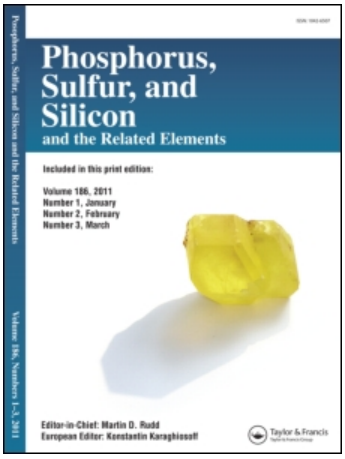
This article was downloaded by:
On: *28 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis and Antimicrobial Activity of Some New Cyanopyridines, Isoxazoles, Pyrazoles, and Pyrimidines Bearing Sulfonamide Moiety

Osama S. Moustafa[a]; Ragaa A. Ahmad[a]
[a] Assiut University, Assiut, Egypt

Online publication date: 27 October 2010

To cite this Article Moustafa, Osama S. and Ahmad, Ragaa A.(2003) 'Synthesis and Antimicrobial Activity of Some New Cyanopyridines, Isoxazoles, Pyrazoles, and Pyrimidines Bearing Sulfonamide Moiety', Phosphorus, Sulfur, and Silicon and the Related Elements, 178: 3, 475 — 484
To link to this Article: DOI: 10.1080/10426500307933
URL: http://dx.doi.org/10.1080/10426500307933

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Phosphorus, Sulfur and Silicon, 2003, Vol. 178:475–484
Copyright © 2003 Taylor & Francis
1042-6507/03 $12.00 + .00
DOI: 10.1080/10426500390170606

Taylor & Francis
Taylor & Francis Group

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW CYANOPYRIDINES, ISOXAZOLES, PYRAZOLES, AND PYRIMIDINES BEARING SULFONAMIDE MOIETY

Osama S. Moustafa and Ragaa A. Ahmad
Assiut University, Assiut, Egypt

(Received April 10, 2002; accepted July 22, 2002)

*Reaction of p-aminoacetophenone **1** with* p-*substituted benzenesulfonyl chloride **2a**,**b** in pyridine afforded p-acetyl derivatives **3a**,**b**, which was then condensed with araldehydes to yield the corresponding chalcones **4a–f**. On condensation of latter chalcones with malononitrile afford cyanopyridines **5a–f**, the reaction of chalcones **4a–f** with hyroxylamine hydrochloride furnished isoxazoles **6a–f**, while condensation of chalcones with hyrazine hydrate afforded pyrazoline derivatives **7**, **8**. Urea or thiourea was reacted with chalcone **4b** to yield pyrimidine derivatives **9**, **10**. The reaction of sulphonylchlorides **2a**,**b** with* P-*aminobenzophenone yield p-[(benzensulphonyl)amido]benzophenone **11a**,**b**, which was then condensed with hydrazine hydrate to give the corresponding hydazone derivatives **12a**,**b**.*

Keywords: Antimicrobial activity; cyanopyridines; isoxazoles; pyrazoles and pyrimidines; sulfonamide; synthesis

