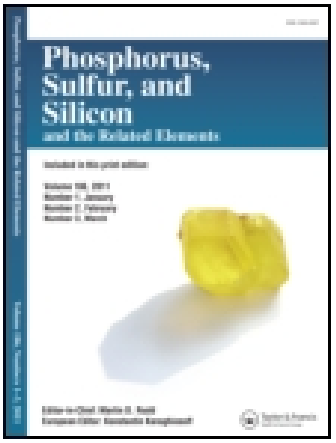


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Molecular Iodine as a Versatile Reagent for the Synthesis of Thiazoloquinoline—A Potential Antibacterial Agent

R. Subashini [a] & F. Nawaz Khan [a]
[a] Organic and Medicinal Chemistry Laboratory, School of Advanced Sciences , VIT University , Vellore, Tamil Nadu, India
Published online: 07 Mar 2011.

To cite this article: R. Subashini & F. Nawaz Khan (2011) Molecular Iodine as a Versatile Reagent for the Synthesis of Thiazoloquinoline—A Potential Antibacterial Agent, Phosphorus, Sulfur, and Silicon and the Related Elements, 186:3, 450-456, DOI: 10.1080/10426507.2010.503209

To link to this article: http://dx.doi.org/10.1080/10426507.2010.503209

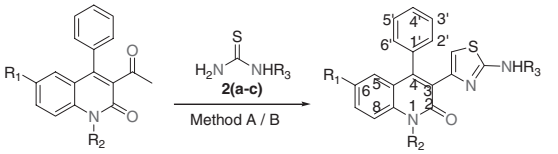
Phosphorus, Sulfur, and Silicon, 186:450–456, 2011

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426507.2010.503209

MOLECULAR IODINE AS A VERSATILE REAGENT FOR THE SYNTHESIS OF THIAZOLOQUINOLINE—A POTENTIAL ANTIBACTERIAL AGENT

R. Subashini and F. Nawaz Khan
Organic and Medicinal Chemistry Laboratory, School of Advanced Sciences, VIT University, Vellore, Tamil Nadu, India

GRAPHICAL ABSTRACT



1(a-g) 3(a-i)

Compound 1 or 3	R_1	R_2	R_3
a	-Cl	$-CH_3$	-H
b	-Cl	$-CH_3$	$-CH_3$
c	-Cl	$-CH_3$	$-NH_2$
d	-Cl	$-C_2H_5$	-H
e	-Cl	$-C_2H_5$	$-CH_3$
f	-Cl	$-CH_2Ph$	$-CH_3$
g	-H	$-CH_3$	-H
h	-H	$-CH_3$	$-CH_3$
i	-H	$-C_2H_5$	-H

Abstract *A series of 3-(2-aminothiazol-4-yl)quinolin-2[1*H*]-ones **3** was prepared by neat reaction of quinolin-2[1*H*]-ones **1** with thioureas **2** in the presence of molecular iodine. The synthesized compounds were evaluated for their in vitro antimicrobial activities against* Escherichia coli*,* Paedococcus sp.*,* Lactobacillus*,* Yersinia enterocolitica*, and* Staphylococcus aureus*. The green chemical approach for the synthesis of thiazoloquinolinone **3** was performed under neat conditions using molecular iodine as catalyst as well as reaction medium.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords 2-Aminothiazole, 3-(2-aminothiazol-4-yl)quinolin-2(1*H*)-ones; antibacterial activity; quinoline; thioureas

Received 13 April 2010; accepted 18 June 2010.
The authors wish to express their gratitude to the Indian Institute of Science, SAIF, Bangalore and Indian Institute of Technology, Chennai and Syngene International Limited for their support of NMR, HRMS facilities.
Address correspondence to F. Nawaz Khan, Organic and Medicinal Chemistry Laboratory, School of Advanced Sciences, VIT University, Vellore, Tamil Nadu 632014, India. E-mail: nawaz_f@yahoo.co.in

