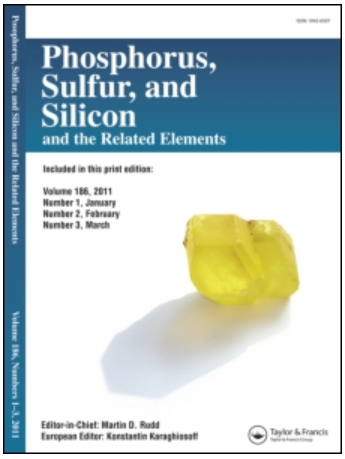

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis of Some New Fused and Spiro 1,4-Benzoxazine Derivatives

H. M. Moustafa[a]
[a] Chemistry Department, Faculty of Science, Sohag, Egypt

To cite this Article Moustafa, H. M.(2005) 'Synthesis of Some New Fused and Spiro 1,4-Benzoxazine Derivatives', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 1, 205 — 216
To link to this Article: DOI: 10.1080/104265090508460
URL: http://dx.doi.org/10.1080/104265090508460

Phosphorus, Sulfur, and Silicon, 180:205–216, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090508460

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Synthesis of Some New Fused and Spiro 1,4-Benzoxazine Derivatives

H. M. Moustafa
Chemistry Department, Faculty of Science, Sohag, Egypt

4-Methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one ***1*** *reacted with* CS_2 *and halo compounds to give thieno-1,4-benzoxazines* ***2a,b*** *and 2-(1,3-dithiol-2-yliden)-1,4-benzoxazines* ***3a,b****, respectively. Reaction of compound* ***1*** *with cyanoketene S,S diacetal afforded pyrano-1,4-benzoxazine derivatives* ***4,5****. Treatment of compound* ***1*** *with bromine in 1:2 molar ratio afforded 2,2-dibromo derivative* ***6****. Compound* ***6*** *reacted with bidentates, or with* CS_2 *and reactive methylenes to give the corresponding spiro compounds* ***7a–f*** *and* ***8a–d****, respectively. 2-(2-Bromo-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-yliden)malononitrile* ***10*** *was allowed to react with ethyl thioglycolate, aniline or benzylamine to yield thiopyrano-1,4-benzoxazine* ***11*** *or pyrrolo-1,4-benzoxazines* ***12a,b****, respectively. 2-(1-Ethoxy-methyliden)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one 13 reacted with* CS_2 *and reactive methylenes or malononitrile to give spiro dithiolane* ***14a–c*** *and 2-(4-methyl-3-oxo–3,4-dihydro-2H-1,4-benzoxazin-2-ylidenmethyl)malononitrile* ***15****, respectively. Reaction of compound* ***15*** *with some reactive methylene compounds gave the corresponding spiro cyclopentenes* ***16a–c****.*

Keywords 2,2-Dibromo-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one; 2-(2-bromo-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-yliden)malononitrile; 2-(1-ethoxymethyliden)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one; 4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one

INTRODUCTION

The biological activity of many heterocyclic annelated benzoxazines has been reviewed.[1–9] In view of these observations and as a continuation of our previous work[10] we undertook the synthesis of some new fused and spiro heterocyclic systems containing the 1,4-benzoxazine moiety.

Received April 21, 2004; accepted June 22, 2004.
Address correspondence to H. M. Moustafa, Chemistry Department, Faculty of Science, Sohag, Egypt. E-mail: hassa20002000@yahoo.com