Downloaded At: 11:04 28 January 2011

INTRODUCTION

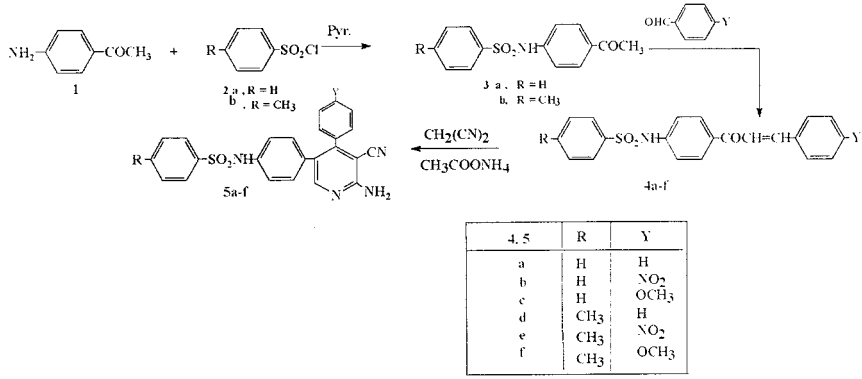
Among the wide variety of heterocycles that have been explored for developing pharmaceutically important molecules, cyanopyridines,[1–3] isoxazoles[4–6] have played an important role in the medicinal chemistry. Bezenesulfonamide derivatives also were reported as elastase inhibitors,[7] carbonic anhydrase, clostridium histolyticum collogenase inhibitors,[8,9] and herbicides and plant growth regulators.[10] They show affinities for ET_A and ET_B receptors in the low nonmolar range and high functional antagonistic potency in vitro,[11] which also exhibits dual action to inhibit the thromboxane receptor and thromboxane

Address correspondence to Osama S. Moustafa, Chemistry Department, Faculty of Science, Assiut University, Assiut, 71516, Egypt. E-mail: oshmous@acc.aun.edu.eg

synthase for cardiovascular and renal diseases.[12] Antiproliferative, antiviral, and antifungal activities have been similarly evaluated.[13] In this respect, and also in continuation of our earlier work on synthesis of different heterocyclic systems that containing highly biological activity,[14–18] these assests prompted us use benzensulfonamide derivative to prepare a new cyanopyridines, isoxazoles, pyrazoles, and pyrimidones with potential biological activity in our search for novel heterocyclic compounds of pharmacological interest. Almost of the synthesized compounds were tested against bacteria and fungi.

RESULTS AND DISCUSSION

As shown in Scheme 1 condensation of *p*-aminoacetophenone **1** with benzensulfonyl chloride **2a** or with *p*-tolunsulfonyl chloride **2b** in pyridine at 0°C yield [benzen (or tolune)-sulfonamido]acetophenone **3a** and **3b** respectively.[21] The key intermediate chalcones **4a–f** required for the synthesis of heterocyclic systems in this article were obtained by condensation of *p*-acetyl derivative **3a–f** with virous aromatic aldehydes. Ring closure of chalcones **4a–f** through reactions with malononitrile in the presence of pyridine gave cyanopyridine derivatives **5a–f** (Scheme 1).

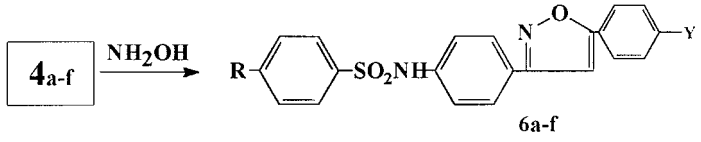


4, 5	R	Y
a	H	H
b	H	NO_2
c	H	OCH_3
d	CH_3	H
e	CH_3	NO_2
f	CH_3	OCH_3

SCHEME 1

Chalcones **4a–f** on reaction with hydroxylamine hydrochloride in the presence of sodium acetate in acetic acid furnished isoxazole derivatives **6a–f** (Scheme 2). Condensation of chalcones **4c**,**f** with hydrazine