INTRODUCTION

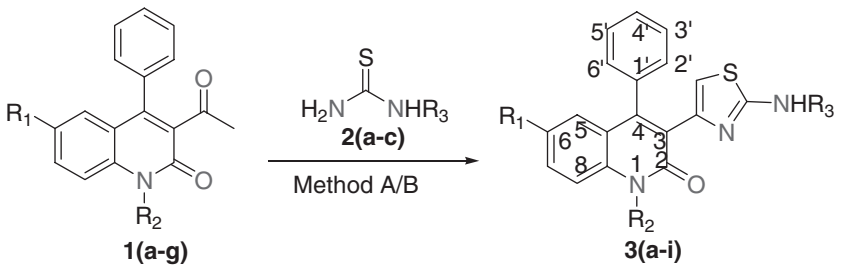
The quinolinenucleus occurs in several natural compounds and pharmacologically active substances[1] displaying a broad range of biological activities such as antiasthmatic,[2] anti-inflammatory,[3] antimalarial,[4] anticancer,[5] antibiotic,[6] antihypertensive,[7] and anti-HIV.[8,9] As a result, several simple and elegant syntheses of substituted quinolines have recently been published.[10] Several drugs based on the quinoline structure have improved therapy of protozoal diseases, especially malaria.[11]

Similarly, the thiazole ring, a structural component of natural compounds such as vitamin B1 (thiamine), penicillin, and carboxylase, has been found to exhibit significant biological activities such as cytotoxic, immunosuppressive, antifungal, and enzyme inhibitory activity.[12] Moreover, among the different aromatic heterocycles, thiazoles occupy a prominent position in the drug discovery process,[13] and this ring structure is found in several marketed drugs. Aminothiazoles are known to be ligands of estrogen receptors[14] as well as a novel class of adenosine receptor antagonists.[15]

In continuation of our interest in heterocyclic molecules,[16–24] in this article, we report a simple and facile, one-pot, two-step, synthesis of novel 3-(2-aminothiazol-4-yl)quinolin-2(1*H*)-ones **3a–i**. Their in vitro antibacterial properties were screened and evaluated. In the present synthesis, iodine played a major role in the one-pot synthesis, resulting in good yields of target compounds.

RESULTS AND DISCUSSION

The synthetic protocol of the title compounds is shown in Scheme 1. The starting material, N-alkylated quinolin-2[1*H*]-one **1,** synthesized by using DMF/K_2CO_3, readily reacted with thioureas **2** in the presence of iodine under solvent free conditions to give 3-(2-aminothiazol-4-yl)quinolin-2[1*H*]-ones **3**. The optimization of the reaction was carried out using bromine (Method A) or iodine (Method B). It should be noted that the reaction of N-alkylated quinolin-2[1*H*]-one **1** with thioureas **2** in the presence of bromine gave less yield of the compound **3**, even after heating for a prolonged reaction time. However, under iodine-mediated conditions, the notorious substrate **1** gave a good yield of thiazolylquinolinone **3** with high purity. All additional attempts to increase the yield in this reaction, however, proved to be futile. Iodine played a major role in the formation of compound **3**, through an iodoacetyl intermediate that condenses with thiourea. Moreover the reaction work up was simpler, i.e., water was added to the reaction mixture and boiled for few minutes so that the product thiazoles were dissolved in distilled water, which was filtered while hot. The filtrate, when neutralized with aqueous NH_3, gave the title compounds **3** in high yield



Scheme 1 Synthesis of 3-(2-aminothiazol-4-yl)quinolin-2(1*H*)-ones.

