3. RESULTS AND DISCUSSIONS

The work carried out towards achieving the proposed plan has been discussed under the following heads:

3.1 Chemical work

3.2 Biological work

3.1 Chemical work

To synthesize the targeted compounds, different synthetic plans have been used. For the purpose of clarity and convenience the chemical work has been discussed under the following subheads:

A. Synthesis of starting materials and intermediates

B. Synthesis of 2-amino-4-chloroalkoxy-5-methoxybenzamides **(40, 41)**

C. Synthesis of 7-(3-substituted aminopropoxy) derivatives of quinazolinones **(54a-59g)**

D. Synthesis of 7-(3-substituted aminoethoxy) derivatives of quinazolinones **(68a-71g)**

E. Synthesis of 4-anilinoquinazoline derivatives **(83a-88c)**

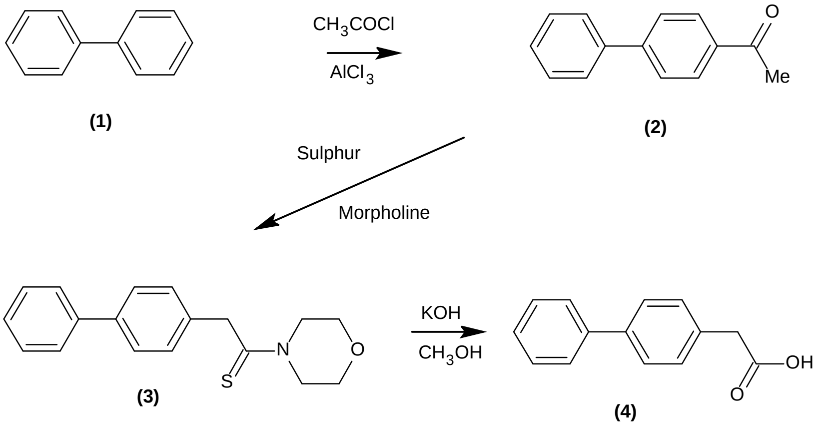
A. Synthesis of starting materials and intermediates

Majority of the stating materials and intermediates used in the synthesis of the targeted compounds were procured from the commercial sources except for a few which could not be procured commercially due to their non-availability or high cost. Such starting materials or intermediates were synthesized in the laboratory by the reported methods. Their syntheses were achieved as discussed below.

A.1 Synthesis of biphenylacetic acid (4)

Biphenylacetic acid was prepared by the reported method as per **Scheme-I**. Biphenyl **(1)** was acetylated by acetyl choride in presence of anhydrous aluminium chloride to obtain the acetylated product **(2)**.

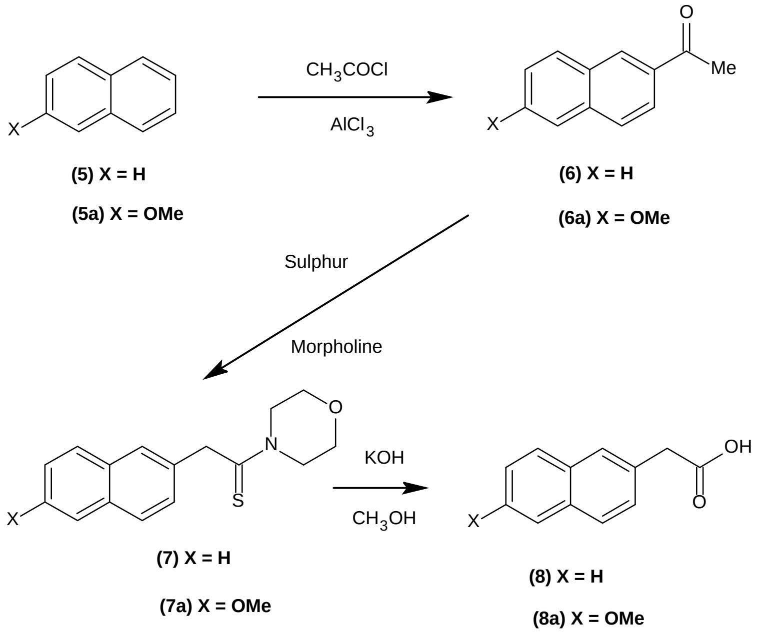
Using Kindler modified Willgerodt synthesis the acetylated product was converted into thiomorpholide **(3)** which was isolated but not characterized. The thiomorpholide **(3)** on basic hydrolysis offered the desired biphenylacetic acid **(4)**.



Scheme-I

A.2 Synthesis of 2-naphthylacetic acid (8)

Naphthalene **(5)** was acetylated by the reported method to obtain 2-acetylnaphthalene **(6)** which was converted into the desired thiomorpholide **(7)** and 2-naphthylacetic acid **(8)** as per the reported procedurer **(Scheme-II)**.



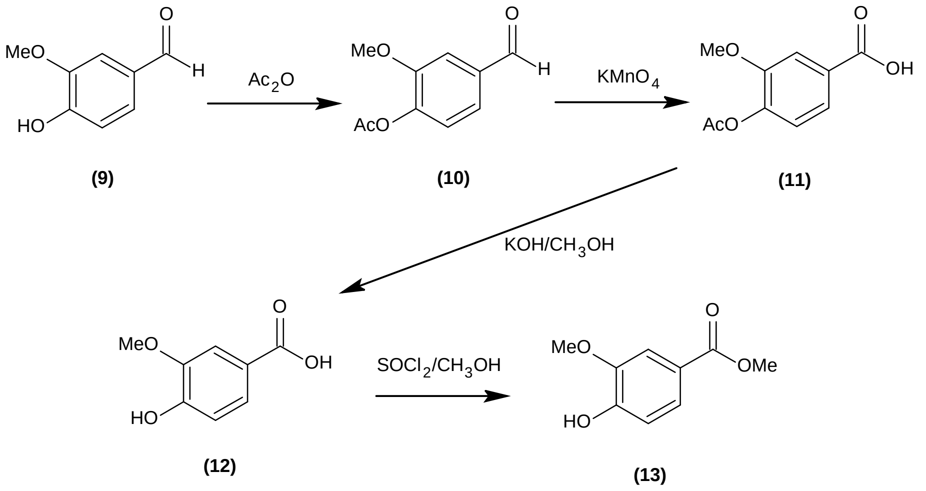
Scheme-II

A.3 Synthesis of 6-methoxy-2-naphthylacetic acid (8a)

Adopting the reported method, neroline **(5a)** was converted into the desired product **(8a)** as per **Scheme-II**

A.4 Synthesis of methyl 4-hydroxy-3-methoxybenzoate (13)

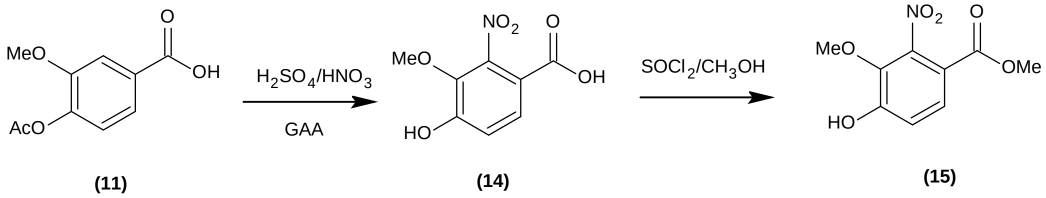
Vanillin **(9)** was acetylated by acetic anhydride-pyridine system to yield the acetylated product **(10)**. The acetylated product **(10)** was oxidized by potassium permanganate to obtain benzoic acid derivative **(11)** which was deacetylated and methylated as per **Scheme-III** to obtain the desired benzoate ester **(13)**. Acetylvanillin **(10)** showed strong peaks in its IR spectrum at 1755 (C=O str. of acetoxy) and 1669 cm^{-1} (C=O str. of aldehyde). The IR spectrum of benzoic acid derivative **(11)** showed characteristic broad band in between 3400- 3000 cm^{-1} (OH str. of acid) and sharp peaks were observed at 1763 (C=O str. of acetoxy) and 1689 cm^{-1} (C=O str. of acid). Compound **(12)** was characterized by the presence of strong peak at 1682 cm^{-1} (C=O str. of acid) and absence of acetoxy C=O str. in its IR spectrum. Benzoate ester **(13)** showed a strong peak in its IR spectrum at 1690 cm^{-1}.



Scheme-III

A.5 Synthesis of methyl 4-hydroxy-3-methoxy-2-nitrobenzoate (15)

Nitration of 4-acetoxy-3-methoxybenzoic acid **(11)** with cold mixture of nitric acid and sulphuric acid (3:2) afforded the nitro derivative **(14)**. It exhibited characteristic IR peaks at 1554 (N=O asym.) & 1377 cm^{-1} (N=O sym.).

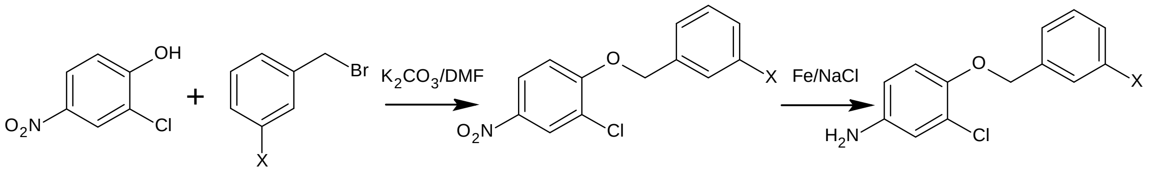


Scheme-IV

Methylation of acid group in compound **(14)** was achieved using thionyl chloride and methanol **(Scheme IV)** to yield compound **(15)**. It showed characteristic ester (C=O) peak at 1685 cm^{-1} in its IR spectrum along with the normal nitro group peaks at 1556 and 1381 cm^{-1}.

A.6 Synthesis of 4-arylmethoxy-3-chloroaniline (21, 22)

2-Chloro-4-nitrophenol (16) was reacted with the desired benzyl bromide **(17, 18)** under mild basic conditions to obtain the desired ethers **(19, 20)**. Reduction of the nitro group in compounds **(19, 20)** was achieved under mild conditions using iron powder and sodium chloride to offer the aniline derivatives **(21, 22)**. The nitro derivatives **(19, 20)** showed characteristic peaks at 1516 & 1342 and 1543 & 1343 cm^{-1} respectively for the nitro group. Both the peaks were missing in the aniline derivatives **(21, 22)** and new peaks for the amino group appeared around 3400 cm^{-1} in their IR spectra.



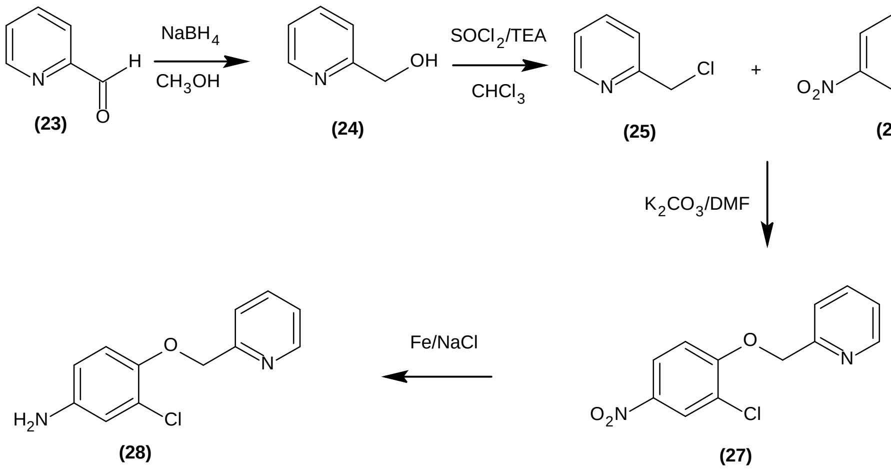
(16) **(17)** X=H **(19)** X=H **(21)** X=H

(18) X=F **(20)** X=F **(22)** X=F

Scheme-V

A.7 Synthesis of 3-chloro-4-(2-pyridinyl)methoxyaniline (28)

Picolinaldehyde **(23)** on sodium borohydride reduction yielded the alcohol **(24)** which on thionyl chloride treatment offered the chloro derivative **(25)**. Reaction of the chloro derivative **(25)** with the phenol **(26)** under mild basic condition gave the ether **(27)**. The ether **(27)** showed typical nitro group stretchings at 1588 and 1354 cm^{-1} in its IR spectrum. Reduction of the nitro group with iron powder and sodium chloride in aq. methanol offered the aniline derivative **(28)** **(Scheme VI)** showing absence of strong nitro group peaks and presence of a band at 3394 cm^{-1} (NH str.) in its IR spectrum.

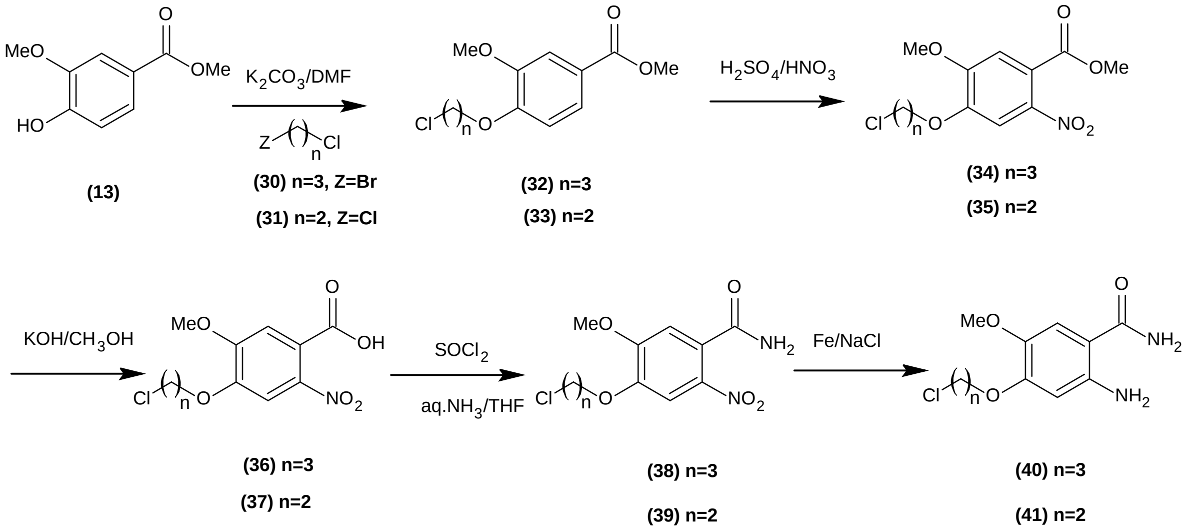


Scheme-VI

B. Synthesis of 2-amino-4-chloroalkoxy-5-methoxybenzamides (40, 41)

The targeted 2-aminobenzamides **(40, 41)** were prepared as per the given **Scheme-VII**. The 4-hydroxybenzoate **(13)** was treated with the dihaloalkane **(30, 31)** to obtain the respective ethers **(32, 33)** under mild basic condition.

The ethers **(32, 33)** showed the characteristic ester (C=O str.) bend at 1709 cm^{-1} and absence of hydroxyl (OH str.) in their IR spectra. Nitration of the ethers **(32, 33)** with a cold mixture of nitric and sulphuric acids (1:1) in acetic acid solution afforded the nitro derivatives **(34, 35)** in pure form. Compound **(34)** exhibited peaks at 1736 (C=O str. of ester), 1526 (N=O asym.) and 1339 cm^{-1} (N=O sym.), while compound **(35)** exhibited peaks at 1719 (C=O str. of ester), 1527 (N=O asym.) and 1361 cm^{-1} (N=O sym.) in their IR spectra.