Downloaded At: 11:04 28 January 2011

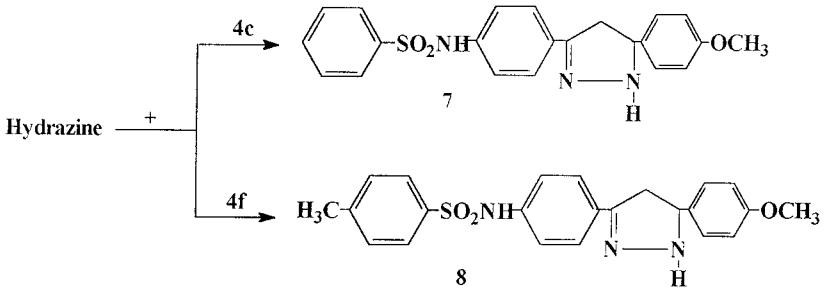


6a-f

6 a-f	R	Y
a	H	H
b	H	NO_2
c	H	OCH_3
d	CH_3	H
e	CH_3	NO_2
f	CH_3	OCH_3

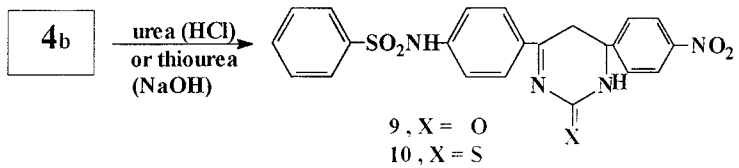
SCHEME 2

Downloaded At: 11:04 28 January 2011



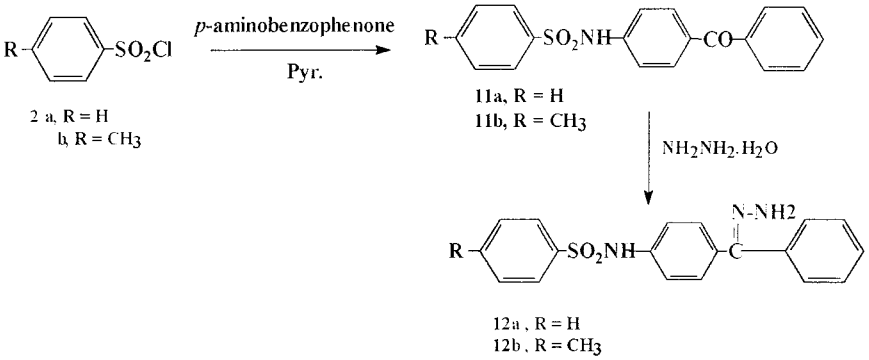
SCHEME 3

hydrate (98%) in ethanol afforded the pyrazoline derivatives **7**, **8** (Scheme 3). The reaction of **4b** with urea in presence of ethanolic hydrogen chloride gave the pyrimidone derivative **9**. Also, reaction of **4b** with thiourea in presence of ethanolic sodium hydroxide afforded the corresponding pyrimidine-2-thione derivative **10** (Scheme 4).



SCHEME 4

Reaction of *p*-aminobenzophenone with benzensulfonyl chloride **2a** at 0°C[19] or with *p*-tolunesulfonyl chloride **2b** furnished benzensulfonamido-N-*p*-pheylbenzoyl derivatives **11a**,**b** Hydrazonlysis of keto compounds **11a**,**b** with hydrazine hydrate afforded the corresponding hydrazone derivatives **12a**,**b** (Scheme 5).



SCHEME 5

ANTIMICROBIAL ACTIVITY

The newly synthesized compounds were screened for their antibacterial activity aganist different three species of bacteria. Gram positive. *Bacillus subtillus*, *Micrococcus luteus*; Gram negative, *Serration rhodenil*; and three species of fungi, *Aspergillus fumigatus*, *Penicllum chrysogen*, and *Fusarium equiseti* using the filter paper technique[20,21] measuring the zone of inhibition in mm at 25 μg concentration. The screening results are summarized in Table I and indicate that, among of tested compounds, there is good growth inhibition aganist Gram positive bacteria, however only two compounds (**3a** and **4f**) showed good growth inhibition against Gram negative bacteria. Concerning the antifungal activaties only two compounds **3e** and **11a** were active aganist fungi, V. B. Patel et al.[22] reported that the activity of the similar compounds (cyanopyridine sulphonamide derivatives) was compared with the known standerd drugs, viz. ampicillin, chloramphenicol, norfloxacin, and griseofulvin.[22]

EXPERIMENTAL

Melting points were determined on a Gallen-Kamp melting point apparatus and are uncorrected. IR spectra were recorded on a Pye-Unicam