Table 1 Substitutents of 3-(2-aminothiazol-4-yl)-quinolin-2[1*H*]-ones

Compound **1** or **3**	R_1	R_2	R_3
a	-Cl	$-CH_3$	-H
b	-Cl	$-CH_3$	$-CH_3$
c	-Cl	$-CH_3$	$-NH_2$
d	-Cl	$-C_2H_5$	-H
e	-Cl	$-C_2H_5$	$-CH_3$
f	-Cl	$-CH_2Ph$	$-CH_3$
g	-H	$-CH_3$	-H
h	-H	$-CH_3$	$-CH_3$
i	-H	$-C_2H_5$	-H

(Table 1). All the synthesized final compounds were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and mass spectral studies. Compound **3a** showed FTIR bands at 3296, 1639, 1518 cm^{-1} due to $-NH_2$, $-C{=}O$, and $-C{=}N$ respectively. The disappearance of $-C{=}O$ at 1705 cm^{-1} of **1a** at C-3 indicates that it had been involved in condensation with thiourea. ^{1}H NMR spectrum of **3a** showed at δ 3.68 (s, 3H, $-N-CH_3$), 6.10 (s, 1H, $-$CH-thiazole), and 6.65 (s, 2H,$-NH_2$).

CONCLUSIONS

This article reports the successful green chemical approach for the synthesis of new 3-(2-aminothiazol-4-yl)quinolin-2[1*H*]-ones **3** using molecular iodine as catalyst under neat condition. The antibacterial activity study revealed that compounds **3a** and **3c** showed good activity against *S. aureus.* Compound **3c** exhibits moderate activity against *B. subtilis* and *Paedococcus*, in comparison to the standard drug ampicillin (see the Supplemental Materials, available online).

EXPERIMENTAL

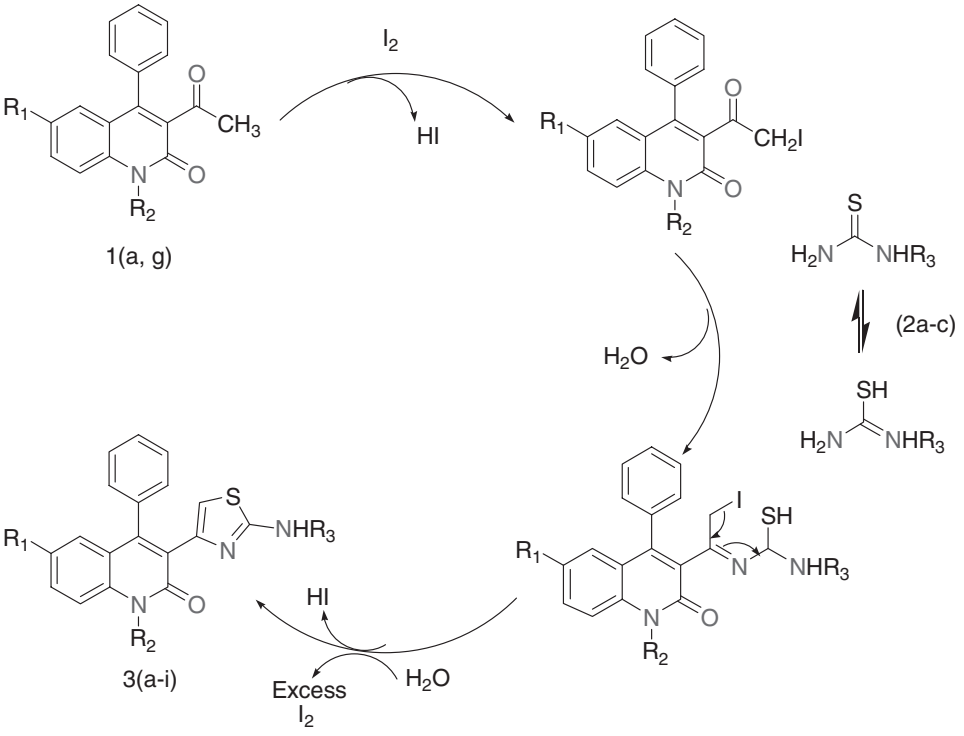
All reagents were purchased from Aldrich Chemical Co. Solvents used were purchased from Rankem Chemicals. TLC was performed on silica gel coated on plates and dried. (SD Fine chemicals). The plates were illuminated under an iodine chamber. Melting points (mp) are uncorrected and were determined using an Elchem Microprocessor–based DT apparatus. FT-IR spectra, as KBr pellets, were recorded on a Nucon Infrared spectrophotometer. ^{1}H NMR (400 and 500 MHz) spectra were recorded on a Bruker 400 and 500 MHz spectrometer in $CDCl_3$ or DMSO (with TMS for ^{1}H as internal references).