RESULTS AND DISCUSSION

Reaction of 4-methyl-3,4-dihydro–2H-1,4-benzoxazin-3-one[11] **1** with CS_2 and reactive halo compounds, namely ethyl chloroacetate and bromo-malononitrile in 1:1:1 molar ratio under phase-transfer catalysis conditions[12] (PTC) using a liquid-solid system (dioxan/K_2CO_3) in the presence of tetrabutylammonium bromide (TBAB) as catalyst afforded thieno[4,3-b]-1,4-benzo-xazine derivatives **2a**,**b** and 2-(1,3-dithiol-2-yliden)-1,4-benzoxazine derivatives **3a**,**b**, respectively. The reaction pathway was assumed to involve the addition of the active methylene group of compound **1** to CS_2 to give the intermediate product which underwent intramolecular cyclization via nucleophilic attack of the carbanion ion onto tautomeric C—OH with elimination of a water molecule to give compounds **2a**,**b**, or via nucleophilic addition of —SH group onto the carbonyl ester in case of compound **3a** or cyano group to give compound **3b**. (*cf.* Scheme 1). The IR and ^{1}H-NMR spectra of compounds **2a**,**b** and **3a**,**b** were consistent with the proposed structures (*cf.* Table I).

Treatment of compound **1** with cyanoketene S,S diacetal[13] afforded 3-cyano-10-methyl-4-methylthio-2-iminopyrano[3,2-b]-1,4-benzoxazine (**4**). This product was treated with dilute HCl to give pyrano[3,2-b]-1,4-benzoxazin-2-one (**5**) (*cf.* Scheme 1). The IR spectra of compounds **4** and **5** revealed the absorption bands corresponding to CN groups at 2203 cm^{-1}. The ^{1}H-NMR spectra showed the peaks of all hydrogen sets of the expected compounds (*cf.* Table I).

Treatment of compound **1** with bromine in 1:2 molar ratio in chloroform at room temperature afforded 2,2-dibromo-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one (**6**). ^{1}H-NMR spectrum of compound **6** showed the disappearance of the methylene group (*cf.* Table I). Compound **6** was investigated as starting material for the synthesis of spiro heterocyclic systems, where it was reacted with ethanolamine, cystamine hydrochloride, 2-mercaptoethanol, 2-aminothiophenol, o-phenylenediamine or thiosemicarbazide using phase-transfer technique [dioxan/K_2CO_3/tetrabutyl-ammonium bromide (TBAB)] to give the corresponding spiro 1,4-benzoxazin-3-one derivatives **7a–f** (*cf.* Scheme 2). The IR and ^{1}H-NMR spectra of compounds **7a–f** are in agreement with the proposed structures (*cf.* Table I).

Using the PTC technique compound **6** reacted with CS_2 and different reactive methylene compounds, namely acetylacetone, ethyl acetoacetate, malononitrile, or ethyl cyanoacetate to give the corresponding dithietane derivatives **8a–d**,[14] respectively (*cf.* Scheme 2).

Bromination of 2-(4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-yliden)-malononitrile[10] **9** with N-bromosuccinimide in chloroform