Downloaded At: 11:04 28 January 2011

TABLE I Antimicrobial Activities of the Synthesized Compounds [Zone of Inhibition in mm]

	Antibacterial activity			Antifungal activity		
Comp. no.	*Bacillus subtillus*	*us luteus*	*Serration rhodenil*	*Aspergillus fumigatus*	*Penicllum chrysogen*	*Fusarium equiseti*
3a	7	—	16	—	—	—
3b	—	—	—	—	—	—
4e	—	—	—	—	—	—
4f	7	—	19	—	—	—
5e	7	—	—	—	—	13
5f	11	—	—	—	—	—
6c	9	—	—	—	—	—
6e	7	—	—	—	—	—
6f	—	14	—	—	—	—
11a	—	—	—	—	—	7
11b	8	—	—	—	—	—
12a	—	—	—	—	—	—

Downloaded At: 11:04 28 January 2011

SP^3-100 spectrophotometer using KBr wafer technique. ^{1}HNMR spectra were measured on a Varian 390-90 MHz NMR spectrometer in a suitable deutreated solvent, using TMS as internal standard. Elemental analyses were performed on a Perkin-Elmer 240°C microanalyzer and all compounds gave results in acceptable range. Melting points, yields, and spectroscopic data are listed in Tables II and III.

Synthesis of *p*-(Benzensulfonamido)acetophenone Derivatives (3a,b)

Method A

To a mixture of *p*-aminoacetophenone **1** (0.01 mmol) in pyridine (0.02 mmol), benzene or tolune sulphonylchloride (0.01 mmol) was added portion-wise with constant stirring. The mixture was refluxed for 3 h in (20 ml) ethanol; the contents were poured onto crushed ice (60 g) and conc. HCl (5 ml) was added. The product seperated was filtered and crystallized from ethanol, yield 67%, m.p. 262°C.

Method B

To a solution of *p*-aminoacetophenone **1** (0.01 mmol in pyridine 10 ml), benzene or tolouene sulphonylchloride (0.01 mmol) was added portion-wise with constant stirring. The mixture was stirred for 30 min at 0°C; the contents were poured onto crushed ice (60 g) and conc. HCl (5 ml) was added. The separated product was filtered and crystallized from ethanol.

TABLE II Physical Data of Compounds **4a–12b**

No.	M.P.°C (Yield%)	Formula mol. wt.	No.	M.P.°C (Yield%)	Formula mol. wt.
4a	175 (83)	$C_{21}H_{17}NO_3S$ 363	**6b**	161 (71)	$C_{21}H_{15}N_3O_5S$ 421
4b	190 (70)	$C_{21}H_{16}N_2O_5S$ 408	**6c**	135 (77)	$C_{22}H_{18}N_2O_4S$ 406
4c	175 (80)	$C_{22}H_{18}NO_4S$ 384	**6d**	125 (69)	$C_{22}H_{18}N_2O_3S$ 390
4d	165 (75)	$C_{22}H_{19}NO_3S$ 377	**6e**	110 (70)	$C_{22}H_{17}N_3O_5S$ 435
4e	173 (77)	$C_{22}H_{18}N_2O_5S$ 422	**6f**	132 (71)	$C_{23}H_{20}N_2O_4S$ 420
4f	182 (68)	$C_{23}H_{21}NO_4S$ 407	**7**	135 (77)	$C_{22}H_{21}N_3O_3S$ 407
5a	162 (72)	$C_{24}H_{18}N_4O_2S$ 426	**8**	125 (68)	$C_{23}H_{23}N_3O_3S$ 421
5b	176 (70)	$C_{24}H_{17}N_5O_4S$ 471	**9**	110 (70)	$C_{22}H_{18}N_4O_5S$ 450
5c	151 (65)	$C_{25}H_{20}N_4O_3S$ 456	**10**	132 (66)	$C_{23}H_{18}N_4O_4S_2$ 418
5d	173 (70)	$C_{25}H_{20}N_4O_2S$ 440	**11b**	108 (75)	$C_{20}H_{17}NO_3S$ 351
5e	157 (65)	$C_{25}H_{19}N_5O_4S$ 485	**12a**	255 (70)	$C_{19}H_{17}N_3O_2S$ 351
5f	145 (62)	$C_{26}H_{22}N_4O_3S$ 470	**12b**	185 (75)	$C_{20}H_{19}N_3O_2S$ 365
6a	148 (68)	$C_{21}H_{16}N_2O_3S$ 376			

