(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 August 2012 (23.08.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/111017 A1

(51) International Patent Classification:
C07D 239/91 (2006.01) *C07D 409/10* (2006.01)
C07D 401/10 (2006.01) *A61K 31/517* (2006.01)
C07D 405/06 (2006.01) *A61P 35/00* (2006.01)

(21) International Application Number:
PCT/IN2011/000228

(22) International Filing Date:
31 March 2011 (31.03.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
391/DEL/2011 15 February 2011 (15.02.2011) IN

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

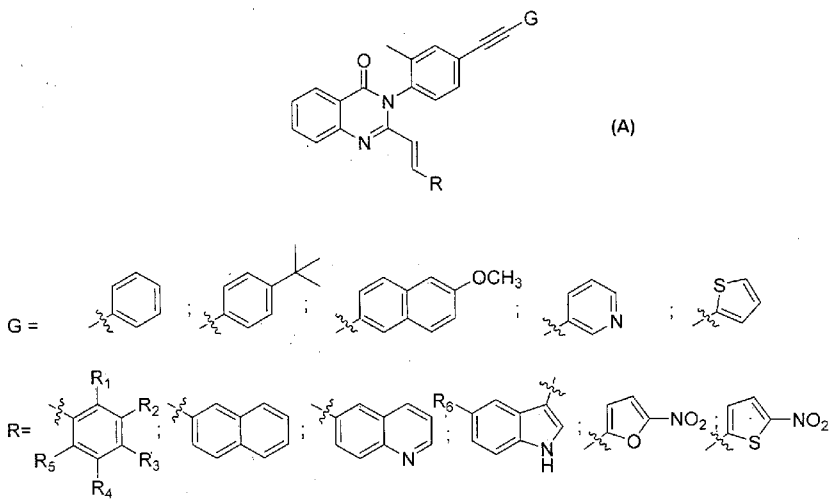
Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *of inventorship (Rule 4.17(iv))*

[Continued on next page]

(54) Title: 3-ARYLETHYNYL SUBSTITUTED QUINAZOLINONE COMPOUNDS



(57) Abstract: The present invention provides 3-arylethynyl substituted quinazolinone compounds of formula (A) as potential anticancer agents against sixty human cancer cell lines. R_1 = H, OH, OCH_3; R_2 = H, OH, CH_3,OCH_3, NO_2; R_3 = H, OH, OCH_3, F, Cl; R_2+R_3 = -OCH_2O-; R_4 = H, OH, CH_3, OCH_3; R_5 = H, OH, CH_3, OCH_3; R_6 = H, OCH_3.

WO 2012/111017 A1

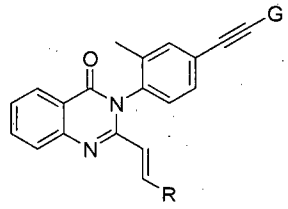
Published:

— *with international search report (Art. 21(3))*

3-ARYLETHYNYL SUBSTITUTED QUINAZOLINONE COMPOUNDS

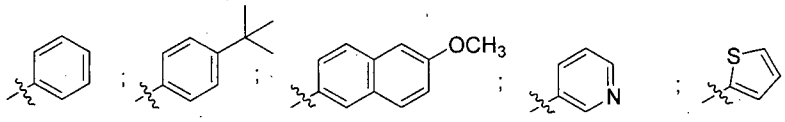
FIELD OF THE INVENTION

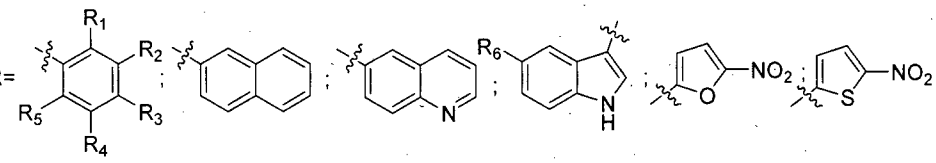
The present invention relates to 3-Arylethynyl substituted quinazolinone compounds of general formula A as potential anticancer agents and a process for the preparation thereof.



General formula A

Wherein,

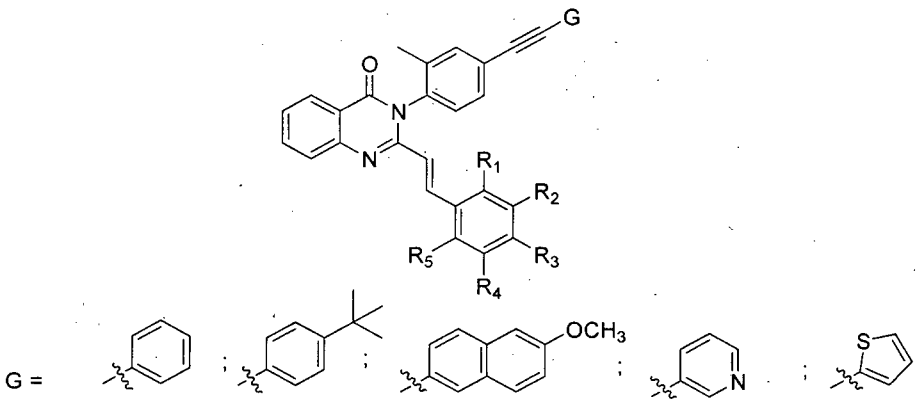
G = 

R= 

R_1= H, OH, OCH_3
R_2= H, OH, CH_3, OCH_3, NO_2
R_3= H, OH, OCH_3, F, Cl
R_2+R_3= $-OCH_2O-$

R_4= H, OH, CH_3, OCH_3
R_5= H, OH, CH_3, OCH_3
R_6= H, OCH_3

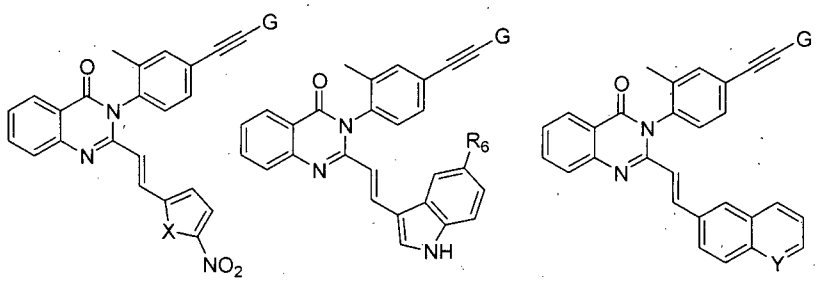
The structural formula of the representative compounds of 3-Arylethynyl substituted quinazolinone compounds of general formula A are:



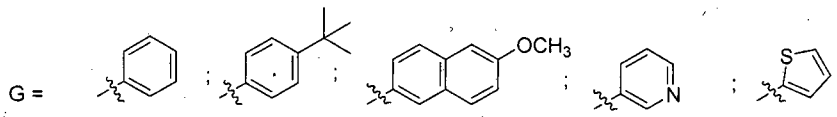
R_1= H, OH, OCH_3
R_2= H, OH, CH_3, OCH_3, NO_2
R_3= H, OH, OCH_3, F, Cl
R_4= H, OH, CH_3, OCH_3
R_5= H, OH, CH_3, OCH_3

R_2+R_3= $-OCH_2O-$ For compounds **4j**, **5j**, **6j**, **7j**, **8j**

Formula **4a-n to 8a-n**



formula 9a-b to 13a-b **formula 14a-b to 18a-b** **formula 19a-b to 23a-b**



R_6= H, OCH_3
X= O, S
Y=CH, N

BACKGROUND OF THE INVENTION

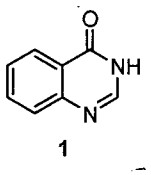
Poly(ADP-ribose)polymerase-1 (PARP-1) a nuclear enzyme bounded to chromatin involved in a variety of physiological functions related to genomic repair, including DNA replication and repair, cellular proliferation and differentiation, and apoptosis. Inhibition of these PARP enzyme results in genomic dysfunction and finally leading to cell death (Ferraris, D. V. *J. Med. Chem.* **2010**, 53, 4561).

Quinazolinone (**1**) is a naturally occurring alkaloid as well as a core structural subunit in a growing class of bioactive natural products and synthetic compounds (Michael, J. P. *Nat. Prod. Rep.* 2004, *21*, 650'' and also D'yakonov, A. L.; Telezhenetskaya, M. V. *Chem. Nat. Comput.* 1997, *33*, 221). Recently various quinazolinone compounds were identified as dual inhibitors of P-glycoprotein (Pgp) and the multidrug resistance associated protein (MRP1). These proteins cause resistance in tumor cells hence inhibition of these proteins were useful in cancer chemotherapy (Wang, S.; Ryder, H.; Pretswell, I.; Depledge, P.;

Milton, J.; Hancox, T. C.; Dale, I.; Dangerfield, W.; Charlton, P.; Faint, R.; Dodda, R.; Hassan, S. *Bioorg. Med. Chem. Lett.* 2002, *12*, 571). Recently a library of quinazollinone compounds containing 2-styryl quinazolinone compounds possessing a defining structural feature, containing 3-substituted aliphatic chain bearing basic nitrogen,exhibiting cytotoxicity against various cancer cell lines.(Liu, J. F.; Kaselj, M.; Isome, Y.; Ye, P.; Sargent, K.; Sprague, K.; Cherrak, D.; Wilson, C. J.; Si, Y.; Yohannes, D.; Ng, S.C. *J Comb Chem.* 2006, *8*, 7-10). Various substituted 2-phenyl-4-quinazolinones and 2,3-dihydro-2-phenyl-4-quinazolinones displayed highly selective cytotoxicity against the ovarian cancer 1A9 and P-gp resistant KB-VIN cell lines and these compounds acts as tubulin polymerization inhibitiors.(Hour, M. J.; Huang, L. J.; Kuo, S. C.; Xia, Y.; Bastow, K.; Nakanishi, Y.; Hamel, E.; Lee, K. H. *J. Med. Chem.* 2000, 43, 4479). Moreover a new class of 4(3*H*)-quinazolinones 2-styryl substituted derivatives (**2**) form an important component of pharmacologically active compounds which exhibit anticancer activity by inhibition of tubulin polymerization.(Jiang, J. B.; Hesson, D. P.; Dusak, B. A.; Dexter, D. L.; Kang, G. J.; Hamel, E. *J. Med. Chem.* 1990, *33*, 1721" and also Raffa, D.; Edler, M. C.; Daidone, G.; Maggio, B.; Merikech, M.; Plescia, S.; Schillaci, D.; Bai, R.; Hamel, E. *Eur. J. Med. Chem.* 2004, *39*, 299). Whereas a novel series containing 2-methyl quinazolinones and 2-aryl quinazolinones act as inhibitors of DNA repair enzyme poly (ADP-ribose) polymerase.(Griffin, R. J.; Srinivasan, S.; Bowman, K.; Calvert, A. H.; Curtin, N. J.; Newell, D.R.; Pemberton, L. C.; Golding, B. T. J. Med. Chem. 1998, 41, 5247).

Recently a series of 3-aryl ethynyl substituted quinoline-8-carboxamide were synthesized and identified as a new class of PARP inhibitors.(Lord, A.M.; Mahon, M. F.; Lloyd, M. D.; Threadgill, M. D. *J. Med. Chem.* 2009, *52,* 868–877) and also a new series of 3-ethynyl-1H-indazoles (**3**) has been synthesized and exhibited low micro molar inhibition against critical components of the PI3K pathway, targeting PI3K, PDK1, and mTOR kinases, These compound displays significant antiproliferative activity both in monolayer human cancer cell cultures and in three dimensional tumor models and these identified as multiple PI3K/PDK1/mTOR inhibitors. (Barile, E.; De, S. K.; Carlson, C. B.; Chen, V.; Knutzen, C.; Riel-Mehan, M.; Yang, L.; Dahl,R.; Chiang, G.; Pellecchia, M.). More recently structure-activity relationship study revealed the rigid triple bond functionality also contributed to the observed antiviral activity and also antiproliferative activity for ethynyltriazole ribonucleosides which are showing potent apoptosis-induced antiproliferative activity against pancreatic cancer MiaPaCa-2 cells both in vitro and in vivo The role of ethynyl group may be due to appended π-conjugated systems to offer helpful binding properties with the corresponding biological targets via the stronger interactions afforded by a larger aromatic binding surface and better shape complementary conjugated system.(Wan J, Xia Y, Liu Y, Wang M, Rocchi P, Yao J, Qu F, Neyts J, Iovanna JL, Peng L. *J. Med. Chem.* 2009, *52,* 1144–1155).

Keeping this aspect in mind, various aryl ethynyl groups are incorporated at *N*-3 position of quinazolinones. Further structural modifications have also been carried out at position 2 of quinazolinone ring. Thereby, the newly designed and synthesized molecules comprising of quinazolinone and phenyl ethynyl moiety could possess promising anticancer activity that might work through inhibition of PARP. Additionally, these are structurally simple small molecules.



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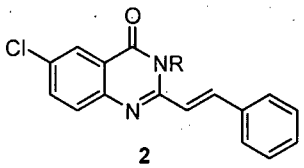

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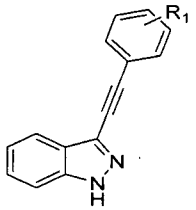


3

OBJECTIVES OF THE INVENTION

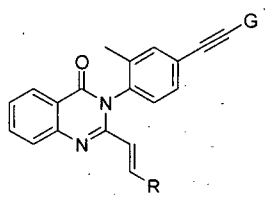
The main objective of the present invention is to provide 3-Arylethynyl substituted quinazolinone compounds of general formula A.

Another objective of the present invention is to provide process for the preparation of 3-Arylethynyl substituted quinazolinone compounds of general formula A.

Still another objective of the present invention is to provide 3-Arylethynyl substituted quinazolinone compounds of general formula A as potential anticancer agents.

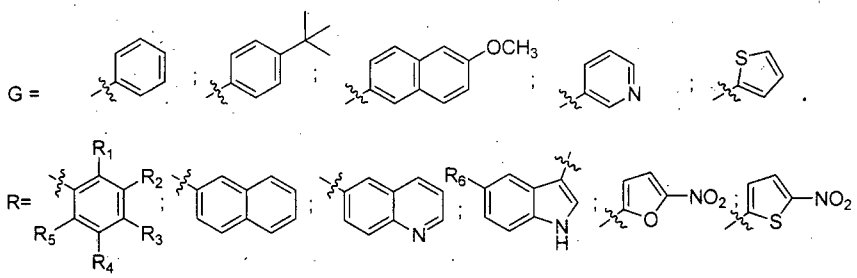
SUMMARY OF THE INVENTION

Accordingly, present invention provides 3-Arylethynyl substituted quinazolinone compounds of general formula A

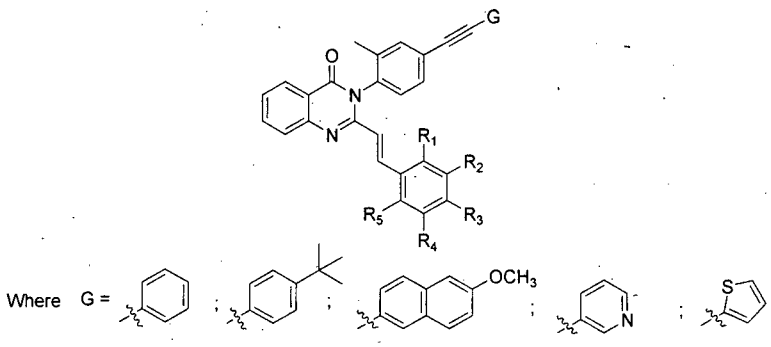


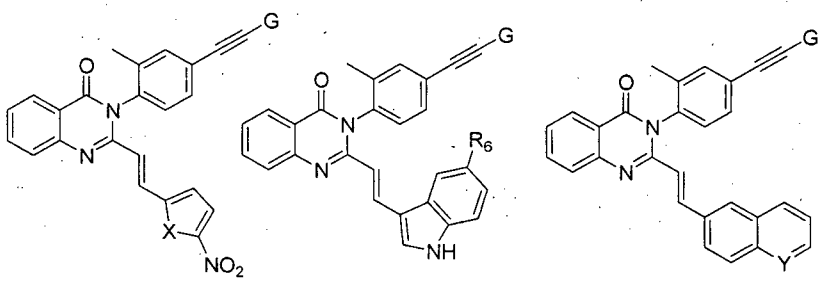
General formula A

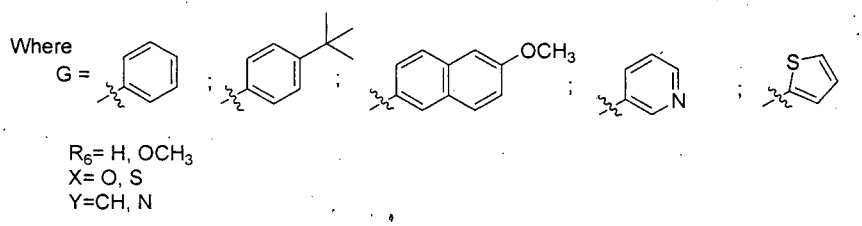
Wherein,



In yet another embodiment of the present invention, structural formulas of the representative group of 3-Arylethynyl substituted quinazolinone compounds are:







