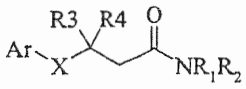
CLAIMS

1. A CNS-active compound having Formula I:

FORMULA I



wherein Ar is an optionally substituted phenyl, optionally substituted naphthyl, optionally substituted tetrahydronaphthyl, optionally substituted indane, or an optionally substituted heterocyclic aryl, wherein up to 5 substituents are optionally present on Ar and each substituent is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, halogen, alkoxy, thioalkyl, sulfoxyalkyl, sulfonylalkyl, alkylene dioxy, haloalkyl, haloalkoxy, OH, CH_2OH, $CONH_2$, CN, acetoxy, $N(alkyl)_2$, benzyl, benzyloxy, α,α-dimethylbenzyl, NO_2, CHO, $CH_3CH(OH)$, acetyl, OCH_2COOH, and an optionally substituted aromatic ring system;

said optionally substituted aromatic ring system being selected from the group consisting of phenyl, phenoxy, and heterocyclic aryl, wherein up to 5 substituents are optionally present on the aromatic ring system, and each substituent is independently selected from the group consisting of: hydrogen, alkyl, cycloalkyl, halogen, alkoxy, thioalkyl, sulfoxyalkyl, sulfonylalkyl, alkylene dioxy, haloalkyl, haloalkoxy, OH, CH_2OH, $CONH_2$, CN, acetoxy, $N(alkyl)_2$, NO_2, CHO, $CH_3CH(OH)$, acetyl, and OCH_2COOH;

R_1 and R_2 are each independently H, optionally substituted alkyl, optionally substituted cycloalkyl, or optionally substituted CW_2phenyl, wherein each W is independently selected from the group consisting of H, methyl and ethyl with the proviso that Ws are not ethyl, and wherein up to 5 substituents are optionally present in the phenyl group or cycloalkyl, and each substituent is independently selected from the group consisting of halogen, alkoxy, thioalkyl, sulfoxyalkyl, sulfonylalkyl, haloalkyl, haloalkoxy, $CONH_2$, CN, acetoxy, $N(alkyl)_2$, NO_2, and acetyl; when one of R_1 or R_2 is H then the other of R_1 or R_2 is $(CH_2)_2SO_3H$, or CHZCOOH, wherein Z is one of the group consisting of H, CH_3, $CH(CH_3)_2$, $CH_2C_6H_5$, $CH_2CH(CH_3)_2$, and $CH(CH_3)CH_2CH_3$; or R_1 and R_2 together are a cycloalkyl;

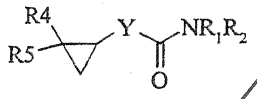
R_3 is one of a hydroxy, alkyl, cycloalkyl, or together with R_4 a cycloalkyl with the proviso that when one of R_3 or R_4 is OH then the other of R_3 or R_4 is not an ethyl;

R_4 is one of an alkyl, cycloalkyl, or together with R_3 cycloalkyl; and

X is one of nothing, methylene, ketone, CHOH, oxygen, NR_1, sulfur, sulfone, or sulfoxide.

2. A CNS-active compound having Formula II:

FORMULA II

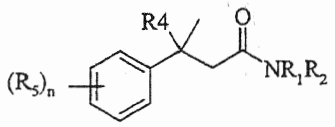


wherein R_1 and R_2 are each independently at least one of H, alkyl, cycloalkyl, or CW_2phenyl, wherein each W is independently selected from the group consisting of H, methyl and ethyl with the proviso that both Ws are not ethyl, and wherein up to 5 substituents may be present in the phenyl or cycloalkyl groups, and each substituent is independently selected from the group consisting of halogen, alkoxy, thioalkyl, sulfoxyalkyl, sulfonylalkyl, haloalkyl, haloalkoxy, $CONH_2$, CN, acetoxy, $N(alkyl)_2$, NO_2, and acetyl; when one of R_1 or R_2 is H then the other of R_1 or R_2 is $(CH_2)_2SO_3H$, or CHZCOOH, wherein Z is one of the group consisting of H, CH_3, $CH(CH_3)_2$, $CH_2C_6H_5$, $CH_2CH(CH_3)_2$, and $CH(CH_3)CH_2CH_3$; or R_1 and R_2 together are a cycloalkyl;

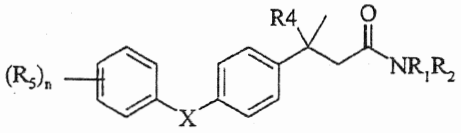
R_4 and R_5 are each independently an optionally substituted phenyl or optionally substituted heterocyclic aryl, wherein up to 5 substituents may be present and each substituent is independently selected from the group consisting of halogen, alkoxy, thioalkyl, sulfoxyalkyl, sulfonylalkyl, haloalkyl, haloalkoxy, CH_2OH, $CONH_2$, CN, acetoxy, $N(alkyl)_2$, NO_2, acetyl, and OCH_2COOH; and

Y is either nothing or methylene.

