dd, *J* = 5.4, 0.6 Hz, Ar-H), 8.58 (1H, d, *J* = 1.5 Hz, Ar-H), 9.62 (1H, dd, *J* = 6.3, 0.6 Hz, Ar-H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 24.27, 25.89, 52.33, 123.47, 125.75, 127.28, 127.85, 128.56, 129.02, 129.23, 130.48, 131.62, 132.16, 132.33, 133.46, 134.67, 144.97, 158.50, 181.51 (C=O). HRMS (ESI) calcd for C₂₁H₁₇N₂OSCl [M]⁺ 380.0750; found [M+H]⁺ 381.0816.

10 Example 15

10-Chloro-6-(4-hydroxypiperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (16)

Product **16** was prepared from **3** and 4-hydroxypiperidine. The gray-yellow solid material was isolated in 84% yield (*R*_f = 0.4 at EA: n-hexane = 1: 1). Mp 224-225 °C. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 1.89 (1H, td, *J* = 7.2, 2.7 Hz, piperidine-CH_a), 1.94 (1H, td, *J* = 6.9, 2.7 Hz, piperidine-CH_a), 2.15-2.21 (2H, m, piperidine-CH_e), 3.19 (2H, td, *J* = 8.4, 2.1 Hz, piperidine-NCH_a), 3.60-3.65 (2H, m, piperidine-NCH_e), 4.01 (1H, sext, *J* = 3.0 Hz, piperidine-CH), 7.61-7.67 (3H, m, Ar-H), 7.71 (1H, td, *J* = 6.3, 1.2 Hz, Ar-H), 7.99 (1H, dd, *J* = 6.3, 0.6 Hz, Ar-H), 8.59 (1H, dd, *J* = 1.5, 0.6 Hz, Ar-H), 9.64 (1H, dd, *J* = 6.3, 0.6 Hz, Ar-H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 34.49, 48.90, 67.80, 123.62, 125.82, 127.54, 127.88, 128.64, 129.11, 129.36, 130.61, 131.29, 132.20, 132.47, 133.63, 134.43, 144.91, 157.83, 181.47 (C=O). HRMS (ESI) calcd for C₂₁H₁₇N₂OSCl [M]⁺ 396.0699; found [M+H]⁺ 397.0757.

Example 16

6-(4-Benzylpiperidin-1-yl)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (17)

Product **17** was prepared from **3** and 4-benzylpiperidine. The yellow solid material was isolated in 90% yield ($R_f = 0.57$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 184-185 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.67 (2H, td, $J = 9.3, 3.0$ Hz, $-\text{CH}_2-$), 1.79-1.89 (1H, m, $-\text{CH}-$), 1.88 (2H, d, $J = 6.9$ Hz, piperidine- CH_2), 2.71 (2H, d, $J = 5.1$ Hz, piperidine- CH_2), 3.00 (2H, td, $J = 9.3, 1.2$ Hz, $-\text{NCH}_2-$), 3.65 (2H, d, $J = 9.3$ Hz, $-\text{NCH}_2-$), 7.20-7.25 (3H, m, Ar-H), 7.31-7.33 (2H, m, Ar-H), 7.60-7.72 (4H, m, Ar-H), 7.98 (1H, dd, $J = 6.3, 0.6$ Hz, Ar-H), 8.59 (1H, d, $J = 1.8$ Hz, Ar-H), 9.62 (1H, dd, $J = 6.6, 0.6$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 32.21, 37.88, 43.30, 51.64, 123.52, 125.79, 125.99, 127.36, 127.87, 128.61, 129.09, 129.17, 129.29, 130.55, 131.49, 132.22, 132.41, 133.54, 134.62, 140.46, 144.98, 147.04, 158.25, 181.55 (C=O). HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{23}\text{N}_2\text{OSCl}$ $[\text{M}]^+$ 471.0130; found $[\text{M}+\text{H}]^+$ 471.1276.

Example 17

6-([1,4'-Bipiperidin]-1'-yl)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (18)

Product **18** was prepared from **3** and 1,4'-bipiperidine. The yellow solid material was isolated in 92% yield ($R_f = 0.15$ at EA: MeOH= 5: 1). Mp 187-189 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.50-1.52 (2H, m, piperidine-H), 1.66-1.67 (3H, m, piperidine-H), 1.86-1.98 (2H, qd, $J = 12.4, 2.8$ Hz, piperidine-H), 2.06 (2H, d, $J = 11.6$ Hz, piperidine-H), 2.54 (1H, t, $J = 10.8$ Hz, piperidine-H), 2.65 (3H, br, piperidine-H), 3.05 (2H, t, $J = 12$ Hz, piperidine-H), 3.73 (2H, d, $J = 12.8$ Hz, piperidine-H), 7.60-7.66 (3H, m, Ar-H), 7.70 (1H, td, $J = 8.0,$

1.2 Hz, Ar-H), 7.98 (1H, d, $J = 8.0$ Hz, Ar-H), 8.58 (1H, s, Ar-H), 9.62 (1H, d, $J = 8.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 24.79, 26.36, 28.24, 50.45, 51.16, 62.40, 123.57, 125.80, 127.42, 127.86, 128.61, 129.08, 129.30, 130.52, 131.41, 132.18, 132.43, 133.56, 134.54, 144.92, 157.92, 181.47 (CO). HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{26}\text{N}_3\text{OSCl}$ $[\text{M}]^+$ 463.1485; found $[\text{M}+\text{H}]^+$ 464.1593.

Example 18

10-Chloro-6-(4-(3-(piperidin-4-yl)propyl)piperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (19)

Product **19** was prepared from **3** and 1,3-di(piperidin-4-yl)propane. The yellow solid material was isolated in 76% yield ($R_f = 0.13$ at CH_2Cl_2). Mp 164-165 °C. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.16 (2H, qd, $J = 11.6, 3.2$ Hz, $-\text{CH}_2-$), 1.20-1.28 (2H, m, $-\text{CH}_2-$), 1.36-1.39 (4H, m, $-\text{CH}_2-$), 1.51-1.58 (4H, m, $-\text{CH}_2-$), 1.70 (2H, d, $J = 13.6$ Hz, $-\text{CH}_2-$), 1.87 (2H, d, $J = 9.6$ Hz, $-\text{CH}_2-$), 2.43 (1H, br, $-\text{NH}$), 2.60 (2H, td, $J = 12.0, 2.0$ Hz, $-\text{CH}_2-$), 2.99 (2H, t, $J = 11.2$ Hz, $-\text{CH}_2-$), 3.10 (2H, d, $J = 12$ Hz, $-\text{CH}_2-$), 3.64 (2H, d, $J = 12.4$ Hz, $-\text{CH}_2-$), 7.59-7.65 (3H, m, Ar-H), 7.68 (1H, td, $J = 8.0, 1.2$ Hz, Ar-H), 8.00 (1H, dd, $J = 11.2, 1.2$ Hz, Ar-H), 8.57 (1H, d, $J = 1.6$ Hz, Ar-H), 9.61 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 23.66, 32.40, 33.24, 35.73, 36.08, 36.86, 37.38, 46.58, 51.76, 123.49, 125.79, 127.30, 127.84, 128.57, 129.05, 129.26, 130.49, 131.55, 132.17, 132.36, 133.50, 134.64, 144.98, 158.34, 181.50 (CO). HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{32}\text{N}_3\text{OSCl}$ $[\text{M}]^+$ 505.1955; found $[\text{M}+\text{H}]^+$ 506.2004.

Example 19

10-Chloro-6-(pyrrolidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (20)

Product **20** was prepared from **3** and pyrrolidine. The solid material was isolated in 86% yield ($R_f = 0.56$ at CH_2Cl_2 : n-hexane = 1: 1). Mp 170-171 °C. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 2.05 (4H, quin, $J = 3.6$ Hz, $-\text{CH}_2-$), 3.76 (4H, t, $J = 6.9$ Hz, $-\text{NCH}_2-$), 7.50 (1H, td, $J = 7.2, 1.5$ Hz, Ar-H), 7.61 (1H, d, $J = 1.5$ Hz, Ar-H₁₁), 7.65 (1H, td, $J = 7.5, 1.5$ Hz, Ar-H), 7.88 (1H, dd, $J = 8.4, 1.5$ Hz, Ar-H), 8.54 (1H, t, $J = 1.5$ Hz, Ar-H), 9.44 (1H, dd, $J = 8.7, 1.5$ Hz, Ar-H). ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) 24.89, 50.52, 121.90, 124.97, 125.17, 126.92, 127.33, 128.42, 128.84, 130.09, 131.77, 131.92, 133.10, 133.32, 144.73, 154.62, 159.91, 181.07 ($\underline{\text{C}}\text{O}$). HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{15}\text{N}_2\text{OSCl}$ $[\text{M}]^+$ 366.0594; found $[\text{M}+\text{H}]^+$ 367.0659.

Example 20

10-chloro-6-(2-oxopiperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one (TC-SCI-B-18) (21)

Product **21** was a yellow solid material which was isolated in 89% yield. Mp: 258-261 °C. ^1H NMR (400 MHz, CDCl_3): δ ppm. 1.25 (1H, d, $J = 4.8$ Hz, piperidone-H), 2.44 (2H, quin, $-\text{CH}_2-$), 2.61 (1H, s, piperidone-H), 2.75 (2H, t, $J = 8.4$ Hz, $-\text{CH}_2-$), 4.11-4.14 (2H, m, $-\text{CH}_2-$), 7.60-7.67 (2H, m, Ar-H), 7.78-7.81 (2H, m, Ar-H), 8.09-8.12 (1H, m, Ar-H), 8.60 (1H, d, $J = 2.0$ Hz, Ar-H), 9.72-9.75 (1H, m, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ ppm. 19.37, 31.47, 41.05, 49.14, 125.25, 126.08, 127.65, 129.29, 129.51, 129.80, 129.88, 130.74, 131.96, 132.26, 132.74, 133.47, 133.91, 145.05, 148.08, 176.14, 181.01.

25 Example 21

10-Chloro-6-methylamino-12H-thiochromeno[2,3-c]quinolin-12-one (N1)

Product **N1** was prepared from **3** and methylamine. The pure compound was obtained as a yellow solid (yield 92%) ($R_f = 0.65$ at CH_2Cl_2). Mp 237-238 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.26 (3H, d, $J = 4.8$ Hz, $-\text{CH}_3$), 4.92 (1H, d, $J = 4.8$ Hz, $-\text{NH}-$),
 5 7.45 (1H, td, $J = 11.2, 1.6$ Hz, Ar-H), 7.58 (1H, d, $J = 8.4$ Hz, Ar-H),
 7.69-7.65 (2H, m, Ar-H), 7.86 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H), 8.56 (1H, d, $J = 1.6$ Hz, Ar-H), 9.45 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 29.38, 120.73, 123.68, 124.65, 125.87, 127.18, 127.49, 129.38, 129.51, 129.62, 131.04, 132.50,
 10 132.53, 134.14, 145.64, 151.21, 180.96 (CO). HRMS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{11}\text{N}_2\text{OSCl}$ $[\text{M}]^+$: 326.0281, found $[\text{M}+\text{H}]^+$: 327.0356.

Example 22

10-Chloro-6-ethylamino-12H-thiochromeno[2,3-c]quinolin-12-one (N2)

15 Product **N2** was prepared from **3** and ethylamine. The pure compound was obtained as a yellow solid (yield 91%) ($R_f = 0.75$ at CH_2Cl_2). Mp 204-205 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.41 (3H, t, $J = 7.2$ Hz, $-\text{CH}_3$), 3.75 (2H, q, $J = 1.6$ Hz, $-\text{CH}_2-$),
 4.81 (1H, br, $-\text{NH}-$), 7.44 (1H, td, $J = 8.4, 1.6$ Hz, Ar-H), 7.58-7.64
 20 (3H, m, Ar-H), 7.83 (1H, d, $J = 8.4$ Hz, Ar-H), 8.56 (1H, d, $J = 1.6$ Hz, Ar-H), 9.44 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 14.79, 37.28, 120.70, 123.50, 124.58, 125.84, 127.18, 127.47, 129.39, 129.47, 129.66, 131.08, 132.50, 132.53, 134.12, 145.67, 150.55, 181.00 (CO). HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{OSCl}$ $[\text{M}]^+$:
 25 340.0437, found $[\text{M}+\text{H}]^+$: 341.0493.

Example 23

10-Chloro-6-propylamino-12H-thiochromeno[2,3-c]quinolin-12

-one (N3)

Product **N3** was prepared from **3** and propylamine. The pure compound was obtained as a yellow solid (yield 85%) (R_f = 0.82 at CH_2Cl_2). Mp 178-179 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.09 (3H, t, J = 7.2 Hz, $-\text{CH}_3$), 1.81 (2H, sext, J = 7.2 Hz, $-\text{CH}_2-$), 3.69 (2H, q, J = 7.2 Hz, $-\text{NCH}_2-$), 4.87 (1H, br, $-\text{NH}-$), 7.44 (1H, td, J = 8.0, 1.2 Hz, Ar-H), 7.58-7.64 (3H, m, Ar-H), 7.82 (1H, d, J = 8.0 Hz, Ar-H), 8.56 (1H, d, J = 1.2 Hz, Ar-H), 9.44 (1H, d, J = 8.8 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 11.68, 22.64, 44.13, 120.67, 123.53, 124.53, 125.82, 127.15, 127.46, 129.38, 129.46, 129.65, 131.05, 132.49, 134.10, 145.66, 150.62, 181.02 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{15}\text{N}_2\text{OSCl}$ $[\text{M}]^+$: 354.0594, found $[\text{M}+\text{H}]^+$: 355.0651.

Example 24

6-(Butylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (N4)

Product **N4** was prepared from **3** and butylamine. The pure compound was obtained as a yellow solid (yield 91%) (R_f = 0.85 at CH_2Cl_2). Mp 147-149 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.03 (3H, t, J = 7.2 Hz, $-\text{CH}_3$), 1.53 (2H, sext, J = 7.2 Hz, $-\text{CH}_2-$), 1.76 (2H, quin, J = 7.2 Hz, $-\text{CH}_2-$), 3.71 (2H, q, J = 6.8 Hz, $-\text{NCH}_2-$), 4.83 (1H, br, $-\text{NH}-$), 7.43 (1H, td, J = 7.6, 1.2 Hz, Ar-H), 7.57-7.64 (3H, m, Ar-H), 7.82 (1H, d, J = 8.4 Hz, Ar-H), 8.55 (1H, d, J = 1.6 Hz, Ar-H), 9.43 (1H, d, J = 8.4 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 13.97, 20.36, 31.54, 42.12, 120.67, 123.53, 124.52, 125.84, 127.16, 127.46, 129.38, 129.46, 129.65, 131.05, 132.48, 132.52, 134.11, 145.68, 150.62, 181.00 (C=O). HRMS (ESI)

m/z calcd for $C_{20}H_{17}N_2OSCl$ $[M]^+$: 368.0750, found $[M+H]^+$: 369.0846.