Scheme-VII

Basic hydrolysis of the ester group in compounds **(34, 35)** was achieved using potassium hydroxide in aq, methanol to afford the respective acid derivatives **(36, 37)**. The acid derivative **(36)** showed peaks at 1707 (C=O str. of acid), 1526 (N=O asym.) and 1339 cm^{-1}(N=O sym.), while compound **(37)** showed peaks at 1700, 1531 (N=O asym.) and 1347 cm^{-1} (N=O sym.) and a new peak appeared around 3050 cm^{-1} (O-H srt. of acid) in their IR spectra.

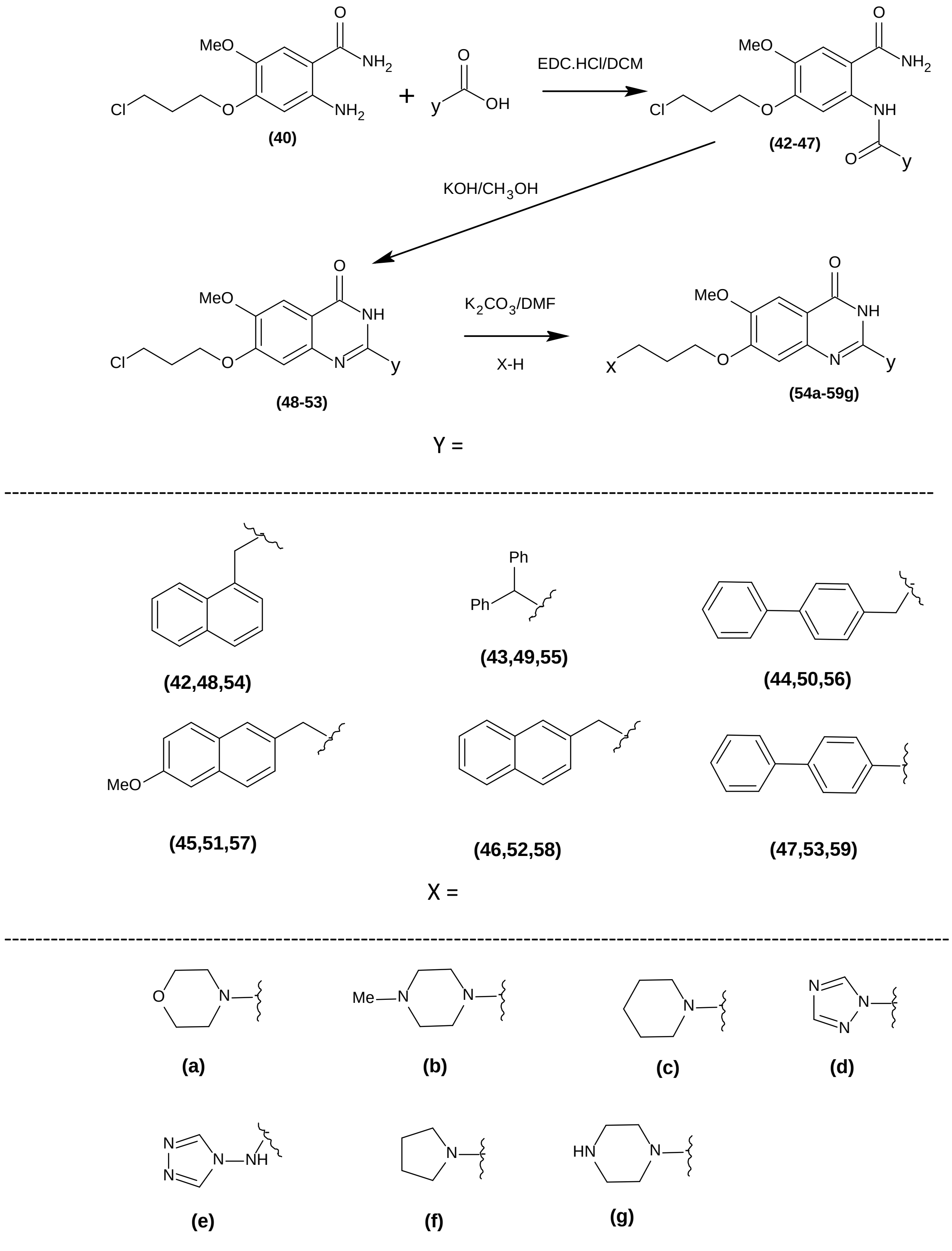
The acid derivatives **(36, 37)** were treated with thionyl chloride and ammonia to afford benzamide derivatives **(38, 39)**. Compound **(38)** showed peaks at 1671 (C=O str. amide-I), 1617 (N-H def., amide II), 1507 (N=O asym.) 1277 (N=O sym.) and 3437 cm^{-1} (N-H str.), while compound **(39)** showed peaks at 1675 (C=O str. amide-I), 1584 (sym., amide II), 1509 (N=O asym.) and 1275 cm^{-1} (N=O sym.) in their IR spectra.

Reduction of the nitro group in compounds **(38, 39)** was achieved under mild conditions using iron powder and sodium chloride in aq. methanol to afford the 2-aminobenzamide derivatives **(40, 41)**. The compound **(40)** showed characteristic peaks at 3371 (N-H str.), 1655 (C=O str., amide-I) and 1613 cm^{-1} (NH sym., amide II), while compound **(41)** exhibited characteristic peaks at 3423 (N-H str.), 1655 (C=O str., amide-I) and 1634 cm^{-1} (NH sym., amide II) in their IR spectra.

C. Synthesis of 7-(3-substituted aminopropoxy) derivatives of quinazolinones (54a-59g)

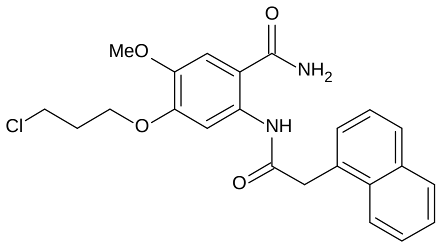
The quinazolinone derivatives **(54a-59g)** were prepared by adopting **Scheme (VIII)**. The anthranilamide derivative **(40)** was reacted with various acids under dehydrating conditions to offer the diamides **(42-47)**. The diamides **(42-47)** were cyclized under basic conditions to yield the quinazolinones **(48-53)**. The chloro group in compounds **(48-53)** was substituted by various amines **(X-H)** to obtain the targeted compounds.

The diamide **(42)** was obtained by coupling the anthranilamide **(40)** with 1-naphthylacetic acid. It showed IR bands at 3393 (N-H asym.), 1659 (C=O str., amide I) and 1616 cm^{-1} (NH band) characteristic for the amide. 2,2-Diphenylacetic acid offered the diamide **(43)** which showed characteristic peaks at 3352, 1669 and 1621 cm^{-1} in its IR spectrum.

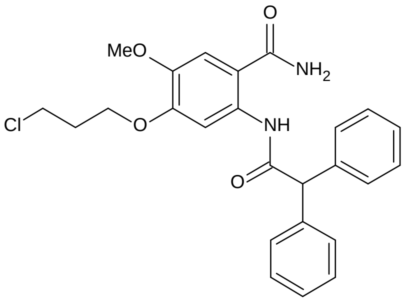


Scheme-VIII

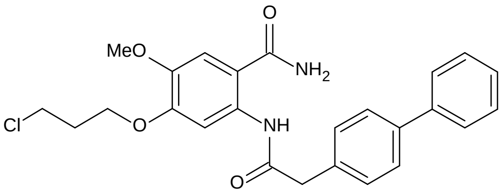
Compound **(44)** was obtained by coupling of the anthranilamide **(40)** with biphenylacetic acid while 2-(6-methoxy-2-naphthyl)acetic acid on coupling offered the diamide **(45)** under dehydrating conditions. Compound **(44)** displayed characteristic peaks at 3394 (N-H asym.), 1664 (C=O str., amide I) & 1622 cm^{-1} (NH sym., amide II) in its IR spectrum while characteristic peaks at 3389, 1653 and 1625 cm^{-1} were observed in the IR spectrum of compound **(45)**.



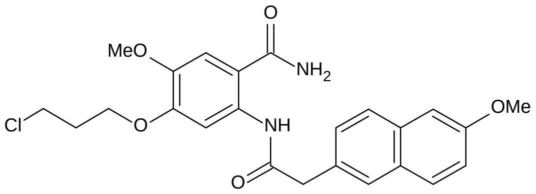
(42) MCR-812



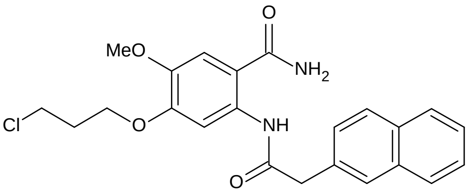
(43) MCR-818



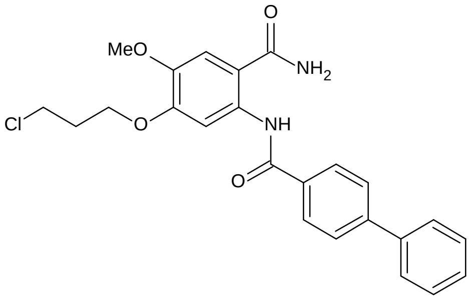
(44) MCR-820



(45) MCR-822



(46) MCR-826

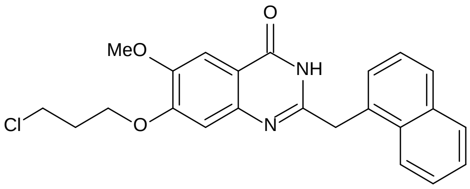


(47) MCR-828

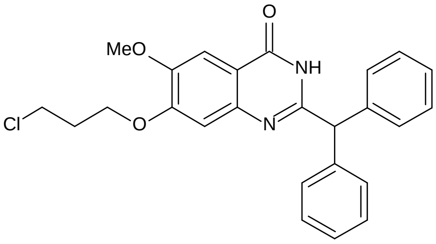
The diamide **(46)** was synthesized by coupling of anthranilamide **(40)** with 2-naphthylacetic acid which was characterized by appearance of peaks at 3345 (N-H asym.), 1660 (C=O str., amide I), and at 1621 cm^{-1} (NH sym., amide II) in its IR spectrum. Compound **(40)** and biphenyl-4-carboxylic acid were coupled to furnish diamide **(47)**. IR spectrum of compound **(47)** displayed peaks at 3361, 1656 and 1617 cm^{-1} characteristic for the amide.

The amides were cyclized to quinazolinones under basic conditions. IR spectrum of compound **(48)** showed characteristic peaks for the amide at 1650 and 1616 cm^{-1}. Further, compound **(48)** was confirmed by peaks at 408 (M^+) and 410 ($M+2^+$) in the mass spectrum. Quinazolinone **(49)** showed characteristic peaks at 1650 for C=O str. (amide I) and 1611 cm^{-1}

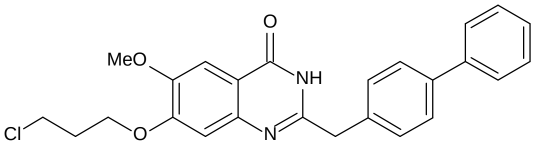
for NH sym. (amide II) in its IR spectrum. Its mass spectrum was characterized by appearance of peaks at 436 (M^+) and 438 ($M+2^+$).



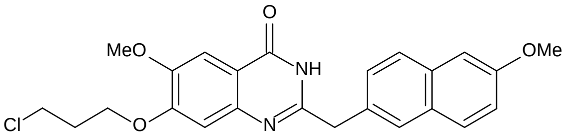
(48) MCR-813



(49) MCR-819

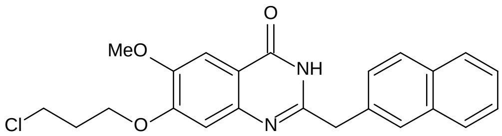


(50) MCR-821

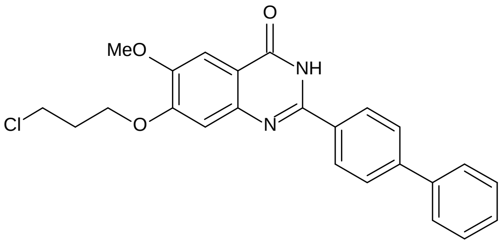


(51) MCR-823

Quinazolinone **(50)** exhibited characteristic IR peaks at 1663 and 1612 cm^{-1}. The mass spectrum of this compound showed peaks at 434 (M^+) and 436 ($M+2^+$). Characteristic peaks at 1663 of C=O str. (amide I) and 1625 cm^{-1} of NH sym. (amide II) were observed in the IR spectrum of compound **(51)**, which also showed peaks at 438 (M^+) and 440 ($M+2^+$) in its mass spectrum.



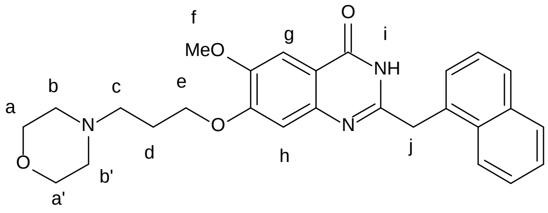
(52) MCR-827



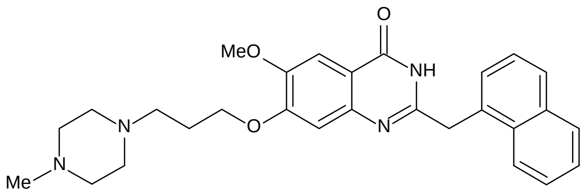
(53) MCR-829

Compound **(52)** was characterized by appearance of peaks at 1660 (C=O str., amide I) and 1621 cm^{-1} (NH sym., amide II) in its IR spectrum. Its mass spectrum showed peaks at 408 (M^+) and 410 ($M+2^+$). IR spectrum of qunazolinone **(53)** showed characteristic amide peaks at 1656 and 1613 cm^{-1}. Compound **(53)** was further characterized by appearance of peaks at 420 (M^+) and 422 ($M+2^+$) in its mass spectrum.

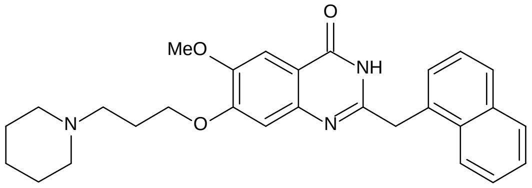
Compound **(54a)** was obtained by reacting compound **(48)** with morpholine. IR spectrum of **54a** showed characteristic peaks for amide at 1651 and 1610 cm^{-1}. Its ^{1}H-NMR spectrum showed broad singlet for NH$_i$ at δ 9.05. The peaks for nine aromatic protons were observed at δ 8.05-7.20 and the two singlets at δ 4.52 & δ 3.95 represented methylene (CH_{2j}) and methoxy (OCH_{3f}) protons respectively. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.27-4.25 & δ 2.56-2.54 respectively. Other two metylene protons (CH_{2d}) were characterized by a multiplet at δ 2.14-2.10. The peaks for four chemically equivalent protons ($CH_{2a/a`}$) of morpholine moiety were observed at δ 3.75-3.73 and the other four ($CH_{2b/b`}$) at δ 2.49. Compound **(54a)** was further confirmed by M^+ peak at 459 in its mass spectrum. Compound **(54b)** was synthesized by treating **48** with N-methylpiperazine in the presence of potassium carbonate**.** Compound **(54b)** was characterized by appearance of peaks at 1653 (C=O str., amide I) and 1612 cm^{-1} (NH sym., amide II) in its IR spectrum. Its mass spectrum was characterized by appearance of M^+ peak at 472.