3. A CNS-active compound having one of the Formulas 1-9:



Formula 1



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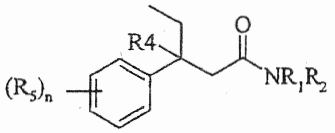
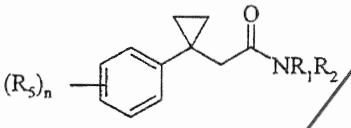


Formula 3



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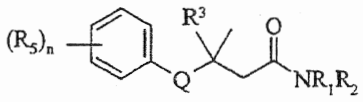
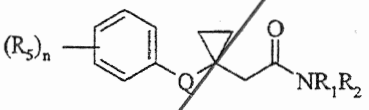
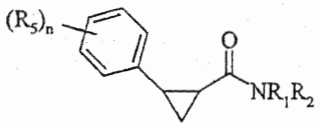


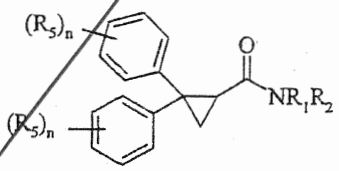
Formula 5



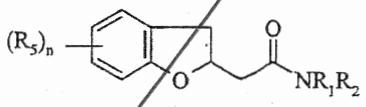
Formula 6



Formula 7



Formula 8



Formula 9

wherein R_1 is one of H, CH_3, C_2H_5, $(CH_2)_2SO_3H$, or CHZCOOH;

Z is one of H, CH_3, $CH(CH_3)_2$, $CH_2C_6H_5$, $CH_2CH(CH_3)_2$, or $CH(CH_3)CH_2CH_3$;

R_2 and R_3 are independently one of H or CH_3;

R_4 is one of H, CH_3, OH, or OCH_3;

R_5 is one of H, Cl, F, CF_3, CN, C1-C5 alkyl, C1-C5 alkoxy, OCF_3 or $CONR_1R_2$;

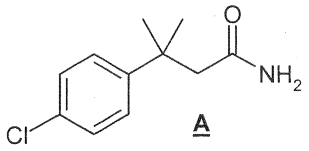
n = 1 - 5;

Q = O, NR_2, C=O, S, SO, or SO_2; and

X = O, NR_2, nothing, C=O, S, SO, or SO_2.

CLAIMS

41. A CNS-active compound having one of Formulas A-~~BA~~, B, D-O, R, S, T, or AW:



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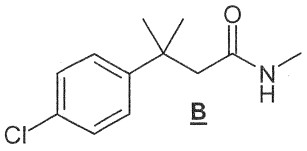

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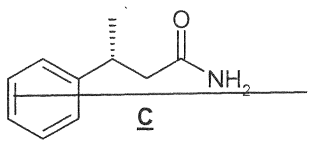

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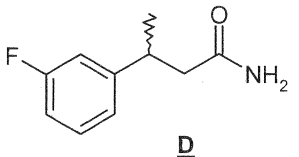

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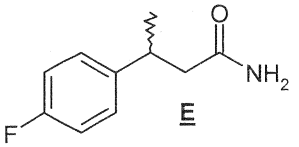

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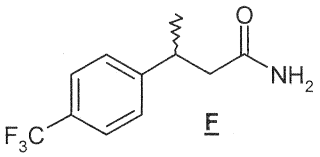

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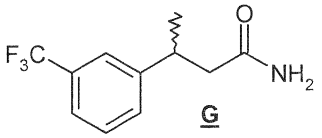

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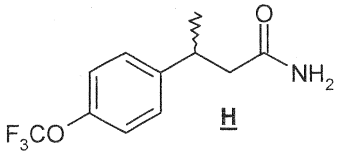

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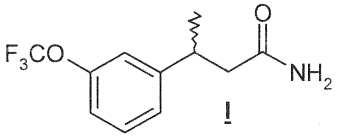

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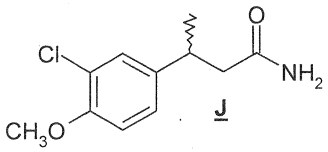