Example 25

5 **10-Chloro-6-isobutylamino-12H-thiochromeno[2,3-c]quinolin-12-one (N5)**

Product **N5** was prepared from **3** and isobutylamine. The pure compound was obtained as a yellow crystal (yield 61%) (R_f = 0.85 at CH_2Cl_2). Mp 159-160 °C (MeOH). 1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.08 (6H, d, J = 6.8 Hz, - CH_3), 2.10 (1H, sep, J = 6.8 Hz, -CH-),
 10 3.56 (2H, t, J = 6.4 Hz, - CH_2 -), 4.94 (1H, br, -NH), 7.44 (1H, t, J = 7.2 Hz, Ar-H), 7.59-7.64 (3H, m, Ar-H), 7.82 (1H, d, J = 8.4 Hz, Ar-H), 8.57 (1H, dd, J = 2.0, 0.8 Hz, Ar-H), 9.43 (1H, d, J = 8.4 Hz, Ar-H).
 ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.50, 28.16, 49.72, 120.67, 123.54, 124.51, 125.82, 127.13, 127.47, 129.39, 129.47, 129.69,
 15 131.02, 132.50, 134.11, 138.34, 145.62, 150.68, 181.02 (CO). HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2OSCl$ $[M]^+$: 368.0750, found $[M+H]^+$: 369.0825.

Example 26

20 **10-Chloro-6-(pentan-3-ylamino)-12H-thiochromeno[2,3-c]quinolin-12-one (N6)**

Product **N6** was prepared from **3** and 3-aminopentane. The pure compound was obtained as a light yellow crystal (yield 65%) (R_f = 0.87 at CH_2Cl_2). Mp 160-161 °C (MeOH). 1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.92 (6H, t, J = 7.6 Hz, - CH_3), 1.69 (4H, quin, J =
 25 6.0 Hz, - CH_2 -), 4.34 (1H, sext, J = 7.2 Hz, -CH-), 6.58 (1H, d, J = 8.0 Hz, Ar-H), 7.36 (1H, t, J = 8.0 Hz, Ar-H), 7.58 (1H, t, J = 8.0 Hz, Ar-H), 7.65 (1H, d, J = 8.0 Hz, Ar-H), 7.90 (1H, dd, J = 8.4, 2.4 Hz,

Ar-H), 8.01 (1H, d, $J = 8.4$ Hz, Ar-H), 8.40 (1H, d, $J = 2.4$ Hz, Ar-H),
 9.34 (1H, d, $J = 8.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm)
 11.21, 26.86, 54.41, 120.16, 123.92, 125.13, 125.81, 127.05, 128.49,
 129.02, 129.37, 129.73, 132.17, 132.55, 133.22, 133.29, 145.69,
 5 151.64, 180.85 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OSCl}$ $[\text{M}]^+$:
 382.0907, found $[\text{M}+\text{H}]^+$: 383.0994, $[\text{M}-\text{H}]^-$: 381.0851.

Example 27

10-Chloro-6-((2-(dimethylamino)ethyl)amino)-12H-thiochrome no[2,3-c]quinolin-12-one (N7)

10 Product **N7** was prepared from **3** and
 N,N -dimethylethylenediamine. The pure compound was obtained as a
 yellow crystal (yield 76%) ($R_f = 0.82$ at EA: MeOH: ammonia water=
 10:5:1). Mp 156-157 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ
 (ppm) 2.36 (6H, s, $-\text{N}(\text{CH}_3)_2$), 2.69 (2H, t, $J = 6.0$ Hz, $-\text{CH}_2\text{N}-$), 3.57
 15 (2H, q, $J = 5.6$ Hz, $-\text{NCH}_2-$), 5.86 (1H, br, $-\text{NH}$), 7.44 (1H, td, $J = 8.0$,
 1.6 Hz, Ar-H), 7.62 (2H, td, $J = 7.6$, 1.6 Hz, Ar-H), 7.65 (1H, dd, $J =$
 8.0, 0.8 Hz, Ar-H), 7.82 (1H, dd, $J = 8.4$, 1.2 Hz, Ar-H), 8.58 (1H, dd,
 $J = 1.6$, 0.4 Hz, Ar-H), 9.46 (1H, dd, $J = 8.8$, 1.2 Hz, Ar-H). ^{13}C NMR
 (100 MHz, CDCl_3): δ (ppm) 39.53, 45.28, 57.57, 120.71, 123.46,
 20 125.90, 127.02, 127.27, 127.57, 129.35, 129.43, 129.56, 131.46,
 132.43, 132.56, 134.02, 145.72, 150.90, 181.05. (C=O). HRMS (ESI)
 m/z calcd for $\text{C}_{20}\text{H}_{18}\text{N}_3\text{OSCl}$ $[\text{M}]^+$: 383.0859, found $[\text{M}+\text{H}]^+$:
 384.0925.

Example 28

25 ***10-Chloro-6-((2-(diethylamino)ethyl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one (N8)***

Product **N8** was prepared from **3** and N,N -diethylethylenediamine.

The pure compound was obtained as a yellow crystal (yield 86%) (R_f = 0.8 at EA: MeOH: ammonia water = 10:5:1). Mp 152-153 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.13 (6H, t, J = 7.2 Hz, -CH₃), 2.64 (4H, q, J = 6.8 Hz, -NCH₂-), 2.82 (2H, t, J = 6.0 Hz, -CH₂N-), 3.70 (2H, q, J = 5.2 Hz, -NCH₂-), 6.08 (1H, br, -NH-), 7.43 (1H, t, J = 7.2 Hz, Ar-H), 7.59-7.64 (3H, m, Ar-H), 7.81 (1H, d, J = 8.4 Hz, Ar-H), 8.57 (1H, d, J = 1.2 Hz, Ar-H), 9.45 (1H, d, J = 8.4 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 12.34, 39.52, 46.81, 50.89, 120.64, 124.25, 124.34, 125.89, 126.96, 127.63, 129.32, 129.41, 129.53, 131.49, 132.37, 132.55, 133.98, 145.79, 150.96, 181.06 ($\underline{\text{CO}}$). HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{22}\text{N}_3\text{OSCl}$ $[\text{M}]^+$: 411.1172, found $[\text{M}+\text{H}]^+$: 412.1262.

Example 29

10-Chloro-6-(2-ethanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one (N9)

Product **N9** was prepared from **3** and ethanolamine. The pure compound was obtained as a yellow crystal (yield 77%) (R_f = 0.65 at EA). Mp 190-192 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.93 (2H, q, J = 4.4 Hz, -NCH₂-), 4.00 (2H, t, J = 4.4 Hz, -CH₂O-), 4.23 (1H, br, -OH), 5.45 (1H, br, -NH), 7.48 (1H, td, J = 8.0, 1.6 Hz, Ar-H), 7.62-7.68 (3H, m, Ar-H), 7.81 (1H, dd, J = 7.6, 0.8 Hz, Ar-H), 8.58 (1H, dd, J = 1.6, 0.4 Hz, Ar-H), 9.45 (1H, dd, J = 8.4, 0.8 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 45.88, 63.59, 120.97, 123.67, 125.12, 125.92, 126.60, 127.50, 129.48, 129.83, 130.15, 130.91, 132.55, 132.69, 134.35, 144.65, 151.32, 180.87 ($\underline{\text{CO}}$). HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{O}_2\text{SCl}$ $[\text{M}]^+$: 356.8260, found $[\text{M}+\text{H}]^+$: 357.0476, $[\text{M}+\text{H}+2]^+$: 359.0455.

Example 30

10-Chloro-6-(3-propanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one (N10)

Product **N10** was prepared from **3** and 3-amino-1-propanol. The
 5 pure compound was obtained as a yellow solid (yield 94%) (R_f = 0.66
 at EA). Mp 201-202 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ
 (ppm) 1.94 (2H, p, J = 6.0 Hz, $-\text{CH}_2-$), 3.72 (2H, t, J = 5.2 Hz,
 $-\text{NCH}_2-$), 3.93 (2H, q, J = 6.0 Hz, $-\text{CH}_2\text{O}-$), 4.41 (1H, br, $-\text{OH}$), 5.38
 (1H, t, J = 5.2 Hz, $-\text{NH}-$), 7.45 (1H, td, J = 7.6, 1.2 Hz, Ar-H),
 10 7.58-7.65 (3H, m, Ar-H), 7.78 (1H, dd, J = 8.4, 0.8 Hz, Ar-H), 8.56
 (1H, dd, J = 2.0, 0.4 Hz, Ar-H), 9.42 (1H, dd, J = 8.4, 1.2 Hz, Ar-H).
 ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 33.23, 38.94, 59.25, 120.72,
 123.44, 124.84, 125.94, 126.32, 127.45, 129.44, 129.92, 130.11,
 130.84, 132.49, 132.64, 134.31, 144.83, 151.33, 180.88 (CO). HRMS
 15 (ESI) m/z calcd for $\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}_2\text{SCl}$ $[\text{M}]^+$: 370.0543, found $[\text{M}+\text{H}]^+$:
 371.0622.

Example 31

10-Chloro-6-(5-pentanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one (N11)

20 Product **N11** was prepared from **3** and 5-amino-1-pentanol. The
 pure compound was obtained as a yellow solid (yield 91%) (R_f = 0.7
 at EA). Mp 158-160 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ
 (ppm) 1.40 (1H, br, $-\text{OH}$), 1.49-1.62 (2H, m, $-\text{CH}_2-$), 1.71 (2H, quin,
 $-\text{CH}_2-$), 1.83 (2H, quin, $-\text{CH}_2-$), 3.74 (4H, quin, $-\text{CH}_2-$), 4.91 (1H, br,
 25 $-\text{NH}$), 7.45 (1H, td, J = 7.6, 1.2 Hz, Ar-H), 7.59 (3H, m, Ar-H), 7.83
 (1H, d, J = 8.4 Hz, Ar-H), 8.57 (1H, d, J = 1.2 Hz, Ar-H), 9.44 (1H, d,
 J = 8.4 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 23.39, 29.17,

32.40, 42.24, 62.83, 120.69, 123.53, 124.60, 125.84, 127.11, 127.48, 129.40, 129.51, 129.71, 131.02, 131.79, 132.53, 134.14, 145.60, 150.58, 181.02 (CO). HRMS (ESI) m/z calcd for $C_{21}H_{19}N_2O_2SCl$ $[M]^+$: 398.0856, found $[M+H]^+$: 399.0914.

5 Example 32

10-Chloro-6-((1-hydroxybutan-2-yl)amino)-12H-thiochromenol[2,3-c]quinolin-12-one (N12)

Product **N12** was prepared from **3** and 2-amino-1-butanol. The pure compound was obtained as a yellow solid (yield 94%) ($R_f = 0.8$ at EA). Mp 203-204 °C (MeOH). 1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.21 (3H, t, $J = 7.6$ Hz, $-CH_3$), 1.71-1.88 (2H, m, $-CH_2-$), 3.79 (1H, dd, $J = 11.2, 1.6$ Hz, $-CH_2-$), 3.99 (1H, dd, $J = 11.2, 2.8$ Hz, $-CH_2-$), 4.34 (1H, quin, $J = 11.2$ Hz, $-NCH-$), 4.59 (1H, br, $-OH$), 5.02 (1H, d, $J = 6.0$ Hz, $-NH-$), 7.44 (1H, td, $J = 8.0, 1.2$ Hz, Ar-H), 7.56 (1H, d, $J = 8.4$ Hz, Ar-H), 7.59 (1H, td, $J = 7.6, 1.2$ Hz, Ar-H), 7.61 (1H, d, $J = 8.4$ Hz, Ar-H), 7.74 (1H, d, $J = 8.4$ Hz, Ar-H), 8.52 (1H, d, $J = 2.0$ Hz, Ar-H), 9.40 (1H, dd, $J = 7.6, 1.2$ Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 10.95, 24.95, 56.89, 67.08, 120.83, 123.68, 124.98, 125.88, 126.51, 127.40, 129.39, 129.75, 130.02, 130.81, 132.38, 132.62, 134.28, 144.53, 151.09, 180.75 (CO). HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_2SCl$ $[M]^+$: 384.0699, found $[M+H]^+$: 385.0790.

Example 33

25 ***10-Chloro-6-((4-methylpentan-2-yl)amino)-12H-thiochromenol[2,3-c]quinolin-12-one (N13)***

Product **N13** was prepared from **3** and 4-methylpentan-2-amine. The pure compound was obtained as a

yellow solid (yield 94%) ($R_f = 0.9$ at CH_2Cl_2). Mp 176-177 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 0.98 (3H, d, $J = 6.8$ Hz, $-\text{CH}_3$), 1.03 (3H, d, $J = 6.8$ Hz, $-\text{CH}_3$), 1.35 (3H, d, $J = 6.4$ Hz, $-\text{CH}_3$), 1.45 (1H, quin, $J = 6.4$ Hz, $-\text{CH}_2-$), 1.66 (1H, quin, $J = 6.8$ Hz, $-\text{CH}_2-$), 1.80 (1H, sep, $J = 6.8$ Hz, $-\text{CH}-$), 4.63 (1H, br, $-\text{NH}$), 4.63-4.66 (1H, m, $-\text{CH}-$), 7.43 (1H, td, $J = 7.6, 1.2$ Hz, Ar-H), 7.58-7.63 (3H, m, Ar-H), 7.81 (1H, d, $J = 8.4$ Hz, Ar-H), 8.56 (1H, d, $J = 1.2$ Hz, Ar-H), 9.43 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 21.38, 22.87, 22.92, 25.40, 45.73, 46.80, 120.55, 123.42, 124.36, 125.80, 127.21, 127.44, 129.38, 129.71, 131.08, 132.47, 132.52, 134.07, 145.76, 150.01, 181.05 ($\underline{\text{CO}}$). HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{19}\text{N}_2\text{OSCl}$ $[\text{M}]^+$: 396.1063, found $[\text{M}+\text{H}]^+$: 397.1142.