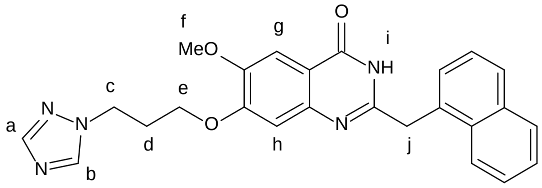
(54a) MCR-814



(54b) MCR-815



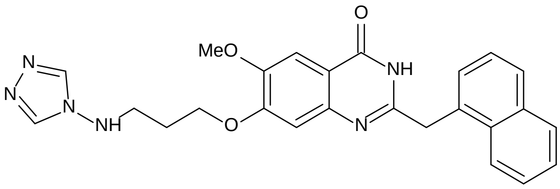
(54c) MCR-817



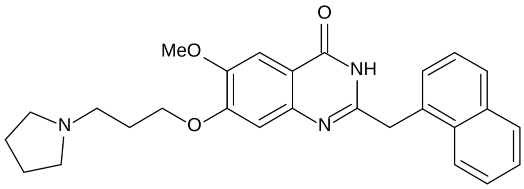
(54d) MCR-816

Compound **(48)** and piperidine were reacted in the presence of potassium carbonate to afford **54c**. Compound **(54c)** showed characteristic peaks at 1658 (C=O str., amide I) and 1611 cm^{-1} (NH sym., amide II). The mass spectrum of this compound showed M^+ peak at 457. While 1,2,4-triazole offered **54d.** Compound **(54d)** showed characteristic peaks at 1670 and 1612 cm^{-1} for amide in its IR spectrum. Its ^{1}H-NMR spectrum showed a peak at δ 9.02 (1H, s, b, NH$_i$). The peak for eleven aromatic protons appeared in between δ 8.25-7.12. Other signals appeared at δ 5.53 (2H, s, CH_{2j}), 4.53-4.50 (2H, t, OCH_{2e}), 4.15-4.12 (2H, t, CH_{2c}), 3.97 (3H, s, OCH_{3f}) and δ 2.54-2.51 (2H, m, CH_{2d}). Its mass spectrum was characterized by appearance of M^+ peak at 441.

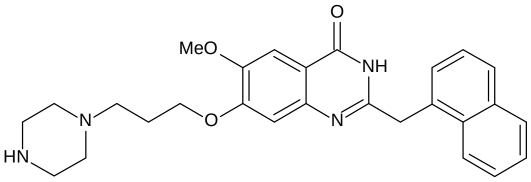
Compound **(54e)** was synthesized from **48** by treating it with 1-amino-1,3,4-triazole . Its IR spectrum showed peaks for C=O str. at 1659 (amide I) and NH sym. (amide II) at 1614 cm^{-1}. Compound **(54e)**, was further confirmed by appearance of M^+ peak at 443 in its mass spectrum. Reaction of pyrrolidine with **48** afforded the targeted compound (**54f)**. IR spectrum of **54f** showed peaks for C=O str. at 1660 (amide I) and NH sym. (amide II) at 1615 cm^{-1}. Compound **54f** was further confirmed by appearance of M^+ peak at 444 in its mass spectrum. Compound **(54g)** was synthesized from **48** by treating it with piperazine in the presence of potassium carbonate. IR spectrum of **54g** showed characteristic amide peaks at 1660 and 1611 cm.$^{-1}$



(54e) MCR-974

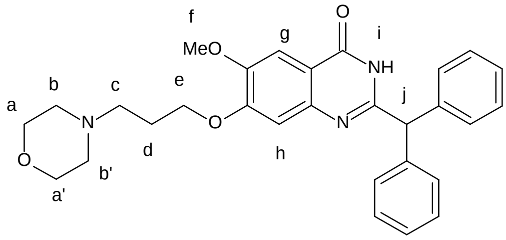


(54f) MCR-975



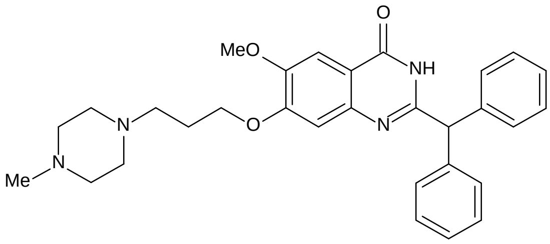
(54g) MCR-976

Compound **(55a)** was obtained by reacting compound **49** with morpholine. IR spectrum of **55a** showed characteristic peaks for amide at 1658 and 1610 cm^{-1}. Further, it was characterized from its ^{1}H-NMR spectrum wherein the signals appeared at δ 9.2 (1H, s ,b, NH$_i$), δ 7.56- 7.16 **(**12H, ArH), 5.60 (1H, s, CH$_j$), 4.22-4.20 (2H, t, CH$_{2e}$), 3.98 (3H, s, OCH$_{3f}$), 3.73-3.71 (4H, t, CH$_{2a/a`}$), 2.58-2.54 (4H, m, CH$_{2b/b`}$), 2.53-2.51 (2H, t, CH$_{2c}$) & 2.13-2.10 (2H, m, CH$_{2d}$). The mass spectrum of this compound showed M^+ peak at 485.

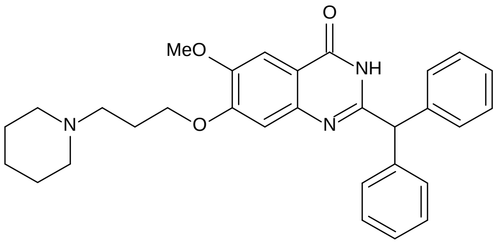


(55a) MCR-961

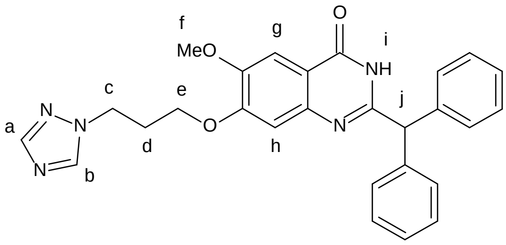
Compound **(55b)** was synthesized by treating **49** with *N*-methylpiperazine in the presence of potassium carbonate**.** Compound **(55b)** was characterized by appearance of peaks at 1659 (C=O str., amide I) and 1611 cm^{-1} (NH sym., amide II) in its IR spectrum. Further, compound **(55b)** was confirmed by M$^+$ peak at 498 in its mass spectrum.



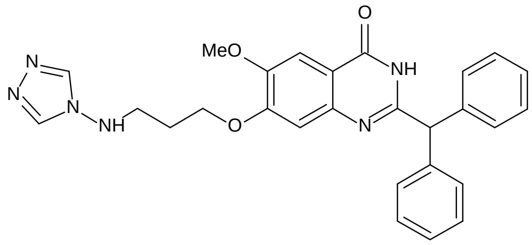
(55b) MCR-962



(55c) MCR-963



(55d) MCR-964

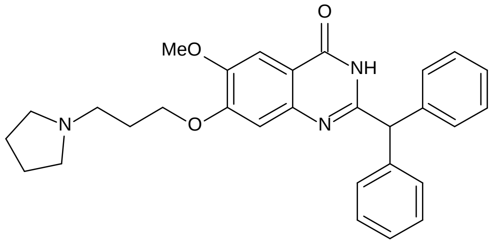


(55e) MCR-966

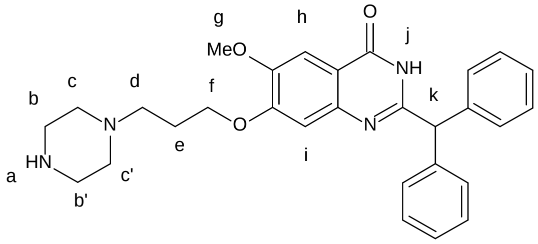
Compound **(49)** and piperidine were reacted in the presence of potassium carbonate to obtain **55c.** Compound **(55c)** displayed characteristic IR peak at 1657 cm^{-1} (C=O str., amide I) and 1611 cm^{-1} (NH sym., amide II). The mass spectrum of this compound showed M$^+$ peak at 483. Compound **(55d)** was synthesized by treating **49** with 1,2,4-triazole. It (**55d)** showed characteristic amide peaks at 1661 and 1605 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum was characterized by appearance of a signal at δ 9.00 (1H, s, b, NH_i) fourteen aromatic protons were appeared in between δ 7.94-7.21. Other protons showed signals at δ 5.55 (1H, s, CH_j), 4.46-4.44 (2H, t, CH_{2e}), 4.07-4.04 (2H, t, CH_{2c}), 3.99 (3H, s, OCH_{3f}) & 2.48-2.44 (2H, m, CH_{2d}). Its mass spectrum was characterized by appearance of M$^+$ peak at 467**.** Reaction of 1-amino-1,3,4-triazole with **49** offered **55e**, Compound **(55e)** showed characteristic peaks at 1661 and 1613 cm^{-1} for amide in its IR spectrum. It was further characterized by appearance of M$^+$ peak at 482 in its mass spectrum**.**

Compound **(55f)** was obtained by treating **49** with pyrrolidine. Compound **(55f)** showed characteristic amide peaks at 1657 and 1611 cm^{-1} in its IR spectrum. Its mass spectrum was characterized by appearance of M$^+$ peak at 469. Compound **(49)** with piperazine offered the piperazine derivative **(55g)**. The IR spectrum of **(55g)** exhibited characteristic peaks at 1661 and 1605 cm^{-1}. It was further characterized from its ^{1}H-NMR spectrum which showed peaks for two NH protons at δ 9.72 (1H, s, NH_j) and δ 3.50 (1H, s,

NH_a). The twelve aromatic protons were appeared in between δ 7.47-7.21. Other signals were observed at δ 5.42 (1H, s, CH_k), 4.17-4.15 (2H, t, CH_{2f}), δ 3.91-3.88 (4H, m, $CH_{2c/c`}$), 2.48-2.46 (2H, t, $CH_{2d}$), 2.41-2.38 (4H, m, $CH_{2b/b`}$) and at δ 1.99-1.95 (2H, m, CH_{2e}). The mass spectrum of this compound **(55g)** showed M^+peak at 484.

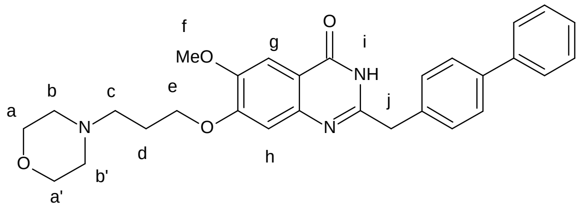


(55f) MCR-965

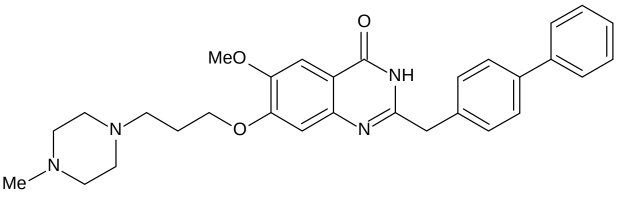


(55g) MCR-1016

Compound **(50)** was treated with morpholine to offer the targeted compound **(56a).** Compound **(56a)** was characterized by appearance of peaks at 1667 (C=O str., amide I) and 1608 cm^{-1}(NH sym., amide II) in its IR spectrum. It gave NMR signals at δ 12.20 (1H, s, NH_i), 7.157-7.12 (m, 11H, ArH), 4.20-4.18 (2H, t, CH_{2e}), 3.99 (2H, s, CH_{2j}), 3.66 (3H, s, OCH_{3f}), 2.54-2.51 (2H, t, CH_{2c}) and 2.06-2.04 (2H, m, CH_{2d}). The peak for eight morpholino protons were observed at δ 3.65-3.63 (2H, m, CH_{2a}), 2.59-2.57 (2H, m, $CH_{2a`}$) and at δ 2.44-2.43 (4H, m, $CH2_{b/b`}$) in its ^1H-NMR spectrum. Its mass spectrum was characterized by appearance of M^+ peak at 485. Compound **(50)** with N-methylpiperazine offered **56b.** It showed characteristic peaks at 1666 and 1606 cm^{-1} for amide in its IR spectrum.

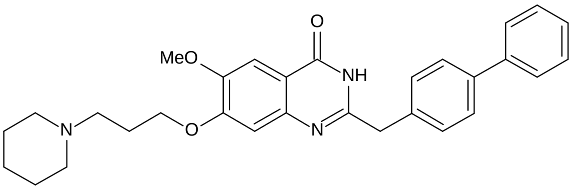


(56a) MCR-955

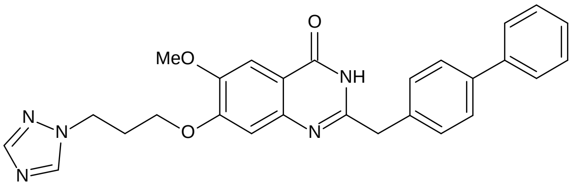


(56b) MCR-1017

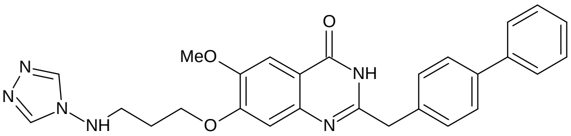
Compound **(50)** was treated with piperidine to afford **56c**. Compound **(56c)** showed characteristic peaks at 1666 and 1609 cm^{-1} in its IR spectrum. 1,2,4-Triazole afforded the targeted compound **(56d)**. Compound **(56d)** exhibited characteristic peaks at 1667 and 1610 cm^{-1} in its IR spectrum. Compound **(50)** was treated with 1-amino-1,3,4-triazole in the presence of potassium carbonate to obtain **56e.** It showed characteristic peaks at 1667 and 1611 cm^{-1} for amide in its IR spectrum. Compound **(56f)** was obtained by substitution of chloro in compound **(50)** with pyrrolidine. It showed characteristic peaks at 1666 and 1609 cm^{-1} for amide in its IR spectrum.



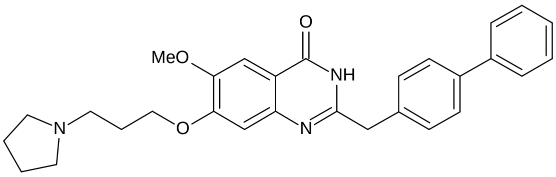
(56c) MCR-956



(56d) MCR-957

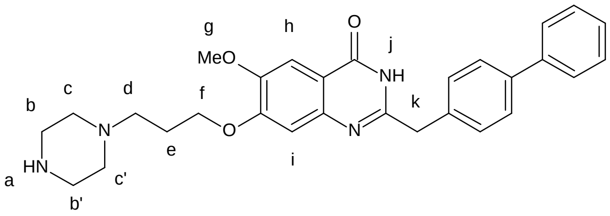


(56e) MCR-959



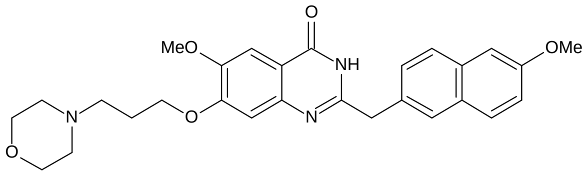
(56f) MCR-958

Compound **(50)** was treated with piperazine to offer the targeted compound **(56g)**. It showed characteristic peaks at 1667 and 1609 cm^{-1} for amide in its IR spectrum. Its ^{1}H-NMR spectrum showed broad peak at δ 8.61 for NH$_j$ and the eleven aromatic protons were observed in between δ 7.82-7.18. There was a triplet at δ 4.25-4.23 which was characterized for two methylene protons (CH_{2f}) and a singlet at δ 4.12 (CH_{2k}). The three methoxy protons were characterized by a sharp signal at δ 3.98 as singlet. Broad signal was obtained at δ 3.61 for NH$_a$ proton. The four chemically equivalent protons (CH2$_{c/c'}$) of piperazine appeared as multiplet at δ 2.94-2.92 and other four protons (CH2$_{b/\,b'}$) appeared at δ 2.49-2.47. A triplet at δ 2.56.2.53 indicated methylene protons (CH_{2d}) and multiplet at δ 2.15-2.11 characterized the (CH_{2e}) protons. The mass spectrum of this compound **(56g)** showed M$^+$ peak at 484.