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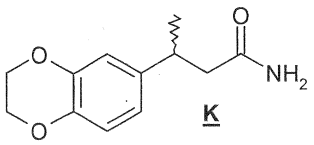

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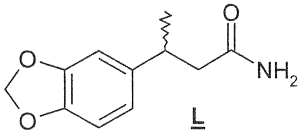

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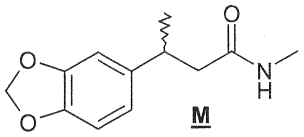

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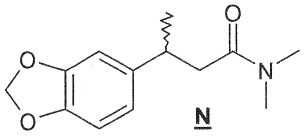

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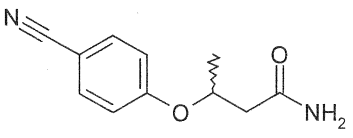

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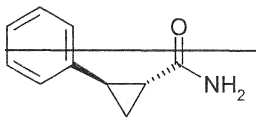

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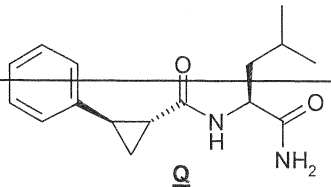
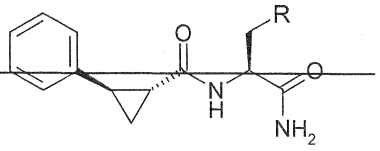
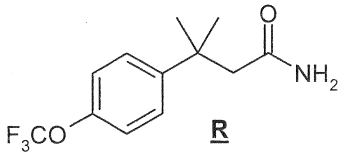


Q



Q-1, R = CH_3
Q-2, R = H



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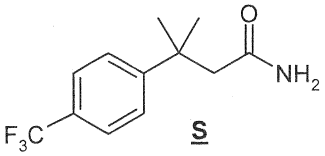

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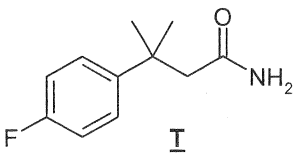

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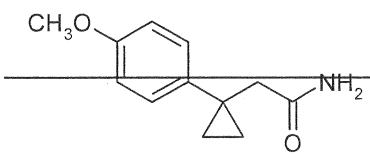

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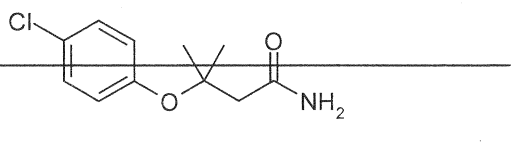