Example 34

15 **6-((2-Aminoethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (N14)**

Product **N14** was prepared from **3** and 1,2-diaminoethane. The pure compound was obtained as a yellow solid (yield 90%) ($R_f = 0.6$ at EA: MeOH: ammonia water = 10: 5: 1). Mp 193-194 °C (MeOH). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ (ppm) 2.90 (2H, t, $J = 6.0$ Hz, $-\text{CH}_2-$), 3.59 (2H, t, $J = 6.0$ Hz, $-\text{CH}_2-$), 7.36 (1H, t, $J = 8.0$ Hz, Ar-H), 7.59 (1H, t, $J = 8.0$ Hz, Ar-H), 7.66 (1H, d, $J = 8.0$ Hz, Ar-H), 7.85 (1H, d, $J = 7.2$ Hz, Ar-H), 7.96 (1H, d, $J = 8.8$ Hz, Ar-H), 8.35 (1H, br, Ar-H), 9.32 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ (ppm) 40.79, 45.06, 120.24, 124.08, 125.31, 125.84, 127.00, 128.39, 128.83, 129.32, 129.69, 132.06, 132.33, 133.12, 133.26, 145.58, 151.52, 180.65 ($\underline{\text{CO}}$). HRMS (ESI) m/z calcd for

$C_{18}H_{14}N_3OSCl$ $[M]^+$: 355.0546, found $[M+H]^+$: 356.0641.

Example 35

10-Chloro-6-((2-((2-hydroxyethyl)amino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N15)

5 Product **N15** was prepared from **3** and *N*-(2-hydroxyethyl)ethylenediamine. The pure compound was obtained as a yellow solid (yield 58%) (R_f = 0.63 at EA: MeOH: ammonia water = 10: 5: 1). Mp 141-143 °C (MeOH). 1H NMR (400 MHz, DMSO- d_6): δ (ppm) 2.69 (2H, t, J = 5.6 Hz, -CH₂-), 2.90 (2H, t, J = 6.0 Hz, -CH₂-), 3.51 (2H, t, J = 5.6 Hz, -CH₂-), 3.65 (2H, t, J = 6.0 Hz, -CH₂-), 7.10 (1H, br, -NH-), 7.32 (1H, t, J = 7.2 Hz, Ar-H), 7.55 (1H, t, J = 7.2 Hz, Ar-H), 7.62 (1H, d, J = 8.4 Hz, Ar-H), 7.76 (1H, t, J = 7.2 Hz, Ar-H), 7.86 (1H, d, J = 8.4 Hz, Ar-H), 8.25 (1H, d, J = 2.0 Hz, Ar-H), 9.26 (1H, d, J = 8.4 Hz, Ar-H). ^{13}C NMR (100 MHz, DMSO- d_6): δ (ppm) 41.90, 48.16, 51.80, 60.72, 120.13, 123.96, 125.14, 125.81, 126.94, 128.26, 128.65, 129.16, 129.60, 131.82, 132.11, 132.96, 133.19, 145.50, 151.35, 180.45 ($\underline{CO}$). HRMS (ESI) m/z calcd for $C_{20}H_{18}N_3O_2SCl$ $[M]^+$: 399.8938, found $[M+H]^+$: 400.0880.

20 Example 36

10-Chloro-6-((2-morpholinoethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N16)

Product **N16** was prepared from **3** and 4-(2-aminoethyl)morpholine. The pure compound was obtained as a yellow solid (yield 87%) (R_f = 0.48 at EA). Mp 189-190 °C (MeOH). 1H NMR (400 MHz, CDCl₃): δ (ppm) 2.63 (4H, br, -CH₂-), 2.81 (2H, br, -CH₂-), 3.81 (6H, br, -CH₂-), 5.92 (1H, br, -NH-), 6.70 (2H, d, J =

8.4 Hz, Ar'-H), 7.45 (1H, td, $J = 7.8, 1.6$ Hz, Ar-H), 7.60-7.64 (3H, m, Ar-H), 7.81 (1H, d, $J = 8.4$ Hz, Ar-H), 8.57 (1H, s, Ar-H), 9.46 (1H, dd, $J = 8.8, 1.2$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 38.28, 53.31, 56.52, 67.13, 120.73, 123.94, 124.58, 125.91, 127.01, 127.56, 129.37, 129.49, 129.64, 131.27, 132.47, 132.54, 134.10, 145.66, 150.76, 180.99 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}_2\text{SCl}$ $[\text{M}]^+$: 425.0965, found $[\text{M}+\text{H}]^+$: 426.1058, $[\text{M}-\text{H}]^-$: 424.0885.

Example 37

10 **10-Chloro-6-((3-(dimethylamino)propyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N17)**

Product **N17** was prepared from **3** and 3-(dimethylamino)-1-propylamine. The pure compound was obtained as a yellow crystal (yield 43%) ($R_f = 0.71$ at EA: MeOH: ammonia water = 10: 5: 1). Mp 194-195 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.92 (2H, quin, $J = 6.0$ Hz, $-\text{CH}_2-$), 2.41 (6H, s, $-\text{N}(\text{CH}_3)_2$), 2.60 (2H, t, $J = 5.6$ Hz, $-\text{CH}_2\text{N}-$), 3.81 (2H, q, $J = 5.6$ Hz, $-\text{NCH}_2-$), 7.95 (1H, br, $-\text{NH}$), 7.40 (1H, td, $J = 7.6, 1.6$ Hz, Ar-H), 7.56-7.63 (4H, m, Ar-H), 7.80 (1H, d, $J = 8.4$ Hz, Ar-H), 8.57 (1H, d, $J = 2.4$ Hz, Ar-H), 9.44 (1H, dd, $J = 7.6, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 24.83, 43.64, 45.68, 59.72, 120.46, 123.97, 124.56, 125.84, 126.83, 127.54, 129.32, 129.48, 131.84, 132.29, 132.56, 133.86, 146.01, 151.27, 181.14 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{20}\text{N}_3\text{OSCl}$ $[\text{M}]^+$: 397.1016, found $[\text{M}+\text{H}]^+$: 398.1072.

25 Example 38

10-Chloro-6-((3-(diethylamino)propyl)amino)-12H-thiochrome no[2,3-c]quinolin-12-one (N18)

Product **N18** was prepared from **3** and 3-(diethylamino)-1-propylamine. The pure compound was obtained as a yellow acicular crystal (yield 70%) ($R_f = 0.68$ at EA: MeOH: ammonia water = 10: 5: 1). Mp 142-143 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.15 (6H, t, $J = 6.8$ Hz, $-\text{CH}_3$), 1.91 (2H, quin, $J = 6.0$ Hz, $-\text{CH}_2-$), 2.66-2.72 (6H, m, $-\text{NCH}_2-$), 3.81 (2H, q, $J = 4.8$ Hz, $-\text{NCH}_2-$), 7.40 (1H, td, $J = 7.2, 1.2$ Hz, Ar-H), 7.55-7.58 (1H, dd, $J = 8.4, 3.6$ Hz, Ar-H), 7.60-7.64 (2H, m, Ar-H), 7.81 (1H, d, $J = 8.0$ Hz, Ar-H), 7.93 (1H, br, Ar-H), 8.58 (1H, t, $J = 2.0$ Hz, Ar-H), 9.45 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 11.44, 24.71, 44.25, 47.09, 53.57, 120.45, 123.99, 124.50, 125.86, 126.87, 127.46, 129.34, 129.43, 131.85, 132.32, 132.57, 133.88, 146.04, 151.30, 181.15 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{SOCl}$ $[\text{M}]^+$: 425.1329, found $[\text{M}+\text{H}]^+$: 426.1396, $[\text{M}-\text{H}]^-$: 424.1284.

Example 39

10-Chloro-6-((3-((2-hydroxyethyl)amino)propyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N19)

Product **N19** was prepared from **3** and *N*-(2-Hydroxyethyl)-1,3-diaminopropane. The pure compound was obtained as a brown solid (yield 75%) ($R_f = 0.65$ at EA: MeOH: ammonia water = 10: 5: 1). Mp 65-67 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.89 (2H, quin, $J = 6.0$ Hz, $-\text{CH}_2-$), 2.15 (2H, br, $-\text{OH}$ & $-\text{NH}-$), 2.85 (4H, quin, $-\text{CH}_2-$), 3.74 (2H, t, $J = 6.0$ Hz, $-\text{CH}_2-$), 3.80 (2H, t, $J = 5.2$ Hz, $-\text{CH}_2-$), 6.53 (1H, br, $-\text{NH}-$), 7.39 (1H, td, $J = 7.6, 0.8$ Hz, Ar-H), 7.44 (1H, d, $J = 8.8$ Hz, Ar-H), 7.50 (1H, dd, $J = 8.4, 2.4$ Hz, Ar-H), 7.58 (1H, td, $J = 7.2, 1.2$ Hz, Ar-H), 7.76 (1H, d, $J = 8.0$ Hz, Ar-H), 8.46 (1H, d, $J = 2.0$ Hz, Ar-H), 9.39 (1H, d, $J =$

8.4 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 28.37, 42.23, 48.74, 51.65, 61.42, 120.48, 123.99, 124.22, 125.85, 126.88, 127.42, 129.13, 129.33, 129.38, 131.23, 132.21, 132.33, 133.95, 145.69, 150.82, 180.92 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}_2\text{SCl}$ $[\text{M}]^+$: 413.0965, found $[\text{M}+\text{H}]^+$: 414.1053, $[\text{M}+\text{H}+2]^+$: 416.1037.

Example 40

10-Chloro-6-((2,3-dihydro-1H-inden-2-yl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N20)

Product **N20** was prepared from **3** and 2-aminoindane. The pure compound was obtained as a brown solid (yield 65%) ($R_f = 0.7$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 251-252 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.02 (1H, d, $J = 5.2$ Hz, indane-H), 3.06 (1H, d, $J = 5.2$ Hz, indane-H), 3.59 (1H, d, $J = 7.2$ Hz, indane-H), 3.63 (1H, d, $J = 7.2$ Hz, indane-H), 5.10 (1H, d, $J = 6.8$ Hz, -NH), 5.23 (1H, q, $J = 5.2$ Hz, indane-H), 7.21-7.25 (2H, m, Ar'-H), 7.28-7.31 (2H, m, Ar'-H), 7.47 (1H, td, $J = 6.8, 1.2$ Hz, Ar-H), 7.58 (1H, d, $J = 8.4$ Hz, Ar-H), 7.61-7.67 (1H, td, $J = 6.8, 1.2$ Hz, Ar-H), 7.87 (1H, d, $J = 7.6$ Hz, Ar-H), 8.57 (1H, d, $J = 2.0$ Hz, Ar-H), 9.46 (1H, dd, $J = 8.8, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 40.41, 53.27, 120.79, 123.60, 124.81, 124.93, 125.84, 126.76, 127.37, 127.46, 129.38, 129.51, 129.71, 131.02, 132.50, 132.54, 134.12, 141.29, 145.56, 150.20, 181.00 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{17}\text{N}_2\text{OSCl}$ $[\text{M}]^+$: 428.0750; found $[\text{M}+\text{H}]^+$: 429.0822.

Example 41

10-Chloro-6-(cyclohexylamino)-12H-thiochromeno[2,3-c]quinolin-12-one (N21)

Product **N21** was prepared from **3** and cyclohexylamine. The

pure compound was obtained as a brown solid (yield 91%) ($R_f = 0.7$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 196-197 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.25-1.40 (4H, m, cyclohexylamine- CH_2), 1.49-1.60 (2H, m, cyclohexylamine- CH_2), 1.70-1.74 (2H, m, cyclohexylamine- CH_2), 1.79-1.84 (2H, m, cyclohexylamine- CH_2), 2.21 (2H, dd, $J = 8.8, 3.2$ Hz, cyclohexylamine- CH_2), 4.30 (1H, sep, $J = 3.6$ Hz, cyclohexylamine-CH), 4.72 (1H, d, $J = 6.8$ Hz, -NH-), 7.41 (1H, t, $J = 8.0$ Hz, Ar-H), 7.51-62 (3H, m, Ar-H), 7.79 (1H, d, $J = 8.0$ Hz, Ar-H), 8.51 (1H, d, $J = 1.6$ Hz, Ar-H), 9.41 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 24.94, 25.92, 33.10, 50.26, 120.51, 123.50, 124.34, 125.77, 127.11, 127.37, 129.27, 129.35, 129.60, 131.01, 132.37, 132.41, 134.00, 145.66, 149.75, 180.95 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{19}\text{N}_2\text{OSCl}$ $[\text{M}]^+$: 394.0907; found $[\text{M}+\text{H}]^+$: 395.0991.

Example 42

6-((1-Benzylpiperidin-4-yl)amino)-10-chloro-12H-thiochromen-2-ylidenequinolin-12-one (N22)

Product **N22** was prepared from **3** and 1-benzylpiperidin-4-amine. The pure compound was obtained as a brown solid (yield 62%) ($R_f = 0.77$ at EA). Mp 194-196 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 1.62-1.72 (2H, m, piperidine-H), 2.24 (2H, d, $J = 13.2$ Hz, piperidine-H), 2.32 (2H, t, $J = 11.2$ Hz, piperidine-H), 2.92 (2H, d, $J = 11.6$ Hz, piperidine-H), 3.59 (2H, s, - CH_2 -), 4.35 (1H, sext, $J = 6.4$ Hz, piperidine-CH), 4.75 (1H, d, $J = 7.2$ Hz, -NH), 7.26-7.30 (1H, m, Ar'-H), 7.36-7.38 (4H, m, Ar'-H), 7.44 (1H, td, $J = 7.6, 0.8$ Hz, Ar-H), 7.59-7.64 (3H, m, Ar-H), 7.80 (1H, d, $J = 7.6$ Hz, Ar-H), 8.56 (1H, d, $J = 1.6$ Hz, Ar-H), 9.43 (1H, d, $J = 8.8$ Hz, Ar-H). ^{13}C NMR (100 MHz,

CDCl₃): δ (ppm) 32.26, 48.63, 52.35, 63.22, 120.63, 123.47, 124.57, 125.81, 127.07, 127.12, 127.47, 128.25, 129.21, 129.35, 129.44, 129.74, 130.99, 132.46, 132.52, 134.10, 138.37, 145.57, 149.76, 181.00 (CO). HRMS (ESI) m/z calcd for C₂₈H₂₄N₃OSCl [M]⁺:
 5 485.1329; found [M+H]⁺: 486.1379.

Example 43

10-Chloro-6-((thiophen-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N23)

Product **N23** was prepared from **3** and 2-thiophenemethylamine.

10 The pure compound was obtained as a brown solid (yield 78%) (R_f = 0.7 at CH₂Cl₂: n-hexane = 2: 1). Mp 178-180 °C (MeOH). ¹H NMR (400 MHz, CDCl₃): δ (ppm) 5.07 (1H, d, J = 5.2 Hz, -NCH₂-), 5.17 (1H, br, -NH-), 7.00 (1H, t, J = 4.4 Hz, thiophene-H), 7.16 (1H, d, J = 3.2 Hz, thiophene-H), 7.25 (1H, d, J = 0.8 Hz, thiophene-H), 7.47 (1H,
 15 t, J = 8.0 Hz, Ar-H), 7.52 (1H, d, J = 8.4 Hz, Ar-H), 7.58 (1H, d, J = 8.4 Hz, Ar-H), 7.65 (1H, t, J = 7.6 Hz, Ar-H), 7.89 (1H, d, J = 8.0 Hz, Ar-H), 8.53 (1H, s, Ar-H), 9.46 (1H, d, J = 8.4 Hz, Ar-H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 41.14, 121.06, 123.58, 125.05, 125.47, 125.89, 126.47, 126.73, 127.29, 127.45, 129.33, 129.57, 129.71,
 20 130.94, 132.39, 132.51, 134.12, 141.36, 145.20, 149.82, 180.80 (CO). HRMS (ESI) m/z calcd for C₂₁H₁₃N₂OS₂Cl [M]⁺: 408.0158; found [M+H]⁺: 409.0251, [M-H]⁻: 407.0085.

