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Synthesis and Anti-Oxidant Activity of Phenol and Aldehyde Derivatives of Sulfonyl Chloride Quinoxaline

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ABSTRACT

N, N'-diprotonation is very easier for pyrazine Synthesis of 2, 3-diphenylquinoxaline by phenylene-diamine in 16 ml of rectified spirit was added & combine solution was warm in water bath for 30 min. added water until slight colorless persist & allow to cool recrystallize the product in ethanol. Synthesis of 2, 3-diphenylquinoxaline 7-sulfonylchloride (R) using chlorosulfonic acid under ice-cold condition, thenSynthesis of 2-hydroxyphenyl-2,3-diphenylquinoxaline-7-sulphonate (R1) throughresorcinol with 3ml pyridine &sulphonyl chloride derivative, Synthesis of 2-formylphenyl-2,3-diphenylquinoxaline-7-sulphonate (R7)obtained by reaction of salicylaldehyde with pyridine &sulphonyl chloride derivative then Synthesis of 3-formylphenyl-2,3-diphenylquinoxaline-7-sulphonate (R9) obtained by heating on water bath mixture of 3-hydroxybenzaldehyde with pyridine &sulphonyl chloride, Synthesized quinoxaline derivatives were subjected to antioxidant activity.Hydrogen peroxide solution (40 mM) was prepared with standard phosphate buffer (pH 7.4). Different concentration of the compound stock solution and 4ml distilled water was added to 0.6 ml of hydrogen peroxide solution. Absorbance was determined at 230 nm after 10 min against a blank solution containing phosphate buffer without hydrogen peroxide. DPPH radical scavenging activity was measured using the method of Cotelle*et al.* with some modifications. 3 ml of reaction mixture containing 0.2 ml of DPPH (100 µM in methanol) 2.8 ml of test solution, at various concentrations (5, 10, 20, 40, 80, 160 320 µg/ml) of the extract fractions was incubated at 37°C for 30 min absorbance of the resulting solution was measured at 517 nm using Beckman model DU-40 spectrophotometer. Most of the derivatives have shown comparable antioxidant activity in relation to standard Ascorbic acid and DPPH

Keywords: DPPH,Quinoxaline, Antioxidant activity,Sulfonyl chloride quinoxaline.

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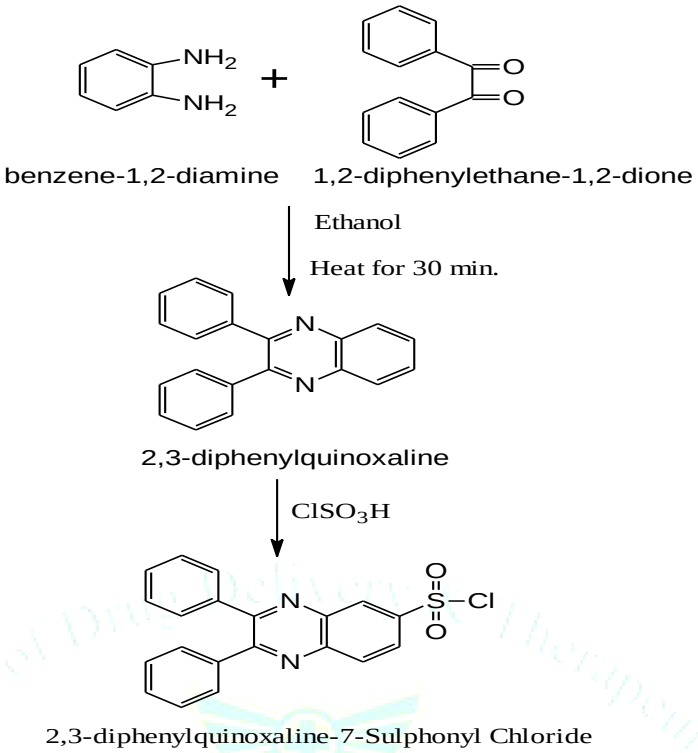
1. INTRODUCTION:

