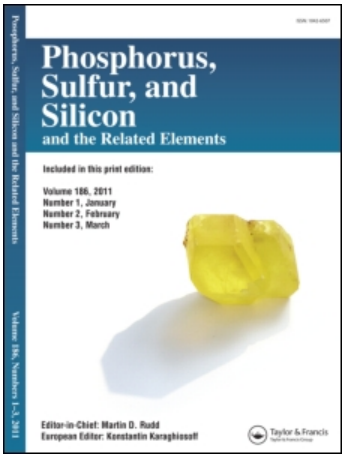


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

A Facile One-Pot Microwave-Induced Synthesis of Some Novel Selenolo[2,3-*b*]quinoline Derivatives under Solvent-Free Conditions

M. Raghavendra[a]; Halehatty S. Bhojya Naik[a]; Bailure S. Sherigara[a]
[a] Department of P G Studies and Research in Industrial Chemistry, School of Chemical Sciences, Kuvempu University Shankaraghatta, Karnataka, India

To cite this Article Raghavendra, M. , Bhojya Naik, Halehatty S. and Sherigara, Bailure S.(2008) 'A Facile One-Pot Microwave-Induced Synthesis of Some Novel Selenolo[2,3-*b*]quinoline Derivatives under Solvent-Free Conditions', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 6, 1501 — 1509
To link to this Article: DOI: 10.1080/10426500701690855
URL: http://dx.doi.org/10.1080/10426500701690855

Phosphorus, Sulfur, and Silicon, 183:1501–1509, 2008

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701690855

Taylor & Francis
Taylor & Francis Group

A Facile One-Pot Microwave-Induced Synthesis of Some Novel Selenolo[2,3-*b*]quinoline Derivatives under Solvent-Free Conditions

M. Raghavendra, Halehatty S. Bhojya Naik, and Bailure S. Sherigara
Department of P G Studies and Research in Industrial Chemistry, School of Chemical Sciences, Kuvempu University Shankaraghatta, Karnataka, India

A rapid, solvent free microwave assisted synthetic strategy has been developed for the synthesis of some selenolo[2,3-b]quinoline derivatives using potassium carbonate by the reaction between 2-seleno-3-formyl-quinolines ***(2a–d)*** *with 2-chloroacetamide and phenacylbromide. This method found to be very effective, products obtained in high yield, isolation is just treating the reaction mixture with water.*

Keywords Microwave irradiation; quinolines; selenolo[2,3-*b*]quinolines; solvent-free conditions

INTRODUCTION

The use of microwave for the synthesis of organic compounds under solvent-free conditions proved to be efficient safe and environmentally benign techniques that with shorter reaction time, high yields, and easier manipulation. Additionally, it can also avoid the use of poisonous and expensive solvent, and as such can be environmentally benign, and make manipulations much easier.[1–2]

Several polycyclic analogues of natural or synthetic antitumor agents are well known, and have attracted considerable interest because of their significant anticancer activity.[3] There is a evidence that the antitumor activity is due to these compounds intercalation between the

Received 17 January 2007; accepted 8 August 2007.
M. Raghavendra is thankful to the Chairman, Kuvempu University, Shankaraghatta, for providing research facilities and the Head of the Sophisticated Instruments Facility, IISc, Bangalore, for spectral data.
Address correspondence to Halehatty S. Bhojya Naik, Department of P G Studies and Research in Industrial Chemistry, School of Chemical Sciences, Kuvempu University, Shankaraghatta, Karnataka, India. E mail: hsb_naik@rediffmail.com

base pairs of DNA and interference with normal functioning of the enzyme topoisomerase II, which is involved in the breaking and releasing of DNA strands.[4] The intercalative binding of these drugs is due to the presence of planar linearly fused tri and tetra cyclic systems.

Further, the biological and pharmaceutical activities of different selenium compounds are gains special interest because it has been associated with modification of metal toxicity[5] and with prevention of cancer.[6] In addition to naturally occurring selenium compounds, certain synthetic organoselenium compounds such as *p*-methoxybenzeneselenol, benzylselenocyanate, 1,4-phenylenebisselenocyanate were found to inhibit azoxymethane-induced hepatocarcinogenesis in female F 344 rats without clinical signs of toxicity,[7–9] *p*-methoxybenzyl selenocyanate and 1, 4-phenylenebis (methylene) selenocyanate prevented both precancerous cell growth and tumor growth in animals after being treated with a colorectal cancer-inducing agent with no side effects.[10] Moreover, some patented phenylaminoalkyl selenides confirmed antihypertensive properties.