Example 44

10-Chloro-6-((cyclohexylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N24)

Product **N24** was prepared from **3** and cyclohexylmethanamine. The pure compound was obtained as a brown solid (yield 79%) (R_f =

0.7 at CH₂Cl₂: n-hexane = 2: 1). Mp 165-166 °C (MeOH). ¹H NMR (400 MHz, CDCl₃): δ (ppm) 1.07 (1H, d, *J* = 11.2 Hz, cyclohexyl-CH₂), 1.30 (1H, d, *J* = 11.2 Hz, cyclohexyl-CH₂), 1.23 (2H, q, *J* = 11.6 Hz, cyclohexyl-CH₂), 1.31 (2H, q, *J* = 11.6 Hz, cyclohexyl-CH₂), 1.78-1.81 (4H, m, cyclohexyl-CH₂), 1.90 (2H, d, *J* = 12.4 Hz, cyclohexyl-CH₂), 3.53 (2H, t, *J* = 6.0 Hz, -NCH₂-), 4.85 (1H, br, -NH-), 7.40 (1H, t, *J* = 7.2 Hz, Ar-H), 7.51 (1H, d, *J* = 8.8 Hz, Ar-H), 7.55 (1H, d, *J* = 1.6 Hz, Ar-H), 7.60 (1H, t, *J* = 8.0 Hz, Ar-H), 7.79 (1H, d, *J* = 8.0 Hz, Ar-H), 8.50 (1H, d, *J* = 1.2 Hz, Ar-H), 9.41 (1H, d, *J* = 8.4 Hz, Ar-H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 25.97, 26.52, 31.23, 37.63, 48.50, 120.59, 123.57, 124.41, 125.80, 127.10, 127.38, 129.26, 129.38, 129.45, 130.95, 132.33, 132.41, 134.02, 145.58, 150.64, 180.87 (C=O). HRMS (ESI) *m/z* calcd for C₂₃H₂₁N₂OCl [M]⁺: 408.1063; found [M+H]⁺: 409.1115.

Example 45

6-(Benzylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (N25)

Product **N25** was prepared from **3** and benzylamine. The pure compound was obtained as a brown solid (yield 93%) (*R_f* = 0.67 at CH₂Cl₂: n-hexane = 2: 1). Mp 194-195 °C (MeOH). ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.94 (2H, d, *J* = 5.2 Hz, -CH₂-), 5.16 (1H, br, -NH-), 7.33-7.51 (6H, m, Ar-H), 7.58-7.67 (3H, m, Ar-H), 7.87 (1H, d, *J* = 8.0 Hz, Ar-H), 8.59 (1H, d, *J* = 2.0 Hz, Ar-H), 9.47 (1H, d, *J* = 8.0 Hz, Ar-H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 37.63, 120.98, 123.54, 124.89, 125.87, 127.26, 127.50, 127.63, 128.24, 128.79, 129.43, 129.57, 129.85, 131.02, 132.58, 134.18, 138.82, 145.48, 150.33, 181.00 (C=O). HRMS (ESI) *m/z* calcd for C₂₃H₁₅N₂OSCl [M]⁺:

402.0594; found $[M+H]^+$: 403.0692.

Example 46

10-Chloro-6-((pyridin-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N26)

5 Product **N26** was prepared from **3** and 2-picolylamine. The pure compound was obtained as a brown solid (yield 93%) ($R_f = 0.25$ at EA). Mp 187-189 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 5.01 (2H, d, $J = 4.0$ Hz, $-\text{CH}_2-$), 6.79 (1H, br, $-\text{NH}-$), 7.24-7.28 (1H, m, Ar'-H), 7.45 (2H, t, $J = 7.2$ Hz, Ar'-H & Ar-H), 7.61-7.67 (3H, m, Ar-H), 7.73 (1H, td, $J = 7.6, 1.6$ Hz, Ar-H), 7.86 (1H, d, $J = 8.4$ Hz, Ar-H), 8.58 (1H, d, $J = 2.0$ Hz, Ar-H), 8.67 (1H, d, $J = 4.8$ Hz, Ar'-H), 9.47 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 46.74, 120.81, 122.37, 124.19, 124.61, 125.93, 127.04, 127.60, 129.33, 129.44, 129.60, 131.40, 132.46, 132.52, 134.03, 136.94, 145.62, 148.94, 150.43, 156.58, 181.00 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{14}\text{N}_3\text{OSCl}$ $[M]^+$: 403.0546; found $[M+H]^+$: 404.0615.

Example 47

6-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (N27)

20 Product **N27** was prepared from **3** and piperonylamine. The pure compound was obtained as a brown solid (yield 90%) ($R_f = 0.88$ at EA). Mp 205-206 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 4.82 (2H, t, $J = 5.2$ Hz, $-\text{NCH}_2-$), 5.08 (1H, br, $-\text{NH}-$), 5.97 (2H, s, $-\text{OCH}_2\text{O}-$), 6.82 (1H, d, $J = 8.0$ Hz, Ar'-H), 6.96 (1H, d, $J = 8.0$ Hz, Ar'-H), 7.00 (1H, d, $J = 1.2$ Hz, Ar'-H), 7.47 (1H, td, $J = 8.0, 1.2$ Hz, Ar-H), 7.57 (1H, d, $J = 8.8$ Hz, Ar-H), 7.60-7.66 (2H, m, Ar-H), 7.86 (1H, d, $J = 8.0$ Hz, Ar-H), 8.62 (1H, d, $J = 2.0$ Hz, Ar-H), 9.46 (1H, d,

$J = 8.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 46.30, 101.10, 108.40, 108.85, 120.95, 121.58, 123.52, 124.88, 125.86, 127.23, 127.46, 129.39, 129.56, 129.76, 130.98, 132.48, 132.55, 132.61, 134.15, 145.42, 147.07, 147.92, 150.21, 180.93 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{15}\text{N}_2\text{O}_3\text{SCl}$ $[\text{M}]^+$: 446.0492; found $[\text{M}+\text{H}]^+$: 447.0586, $[\text{M}-\text{H}]^-$: 445.0440.

Example 48

10-Chloro-6-((2-methoxybenzyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N28)

Product **N28** was prepared from **3** and 2-methoxybenzylamine. The pure compound was obtained as a brown solid (yield 82%) ($R_f = 0.65$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 223-224 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.95 (3H, s, $-\text{OCH}_3$), 4.93 (2H, d, $J = 5.6$ Hz, $-\text{NCH}_2-$), 5.57 (1H, t, $J = 5.6$ Hz, $-\text{NH}-$), 5.97 (2H, s, $-\text{OCH}_2\text{O}-$), 6.94-7.00 (2H, m, Ar'-H), 7.30 (1H, td, $J = 8.0, 2.0$ Hz, Ar'-H), 7.45 (1H, td, $J = 8.0, 1.6$ Hz, Ar'-H), 7.51 (1H, d, $J = 7.2$ Hz, Ar'-H), 7.59-7.66 (3H, m, Ar-H), 7.89 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H), 8.57 (1H, dd, $J = 2.0, 0.8$ Hz, Ar-H), 9.45 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 42.33, 55.49, 110.47, 120.68, 120.81, 123.90, 124.59, 125.82, 126.68, 127.20, 127.52, 128.88, 129.38, 129.44, 129.71, 130.49, 131.23, 132.46, 132.54, 134.04, 145.59, 150.62, 157.89, 181.04 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{17}\text{N}_2\text{O}_2\text{SCl}$ $[\text{M}]^+$: 432.0699; found $[\text{M}+\text{H}]^+$: 433.0783.

Example 49

Product **N29** was prepared from **3** and 2-methoxybenzylamine. The pure compound was obtained as a brown solid (yield 82%) ($R_f = 0.65$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 223-224 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.95 (3H, s, $-\text{OCH}_3$), 4.93 (2H, d, $J = 5.6$ Hz, $-\text{NCH}_2-$), 5.57 (1H, t, $J = 5.6$ Hz, $-\text{NH}-$), 5.97 (2H, s, $-\text{OCH}_2\text{O}-$), 6.94-7.00 (2H, m, Ar'-H), 7.30 (1H, td, $J = 8.0, 2.0$ Hz, Ar'-H), 7.45 (1H, td, $J = 8.0, 1.6$ Hz, Ar'-H), 7.51 (1H, d, $J = 7.2$ Hz, Ar'-H), 7.59-7.66 (3H, m, Ar-H), 7.89 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H), 8.57 (1H, dd, $J = 2.0, 0.8$ Hz, Ar-H), 9.45 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 42.33, 55.49, 110.47, 120.68, 120.81, 123.90, 124.59, 125.82, 126.68, 127.20, 127.52, 128.88, 129.38, 129.44, 129.71, 130.49, 131.23, 132.46, 132.54, 134.04, 145.59, 150.62, 157.89, 181.04 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{17}\text{N}_2\text{O}_2\text{SCl}$ $[\text{M}]^+$: 432.0699; found $[\text{M}+\text{H}]^+$: 433.0783.

Product **N29** was prepared from **3** and 2-methoxybenzylamine. The pure compound was obtained as a brown solid (yield 82%) ($R_f = 0.65$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 223-224 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.95 (3H, s, $-\text{OCH}_3$), 4.93 (2H, d, $J = 5.6$ Hz, $-\text{NCH}_2-$), 5.57 (1H, t, $J = 5.6$ Hz, $-\text{NH}-$), 5.97 (2H, s, $-\text{OCH}_2\text{O}-$), 6.94-7.00 (2H, m, Ar'-H), 7.30 (1H, td, $J = 8.0, 2.0$ Hz, Ar'-H), 7.45 (1H, td, $J = 8.0, 1.6$ Hz, Ar'-H), 7.51 (1H, d, $J = 7.2$ Hz, Ar'-H), 7.59-7.66 (3H, m, Ar-H), 7.89 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H), 8.57 (1H, dd, $J = 2.0, 0.8$ Hz, Ar-H), 9.45 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 42.33, 55.49, 110.47, 120.68, 120.81, 123.90, 124.59, 125.82, 126.68, 127.20, 127.52, 128.88, 129.38, 129.44, 129.71, 130.49, 131.23, 132.46, 132.54, 134.04, 145.59, 150.62, 157.89, 181.04 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{17}\text{N}_2\text{O}_2\text{SCl}$ $[\text{M}]^+$: 432.0699; found $[\text{M}+\text{H}]^+$: 433.0783.

3,4-dimethoxybenzylamine. The pure compound was obtained as a brown solid (yield 84%) ($R_f = 0.66$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 251-252 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.89 (3H, s, - OCH_3), 3.90 (3H, s, - OCH_3), 4.86 (2H, d, $J = 4.8$ Hz, - NCH_2 -), 5.11 (1H, t, $J = 5.2$ Hz, -NH-), 6.89 (1H, d, $J = 8.0$ Hz, Ar'-H), 7.05 (1H, dd, $J = 8.0, 2.0$ Hz, Ar'-H), 7.08 (1H, d, $J = 2.0$ Hz, Ar'-H), 7.48 (1H, td, $J = 7.6, 1.2$ Hz, Ar-H), 7.60 (1H, dd, $J = 8.4, 0.4$ Hz, Ar-H), 7.65 (1H, dd, $J = 8.4, 1.5$ Hz, Ar-H), 7.66 (1H, td, $J = 8.0, 1.2$ Hz, Ar-H), 7.88 (1H, dd, $J = 8.4, 0.8$ Hz, Ar-H), 8.59 (1H, dd, $J = 1.5, 0.4$ Hz, Ar-H), 9.48 (1H, dd, $J = 8.4, 1.2$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 46.45, 55.96, 55.99, 111.31, 111.82, 120.59, 120.99, 123.56, 124.88, 125.91, 127.20, 127.50, 129.45, 129.60, 129.88, 131.04, 131.34, 132.59, 134.21, 145.52, 148.63, 149.20, 150.34, 181.01 (CO). HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}_3\text{SCl}$ $[\text{M}]^+$: 462.0805; found $[\text{M}+\text{H}]^+$: 463.0900, $[\text{M}-\text{H}]^-$: 461.0754.

Example 50

10-Chloro-6-(phenethylamino)-12H-thiochromeno[2,3-c]quinolin-12-one (N30)

Product **N30** was prepared from **3** and phenethylamine. The pure compound was obtained as a brown solid (yield 94%) ($R_f = 0.52$ at CH_2Cl_2 : n-hexane = 2: 1). Mp 151-152 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.10 (2H, t, $J = 6.8$ Hz, - CH_2 -), 3.98 (2H, q, $J = 6.4$ Hz, - NCH_2 -), 4.91 (1H, t, $J = 4.8$ Hz, -NH-), 7.27-7.39 (5H, m, Ar'-H), 7.45 (1H, t, $J = 8.0$ Hz, Ar-H), 7.54 (1H, d, $J = 8.4$ Hz, Ar-H), 7.59 (1H, d, $J = 1.2$ Hz, Ar-H), 7.63 (1H, t, $J = 7.6$ Hz, Ar-H), 7.85 (1H, d, $J = 8.4$ Hz, Ar-H), 8.54 (1H, d, $J = 1.6$ Hz, Ar-H), 9.44 (1H, d, $J = 8.4$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 35.33, 43.52,

120.77, 123.66, 124.69, 125.85, 126.56, 127.23, 127.50, 128.73, 128.94, 129.33, 129.48, 129.50, 131.03, 132.54, 134.08, 139.30, 145.57, 150.36, 180.94 ($\underline{\text{CO}}$). HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{17}\text{N}_2\text{OSCl}$ $[\text{M}]^+$: 416.9226; found $[\text{M}+\text{H}]^+$: 417.0857, $[\text{M}+\text{H}+2]^+$: 419.0834.