Downloaded At: 11:04 28 January 2011

Condensation of Acetyl Compound 3 with Aromatic Aldehydes

Synthesis of Chalcones (4a–f)

A mixture of acetyl compound **3** (0.01 mmol) and aromatic aldehydes (0.01 mmol) in ethanol (20 ml), and NaOH (40%, 5 ml) was stirred for 5 h. The contents were poured onto crushed ice, isolated by acidifaction (HCl, 5 ml), and crystallized from ethanol.

Reactions of Chalcones 4a–c with Malononitrile

Synthesis of Cyanopyridines (5a–f)

A mixture of chalcone **4a–f** (0.1 mmol), malononitrile (0.1 mmol), and ammonium acetate (0.8 mmol) was refluxed in ethanol (30 ml) for 6 h in a water-bath. The cooled contents were then poured onto crushed ice with constant stirring; the resulting solid was washed with water and the residue was crystallized from proper solvent.

TABLE III Spectroscopic Data of Compounds **3–12**

Comp. no.	IR (ν cm^{-1})/^{1}HNMR δ (ppm)
3a	3200 (NH), 1670 (C═O), 1620 (C═N), 1160–1350 (S═O); ($CDCl_3$): δ 2.4 (s, 3H, CH_3), δ 7.2–8.0 (m, 9H, Ar-H), δ 8.8 (s, 1H, NH)
3b	3230 (NH), 1660 (C═O), 1165–1350 (str. S═O); ($CDCl_3$): δ 2.3 (s, 3H, CH_3), δ 2.45 (s, 3H, CH_3), δ 7.4–8.2 (m, 8H, Ar-H), δ 8.95 (s, 1H, NH)
4a	3250 (NH), 2980 (CH-alph.), 1680 (C═O), 1160 (S═O); (DMSO-d_6): δ 7.4–8.00 (m, 16H, Ar-H and CH═CH), δ 8.9 (s, 1H, NH)
4b	3230 (NH), 2980 (CH-alph.), 1670 (C═O), 1165–1350 (str. S═O); (CF_3COOD): δ 7.4–8.2 (m, 15H, Ar-H and CH═CH), δ 8.95 (s, 1H, NH)
4c	3200 (NH), 2980 (CH-alph.), 1655 (C═O), 1165–1350 (str. S═O); (DMSO-d_6): δ 2.3 (s, 3H, CH_3), δ 7.5–8.4 (m, 15H, Ar-H and CH═CH), δ 8.95 (s, 1H, NH)
4d	3400 (NH), 2950 (CH-alph.), 1650 (C═O), 1170–1350 (str. S═O); (DMSO-d_6): δ 2.3 (s, 3H, CH_3), δ 7.3–8.2 (m, 15h, Ar-H and CH═CH), δ 8.75 (s, 1H, NH)
4e	3200 (NH), 2850 (CH-alph.), 1680 (C═O), 1170–1350 (str. S═O); (DMSO-d_6): δ 2.4 (s, 3H, CH_3), δ 7.4–8.0 (m, 14H, Ar-H and CH═CH), δ 8.6 (s, 1H, NH)