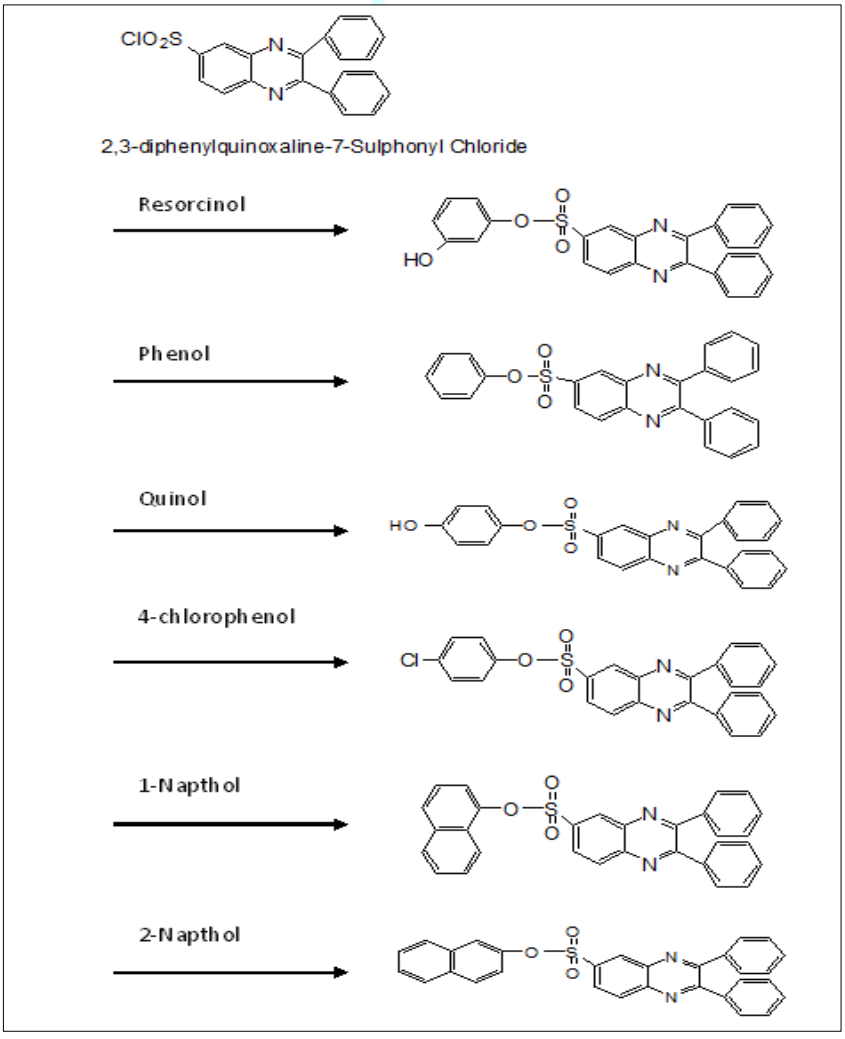
Pharmaceutical chemistry is the chemistry of substances used in medicine. It embraces the main branches of chemistry: radiochemistry, analytical, general, and physical and organic chemistry. Pharmaceutical chemistry is concerned more with physically and chemically oriented phases of drug action or availability such as pharmacokinetics, thermodynamics and the assay of drugs in drug system. Heterocyclic compounds are those cyclic compounds whose ring contain besides, carbon, one or more atoms of other elements. The non-carbon atoms such rings are referred to ashetero atoms. The most common hetero atoms are nitrogen, sulphur and oxygen. The heterocyclic compounds having lesser common atoms such phosphorus, tin, boron, silicon, bromine, etc. have been a subject of much investigation in recent years. The heterocyclic compounds having three to six carbons in the ring are numerous, but only those having five or six atoms in the ring are by far the most important. Quinoxalines are becoming the attractive target of extensive research due to its inherent diverse properties. Various potential activities of the quinoxalines have been explored recently like, antimicrobial agents, cytotoxic agents, anti-tubercular, anxiolytic, anti-HIV, anti-inflammatory, antioxidant etc. In the recent year, 2, 3 Disubstitutedquinoxalines reported to posse's significant antimicrobial potential against bacteria, fungi, and mycobacterium (Ganapaty S. *et al* 2007). Designs of quinoxaline antibiotics have undertaken by several workers, but they possess limited application due to their toxic effect. According to conclusion derived in literature survey, it was worthwhile to introduced lipophillic moiety into the 2,3 diphenylquinoxaline system to make the structure as DNA targeted potent antimicrobial agent the sulfonate have created considerable attention as carrier and lipophillic core in the area of synthetic medicinal chemistry. Based on the observation and in connection with earlier studies (Ganapaty*etal*, 2007), the present work was undertaken synthesize some new phenol &aldehyde derivatives of 2, 3 diphenylquinoxaline 7 sulphonyl chloride which are more potential as antibacterial than parent quinoxalines.