Example 51

10-Chloro-6-((4-methoxyphenethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one (N31)

Product **N31** was prepared from **3** and 2-(4-methoxyphenyl)ethylamine. The pure compound was obtained as a yellow solid (yield 95%) ($R_f = 0.89$ at CH_2Cl_2). Mp 214-215 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.03 (2H, t, $J = 6.8$ Hz, $-\text{CH}_2-$), 3.81 (3H, s, $-\text{OCH}_3$), 3.94 (2H, q, $J = 6.4$ Hz, $-\text{NCH}_2-$), 4.90 (1H, t, $J = 4.8$ Hz, $-\text{NH}-$), 6.90 (2H, d, $J = 8.4$ Hz, $\text{Ar}'\text{-H}$), 7.23 (2H, d, $J = 8.4$ Hz, $\text{Ar}'\text{-H}$), 7.45 (1H, t, $J = 7.6$ Hz, Ar-H), 7.55 (1H, d, $J = 8.8$ Hz, Ar-H), 7.59 (1H, d, $J = 2.0$ Hz, Ar-H), 7.63 (1H, t, $J = 7.6$ Hz, Ar-H), 7.85 (1H, d, $J = 8.0$ Hz, Ar-H), 8.54 (1H, d, $J = 2.0$ Hz, Ar-H), 9.44 (1H, d, $J = 8.8$ Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 34.39, 43.68, 55.31, 114.13, 120.76, 123.67, 124.67, 125.85, 127.22, 127.52, 129.36, 129.49, 129.68, 129.87, 131.05, 131.24, 132.48, 134.09, 145.59, 150.41, 158.31, 180.99 ($\underline{\text{CO}}$). HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}_2\text{SCl}$ $[\text{M}]^+$: 446.0856; found $[\text{M}+\text{H}]^+$: 447.0938.

Example 52

6-((4-Aminophenethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one (N32)

Product **N32** was prepared from **3** and 2-(4-aminophenyl)ethylamine. The pure compound was obtained as a

yellow solid (yield 82%) (R_f = 0.52 at CH_2Cl_2). Mp 208-210 °C (MeOH). ^1H NMR (400 MHz, CDCl_3): δ (ppm) 2.97 (2H, t, J = 6.8 Hz, $-\text{CH}_2-$), 3.63 (2H, br, $-\text{NH}_2$), 3.91 (2H, q, J = 6.4 Hz, $-\text{NCH}_2-$), 4.91 (1H, t, J = 4.8 Hz, $-\text{NH}-$), 6.70 (2H, d, J = 8.4 Hz, $\text{Ar}'\text{-H}$), 7.09 (2H, d, J = 8.0 Hz, $\text{Ar}'\text{-H}$), 7.44 (1H, t, J = 7.6 Hz, Ar-H), 7.55 (1H, d, J = 8.0 Hz, Ar-H), 7.60 (1H, d, J = 8.4 Hz, Ar-H), 7.63 (1H, t, J = 7.6 Hz, Ar-H), 7.84 (1H, d, J = 8.0 Hz, Ar-H), 8.54 (1H, d, J = 2.0 Hz, Ar-H), 9.44 (1H, d, J = 8.4 Hz, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 34.37, 43.70, 115.52, 120.72, 123.73, 124.59, 125.83, 127.19, 127.51, 129.06, 129.31, 129.45, 129.59, 129.75, 131.09, 132.42, 134.04, 144.89, 145.60, 150.45, 180.96 (C=O). HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{16}\text{N}_3\text{OSCl}$ $[\text{M}]^+$: 431.0859; found $[\text{M}+\text{H}]^+$: 432.0950.

Example 53

2-(10-Chloro-12-oxo-12H-thiochromeno[2,3-c]quinolin-6-yl)guanidine (TC-SCI-A-41) (N33)

Product **N33** was a yellow solid (yield 85%). Mp: 370 °C.(dec.) ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ ppm. 7.40 (3H, td, J = 8.4, 1.2 Hz, Ar-H & $-\text{NH}_2$), 7.59 (1H, td, J = 8.7, 1.2 Hz, Ar-H), 7.59 (1H, dd, J = 8.4, 0.8 Hz, Ar-H), 7.83 (1H, dd, J = 8.4, 2.0 Hz, Ar-H), 7.95 (1H, d, J = 8.8 Hz, Ar-H), 8.40 (1H, d, J = 2.4 Hz, Ar-H), 9.49 (1H, dd, J = 8.4, 0.8 Hz, Ar-H). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ ppm. 120.77, 124.49, 125.86, 126.82, 128.11, 128.60, 129.21, 129.85, 132.13, 132.52, 132.68, 136.17, 136.80, 144.49, 159.19, 181.16. HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{11}\text{N}_4\text{OSCl}$ $[\text{M}]^+$ 354.0342; found $[\text{M}+\text{H}]^+$ 355.0438.

Example 54

10-Chloro-6-(piperidin-1-ylamino)-12H-thiochromeno[2,3-c]quinolin-12-one (TC-SCI-A-26) (N34)

Product **N34** was a yellow solid (yield 60%). Mp: 180-181 °C. ¹H NMR (400 MHz, CDCl₃): δ ppm. 1.72-1.74 (2H, m, -CH₂-), 1.89 (4H, quin, *J* = 5.2 Hz, -CH₂-), 3.32 (4H, *J* = 4.8 Hz, -CH₂-), 7.36 (1H, tt, *J* = 8.7, 2.1 Hz, Ar-H₁₀), 7.47 (1H, dd, *J* = 8.4, 2.7 Hz, Ar-H₈), 7.61-7.73 (3H, m, Ar-H), 8.00 (1H, d, *J* = 8.0 Hz, Ar-H), 8.59 (1H, d, *J* = 2.0 Hz, Ar-H), 9.63 (1H, d, *J* = 8.8 Hz, Ar-H). ¹³C NMR (100 MHz, CDCl₃): δ ppm. 24.28, 25.91, 52.36, 123.49, 125.77, 127.32, 127.90, 128.59, 129.06, 129.27, 130.51, 131.66, 132.18, 132.39, 133.49, 134.70, 144.98, 158.53, 181.58.

10 **Pharmacological activity assay**

In pharmacological tests, compounds synthesized chemically including **2-21**, **N-1** to **N-34** (a total of 54 drugs) are subjected to the following pharmacological activity tests: (1) MTT assay; (2) Topoisomerase I and II activities assay; (3) cytotoxicity assays
 15 conducted by NCI on the 26 screened compounds in 60 cancer cell lines.

Example 55

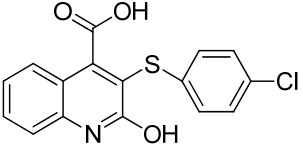
MTT assay for cell cytotoxicity

All of synthesis compounds were evaluated cell cytotoxicity by
 20 using MTT colorimetric assay on PC-3 and DU-145 cell lines. DU-145 and PC-3 are human hormone-refractory (androgen-independent) prostatic cancer cell lines from American Type Culture Collection (HTB-81™, ATCC, Rockville, MD)¹²⁵ and Bioresource Collection and Research Center (60122, BCRC,
 25 Taiwan)¹²⁶, respectively. Two of the "classical" cell lines were cultivated in RPMI-1640 medium supplemented with 5% fetal bovine

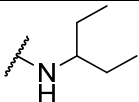
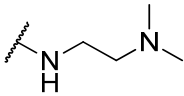
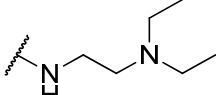
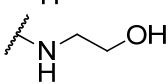
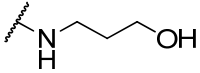
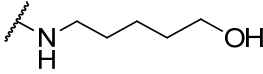
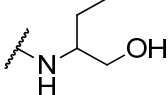
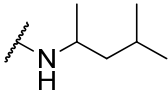
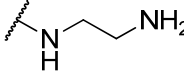
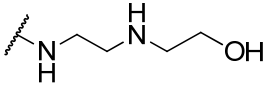
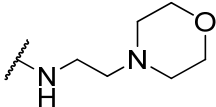
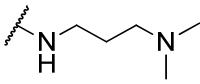
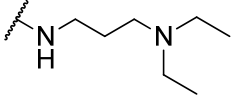
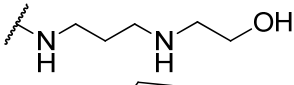
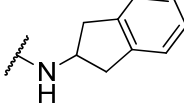
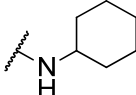
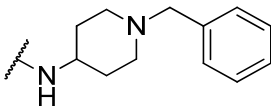
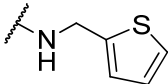
serum (v/v), 100 U/mL penicillin, and 50 mg/mL streptomycin. Approximately 2×10^3 cells were seeded into each well of a 96-well plate and incubated in 5% CO₂ at 37 °C for 24 h. To evaluate the *in vitro* cytotoxicity, all the synthetic compounds were dissolved in DMSO, prepared immediately before the experiments and diluted into the complete medium before being added to each well of a 96-well plate. Each compound was then added to the culture medium for designated various concentrations (0.15, 0.5, 1.5, 5, 15 μ M). After 72 h, an amount of 100 μ L of MTT (1 mg/mL) was added to each well, and the samples were incubated at 37 °C for 4 h. After removing the MTT solution, 100 μ L of DMSO was added to each well and incubated at 37 °C for another 20 mins. The absorbency at 560 nm was measured by using an ELISA reader.

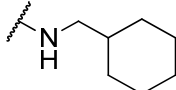
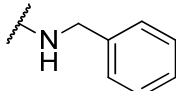
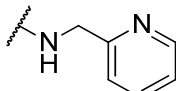
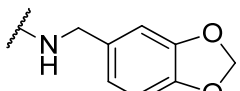
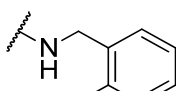
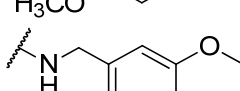
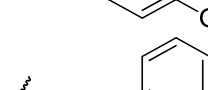
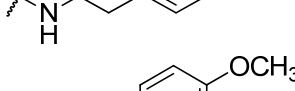
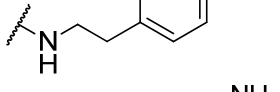
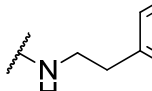
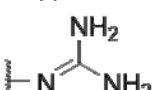
Results are expressed as mean values of at least three independent experiments. The IC₅₀ values of testing compounds were described in Table 1.

Table1. Effects of 10-Chloro-12*H*-thiochromeno[2,3-*c*]quinolin-12-one derivatives on cytotoxicity by MTT assay.

No.	R substitutions	MTT assay (IC ₅₀ $\pm$ SD) ^a	
		DU-145 (μ M)	PC-3 (μ M)
2		> 15	> 15
3		> 15	> 15
4		> 15	10.10 $\pm$ 1.81
5		10.84 $\pm$ 6.55	3.89 $\pm$ 0.54
6		> 15	> 15

7		5.01 ± 1.68	2.84 ± 0.64
8		12.94 ± 0.26	7.18 ± 2.45
9		> 15	12.04 ± 3.41
10		> 15	> 15
11		> 15	> 15
12		> 15	> 15
13		> 15	> 15
14		> 15	> 15
15		13.38 ± 2.87	> 15
16		11.12 ± 4.18	9.55 ± 2.42
17		> 15	> 15
18		10.23 ± 2.03	14.16 ± 1.41
19		9.02 ± 1.20	6.36 ± 0.17
20		> 15	> 15
21		11.12 ± 4.18	9.55 ± 2.42
N1		11.65 ± 5.15	14.48 ± 2.70
N2		6.70 ± 1.62	5.18 ± 2.20
N3		7.64 ± 2.74	7.41 ± 3.43
N4		10.35 ± 2.46	10.11 ± 1.32
N5		> 15	> 15

N6		> 15	> 15
N7		5.94 ± 3.45	2.25 ± 0.61
N8		1.73 ± 0.72	1.11 ± 0.69
N9		11.55 ± 7.23	7.48 ± 3.35
N10		5.94 ± 2.03	6.31 ± 4.11
N11		4.95 ± 0.58	8.38 ± 3.39
N12		6.74 ± 2.14	7.05 ± 2.48
N13		14.16 ± 1.18	10.38 ± 2.30
N14		1.80 ± 0.40	1.64 ± 0.55
N15		3.81 ± 1.88	3.44 ± 1.81
N16		>15	>15
N17		2.70 ± 0.16	2.27 ± 0.09
N18		3.53 ± 1.05	2.22 ± 0.21
N19		1.50 ± 1.32	1.98 ± 0.72
N20		4.86 ± 0.99	6.20 ± 2.52
N21		8.06 ± 2.08	7.51 ± 0.22
N22		8.39 ± 1.84	6.47 ± 0.30
N23		14.65 ± 3.84	> 15

N24		13.55 ± 3.88	14.80 ± 3.26
N25		13.49 ± 0.69	11.16 ± 1.55
N26		14.75 ± 1.99	14.20 ± 2.22
N27		11.82 ± 5.83	> 15
N28		9.61 ± 4.88	6.01 ± 3.31
N29		4.86 ± 0.99	6.20 ± 2.52
N30		> 15	> 15
N31		> 15	> 15
N32		13.59 ± 1.39	10.11 ± 0.94
N33		8.11 ± 1.37	6.13 ± 6.98
N34		9.06 ± 1.95	8.22 ± 1.02
-	Mitoxantrone	0.10 ± 0.01	0.39 ± 0.02
-	Doxorubicin	0.12 ± 0.03	0.63 ± 0.26
-	Camptothecin	0.10 ± 0.01	0.10 ± 0.01
-	Etoposide (VP-16)	0.40 ± 0.01	4.33 ± 0.86

^a SD: standard derivatives, all experiments were independently performed at least three times.

Besides, compounds N7, N8, N14, N15, N17, and N18 containing more than one nitrogen atom in the side chains showed the outstanding cytotoxic activities than having a hydroxyl group, alkyl

group, or aromatic rings. Compounds **5**, **7**, **8**, **16**, **19**, **N2**, **N7**, **N8**, **N9**, **N14**, **N15**, **N16**, **N17**, **N18**, **N19**, and **N25** were selected for TOPs activities assay.

Example 56

5 Topoisomerase I and II activities assay

According to the cell cytotoxicity, compounds **5**, **7**, **8**, **16**, **19**, **N2**, **N7**, **N8**, **N9**, **N14-N19**, and **N25** were also selected for primary TOP I and II activities assays at 25 and/or 50 μ M (Fig. 2-4). In TOP I activity assay, compounds **7**, **N7**, **N14**, **N15**, **N17**, **N18**, and **N25** were showed
 10 more potent inhibitory effects than CPT and selected for further evaluation by using five different concentrations (Figure 4). The IC₅₀ value of compounds **7**, **N7**, **N14**, **N15**, **N18**, **N19**, and **N25** were about 10, 10, 1, 5, 25, 5, and 25 μ M, respectively (detect by TopoGEN TG2005H, TG-2000H-1).

15 We also performed TOP II-catalyzed relaxation of plasmid DNA assays(Fig. 5-7) to evaluate if compounds could inhibit TOP II. Respond to our drug design, compounds **7**, **N7**, **N8**, **N14**, **N15**, **N18**, and **N19** were showed more potent inhibitory effects than the positive agent VP-16 and selected for further evaluation by using five different
 20 concentrations (Figure 7). The IC₅₀ value of compounds **7**, **N7**, **N8**, **N14**, **N15**, **N18**, and **N19** were about 10, 10, 1, 10, 5, 1, and 1 μ M, respectively (detect by TopoGEN TG2005H, TG-2000H-1).