In yet another embodiment of the present invention, said compounds are useful as anticancer agent.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of general formula A, wherein chemical formula of the compounds are:

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-methylstyryl)quinazolin-4(3*H*)-one (**4a**);

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4e**);

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(2-methyl-4-phenylethynyl) phenyl) quinazolin-4(3*H*)-one (**4g**)

(*E*)-2-(3,4-Dimethoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3H)-one (**4h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one(**4i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(2-methyl-4-(phenylethynyl) phenyl) quinazolin-4(3*H*)-one (**4j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(2-methyl-4-phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4k**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (**4l**);

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4m**);

(*E*)-2-(4-Chlorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4n**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-methylstyryl) quinazolin-4(3H)-one (**5a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxystyryl) quinazolin-4(3*H*)-one (**5b**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2,5-dihydroxystyryl)quinazolin-4(3*H*)-one (**5c**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)phenyl)-2-(2,4-dihydroxystyryl) quinazolin-4(3*H*)-one (**5d**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxy-3-nitrostyryl) quinazolin-4(3*H*)-one (**5e**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-methoxystyryl) quinazolin-4(3*H*)-one (**5f**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxy-3-methoxystyryl) quinazolin-4(3*H*)-one (**5g**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(3,4-dimethoxystyryl) quinazolin-4(3*H*)-one (**5h**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2,4-dimethoxystyryl)quinazolin-4(3*H*)-one (**5i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(4-((4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**5j**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxy-3,5-dimethylstyryl) quinazolin-4(3*H*)-one (**5k**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (**5l**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-fluorostyryl) quinazolin-4(3*H*)-one (**5m**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-chlorostyryl) quinazolin-4(3*H*)-one (**5n**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-methylstyryl)quinazolin-4(3*H*)-one (**6a**);

(*E*)-2-(4-Hydroxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6e**);

(*E*)-2-(4-methoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6g**);

(*E*)-2-(3,4-Dimethoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6k**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (**6l**);

(*E*)-2-(4-Fluorostyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6m**);

(*E*)-2-(4-Chlorostyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6n**)

(E)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-methylstyryl)quinazolin-4(3*H*)-one (**7a**);

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7e**);

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7g**);

(*E*)-2-(3,4-Dimethoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**7k**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (**7l**);

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl)quinazolin-4(3*H*)-one(**7m**);

(*E*)-2-(4-Chlorostyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl)quinazolin-4(3*H*)-one(**7n**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-methylstyryl) quinazolin-4(3*H*)-one (**8a**);

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl)quinazolin-4(3*H*)-one (**8b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**8c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8e**);

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**8f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**8g**);

(*E*)-2-(3,4-Dimethoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**8h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8i**);

(*E*)-2-(2-(Benzo[d][1,3]dioxol-5-yl)vinyl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**8k**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (**8l**);

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3H)-one (**8m**);

(*E*)-2-(4-Chlorostyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8n**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3H)-one (**9a**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**9b**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**10a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl) quinazolin-4(3*H*)-one (**10b**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**11a**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**11b**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**12a**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**12b**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**13a**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**13b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**14a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(2-methyl-4-(phenylethynyl) phenyl) quinazolin-4(3*H*)-one (**14b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(4-((4-*tert*-butylphenyl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**15a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-methoxy-1H-indol-3-yl)vinyl)quinazolin-4(3*H*)-one (**15b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**16a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**16b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(2-methyl-4-(pyridin-3-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**17a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(2-methyl-4-(pyridin-3-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**17b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**18a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl)quinazolin-4(3*H*)-one(**18b**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(naphthalen-2-yl)vinyl) quinazolin-4(3*H*)-one (**19a**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(quinolin-6-yl)vinyl) quinazolin-4(3*H*)-one (**19b**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(naphthalen-2-yl)vinyl) quinazolin-4(3*H*)-one (**20a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(quinolin-6-yl)vinyl)quinazolin-4(3*H*)-one (**20b**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(naphthalen-2-yl)vinyl)quinazolin-4(3H)-one (**21a**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(quinolin-6-yl)vinyl)quinazolin-4(3*H*)-one (**21b**);

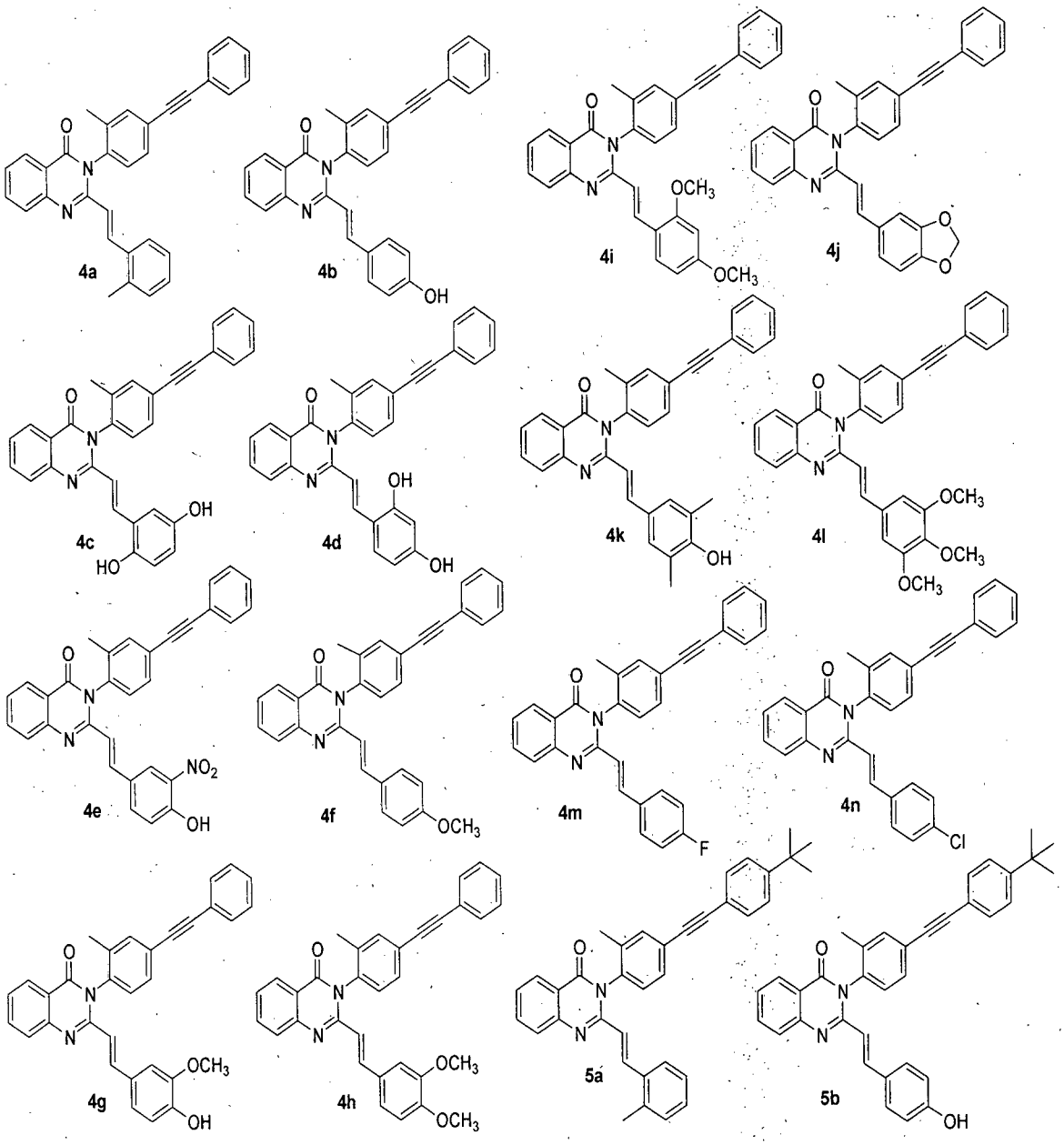
(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(naphthalen-2-yl)vinyl)quinazolin-4(3*H*)-one (**22a**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(quinolin-6-yl)vinyl)quinazolin-4(3*H*)-one (**22b**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(naphthalen-2-yl)vinyl)quinazolin-4(3*H*)-one (**23a**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(quinolin-6-yl)vinyl) quinazolin-4(3*H*)-one (**23b**).