2. MATERIALS AND METHODS:

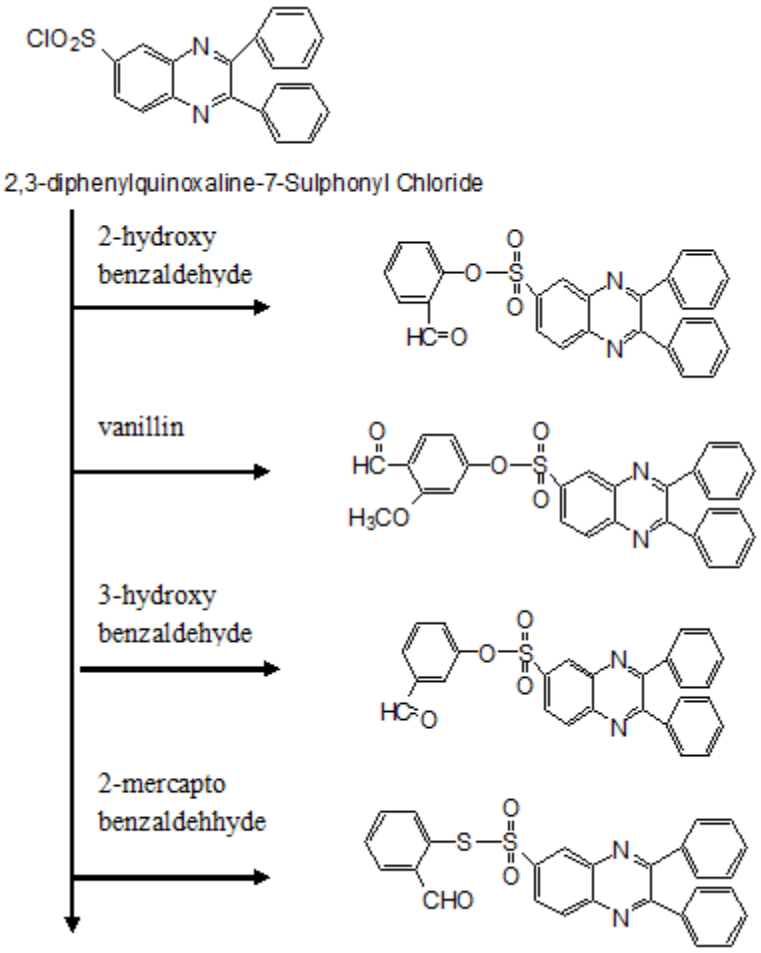
Synthetic Scheme 1:



2.1 Synthetic Scheme 2:



2.2 Synthetic Scheme 3:



2.3 Experimental Procedure:

2.3.1 Synthesis of 2, 3-diphenylquinoxaline

To warm solution of 4.2 gram of benzyl in 16 ml of rectified spirit, the solution of 2.2ml of o-phelynediamine in 16 ml of rectified spirit was added & combine solution was warm in water wath for 30 min. added water until slight colourless persist & allow to cool. Filter & recrystallize the product in ethanol.