General Procedure for the Synthesis of 3-(2-Aminothiazol-4-yl)-quinolin-2[1*H*]-ones 3 (a–i)

Method A. To a mixture of N-substituted quinolin-2[1*H*]-ones **1** (1 mmol) and thioureas **2** (20 mmol), bromine (20 mmol) was added dropwise. Then the mixture was heated on a water bath overnight. Reaction completion was monitored by TLC using pet. ether:EtOAc (3:2). Upon completion of the reaction, water was added and refluxed on a water bath and filtered while hot. Then the solution was made alkaline by adding a strong

ammonia solution. The solid separated was filtered and purified by column chromatography to afford products **3a–i** as yellow amorphous solids (38–41% yield).

Method B. A mixture of N-substituted quinolin-2[1*H*]-ones **1** (1 mmol), thioureas **2** (20 mmol), and iodine (10 mmol) was heated on water bath for 6–8 h. The reaction completion was monitored by TLC using pet. ether:EtOAc (3:2). The mixture was cooled and diluted with water, then heated until most of the solid dissolved. It was filtered while hot, then the filtrate was cooled and made alkaline by adding a strong ammonia solution. The solid was filtered, washed with water, and recrystallized form acetone to afford products **3a–i** as yellow amorphous solids (78–89% yield). The purity of quinolinone-thioazoles was ascertained by spectral analysis (Scheme 2).



Scheme 2 Plausible mechanistic pathway for the formation of thiazoloquinolinones **3a–i**.

1-Methyl-3-(2-aminothiazol-4-yl)-4-phenyl-6-chloroquinolin-2(*1H*)-one (3a). Yield: 89%. Mp: 210°C. IR (KBr, cm^{-1}) υ: 3296 (−NH_2), 1639 (−C=O), 1518 (−C=N). ^{1}H NMR (400 MHz, DMSO-d6, δ, ppm): 3.68 (s, 3H, N−CH_3); 6.10 (s, 1H, CH-Thiazole); 6.65 (s, 2H, −NH_2); 6.95 (s, 1H, CH-5); 7.18 (m, 2H, CH-2′, CH-6′); 7.36 (m, 3H, CH-3′, CH-4′, CH-5′); 7.65 (m, 2H, CH-7, CH-8). ^{13}C NMR (100 MHz, DMSO-d6, δ, ppm): 30.3 (N-CH_3), 107.3 (C-5-Thiazole), 117.5, 122.1, 126.4, 126.7, 2 × 128.4, 128.7, 2 × 129.4, 130.7, 135.8 (C-Cl), 136.0, 138.4 (C-4- Thiazole), 145.0, 147.4, 160.3 (−C=O), 167.1 (C-NH_2). Mol. formula: $C_{19}H_{14}ClN_3OS$ requires 367.0546: HRMS: m/z 367.1063 (M+).

1-Methyl-3-(2-(methylamino)thiazol-4-yl)-4-phenyl-6-chloroquinolin-2 (*1H*)-one (3b). Yield: 82.3%. Mp: 130–132°C. IR (KBr, cm^{-1}) υ: 3371 (−NH), 1632

(−C=O), 1513 (−C=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 2.82 (s, 3H, Thiazole -N-CH_3); 3.80 (s, 3H, N-CH_3); 5.13 (s, 1H, -NH); 6.16 (s, 1H, CH- Thiazole); 7.18 (m, 2H, CH-5, CH-7); 7.37 (m, 5H, CH-2′, 3′, 4′, 5′, 6′); 7.49—7.51 (d, 1H, CH-8). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.2 (Thiazole -N-CH_3), 32.6 (N-CH_3), 109.1, 114.5, 122.0, 124.7, 2 × 128.2, 128.5, 3 × 130.2, 2 × 130.1, 130.5, 131.4, 135.2, 141.8, 164.1 (C=O), 164.8 (C-NH_2). Mol. formula: $C_{20}H_{16}ClN_3OS$ requires 381.0703 : HRMS: m/z 381.1352 (M+).