In yet another embodiment of the present invention, structural formulae of the 3-Arylethynyl substituted quinazolinone compounds of general formula A are: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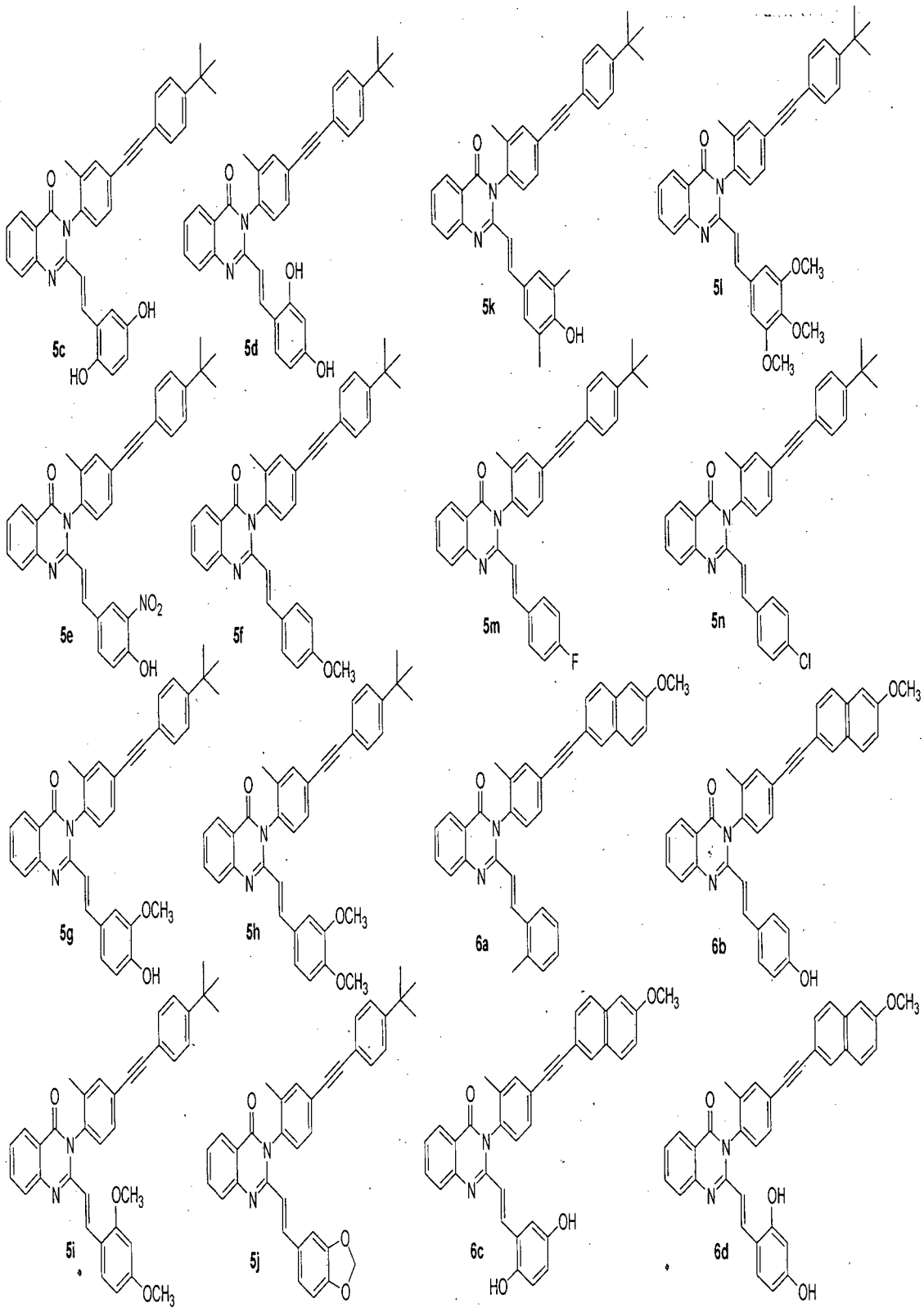
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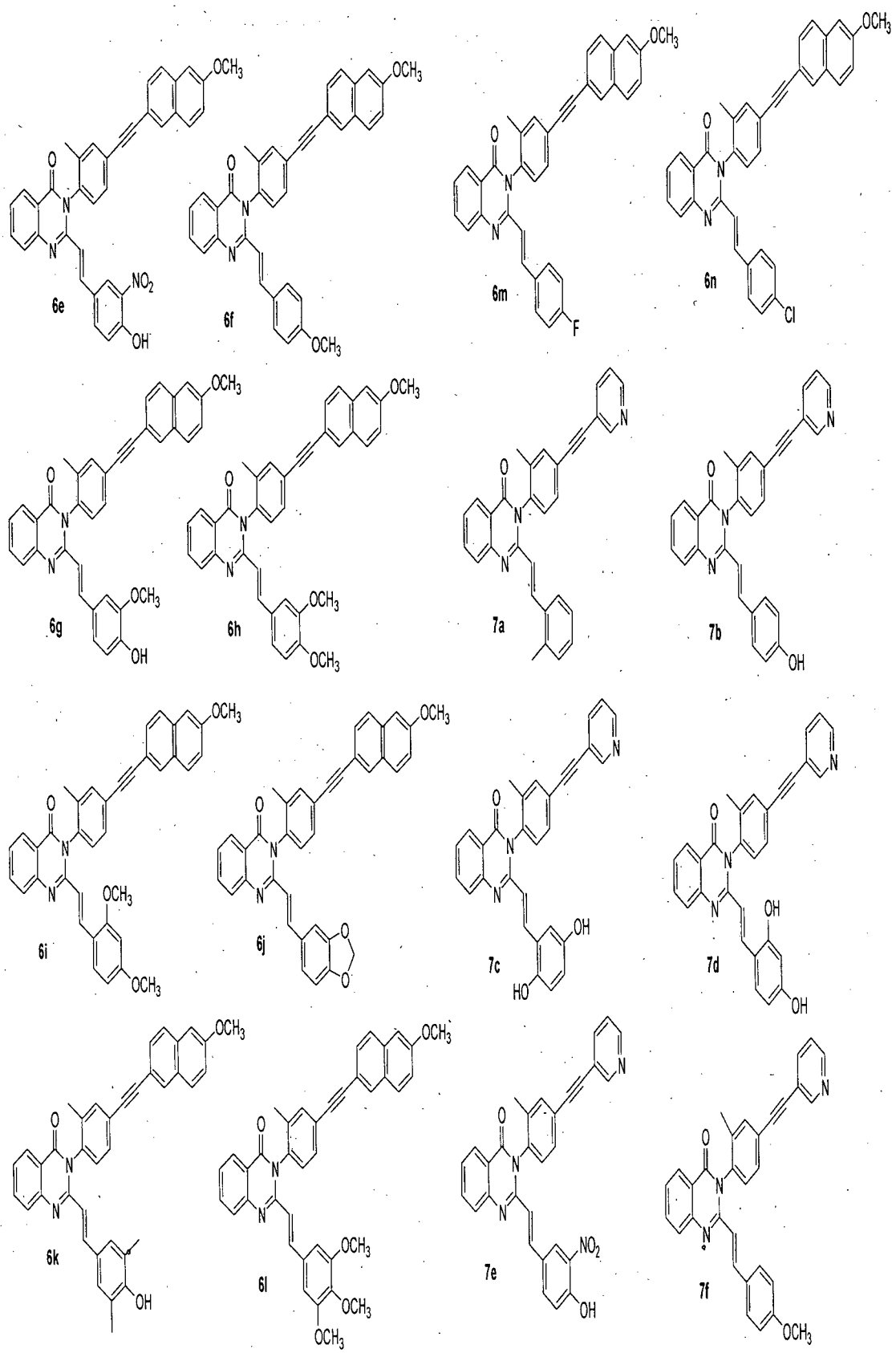
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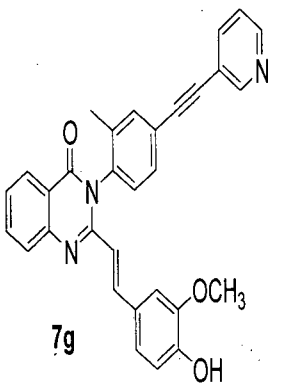
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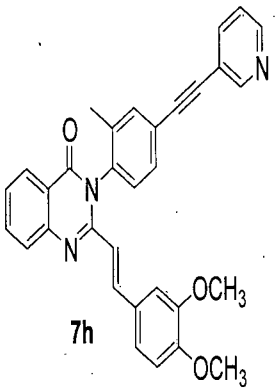
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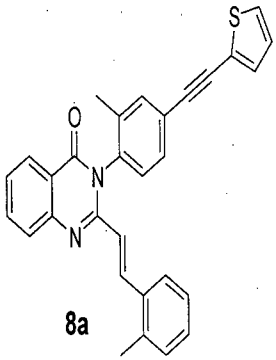
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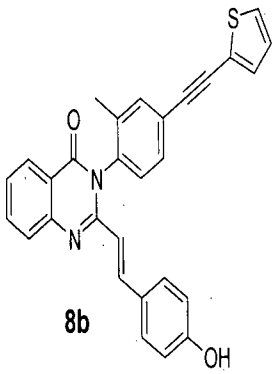
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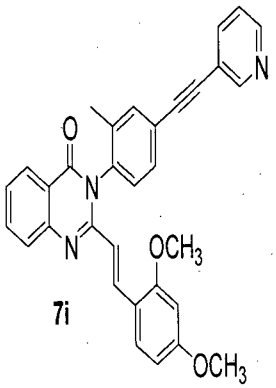
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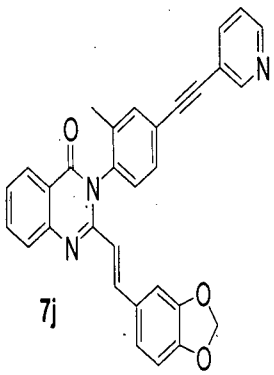
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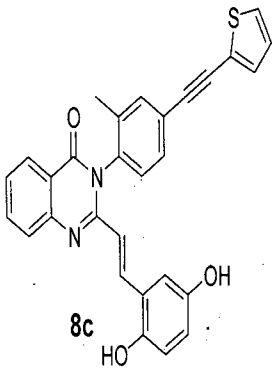
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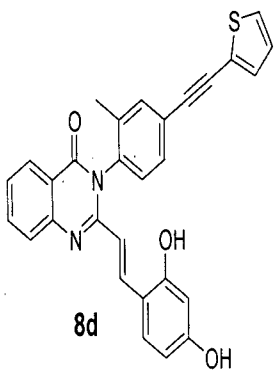
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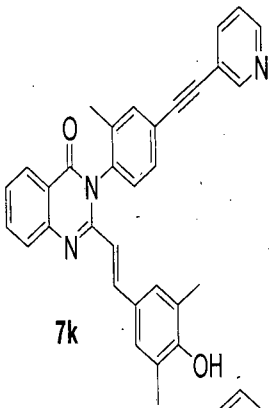
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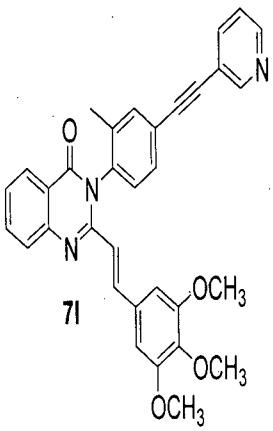
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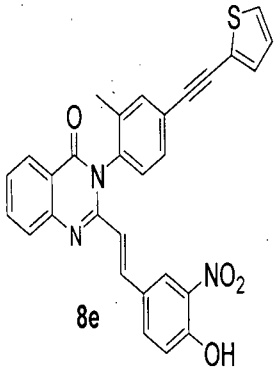
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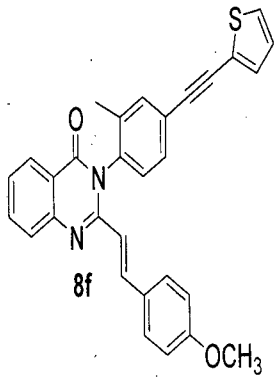
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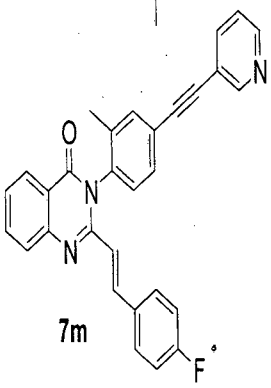
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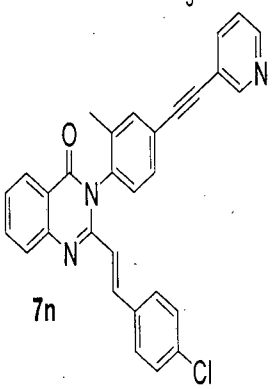
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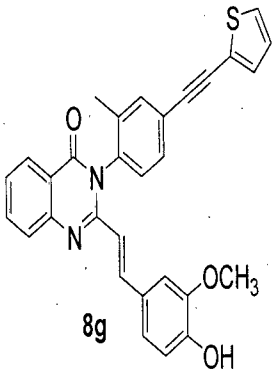
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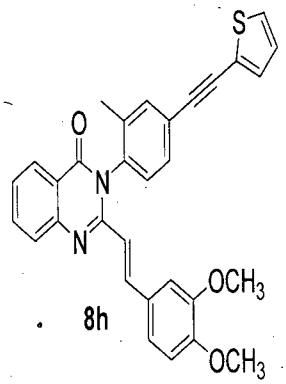
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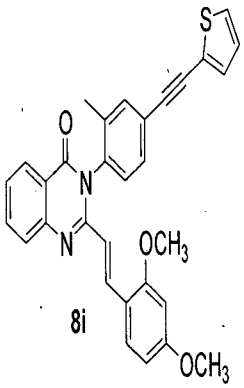
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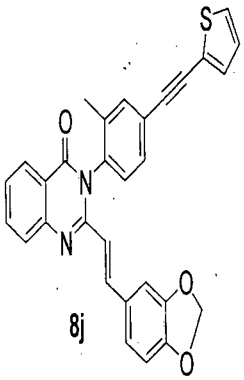
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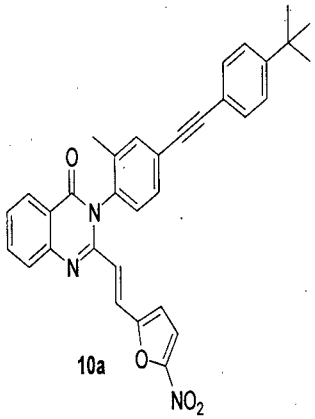
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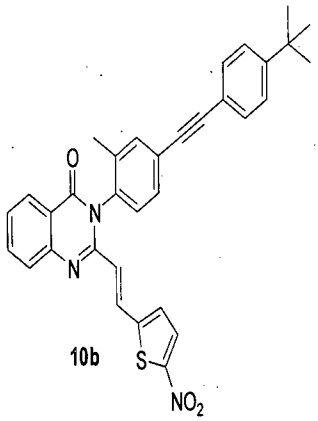
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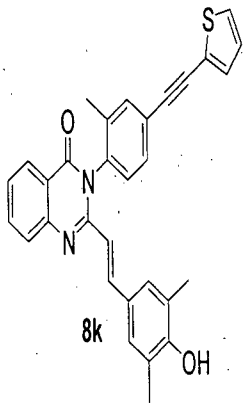
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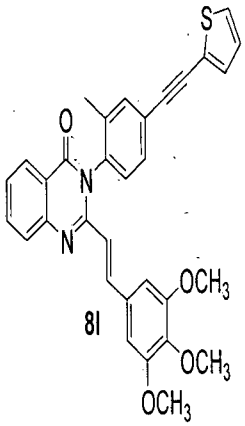
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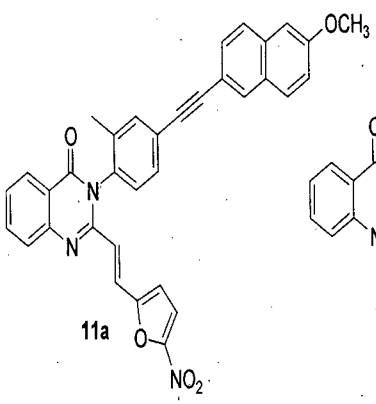
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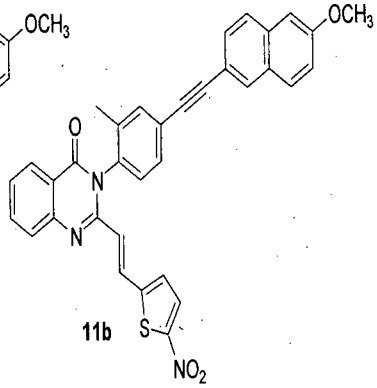
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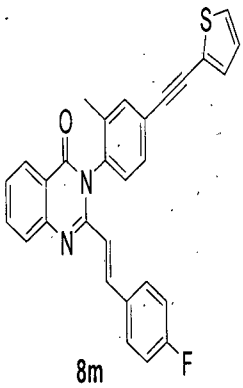
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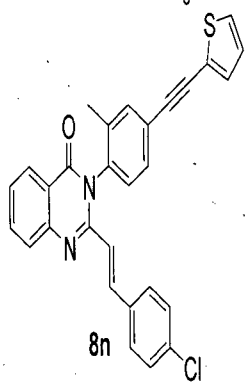
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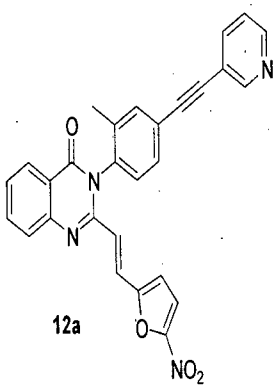
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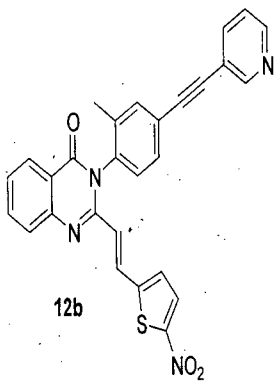
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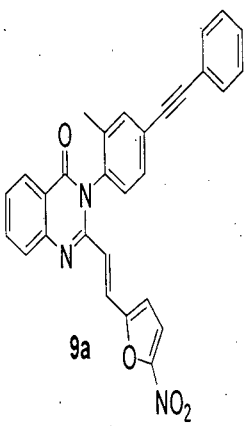
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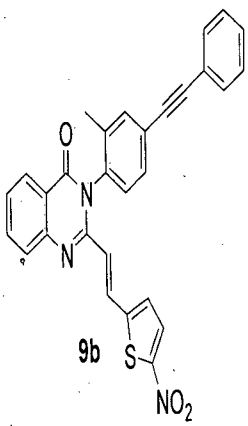
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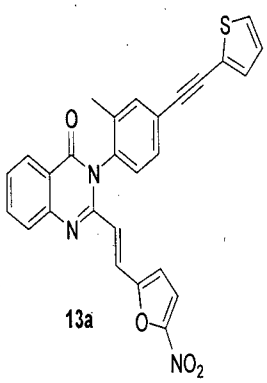
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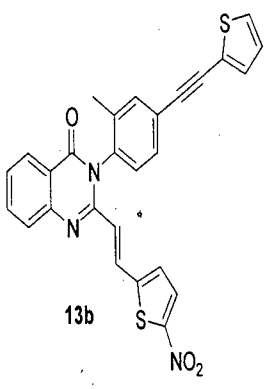
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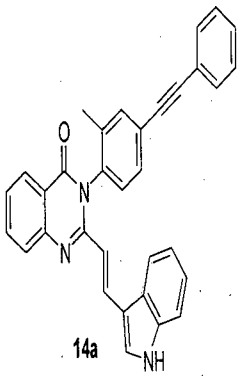
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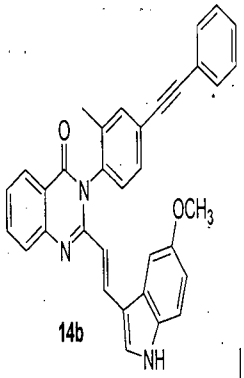
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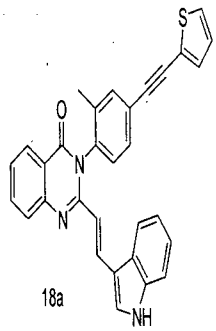
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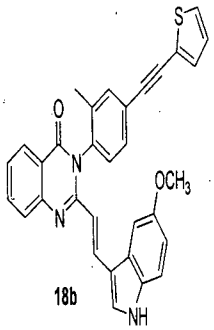
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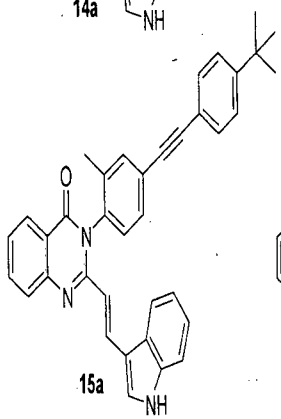
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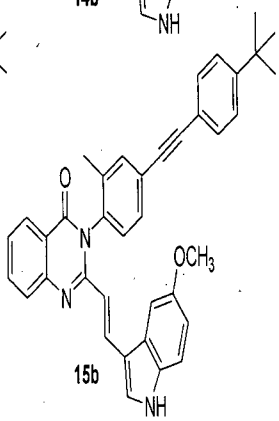
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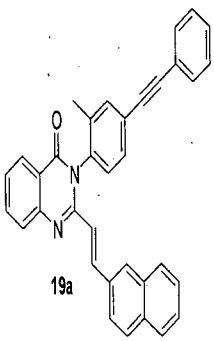
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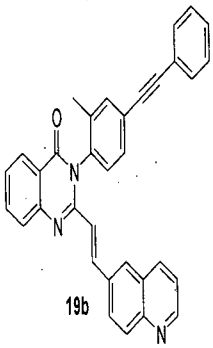
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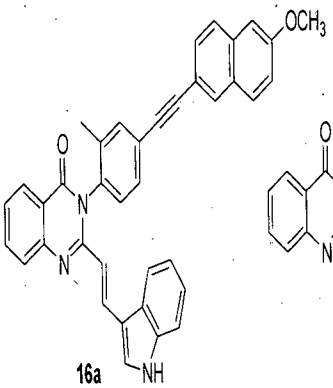
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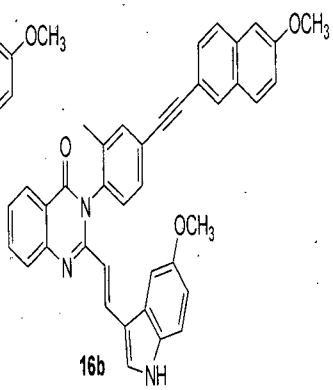
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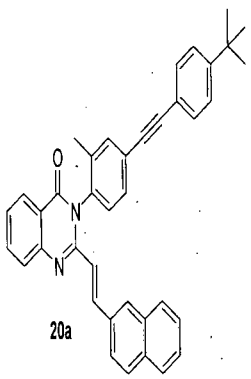
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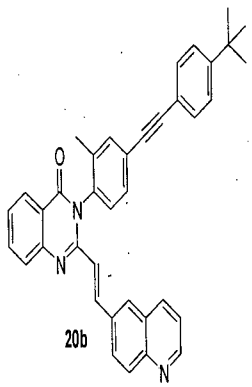
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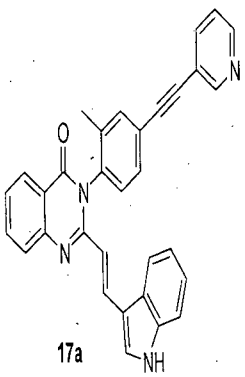
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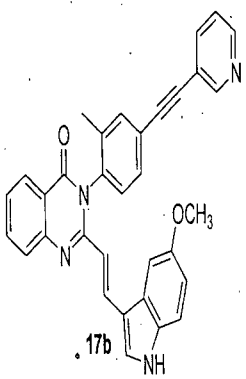
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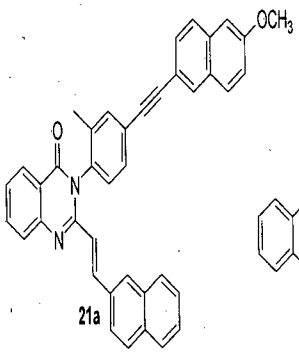
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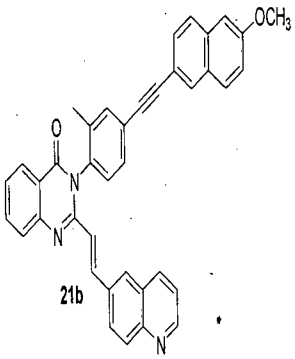
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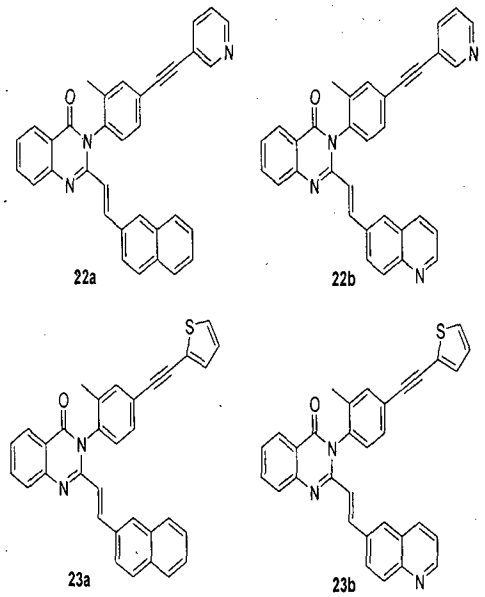