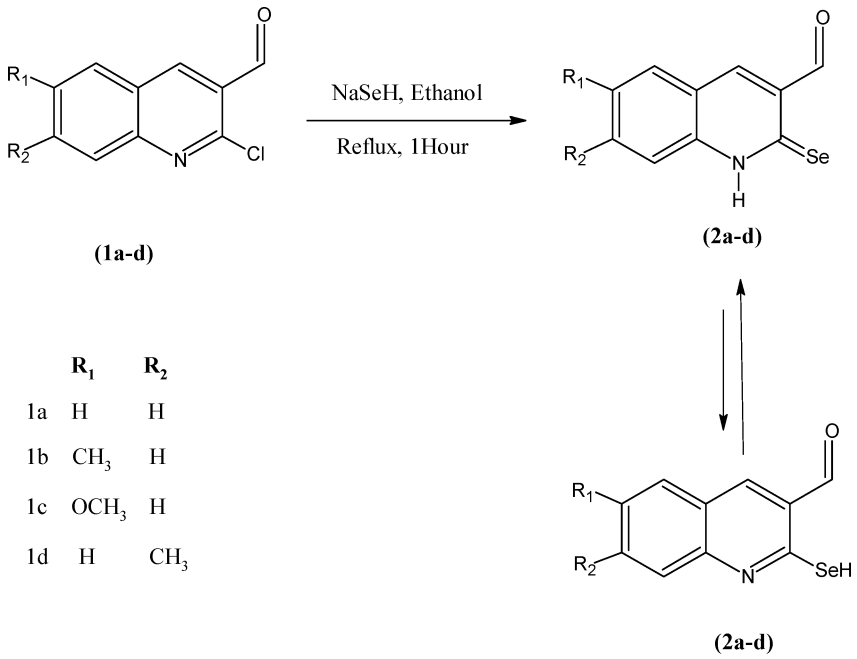
On the other hand, five- and six-membered heterocyclic compounds containing one or two heteroatom fused to quinoline ring in a linear fashion are found in natural products, as well as in synthetic compounds of biological interest have antitumor and anticancer properties.[11,12] They are also known to exhibit antiallergenic,[13] antifungal,[14] hypocholesterolemic, hypolemic,[15] antibacterial,[16] and antiviral[17] properties. In addition, various condensed quinolines were studied for their intercalative DNA binding, cytotoxic, and antitumor activities.[18]

Due to their great biological properties, compounds containing the quinoline system have been the subject of many synthetic studies. In these directions, there has been increasing interest in the synthesis of quinoline containing Se moieties to obtain improved chemoprevention with lower toxic activity. So, in continuation of our studies on synthesis of condensed quinolines[19] by taking the advantage of microwave, we wish to report on synthesis of novel selenolo[2,3-*b*]quinoline derivatives under solvent free microwave irradiation conditions.

RESULTS AND DISCUSSION

The starting compounds 2-chloro-3-formylquinoline (**1a–d**), were prepared according to literature method.[20] The compounds 2-seleno-3-formylquinoline (**2a–d**) were prepared by the action of sodium hydroselenide on 2-chloro-3-formylquinolines (**1a–d**) (Scheme 1).

A wide range of substituted selenolo[2,3-*b*]quinolines such as (**3a–d**), and (**4a–d**) were prepared by treating (**2a–d**) with phenacylbromide and 2-chloroacetamide under solvent free microwave irradiation conditions



(1a-d)

(2a-d)

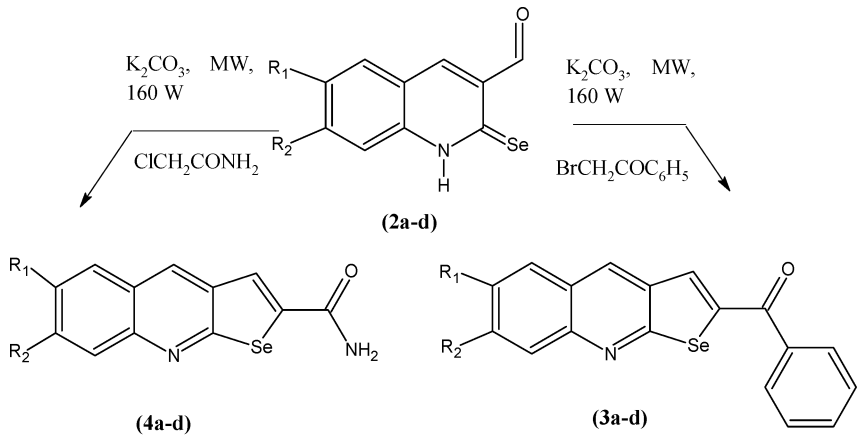
(2a-d)