Example 57

National Cancer Institute Cancer Cell Cytotoxicity assay:

25 The test results shown in this section are the compound

cytotoxicities in vitro against cancer cell lines National Cancer Institute (NCI)'s anticancer drug screen and 26 compounds (2, 3, 4, 5, 6, 8, 10, 11, 12, 13, N1, N2, N6, N7, N9, N12, N13, N14, N16, N17, N19, N21, N25, N27, N30, N31) screened. In the first stage, 5 cytotoxicity of the 26 compounds at the concentration of 10 μ M was conducted on 60 cell lines and SRB assay was performed after 48 hours of incubation. The results are shown in Tables 2 to 4 and are represented by growth percentage.

Furthermore, among five compounds were active drugs for 10 further their cytostatic and cytotoxic activities against the 60 cell panel by using five dose studies (0.01, 0.1, 1, 10 and 100 μ M) (Table 5).

Many changes and modifications in the above described embodiment of the invention can, of course, be carried out without departing from the scope thereof. Accordingly, to promote the 15 progress in science and the useful arts, the invention is disclosed and is intended to be limited only by the scope of the appended claims.

Table 2. *In-vitro* anticancer activity of compounds 2, 3, 4, 5, 6, 8, 10, 11, 12, and 13 in NCI's drug screen program.

Panel/Cell line	Compounds/ Growth percent ^a									
	2	3	4	5	6	8	10	11	12	13
	NSC763977	NSC771780	NSC777199	NSC777200	NSC777202	NSC777175	NSC777176	NSC777177	NSC777178	NSC777179
Leukemia										
CCRF-CEM	98.31	93.12	107.78	106.56	99.42	91.60	83.46	95.42	98.41	88.02
HL-60(TB)	105.63	99.34	109.82	89.47	107.16	96.19	93.81	100.96	113.79	93.38
K-562	112.29	101.04	107.08	95.83	99.71	72.98	35.47	87.84	112.37	81.18
MOLT-4	97.25	98.04	100.41	80.62	97.52	87.97	70.01	90.91	107.23	89.31
RPMI-8226	98.10	100.19	100.99	102.86	98.20	91.11	84.87	96.63	99.93	89.54
SR	106.33	89.02	96.00	88.18	95.68	86.41	79.07	85.15	103.11	88.91
Non-small cell lung cancer										
A549/ATCC	107.34	104.74	95.25	100.46	94.16	99.80	95.49	106.37	98.54	92.97
EKVX	89.47	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.
HOP-62	116.47	82.02	90.80	69.64	43.62	49.41	67.83	87.72	86.00	70.77
HOP-92	72.97	90.83	93.13	80.11	58.65	17.97	39.64	70.17	81.27	60.43
NCI-H226	105.64	83.41	99.58	98.57	96.20	85.67	89.29	88.98	87.10	88.01
NCI-H23	92.61	85.12	88.96	80.14	77.00	81.11	84.75	89.94	93.80	95.21
NCI-H322M	101.10	100.12	90.87	90.77	83.74	77.04	82.85	88.92	84.41	88.41
NCI-H460	104.20	103.14	96.92	101.23	88.86	96.05	93.71	95.57	103.24	99.28
NCI-H522	81.64	96.81	86.60	92.71	70.42	98.78	94.76	96.69	93.50	89.60
Colon cancer										
COLO 205	108.65	112.15	93.69	97.94	89.67	90.06	88.90	105.64	111.67	99.24
HCC-2998	100.97	123.28	101.48	104.67	97.20	96.87	103.49	99.32	105.23	108.75
HCT-116	103.87	102.27	86.20	89.48	74.26	80.94	69.33	98.59	105.36	85.71
HCT-15	107.80	102.28	98.11	107.99	89.27	93.94	82.92	94.51	99.81	93.81
HT29	101.41	99.73	96.78	102.69	87.73	78.65	63.19	102.71	99.94	83.73
KM12	112.61	111.27	102.45	98.03	96.40	110.71	101.86	107.75	113.15	88.68
SW-620	96.92	99.06	101.39	103.05	105.18	95.50	88.11	93.08	100.20	96.18
CNS cancer										
SF-268	113.60	109.60	95.26	94.12	77.86	82.98	87.80	100.42	103.82	103.56
SF-295	98.99	90.26	99.93	86.35	48.82	91.69	100.32	94.34	99.23	93.62
SF-539	110.22	89.02	93.21	86.13	72.72	85.30	86.18	108.56	100.06	82.38
SNB-19	97.17	107.89	101.37	89.36	76.46	87.07	84.81	95.52	105.57	99.37
SNB-75	82.18	77.88	66.63	52.28	15.29	42.15	77.64	82.62	94.73	76.88
U251	99.59	101.71	101.85	99.18	93.55	92.52	83.31	96.69	96.09	98.58
Melanoma										
LOX IMVI	90.46	90.53	92.07	91.21	86.53	87.47	87.79	94.22	95.15	89.82
MALME-3M	107.05	95.87	93.26	94.19	89.70	108.36	119.20	112.36	121.84	118.84
M14	106.90	106.18	94.76	88.40	94.36	102.15	101.70	93.00	104.02	110.35
MDA-MB-435	102.02	100.64	103.18	103.83	107.18	105.80	98.24	96.99	102.39	102.07
SK-MEL-2	119.91	95.54	103.04	105.52	87.26	97.53	104.06	107.37	104.26	98.77
SK-MEL-28	98.95	101.80	116.59	112.31	96.60	107.92	100.66	104.19	104.22	111.28
SK-MEL-5	98.07	97.42	100.69	99.74	97.92	99.54	94.13	98.38	103.57	95.88
UACC-257	121.83	104.47	108.36	108.09	109.22	100.55	102.79	95.39	93.68	110.91
UACC-62	102.05	89.69	105.86	96.15	87.80	99.27	91.36	96.00	104.48	87.86
Ovarian cancer										
IGROV1	103.57	96.06	78.35	71.44	68.16	80.08	71.67	93.49	91.38	80.90
OVCAR-3	121.29	111.27	106.37	96.60	79.65	89.13	93.92	101.69	109.63	96.54
OVCAR-4	98.41	87.91	N.T.	N.T.	N.T.	94.93	85.35	102.43	94.29	96.75
OVCAR-5	112.47	100.07	111.17	106.70	98.05	98.14	95.70	111.92	108.10	95.97
OVCAR-8	114.68	101.62	100.55	91.82	68.53	89.44	84.95	98.54	90.34	83.66
NCI/ADR-RES	97.75	102.80	96.84	96.10	87.86	81.35	92.05	98.31	100.81	98.16
SK-OV-3	N.T. ^b	101.32	94.40	58.94	41.57	75.11	95.12	94.79	100.39	77.18
Renal cancer										
786-0	104.44	105.25	99.76	99.15	87.00	90.48	85.58	105.57	101.58	99.31
A498	N.T.	106.06	107.74	96.29	97.06	79.33	62.20	94.17	81.04	94.15
ACHN	113.47	86.84	95.52	74.89	64.81	89.73	83.05	96.39	94.99	82.54
CAKI-1	76.26	94.31	N.T.	N.T.	N.T.	87.50	87.87	94.03	97.83	90.00
RXF 393	113.90	102.55	116.94	109.68	83.17	88.57	70.31	100.71	107.68	108.61
SN12C	95.83	95.92	101.14	98.74	99.49	83.03	86.81	97.70	102.66	96.81
TK-10	118.09	108.56	113.26	113.30	64.75	97.07	93.19	124.99	112.45	86.24
UO-31	68.91	66.06	76.44	74.69	73.81	48.97	42.34	64.91	63.85	73.11
Prostate cancer										
PC-3	93.23	91.59	91.90	92.46	81.25	84.81	77.99	89.12	90.66	79.80
DU-145	115.22	114.27	99.80	104.27	92.93	103.45	96.26	111.61	111.15	110.81
Breast cancer										
MCF7	91.95	82.58	69.90	65.39	22.19	76.60	51.73	68.32	74.16	50.59
MDA-MB-231/ATCC	95.70	84.28	81.80	78.12	71.03	57.30	55.49	89.11	94.34	71.53
HS 578T	88.33	95.14	113.28	66.51	60.38	65.57	76.01	76.42	85.20	83.27
BT-549	124.20	110.01	85.17	94.85	92.96	96.25	90.05	114.05	123.95	113.81
T-47D	99.59	110.10	77.89	68.46	37.66	82.24	87.22	89.22	104.57	80.00
MDA-MB-486	104.57	98.57	100.33	103.54	29.91	102.02	81.67	98.53	86.34	39.67
Mean	102.11	98.11	97.17	92.10	80.59	86.81	84.06	96.19	99.30	90.52
Delta	33.20	32.05	30.54	39.82	65.30	68.64	48.59	31.28	35.45	50.85
Range	55.29	57.22	50.31	61.02	93.93	92.74	83.73	60.08	60.10	79.17

^a Data obtained from NCI *in vitro* 60-cell drug screen program at 10⁻⁵ molar concentration. ^b N.T. = No test.

Table 3. Growth percentage of compounds N1, N2, N6, N7, N9, N12, N13, and N14 in the NCI *in vitro* 60-cell Drug Screen Program.

Panel/Cell line	Compounds/ Growth percent ^a							
	N1	N2	N6	N7	N9	N12	N13	N14
	NSC775512	NSC771784	NSC775513	NSC771785	NSC771786	NSC772854	NSC772855	NSC772865
Leukemia								
CCRF-CEM	79.77	88.62	93.72	-53.54	81.07	70.00	98.57	-39.61
HL-60(TB)	131.66	103.33	141.93	-47.40	104.58	96.29	103.96	-47.50
K-562	40.69	77.52	95.25	-58.60	68.23	46.86	106.64	-57.17
MOLT-4	86.86	92.27	103.08	-56.34	78.76	61.79	93.68	-58.82
RPMI-8226	93.10	79.66	108.60	-37.68	83.81	73.50	97.78	-27.48
SR	47.76	84.32	104.59	-34.76	60.44	62.38	97.29	-51.67
Non-small cell lung cancer								
A549/ATCC	51.68	61.84	91.04	23.38	80.72	69.86	101.98	-88.76
EKVX	N.T. ^b	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.
HOP-62	79.39	57.49	95.32	56.42	81.90	55.91	88.69	-97.40
HOP-92	59.15	-0.07	83.26	-10.12	63.17	N.T.	N.T.	N.T.
NCI-H226	73.53	41.31	79.22	58.08	83.55	77.56	87.55	28.55
NCI-H23	44.39	86.29	94.17	72.59	86.06	81.25	95.10	-5.25
NCI-H322M	60.89	74.88	92.45	49.16	79.00	58.98	85.51	-50.28
NCI-H460	73.84	53.33	99.42	-71.14	100.97	83.78	95.17	-62.39
NCI-H522	97.00	80.75	99.02	-8.99	76.94	64.07	102.30	-66.59
Colon cancer								
COLO 205	94.82	82.36	107.68	-82.85	99.13	68.37	93.45	-87.22
HCC-2998	105.34	98.02	119.79	-83.65	101.55	99.61	112.26	-90.43
HCT-116	32.49	48.13	99.01	-96.59	93.62	73.42	90.30	-48.19
HCT-15	68.73	79.72	95.35	-30.05	78.61	77.58	96.97	-45.92
HT29	114.79	68.21	116.70	-84.24	87.36	78.24	121.02	-83.30
KM12	68.75	85.79	94.04	-77.07	91.93	82.37	105.66	-85.99
SW-620	84.37	84.65	104.94	-67.82	97.18	84.32	92.80	-66.88
CNS cancer								
SF-268	70.58	78.23	102.86	39.05	95.06	76.71	105.52	-67.65
SF-295	89.04	69.49	104.18	-32.59	92.50	89.58	95.92	-74.29
SF-539	59.86	60.35	95.09	48.73	90.56	83.86	N.T.	2.13
SNB-19	96.48	84.19	99.01	55.44	90.96	93.87	106.79	40.06
SNB-75	67.29	12.12	73.24	33.36	90.05	31.01	85.02	-43.13
U251	85.19	76.58	97.05	-39.75	84.10	74.49	105.12	N.T.
Melanoma								
LOX IMVI	44.95	80.61	89.35	-84.12	86.96	79.25	98.90	N.T.
MALME-3M	72.46	77.31	92.36	-4.32	104.86	58.66	95.93	-48.42
M14	105.85	91.72	107.34	-92.77	107.09	85.38	94.27	-55.62
MDA-MB-435	84.97	80.67	108.13	-64.64	94.98	92.11	108.08	-85.39
SK-MEL-2	110.10	76.15	104.97	-7.83	86.80	N.T.	N.T.	N.T.
SK-MEL-28	83.41	93.07	98.40	-76.79	100.76	82.86	106.87	-96.20
SK-MEL-5	80.13	73.99	90.08	18.83	97.36	87.19	90.71	68.64
UACC-257	91.23	75.21	99.44	-48.22	89.33	95.71	114.40	-67.35
UACC-62	77.66	69.06	83.74	-76.58	76.52	76.17	96.09	-96.67
Ovarian cancer								
IGROV1	67.97	59.26	80.40	33.20	88.51	66.54	74.77	-77.31
OVCAR-3	N.T.	76.51	N.T.	19.74	103.35	96.34	115.22	-84.15
OVCAR-4	71.33	23.19	98.77	60.67	102.67	83.23	86.07	-20.15
OVCAR-5	86.91	92.93	99.96	24.27	101.56	88.01	101.36	-52.16
OVCAR-8	31.61	62.54	95.31	1.22	78.13	68.74	92.79	-74.59
NCI/ADR-RES	70.95	88.61	101.32	23.00	91.54	77.02	98.47	-42.68
SK-OV-3	88.67	28.90	99.71	70.10	104.57	58.93	86.70	12.25
Renal cancer								
786-0	95.51	23.87	108.84	43.11	104.43	82.86	99.74	-57.40
A498	82.89	61.02	103.44	43.17	65.78	74.62	75.01	60.29
ACHN	84.47	43.77	84.92	7.55	82.25	69.12	91.24	-92.31
CAKI-1	68.09	72.44	73.26	34.60	89.29	59.29	86.38	-75.30
RXF 393	84.52	34.56	93.23	-15.29	92.81	71.61	98.67	-87.22
SN12C	92.52	85.67	94.28	48.67	92.52	81.98	95.41	-93.98
TK-10	81.21	47.11	138.89	-89.05	78.14	77.45	123.23	-28.04
UO-31	65.34	32.06	78.57	21.83	51.97	51.01	78.64	-92.77
Prostate cancer								
PC-3	61.41	77.80	84.63	33.32	71.70	58.35	86.33	-97.71
DU-145	80.29	87.67	109.54	-80.85	102.77	87.04	113.48	-96.35
Breast cancer								
MCF7	23.26	17.54	67.12	-85.41	29.66	40.92	73.82	-98.38
MDA-MB-231/ATCC	66.58	48.66	77.83	-37.28	66.62	58.29	84.22	-84.52
HS 578T	82.63	36.37	89.81	34.31	83.24	52.66	89.33	50.82
BT-549	108.49	100.10	109.76	91.29	131.62	85.96	103.61	78.49
T-47D	42.13	38.28	73.62	26.06	74.45	46.94	73.76	-82.45
MDA-MB-486	8.75	26.29	95.79	12.81	39.59	80.85	96.02	-62.13
Mean	75.06	65.97	96.94	-11.06	86.33	73.52	96.33	-51.89
Delta	66.31	66.04	29.82	85.53	56.67	42.51	22.57	46.49
Range	122.91	103.40	74.81	187.88	101.96	68.60	49.47	176.87

^aData obtained from NCI *in vitro* 60-cell drug screen program at 10⁻⁵ molar concentration. ^bN.T. = No test.