In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds are useful as anticancer agent.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against sixty human cancer cell lines derived from nine cancer types leukemia cell line, non small cell lung cell line, colon cell line, CNS cell line, renal cell line, prostate cell line, ovarian cell line, breast and melanoma cell line.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against six leukemia cancer cell lines (CCRF-CEM, HL-60, K-562, MOLT-4, SR and RPMI-8226) for GI_{50} are in the range of 1.66 to 3.26, 0.634 to 1.54, 2.45 to 3.85 and 0.395 to 4.66 μM, respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against nine non-small cell lung cancer cell lines (A549/ATCC, EKVX, HOP-62, HOP-92, NCI-H226, NCI-H23, NCI-H322M, NCI-H460 and NCI-H522) for GI_{50} are in the range of 2.22 to 13.1, 1.24 to 1.71, 1.82 to 6.09 and 2.48 to 40.5 μM, respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against seven colon cancer cell line (COLO 205, HCC-2998, HCT-116, HCT-15, HT29, KM12 and SW-620) for GI_{50} are in the

range of 1.99 to 4.08, 1.03 to 1.95, 1.81 to 3.33 and 1.22 to 17.2 μM, respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against six CNS cancer cell line (SF-268, SF-295, SF-539, SNB-19, SNB-75 and U251) for GI_{50} are in the range of 2.85 to 6.91, 1.30 to 1.62, 1.87 to 7.90, 7.40 μM, respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** said compoundsexhibiting an *in vitro* anticancer activity against eight renal cancer cell line (786-0, A498, ACHN, CAKI-1, SN12C, TK-10, UO-31 and RXF 393) for are in the range of 1.56 to 3.77, 0.370 to 2.15, 1.88 to 5.08, 4.91μM, respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** exhibiting an *in vitro* anticancer activity against two prostate cancer cell line (PC-3, DU-145) for GI_{50} are 3.24 to 4.87, 0.419 to 2.19, 3.42 to 3.67 μM, respectively at an exposure period of at least 48 h.

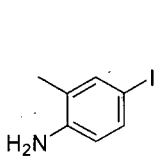
In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against seven ovarian cancer cell lines (IGROV1, OVCAR-3, OVCAR-4, OVCAR-5, OVCAR-8, NCI/ADR-RES and SK-OV-3) for GI_{50} are in the range of 3.09 to 20.6, 1.39 to 2.45, 2.23 to 10.9 and 19.3μM respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against six breast cancer cell line (MCF-7, MDA-MB-231/ATCC, HS 578T, TD-47D , MDA-MB-468 and BT-549) for GI_{50} are in the range of 2.02 to 3.89, 1.14 to 1.61, 2.20 to 8.60, 3.80 to 63.8 μM, respectively at an exposure period of at least 48 h.

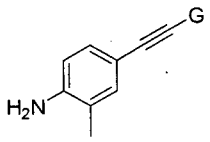
In yet another embodiment of the present invention, 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** exhibiting an *in vitro* anticancer activity against nine melanoma cancer cell line (LOX IMVI, MALME-3M, M14, MDA-MB-435, SK-MEL-2, SK-MEL-28, SK-MEL-5, UACC-257 and UACC-62) for GI_{50} are in the range of 1.77 to 4.54, 1.35 to 1.67, 1.49 to 8.42 and 1.85 to 42.6 μM, respectively at an exposure period of at least 48 h.

In yet another embodiment of the present invention, a process for the preparation of 3-arylethynyl substituted quinazolinone compounds of general formula A and the said process comprising the steps of:

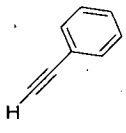
i. treating 4-iodo-2-methylbenzenamine (**24**) with substituted aryl (hetero) ethynyl compounds of formulae (**25a-e**) which represent phenyl, 4-*tertiary* butyl phenyl, 6-methoxy naphthaalene, 3-pyridyl, 2-thiophenyl ethynyl compounds by employing Sonagashira coupling conditions using $Pd(PPh_3)_4$ as catalyst, CuI as cocatalyst, butyl amine as base and ether as solvent and kept the reaction for 6-8 h to gave 2-methyl-4-(phenylethynyl)benzenamine compounds (**26a-e**) wherein G represent phenyl, 4-*tertiary*-butyl phenyl, 6-methoxy naphthalene, 3-pyridyl, 2-thiophenyl;



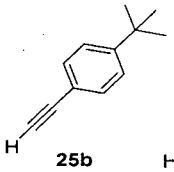
24



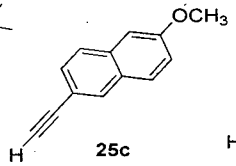
26a-e



25a



25b



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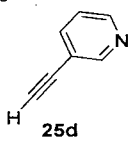
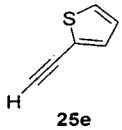
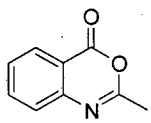


25d



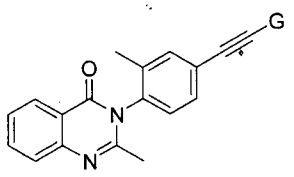
25e

ii. treating anthranilic acids (**27**) with acetic anhydride at temperature in the range of 150-155 °C for period in the range of 30-45min afforded 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one compound (**28**);



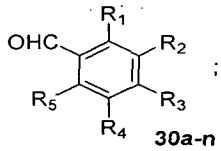
28

iii. mixing 2-methyl-4-(phenylethynyl)benzenamine compounds (**26a-e**) as obtained in step (i) with 2-methyl-4*H*-benzo[*d*][1,3] oxazin-4-one (**28**) as obtained in step (ii) in acetic acid was heated under reflux conditions (120-125 °C) for 8-10 h afford 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**29a-e**);

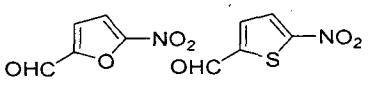


29a-e

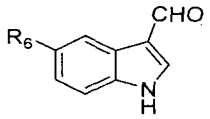
iv. treating 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**29a-e**) as obtained in step (iii) with aldehydes of formula **30a-n**, **31a-b**, **32a-b** and **33a-b** in acetic acid was heated under reflux conditions (120-125 °C) for 8-10 h to obtain the final compounds **4a-n** to **8a-n**, **9a-b** to **23a-b** of general formula A.



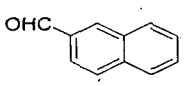
30a-n



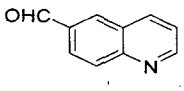
31a **31b**



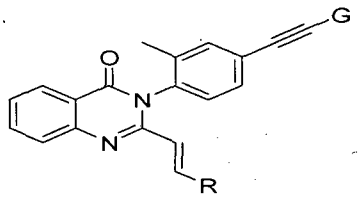
32a; R_6 = H
32b; R_6 = OCH_3



33a



33b



4a-i to **8a-i**; **9a-b** to **23a-b**

BRIEF DISCRIPTION OF THE DRAWING

Figure 1 represents structural formula of compounds of formula 30a-n, 31a-b, 32a-b, 33a-b, 25a-e, 26a-e, 29 a-e.

Scheme 1 represent the flow diagram for the preparation of compound of general formula A wherein reagent and conditions are (i)substituted phenyl acetylenes, $Pd(PPh_3)_4$, CuI, $BuNH_2$, ether, rt (room temperature 25 to 30°C), 6h; (ii)Ac_2O, 150 °C, 30 min; (iii)aryl ethynyl anilines, AcOH, reflux, 8h; (iv)Substituted aldehydes, AcOH, reflux, 8h.

DETAILED DESCRIPTION OF THE INVENTION

3-Arylethynyl substituted quinazolinone compounds have shown promising anticancer activity in various cell lines. The molecules synthesized are of immense biological significance. This resulted in design and synthesis of new congeners as illustrated in Scheme-1, which comprise:

i. Sonagasira coupling reaction between various phenyl acetylenes and 4-iodo-2-methylbenzenamine.

ii. Cyclization of anthranilic acid on reaction with acetic anhydride at 150 °C for 30 min.

iii. Insertion reaction of 2-methyl-4-(phenylethynyl)benzenamine and 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one in acetic acid under reflux conditions afforded 2-methyl-3-(2-methyl-4-(phenylethynyl) phenyl) quinazolin-4(3*H*)-one.

iv. The synthesis of 3-Arylethynyl substituted quinazolinone compounds as potential anticancer agents were synthesized by the reaction of 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one with various substituted aldehydes at room temparature to gave the final compounds.

v. Purification by column chromatography using different solvents like ethyl acetate, hexane, chloroform and methanol.

The 3-arylethynyl substituted quinazolinone compounds exhibited significant anticancer activity against sixty human cancer cell lines.

EXAMPLES

The following examples are given by way of illustration of the present invention and therefore should not be construed to limit the scope of the present invention.

Example 1

(*E*)-2-(4-hydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (4b)

4-iodo-2-methylbenzenamine (**24,** 233mg, 1 mmol) on reaction with ethynyl benzene (**25a,** 102 mg, 1mmol) by employing Sonagashira coupling conditions using $Pd(PPh_3)_4$ (69.3 mg, 0.06 equiv) as catalyst, CuI (22.8 mg, 0.12equiv) as cocatalyst, butyl amine (261 mg, 3 equiv) as base and ether as solvent and kept the reaction for 6h. After completion of the reaction as indicated by TLC and the reaction mixture is extracted into ether (4x25 mL) from the aqueous layer and concentrated in vacuo. The compound was further purified by column chromatography using 60-120 silica gel (ethyl acetate/hexane,1:9) to obtain 2-methyl-4-(phenylethynyl)benzenamine compound (**26a**) as pure product. Anthranilic acid (**27,** 137 mg, 1mmol) on reaction with acetic anhydride at 150 °C and reflux for 30 min, after completion of reaction aqueous sodium bicarbonate solution is added and extracted in ethyl acetate (4x25 mL) from the aqueous layer and concentrated in vacuo afforded 2-methyl 4*H*-benzo [*d*][1,3] oxazin-4-one compound (**28**) as pure product. To a stirred solution of 2-methyl-4-(phenylethynyl)benzenamine (**26a,** 207 mg, 1mmol) with 2-methyl-4*H*-benzo [*d*][1,3]oxazin-4-one (**28,** 161 mg, 1mmol) in acetic acid and reflux for 8h. After completion of the reaction as indicated by TLC. The reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4 afforded 2-methyl-3-(2-methyl-4-(phenylethynyl) phenyl)quinazolin-4(3*H*)-one (**29a**). Reaction of 2-methyl-3-(2-methyl-4-(phenyl

ethynyl)phenyl)quinazolin-4(3*H*)-one (**29a,** 350 mg, 1mmol) with 4-hydroxy benzaldehyde (**30b,** 122 mg, 1mmol) was taken in acetic acid Then the resulting mixture was stirred under reflux conditions for 8 h and then the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4.The resulting product (**4b**) was purified by column chromatography employing EtOAc/Hexane as an eluent.

Mp 161-162 °C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 8.29 (s, 1H), 8.27 (d, *J* = 15.1 Hz, 1H), 7.77 (d, *J* = 3.6 Hz, 2H), 7.57 (d, *J* = 9.4, 1H), 7.52 (dd, *J* = 3.9, 7.5 Hz, 2H), 7.46 (t, *J* = 3.9 Hz, 1H), 7.40-7.27 (m, 3H), 7.26-7.06 (m, 6H), 6.25 (d, *J* = 15.3 Hz, 1H), 2.16 (s, 3H); LRMS(ESI, *m/z*) 455 $(M)^+$.

Example 2

(*E*)-2-(2,5-dihydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (4c)

4-iodo-2-methylbenzenamine **24** (233 mg, 1 mmol) on reaction with ethynyl benzene (**25a,** 102 mg, 1mmol) by employing Sonagashira coupling conditions using $Pd(PPh_3)_4$ (69.3 mg, 0.06 equiv) as catalyst, CuI (22.8 mg, 0.12equiv) as cocatalyst, butyl amine (261 mg, 3 equiv) as base and ether as solvent and kept the reaction for 6h. After completion of the reaction as indicated by TLC and the reaction mixture is extracted into ether (4x25 mL) from the aqueous layer and concentrated in vacuo. The compound was further purified by column chromatography using 60-120 silica gel (ethyl acetate/hexane,1:9) to obtain 2-methyl-4-(phenylethynyl)benzenamine compounds (**26a)** as pure product. Anthranilic acid (**27,** 137 mg, 1mmol) on reaction with acetic anhydride at 150 °C and reflux for 30 min, after completion of reaction aqueous sodium bicarbonate solution is added and extracted in ethyl acetate (4x25 mL) from the aqueous layer and concentrated in vacuo afforded 2-methyl 4*H*-benzo [*d*][1,3] oxazin-4-one compound (**28**) as pure product. To a stirred solution of 2-methyl -4-(phenylethynyl)benzenamine (**26a,** 207 mg, 1mmol) with 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**28,** 161 mg, 1mmol) in acetic acid and reflux for 8h. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4 afforded 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**29a**). Reaction of 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**29a,** 350 mg, 1mmol) with 2,5-dihydroxy benzaldehyde (**30c,** 138 mg, 1 mmol) was taken in acetic acid Then the resulting mixture was stirred under reflux conditions for 8 h and then the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4.The resulting product (**4c**) was purified by column chromatography employing EtOAc/Hexane as an eluent.

Mp 170-172 °C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 8.26 (s, 1H), 8.02 (d, *J* = 15.2 Hz, 1H), 7.88-7.62 (m, 3H), 7.57-7.33 (m, 6H), 7.26-7.16 (m, 3H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.52 (d, *J* = 15.2 Hz, 1H), 1.82 (s, 3H); LRMS(ESI, *m/z*) 471 $(M)^+$.