	R_1	R_2
1a	H	H
1b	CH_3	H
1c	OCH_3	H
1d	H	CH_3

SCHEME 1

in one pot to furnished the title compounds in good yields as shown in (Scheme 2). The reaction was known[21] to proceed through replacing halogen of the reactants by selenium moiety, the carbanion results in the intermediate by base, adds on the aldehydic carbon with simultaneous elimination of water resulting in the formation of products with good yields. The structural elucidation of all the newly synthesized compounds was established based on their IR, ^{1}H NMR and mass spectral data. (which are presented in the experimental section).

As an example, the IR spectrum of (**3a**) showed an absence of tautomeric SeH, NH, groups and CHO stretching frequency in the region of 3150–3300, and 1650 cm^{-1}, which appeared in the 2-seleno-3-formylquinoline (**2a**) were found to be absent in the IR spectrum of (**3a**). The ^{1}H NMR spectrum of **2a** exhibits singlet at δ 5.8 ppm corresponding to tautomeric SeH, NH, group and singlet at δ 10.35 ppm corresponding to −CHO group, the singlet in the intermediate near at δ 4.2 ppm corresponding to an unreacted –$SeCH_2$ group were found to be absent in (**3a**) indicates the attachment of the reactive partner to quinoline moiety. Further, compound (**3a**) showed signal at δ 8.50 for C4-H proton and signal at δ 8.62 for C3-H proton, this might be due to hydrogen



	R_1	R_2
3a	H	H
3b	CH_3	H
3c	OCH_3	H
3d	H	CH_3
4a	H	H
4b	CH_3	H
4c	OCH_3	H
4d	H	CH_3

SCHEME 2

bonding and anisotropy effect of the adjacent carbonyl groups. The other aromatic protons resonated at δ 7.50–8.16 (4H). Finally, the structure assigned was confirmed by its mass spectrum through the appearance of a molecular ion peak at m/z 334 [M^+]. The melting points, percentage of yield and elemental data were shown in Table I.

MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. The FT-IR spectra were recorded on NICOLETAVATAR 360-FTIR instrument by using KBr pellets. The ^{1}H NMR were recorded on a BRUCKER AMX-400 spectrometer operating at 400 MHz. Mass spectra were recorded on AGILENT LC-MSD-TRAP-XCT mass spectrometer

TABLE I Characterization Data of the Newly Synthesized Compounds

Compound no.	Microwave irradiation/Reflux M.P. (°C)	Yield (%)	Time/hr/min	Mol. formula	Elemental analysis Calcd./Found (%) C	H	N
2a	255	91	1hour	$C_{10}H_7NOSe$	50.84	2.96	5.93
					50.80	3.00	5.99
2b	247	90	1hour	$C_{11}H_9N0Se$	52.81	3.63	5.60
					52.81	3.63	3.63
2c	266	92	1hour	$C_{11}H_9N0_2Se$	49.64	3.41	5.26
					49.64	3.43	5.28
2d	240	90	1hour	$C_{11}H_9N0Se$	52.81	3.63	5.60
					52.81	3.63	5.60
3a	235	89	7	$C_{18}H_{11}NOSe$	64.28	3.27	4.16
					64.30	3.24	4.12
3b	208	88	8	$C_{19}H_{13}NOSe$	65.14	3.71	4.00
					65.18	3.68	4.06
3c	231	85	7	$C_{19}H_{13}NO_2Se$	62.29	3.55	3.82
					62.32	3.52	3.86
3d	208	88	8	$C_{19}H_{13}NOSe$	65.14	3.71	4.00
					65.20	3.73	3.96
4a	237	89	8	$C_{12}H_8N_2OSe$	52.36	2.90	10.18
					52.39	2.94	10.20
4b	217	90	8	$C_{13}H_{10}N_2OSe$	53.97	3.46	9.68
					53.94	3.42	9.64
4c	229	88	8	$C_{13}H_{10}N_2O_2Se$	51.14	3.27	9.18
					51.16	3.30	9.22
4d	225	90	8	$C_{13}H_{10}N_2OSe$	53.97	3.46	9.68
					53.94	3.42	9.64

Elemental analyses were done on Vario EL. CHNOS elemental analyzer.