1-Methyl-3-(2-hydrazinothiazol-4-yl)-4-phenyl-6-chloroquinolin-2(*1H*)-one (3c). Yield: 79.6%. Mp: 250–252°C. IR (KBr, cm^{-1}) υ: 3436 (−NH), 3357 (−NH_2), 1637 (−C=O), 1572 (−C=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 2.01—2.03 (d, 2H, J = 8 Hz, NH_2- Thiazole); 3.80 (s, 3H, N-CH_3); 7.01 (s, 1H, CH- Thiazole); 7.17 (m, 2H, CH-5,7); 7.50 (m, 5H, CH-2′, 3′, 4′, 5′, 6′); 7.61–7.63 (d, 1H, CH-8); 8.42 (t, 1H, NH- Thiazole). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.6 (N-CH_3), 109.1, 114.5, 122.0, 124.7, 2 × 128.2, 128.5, 3 × 130.2, 2 × 130.1, 130.5, 131.4, 135.2, 141.8, 164.1 (C=O), 164.8 (C-NH_2). Mol. formula: $C_{19}H_{15}ClN_4OS$ requires 382.0655 : HRMS: m/z 381.9078 (M+).

1-Ethyl-3-(2-aminothiazol-4-yl)-4-phenyl-6-chloroquinolin-2(*1H*)-one (3d). Yield: 82.1%. Mp: 170–172°C. IR (KBr, cm^{-1}) υ: 3437 (−NH_2), 1629 (−C=O), 1519 (−C=N). ^{1}H NMR (500 MHz, DMSO-d6, δ ppm): 1.26 (t, 3H, N-$CH_2\underline{CH_3}$); 4.34 (q, 2H, N-$\underline{CH_2}CH_3$); 6.10 (s, 1H, CH- Thiazole); 6.69 (s, 2H, -NH_2); 6.97 (s, 1H, CH-5); 7.19 (m, 2H, CH-2′, 6′); 7.38 (m, 3H, CH-3′, 4′, 5′); 7.69 (m, 2H, CH-7,8). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 13.0 (N-$CH_2\underline{CH_3}$), 37.9 (N-$\underline{CH_2}CH_3$), 107.4, 117.2, 122.4, 2 × 126.2, 127.0, 3 × 128.4, 2 × 129.4, 2 × 130.8, 135.9, 137.3, 147.5, 159.8 (C=O), 167.1 (C-NH_2). Mol. formula: $C_{20}H_{16}ClN_3OS$ requires 381.0703 : (ESI): HRMS: m/z 381.5604 (M+).

1-Ethyl-3-(2-(methylamino)thiazol-4-yl)-4-phenyl-6-chloroquinolin-2(*1H*)-one (3e). Yield: 80.7%. Mp: 140°C. IR (KBr, cm^{-1}) υ: 3432 (-NH_2), 1632 (−C=O), 1556 (−C=N). ^{1}H NMR (500 MHz, DMSO-d6, δ, ppm): 1.25 -1.28 (t, 3H, N-$CH_2\underline{CH_3}$); 2.49 (s, 3H, 2′NH-CH_3); 4.34–4.36 (q, 2H, N-$\underline{CH_2}CH_3$); 6.45 (s, 1H, CH- Thiazole); 6.97 (s, 1H, -NH); 7.37 (m, 3H, CH-5, 2′, 6′); 7.38 (m, 3H, CH-3′, 4′, 5′); 7.66 (m, 2H, CH-7,8). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 13.1 (N-$CH_2\underline{CH_3}$), 30.3 (Thiazole-N-CH_3), 37.3 (N-$\underline{CH_2}CH_3$), 109, 114.1, 121.9, 124.1, 2 × 127.9, 128.0, 3 × 129.8, 2 × 130, 130.2, 130.9, 135, 140.9, 163.5 (C=O), 164.5 (C-NH-). Mol. formula: $C_{21}H_{18}ClN_3OS$ requires 395.0859 : HRMS: m/z 395.6901 (M+).