Example 3

(*E*)-3-(4-((4-*tert*-butylphenyl)ethynyl)phenyl)-2-(2,4-dihydroxystyryl) quinazolin-4(3*H*)-one (5d)

4-iodo-2-methylbenzenamine **24** (233mg, 1 mmol) on reaction with 1-*tert*-butyl-4-ethynylbenzene (**25b,** 158 mg,1 mmol) by employing Sonagashira coupling conditions using $Pd(PPh_3)_4$ (69.3 mg, 0.06 equiv) as catalyst, CuI (22.8 mg, 0.12equiv) as cocatalyst, butyl amine (261 mg, 3 equiv)as base and ether as solvent and kept the reaction for 6h. After completion of the reaction as indicated by TLC and the reaction mixture is extracted into ether (4x25 mL) from the aqueous layer and concentrated in vacuo. The compound was further purified by column chromatography using 60-120 silica gel (ethyl acetate/hexane,1:9) to obtain 4-((4-*tert*-butylphenyl) ethynyl)-2-methyl benzene amine (**26b)** as pure product. Anthranilic acid (**27,** 137 mg, 1mmol) on reaction with acetic anhydride at 150 °C and reflux for 30 min, after completion of reaction aqueous sodium bicarbonate solution is added and extracted in ethyl acetate (4x25 mL) from the aqueous layer and concentrated in vacuo afforded 2-methyl 4*H*-benzo [*d*][1,3]oxazin-4-one compound (**28**) as pure product. To a stirred solution of 4-((4-*tert*-butylphenyl)ethynyl)-2-methylbenzenamine (**26b,** 263 mg, 1 mmol) with 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**28,** 161 mg, 1mmol) in acetic acid and reflux for 8h After completion of the reaction as indicated by TLC. then the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4 afforded 3-(4-((4-*tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**29b**). Reaction of 3-(4-((4-*tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-methyl quinazolin-4(3*H*)-one (**29b,** 406 mg, 1mmol) with 2,4-dihydroxybenzaldehyde (**30d,** 138 mg, 1mmol) was taken in acetic acid Then the resulting mixture was stirred under reflux conditions for 8 h and then the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4.The resulting product (**5d**) was purified by column chromatography employing EtOAc/Hexane as an eluent.

Mp 93-95 °C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 8.23 (d, *J* = 15.9 Hz, 1H), 8.20 (s, 1H), 7.79-7.66 (m, 3H), 7.51-7.34 (m, 6H), 7.26 (s, 1H), 7.10 (d, *J* = 8.3 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.21 (d, *J* = 15.2 Hz, 1H), 6.18 (s, 1H), 2.06 (s, 3H), 1.14 (s, 9H); LRMS(ESI, *m/z*) 527 $(M)^+$

Example 4

(*E*)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (6l)

4-iodo-2-methylbenzenamine **24** (233 mg, 1 mmol) on reaction with 2-ethynyl-6-methoxynaphthalene (**25c,** 182mg, 1 mmol) by employing Sonagashira coupling conditions using $Pd(PPh_3)_4$ (69.3 mg, 0.06 equiv) as catalyst, CuI (22.8 mg, 0.12 equiv) as cocatalyst, butyl amine (261 mg, 3 equiv) as base and ether as solvent and kept the reaction for 6h. After completion of the reaction as indicated by TLC and the reaction mixture is extracted into ether (4x25 mL) from the aqueous layer and concentrated in vacuo. The compound was further purified by column chromatography using 60-120 silica gel (ethyl acetate/hexane,1:9) to obtain 4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methyl benzenamine (**26c**) as pure product. Anthranilic acid (**27,** 137 mg, 1mmol) on reaction with acetic anhydride at 150 °C and reflux for 30 min, after completion of reaction aqueous sodium bicarbonate solution is added and extracted in ethyl acetate (4x25 mL) from the aqueous layer and concentrated in vacuo afforded 2-methyl-4*H*-benzo [*d*][1,3]oxazin-4-one compound (**28**) as pure product. To a stirred solution of 4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylbenzenamine (**26c**) with 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**28,** 161 mg, 1mmol) in acetic acid and reflux for 8h After completion of the reaction as indicated by TLC. then the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4 afforded 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**29c**). Reaction of 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**29c,** 430 mg, 1 mmol) with 3,4,5-trimethoxybenzaldehyde (**30l,** 196 mg, 1 mmol) was taken in acetic acid Then the resulting mixture was stirred under reflux conditions for 8 h and then the reaction mixture was quenched with $NaHCO_3$ and extracted in ethyl acetate (4x25 mL) from the ice cold aqueous layer and dried over anhydrous Na_2SO_4.The resulting product (**6l**) was purified by column chromatography employing EtOAc/Hexane as an eluent.

Mp 129-130 °C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 8.79 (t, *J*=8.5, 1H), 7.99 (s, 1H), 7.87 (d, *J* =14.5 Hz, 1H), 7.81-7.63 (m, 5H), 7.59-7.44 (m, 3H), 7.24 (d, *J* = 10.2 Hz, 1H), 7.14 (dd, *J*=2.9, 7.7 Hz, 2H), 7.08 (s, 1H), 6.49 (s, 1H), 6.41 (d, *J* = 15.3 Hz, 1H), 3.93 (s, 3H), 3.80 (s, 9H), 2.20 (s, 3H); LRMS(ESI, *m/z*) 609 $(M)^+$

BIOLOGICAL ACTIVITY

Some of biological activity studies were carried out at the National Cancer Institute (NCI), Maryland, USA.

Anticancer Activity: The compounds were evaluated for anticancer activity against sixty human cancer cells derived from nine cancer types (leukemia cell line, non-small-cell lung cell line, colon cell line, CNS cell line, melanoma cell line, ovarian cell line, prostate cell line, renal cell line and breast cancer cell line) as shown in Table 1. For each compound, dose response curves for each cell line were measured at a minimum of five concentrations at 10 fold dilutions. A protocol of 48 h continuous drug exposure was used and a sulforhodamine B (SRB) protein assay was used to estimate cell viability or growth.

Table 1: The GI_{50} (the concentration needed to reduce the growth of treated cells to half that of untreated cells) values for compounds **4b, 4c, 5d, and 6l** in sixty cancer cell lines

Cancer panel/cell line	Growth Inhibition GI_{50} (μM)			
	NSC : 754027 **(4b)**	NSC : 754031 **(4c)**	NSC753534 **(5d)**	NSC;754032 **(6l)**
Leukemia				
CCRF-CEM	3.26	1.54	3.85	-[b]
HL-60(TB)	1.66	0.634	-[a]	0.686
K-562	2.00	1.42	3.28	0.882
MOLT-4	2.36	1.14	2.45	4.66
SR	2.45	1.10	2.45	0.395
RPMI-8226	2.33	1.26	3.10	0.821
Non-small lung				
A549/ATCC	3.14	1.28	2.83	-[b]
EKVX	2.43	1.24	3.67	24.1
HOP-62	13.1	1.71	5.88	-[b]
HOP-92	2.50	1.54	2.82	-[b]
NCI-H226	3.99	1.52	2.17	-[b]
NCI-H23	3.62	1.48	2.42	40.5
NCI-H322M	2.93	1.62	6.09	-[b]
NCI-H460	2.22	1.57	1.82	2.48
NCI-H522	2.26	1.29	1.83	-[b]

Colon				
COLO 205	1.99	1.48	3.02	6.96
HCC-2998	2.35	1.36	1.93	-[b]
HCT-116	2.66	1.46	2.89	3.53
HCT-15	2.50	1.03	2.74	1.22
HT29	3.33	1.95	2.08	3.41
KM12	3.24	1.65	3.33	4.30
SW-620	4.08	1.71	1.81	17.2
CNS				
SF-268	4.56	1.31	4.82	-[b]
SF-295	2.85	1.35	3.83	-[b]
SF-539	5.65	1.60	4.37	-[b]
SNB-19	6.91	1.62	7.90	-[b]
SNB-75	3.66	1.30	1.87	-[b]
U251	4.33	1.45	2.11	7.40
Ovarian				
IGROV1	20.6	2.45	7.48	-[b]
OVCAR-3	3.60	1.49	2.23	19.3
OVCAR-4	3.17	2.40	3.15	-[b]
OVCAR-5	4.59	1.39	4.25	-[b]
OVCAR-8	3.98	1.94	3.55	-[b]
NCI/ADR-RES	3.09	2.06	3.17	-[b]
SK-OV-3	9.91	1.83	10.9	-[b]
Renal				
786-0	3.65	1.74	5.08	-[b]
A498	1.56	0.370	2.98	-[b]
ACHN	2.46	1.44	3.26	-[b]
CAKI-1	3.30	2.15	2.87	4.91
SN12C	3.77	1.62	1.88	-[b]
TK-10	2.62	2.03	3.82	-[b]
UO-31	2.06	1.16	2.63	-[b]

RXF 393	-[a]		1.88	-[b]
Prostate				
PC-3	3.24	2.19	3.67	-[b]
DU-145	4.87	0.419	3.42	-[b]
Breast				
MCF7	2.72	1.45	2.39	63.8
MDA-MB-231/ATCC	3.89	1.56	3.06	37.0
HS 578T	2.48	1.54	2.20	-[b]
BT-549	-[a]	-[a]	8.60	-[a]
T-47D	2.02	1.14	3.85	-[b]
MDA-MB-468	3.78	1.61	2.20	3.80
Melanoma				
LOX IMVI	2.78	1.37	1.49	5.96
MALME-3M	2.12	1.50	8.42	42.6
M14	3.26	1.54	5.91	12.7
MDA-MB-435	2.82	1.67	3.08	-[b]
SK-MEL-2	1.93	1.40	3.52	-[b]
SK-MEL-28	4.54	1.53	2.42	-[b]
SK-MEL-5	1.77	1.35	1.77	1.85
UACC-257	4.18	1.56	6.91	6.24
UACC-62	3.48	1.52	3.52	2.19

–[a] not done on that cell line ; -[b] means GI_{50} values not attained at the concentrations used.

Table 2: The mean graph midpoint values (MG_MID) of $Log_{10}GI_{50}$ (log values of concentration in mol/L causing 50% inhibition of net cell growth) values for compounds **4b**, **4c**, **5d** and **6l** in sixty cancer cell lines.

Cancer cell lines $Log_{10} GI_{50}$	**4b**	**4c**	**5d**	**6l**
Leukemia	-5.64	-5.94	-5.53	-5.67
Non-small cell lung	-5.47	-5.83	-5.53	-4.32
Colon	-5.55	-5.83	-5.60	-5.16

CNS	-5.35	-5.85	-5.43	-4.18
Melanoma	-5.54	-5.83	-5.45	-4.79
Ovarian	-5.33	-5.72	-5.34	-4.10
Renal	-5.52	-5.86	-5.54	-4.16
Prostate	-5.40	-6.17	-5.45	-4.00
Breast	-5.54	-5.84	-5.49	-4.51

Table 3: The mean graph midpoint values (MG_MID) of Log_{10} LC_{50} values (log value of the concentration of compounds leading to 50% net cell death) for compounds **4b**, **4c**, **5d** and **6l** in sixty cancer cell lines.

Cancer cell lines $Log_{10}LC_{50}$	**4b**	**4c**	**5d**	**6l**
Leukemia	>-4.00	-4.40	>-4.00	>-4.00
Non-small cell lung	-4.04	-4.91	-4.51	>-4.00
Colon	-4.15	-5.23	-5.41	>-4.00
CNS	>-4.00	-5.15	-4.35	>-4.00
Melanoma	-4.16	-5.22	-4.02	>-4.00
Ovarian	>-4.00	-4.61	-4.19	>-4.00
Renal	>-4.00	-4.93	-4.5	>-4.00
Prostate	>-4.00	-4.68	-4.24	>-4.00
Breast	>-4.00	-4.66	-4.25	>-4.00

Table 4: The mean graph midpoint values (MG_MID) of $log_{10}TGI$ (log value of concentration of the compound resulting in total inhibition of net cell growth) for compounds **4b**, **4c**, **5d** and **6l** in sixty cancer cell lines.

Cancer cell lines $Log_{10}TGI_{50}$	**4b**	**4c**	**5d**	**6l**
Leukemia	-4.49	-5.38	-4.72	>-4.00
Non-small cell lung	-4.32	-5.44	-4.45	>-4.00
Colon	-4.83	-5.53	-5.15	>-4.00

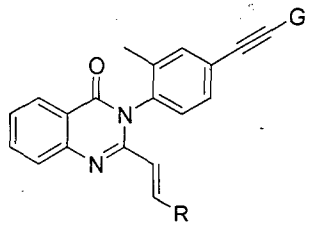
CNS	-4.21	-5.50	-4.83	>-4.00
Melanoma	-4.79	-5.52	-4.96	>-4.00
Ovarian	-4.23	-5.31	-4.77	>-4.00
Renal	-4.65	-5.43	-4.97	>-4.00
Prostate	>- 4.00	-5.43	-4.83	>-4.00
Breast	-4.58	-5.39	-4.93	>-4.00

ADVANTAGES OF THE INVENTION

1. The present invention provides 3-arylethynyl substituted quinazolinone compounds of general formula A.
2. It also provides a process for the preparation of 3-arylethynyl substituted quinazolinone compounds of general formula A.

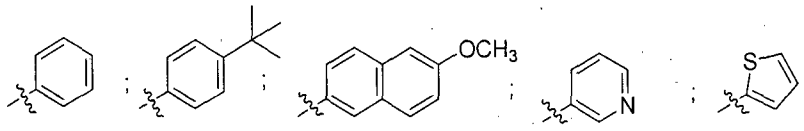
We claim

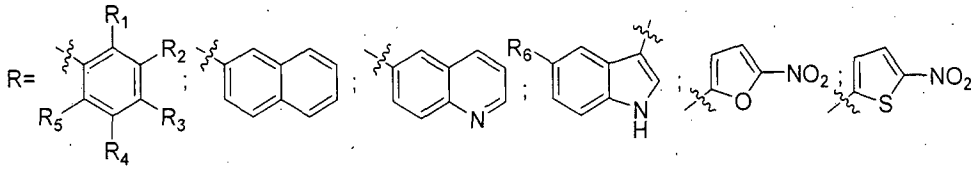
1. 3-Arylethynyl substituted quinazolinone compounds of formula A:



General formula A

Wherein,

G = 

R= 

R_1= H, OH, OCH_3
R_2= H, OH, CH_3, OCH_3, NO_2
R_3= H, OH, OCH_3, F, Cl
R_2+R_3= $-OCH_2O-$

R_4= H, OH, CH_3, OCH_3
R_5= H, OH, CH_3, OCH_3
R_6= H, OCH_3

2. 3-Arylethynyl substituted quinazolinone compounds of general formula A as claimed in claim 1, wherein chemical formula of the compounds are:

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-methylstyryl)quinazolin-4(3*H*)-one (**4a**);

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4e**);

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(2-methyl-4-phenylethynyl) phenyl) quinazolin-4(3*H*)-one (**4g**)

(*E*)-2-(3,4-Dimethoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3H)-one (**4h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one(**4i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(2-methyl-4-(phenylethynyl) phenyl) quinazolin-4(3*H*)-one (**4j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(2-methyl-4-phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**4k**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (**4l**);

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4m**);

E)-2-(4-Chlorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**4n**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-methylstyryl) quinazolin-4(3H)-one (**5a**);

E)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxystyryl) quinazolin-4(3*H*)-one (**5b**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2,5-dihydroxystyryl)quinazolin-4(3*H*)-one (**5c**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)phenyl)-2-(2,4-dihydroxystyryl) quinazolin-4(3*H*)-one (**5d**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxy-3-nitrostyryl) quinazolin-4(3*H*)-one (**5e**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-methoxystyryl) quinazolin-4(3*H*)-one (**5f**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxy-3-methoxystyryl)quinazolin-4(3*H*)-one (**5g**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(3,4-dimethoxystyryl) quinazolin-4(3*H*)-one (**5h**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2,4-dimethoxystyryl)quinazolin-4(3*H*)-one (**5i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(4-((4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**5j**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-hydroxy-3,5-dimethylstyryl)quinazolin-4(3*H*)-one (**5k**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (**5l**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-fluorostyryl) quinazolin-4(3*H*)-one (**5m**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(4-chlorostyryl) quinazolin-4(3*H*)-one (**5n**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-methylstyryl)quinazolin-4(3*H*)-one (**6a**);

(*E*)-2-(4-Hydroxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6e**);

(*E*)-2-(4-methoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6g**);

(*E*)-2-(3,4-Dimethoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**6k**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (**6l**);

(*E*)-2-(4-Fluorostyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6m**);

(*E*)-2-(4-Chlorostyryl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (**6n**)

(E)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-methylstyryl)quinazolin-4(3*H*)-one (**7a**);

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7e**);

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7g**);

(*E*)-2-(3,4-Dimethoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7i**);

(*E*)-2-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**7j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**7k**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (**7l**);

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl)quinazolin-4(3*H*)-one(**7m**);

