

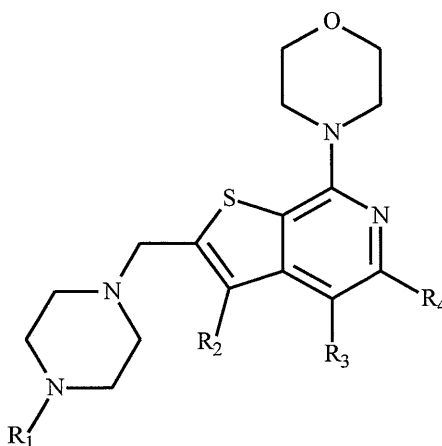
Another objective of the present invention is to provide a series of novel substituted 7-(morpholinyl)-2-(N-piperazinyl)-methylthieno[2,3-c] pyridines of general formula I defined above and their pharmaceutically acceptable salts which are potent and selective PI3 kinase inhibitors and are therefore beneficial in the treatment and prevention of various human ailments such as cancer.

Yet another objective of the present invention is to provide a novel series of substituted 7-(morpholinyl)-2-(N-piperazinyl)-methylthieno [2,3-c]pyridines of general formula I defined above and their pharmaceutically acceptable salts having excellent in-vivo activity against solid tumors such as lung, pancreatic etc.

Another objective of the present invention is to provide a process for the preparation of a series of novel substituted 7-(morpholinyl)-2-(N-piperazinyl)-methylthieno [2, 3-c] pyridines of general formula I defined above and their pharmaceutically acceptable salts.

Summary

In one aspect of the present disclosure, there is provided a 7-(Morpholinyl)-2-(N-piperazinyl)methyl thieno[2, 3-c]pyridine compound of Formula-I or a pharmaceutically acceptable salt thereof,



Formula-I

wherein:

R₁ is H, C₁–C₆ alkyl, C₃–C₆ cycloalkyl, -C(O)R₅, -S(O)₂R₅, -C(O)₂R₅, C₁–C₆ alkyl substituted with R₆, C₃–C₆ cycloalkyl substituted with R₆, aryl, aryl substituted with R₆ or heteroaryl substituted with R₆;

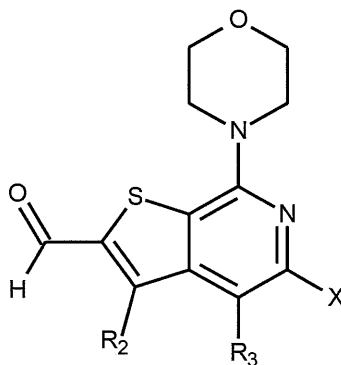
5 R₂, R₃ and R₄ are each independently H, -OH, -SH, halo, amino, cyano, -nitro, C₁–C₆ alkyl, C₃–C₆ cycloalkyl, aryl, -C(O)R₅, -S(O)₂R₅, -C(O)₂R₅, -C=C(H)-R₆, aminocarbonyl substituted with R₆, alkylamino group substituted with R₆ and optionally containing C₃–C₆ cycloalkyl, -alkylaminocarbonyl, heteroaryl optionally substituted with H or amino, fused bicyclic or tricyclic heteroaryl containing 1, 2 or 3 heteroatoms
10 selected from N, O and S, or aryl optionally substituted with hydroxyl, hydroxylalkyl, amino, aminoalkyl, aminocarbonyl, cyano, halogen, aryloxy or R₆;

R₅ is H, alkyl, amino, aryl substituted with R₆, heteroaryl substituted with R₆, fused heteroaryl substituted with R₆ or -trifluoromethyl;

R₆ is H, hydroxy, halogen, cyano, nitro, amino or C₁–C₆ alkyl.