2.3.2 *Synthesis of 2-hydroxyphenyl-2,3-diphenylquinoxaline-7-sulphonate(R1)*

Mix 1.17gm of resorcinol with 3ml pyridine & 2.34 gm of sulphonyl chloride derivative &heat on water bath for 1 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.3*Synthesis of Phenyl-2,3-diphenylquinoxaline-7-sulphonate (R2)*

Mix 1 gm of phenol with 2.5ml pyridine & 2 gm of sulphonyl chloride derivative & heat on water bath for 1 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.4 Synthesis of 4-hydroxyphenyl-2,3-diphenylquinoxaline-7-sulphonate(R3)

Mix 1.17 gm of quinol with 3ml pyridine & 2.34 gm of sulphonyl chloride derivative &heat on water bath for 55min pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present & them with cold water , recrystallized from methanol or ethanol.

4.3.2.4 Synthesis of 4-Chlorophenyl-2,3-diphenylquinoxaline-7-sulphonate(R4)

Mix 1.36 gm of 4-chloro phenol with 3.4ml pyridine & 2.72 gm of sulphonyl chloride derivative &heat on water bath for 1 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.5 Synthesis of Napthalene-1-yl-2,3-diphenylquinoxaline-7-sulphonate(R5)

Mix 1.54gm of 1-naphthol with 3.85ml pyridine & 3.08 gm of sulphonyl chloride derivative &heat on water bath for 2 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.6 Synthesis of Napthalene-2-yl-2,3-diphenylquinoxaline-7-sulphonate (R6)

Mix 1.54 gmof 2-naphthol with 3.85ml pyridine & 3.08 gm of sulphonyl chloride derivative &heat on water bath for

2.15 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.7 Synthesis of 2-formylphenyl-2,3-diphenylquinoxaline-7-sulphonate(R7)

Mix 1.29 gm of salicylaldehyde with 3.22ml pyridine & 2.58 gm of sulphonyl chloride derivative &heat on water bath for 1.5 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.8Synthesis of 4-formyl-3-methoxyphenyl-2,3-diphenylquinoxaline-7-sulphonate (R8)

Mix 1.61 gm of vanillin with4.02 ml pyridine & 3.22 gm of sulphonyl chloride derivative & heat on water bath for 3 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.9Synthesis of 3-formylphenyl-2,3-diphenylquinoxaline-7-sulphonate(R9)

Mix 1.29 gm of 3-hydroxybenzaldehyde with 3.22ml pyridine & 2.58 gm of sulphonyl chloride derivative &heat on water bath for 2.15 hr. pour into 25 ml of cold water & stir until the oil solidifies , filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water , recrystallized from methanol or ethanol.

2.3.10 Synthesis of S-2-formylphenyl-2,3-diphenylquinoxaline-7-sulphonate(R10)

Mix 1.46 gm of 2-mercapto benzaldehyde with 3.67ml pyridine & 2.92 gm of sulphonyl chloride derivative &heat on water bath for 2 hr. pour into 25 ml of cold water & stir until the oil solidifies, filter wash with cold dilHCl to remove pyridine and cold dilNaOH to remove any phenol present &them with cold water, recrystallized from methanol or ethanol.

3. PHARMACOLOGICAL ACTIVITY:

3.2 Antioxidant Screening

3.2.1 Hydrogen Peroxide Scavenging Assays

Hydrogen peroxide solution (40 mM) was prepared with standard phosphate buffer (pH 7.4). Different concentration of the compound stock solution and 4ml distilled water was added to 0.6 ml of hydrogen peroxide solution. Absorbance was determined at 230 nm after 10 min against a blank solution containing phosphate buffer without hydrogen peroxide. The percentage scavenging activity at different concentrations of the different derivatives compared with the standard, ascorbic acid.

$$\% \text{ Inhibition} = (Ac - At/Ac) \times 100$$

Where, Ac – Absorbance of control and At – Absorbance of test

3.2.21,1-Diphenyl-2, Picryl Hydrazyl Method (DPPH)

DPPH radical scavenging activity was measured using the method of Cotelle*et al.* with some modifications. 3 ml of reaction mixture containing 0.2 ml of DPPH (100 µM in methanol) 2.8 ml of test solution, at various concentrations (5, 10, 20, 40, 80, 160 320 µg/ml) of the extract fractions was incubated at 37°C for 30 min absorbance of the resulting solution was measured at 517 nm using Beckman model DU-40 spectrophotometer. The percentage inhibition of DPPH radical was calculated by comparing the results of the test with those of the control (not treated with extract) using the following equation: (Navkar S. et al, 2010).