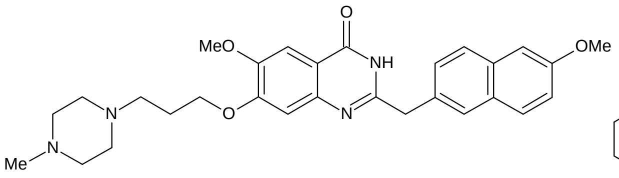


(56g) MCR-960

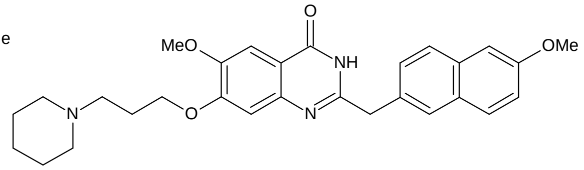
Compound **(51)** was treated with morpholine to offer the targeted compound **(57a)**. Compound **(57a)** showed characteristic amide peaks at 1666 and 1613 cm^{-1} in its IR spectrum. Compound **(51)** was treated with N-methylpiperazine in the presence of potassium carbonate to obtain **57b.** Compound **(57b)** showed characteristic peaks at 1664 cm^{-1} for C=O str. (amide I) and 1609 cm^{-1} for NH sym. (amide II) in its IR spectrum. With piperidine, compound **(51)** offered the derivative **(57c).** Compound **(57c)** showed characteristic peaks at 1664 and 1611 cm^{-1} in its IR spectrum.



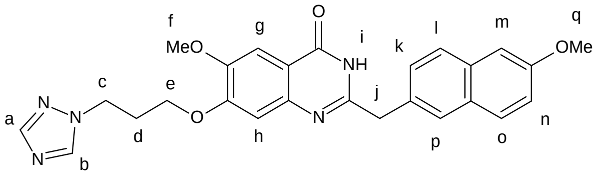
(57a) MCR-977



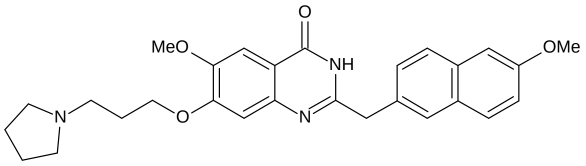
(57b) MCR-1015



(57c) MCR-978

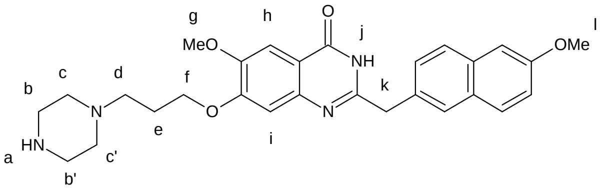


(57d) MCR-979



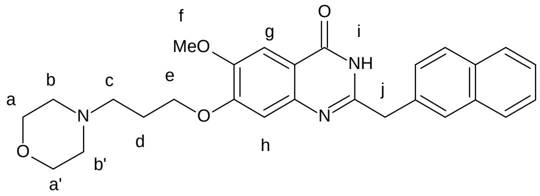
(57f) MCR-980

Compound **(51)** on reaction with with 1,2,4-triazole afforded the targeted compound **(57d).** IR spectrum of compound **(57d)** showed characteristic peaks at 1667 and 1609 cm^{-1}. Its ^{1}H-NMR spectrum displayed signals at δ 12.24 (1H, s, b, NH_i), 8.40-7.05 (m, 10H, ArH), 4.41-4.39 (2H, t, OCH_{2e}), 3.89 (3H, s, OCH_{3q}), 3.87 (3H, s, OCH_{3f}), 2.61-2.59 (2H, m, CH_{2c}) and at δ 2.37-2.35 (2H, m, CH_{2d}). Its mass spectrum was characterized by appearance of M^+ peak at 471. Compound **(51)** was reacted with pyrrolidine in presence of potassium carbonate to obtain **57f.** Compound **(57f)** showed characteristic peaks at 1664 cm^{-1} and 1611 cm^{-1} for amide in its IR spectrum.



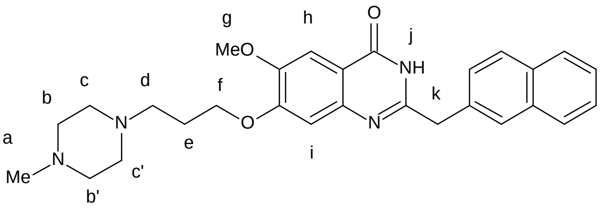
(57g, MCR- 981)

Compound **(51)** was treated with piperazine in the presence of potassium carbonate to obtain **57g**. Compound **(57g)** showed characteristic peaks for amide at 1663 and 1607 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlets at δ 10.81 & δ 8.52 for NH_a and NH_j. The eight aromatic protons appeared in between δ 7.72- 7.13, three singlets at δ 4.23, 3.98 & 3.91 indicated (CH_{2k}, OCH_{3g} and OCH_{3l}) protons respectively. The peaks at δ 4.26-4.24 and δ 2.55-2.53 as triplets represented methylene protons of (CH_{2f} and CH_{2d}). The methylene protons (CH_{2c}) appered as multiplet at δ 2.13-2.10, four methylene protons ($CH_{2c/c'}$) were at δ 2.91 and the signal for other four methylene protons ($CH_{2b/b'}$) of piperazine moiety appeared at δ 2.47-2.43. The mass spectrum of this compound **(57g)** showed M^+ peak at 488.

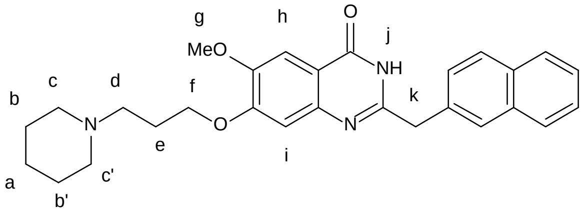


(58a) MCR-967

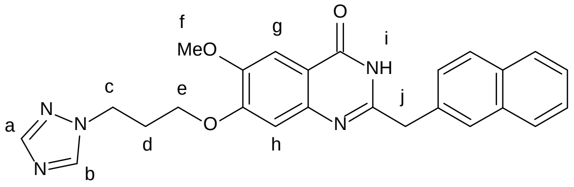
Reaction of **52** and morpholine in the presence of potassium carbonate offered compound **(58a)**. The IR spectrum of **58a** displayed peaks at 1666 and 1611 cm^{-1}. This compound **(58a)** was further characterized from its ^{1}H-NMR data, which showed broad singlet at δ 9.80 for NH_i proton. The nine aromatic protons were appeared in between δ 7.83-7.43. Other protons showed peaks at δ 4.36-4.34 (2H, t, OCH_{2e}), 4.31 (2H, s, CH_{2j}), 3.98 (3H, s, OCH_{3f}), 3.73-3.70 (4H, m, $CH_{2a/a`}$), 2.56-2.54 (2H, t, $CH_{2c}$), 2.43-2.41 (4H, m, $CH_{2b/b`}$) and at δ 2.09-2.07 (2H, m, CH_{2d}). Its mass spectrum was characterized by appearance of M^+ peak at 459. Compound **(58b)** was synthesized by treating **52** with N-methylpiperazine. Compound **(58b)** showed characteristic peaks for amide at 1665 and 1610 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum displayed amine protons NH_j as broad singlet at δ 10.20. The nine aromatic protons appeared in the region between δ 7.86-7.15. The signals at δ 4.47-4.45 and δ 4.25-4.23 as triplets indicated methylene protons (CH_{2f}) and (CH_{2d}) respectively. The multiplet at δ 2.14-2.12 represented methylene protons (CH_{2e}) and the other two methylene protons (CH_{2k}) appeared as singlet at δ 4.37. The methoxy protons were characterised by sharp singlet at δ 3.97. The peak at δ 2.26 as singlet was for N-methyl protons. Two methylene protons of N-piperazine moiety appeared at δ 3.93 and the rest six protons gave a multiplet at δ 2.58-2.54 in its spectrum. The mass spectrum of this compound showed M^+ peak at 472. Compound **(52)** and piperidine were reacted in the presence of potassium carbonate to afford **58c.** IR spectrum of compound **(58c)** displayed characteristic peaks at 1666 and 1611 cm^{-1}. Its ^{1}H-NMR spectrum showed signal for NH_j at δ 10.13; the signals for the nine aromatic protons appeared in between δ 7.77-7.10. Other characteristic peaks observed in its spectrum were at δ 4.19-4.17 (2H, t, CH_{2f}), 4.16 (2H, s, CH_{2k}), 3.87-3.85 (2H, m, CH_{2d}), 3.83 (3H, s, OCH_{3g}), 3.66-3.63 (4H, m, $CH_{2c/c`}$), 2.48-2.46 ( 4H, m, $CH_{2b/b`}$), 2.37-2.34 (2H, m, CH_{2a}), and at δ 2.04-2.02 (2H, m, CH_{2e}). Its mass spectrum was characterized by appearance of M^+ peak at 457.



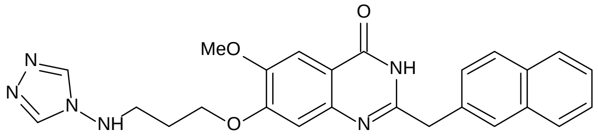
(58b) MCR-968



(58c) MCR-969

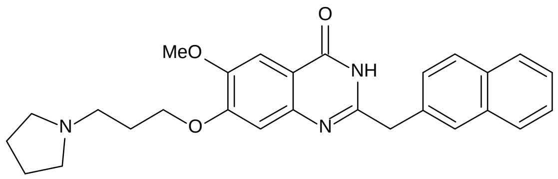


(58d) MCR-970

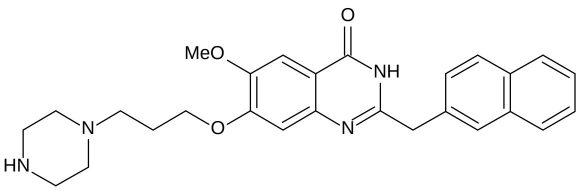


(58e) MCR-972

Compound **(52)** and 1,2,4-triazole were reacted in the presence of potassium carbonate to afford **58d.** IR spectrum of compound **(58d)** showed characteristic amide peaks at 1667 and 1610 cm^{-1}. Its ^1H-NMR spectrum showed signal for NH_i at δ 8.96; the signals for the eleven aromatic protons appeared in between δ 7.99-7.12. Other characteristic peaks observed in its spectrum were at δ 4.52-4.50 (2H, t, CH_{2e}), 4.15-4.13 (2H, t, CH_{2j}), 4.06 (3H, s, OCH_{3f}), δ 2.53-4.51 (2H, t, CH_2c), and at δ 1.72 (2H, s, CH_{2d}). Its mass spectrum was characterized by appearance of M^+ peak at 441. Compound **(52)** and 1-amino-1,3,4-triazole afforded **58e.** IR spectrum of compound **(58e)** displayed characteristic amide peaks at 1667 and 1610 cm^{-1}. Its mass spectrum was characterized by appearance of M^+ peak at 456.



(58f) MCR-971

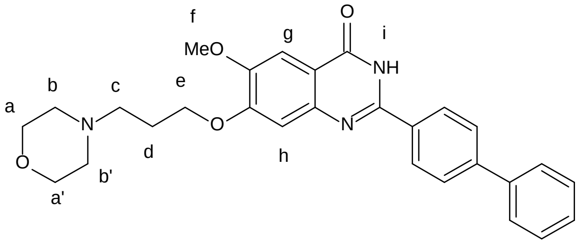


(58g) MCR-973

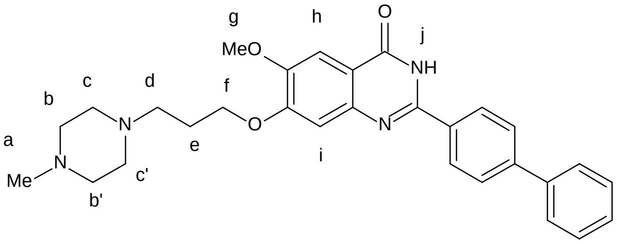
The targeted compound **(58f)** was synthesized by treating **52** with pyrrolidine. Compound **(58f)** displayed characteristic IR peaks at 1662 cm^{-1} (C=O str., amide I) and 1611

cm^{-1} (NH sym., amide II). The mass spectrum of this compound showed M^+ peak at 443. With piperazine, compound **(52)** offered compound **(58g)**. It showed characteristic peaks at 1667 and 1610 cm^{-1} in its IR spectrum.

Compound **(53)** and morpholine were reacted in the presence of potassium carbonate to obtain **59a.** Compound **(59a)** showed characteristic amide peaks at 1667 and 1609 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed peaks at δ 11.1 (1H, s, b, NH_i), 8.28- 7.25 (11H, Ar*H*), 4.42-4.40 (2H, t, CH_{2e}), 4.05 (3H, s), 2.58-2.56 (2H, t, CH_{2c}) & 2.14-2.12 (2H, m, CH_{2d}). The peak for four morpholino protons ($CH_{2a/a'}$) appeared at δ 3.83-3.79 and the other four ($CH_{2b/b'}$) protons appeared at δ 2.54-2.50 as multiplets. The mass spectrum of this compound showed M^+ peak at 471. **59b** was synthesized by treating **53** with N-methylpiperazine. IR spectrum of **59b** displayed characteristic peaks at 1667 and 1609 cm^{-1}. Its ^{1}H-NMR spectrum showed signals at 10.08 (1H, s, NH_j) and two singlets were observed at δ 7.64 and δ 7.26 for protons (ArH_h & ArH_i) of quinazolinone moiety respectively. The nine protons of the biphenyl moiety appeared in between δ 8.21- 7.27. The peak for two methylene protons (OCH_{2f}) was observed as triplet at δ 4.51-4.49. The methoxy protons (OCH_{3g}) appeared at δ 3.95 as singlet; the peak for rest four methylene protons (CH_{2d} and CH_{2e}) were observed at δ 2.57-2.55 as multiplets. The methyl protons (CH_{3a}) showed characteristic singlet at δ 2.29. Signals for the eight methylene protons of the N-methylpiperazine appeared at δ 2.51-2.47 (6H, m) and at δ 2.32-2.30 (2H, m). Its mass spectrum was characterized by appearance of M^+ peak at 484.

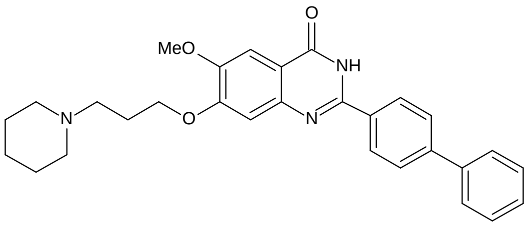


(59a) MCR-948

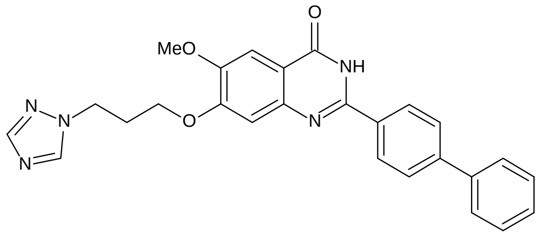


(59b) MCR-949

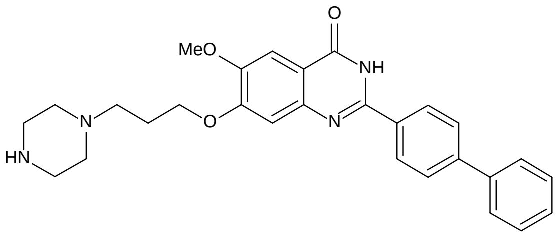
With piperidine, compound **(53)** afforded compound **(59c)**. IR spectrum of compound **(59c)** showed characteristic amide peaks at 1656 and 1609 cm^{-1}. Compound **(59d)** was synthesized by treating **53** with 1,2,4-triazole in presence of potassium carbonate. IR spectrum of **59d** displayed characteristic amide peaks at 1656 and 1610 cm^{-1}. Its mass spectrum was characterized by appearance of M^+ peak at 453. Compound **(59g)** was synthesized by treating **53** with piperazine in the presence of potassium carbonate. IR spectrum of **59g** displayed characteristic amide peaks at 1659 and 1607 cm^{-1}.



