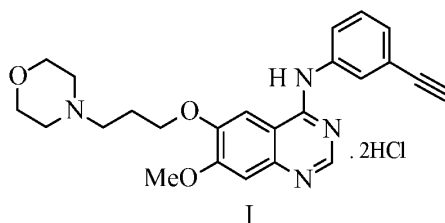
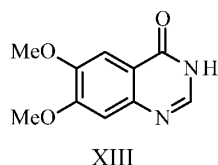


We Claim:

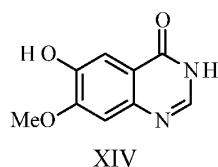
1. A process for the preparation of N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine dihydrochloride of formula-I comprising the steps of :



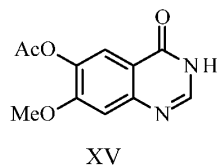
- i) selective demethylation of 6,7-dimethoxy-quinazoline-4(3H)-one of formula-XIII



- using de-methylating agent to get 6-hydroxy-7-methoxy-quinazoline-4(3H)-one of formula-XIV,

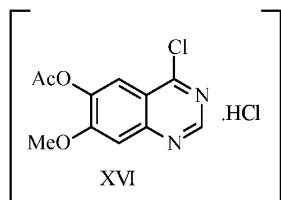


- ii) protecting 6-hydroxy-7-methoxy-quinazoline-4(3H)-one of formula-XIV using acylating agent to get 6-acetoxy-7-methoxy-quinazoline-4(3H)-one of formula-XV,

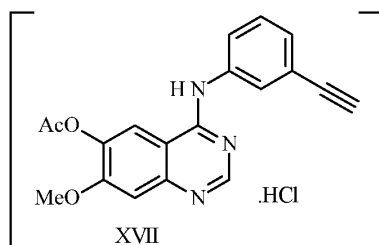


- iii) chlorination of 6-acetoxy-7-methoxy-quinazoline-4(3H)-one of formula-XV with chlorinating agent in the presence of catalyst in an organic solvent to get (4-

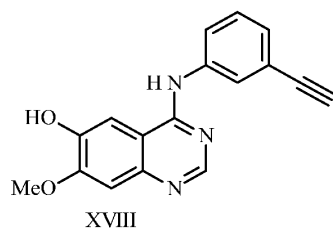
chloro-7-methoxy-quinazolin-6-yl) acetate hydrochloride of compound of formula-XVI,



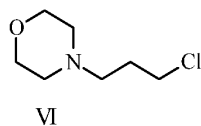
which is reacted in-situ with 3-ethynylaniline of formula-III in alcoholic solvent medium to get [4-(3-ethynylanilino)-7-methoxy-quinazolin-6-yl] acetate hydrochloride of formula-XVII,



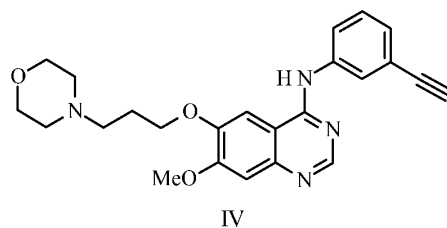
which is further subjected to de-protection of acetoxymethyl moiety using aqueous alcoholic medium to get 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII,



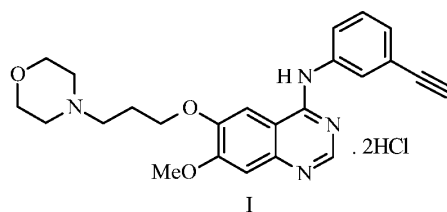
iv) condensing 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII with 3-morpholinopropyl chloride of formula-VI,



in dimethylformamide-potassium carbonate medium to get N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine of formula-IV,



- v) converting N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine of formula-IV to dihydrochloride salt of formula-I using hydrochloric acid gas dissolved in organic solvent medium,



- v) optionally purification of N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine dihydrochloride of formula-I from alcoholic solvent or organic solvent mixture.