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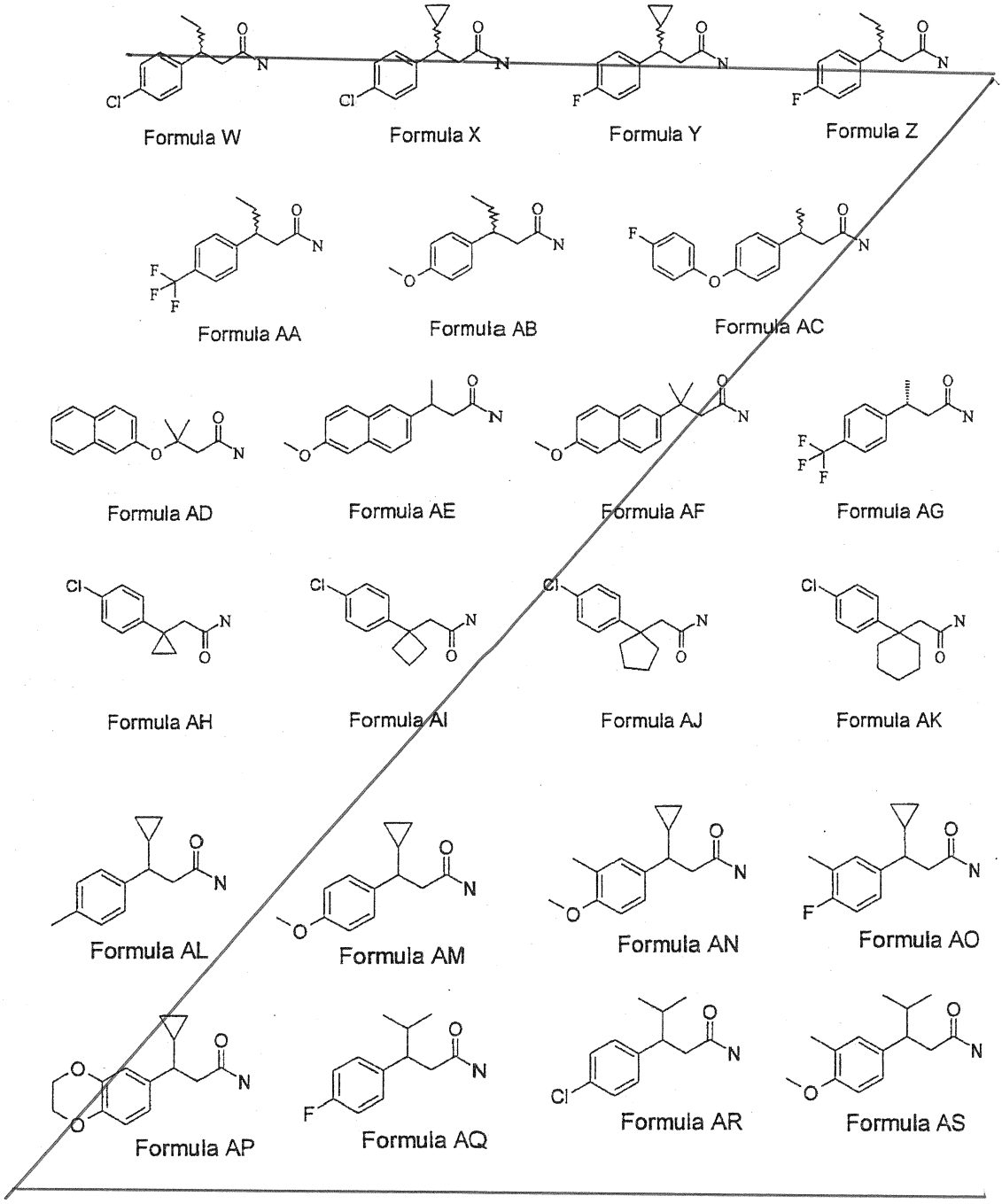
Formula W
Formula X
Formula Y
Formula Z
Formula AA
Formula AB
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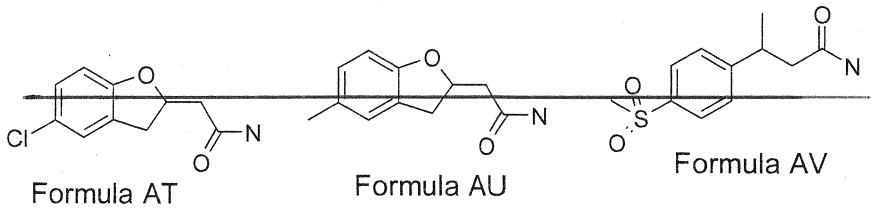
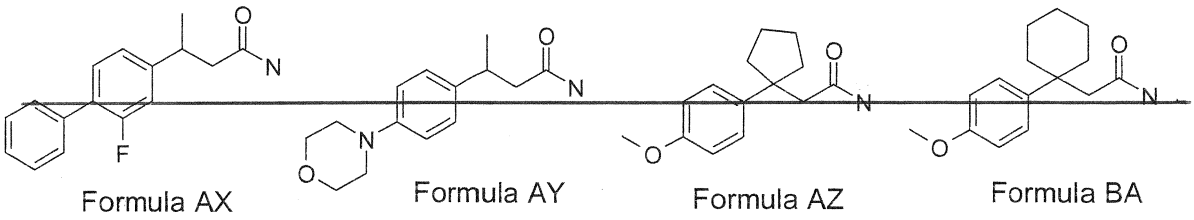
Formula AS





52. A pharmaceutical composition ~~for modulating CNS activity~~, the composition comprising:

a pharmaceutically-acceptable carrier; and

a CNS-active compound of ~~one of claims 1-4~~claim 1 combined with the carrier.

63. A pharmaceutical composition as in claim ~~5~~2, further comprising an excipient.

74. A pharmaceutical composition as in claim ~~5~~2, wherein the CNS-active compound is present in a therapeutically effective amount ~~to modulate CNS activity~~.

85. A pharmaceutical composition as in claim ~~7~~4, wherein the therapeutically effective amount is sufficient for at least one of the following:

to provide anticonvulsant activity to a subject;

to treat and/or prevent convulsions in a subject;

to treat and/or prevent seizures in a subject;

to treat and/or prevent spasticity in a subject;

to treat and/or prevent affective mood disorders in a subject;

to treat and/or prevent bipolar mood disorder in a subject;

to treat and/or prevent chronic headaches in a subject;

to treat and/or prevent cluster headaches in a subject;

to treat and/or prevent migraine headaches in a subject;

to treat and/or prevent restlessness syndromes in a subject;

to treat and/or prevent neuropathic pain in a subject; or

to treat and/or prevent movement disorders in a subject.