(59c, MCR-950)



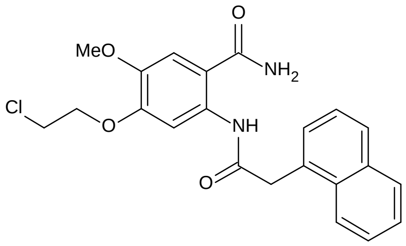
(59d, MCR-951)



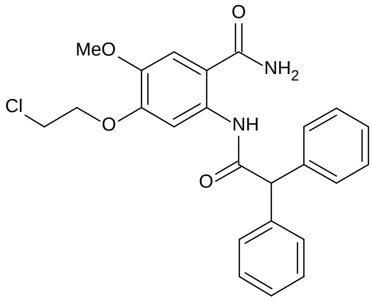
(59g, MCR-954)

D. Synthesis of 7-(2-substitutedaminoethoxy) derivatives of quinazolinones (68a-71g)

Scheme IX was adopted for the synthesis of the targeted compounds **(68a-71g)**. The anthranilamide derivative **(41)** was condensed with various carboxylic acids to obtain the diamides **(60-63)** as described earlier. The cyclisation of the diamides **(60-63)** under basic conditions offered quinazolinones **(64-67)**. The targeted compounds **(68a-71g)** were prepared by the substitution of the chloro groups by various amines **(X – H)**.

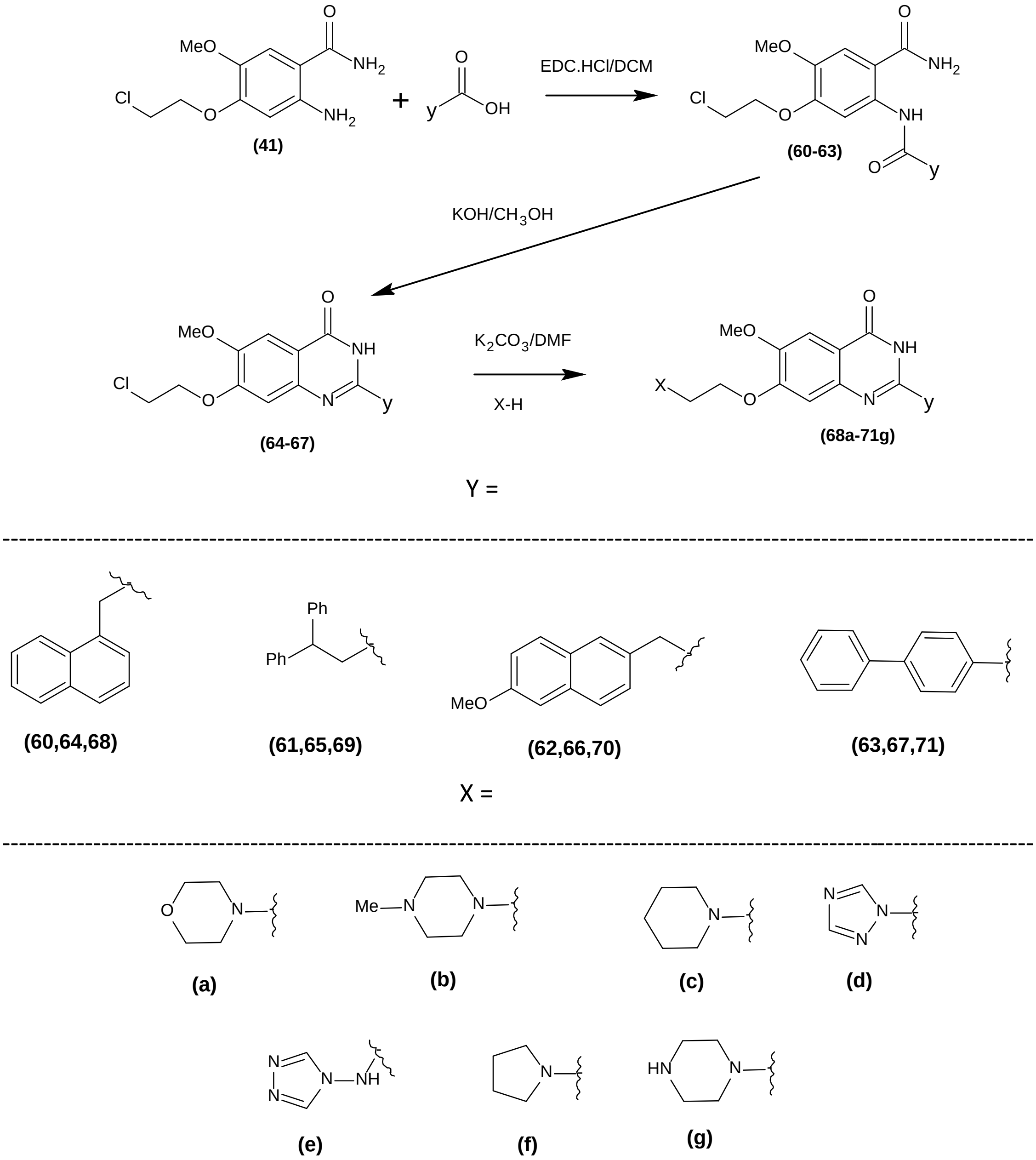


(60)



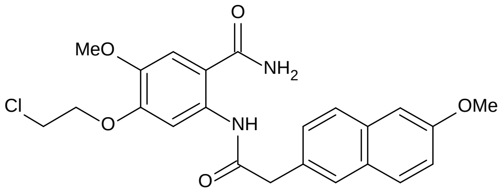
(61)

Diamide **(60)** was obtained by condensation of compound **(41)** and 2-(1-naphthyl)acetic acid. It showed characteristic IR peaks at 3395 cm^{-1} (N-H asym.), 1659 cm^{-1} (- C=O str., amide I) and 1617 cm^{-1} (NH sym., amide II). Compound **(41)** and 2,2-diphenylacetic acid were coupled to furnish diamide **(61).** IR spectrum of compound **(61)** showed characteristic peaks at 3393, 1664 and 1620 cm^{-1}.

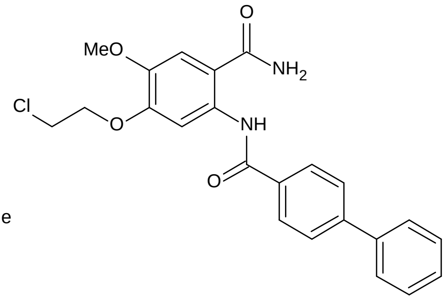


Scheme-IX

Compound **(41)** and 2-(6-methoxy-2-naphthyl)acetic acid were coupled to obtain compound **(62)**. Characteristic peaks at 3389, 1662 and 1617 cm^{-1} were observed in the IR spectrum of compound **(62)**. Biphenyl-4-carboxylic acid yielded compound **(63)** by reacting it with compound **(41)**. IR spectrum of compound **(63)** displayed characteristic peaks at 3369, 1658 and 1612 cm^{-1}.

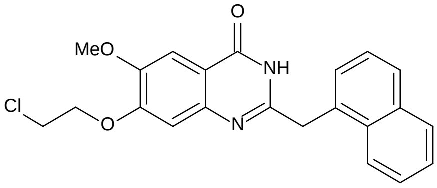


(62)

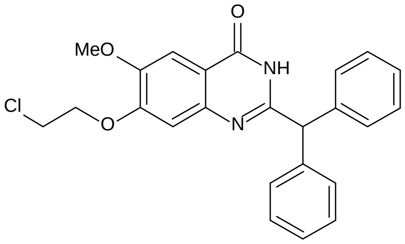


(63)

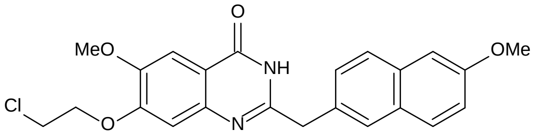
The diamides **(60-63)** were cyclized in basic conditions by refluxing them in methanolic KOH solution. IR spectrum of compound **(64)** showed characteristic amide peaks at 1650 and 1608 cm^{-1}. Compound **(64)** was further confirmed by peaks at 394 (M^{+}) and 396 (M+2^{+}) in its mass spectrum. Compound **(65)** showed characteristic peaks at 1658 (C=O str., amide I) and 1610 cm^{-1} (NH sym., amide II) in its IR spectrum. Its mass spectrum was characterized by appearance of peaks at 420 (M^{+}) and 422 (M+2^{+}).



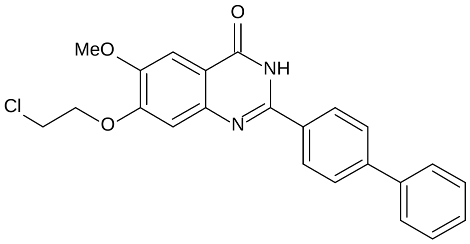
(64)



(65)



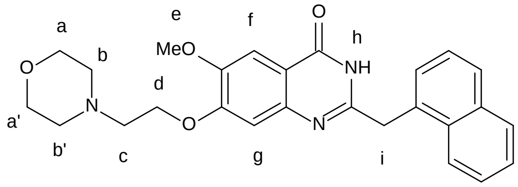
(66)



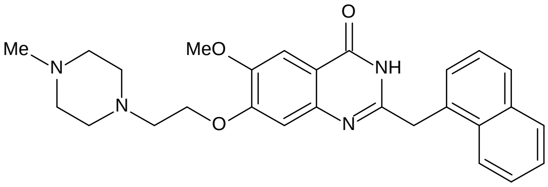
(67)

Characteristic peaks for amide at 1660 and 1608 cm^{-1} were observed in the IR spectrum of compound **(66)**. The mass spectrum of this compound showed peaks at 424 (M^{+}) and 426 (M+2^{+}). The IR spectrum of compound **(67)** showed peaks for C=O str. at 1657 cm^{-1} (amide I) and NH sym. at 1610 cm^{-1}(amide II). Compound **(67)** was further characterized by appearance of peaks at 406 (M^{+}) and 408 (M+2^{+}) in its mass spectrum.

Compound **(64)** was treated with morpholine to offer **68a,** which showed characteristic amide peaks at 1663 and 1612 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum displayed signals at δ 9.81 (1H, s, b, NH_{h}), 8.42-7.28 (9H, ArH), 4.38 (2H s, CH_{2i}), 4.18-4.16 (2H, t, OCH_{2d}), 3.87 (3H, s, OCH_{3e}), 3.62-3.59 (4H, m, $CH_{2a/a`}$), 2.77-2.75 (2H, t, $CH_{2c}$) and at $\delta$ 2.53-2.51 (4H, m, $CH_{2b/b`}$). N-Methyl piperazine with compound **(64)** offered the targeted compound **(68b)**. It showed characteristic amide peaks at 1668 and 1616 cm^{-1} in its IR spectrum.

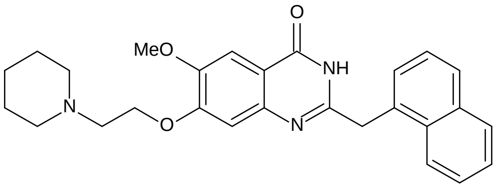


(68a) MCR-982

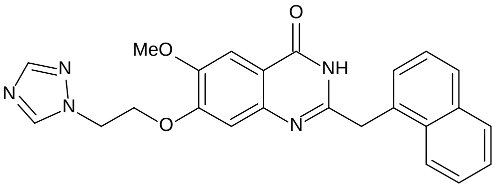


(68b) MCR-983

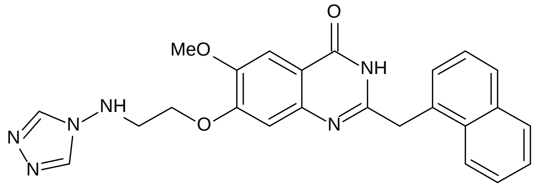
Reaction of piperidine with compound **(64)** afforded targeted product **(68c)**, which showed characteristic peak at 1673 cm^{-1} for C=O str. (amide I) and 1612 cm^{-1} for NH sym. (amide II) in its IR spectrum. Compound **(64)** was treated with 1,2,4-triazole in the presence of potassium carbonate to obtain compound **(68d)**. It showed characteristic amide peaks at 1656 and 1612 cm^{-1} in its IR spectrum. .



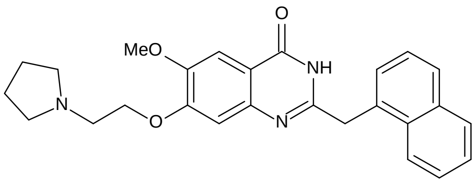
(68c) MCR-984



(68d) MCR-986



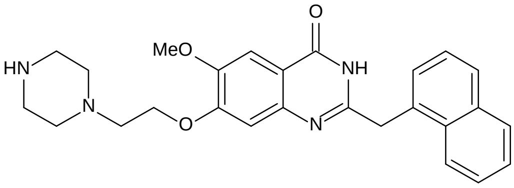
(68e) MCR-987



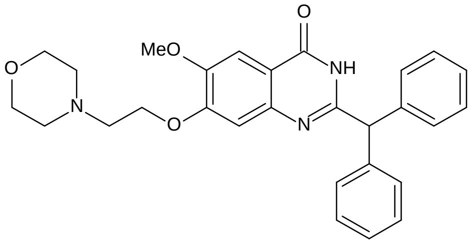
(68f) MCR-985

1-Amino-1,3,4-triazole offered compound **(68e)**, which showed characteristic amide peaks at 1668 and 1611 cm^{-1} in its IR spectrum, while pyrrolidine on reacting with compound **(64)** furnished compound **(68f).** It showed characteristic amide peaks at 1669 and 1611 cm^{-1} in IR spectrum.

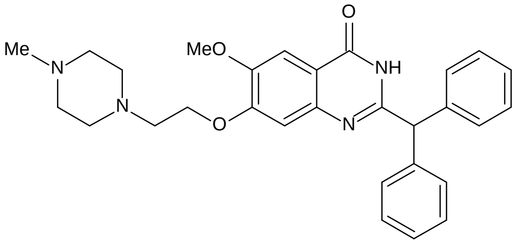
Reaction of piperazine with compound **(64)** afforded the targeted product **(68g)**, which showed characteristic amide peaks at 1667 and 1611 cm^{-1} in its IR spectrum.