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In another aspect of the present disclosure, there is provided a compound of Formula-III,



Formula-III

wherein:

20 R₂ and R₃ are each independently H, -OH, -SH, halo, amino, cyano, -nitro, C₁–C₆ alkyl, C₃–C₆ cycloalkyl, aryl, -C(O)R₅, -S(O)₂R₅, -C(O)₂R₅, -C=C(H)-R₆, aminocarbonyl substituted with R₆, alkylamino group substituted with R₆ and optionally containing C₃–C₆ cycloalkyl, -alkylaminocarbonyl, heteroaryl optionally substituted with H or amino,

fused bicyclic or tricyclic heteroaryl containing 1, 2 or 3 heteroatoms selected from N, O and S, or aryl optionally substituted with hydroxyl, hydroxylalkyl, amino, aminoalkyl, aminocarbonyl, cyano, halogen, aryloxy or R₆; and X is a halogen.

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In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

- (a) a therapeutically effective amount of a compound as defined herein or pharmaceutically acceptable salt thereof; and
- 10 (b) a pharmaceutically acceptable carrier, diluent or vehicle.

In another aspect of the present disclosure, there is provided a use of a compound as defined herein or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of cancer.

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Detailed description of the invention

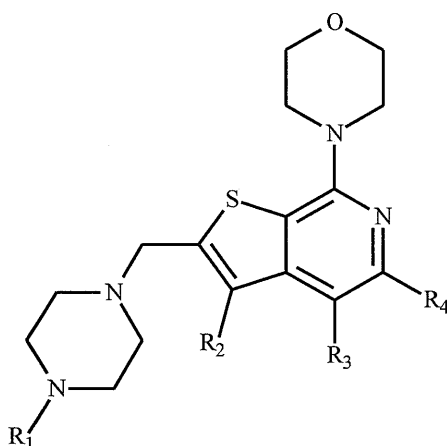
The compounds in accordance with the present invention, being potent and selective PI3 kinase inhibitors are therefore beneficial in the treatment and prevention of various human ailments such as cancer.

- 20 The present invention relates to compounds of formula-I and pharmaceutically acceptable salts thereof, may be prepared by any process known to be applicable to the chemically related compounds.

The invention relates to novel substituted 7-(morpholinyl)-2-(N-piperazinyl) methyl thieno [2, 3-c] pyridines of the formula-I,

CLAIMS

1. A 7-(Morpholinyl)-2-(*N*-piperazinyl)methyl thieno[2, 3-*c*]pyridine compound of Formula-I or a pharmaceutically acceptable salt thereof,



Formula-I

wherein:

R_1 is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, $-C(O)R_5$, $-S(O)_2R_5$, $-C(O)_2R_5$,

C_1-C_6 alkyl substituted with R_6 , C_3-C_6 cycloalkyl substituted with R_6 , aryl, aryl substituted with R_6 or heteroaryl substituted with R_6 ;

R_2 , R_3 and R_4 are each independently H, $-OH$, $-SH$, halo, amino, cyano, $-nitro$, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, aryl, $-C(O)R_5$, $-S(O)_2R_5$, $-C(O)_2R_5$, $-C=C(H)-R_6$, aminocarbonyl substituted with R_6 , alkylamino group substituted with R_6 and optionally containing C_3-C_6 cycloalkyl, $-alkylaminocarbonyl$, heteroaryl optionally substituted with H or amino, fused bicyclic or tricyclic heteroaryl containing 1, 2 or 3 heteroatoms selected from N, O and S, or aryl optionally substituted with hydroxyl, hydroxylalkyl, amino, aminoalkyl, aminocarbonyl, cyano, halogen, aryloxy or R_6 ;

R_5 is H, alkyl, amino, aryl substituted with R_6 , heteroaryl substituted with R_6 , fused heteroaryl substituted with R_6 or $-trifluoromethyl$;

R_6 is H, hydroxy, halogen, cyano, nitro, amino or C_1-C_6 alkyl.