4f	3200 (NH), 2900 (CH-alph.), 1660 (C═O), 1160–1350 (str. S═O); (DMSO-d_6): δ 2.5 (s, 3H, CH_3), δ 7.2–7.9 (m, 14H, Ar-H and CH═CH), δ 9.1 (s, 1H, NH)
5a	3320, 3180 (NH, NH_2), 2220 (CN), 1160–1350 (S═O); (CF_3COOD): δ 7.3–8.1 (m, 15H, Ar-H and CH, pyr.), δ 9.86 (s, 1H, NH)
5b	3300, 3200 (NH, NH_2), 2220 (CN) 1160–1350 (S═O); (DMSO-d_6): δ 2.46 (s, 2H, NH_2), δ 7.5–8.4 (m, 14H, Ar-H and CH, pyr.), δ 9.6 (s, 1H, NH)
5c	3200–3420 (NH, NH_2), 2220 (CN), 1150–1350 (str. S═O); (CF_3COOD): δ 2.4 (s, 3H, CH_3), δ 7.5–8.4 (m, 14H, Ar-H and CH, pyr.), δ 9.80 (s, 1H, NH)
5d	3300, 3400 (NH, NH_2), 2210 (CN), 1620 (C═N), 1160–1350 (str. S═O); (CF_3COOD): δ 2.3 (s, 3H, CH_3), δ 7.3–8.2 (m, 14H, Ar-H and CH, pyr.)
5e	3300, 3200 (NH, NH_2), 2210 (CN), 1610 (C═N), 1170–1350 (str. S═O); (DMSO-d_6): δ 2.35 (s, 3H, CH_3), δ 2.8 (s, 2H, NH_2), δ 7.2–8.1 (m, 13H, Ar-H), δ 9.6 (s, 1H, NH)
5f	3200, 3350 (NH, NH_2), 2220 (CN), 1620 (C═N), 1160–1350 (str. S═O); (DMSO-d_6): δ 2.1 (s, 3H, CH_3), δ 2.35 (s, 3H, OCH_3), δ 2.75 (s, 2H, NH_2), δ 7.6–8.2 (m, 13H, Ar-H and CH, pyr.), δ 9.88 (s, 1H, NH)
6a	3250 (NH), 1620 (C═N), 1160–1350 (str. S═O); (CF_3COOD): δ 7.5–8.3 (m, 14H, Ar-H), δ 8.8 (s, 1H, CH)
6b	3240 (NH), 2950, 1600 (C═N), 1165–1350 (str. S═O); (DMSO-d_6): δ 7.2–8.1 (m, 13H, Ar-H), δ 8.9 (s, 1H, CH), δ 9.7 (s, 1H, NH)
6c	3250 (NH), 1590 (C═N), 1165–1350 (str. S═O); (DMSO-d_6): δ 2.33 (s, 3H, CH_3), δ 7.4–8.0 (m, 13H, Ar-H), δ 8.8 (s, 1H, CH), δ 9.5 (s, 1H, NH)
6d	3280 (NH), 1620 (C═N), 1165–1350 (str. S═O); (DMSO-d_6): δ 2.4 (s, 3H, CH_3), δ 7.2–8.1 (m, 13H, Ar-H), δ 8.87 (s, 1H, CH), δ 9.5 (s, 1H, NH)
6e	3220 (NH), 1600 (C═N); (DMSO-d_6): δ 2.3 (s, 3H, CH_3), δ 7.2–8.1 (m, 12H, Ar-H), δ 8.9 (s, 1H, CH), δ 9.55 (s, 1H, NH)
6f	3200 (NH), 1610 (C═N); (DMSO-d_6): δ 2.45 (s, 3H, CH_3), δ 7.2–8.1 (m, 12H, Ar-H), δ 8.92 (s, 1H, CH), δ 9.72 (s, 1H, NH)
7	3300–3100 (NH), 1610 (C═N), 1160–1350 (str. S═O); (DMSO-d_6): δ 2.45 (s, 3H, CH_3), δ 4.35 (s, 2H, CH_2), δ 7.2–8.1 (m, 13H, Ar-H), δ 8.92, 9.7 (2s, 2H, 2NH)