Table 4. Growth percentage of compounds **N16**, **N17**, **N19**, **N21**, **N25**, **N27**, **N30**, and **N31** in the NCI *in vitro* 60-cell Drug Screen Program.

Panel/Cell line	Compounds/ Growth percent ^a							
	N16	N17	N19	N21	N25	N27	N30	N31
	NSC777203	NSC775511	NSC777201	NSC772866	NSC772867	NSC775508	NSC775509	NSC775510
Leukemia								
CCRF-CEM	82.21	69.06	-54.78	92.23	102.34	88.86	114.29	100.93
HL-60(TB)	104.97	77.32	-37.88	107.06	98.82	112.12	105.68	94.27
K-562	17.67	47.53	-66.94	102.86	90.61	80.37	82.82	91.76
MOLT-4	80.91	70.71	-47.57	92.42	92.42	87.55	87.33	82.02
RPMI-8226	92.20	78.66	5.53	94.56	88.54	96.35	77.36	99.98
SR	67.74	48.48	-51.40	85.52	85.46	79.57	89.88	94.13
Non-small cell lung cancer								
A549/ATCC	95.12	81.19	-61.45	85.28	68.33	104.74	88.44	93.49
EKVX	N.T. ^b	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.
HOP-62	67.97	86.73	36.97	101.46	66.53	78.01	103.19	90.07
HOP-92	58.79	40.76	23.01	N.T.	N.T.	45.39	73.02	67.57
NCI-H226	94.09	81.01	86.75	93.26	79.35	53.50	77.00	72.39
NCI-H23	83.07	100.25	54.26	91.11	74.37	79.93	89.89	92.72
NCI-H322M	76.96	82.29	10.05	91.10	91.00	73.65	117.72	99.19
NCI-H460	100.49	88.06	-80.98	91.29	64.41	76.71	95.11	98.14
NCI-H522	76.66	98.76	-59.68	83.95	75.71	78.43	93.93	93.69
Colon cancer								
COLO 205	79.39	91.35	-87.17	103.96	80.79	87.63	100.02	105.41
HCC-2998	90.51	108.36	-74.47	109.83	95.77	N.T.	113.77	105.27
HCT-116	81.64	70.19	-91.19	65.37	66.87	69.98	85.77	98.46
HCT-15	58.81	80.92	-76.47	91.71	71.76	77.41	91.82	100.67
HT29	43.13	90.98	-83.53	105.11	77.16	82.91	109.15	120.78
KM12	68.16	97.75	-83.29	112.90	80.34	87.96	90.99	109.46
SW-620	99.65	91.74	-81.48	87.98	78.97	76.95	93.45	97.10
CNS cancer								
SF-268	79.49	87.67	17.28	92.06	73.68	93.24	101.32	100.14
SF-295	102.17	95.14	-93.00	92.22	74.33	94.39	95.46	95.31
SF-539	76.72	87.85	-47.59	91.20	80.59	77.12	97.86	95.67
SNB-19	90.44	97.83	46.07	106.72	102.93	97.62	100.86	96.74
SNB-75	60.74	60.99	23.66	81.91	14.83	57.14	68.76	74.50
U251	76.34	84.19	-66.76	N.T.	N.T.	81.03	96.78	98.72
Melanoma								
LOX IMVI	67.43	66.16	-82.79	N.T.	N.T.	78.69	89.03	87.78
MALME-3M	78.79	100.91	-34.30	93.42	77.59	81.64	122.61	99.74
M14	99.59	103.73	6.12	103.41	87.29	94.93	97.97	100.06
MDA-MB-435	98.93	93.04	-88.95	106.98	89.58	91.64	106.06	104.49
SK-MEL-2	94.52	106.47	53.64	N.T.	N.T.	95.57	106.33	113.12
SK-MEL-28	98.56	99.63	-94.33	101.79	84.20	88.24	98.94	99.41
SK-MEL-5	91.61	91.73	62.02	97.00	92.81	79.86	89.49	85.38
UACC-257	106.52	107.40	45.70	103.68	83.24	N.T.	109.29	98.66
UACC-62	94.58	102.63	-77.63	93.23	89.20	72.96	74.67	80.17
Ovarian cancer								
IGROV1	74.11	87.27	-43.25	83.31	53.42	67.81	N.T.	86.73
OVCAR-3	97.14	N.T.	N.T.	91.85	76.59	N.T.	N.T.	N.T.
OVCAR-4	N.T.	94.63	12.32	72.10	27.24	53.73	79.53	79.00
OVCAR-5	68.98	106.26	-65.05	98.06	91.27	84.38	102.03	100.83
OVCAR-8	92.43	98.38	9.89	74.91	68.33	79.45	95.61	97.83
NCI/ADR-RES	77.03	96.94	26.35	95.71	77.36	91.11	96.51	103.78
SK-OV-3	85.34	99.91	76.48	94.54	36.71	82.87	102.16	96.11
Renal cancer								
786-0	83.16	93.30	-17.60	97.69	72.48	95.83	108.00	100.71
A498	80.54	78.57	61.88	93.00	86.46	75.91	83.22	99.56
ACHN	91.61	86.20	-96.96	97.31	51.82	58.48	90.85	91.19
CAKI-1	N.T.	84.31	N.T.	72.76	80.38	75.09	81.04	85.75
RXF 393	93.21	76.32	43.67	97.03	71.08	74.20	96.74	88.50
SN12C	95.98	83.63	78.75	89.12	87.82	85.53	86.54	94.23
TK-10	76.67	108.89	-92.61	127.96	75.80	116.79	122.13	132.57
UO-31	54.16	72.62	24.54	72.52	65.31	80.98	75.82	72.12
Prostate cancer								
PC-3	67.82	81.31	-26.98	75.02	72.70	78.54	87.25	84.95
DU-145	93.09	97.29	-71.03	104.25	74.80	72.44	100.17	107.03
Breast cancer								
MCF7	51.69	51.20	-72.49	46.14	16.01	43.53	60.91	59.13
MDA-MB-231/ATCC	59.20	73.39	-66.53	77.17	32.67	54.65	79.55	82.31
HS 578T	89.65	87.67	64.69	94.22	34.73	70.49	87.62	87.49
BT-549	91.21	99.81	98.48	105.53	97.19	111.06	106.85	105.24
T-47D	47.63	79.82	16.26	72.43	38.08	74.41	71.96	69.90
MDA-MB-486	74.34	43.26	-24.00	108.92	-9.83	60.47	63.11	53.93
Mean	80.38	85.32	-21.33	92.62	71.97	80.18	93.22	93.38
Delta	62.71	44.56	75.63	46.48	81.80	36.65	32.31	39.45
Range	88.85	68.13	195.44	81.82	112.76	73.26	61.70	78.64

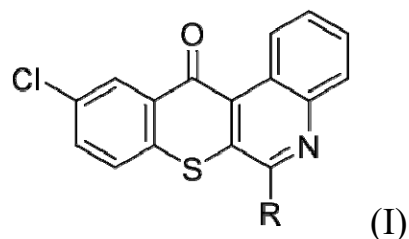
^aData obtained from NCI *in vitro* 60-cell drug screen program at 10⁻⁵ molar concentration. ^bN.T. = No test.

Table 5. *In vitro* antitumor activity (GI₅₀ in μ M), toxicity (LC₅₀ in μ M) and TGI data of selected compounds N2, N7, N14, N19, and N25.

Panel/Cell line (μ M)	N2 (NSC771784)			N7 (NSC771785)			N14 (NSC772865)			N19 (NSC777201)			N25 (NSC772867)		
	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀
Leukemia															
CCRF-CEM	> 100	> 100	> 100	1.63	3.41	7.15	1.75	3.65	7.64	1.83	3.80	-	> 100	> 100	> 100
HL-60(TB)	> 100	> 100	> 100	1.76	3.49	6.95	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.
K-562	> 100	> 100	> 100	1.33	3.00	6.74	1.69	3.65	7.84	1.73	-	> 100	> 100	> 100	> 100
MOLT-4	> 100	> 100	> 100	1.71	3.40	6.74	2.02	3.96	7.77	1.88	-	-	> 100	> 100	> 100
RPMI-8226	> 100	> 100	> 100	1.76	3.68	7.69	2.26	4.92	62.30	1.84	4.21	-	> 100	> 100	> 100
SR	> 100	> 100	> 100	1.70	3.73	8.14	1.81	4.30	> 100	1.98	4.55	> 100	> 100	> 100	> 100
Non-small cell lung cancer															
A549/ATCC	48.1	> 100	> 100	1.66	3.17	6.06	1.83	3.50	6.68	1.76	3.30	-	14.40	> 100	> 100
EKVX	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.
HOP-62	13.30	35.20	93.10	1.54	2.92	5.56	1.47	2.92	-	1.38	2.89	-	2.43	5.92	27.70
HOP-92	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	1.03	3.05	9.04	1.23	4.58	26.70	1.75	7.53	53.60
NCI-H226	33.20	> 100	> 100	1.84	4.38	24.30	1.36	2.95	-	1.90	4.46	> 100	1.84	-	> 100
NCI-H23	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	1.72	3.37	6.63	1.89	3.68	-	15.20	> 100	> 100
NCI-H322M	69.50	> 100	> 100	1.74	3.18	5.81	1.65	3.34	6.74	1.80	3.56	7.03	> 100	> 100	> 100
NCI-460	> 100	> 100	> 100	1.76	3.38	6.50	1.69	3.45	7.05	1.66	3.35	-	5.00	> 100	> 100
NCI-H522	24.80	> 100	> 100	1.59	3.07	5.90	1.86	3.59	6.92	1.85	3.56	-	25.30	> 100	> 100
Colon cancer															
COLO 205	> 100	> 100	> 100	1.66	3.17	6.05	1.73	3.57	-	1.63	3.37	-	-	> 100	> 100
HCC-2998	> 100	> 100	> 100	1.68	3.38	6.82	2.03	4.06	8.14	1.58	3.42	-	> 100	> 100	> 100
HCT-116	6.31	> 100	> 100	1.57	3.18	6.45	1.63	2.99	5.47	1.60	3.05	-	5.59	> 100	> 100
HCT-15	> 100	> 100	> 100	1.59	3.14	6.21	1.58	3.12	6.16	1.61	3.25	6.57	8.75	> 100	> 100
HT29	> 100	> 100	> 100	1.65	3.36	6.88	1.78	3.29	6.09	2.05	4.00	7.82	-	> 100	> 100
KM12	> 100	> 100	> 100	1.78	3.28	6.03	1.67	3.11	5.79	1.67	3.31	-	48.30	> 100	> 100
SW-620	> 100	> 100	> 100	1.71	3.29	6.36	1.67	3.42	7.02	1.63	3.30	-	-	> 100	> 100
CNS cancer															
SF-268	22.10	> 100	> 100	1.57	3.16	6.35	1.59	3.23	6.55	1.67	3.35	-	13.80	> 100	> 100
SF-295	12.20	35.20	> 100	1.73	3.21	5.98	1.79	3.63	-	1.73	3.33	-	3.50	16.50	> 100
SF-539	10.10	58.50	> 100	1.68	3.08	5.67	1.57	2.95	5.52	1.70	3.22	6.11	4.49	46.40	> 100
SNB-19	26.60	81.10	> 100	1.54	3.07	6.10	1.65	3.18	-	1.64	3.26	-	8.56	> 100	> 100
SNB-75	4.96	22.00	60.20	1.28	3.69	12.10	1.09	2.31	4.90	1.28	2.56	5.14	1.45	3.78	9.91
U251	16.90	67.90	> 100	1.48	2.84	5.44	1.63	3.07	5.78	1.73	3.22	-	4.41	25.10	> 100
Melanoma															
LOX IMV1	> 100	> 100	> 100	1.68	3.24	6.24	1.68	3.16	5.96	1.80	3.80	-	> 100	> 100	> 100
MALME-3M	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	1.98	3.96	7.93	2.15	4.33	-	> 100	> 100	> 100
M14	> 100	> 100	> 100	1.85	3.44	6.40	1.83	3.35	6.14	1.83	3.53	6.82	> 100	> 100	> 100
MDA-MB-435	> 100	> 100	> 100	1.71	3.22	6.05	1.82	3.59	-	1.59	2.99	5.62	> 100	> 100	> 100
SK-MEL-2	16.3	43.2	> 100	1.80	3.32	6.12	1.98	3.95	7.87	2.05	3.77	6.90	10.60	31.90	96.50
SK-MEL-28	> 100	> 100	> 100	1.81	3.27	5.89	1.75	3.15	5.66	1.89	3.56	-	-	> 100	> 100
SK-MEL-5	-	> 100	> 100	1.57	3.59	8.21	1.51	2.87	5.44	1.60	3.00	5.63	4.23	> 100	> 100
UACC-257	> 100	> 100	> 100	1.74	3.21	5.93	1.90	3.56	6.70	1.86	3.44	6.33	> 100	> 100	> 100
UACC-62	22.3	> 100	> 100	1.70	3.16	5.88	1.67	3.30	6.52	1.81	3.40	6.39	16.90	> 100	> 100
Ovarian cancer															
IGROV1	11.90	54.40	> 100	1.70	3.34	6.58	1.61	3.45	-	1.66	3.60	-	4.64	> 100	> 100
OVCAR-3	52.40	> 100	> 100	1.61	3.00	5.58	N.T.	N.T.	N.T.	1.79	3.51	-	N.T.	N.T.	N.T.
OVCAR-4	> 100	> 100	> 100	1.19	2.75	6.35	1.52	3.15	6.54	1.60	3.23	-	15.00	3.74	-
OVCAR-5	> 100	> 100	> 100	1.45	2.91	5.83	1.46	2.88	5.66	1.63	3.50	7.53	> 100	> 100	> 100
OVCAR-8	17.70	> 100	> 100	1.64	3.15	6.06	1.89	4.12	-	1.75	3.32	-	7.75	> 100	> 100
NCI/ADR-RES	33.50	> 100	> 100	1.67	3.17	6.00	1.88	3.67	-	1.82	3.63	-	43.00	> 100	> 100
SK-OV-3	11.10	35.20	> 100	1.68	3.06	5.58	1.78	3.38	6.42	1.68	3.38	6.80	3.56	13.90	> 100
Renal cancer															
786-0	10.5	33.8	> 100	1.84	3.45	6.46	1.76	3.20	5.81	1.72	3.37	-	9.55	48.70	> 100
A498	15.3	91.3	> 100	2.70	9.44	3.52	1.45	4.99	29.20	1.27	3.62	15.00	8.05	39.20	> 100
ACHN	8.66	> 100	> 100	1.63	3.07	5.77	1.44	2.76	5.29	1.67	3.22	-	4.02	> 100	> 100
CAKI-1	26.4	> 100	> 100	1.43	2.80	5.49	1.56	3.27	-	1.33	2.69	5.45	6.07	> 100	> 100
RXF 393	13.1	44.6	> 100	1.60	3.41	7.29	N.T.	N.T.	N.T.	1.64	3.20	-	N.T.	N.T.	N.T.
SN12C	75.3	> 100	> 100	1.59	3.12	6.12	1.45	3.02	-	1.70	3.39	6.80	24.90	> 100	> 100
TK-10	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	2.06	3.58	6.21	2.09	3.74	6.69	5.02	22.30	> 100
UO-31	29.4	> 100	> 100	1.19	2.50	5.22	1.29	2.78	5.96	1.36	2.94	6.35	57.80	> 100	> 100
Prostate Cancer															
PC-3	> 100	> 100	> 100	1.47	2.90	5.74	1.55	2.99	5.76	1.51	2.92	5.66	56.90	> 100	> 100
DU-145	> 100	> 100	> 100	1.87	3.34	5.99	1.81	3.20	5.66	1.76	3.31	6.25	5.50	> 100	> 100
Breast cancer															
MCF7	0.047	> 100	> 100	1.23	2.66	5.71	1.28	2.81	-	1.05	2.60	-	0.04	18.60	> 100
MDA-MB-231/ATCC	10.10	65.5	> 100	1.20	2.51	5.28	1.31	2.65	5.35	1.36	2.86	6.02	2.36	34.80	> 100
HS 578T	9.64	65.5	> 100	1.74	4.02	9.27	1.69	3.90	-	1.29	3.53	9.64	2.94	21.20	> 100
BT-549	9.87	> 100	> 100	8.91	2.27	5.33	2.15	5.35	62.00	1.67	3.15	-	20.50	> 100	> 100
T-47D	N.T.	N.T.	N.T.	N.T.	N.T.	N.T.	1.56	3.37	-	1.50	3.43	-	1.26	7.11	> 100
MDA-MB-468	0.040	> 100	> 100	1.47	3.28	7.34	1.27	2.80	6.15	1.06	2.56	6.20	0.03	0.66	63.10
Mean	28.84	83.18	100	1.66	3.39	6.92	1.66	3.39	7.94	1.66	3.39	9.55	11.22	53.70	91.20