2. A process according to claim 1, wherein, in step (i),
 - (a) de-methylating agent employed can be selected from DL-Methionine-sulfuric acid mixture, aqueous hydrobromic acid or pyridine hydrochloride medium
 - (b) the temperatures at which de-methylation performed can be from 25-100°C,
 - (c) base employed can be selected from aqueous ammonia, aqueous sodium hydroxide, aqueous potassium hydroxide or any other equivalent inorganic base
3. A process according to claim 1, wherein step (ii),
 - (a) The acylating agent can be selected from acetic anhydride, acetyl chloride,
 - (b) organic solvent employed in step (ii) is selected from methylene chloride or chloroform medium,

- (c) the temperature at which the acylation in step (ii) can be performed is in the range of 0-150°C,
 - (d) optionally in step (ii) 6-acetoxy-7-methoxy-quinazoline-4(3H)-one of formula-XV can be obtained by crystallization from dimethylformamide.
4. A process according to claim 1, wherein step (iii),
- (a) chlorination of 6-acetoxy-7-methoxy-quinazoline-4(3H)-one of formula-XV is performed with chlorinating agent selected from oxalyl chloride, phosphorous oxychloride, thionyl chloride,
 - (b) the catalyst used in chlorination of 6-acetoxy-7-methoxy-quinazoline-4(3H)-one of formula-XV in step (iii) is selected from dimethylformamide or pyridine,
 - (c) the solvent employed in chlorination of 6-acetoxy-7-methoxy-quinazoline-4(3H)-one of formula-XV in step (iii) is selected from methylene chloride or chloroform
 - (d) the base employed in step (iii) during work-up is selected from sodium bicarbonate, potassium bicarbonate, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate,
 - (e) in step (iii) of the present invention, the wet product of (4-chloro-7-methoxy-quinazolin-6-yl) acetate hydrochloride of compound of formula-XVI is condensed further with 3-ethynylaniline of formula-III in isopropyl alcohol medium to get [4-(3-ethynylanilino)-7-methoxy-quinazolin-6-yl] acetate hydrochloride of formula-XVII,
 - (f) The temperature at which the condensation is performed in step (iii) is at room temperature or at reflux temperature,
 - (g) de-protection of the resulting compound of [4-(3-ethynylanilino)-7-methoxy-quinazolin-6-yl] acetate hydrochloride of formula-XVII is performed with aqueous base solution wherein the base is selected from potassium hydroxide or sodium hydroxide,

- (h) the organic solvent employed in de-protection of [4-(3-ethynylanilino)-7-methoxy-quinazolin-6-yl] acetate hydrochloride of formula-XVII is selected from methanol or isopropyl alcohol,
 - (i) the temperature at which de-protection is carried out is in the range of 25-70°C preferably at 40-50°C,
5. A process according to claim 1, wherein step (iv),
- (a) the base employed in the condensation step of 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII with 3-morpholinopropyl chloride of formula-VI is potassium carbonate,
 - (b) the solvent employed in condensation of 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII with 3-morpholinopropyl chloride of formula-VI is dimethylformamide,
 - (c) the temperature at which condensation of 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII with 3-morpholinopropyl chloride of formula-VI performed is in the range of 20-100°C preferably at 60-70°C,
 - (d) purification the resulting N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine of formula-IV by crystallization is selected from an organic solvent or organic solvent mixture selected from methanol, ethanol, isopropyl alcohol, cyclohexane, toluene, n-heptane, methyl t-butyl ether, isopropyl ether or its mixture.
6. A process according to claim 1, wherein, in step (v),
- (a) N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholino propoxy)quinazolin-4-amine of formula-IV is optionally converted to N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy) quinazolin-4-amine dihydrochloride of formula-I using hydrochloric acid, dry hydrochloric acid gas dissolved in methanol, ethanol or isopropyl alcohol, acetone, ethylacetate,
 - (b) the organic solvent employed for hydrochloride salt formation is selected from methanol, ethanol or isopropyl alcohol,

(c) The isolated product of N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy) quinazolin-4-amine dihydrochloride of formula-I having following physical and crystal characteristics

(i) FT-IR (λ , cm⁻¹): 3406 (N-H str); 3063, 3000 (Aromatic -C-H str); 2943, 2838 (Aliphatic -C-H str); 2623 (br, due to HCl salt); 2100 (-C $\equiv$ C- str); 1633 (-C=N- str); 1438 (N-H bending); 1282 (-C-N str); 1219, 1159, 1002 (-C-O str)