General Method for the Preparation of 2-Seleno-3-formylquinoline (2a)

Solution of sodium hydrogen selenide [freshly prepared from finely divided selenium powder (1 g, 0.013 mol) and sodium borohydride (1 g, 0.026 mol) in water (50 ml)],[22]was added to 2-chloro-3-formylquinoline **(1a)** (1.91 g, 0.01 mol) in ethanol (80 ml). The reaction mixture was refluxed on water bath for one hour, cooled, poured to ice water (100 ml) and neutralized with dilute hydrochloric acid (4N) the resultant solid,

2-seleno-3-formyl quinoline obtained was filtered, washed with water (300 ml) dried and recrystallized from alcohol.

Yield: IR (KBr) cm^{-1} 3150–3300 (tautomeric form of -NH, SeH), 1650 (CHO) 1180 (C=Se). ^1H NMR (400 MHz, DMSO-d_6) 5.8 (tautomeric form of -NH, SeH), 10.35 (-CHO), 7.25–8.35 (m, 5H, Ar-H). MS m/z: 236 (M^+).

2-Seleno-6-methylquinoline-3-carbaldehyde (2b)

Prepared from methyl derivative of quinoline **1b**.

IR (KBr) cm^{-1} 3155–3310 (tautomeric form of —NH, SeH), 1650 (CHO) 1180 (C=Se). ^1H NMR (400 MHz, DMSO-d_6) 2.60 (3H, s, CH_3), 5.85 (tautomeric form of —NH, SeH), 10.35 (—CHO) 7.20–8.30 (m, 4H, Ar-H). MS m/z: 250 (M^+).

2-Seleno-6-methoxy-3-carbaldehyde (2c)

Prepared from methoxy derivative of quinoline **1c**.

IR (KBr) cm^{-1} 3160–3300 tautomeric form of (—NH, SeH) 1650 (CHO) 1180 (C=Se). ^1H NMR (400 MHz, DMSO-d_6) 3.95 (3H, s, OCH_3), 5.90 (tautomeric form of —NH, SeH), 10.40 (—CHO) 7.35–8.40 (m, 4H, Ar—H). MS, m/z 266 (M^+).

2-Seleno-7-methylquinoline-3-carbaldehyde (2d)

Prepared from methyl derivative of quinoline **1d**.

IR (KBr) cm^{-1} 3155–3310 (tautomeric form of —NH, SeH), 1650 (CHO) 1182 (C=Se). ^1H NMR (400 MHz, DMSO-d_6) 2.65 (3H, s, CH_3), 5.85 (tautomeric form of —NH, SeH), 10.35 (—CHO) 7.25–8.37 (m, 4H, Ar—H). MS m/z: 250 (M^+).

General Procedure: Synthesis 1-Selenolo[2,3-*b*]quinolin-2-ylethanone

A mixture of **2a** (2.360 g, 10 mmol), phenacyl bromide (1.99 g, 10 mmol) and potassium carbonate (1.380 g, 20 mmol) were ground for uniform mixing. The mixture was then subjected to microwave radiation in a domestic microwave oven for 8 min at an interval of 1 min at 160 W as required to complete the reaction (TLC). The reaction mixture was then poured into water, stirred, filtered and dried. The crude product was recrystallized from aqueous DMF to give 2.990 g (89%) of **3a**. All the other compounds were prepared in a similar way with 85–88% yield.

Selenolo[2,3-*b*]quinolin-2-yl(phenyl)methanone (3a)

Prepared according to the general method of preparation.

Solid; (89%), MS, m/z 336 (M+); IR (KBr) (cm^{-1}): 1640 (CO), ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 8.52 (s, C_3-H), 8.25 (s, C_4-H), 7.50–8.16 (9H, m, Ar-H).

(6-Methylselenolo[2,3-*b*]quinolin-2-yl)(phenyl)methanone (3b)

Prepared according to the general method of preparation.

Solid; (88%), MS, m/z 350 (M+); IR (KBr) (cm^{-1}): 1643 (CO), ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 2.45 (3H, s, Ar-CH_3), 8.58 (s, C_3-H), 8.24 (s, C_4-H), 7.55–8.13 (8H, m, Ar-H).

(6-Methoxyselenolo[2,3-*b*]quinolin-2-yl)(phenyl)methanone (3c)

Prepared according to the general method of preparation.