(Continued on next page)

Downloaded At: 11:04 28 January 2011

TABLE III Spectroscopic Data of Compounds **3–12** *(Continued)*

Comp. no.	IR (ν cm^{-1})/^{1}HNMR δ (ppm)
8	3280–3120 (NH), 1620 (C═N), 1160–1350 (str. S═O); (DMSO-d_6): δ 2.1, 2.45 (2s, 6H, $2CH_3$), δ 4.2 (s, 2H, CH_2), δ 7.2–8.1 (m, 12H, Ar-H), δ 8.90, 9.75 (2s, 2H, 2NH)
9	3200–3100 (NH), 1670 (C═O), 1630 (C═N), 116–1350 (str. S═O); (DMSO-d_6): δ 4.25 (s, 2H, CH_2), δ 7.2–8.1 (m, 13H, Ar-H), δ 8.87, 9.57 (2s, 2H, 2NH)
10	3300–3100 (NH), 1610 (C═N), 1160–1350 (str. S═O)
11b	3250 (NH), 1680 (CO), 1610 (C═N), 1165–1360 (str. S═O); ($CDCl_3$): δ 2.3 (s, 3H, CH_3), δ 7.2–8.1 (m, 13H, Ar-H), δ 9.5 (s, 2H, NH)
12a	3300–3100 (NH, NH_2), 1610 (C═N), 116–1350 (str. S═O); (CF_3COOD): δ 7.3–8.2 (m, 14H, Ar-H)
12b	3500–3200 (NH, NH_2), 1610 (C═N), 1150–1360 (str. S═O); (CF_3COOD): δ 2.3 (s, 3H, CH_3), δ 7.2–8.3 (m, 13H, Ar-H)

Downloaded At: 11:04 28 January 2011

Reactions of Chalcones (4a–c) with Hyroxylamine Hydrochloride

Synthesis of Isoxazoles (6a–f)

Anhydroyus sodium acetate dissolved in a minimum amount of hot acetic acid was added to the solution of hyroxylamine hydrochloride in ethanol (20 ml). This solution was added to a solution of chalcones **4a–f** in ethanol (20 ml). The mixture was refluxed for 6 h, concentrated, and neutralized with NaOH. The isolated product was then filtered and crystallized from ethanol.

Synthesis of Pyrazolines (7, 8)

A mixture of **2b** (0.005 mmol), hyrazine hydrate (98%, 0.005 mmol), and ethanol (25 ml) was refluxed for 8 h then cooled, filtered, and crystallized from ethanol as yellowish crystals.

Synthesis of 4-[(Benzensulfonyl)anilino]-6-*p*-nitrophenyl-2-oxo-1,2,5,6-tetrahydropyrimidine (9)

To (0.1 gm, 0.015 mmol) of urea in (20 ml) ethanol. (5 ml) of conc. HCl was added to the formed solution of **2b** (0.001 mmol). The mixture was heated at reflux temperature for 8 h then concentrated to 1/3 its volume and cooled. The mixture was neutralized with cold NH_4OH and the precipitated material was crystallized from ethanol as yellow crystals.

Synthesis of 4-[(Benzensulfonyl)anilino]-6-*p*-nitrophenyl-2-thioxo-1,2,5,6-tetrahydropyrimidine (10)

A mixture of **2b** (0.1 mmol), thiourea (0.1 mmol), and NaOH (0.1 gm, in ethanol 30 ml) was refluxed for 5 h, then concentrated, cooled, and filtered. The precipitate was crystallized from abs. ethanol as red crystals.

p-[(Benzenesulfonyl)amino]benzophenone (11a)

The title compound was prepared as literature,[19] m.p. 106–107°C.

p-[(Tolunesulfonyl)amino]benzophenone (11b)

The title compound was synthesized following a procedure analogous to that for compound **11a**.