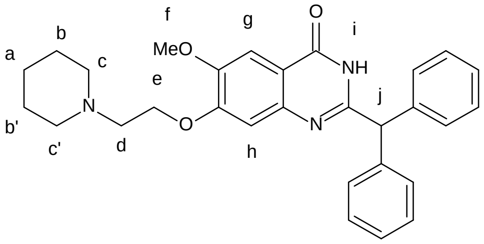
(68g) MCR-988



(69a) MCR-1000



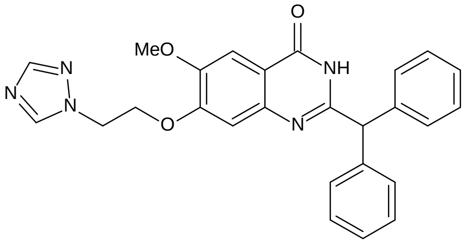
(69b) MCR-1001



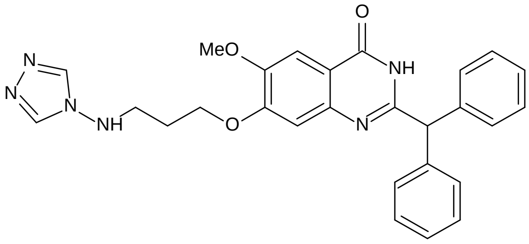
(69c) MCR-1002

Morpholine with compound **(65)** furnished the targeted compound **(69a)**. Its IR spectrum showed characteristic peaks at 1659 and 1609 cm^{-1}. N-Methylpiperazine offered compound **(69b)**. Its IR spectrum showed peaks for C=O str. at 1662 cm^{-1} (amide I) and NH sym. (amide II) at 1613 cm^{-1}. Compound **(69c)** was obtained by reacting quinazolinone **(65)** with piperidine. IR spectrum of **69c** showed characteristic amide peaks at 1656 and 1612 cm^{-1}. ^{1}H-NMR spectrum of **69c** showed broad band for NH_i proton at δ 12.28 as a singlet. All twelve aromatic protons displayed their peaks in between δ 7.44- 7.07. Further, the spectrum showed singlet at δ 5.42 for CH_j proton. The signals for four methylene protons of ethoxy (CH_{2d} & CH_{2e}) were obtained at δ 4.20-4.18 and 2.76-2.74 as triplets respectively. Sharp singlet was observed at δ 3.88 representing the peak for methoxy ($OCH_{3f)}$ protons. The protons of piperidine moiety were observed at δ 2.49-2.46 (4H, m, $CH_{2c/c`}$), 1.54-1.51 (4H, m, $CH_{2b/b`}$) & 1.43-1.41 (2H, m, CH_{2a}). The mass spectrum of this compound showed M^{+} peak at 455.

Compound (**69d)** was synthesized by treating quinazolinone **(65)** with 1,2,4-triazole. IR spectrum of **69d** showed characteristic peaks for C=O str. at 1670 cm^{-1} (amide I) and NH sym. (amide II) at 1617 cm^{-1}. Compound (**69e)** was synthesized by treating compound **(65)** with 1-amino-1,3,4-triazole in the presence of potassium carbonate. IR spectrum of **(69e)** showed characteristic peaks at 1664 and 1612 cm^{-1}. Pyrrolidine on reaction with compound **(65)** offered compound **(69f)**. Its IR spectrum showed peaks at 1656 and 1612 cm^{1}. Piperazine afforded compound **(69g)**. Its IR spectrum showed characteristic amide peaks at 1668 and 1598 cm^{-1}

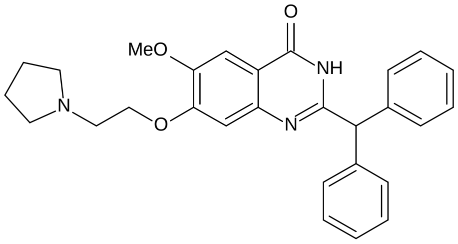


(69d) MCR-1003)

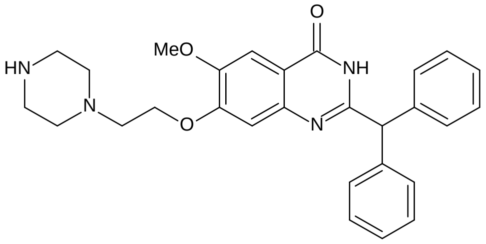


(69e) MCR-1005)

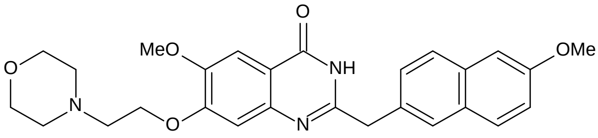
.

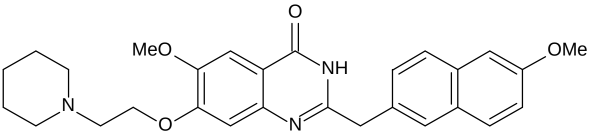


(69f) MCR-1004



(69g) MCR-1006

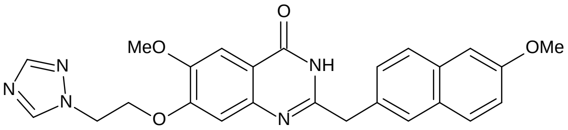




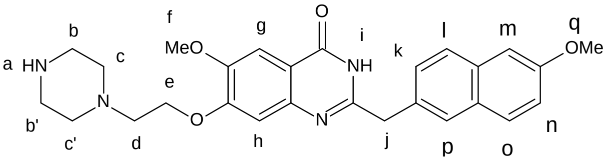
(70a) MCR-989

(70c) MCR-990

Morpholine with compound **(66)** offered the targeted compound **(70a).** It was characterized by appearance of peaks at 1666 cm^{-1} (C=O str., amide I) and 1619 cm^{-1} (NH sym., amide II) in its IR spectrum. Compound **(66)** with piperidine yielded compound **(70c).** Compound **(70c)** showed characteristic peaks at 1665 (C=O str., amide I) and 1611 cm^{-1}(NH sym., amide II) in its IR spectrum. Compound **(70d)** was obtained by reacting compound **(66)** with 1,2,4-triazole. It was characterized by peaks at 1666 (C=O str., amide I) and 1612 cm^{-1}(NH sym., amide II) in its IR spectrum. Compound **(66)** was treated with piperazine to obtain compound **(70g).** Compound **(70g)** was characterized by appearance of peaks at 1656 cm^{-1} (C=O str., amide I) and 1612 cm^{-1} (NH sym., amide II) in its IR spectrum. Its ^{1}H-NMR spectrum showed two broad singlets at δ 12.32 & 8.62 which represented peak for NH$_i$ & NH$_a$ respectively. The signals for eight aromatic protons were observed in between δ 7.91-7.07; the presence of six methoxy protons (OCH$_{3q}$ & OCH$_{3f}$) was confirmed by the appearance of singlets at δ 3.91 and δ 3.87 respectively. The signal for methylene protons CH$_{2j}$ appeared at δ 3.95-3.93 as singlet; the four methylene protons (2H, CH$_{2e}$ & 2H, CH$_{2d}$) showed peaks at δ 4.20-4.18 & 2.81-2.79 respectively. The protons of piperazine moiety showed peaks at δ 2.79-2.76 (4H, m, CH2$_{b/b`}$) and 2.49-2.46 (4H, m, CH$_{2c/c`}$).

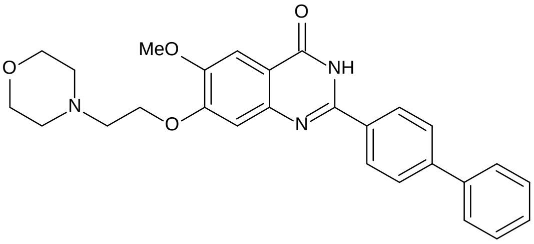


(70d) MCR-991

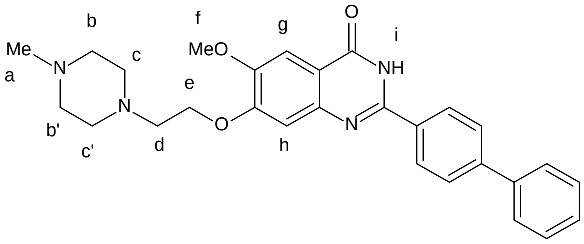


(70g) MCR-992

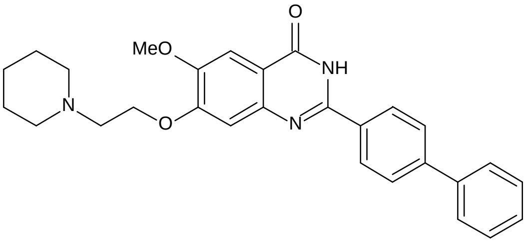
Reaction of morpholine with compound **(67)** afforded the targeted product **(71a).** Compound **(71a)** showed characteristic amide peaks at 1656 and 1610 cm^{-1} in its IR spectrum. Compound **(71b)** was synthesized by treating quinazolinone **(67)** with N-methylpiperazine. Compound **(71b)** showed characteristic amide peaks at 1656 and 1609 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum displayed peak at δ 11.93 (1H, s, b, NH$_i$). The peaks for eleven aromatic protons were observed in between δ 8.31- 7.18. Other peaks in the



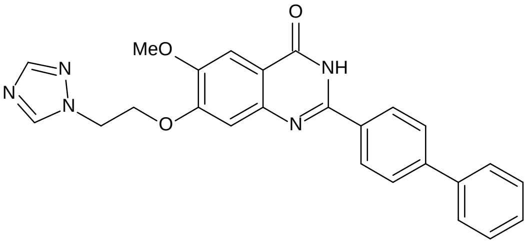
(71a) MCR-993



(71b) MCR-994



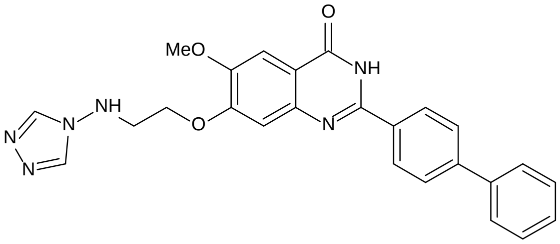
(71c) MCR-995



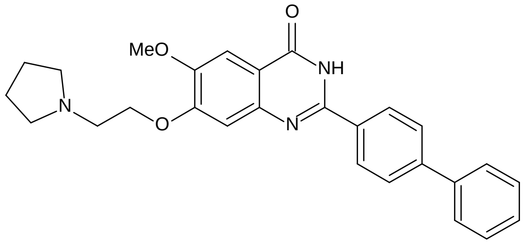
(71d) MCR-996

spectrum were at δ 4.26-4.24 (2H, t, OCH_{2e}), 3.91 (3H, s, OCH_{3f}), 2.82-2.80 (2H, t, CH_{2d}), 2.56-2.53 (4H, m, $CH2_{c/c`}$), 2.39-2.36 (4H, m, $CH_{2b/b`}$) and at 2.19 (3H, s, CH_{3a}). Compound **(71c)** was obtained by treating quinazolinone **(67)** with piperidine in the presence of potassium carbonate**.** Compound **(71c)** showed characteristic amide peaks at 1656 and 1609 cm^{-1} in its IR spectrum. 1,2,4-Triazole afforded compound **(71d)**, It showed characteristic amide peaks at 1657 and 1611 cm^{-1} in its IR spectrum.

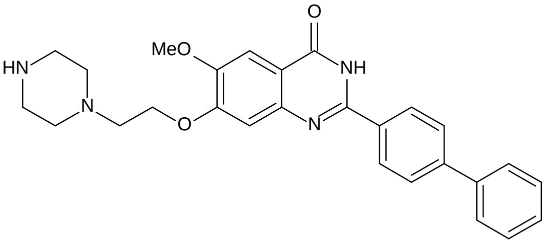
Compound **(71e)** was synthesized by treating quinazolinone **(67)** with 1-amino-1,3,4-triazole. Compound **(71e)** showed characteristic amide peaks at 1658 and 1609 cm^{-1} in its IR spectrum. Pyrrolidine offered compound **(71f)** which showed characteristic peaks at 1656 cm^{-1} for C=O str. (amide I) and 1610 cm^{-1} for NH sym. (amide II) in its IR spectrum.



(71e) MCR-998



(71f) MCR-997

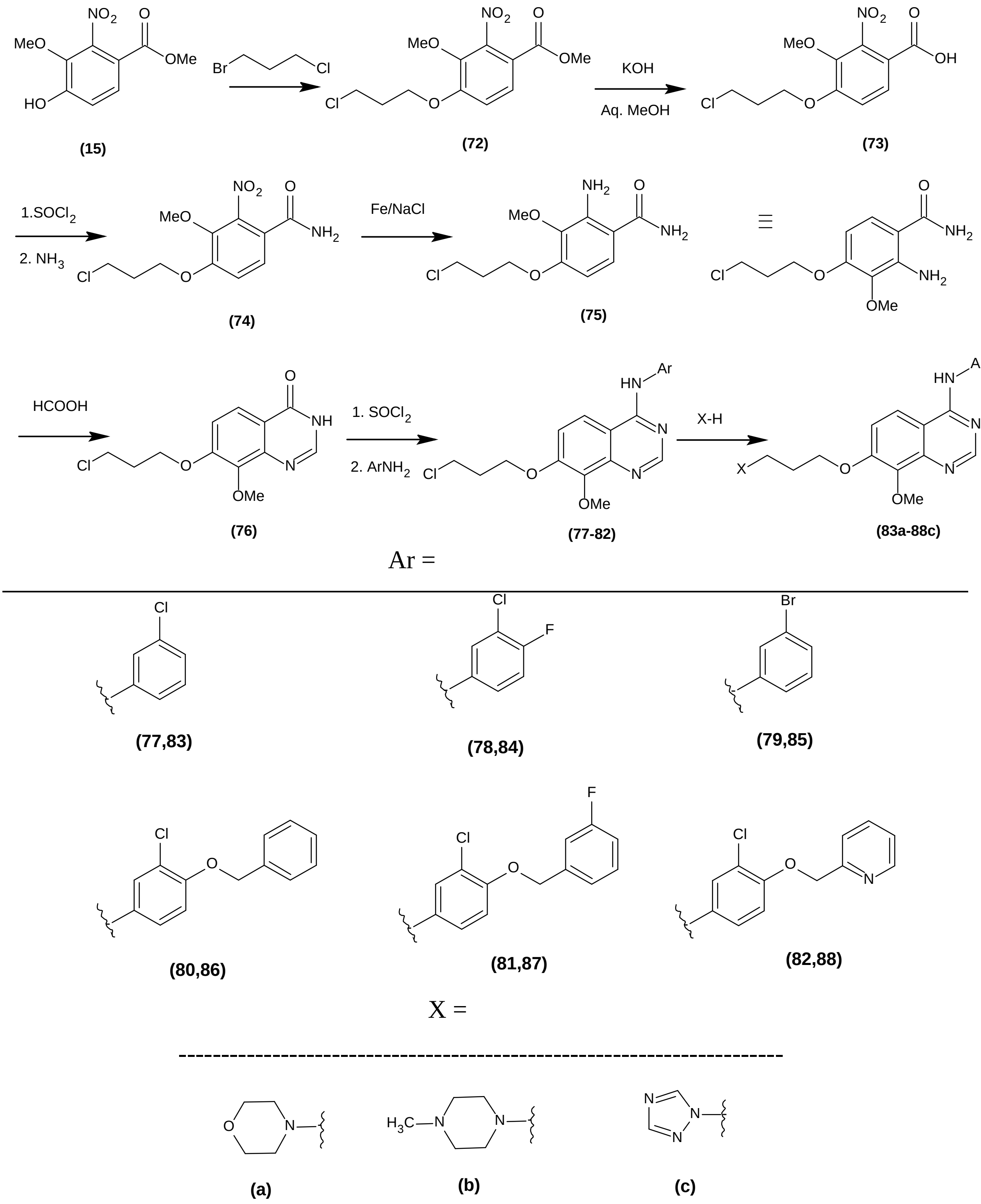


(71g) MCR-999

Compound **(71g)** was obtained by treating quinazolinone **(67)** with piperazine in the presence of potassium carbonate**.** Compound **(71g)** showed characteristic amide peaks at 1658 and 1609 cm^{-1} in its IR spectrum.