What is claimed is:

1. A compound as shown in formulation (I):



wherein the R is selected from the groups consisting of:

- 5 i) 2-oxopiperidin-1-yl ;
 - ii) $\text{NH}(\text{C}_n\text{H}_{2n+1})$, wherein $1 \leq n \leq 10$;
 - iii) $\text{NH}(\text{CH}_2)_n\text{R}_1$, $0 \leq n \leq 10$, wherein R_1 is selected from the
 groups consisting of: $\text{N}(\text{CH}_3)_2$, $\text{C}(\text{NH}_2)_2$, linear alkyl chains
 of $\text{NH}(\text{CH}_2)_n\text{H}$, alkyl groups with substituted side chains,
 10 alkyl side chains with a substituted amino group and alkyl
 side chains with a substituted hydroxy group;
 - iv) $\text{NH}(\text{CH}_2)_n\text{R}_2$, $0 \leq n \leq 10$, wherein R_2 is selected from the
 groups consisting of: benzene rings, C_{3-12} cycloalkyl groups
 and heterocyclic groups of which contain 1 to 3 heteroatoms
 15 selected from O, S and N, wherein the ortho-, para- and meta-
 position can be further selected independently from one of
 the groups consisting of: Methoxyl group, amino group,
 benzene rings, C1-C3 alkyl group containing amino, nitro, or
 hydroxyl substituted groups and C_{3-12} heterocyclic groups;
 20 wherein the C_{3-12} heterocyclic groups which contain 1 to 3
 heteroatoms selected from O, S and N;
 and their pharmaceutically acceptable salts, and stereoisomers.
2. The compound according to claim 1, wherein the functional group
 i) ~ iii) are selected from the group consisting of

- 2-oxopiperidin-1-yl, methylamino, ethylamino, propylamino, butylamino, isobutylamino, pentan-3-ylamino, (2-(dimethylamino)ethyl)amino, (2-(diethylamino)ethyl)amino, 2-ethanolamino, 3-propanolamino, 5-pentanolamino,
- 5 (1-hydroxybutan-2-yl)amino, (4-methylpentan-2-yl)amino, (2-Aminoethyl)amino, (2-((2-hydroxyethyl)amino)ethyl)amino, (2-morpholinoethyl)amino, (3-(dimethylamino)propyl)amino, (3-(diethylamino)propyl)amino, (3-((2-hydroxyethyl)amino)propyl)amino,
- 10 (2,3-dihydro-1H-inden-2-yl)amino, cyclohexylamino, (1-Benzylpiperidin-4-yl)amino, (thiophen-2-ylmethyl)amino, (cyclohexylmethyl)amino, benzylamino, (pyridin-2-ylmethyl)amino, (Benzo[d][1,3]dioxol-5-ylmethyl)amino,
- 15 (2-methoxybenzyl)amino, (3,4-dimethoxybenzyl)amino, phenethylamino, (4-methoxyphenethyl)amino, (4-aminophenethyl)amino, guanidine and piperidin-1-ylamino.
3. The compound according to claim 1, wherein the compound is selected from the group consisting of:
- 20 10-Chloro-6-(2-oxopiperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-methylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-ethylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 25 10-Chloro-6-propylamino-12H-thiochromeno[2,3-c]quinolin-12-one,

- 6-(Butylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-isobutylamino-12H-thiochromeno[2,3-c]quinolin-12-one,
- 5 10-Chloro-6-(pentan-3-ylamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-(dimethylamino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-(diethylamino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10 10-Chloro-6-(2-ethanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(3-propanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 15 10-Chloro-6-(5-pentanolamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((1-hydroxybutan-2-yl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((4-methylpentan-2-yl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 20 6-((2-Aminoethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-((2-hydroxyethyl)amino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 25 10-Chloro-6-((2-morpholinoethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((3-(dimethylamino)propyl)amino)-12H-thiochrom

- eno[2,3-c]quinolin-12-one,
 10-Chloro-6-((3-(diethylamino)propyl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 10-Chloro-6-((3-((2-hydroxyethyl)amino)propyl)amino)-12H-th
 5 iochromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((2,3-dihydro-1H-inden-2-yl)amino)-12H-thiochro
 meno[2,3-c]quinolin-12-one,
 10-Chloro-6-(cyclohexylamino)-12H-thiochromeno[2,3-c]quino
 lin-12-one,
 10 6-((1-Benzylpiperidin-4-yl)amino)-10-chloro-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 10-Chloro-6-((thiophen-2-ylmethyl)amino)-12H-thiochromeno[
 2,3-c]quinolin-12-one,
 10-Chloro-6-((cyclohexylmethyl)amino)-12H-thiochromeno[2,3
 15 -c]quinolin-12-one,
 6-(Benzylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-1
 2-one,
 10-Chloro-6-((pyridin-2-ylmethyl)amino)-12H-thiochromeno[2,
 3-c]quinolin-12-one,
 20 6-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)-10-chloro-12H-thio
 chromeno[2,3-c]quinolin-12-one,
 10-Chloro-6-((2-methoxybenzyl)amino)-12H-thiochromeno[2,3-
 c]quinolin-12-one,
 10-Chloro-6-((3,4-dimethoxybenzyl)amino)-12H-thiochromeno[
 2,3-c]quinolin-12-one,
 25 10-Chloro-6-(phenethylamino)-12H-thiochromeno[2,3-c]quinoli
 n-12-one,

- 10-Chloro-6-((4-methoxyphenethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
 6-((4-Aminophenethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
 5 2-(10-Chloro-12-oxo-12*H*-thiochromeno[2,3-c]quinolin-6-yl)guanidine,
 10-Chloro-6-(piperidin-1-ylamino)-12*H*-thiochromeno[2,3-c]quinolin-12-one,
 and their salts.
- 10 4. A pharmaceutical composition comprising the effective dosage compound according to claim 1 and at least one pharmaceutically acceptable vehicle, diluent or excipient.
5. Use of the pharmaceutical composition according to claim 4 in the preparation of a medicament for the treatment of cancer.
- 15 6. The use according to claim 5, wherein the treatment of cancer is achieved by inhibiting Topoisomerase I activity.
7. The use according to claim 5, wherein the treatment of cancer is achieved by inhibiting Topoisomerase II activity.
8. The use according to claim 5, wherein the cancers are selected
 20 from the groups consisting of leukemia, non-small cell lung cancer, colorectal cancer, central nervous system (CNS) cancer, melanoma, ovarian cancer, renal cancer, prostate cancer and breast cancer.
9. A method for preparation of the compound according to claim 1 derivatives, wherein the method comprising:
- 25 (1) mix isatin, 2-((4-chlorophenyl)thio)acetic acid and sodium acetate was heated at 150 °C for 1 h, after cooling the mixture was added acetic acid, the precipitate was collected, washed

with acetic acid, water and n-hexane, and obtained compound 2 (3-((4-Chlorophenyl)thio)-2-hydroxyquinoline-4-carboxylic acid);

- (2) a solution of compound 2 (3-((4-Chlorophenyl)thio)-2-hydroxyquinoline-4-carboxylic acid) in phosphoryl trichloride was heated at 150 °C for 48 h, after cooling the mixture was poured into water 0 °C, the precipitate was collected by filtration, then added into 10% NaHCO₃ with vigorous stirring for 1 h, the resulting precipitate was collected and washed with H₂O, the crude solid was recrystallized by dichloromethane to give compound 3 (6,10-Dichloro-12H-thiochromeno[2,3-c]quinolin-12-one);
- (3) a solution of compound 3 (6,10-Dichloro-12H-thiochromeno[2,3-c]quinolin-12-one), appropriate piperidin-2-one and sodium carbonate in DMSO was refluxed for 10 hours, then the reaction was added ice-water, the precipitate was filtered, washed with water/methanol and collected to get compound 21:
10-Chloro-6-(2-oxopiperidin-1-yl)-12H-thiochromeno[2,3-c]quinolin-12-one respectively;
- (4) a solution of compound 3 (6,10-Dichloro-12H-thiochromeno[2,3-c]quinolin-12-one) in DMSO was added appropriate primary amines and refluxed for 8 hours, after cooled the reaction was added water, the precipitate was filtered and washed with water and methanol to collect compound N1~N34:
10-Chloro-6-methylamino-12H-thiochromeno[2,3-c]quinolin-

- 12-one,
 10-Chloro-6-ethylamino-12H-thiochromeno[2,3-c]quinolin-1
 2-one,
 10-Chloro-6-propylamino-12H-thiochromeno[2,3-c]quinolin-
 5 12-one,
 6-(Butylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-
 12-one,
 10-Chloro-6-isobutylamino-12H-thiochromeno[2,3-c]quino
 lin-12-one,
 10 10-Chloro-6-(pentan-3-ylamino)-12H-thiochromeno[2,3-c]qu
 inolin-12-one,
 10-Chloro-6-((2-(dimethylamino)ethyl)amino)-12H-thiochro
 meno[2,3-c]quinolin-12-one,
 10-Chloro-6-((2-(diethylamino)ethyl)amino)-12H-thiochrome
 15 no[2,3-c]quinolin-12-one,
 10-Chloro-6-(2-ethanolamino)-12H-thiochromeno[2,3-c]quin
 olin-12-one,
 10-Chloro-6-(3-propanolamino)-12H-thiochromeno[2,3-c]qui
 nolin-12-one,
 20 10-Chloro-6-(5-pentanolamino)-12H-thiochromeno[2,3-c]qui
 nolin-12-one,
 10-Chloro-6-((1-hydroxybutan-2-yl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 10-Chloro-6-((4-methylpentan-2-yl)amino)-12H-thiochromen
 25 o[2,3-c]quinolin-12-one,
 6-((2-Aminoethyl)amino)-10-chloro-12H-thiochromeno[2,3-c
]quinolin-12-one,

- 10-Chloro-6-((2-((2-hydroxyethyl)amino)ethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-morpholinoethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 5 10-Chloro-6-((3-(dimethylamino)propyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((3-(diethylamino)propyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((3-((2-hydroxyethyl)amino)propyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2,3-dihydro-1H-inden-2-yl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-(cyclohexylamino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 15 6-((1-Benzylpiperidin-4-yl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((thiophen-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((cyclohexylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 20 6-(Benzylamino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((pyridin-2-ylmethyl)amino)-12H-thiochromeno[2,3-c]quinolin-12-one,
- 25 6-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)-10-chloro-12H-thiochromeno[2,3-c]quinolin-12-one,
- 10-Chloro-6-((2-methoxybenzyl)amino)-12H-thiochromeno[2

,3-c]quinolin-12-one,
 10-Chloro-6-((3,4-dimethoxybenzyl)amino)-12H-thiochrome
 no[2,3-c]quinolin-12-one,
 10-Chloro-6-(phenethylamino)-12H-thiochromeno[2,3-c]quin
 5 olin-12-one,
 10-Chloro-6-((4-methoxyphenethyl)amino)-12H-thiochromen
 o[2,3-c]quinolin-12-one,
 6-((4-Aminophenethyl)amino)-10-chloro-12H-thiochromeno[
 2,3-c]quinolin-12-one,
 10 2-(10-Chloro-12-oxo-12*H*-thiochromeno[2,3-c]quinolin-6-yl)
 guanidine, and
 10-Chloro-6-(piperidin-1-ylamino)-12*H*-thiochromeno[2,3-c]
 quinolin-12-one respectively.

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