2. A compound according to claim 1 or a pharmaceutically acceptable salt thereof, which compound is:

i) 5-[3-methyl-2-[(4-methyl sulfonyl)piperazin-1-yl) methyl]-7-morpholino-thieno[2,3-c]pyridin-5-yl]pyrimidin-2-amine;

5 ii) 5-[2-[(4-methylsulfonyl piperazin-1-yl)methyl]-7-morpholino-thieno[2,3-c]pyridin-5-yl]pyrimidin-2-amine;

iii) 4-[5-(1H-indazol-4-yl)-2-[(4-methylsulfonyl piperazin-1-yl) methyl] thieno [2, 3-c] pyridin-7-yl] morpholine;

10 iv) [3-[2-[(4-methylsulfonyl piperazin-1-yl)methyl] -7-morpholino-thieno[2,3-c]pyridin-5-yl]phenyl] methanol;

v) 3-[2-[(4-methylsulfonyl piperazin-1-yl)methyl]-7-morpholino-thieno[2,3-c]pyridin-5-yl]aniline;

vi) 4-[5-(1H-indazol-4-yl)-3-methyl-2-[(4-methyl sulfonyl piperazin-1-yl) methyl]thieno [2,3-c] pyridin-7-yl]morpholine;

15 vii) [3-[3-methyl-2-[(4-methyl sulfonyl)piperazin-1-yl) methyl]-7-morpholino-thieno[2,3-c]pyridin-5-yl]phenyl]methanol;

viii) 3-[3-methyl-2-[(4-methyl sulfonyl)piperazin-1-yl) methyl]-7-morpholino-thieno[2,3-c]pyridin-5-yl]aniline;

20 ix) 5-[3-methyl-2-[(4-methylsulfonyl)piperazin-1-yl)methyl]-7-morpholino-4-nitro-thieno[2,3-c]pyridin-5-yl]pyrimidin-2-amine;

x) 5-(2-amino-pyrimidin-5-yl)-3-methyl-2-[(4-methylsulfonyl piperazin-1-yl)methyl]-7-morpholino-thieno[2,3-c]pyridin-4-amine;

xi) 5-[3-methyl-2-[(4-methylsulfonyl)piperazin-1-yl)methyl]-7-morpholino-4-nitro-thieno[2,3-c]pyridin-5-yl]pyrimidin-2,4-diamine; or

25 xii) 5-[4-amino-3-methyl-2-[(4-methylsulfonyl)piperazin-1-yl)methyl]-7-morpholino-thieno[2,3-c]pyridin-5-yl]pyrimidine-2,4-diamine.

R₂ and R₃ are each independently H, -OH, -SH, halo, amino, cyano, -nitro, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, -C(O)R₅, -S(O)₂R₅, -C(O)₂R₅, -C=C(H)-R₆, aminocarbonyl substituted with R₆, alkylamino group substituted with R₆ and optionally containing C₃-C₆ cycloalkyl, -alkylaminocarbonyl, heteroaryl optionally substituted with H or amino, fused bicyclic or tricyclic heteroaryl containing 1, 2 or 3 heteroatoms selected from N, O and S, or aryl optionally substituted with hydroxyl, hydroxylalkyl, amino, aminoalkyl, aminocarbonyl, cyano, halogen, aryloxy or R₆;

and X is a halogen.

10 6. A compound according to claim 5, which compound is:

- i) 5-bromo-3-methyl-7-morpholino-4-nitro-thieno[2,3-c]pyridine-2-carbaldehyde;
- ii) 5-bromo-3-methyl-7-morpholino-thieno[2,3-c]pyridine-2-carbaldehyde; or
- iii) 5-bromo-7-morpholino-thieno [2, 3-c] pyridine-2-carbaldehyde.

15 7. A pharmaceutical composition comprising:

- (a) a therapeutically effective amount of a compound as defined in claim 1 or claim 2 or pharmaceutically acceptable salt thereof; and
- (b) a pharmaceutically acceptable carrier, diluent or vehicle.

20 8. Use of a compound as defined in claim 1 or claim 2 or a pharmaceutically acceptable salt therefore for the manufacture of a medicament for the treatment of cancer.

9. The use according to claim 8, wherein the cancer is lung cancer, pancreatic cancer, prostate cancer, breast cancer or brain cancer.

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10. The use according to claim 8 or claim 9 wherein an effective anticancer amount of the compound or pharmaceutically acceptable salt thereof is to be administered orally, parenterally or rectally to a human.