E. Synthesis of 4-anilinoquinazoline derivatives (83a-88c)

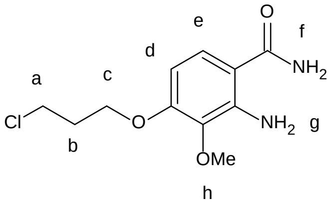
The phenol derivative **(15)** was alkylated using 1-bromo-3-chloropropane under basic conditions to offer the ether **(72)**. The ester group in compound **(72)** was hydrolyzed under basic conditions and the acid **(73)** so obtained was chlorinated using thionyl chloride to yield the acyl chloride. Without chacterization, the acid chloride was given ammonia treatment to afford the amide **(74)**. Nitro group in compound **(74)** was reduced by using iron powder and aqueous sodium chloride to yield the amine **(75)**. The anthranilamide derivative **(75)** on



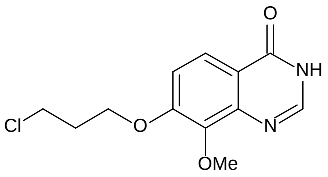
Scheme-X

cyclisation with formic acid yielded the quinazolinone derivative **(76)**. Treatment of the quinazolinone with thionyl chloride followed by nucleophilic substitution with the required aniline derivative offered the 4-aniline substituted quinazolines **(77-82)**. Substitution of the chloro group in the side chain with various amines gave the desired targeted compounds **(83a-88c)** as per **Scheme-X**.

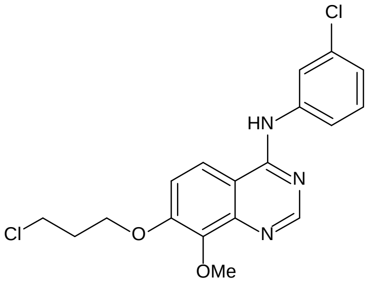
Compound **(72)** showed characteristic ester peak at 1723 cm^{-1} (C=O str.) while compound **(73)** exhibited a characteristic keto peak at 1692 cm^{-1} in their IR spectra. Compound **(74)** was characterized by presence of peaks at 3366 (N-H asym.), 1664 (C=O str., amide I) & 1622 cm^{-1} (NH sym., amide II) while compound **(75)** was characterized by presence of peaks for amino group at 3499 (N-H str.), 1655 C=O str. (amide-I) and NH sym. at 1616 cm^{-1} (amide II) in their IR spectra. Compound **(75)** was further characterized from its ^{1}H-NMR spectral data. The two aromatic protons (ArH$_e$ & ArH$_d$) appeared at δ 8.04-8.02 & 7.19-7.17 respectively as doublets and the two protons of amide (NH$_f$) showed peak at δ 8.18. The methoxy protons (OCH$_{3h}$) were characterized by appearance of singlet at δ 4.72. It showed two triplets at δ 5.11-5.09 & 4.69-4.67 which belonged to methylene protons CH$_{2a}$ & CH$_{2c}$ respectively and the other two methylene protons CH$_{2b}$ were characterized by a multiplet at δ 3.22-3.19. Compound **(76)** showed characteristic IR peaks at 1655 and 1613 cm^{-1} and molecular ion peak at 268.5 m/z in its mass spectrum.



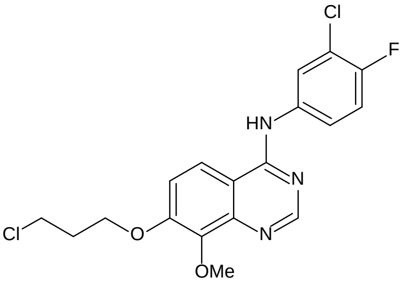
(75)



(76)



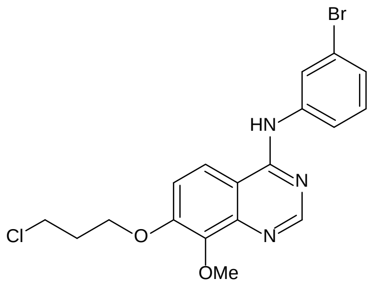
(77)



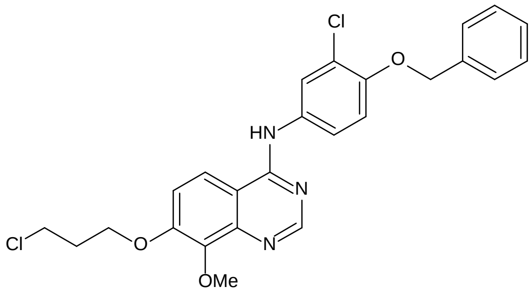
(78)

Compound **(77)** was synthesized by the reaction of quinazolinone **(76)** and 3-chloroaniline as per **Scheme-X**. Compound **(77)** showed characteristic peak at 3325 cm^{-1} (N-

H asym.) in its IR spectrum. 3-Chloro-4-fluoroaniline offered compound **(78)** which showed characteristic peak at 3375 cm^{-1} (N-H asym.) in its IR spectrum.

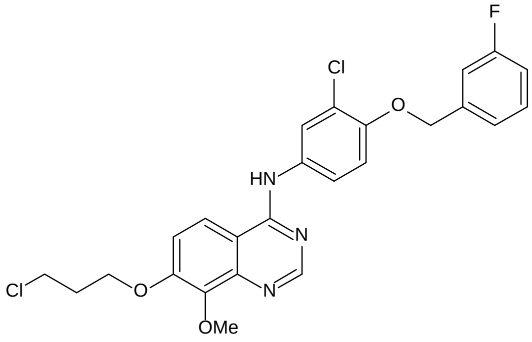


(79)

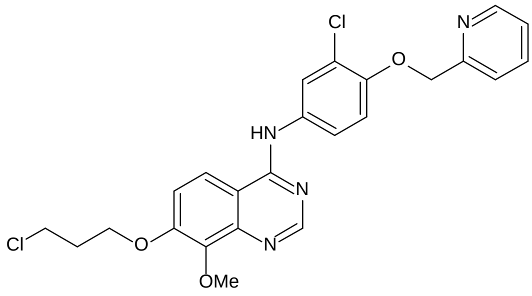


(80)

Compound **(79)** was obtained by reaction of compound **(76)** and 3-bromoaniline. IR spectrum of compound **(79)** showed characteristic peak at 3337 cm^{-1} (N-H asym.). 4-(Benzyloxy)-3-chloroaniline offered compound **(80)** from the quinazolinone **(76)** and aniline derivative **(21)** which showed characteristic peak at 3326 cm^{-1} (N-H asym.) in its IR spectrum.



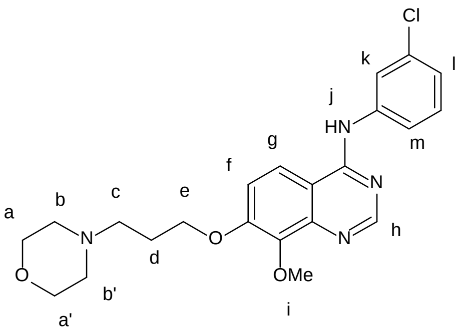
(81)



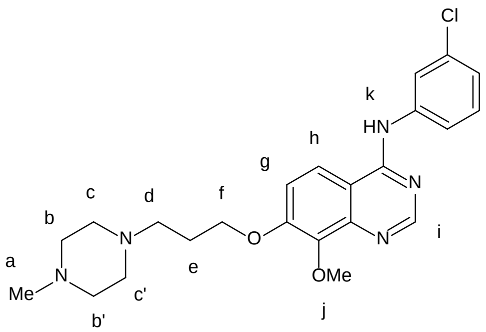
(82)

Compound **(81)** was synthesized by reaction of compound **(76)** and 3-chloro 4-(3-fluorobenzyloxy)aniline **(22)**. The IR spectrum of compound **(81)** showed characteristic peak at 3339 cm^{-1} (N-H asym.). 3-Chloro-4-(2-pyridinyl)methoxyaniline **(28)** on reaction with quinazolinone **(76)** as per **Scheme-X** offered compound **(82)**. It showed characteristic peak at 3445 cm^{-1} (N-H asym.) in its IR spectrum.

Compound **(77)** on reaction with morpholine afforded compound **(83a).** IR spectrum of **(83a)** showed peaks at 3168 (N-H asym.) and 1081 cm^{-1} (for ether). Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 8.79. The peaks for seven aromatic protons were observed in between δ 7.92-7.12 and a singlet at δ 4.03 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.27-4.25 & δ 2.67-2.65 respectively. Other two metylene protons (CH_{2d}) were characterized by a multiplet at δ 2.12-2.10. The peak for four chemically equivalent protons ($CH_{2a/a`}$) of morpholine moiety were observed at δ 3.77 and the other four $CH_{2b/b`}$ appeared at δ 2.56. Compound **(83b)** was obtained by reaction of compound **(77)** with N-methylpiperazine. IR spectrum of **(83b)** showed characteristic peaks at 3254 (N-H asym.) and 1083 cm^{-1} (for ether). Its ^1H-NMR spectrum showed broad singlet for NH_k at δ 8.11. The peaks for seven aromatic protons were observed in between δ 7.86-7.11 and a singlet at δ 3.89 represented methoxy (OCH_{3j}) protons. The methylene protons (CH_{2f} and CH_{2d}) showed triplets at δ 4.24-4.22 & δ 2.47-2.45 respectively. Other two metylene protons (CH_{2e}) were characterized by a multiplet at δ 1.95-1.93. The peaks for the protons of N-methylpiperazine appeared as multiplet between δ 2.33-2.30. 1,2,4- Triazole on reaction with compound **(77)** offered the desired compound **(83c).** IR spectrum of **83c** showed peaks at 3354 (N-H asym.) and 1088 cm^{-1} (characteristic for ether). Its ^1H-NMR spectrum showed broad singlet for NH_j at δ 9.69. The peaks for nine aromatic protons were observed in between δ 8.58-7.03 and a singlet at δ 3.97 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.45-4.43 & δ 4.18-4.16 respectively. Other two metylene protons (CH_{2d}) were characterized by multiplet at δ 2.37-2.35. Compound **(78)** was treated with morpholine in the presence of potassium carbonate to obtain compound **(84a).** IR spectrum of **84a** showed peaks at 3161 (N-H asym.) and 1080 cm^{-1} (for ether). Its ^1H-NMR spectrum showed broad singlet for NH_j at δ 8.75. The peaks for six aromatic protons were observed in between δ 7.90-7.15 and a singlet at δ 4.07 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.27-4.24 & δ 2.59-2.57 respectively. Other two metylene protons (CH_{2d}) were

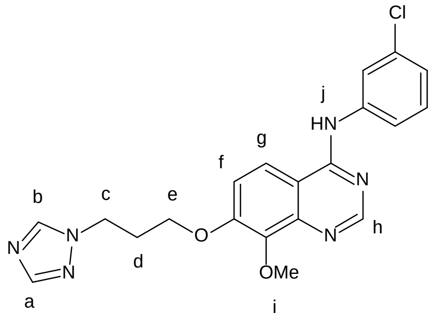


(83a)

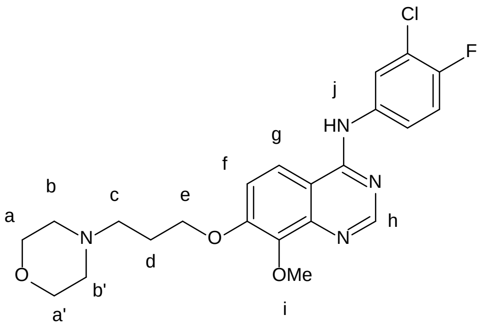


(83b)

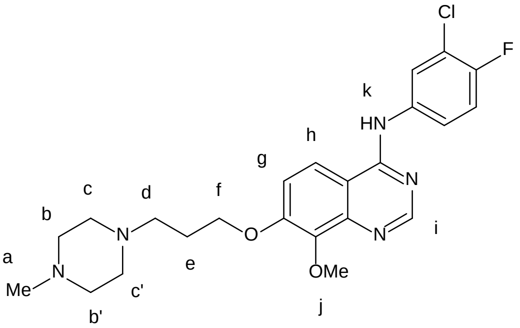
characterized by a multiplet at δ 2.07-2.05. The peak for four chemically equivalent protons ($CH_{2a/a`}$) of morpholine moiety were observed at δ 3.72 and the other four ($CH_{2b/b`}$) appeared at δ 2.48.



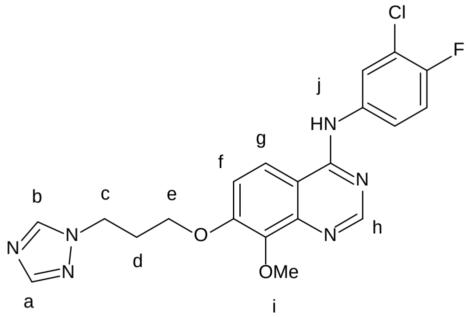
(83c)



(84a)



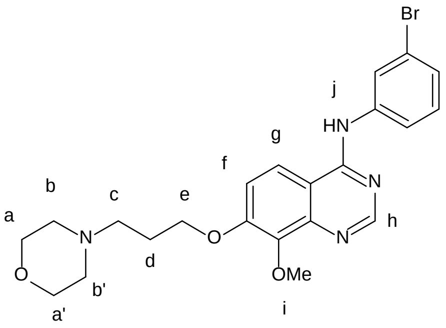
(84b)



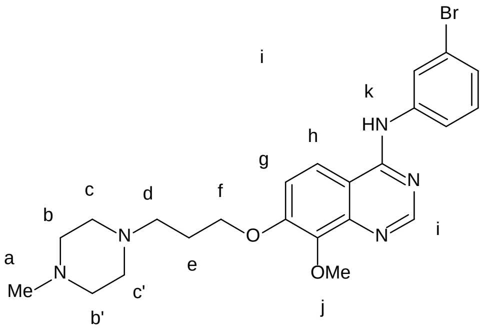
(84c)

N-Methylpiperazine on reaction with compound **(78)** offered compound **(84b).** Its IR spectrum showed characteristic peaks at 3260 cm^{-1} (N-H asym.) and at 1085 cm^{-1} (for ether). Its ^{1}H-NMR spectrum showed broad singlet for NH_k at δ 8.74. The peaks for seven aromatic protons were observed in between δ 7.92-7.16 and a singlet at δ 4.07 represented methoxy (OCH_{3j}) protons. The methylene protons (CH_{2f} and CH_{2d}) showed triplets at δ 4.25-4.23 & δ 2.61-2.59 respectively. Other two metylene protons (CH_{2e}) were characterized by multiplet at δ 2.08-2.05. The peak for the protons of N-methyl appeared as singlet at δ 2.29. 1,2,4-Triazole on reaction with chloro derivative **(78)** offered compound **(84c)** which showed characteristic peaks at 3275 cm^{-1} (N-H asym.) and 1090 cm^{-1} (for ether) in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 9.72. The peaks for nine aromatic protons were observed in between δ 8.60-7.33 and a singlet at δ 4.02 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.51-4.48 & δ 4.23-4.20 respectively. Other two metylene protons (CH_{2d}) were characterized by multiplet at δ 2.42-2.39.

Compound **(79)** was treated with morpholine to obtain the targeted compound **(85a).** The IR spectrum of **85a** showed peaks at 3255 and 1082 cm^{-1}. Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 9.56. The peaks for seven aromatic protons were observed in between δ 8.56-7.18 and a singlet at δ 3.94 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.23-4.21 & δ 2.54-2.51 respectively. Other two metylene protons (CH_{2d}) were characterized by multiplet at δ 2.02-1.99. The peaks for four chemically equivalent protons ($CH_{2a/a`}$) of morpholine moiety were observed at δ 3.61 and the other four ($CH_{2b/b`}$) protons appeared at δ 2.4. N-Methylpiperazine offered compound **(85b)** which showed characteristic IR peaks at 3247 and 1083 cm^{-1}. Its ^{1}H-NMR spectrum showed broad singlet for NH_k at δ 8.78. The peaks for seven aromatic protons were observed in between δ 8.04-7.27 and a singlet at δ 4.00 represented methoxy (OCH_{3j}) protons. The methylene protons (CH_{2f} and CH_{2d}) showed triplets at δ 4.25-4.23 & δ 2.33-2.31 respectively. Other two metylene protons (CH_{2e}) were characterized by a multiplet at δ 2.13-2.09. The peaks for the protons of piperazine appeared as multiplet between δ 2.29-2.22. Appearance of a singlet at δ 2.21 signifies presence of protons of N-methyl group.