1-Benzyl-3-(2-(methylamino)thiazol-4-yl)-4-phenyl-6-chloro-quinolin-2(*1H*)-one (3f). Yield: 78.2%. Mp: 222–226°C. IR (KBr, cm^{-1}) υ: 3462 (-NH_2), 1623(−C=O), 1515(−C=N). ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 5.41 (s, 2H, N-CH_2); 6.12 (s, 1H, CH- Thiazole); 6.40 (s, 1H, -NH_2); 7.23 (d, 1H, CH-7, J = 2.5); 7.27 (s, 1H, CH-5); 7.36 (m, 5H, Ar-H, -CH_2-Ph); 7.51 (m, 5H, Ar-H, 4-Ph); 7.74 (d, 1H, CH-8, J = 2.5). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 48.1 (N-$\underline{CH_2}$-C_6H_5), 30.3 (Thiazole-N-CH_3), 108.8, 114.3, 121.7, 124.3, 5 × 127.8, 3 × 128.2, 3 × 129.9, 3 × 130.1, 130.4, 130.9, 134.9, 140.7, 163.2 (C=O), 164.9 (C-NH-). Mol. formula: $C_{26}H_{20}ClN_3OS$ requires 457.1016 : HRMS: m/z 457.0097 (M+).

1-Methyl-3-(2-aminothiazol-4-yl)-4-phenylquinolin-2(*1H*)-one (3g). Yield: 81%. Mp: 167–169°C. IR (KBr, cm^{-1}) υ: 3439 (−NH_2), 1631 (−C=O),1503 (−C=N). ^{1}H NMR (500 MHz, DMSO-d6, δ, ppm); 3.81 (s, 3H, N-CH_3); 5.53 (s, 2H, -NH_2); 6.05 (s, 1H, CH- Thiazole); 7.40 (m, 9H, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 30.2 (N-$\underline{CH_3}$), 108.9, 121.8, 3 × 127.7, 3 × 129.7, 3 × 130.1, 2 × 130.3, 130.8,

135.2, 140.7, 163.3 (C=O), 164.2 (C-NH_2). Mol. formula: $C_{19}H_{15}N_3OS$ requires 333.0936 : HRMS: m/z 333.4634 (M+).

1-Methyl-3-(2-(methylamino)thiazol-4-yl)-4-phenylquinolin-2(*1H*)-one (3h). Yield: 79%. Mp: 233°C. IR (KBr, cm^{-1}) υ: 3392 (−NH), 1637 (−C=O), 1506 (−C=N). ^{1}H NMR (500 MHz, DMSO-d6, δ, ppm); 2.72 (s, 3H, 2′-$NHCH_3$); 3.81 (s, 3H, N-CH_3); 5.80 (s, 1H, −NH); 6.18 (s, 1H, CH-5′); 7.02–7.57 (m, 9H, Ar-H). ^{13}C NMR (125 MHz, DMSO, δ, ppm): 30.7 (N-CH_3), 107.7 (C-5-Thiazole), 117.2, 122.4, 126.2, 126.9, 2 × 128.5, 3 × 128.9, 2 × 129.7, 133, 136.1, 138.0 (C-4- Thiazole), 145.2, 147.8, 161.5 (-C=O), 169 (C-NH_2). Mol. formula: $C_{20}H_{17}N_3OS$ requires 347.1092 : HRMS: m/z 347.3448 (M+).