Solid; (85%), MS, m/z 366 (M+); IR (KBr) (cm^{-1}): 1640 (CO), ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 3.95 (3H, s, Ar-OCH_3), 8.60 (s, C_3-H), 8.24 (s, C_4-H), 7.58–8.12 (8H, m, Ar-H).

(6-Methylselenolo[2,3-*b*]quinolin-2-yl)(phenyl)methanone (3d)

Prepared according to the general method of preparation.

Solid; (88%), MS, m/z 350 (M+); IR (KBr) (cm^{-1}): 1645 (CO), ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 2.47 (3H, s, Ar-CH_3), 8.58 (s, C_3-H), 8.26 (s, C_4-H), 7.55–8.15 (8H, m, Ar-H).

Selenolo[2,3-*b*]quinoline-2-carboxamide (4a)

Prepared according to the general method of preparation.

Solid; (89%), MS, m/z 275 (M+); IR (KBr) (cm^{-1}): 3350-3175 ($CONH_2$), 1630 (CO). ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 7.42 (2H, b s, $CONH_2$), 8.50 (s, C_3-H), 8.20 (s, C_4-H), 7.54–8.05 (4H, m, Ar-H).

6-Methylselenolo[2,3-*b*]quinoline-2-carboxamide (4b)

Prepared according to the general method of preparation.

Solid; (90%), MS, m/z 289 (M+); IR (KBr) (cm^{-1}): 3360–3185 ($CONH_2$), 1625 (CO). ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 2.40

(3H, s, Ar-CH_3), 7.42(2H, b s, $CONH_2$) 8.56 (s, C_3-H), 8.25 (s, C_4-H), 7.62– 8.12 (3H, m, Ar-H).

6-Methoxyselenolo[2,3-*b*]quinoline-2-carboxamide (4c)

Prepared according to the general method of preparation.

Solid; (88%), MS, m/z 305 (M+); IR (KBr) (cm^{-1}): 3360–3190 ($CONH_2$), 1625 (CO). ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 3.90 (3H, s, Ar-OCH_3), 7.45(2H, b s, $CONH_2$) 8.53 (s, C_3-H), 8.26 (s, C_4-H), 7.65–8.14 (3H, m, Ar-H).

6-Methylselenolo[2,3-*b*]quinoline-2-carboxamide (4d)

Prepared according to the general method of preparation.

Solid; (90%), MS, m/z 289 (M+); IR (KBr) (cm^{-1}): 3370–3195 ($CONH_2$), 1630 (CO). ^{1}H NMR (400 MHz) (DMSO-d6) (δ) ppm: 2.45 (3H, s, Ar-CH_3), 7.40(2H, b s, $CONH_2$) 8.60 (s, C_3-H), 8.25 (s, C_4-H), 7.62–8.15 (3H, m, Ar-H).

REFERENCES

[1] (a) S. Caddick, *Tetrahedron.* **51,** 10403 (1995); (b) A. R. Katritzky and K. S. Sandeep, *Arkivoc.*, **(xiii),** 68 (2003).

[2] C. B. Khour, C. B. Darth, A. Lalnger, and M. E. Daves, *J. Catal.*, **149,** 195 (1994).

[3] (a) W. D. Kingsbury, J. C. Boehm, D. R. Jakas, K. G. Holden, S. M. Hecht, G. Gallagher, M. J. Caranfa, F. L. McCabe, L. F. Faucette, R. K. Johnson, and R. P. Hertzberg, *J. Med. Chem.*, **34,** 98 (1991); (b) M. C. Woni, A. W. Nicholas, G. Manikumar, and M. E. Wall, *J. Med. Chem*., **30,** 1774 (1987); (c) M. J. Luzzio, J. M. Besterman, D. L. Emerson, M. G. Evans, K. Lackey, P. L. Leitner, G. McIntyre, B. Morton, P. L. Myers, M. Peel, J. M. Sisco, D. D. Sternbach, W. Q. Tong, A. Truesdale, D. E. Uehling, A. Vuong, and J. Yates, *J. Med. Chem*. **38,** 395 (1995); (d) M. E. Wall, M. C. Wani, A. W. Nicholas, G. Manikumar, C. Tele, A. Moore, D. Truesdale, P. Leitner, and J. M. Besterman, *J. Med. Chem.*, **36,** 2689 (1993); (e) G. W. Gribble, *Advances in Heterocyclic Natural Products Synthesis.*, **1,** 43 (1990).

[4] B. Gatto, G. Capranico, and M. Palumbo, *Curr. Pharacol. Design*, **5,** 195 (1999).