% inhibition=(1–absorbance of test/absorbance of control)×100

4. RESULT AND DISCUSSION:

4.1Antioxidant Screening

4.1.1 Hydrogen peroxide scavenging activity

Table 1: Hydrogen peroxide scavenging assay

Concentration	50 µg/ml	100 µg/ml	200 µg/ml
R1	45.2	65.30	72.27
R3	36.8	56.93	85.27
R4	18.4	18.53	28.00
R7	34.5	49.80	87.28
R10	30.45	40.52	84.24
Ascorbic acid	49.4	71.32	89.96

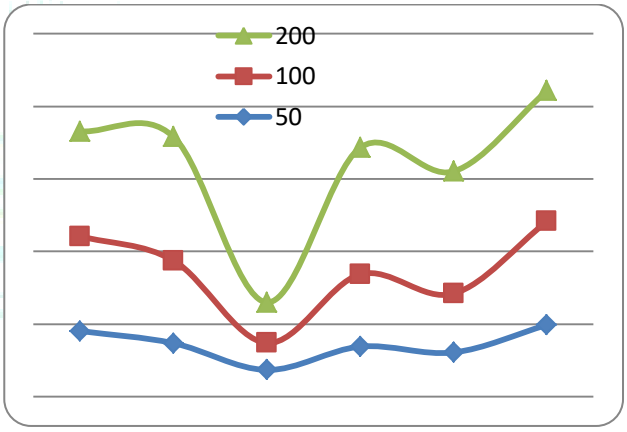


Figure 1: Hydrogen peroxide scavenging assay

4.1.2: 1, 1 diphenyl 2, picryl hydrazyl Method (DPPH)

Table 2:*1, 1 diphenyl 2, picryl hydrazyl Method (DPPH)*

Concentration	100mcg/ml	200mcg/ml	400mcg/ml
R1	71.16	83.03	91.92
R3	71.04	83.48	89.26
R4	76.89	88.57	97.54
R7	85.71	86.21	88.00
R10	74.81	87.93	95.96

CONCLUSION:

The newly synthesized phenol and aldehydes derivatives were screened for antioxidant activity. The results of pharmacological screenings are satisfactory. Most of the derivatives have shown comparable antioxidant activity in relation to standard Ascorbic acid and DPPH at 100, 200 and 400mcg/ml were found 85.71,86.21 and 88.00 for R7 respectively.