1-Ethyl-3-(2-aminothiazol-4-yl)-4-phenylquinolin-2(*1H*)-one (3i). Yield: 80.3%. Mp: 194–196°C. IR (KBr, cm^{-1}) υ: 3439 (−NH_2), 1631 (−C=O), 1503 (−C=N). ^{1}H NMR (500 MHz, DMSO-d6, δ, ppm): 1.48 (t, 3H, N-CH_2*CH_3*); 2.80 (q, 2H, N-*CH_2*CH_3), 4.41 (s, 2H, -NH_2), 6.17 (s, 1H, CH- Thiazole), 7.37 (m, 9H, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 13 (N-CH_2*$\underline{CH_3}$*), 37.5 (N-*$\underline{CH_2}$*CH_3), 107.2, 122.1, 127.4, 3 × 128.0, 128.2, 3 × 129.4, 2 × 129.5, 130.6, 131.2, 138.3, 139, 162 (C=O), 163 (C-NH_2). Mol. formula: $C_{20}H_{17}N_3OS$ requires 347.1092 : HRMS: m/z 346.8739(M+).

REFERENCES

1. (a) Maguire, M. P.; Sheets, K. R.; Vety, K. M.; Spada, A. P.; Zilberstein, A. *J. Med. Chem.* **1994**, *37*, 2129–2137; (b) Roma, G.; Braccio, M. D.; Grossi, G.; Mattioli, F.; Ghia, M. *Eur. J. Med. Chem.* **2000**, *35*, 1021–1035 (c) Chen, Y. L.; Fang, K. C.; Sheu, J. Y.; Hsu, S. L.; Tzeng, C. C. *J. Med. Chem.* **2001**, *44*, 2374–2377.
2. Doube, D.; Blouin, M.; Brideau, C.; Chan, C.; Desmarais, C.; Ethier, D.; Falgueyret, J. P.; Friesen, R. W.; Girard, M.; Girard, Y.; Guay, J.; Tagari, P.; Young, R. N. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1255–1260.
3. Leatham, P. A.; Bird, H. A.; Wright, V.; Seymour, D.; Gordon, A. *Eur. J. Rheumatol. Inflamm.* **1983**, *6*, 209–211.
4. Arcadi, A.; Chiarini, M.; Giuseppe, S. D.; Marinelli, F. *Synlett* **2003**, 203–206, and references cited therein.
5. Denny, W. A.; Wilson, W. R.; Ware, D. C.; Atwell, G. J.; Milbank, J. B.; Stevenson, R. J. U.S. Patent, 7064117, 2006.
6. Mahamoud, A.; Chevalier, J.; Davin-Regli, A.; Barbe, J.; Pages, J.-M. *Current Drug Targets* **2006**, *7*, 843–847.
7. Muruganantham, N.; Sivakumar, R.; Anbalagan, N.; Gunasekaran, V.; Leonard, J. T. *Biol. Pharm. Bull.* **2004**, *27*, 1683–1687.
8. Wilson, W. D.; Zhao, M.; Patterson, S. E.; Wydra, R. L.; Janda, L.; Strekowski, L. *Med. Chem. Res*. **1992**, *2*, 102–110.
9. Strekowski, L.; Mokrosz, J. L.; Honkan, V. A.; Czarny, A.; Cegla, M. T.; Patterson, S. E.; Wydra, R. L.; Schinazi, R. F. *J. Med. Chem.* **1991**, *34*, 1739–1746.
10. (a) Lin, X. F.; Cui, S. L.; Wang, Y. G. *Tetrahedron Lett.* **2006**, *47*, 3127–3130; (b) Sakai, N.; Aoki, D.; Hamajima, T.; Konakahara, T. *Tetrahedron Lett.* **2006**, *47*, 1261–1265; (c) Sakai, N.; Annaka, K.; Konakahara, T. *J. Org. Chem.* **2006**, *71*, 3653–3655; (d) Tanaka, S. Y.; Yasuda, M.; Baba, A. *J. Org. Chem.* **2006**, *71*, 800–803 (e) Wang, G. W.; Jia, C. S.; Dong, Y. W. *Tetrahedron Lett.* **2006**, *47*, 1059–1063; (f) Wang, X.; Dixon, S.; Kurth, M. J.; Lam, K. S. *Tetrahedron Lett.* **2005**, *46*, 5361–5364; (g) De, S. K.; Gibbs, R. A. *Tetrahedron Lett.* **2005**, *46*, 1647–1649; (h) Taguchi, K.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2005**, *46*, 4539–4542; (i) Kobayashi, K.; Yoneda, K.; Miyamoto, K.; Morikawa, O.; Konishi, H. *Tetrahedron* **2004**, *60*, 11639–11645; (j) Zhang, X.; Campo, M. A.; Yao, T.; Larock, R. C. *Org. Lett.* **2004**, *7*, 763–766.