Synthesis of Hydrazones (12a,b)

A solution of ketone compound **8** (0.01 mmol) and hydrazine hydrate (0.01 mmol) in ethanol (30 ml) was heated under reflux for 1 h. The reaction mixture was cooled, the solid separated, and filtered and crystalized from ethanol as yellowish crystals.

Downloaded At: 11:04 28 January 2011

REFERENCES

[1] E. D. Barton-John and F. M. Freeman-Peter, Ger. Offen Brit. Appl. 2, 029, 079 (1971); *C. A.*, **74,** 99891d (1971).
[2] V. E. B. Leung-Werke, *C. A.*, **63,** 6879 (1965).
[3] J. J. Baldwin, A. Scriabine, C. T. Ludden and G. Morgen, *Experientia*, **35**(5), 653 (1979); *C. A.*, **91,** 83212y (1979).
[4] R. Jain and D. D. Agarwal, *J. Indian Chem. Soc.*, **72,** 825 (1995).
[5] I. A. Shehata and R. A. Glannon, *J. Heterocyclic Chem.*, **24,** 1291 (1987).
[6] J. J. Talley, U.S. Appl. 473, 884 (1999); *C. A.*, **130,** 110269e (1999).
[7] B. E. Kornberg and S. S. Nikam, (Warner-Lambert Company, USA, 2000); *C. A.*, **133,** 135328y (2000).
[8] C. E. Mowbray and A. Stobie, (Pfizer Research and Development Company, UK 1997); *C. A.*, **127,** 262701r (1997).
[9] K. Nakia, Y. Ogawa, A. Yamada, T. Chiba and H. Takasugi, *Appl. Wo.*, **32,** 858 (1997); *C. A.*, **127,** 293248c (1997).
[10] M. Kato, T. Fujita, K. Kawabata and H. Ohno (Ono Pharmaceutical Co. Ltd., Japan); *C. A.*, **129,** 175653z (1998).
[11] S. Andrea, B. Fabrizio, A. I. Marc and T. S. Calaudin, *J. Med. Chem.*, **43**(2), 292 (2000).
[12] S. Andrea and T. S. Calaudin, *Eur. J. Med. Chem.*, **35,** 299 (2000).
[13] H. Kehne, L. Willms, K. Bauer, H. Bieringer and C. Rosinger, Ger. Offen. DE **19,** 611, 355 (1997); *C. A.*, **127,** 293245z (1997).
[14] O. S. Moustafa, *Afinidad*, **491,** 39 (2001).

[15] O. S. Moustafa, *Phosphorus*, *Sulfur, and Silicon*, **155,** 235 (1999).
[16] O. S. Moustafa, *Phosphorus*, *Sulfur, and Silicon*, **167,** 101 (2000).
[17] a) O. S. Moustafa, *J. Chinese Chem. Soc.*, **47**(2), 351(2000); b) O. S. Moustafa and Y. A. El-Ossialy, *J. Chinese Chem. Soc.*, **49**(1), 107 (2002).
[18] O. S. Moustafa, M. Z. A. Badr and E. M. Kamel, *Pharmazie*, **55**(12), 896 (2000).
[19] T. Kumiko, W. P. Jonathan and J. L. Rachard, *J. Org. Chem.*, **60,** 156 (1995).
[20] A. W. Bauer, W. W. M. Kriby, J. C. Sherris and M. Turck, *Am. J. Clin. Pathol.*, **45,** 493 (1966).
[21] N. Kalyoncuoglu, S. Rollas, D. Sur-Altiner, Y. Yegenoglu and O. Ang, *Pharmazie*, **47,** 769 (1992).
[22] V. B. Patel, S. D. Sorathiya and A. R. Parikh, *Indian J. Chem.*, **36B,** 822 (1997).

Downloaded At: 11:04 28 January 2011