REFERENCES

1. Darabi HR, Yu K, Toral-Barza L, Hollander I, Zask A, Discovery of 2- arylthieno[3,2-d]pyrimidines containing 8-oxa-3-azabi-cyclo[3.2.1]octane in the 4- position as potent inhibitors of mTOR with selectivity over PI3K. Bioorg Med Chem Lett 2017; 20 (1):375-9.
2. M.M.Ali et.al.; T. B., Antimicrobial activity of long-chain (E)-3-alken-2-ones. Bioorg Med Chem Lett 2017; 20 (6):1819-20.
3. Vicente E., *et al,* Synthesis and structure –activity relationship of 3-furyl and 3-thienylquinoxaline-2-carbonitrile 1,4-di-N-oxide derivatives against Plasmodium falciparum,"http://www.usc.es/congresos/ecsoc/11/ECSOC11.htm(accessed November 13,2007).
4. Asuncion Burgueteet *al.,* synthesis and anti-inflammatory/antioxidant activities of some new ring substituted 3-phenyl-1-(1, 4-di-N-oxide quinoxaline-2-yl)-2-propen-1-one derivative, *Bioorganic and Medicinal Chemistry Letters* 2007; *17*:6439-6443.
5. Sandra Piras et *al*., Quinoxaline Chemistry, Synthesis of Methyl [4-(Substituted 2-quinoxalinyloxy) Phenyl] acetate and evaluation of anticancer activity, *IL FARMCO* 2004; *59*:185-194
6. Iveta Wiedermannova *et al*., Synthesis of some arylhydrazones of 2-oxo-6,7,dichloro-1, 2-dihydroquinoxaline carbaldehyde, *ActaUniversitatisPalackianaeOlomucensisFacultasRerumNaturalium* , 2002; *46*:771.
7. Hossein Reza Darabi et al, A recyclable and highly effective sulfamic acid/MeOH catalytic system for the synthesis of quinoxalines at room temperature, Catalysis Communications 2007; 8:389–392.
8. Fang Dong, et al, A practical and efficient synthesis of quinoxaline derivatives catalyzed by task-specific ionic liquid, Catalysis Communications 2008; 9:317–320.
9. Bhosale RS, Sarda SR, Ardhapure SS, Jadhav WN, Bhusareb SR, Pawar RP, An efficient protocol for the synthesis of quinoxaline derivatives at room temperature using molecular iodine as the catalyst, Tetrahedron Letters 2005; 46:7183–7186.
10. Dae-Kee Kim, Sun Hee Jung, Ho Soon Lee, Purushottam M. Dewang, Synthesis and biological evaluation of benzenesulfonamide-substituted 4-(6-alkylpyridin-2-yl)-5-(quinoxalin-6-yl)imidazoles as transforming growth factor-b type 1 receptor kinase inhibitors, European Journal of Medicinal Chemistry 2009; 44:568-576.
11. Kumar A, Kumar S, Saxena A, De A, Mozumdar S, Ni-nanoparticles: An efficient catalyst for the synthesis of quinoxalines, Catalysis Communications 2008; 9:778–784.
12. Srinivas C, Naga Sesha C, Pavan Kumar S, VaidyaJayathirthaRao, SrinivasanPalaniappan, "Efficient, convenient and reusable polyaniline-sulfate salt catalyst for the synthesis of quinoxaline derivatives", Journal of Molecular Catalysis A: Chemical 2007; 265:227–230.
13. Bi Bi Fatemeh Mirjalili, Ali Akbari, Nano-TiO2: An eco-friendly alternative for the synthesis of quinoxalines, Chinese Chemical Letters 2011; 22:753–756.
14. Hasaninejad A, Zare A, Shekouhy M, Moosavi-Zare AR, Bentonite Clay K-10 as an EfficientReagent for the Synthesis of Quinoxaline Derivatives at Room Temperature, E-Journal of Chemistry, 2009; 6(S1):S247- S253.
15. Rajurkar R.M, Agrawal V.A, Thonte S.S, Ingale R.G, Heterocyclic Chemistry Of Quinoxaline And Potential Activities Of Quinoxaline Derivatives, *Pharmacophore* 2010; 1(2):65-76.
16. Budakoti A, RooufBhat A, Azam A, Synthesis of new 2-(5-substituted-3-phenyl-2-pyrazolinyl)-1,3-thiazolino[5,4-b]quinoxaline derivatives and evaluation of their antiamoebic activity, European Journal of Medicinal Chemistry 2009; 44:1317-1325.
17. Fonseca T, Gigante B, Marques MM, Gilchrist TL, Clercq ED, Synthesis and antiviral evaluation of benzimidazoles, quinoxalines and indoles from dehydroabietic acid, Bioorganic & Medicinal Chemistry 2004; 12:103–112.
18. Xu B, Sun Y, Guo Y, Cao Y, Yu Y, Synthesis and biological evaluation of N4-(hetero)arylsulfonylquinoxalinones as HIV-1 reverse transcriptase inhibitors, Bioorganic & Medicinal Chemistry 2009; 17:2767–2774.