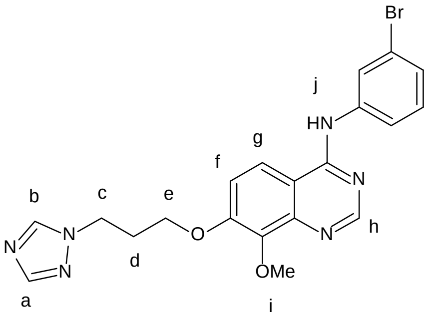
(85a)



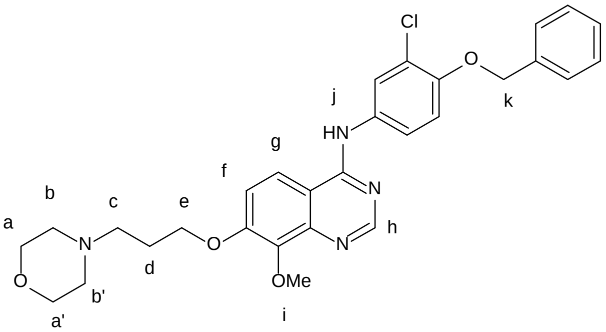
(85b)

1,2,4-Triazole offered compound **(85c)** which showed characteristic peaks at 3360 and 1089 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 9.66. The peaks for nine aromatic protons were observed in between δ 8.57-7.17 and a singlet at δ 3.97 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.45-4.43 & δ 4.17-4.14 respectively. Other two metylene protons (CH_{2d}) were characterized by a multiplet at δ 2.37-2.34. Compound **(80)** was treated with morpholine to afford the desired compound **(86a).** IR spectrum of **(86a)** showed peaks at 3262 (N-H asym.) and 1084 cm^{-1} (for ether). Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 8.70. The peaks for eleven aromatic protons were observed in between δ 7.77-6.95 and a singlet at δ 4.11 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e}

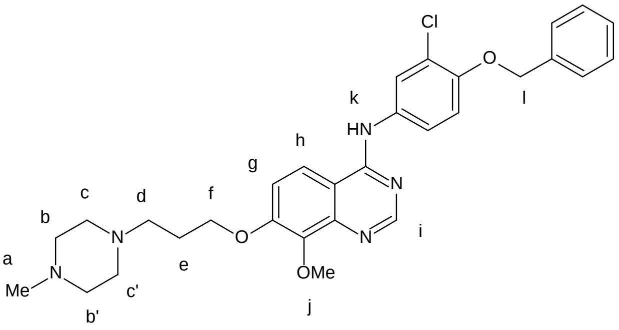
and CH_{2c}) showed triplets at δ 4.26-4.23 & δ 2.59-2.57 respectively. Other two methylene protons (CH_{2d}) were characterized by a multiplet at δ 2.08-2.05. Methylene protons (CH_{2k}) were characterized by a singlet at δ 5.14. The peak for four chemically equivalent protons ($CH_{2a/a`}$) of morpholine moiety were observed at δ 3.72 and the other four ($CH_{2b/b`}$) protons appeared at δ 2.48.



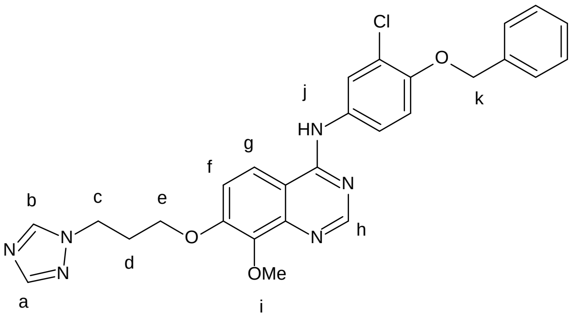
(85c)



(86a)



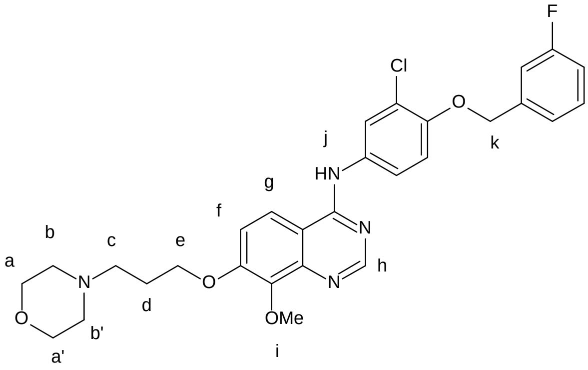
(86b)



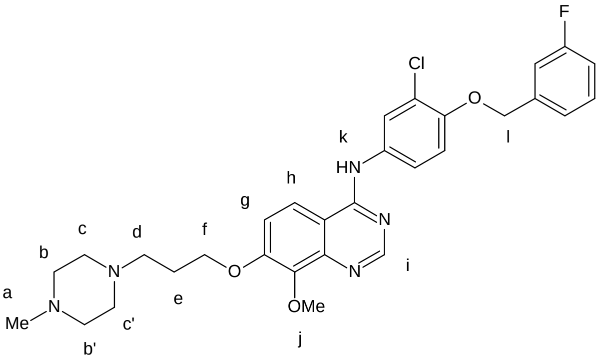
(86c)

N-Methylpiperazine on reaction with chloro derivative **(80)** offered compound **(86b).** The IR spectrum of **86b** showed characteristic peaks at 3139 and 1076 cm^{-1}. Its ^1H-NMR spectrum showed broad singlet for NH_k at δ 8.73. The peaks for eleven aromatic protons were observed in between δ 7.78-6.96. The methylene protons (CH_{2d}) showed triplet at 2.61-2.58. Other two metylene protons (CH_{2e}) were characterized by a multiplet at δ 2.08-2.04. The peaks for four chemically equivalent protons ($CH_{2b/b'}$) of N-methylpiperazine appeared at δ 2.32 and the other four ($CH_{2c/c'}$) at δ 1.79. 1,2,4- Triazole offered compound **(86c).** IR spectrum of **86c** showed characteristic peaks at 3139 and 1076 cm^{-1}. Its ^1H-NMR spectrum showed broad singlet for NH_j at δ 9.54. The peaks for thirteen aromatic protons were observed in between δ 8.52-7.01. Singlet at δ 5.19 represented methylene protons (CH_{2k}) and singlet at δ 4.03 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and

CH_{2c}) showed triplets at δ 4.51-4.48 & δ 4.20-4.18 respectively. Other two metylene protons (CH_{2d}) were characterized by a multiplet at δ 2.45-2.41.



(87a)



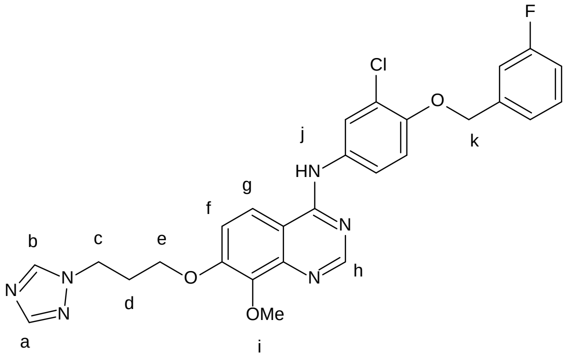
(87b)

Compound **(81)** was treated with morpholine to afford the targeted compound **(87a).** It showed characteristic IR peaks at 3145 and 1115 cm^{-1}. Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 8.73. The peaks for ten aromatic protons were observed in between δ 7.75-6.98 and a singlet at δ 4.07 represent methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.27-4.24 & δ 2.59-2.57 respectively. Other two methylene protons (CH_{2d}) were characterized by a multiplet at δ 2.08-2.04. The peaks for four chemically equivalent protons ($CH_{2a/a`}$) of morpholine moiety were observed at δ 3.72 and the other four ($CH_{2b/b`}$) appeared at δ 2.48.

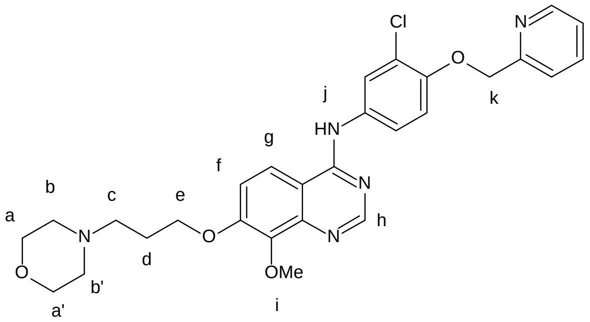
N-Methylpiperazine offered compound **(87b)** which showed characteristic peaks at 3179 and 1087 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlet for NH_k at δ 8.73. The peaks for ten aromatic protons were observed in between δ 7.77-6.95. Singlet of methylene protons (CH_{2l}) appeared at δ 5.14. Singlet at δ 4.07 represented methoxy (OCH_{3j}) protons. The methylene protons (CH_{2f} and CH_{2d}) showed triplets at 4.26-4.23 and 2.60-2.58 respectively. Other two metylene protons (CH_{2e}) were characterized by a multiplet at δ 2.09-2.05.

1,2,4-Triazole offered compound **(87c)** which showed characteristic peaks at 3257 and 1088 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlet for NH_j at δ 9.53. The peaks for twelve aromatic protons were observed in between δ 8.58-7.27. Singlet at δ 5.18 represented methylene protons (CH_{2k}) and a singlet at δ 4.03 represented methoxy (OCH_{3i}) protons. The methylene protons (CH_{2e} and CH_{2c}) showed triplets at δ 4.52-4.49 & δ

4.20-4.18 respectively. Other two metylene protons (CH$_{2d}$) were characterized by appearance of a multiplet at δ 2.44-2.40.

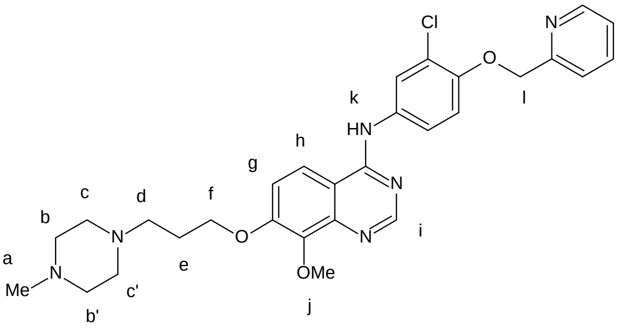


(87c)

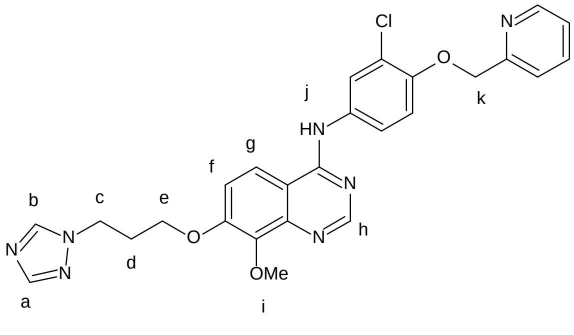


(88a)

Compound **(82)** was treated with morpholine to obtain the targeted compound **(88a).** IR spectrum of **(88a)** showed characteristic peaks at 3132 (N-H asym.) and at 1089 cm^{-1} (for ether). Its ^{1}H-NMR spectrum showed broad singlet for NH$_j$ at δ 8.71. The peaks for ten aromatic protons were observed in between δ 8.58-7.00 and a singlet at δ 4.06 represented methoxy (OCH$_{3i}$) protons. The methylene protons (CH$_{2e}$ and CH$_{2c}$) showed triplets at δ 4.26-4.23 & δ 2.66-2.64 respectively. Other two methylene protons (CH$_{2d}$) were characterized by a multiplet at δ 2.12-2.08. The peak for four chemically equivalent protons (CH$_{2a/a`}$) of morpholine moiety were observed at δ 3.77.3.74 and the other four (CH$_{2b/b`}$) appeared at δ 2.55.



(88b)



(88c)

N-Methylpiperazine offered compound **(88b)** which showed characteristic peaks at 3173 and 1088 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlet for NH$_k$ at δ 8.73. The peaks for ten aromatic protons were observed in between δ 8.59-7.02. Singlet at δ 4.07 represented methoxy (OCH$_{3j}$) protons. The methylene protons (CH$_{2f}$ and CH$_{2d}$) showed triplets at 4.25-4.22 and 2.66-2.64 respectively. Other two metylene protons (CH$_{2e}$)

were characterized by a multiplet at δ 2.09-2.05. Reaction of 1,2,4-triazole offered compound **(88c)** which showed characteristic peaks at 3121 and 1078 cm^{-1} in its IR spectrum. Its ^{1}H-NMR spectrum showed broad singlet for NH$_j$ at δ 8.69. The peaks for twelve aromatic protons were observed in between δ 8.57-6.97. Singlet at δ 4.03 represented methoxy (OCH$_{3i}$) protons. The methylene protons (CH$_{2e}$) appeared as triplet at δ 4.48.4.45. Other two metylene protons (CH$_{2d}$) were characterized by a multiplet at δ 2.48-2.43.

3.2 Biological work

The synthesized compounds were sent to National Cancer Institute-Developmental Therapeutics Program (NCI-DTP) for evaluation for anticancer activity. As per their requirements, the molecular files were to be uploaded on their site for *in silico* selection of

Table 2: Five dose screening results of the selected compounds for anticancer activity on cell lines

Compound	Cell line	GI$_{50}$ (µM)	TGI (µM)
57d (MCR-977)	SR	0.35	41 µM
	HT29	0.57	3.46
	MDA-MB-435	0.28	1.1
	OVCAR-4	0.41	2.0
	A-498	0.47	4.17
58d (MCR-970)	SNB-75	2.0	6.82
	MDA-MB-435	1.15	4.56
	MDA-MB-468	1.95	6.38
56d (MCR-957)	RPMI-8226	0.69	10.0
	NCI-H522	0.54	2.68
	MDA-MB-468	0.43	2.08
58a (MCR-967)	SW-620	0.90	12.5
	SF-268	0.92	14.8
71g (MCR-999)	K-562	1.85	3.59
	EKVX	1.54	3.79
	SNB-75	1.35	2.66
	HS-578T	1.03	2.71

the molecules. Out of the molecular files of total ninety two (92) compounds uploaded, thirty one (31) compounds were selected and evaluated experimentally for single dose assay as anticancer agents on different cell lines. In this study, five compounds showed very good inhibitory activity on different cell lines hence these five compounds were selected for five dose assay **(Table-2)**.

Eli Lilly has started a drug discovery program named, "Open Innovation Drug Discovery" wherein potential compounds for different types of biological activities can be sent to Eli Lilly for evaluation. The compounds are selected by Eli Lilly on the basis of fulfillment of certain parameters fixed by them.

Information for all of the synthesized compounds was sent to the OIDD program. Out of these, twenty four (24) compounds were chosen and screened for different types of biological activities. Result of four compounds for receptor binding studies is given in **Table 3**. The detailed biological screening of the selected compounds is in progress.

Table 3: Screening results of the selected compounds under OIDD program

Compound	**Receptor**	**EC$_{50}$ (μM)**	**IC$_{50}$ (μM)**
57d (MCR-979)	ATP-DLD-1	-	0.06
	ATP-SW-480	0.118	-
	ATP-Colo-320	-	0.039
58d (MCR-970)	Wnt3a C2C12 Osteogen b-catenin	0.766	-
	Wnt3a C2C12 Osteogen Alkphos	0.954	-
56g (MCR-960)	Wnt3a C2C12 Osteogen Alkphos	5.602	-
	PCSK9 Hep G2	-	0.859
57f (MCR-980)	hSETD8 SPA	-	1.379

Analysis of the results would be possible after receiving the report in detail.