(ii) ¹HNMR (DMSO-d₆; 400 MHz, δ ppm): 2.33-2.35 (m, 2H); 3.12 (br, m, 2H); 3.29-3.34 (br, m, 2H); 3.48-3.51 (br, m, 2H); 3.80-3.85 (m, 2H); 3.96-4.0 (m, 5H); 4.28 (s, 1H), 4.38-4.41 (t, 2H); 7.39-7.41 (m, 2H); 7.47-7.51 (t, 1H); 7.83-7.85 (d, 1H); 7.92 (m, 1H); 8.61 (m, 1H); 8.86 (s, 1H); 11.04 (s, 1H), 11.72 & 15.40 (br, s, 2H)

(iii) ¹³CNMR (DMSO-d₆; 100 MHz; δ ppm): 22.72, 15.10, 53.48, 56.49, 63.17, 67.28, 81.21, 82.94, 99.95, 105.64, 107.35, 121.90, 125.28, 127.54, 129.00, 129.17, 135.85, 137.33, 148.73, 148.93, 156.32, 158.13

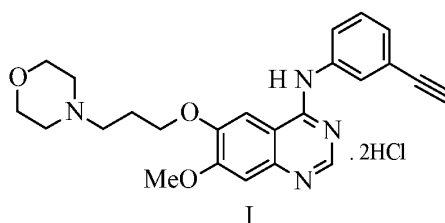
(iv) DSC: Peak observed at 279.55°C

(v) PXRD (2 θ , °): 5.76, 6.76, 7.13, 7.64, 9.81, 12.62, 13.50, 13.97, 14.23, 15.27, 15.77, 17.22, 20.30, 20.60, 21.44, 22.42, 22.95, 24.81, 25.82, 27.37, 28.10, 28.53, 29.60, 30.75, 32.42, 34.15 ($\pm 0.2^\circ$)

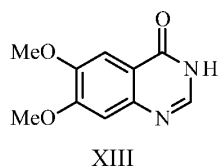
7. A process according to claim 1, wherein, in step (vi),

(a) N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy) quinazolin-4-amine dihydrochloride of formula-I can be purified by crystallization from an organic solvent or organic solvent mixture selected from methanol, ethanol, isopropyl alcohol, cyclohexane, toluene, n-heptane, methyl t-butyl ether, isopropyl ether or its mixture .

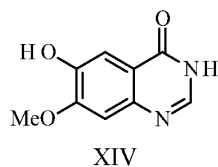
8. A process for the preparation of N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine dihydrochloride of formula-I comprising the steps of :



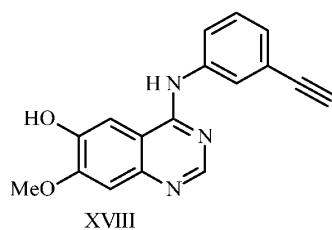
- i) selective demethylation of 6,7-dimethoxy-quinazoline-4(3H)-one of formula-XIII



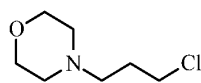
using de-methylating agent to get 6-hydroxy-7-methoxy-quinazoline-4(3H)-one of formula-XIV,



- ii) converting 6-hydroxy-7-methoxy-quinazoline-4(3H)-one of formula-XIV to 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII,

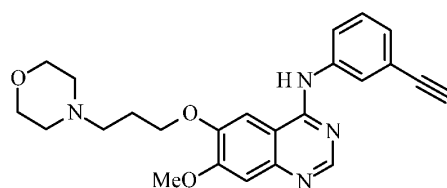


- iii) condensing 4-(3-ethynylanilino)-7-methoxy-quinazolin-6-ol of formula-XVIII with 3-morpholinopropyl chloride of formula-VI,



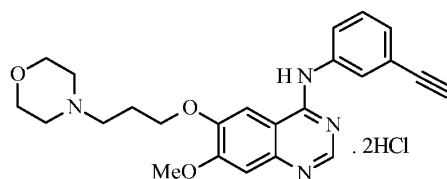
VI

in dimethylformamide-potassium carbonate medium to get N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine of formula-IV,



IV

iv) converting N-(3-ethynylphenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine of formula-IV to dihydrochloride salt of formula-I using hydrochloric acid gas dissolved in organic solvent medium.



I

9. A process according to claim 8, wherein de-methylating agent employed can be selected from DL-Methionine-sulfuric acid mixture, aqueous hydrobromic acid or pyridine hydrochloride medium.