(*E*)-2-(4-Chlorostyryl)-3-(2-methyl-4-(pyridin-3-ylethynyl)phenyl)quinazolin-4(3*H*)-one(**7n**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-methylstyryl) quinazolin-4(3*H*)-one (**8a**);

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl)quinazolin-4(3*H*)-one (**8b**);

(*E*)-2-(2,5-Dihydroxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**8c**);

(*E*)-2-(2,4-Dihydroxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8d**);

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8e**);

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**8f**);

(*E*)-2-(4-Hydroxy-3-methoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**8g**);

(*E*)-2-(3,4-Dimethoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**8h**);

(*E*)-2-(2,4-Dimethoxystyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8i**);

(*E*)-2-(2-(Benzo[d][1,3]dioxol-5-yl)vinyl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8j**);

(*E*)-2-(4-Hydroxy-3,5-dimethylstyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl) quinazolin-4(3*H*)-one (**8k**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(3,4,5-trimethoxystyryl) quinazolin-4(3*H*)-one (**8l**);

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3H)-one (**8m**);

(*E*)-2-(4-Chlorostyryl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl) quinazolin-4(3*H*)-one (**8n**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3H)-one (**9a**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**9b**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**10a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**10b**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3*H*)-one (**11a**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**11b**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**12a**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**12b**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (**13a**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (**13b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**14a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(2-methyl-4-(phenylethynyl) phenyl) quinazolin-4(3*H*)-one (**14b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(4-((4-*tert*-butylphenyl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**15a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-methoxy-1H-indol-3-yl)vinyl)quinazolin-4(3*H*)-one (**15b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**16a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (**16b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(2-methyl-4-(pyridin-3-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**17a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(2-methyl-4-(pyridin-3-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**17b**);

(*E*)-2-(2-(1H-Indol-3-yl)vinyl)-3-(2-methyl-4-(thiophen-2-ylethynyl) phenyl)quinazolin-4(3*H*)-one (**18a**);

(*E*)-2-(2-(5-Methoxy-1H-indol-3-yl)vinyl)-3-(2-methyl-4-(thiophen-2-ylethynyl)phenyl)quinazolin-4(3*H*)-one (**18b**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(naphthalen-2-yl)vinyl) quinazolin-4(3*H*)-one (**19a**);

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(quinolin-6-yl)vinyl) quinazolin-4(3*H*)-one (**19b**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(naphthalen-2-yl)vinyl) quinazolin-4(3*H*)-one (**20a**);

(*E*)-3-(4-((4-*Tert*-butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(quinolin-6-yl)vinyl)quinazolin-4(3*H*)-one (**20b**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(naphthalen-2-yl)vinyl)quinazolin-4(3H)-one (**21a**);

(*E*)-3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-(2-(quinolin-6-yl)vinyl)quinazolin-4(3*H*)-one (**21b**);

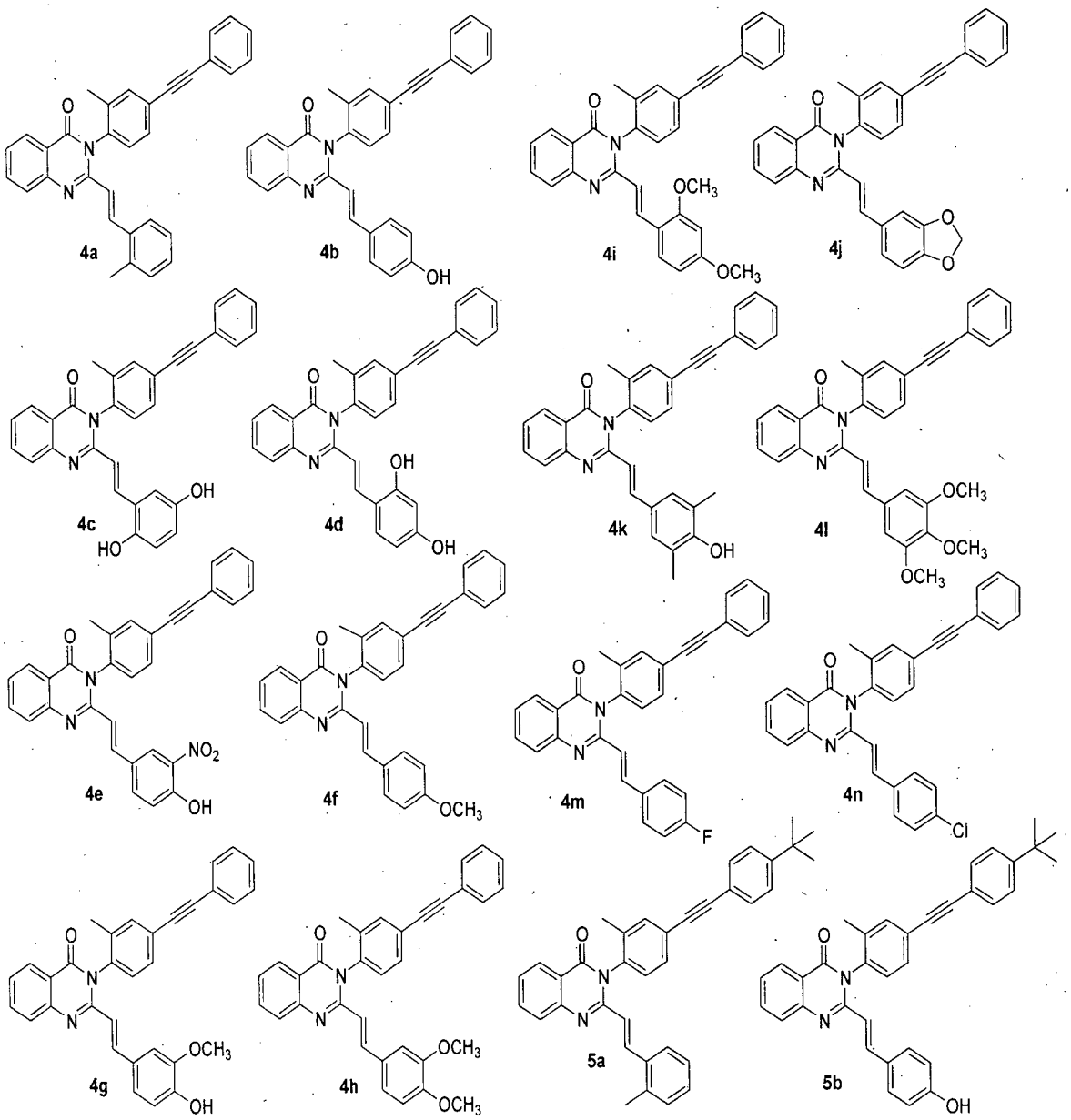
(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(naphthalen-2-yl)vinyl)quinazolin-4(3*H*)-one (**22a**);

(*E*)-3-(2-Methyl-4-(pyridin-3-ylethynyl)phenyl)-2-(2-(quinolin-6-yl)vinyl)quinazolin-4(3*H*)-one (**22b**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(naphthalen-2-yl)vinyl)quinazolin-4(3*H*)-one (**23a**);

(*E*)-3-(2-Methyl-4-(thiophen-2-ylethynyl)phenyl)-2-(2-(quinolin-6-yl)vinyl) quinazolin-4(3*H*)-one (**23b**).

3. 3-Arylethynyl substituted quinazolinone compounds of general formula A as claimed in claim 1, wherein the structural formulae of the representative compounds are: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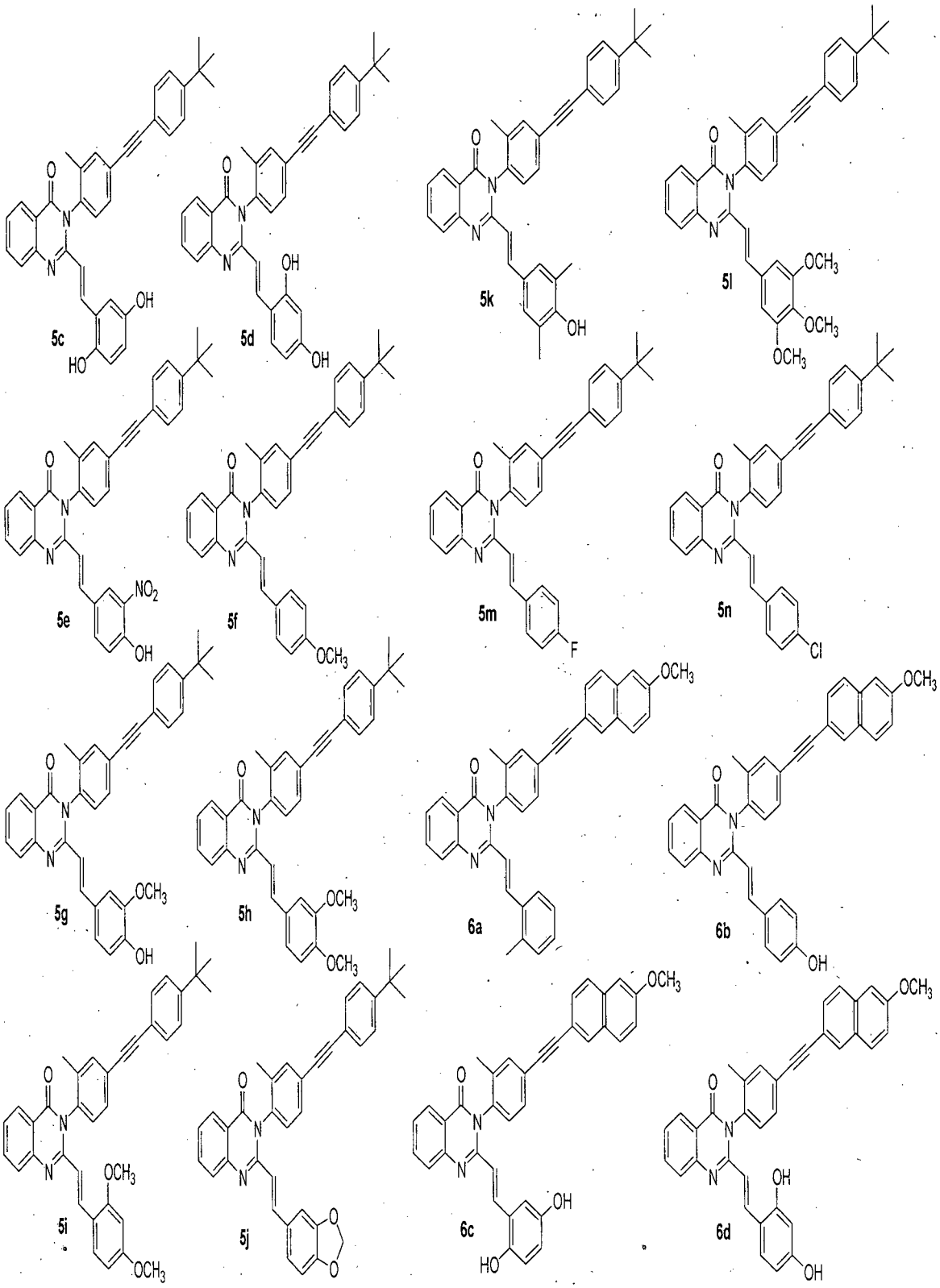
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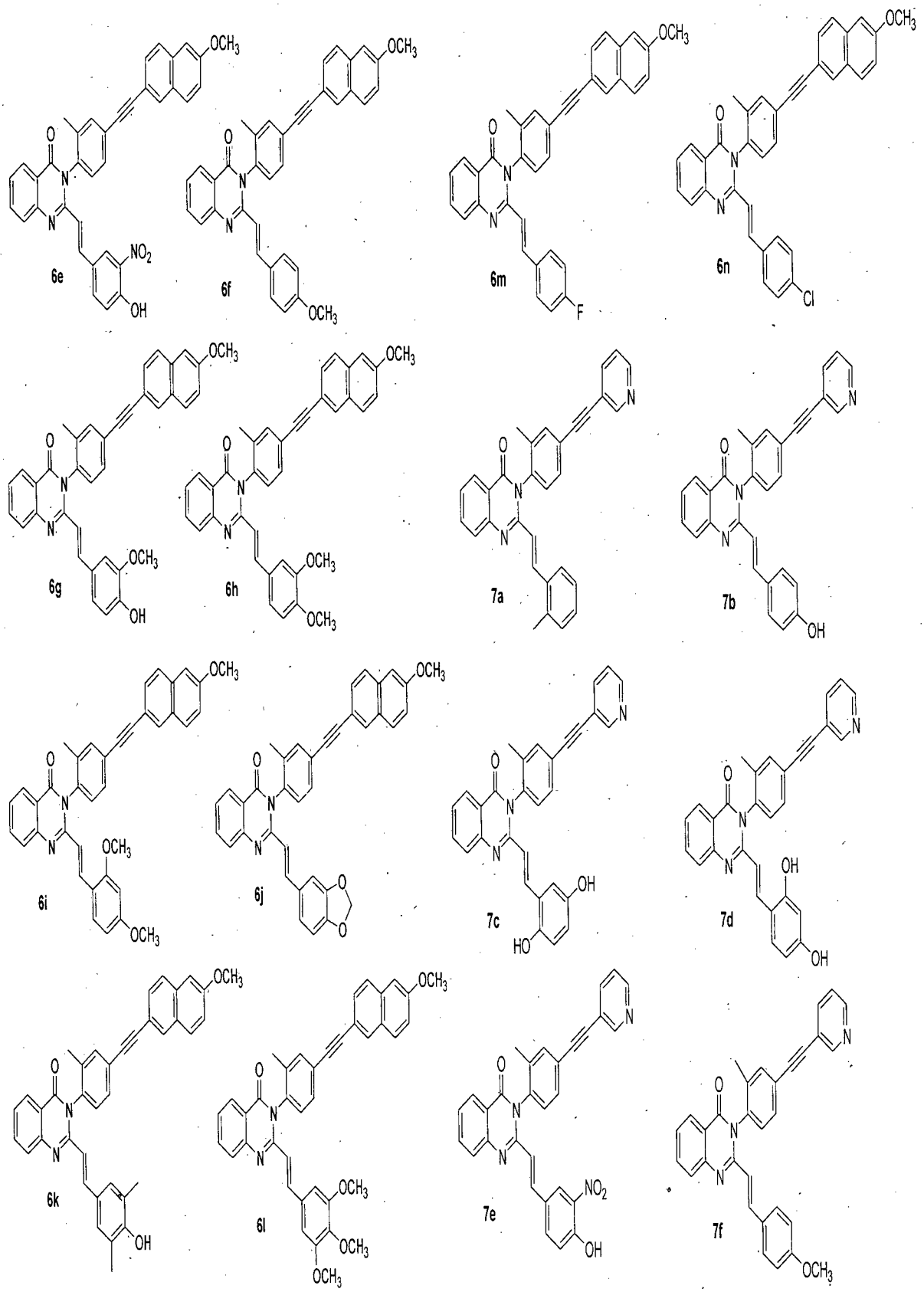
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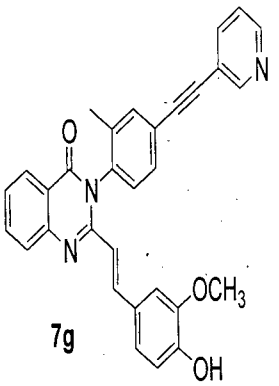

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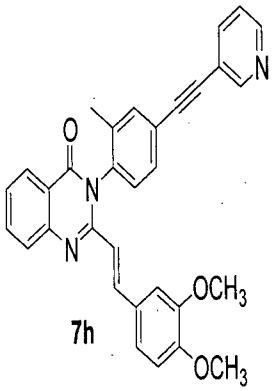

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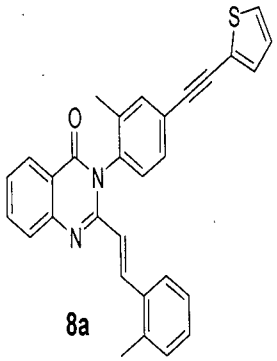

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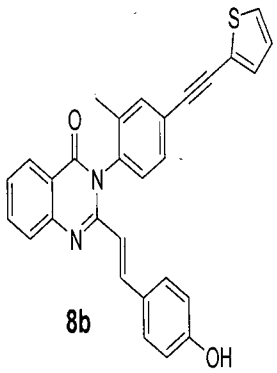