96. The Uuse of a CNS-active compound of one of claims 1-4claim 1 forin the manufacture of a medicament for modulating CNS activitythe treatment of central nervous system diseases and disorders.

107. The use as in claim 96, wherein the CNS-active compound is combined with a pharmaceutically-acceptable carrier.

118. The use as in claim 96, wherein the CNS-active compound is to be administered to the subject in a therapeutically effective amount to modulate CNS activity in the subject.

129. The use as in claim 118, wherein the therapeutically effective amount is sufficient for at least one of the following:

to provide anticonvulsant activity to a subject;

to treat and/or prevent convulsions in a subject;

to treat and/or prevent seizures in a subject;

to treat and/or prevent spasticity in a subject;

to treat and/or prevent affective mood disorders in a subject;

to treat and/or prevent bipolar mood disorder in a subject;

to treat and/or prevent chronic headaches in a subject;

to treat and/or prevent cluster headaches in a subject;

to treat and/or prevent migraine headaches in a subject;

to treat and/or prevent restlessness syndromes in a subject;

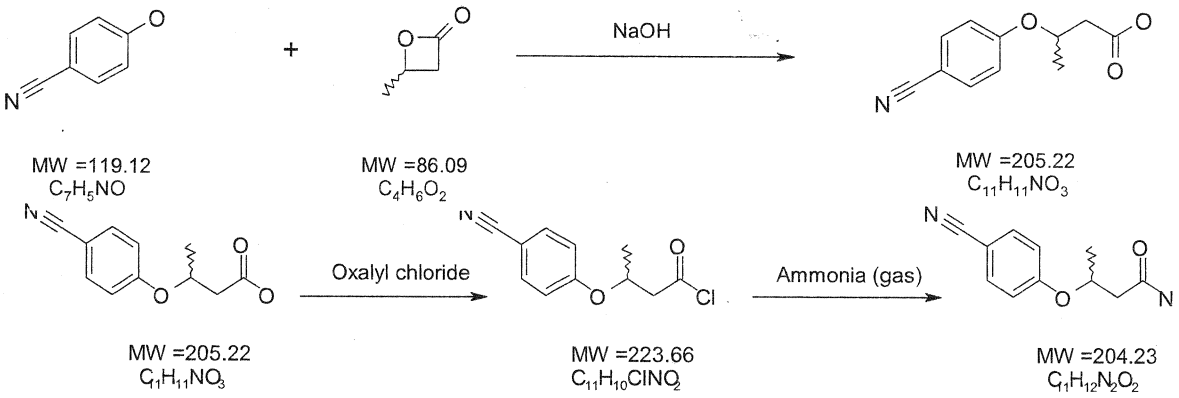
to treat and/or prevent neuropathic pain in a subject: or

to treat and/or prevent movement disorders in a subject.

~~13~~10. The use as in claim ~~11~~8, wherein the therapeutically effective amount is sufficient to treat and/or prevent the symptoms of at least one of anxiety, depression, insomnia, migraine headaches, schizophrenia, Parkinson's disease, spasticity, Alzheimer's disease, bipolar disorder, chronic or neuropathic pain, stroke, chronic neurodegenerative diseases, Huntington's disease, traumatic brain injury, spinal cord injury, or *status epilepticus*.

~~14~~11. The use as in claim ~~11~~8, wherein the therapeutically effective amount is sufficient for a chemical countermeasure.

~~15~~12. A method of manufacturing a CNS-active compound [3-(4-cyanophenoxy)butyramide], the method comprising:



~~16~~13. A method as in claim ~~15~~12, further comprising:

heating 4-cyanophenol in a basic solution at reflux;

adding β-butyrolactone to the refluxing solution;

cooling the solution to room temperature;

preparing a biphasic mixture of the solution by adding water and diethyl ether;

removing a diethyl ether layer after formation;

acidifying the aqueous layer after formation by adding a HCl solution at about *p*H ~2;

extracting the acidified aqueous layer with ethyl acetate;

drying the ethyl acetate layer to yield 3-(4-cyanophenoxy)butyric acid];

preparing a solution of 3-(4-cyanophenoxy)butyric acid in an organic solvent;

treating the solution with oxalyl chloride to obtain [3-(4-cyanophenoxy)butyryl chloride];

bubbling ammonia gas through the solution of 3-(4-cyanophenoxy)butyryl chloride; and

obtaining [3-(4-cyanophenoxy)butyramide] from the solution.