11. Basco, L. K.; Dechy-Cabaret, O.; Ndounga, M.; Meche, F. S.; Robert, A.; Meunier, B. *Antimicrob. Agents Chemother*. **2001**, *45*, 1886–1888.
12. Sperry, J. B.; Wright, D. L. *Curr. Opin. Drug. Discovery Dev.* **2005**, *8*, 723–740.
13. Dolle, R. E.; Le Bourdonnec, B.; Morales, G. A.; Moriarty, K. J.; Salvino, J. M. J. *Comb. Chem.* **2006**, *8*, 597–635.
14. Fink, B. A.; Mortensen, D. S.; Stauffer, S. R.; Aron, Z. D.; Katzenellenbogen, J. A. *Chem. Biol.* **1999**, *6*, 205–219.
15. Van Muijlwijk-Koezen, J. E.; Timmerman, H.; Vollinga, R. C.; Von Drabbe Kunzel, J. F.; De Groote, M.; Visser, S.; Ijzerman, A. P. *J. Med. Chem.* **2001**, *44*, 749–762.
16. Patil, N. T.; Nawaz Khan, F.; Yamamoto, Y. *Tetrahedron Lett.* **2004**, *45*, 8497–8499.
17. Nawaz Khan, F.; Jayakumar, R.; Pillai, C. N. *J. Mol. Catal. A, Chem.* **2003**, *195*, 139–145.
18. Nawaz Khan, F.; Jayakumar, R.; Pillai, C. N. *Tetrahedron Lett.* **2002**, *43*, 6807–6809.
19. Hathwar, V. R.; Manivel, P.; Nawaz Khan, F.; Guru Row, T. N. *Acta Cryst.* **2007**, *E63*, *o*3707.
20. Hathwar, V. R.; Manivel, P.; Nawaz Khan, F.; Guru Row, T. N. *Acta Cryst.* **2007**, *E63*, *o*3708.
21. Syed Tajudeen, S.; Nawaz Khan, F. *Synth. Commun.* **2007**, *37*, 3649–3656.
22. Maiyalagan, T.; Hathwar, V. R.; Manivel, P.; Burcu Arslan, N.; Nawaz Khan, F. *Acta Cryst*. **2008**, *E65*, *o*128.
23. (a) Manivel, P.; Roopan, S. M.; Nawaz Khan, F. *J. Chil. Chem. Soc.* **2008**, *53*, 1609–1610; (b) Manivel, P.; Roopan, S. M.; Nawaz Khan, F. *Indian J. Heterocycl Chem.* **2008**, *18*, 21–24; (c) Roopan, S. M.; Maiyalagan, T.; Nawaz Khan, F. *Can. J. Chem.* **2008**, *86*, 1019–1025.
24. (a) Roopan, S. M.; Reddy, B. R.; Kumar, A. S.; Khan, F. N. *Indian J. Heterocy Chem.* **2009**, *19*, 81–82; (b) Roopan, S. M.; Khan, F. N.; Mandal, B. K. *Tetrahedron Lett.* **2010**, *51*, 2309–2311; (c) Roopan, S. M.; Khan, F. N. *Arkivoc* **2009**, *13*, 161–169.