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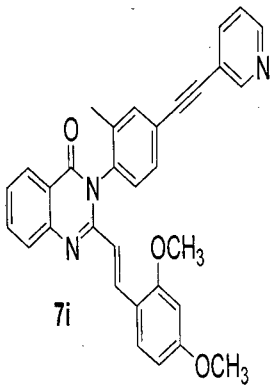

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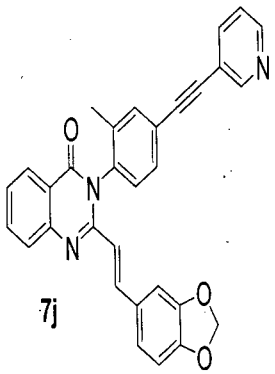

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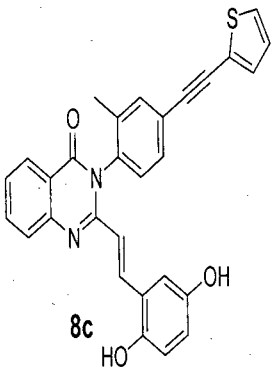

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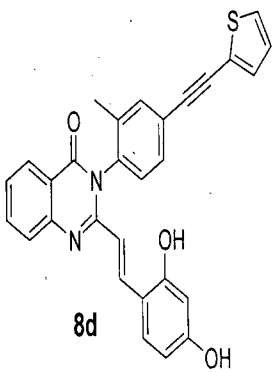

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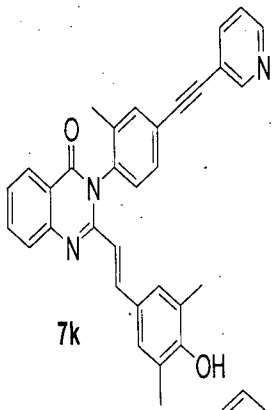

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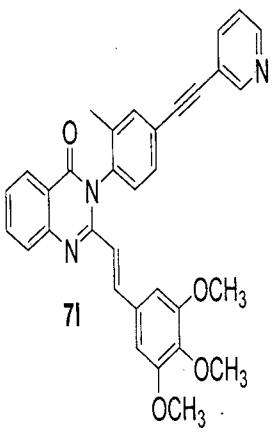

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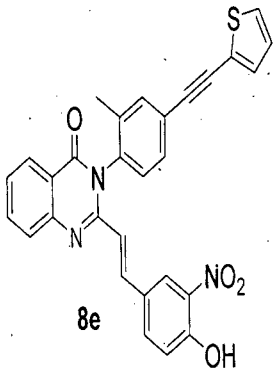

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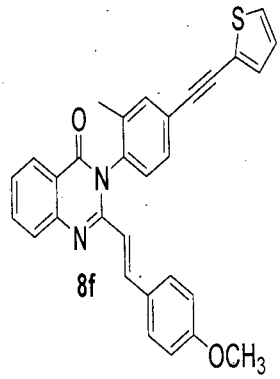

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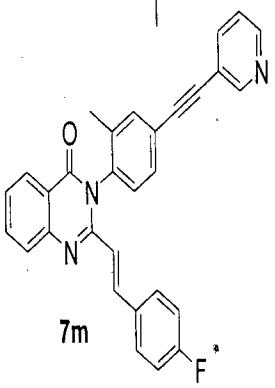

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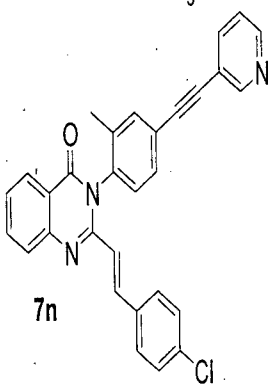

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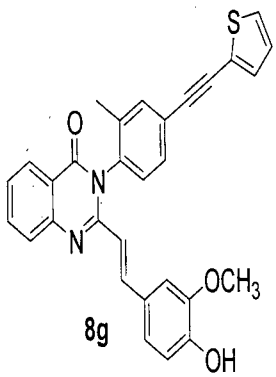

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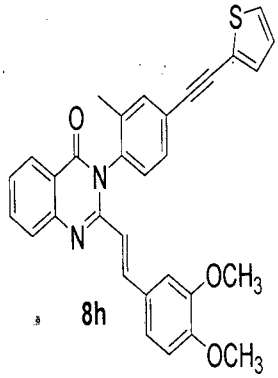

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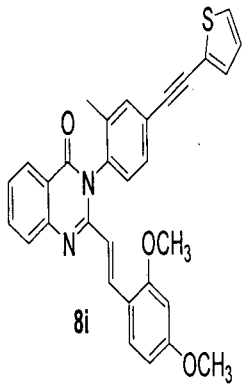
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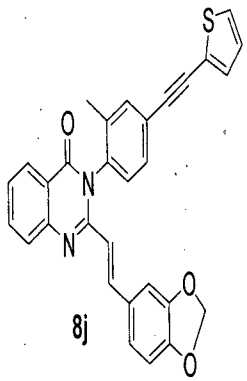
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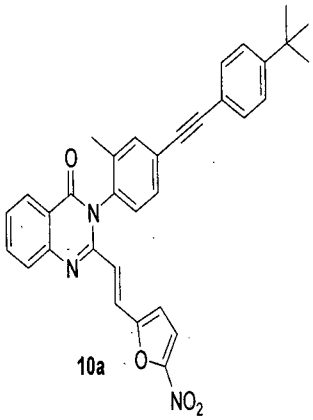
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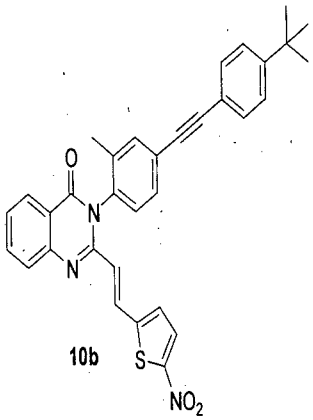
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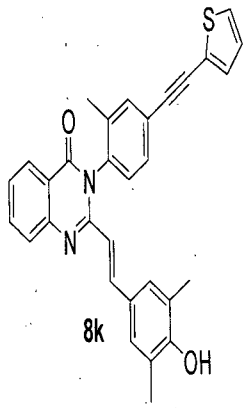
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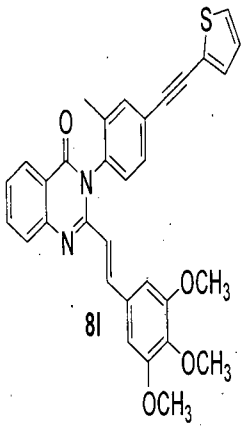
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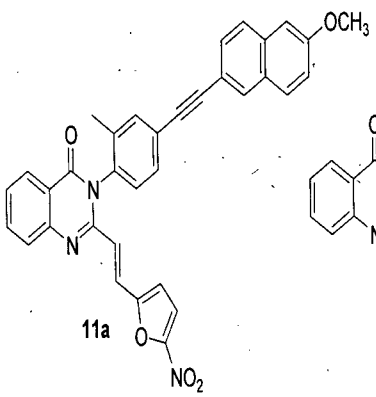
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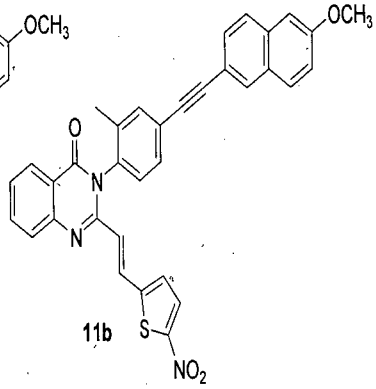
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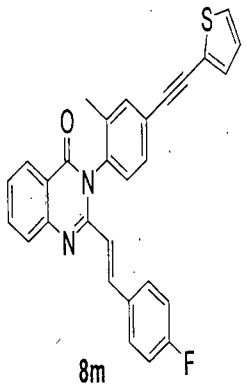
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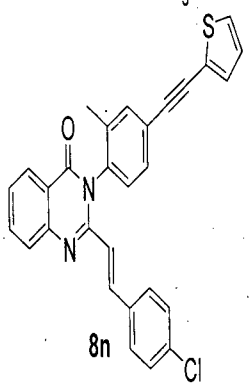
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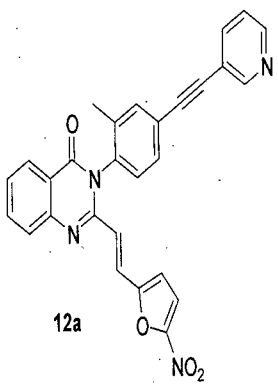
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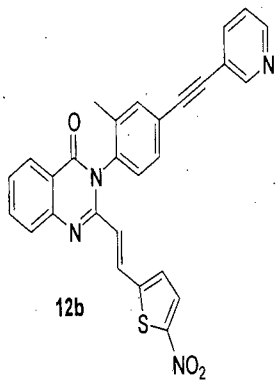
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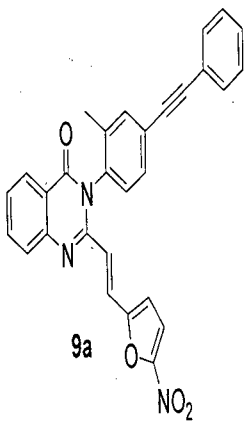
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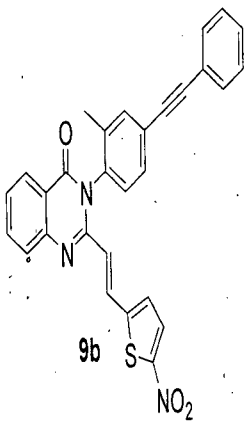
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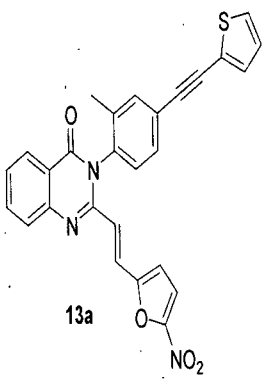
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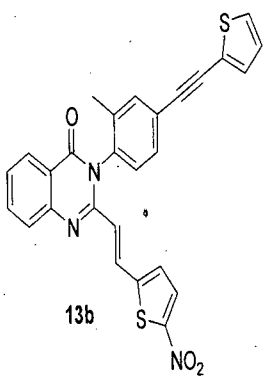
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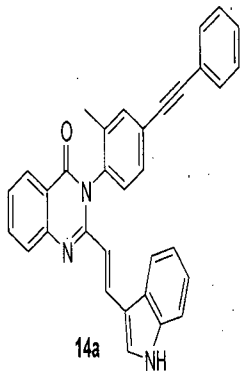
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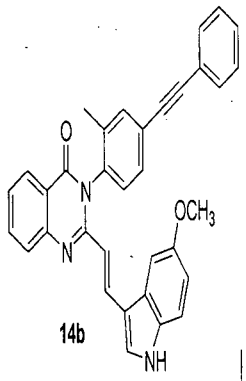
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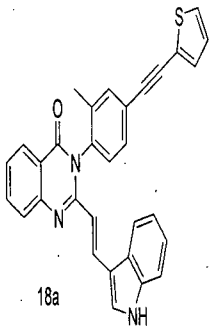
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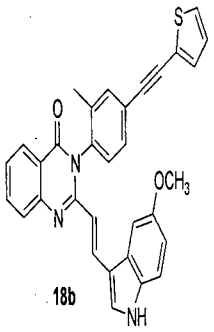
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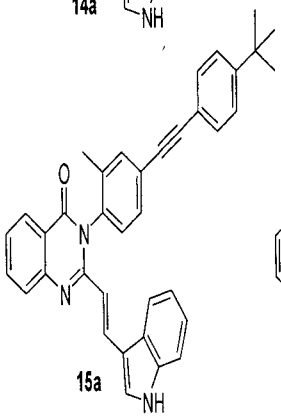
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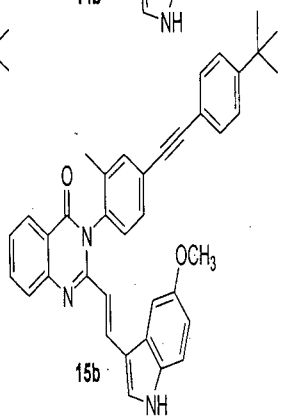
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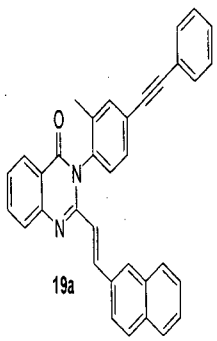
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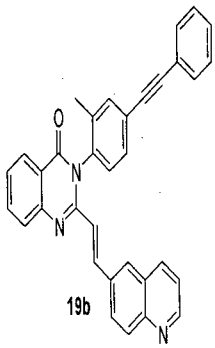
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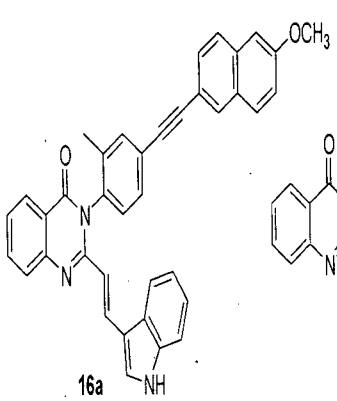
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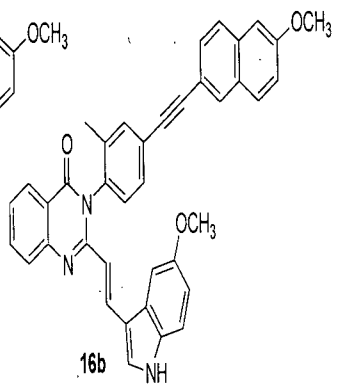
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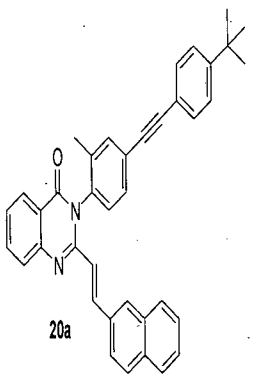
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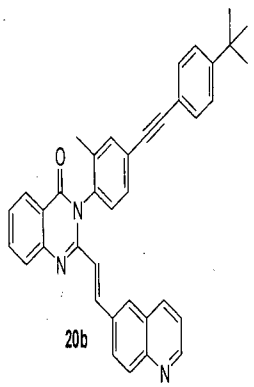
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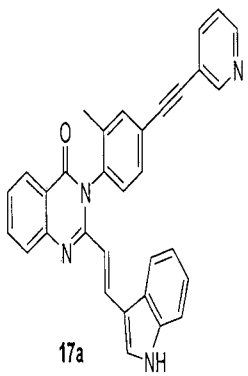
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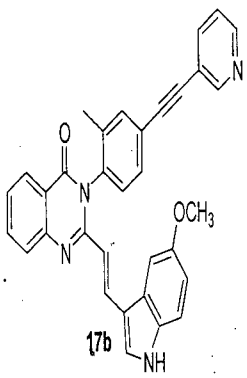
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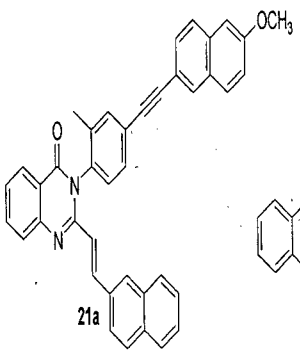
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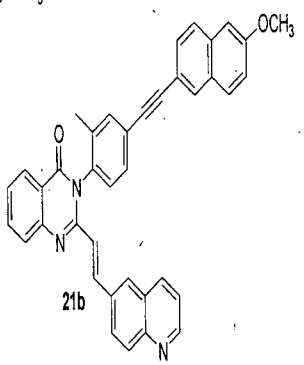
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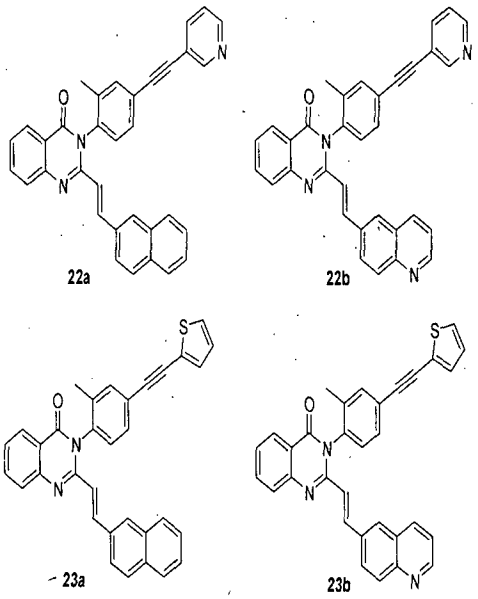


4. 3-Arylethynyl substituted quinazolinone compounds of general formula A as claimed in claim 1, wherein said compounds are useful as anticancer agent.
5. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against sixty human cancer cell lines derived from nine cancer types leukemia cell line, non small cell lung cell line, colon cell line, CNS cell line, renal cell line, prostate cell line, ovarian cell line, breast and melanoma cell line.
6. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against six leukemia cancer cell lines (CCRF-CEM, HL-60, K-562, MOLT-4, SR and RPMI-8226) for GI_{50} are in the range of 1.66 to 3.26, 0.634 to 1.54, 2.45 to 3.85 and 0.395 to 4.66 μM, respectively at an exposure period of at least 48 h.
7. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against nine non-small cell lung cancer cell lines (A549/ATCC, EKVX, HOP-62, HOP-92, NCI-H226, NCI-H23, NCI-H322M, NCI-H460 and NCI-H522) for GI_{50} are in the range of 2.22 to 13.1, 1.24 to 1.71, 1.82 to 6.09 and 2.48 to 40.5 μM, respectively at an exposure period of at least 48 h.
8. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against seven colon cancer cell line (COLO 205, HCC-2998, HCT-116, HCT-15, HT29, KM12 and SW-620) for GI_{50} are in

the range of 1.99 to 4.08, 1.03 to 1.95, 1.81 to 3.33 and 1.22 to 17.2 μM, respectively at an exposure period of at least 48 h.

9. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein exhibiting an *in vitro* anticancer activity against six CNS cancer cell line (SF-268, SF-295, SF-539, SNB-19, SNB-75 and U251) for GI_{50} are in the range of 2.85 to 6.91, 1.30 to 1.62, 1.87 to 7.90, 7.40 μM, respectively at an exposure period of at least 48 h.

10. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against eight renal cancer cell line (786-0, A498, ACHN, CAKI-1, SN12C, TK-10, UO-31 and RXF 393) for are in the range of 1.56 to 3.77, 0.370 to 2.15, 1.88 to 5.08, 4.91μM, respectively at an exposure period of at least 48 h.

11. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against two prostate cancer cell line (PC-3, DU-145) for GI_{50} are 3.24 to 4.87, 0.419 to 2.19, 3.42 to 3.67 μM, respectively at an exposure period of at least 48 h.

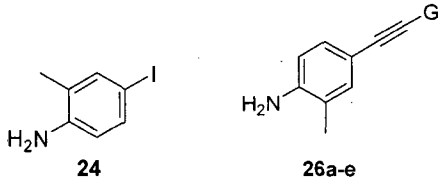
12. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against seven ovarian cancer cell lines (IGROV1, OVCAR-3, OVCAR-4, OVCAR-5, OVCAR-8, NCI/ADR-RES and SK-OV-3) for GI_{50} are in the range of 3.09 to 20.6, 1.39 to 2.45, 2.23 to 10.9 and 19.3μM respectively at an exposure period of at least 48 h.

13. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against six breast cancer cell line (MCF-7, MDA-MB-231/ATCC, HS 578T, TD-47D , MDA-MB-468 and BT-549) for GI_{50} are in the range of 2.02 to 3.89, 1.14 to 1.61, 2.20 to 8.60, 3.80 to 63.8 μM, respectively at an exposure period of at least 48 h.

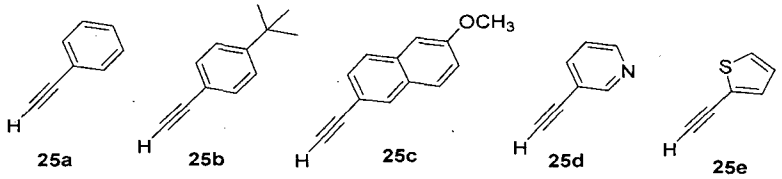
14. 3-Arylethynyl substituted quinazolinone compounds of formula **4b, 4c, 5d** and **6l** as claimed in claim 2, wherein said compounds exhibiting an *in vitro* anticancer activity against nine melanoma cancer cell line (LOX IMVI, MALME-3M, M14, MDA-MB-435, SK-MEL-2, SK-MEL-28, SK-MEL-5, UACC-257 and UACC-62) for GI_{50} are in the range of 1.77 to 4.54, 1.35 to 1.67, 1.49 to 8.42 and 1.85 to 42.6 μM, respectively at an exposure period of at least 48 h.

15. A process for the preparation of 3-arylethynyl substituted quinazolinone compounds of general formula A and the said process comprising the steps of:

i. treating 4-iodo-2-methylbenzenamine (**24**) with substituted aryl (hetero) ethynyl compounds of formulae (**25a-e**) which represent phenyl, 4-*tertiary* butyl phenyl, 6-methoxy naphthaalene, 3-pyridyl, 2-thiophenyl ethynyl compounds by employing Sonagashira coupling conditions using $Pd(PPh_3)_4$ as catalyst, CuI as cocatalyst, butyl amine as base and ether as solvent and kept the reaction for 6-8 h to give 2-methyl-4-(phenylethynyl)benzenamine compounds (**26a-e**) wherein G represent phenyl, 4-*tertiary*-butyl phenyl, 6-methoxy naphthalene, 3-pyridyl, 2-thiophenyl;

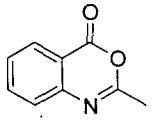


24 **26a-e**



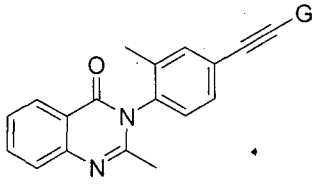
25a **25b** **25c** **25d** **25e**

ii. treating anthranilic acids (**27**) with acetic anhydride at temperature in the range of 150-155 °C for period in the range of 30-45 min afforded 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one compo und (**28**);



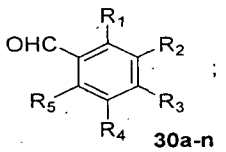
28

iii. mixing 2-methyl-4-(phenylethynyl)benzenamine compounds (**26a-e**) as obtained in step (i) with 2-methyl-4*H*-benzo[*d*][1,3] oxazin-4-one (**28**) as obtained in step (ii) in acetic acid was heated under reflux conditions (120-125 °C) for 8-10 h afford 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**29a-e**);

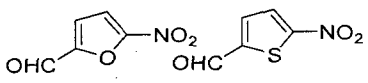


29a-e

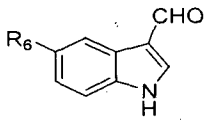
iv. treating 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**29a-e**) as obtained in step (iii) with aldehydes of formula **30a-n**, **31a-b**, **32a-b** and **33a-b** in acetic acid was heated under reflux conditions (120-125 °C) for 8-10 h to obtain the final compounds **4a-n** to **8a-n**, **9a-b** to **23a-b** of general formula A.



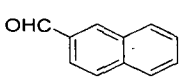
30a-n



31a **31b**



32a; R_6 = H
32b; R_6 = OCH_3



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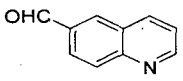
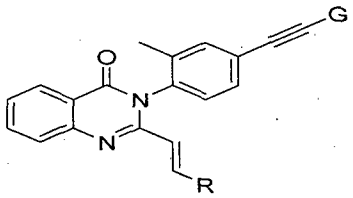
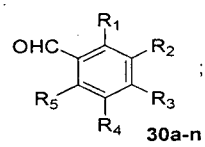


33b

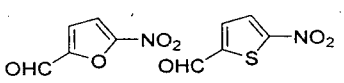


4a-i to **8a-i**; **9a-b** to **23a-b**

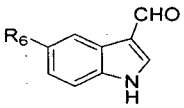
1/2



30a-n

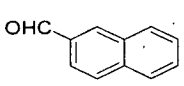


31a 31b

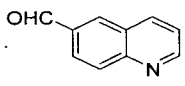


32a; R_6 = H
32b; R_6 = OCH_3

wherein
30a:R_1 = R_2 = R_3 = R_4 = H; R_5= CH_3
30b:R_1 = R_2 = R_4 = R_5 = H; R_3 = OH
30c:R_2 = R_3 = R_5 = H; R_1 = R_4 = OH
30d:R_2 = R_4 = R_5 = H; R_1 = R_3 = OH
30e:R_1 = R_4 = R_5 = H; R_2 = NO_2; R_3 = OH
30f:R_1 = R_2 = R_4 = R_5 = H; R_3 = OCH_3
30g:R_1 = R_4 = R_5 = H; R_2 = OCH_3; R_3 = OH
30h:R_1 = R_4 = R_5 = H; R_2 = R_3 = OCH_3
30i: R_2 = R_4 = R_5 = H; R_1 = R_3 = OCH_3
30j:R_1 = R_4 = R_5 = H; R_2 + R_3 = $-OCH_2O-$
30k:R_1 = R_5 = H; R_2 = R_4 = CH_3; R_3 = OH
30l:R_1 = R_5 = H; R_2 = R_3 = R_4 = OCH_3
30m:R_1 = R_2 = R_4 = R_5 = H; R_3 = F
30n:R_1 = R_2 = R_4 = R_5 = H; R_3 = Cl



33a



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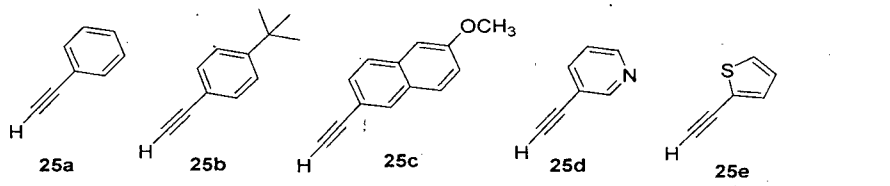
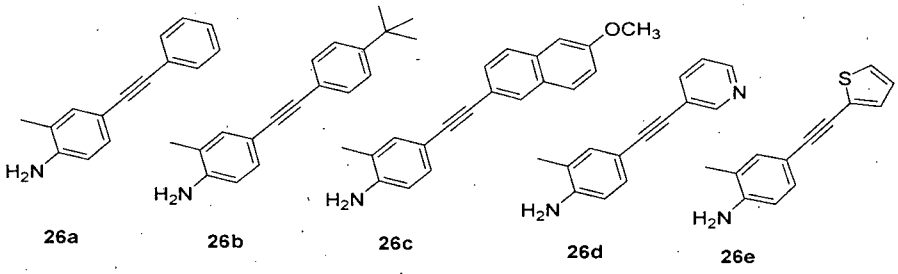
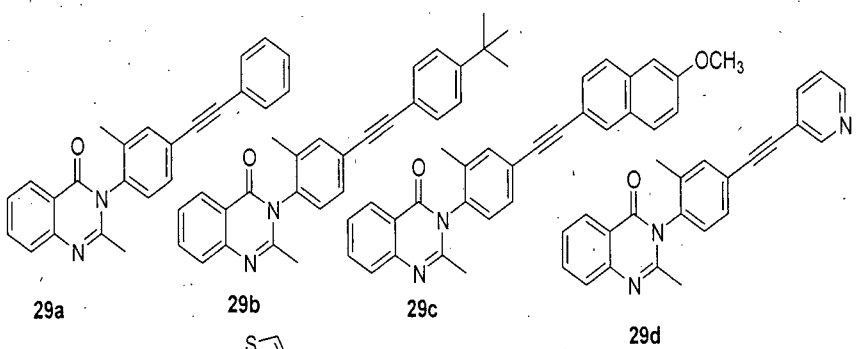


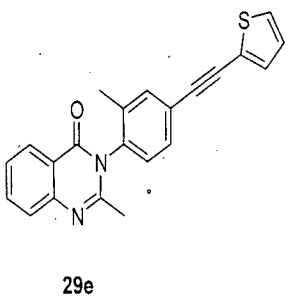
25a 25b 25c 25d 25e



26a 26b 26c 26d 26e

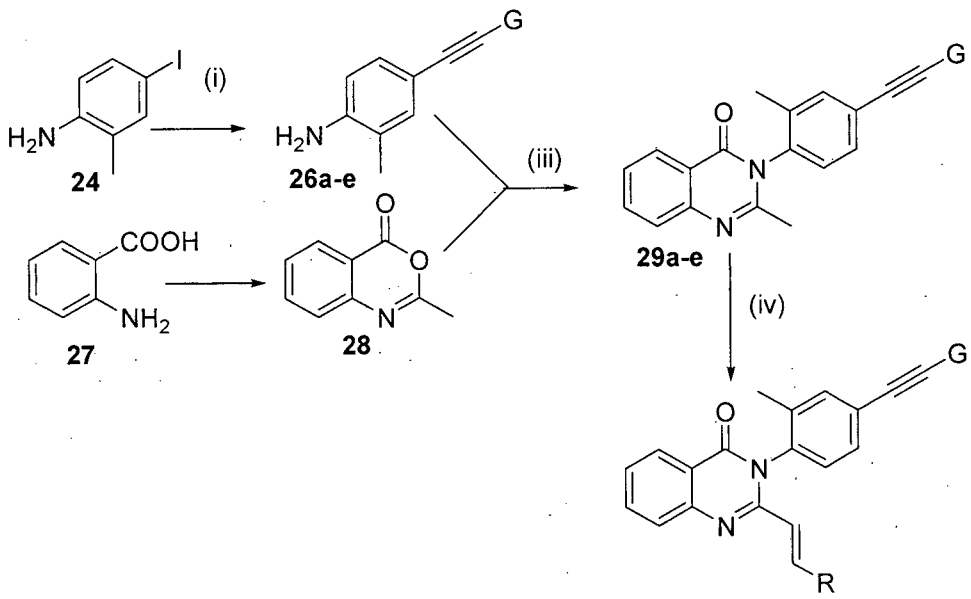


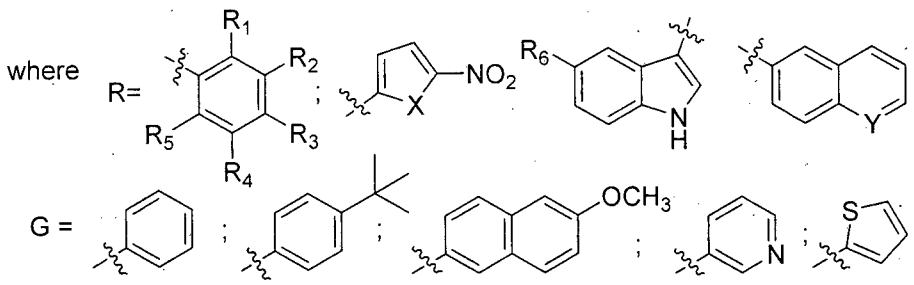
29a 29b 29c 29d



29e

Figure 1





Scheme 1

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2011/000228

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D239/91 C07D401/10 C07D405/06 C07D409/10 A61K31/517 A61P35/00
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JIANG G B ET AL: "SYNTHESIS AND BIOLOGICAL EVALUATION OF 2-STYRYLQUINAZOLIN-4(3H)-ONES, A NEW CLASS OF ANTIMITOTIC ANTICANCER AGENTS WHICH INHIBIT TUBULIN POLYMERIZATION", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 33, no. 6, 1 January 1990 (1990-01-01), pages 1721-1728, XP002917810, ISSN: 0022-2623, DOI: DOI:10.1021/JM00168A029 the whole document	1-15

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 July 2011	28/07/2011

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Weisbrod, Thomas

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2011/000228

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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A	LIU JI-FENG ET AL: "Design and synthesis of a quinazolinone natural product-templated library with cytotoxic activity", JOURNAL OF COMBINATORIAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 8, no. 1, 8 December 2005 (2005-12-08), pages 7-10,suppl., XP009106847, ISSN: 1520-4766, DOI: DOI:10.1021/CC050108G the whole document	1-15
A	Anna-Marie Lord ET AL: "Design, Synthesis, and Evaluation in Vitro of Quinoline-8-carboxamides, a New Class of Poly(adenosine-diphosphate-ribose)polymera se-1 (PARP-1) Inhibitor", Journal of Medicinal Chemistry, vol. 52, no. 3, 12 February 2009 (2009-02-12), pages 868-877, XP55002929, ISSN: 0022-2623, DOI: 10.1021/jm8013629 the whole document	1-15
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International application No
PCT/IN2011/000228

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