[5] L. Magos and M. Webb, *Crit. Rev. Toxicol.*, **8,** 1 (1980).

[6] L. Fishbein, *Toxicology and Environmental Chemistry.*, **12,** 1 (1986).

[7] T. Tanaka, B. S. Reddy, and K. El-Bayoumy, *Japanese J. Cancer Research.*, **76,** 462 (1985).

[8] K. El-Bayoumy, *Cancer Res.*, **45,** 3631 (1985).

[9] B. S. Reddy, T. Tanaka, and K. El-Bayoumy, *J. Natl. Cancer Inst.*, **74,** 1325 (1985).

[10] I. Jibril, E. Abd Alhadi, and Z. Hamadah, *Trans Metals in Chemistry.*, **25,** 407 (2000).

[11] H. Thomys, *Ber. Deut. Pharm. Ges.*, **33,** 68 (1923).

[12] P. R. Loaiza, A. Quintero, R. Rodríguez-Sotres, J. D. Solano, and A. L. Rocha, *Eur. J. Med. Chem.*, **39,** 5 (2004).

[13] T. H. Althuis, S. B. Khadin, L. J. Czuba, P. F. Moore, and H. J. Hess, *J. Med. Chem.*, **23,** 262 (1980).

[14] J. B. Jiang and D. Isaacson.U. S. Patent., 4,656,274 (1987). *Chem. Abstr.*, **107,** 39643 (1987).
[15] R. E. Graeve, J. R. Pociask, and R. G. Stein, U. S. Patent. 3,600,393 (1971).
[16] A. M. Farghaly, N. S. Habib, M. A. Khalil, O. A. El-Sayed, and A. Alaxandria, *J. Pharm. Sci.*, **3,** 90 (1989). *Chem. Abstr.,* **112**, 7420 (1990).
[17] V. Zikan, S. Radl, F. Smejkal, and D. Zelena. Czech. Patent., 233,445 (1986); *Chem. Abstr.*, **106,** 138,447 (1987).
[18] (a) M. Gopal, S. Veeranna, and L. S. Doddamani. *Spect Lett.*, **37,** 347 (2004); (b) V. Nithyadevi and S. P. Rajendran, *Phosphorus, Sulfur, and Silicon,and their related elem.*, **180**, 1849 (2005); (c) M. Gopal, M. S. Shahabuddin, and S. R. Inamdar, *Proc. Indian Acad. Sci. (Chem. Sci).*, **114**, 687 (2002); (d) M. Gopal, S. Shenoy, and L. S. Doddamani, *J. Photochem. Photobiol.*, **72**, 69 (2003); (e) G. J. Atwell, B. F. Cain, and R. N. Seelye, *J. Med. Chem.*, **15,** 611 (1972); (f) B. F. Cain, R. N. Seelye, and G. J. Atwell, *J. Med. Chem.*, **17**, 922 (1974); (g) B. F. Cain, G. J. Atwell, and W. A. Denny, *J. Med. Chem.*, **18,** 1110 (1975); (h) G. W. Rewcastle, G. J. Atwell, D. Chambers, B. C. Gaguley, and W. A. Denny, *J. Med. Chem.*, **29,** 472 (1986).
[19] (a) B. P. Nandeshwarappa, D. B. Arun Kumar, H. S. Bhojya Naik, V. P. Vaidya, and K. M. Mahadevan, *J. Sulfur Chem.*, **26,** 373 (2005); (b) B. P. Nandeshwarappa, D. B. Arun Kumar, H. S. Bhojya Naik, V. P. Vaidya, and K. M. Mahadevan, *Indian J. Chem*., **44B,** 2155 (2005); (c) M. Raghavendra, H. S. Bhojya Naik, and B. S. Sherigara, *J. Sulfur Chem.*, **27,** 347 (2006); (d) H. S. Bhojya Naik, M. S. Ramesh, B. V. Swetha, and T. R. Roopa, *Phosphorous, Sulfur, Silicon and their related elem.*, **181,** 533 (2006).
[20] O. Meth-Cohn, B. Narine, and B. Tarnowski, *J. Chem. Soc. Perkin Trans.*, **1,** 1520 (1981).
[21] V. P. Litvinov, V.Yu. Mortikov, Yu. A. Sharanin, and A. M. Shestopalov, *Synthesis.*, 98 (1985).
[22] D. L. Klayman and T. S. Griffin, *J. Am. Chem. Soc.*, **95,** 197 (1973).