TABLE I Analytical and Spectral Data of the New Compounds

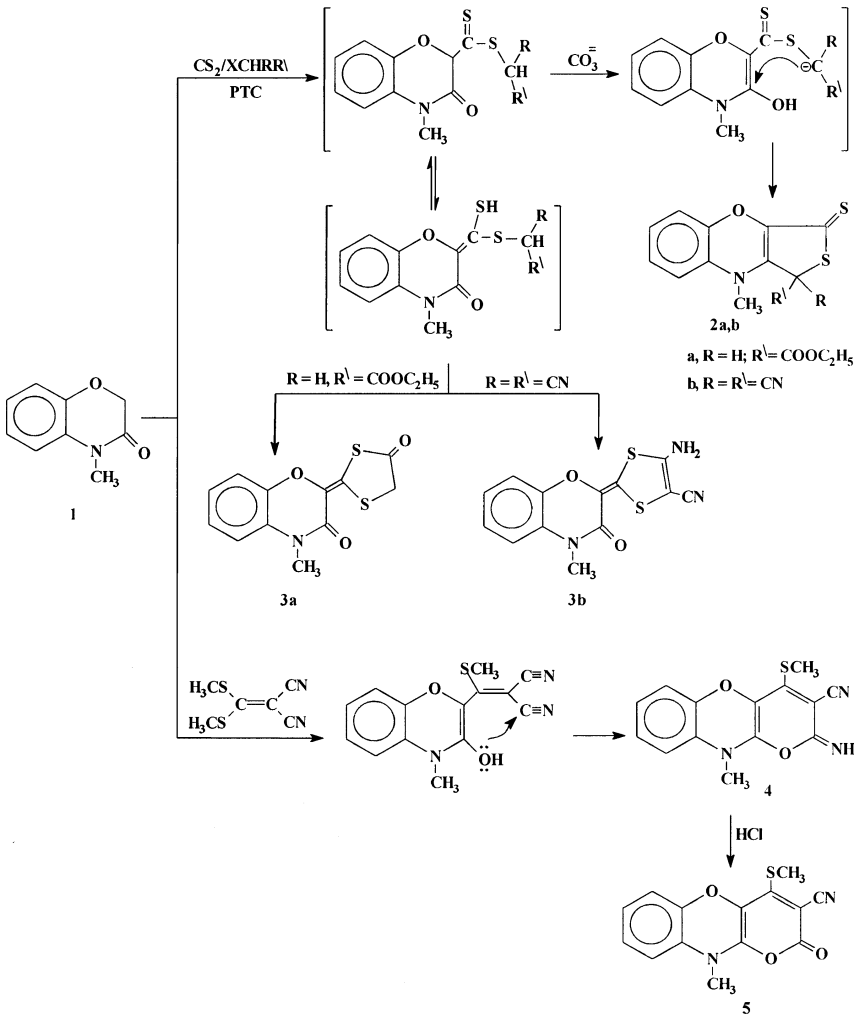
Comp. no.	M.P. (°C) cryst. solvent	Yield (%)	Mole. form. (mol. wt.)	Analytical data cal./found C	H	N	S	IR (cm^{-1})	^{1}H-NMR δ (ppm) a, $CDCl_3$; b, DMSO-d_6
2a	151 ethanol	41	$C_{14}H_{13}NO_3S_2$ (307.38)	54.70 54.38	4.26 4.11	4.55 4.41	20.86 20.64	1200 (C=S), 1711 (C=O).	7.5–7.0 (m, 4H, arom.); 4.3 (s, 1H, CH); 3.9–4.2 (q, 2H, CH_2), 2.9 (s, 3H, NCH_3); 1.4–1.1 (t, 3H, CH_3).[a]
2b	170 ethanol	50	$C_{13}H_7N_3OS_2$ (285.33)	54.72 54.29	2.47 2.31	14.73 14.66	22.47 22.33	1201 (C=S), 2207 (2CN).	7.5–7.0 (m, 4H, arom.); 3.0 (s, 3H, CH_3)[b]
3a	192 ethanol	33	$C_{12}H_9NO_3S_2$ (279.33)	51.59 51.24	3.25 3.13	5.01 4.89	22.96 23.76	1689 (C=O_{amidic}). 1712 (C=O).	7.5–7.0 (m, 4H, arom.); 3.95 (s, 2H, CH_2); 3.0 (s, 3H, CH_3).[a]
3b	184 ethanol	31	$C_{13}H_9N_3O_2S_2$ (303.35)	51.47 51.56	2.99 2.87	13.85 13.88	21.14 20.94	3402, 3319 (NH_2); 2211 (CN); 1688 (C=O).	7.6–7.1 (m, 4H, arom.); 5.0–4.6 (br, 2H, NH_2); 2.9 (s, 3H, CH_3).[a]
4	199–201 dioxan	69	$C_{14}H_{11}N_3O_2S$ (285.31)	58.93 58.60	3.88 3.67	14.73 14.57	11.24 11.11	3279 (NH); 2207 (CN).	11.4–11.2 (br, 1H, NH); 7.5–7.0 (m, 4H, arom.), 2.9 (s, 3H, NCH_3), 2.6 (s, 3H, SCH_3).[b]
5	183 ethanol	81	$C_{14}H_{10}N_2O_3S$ (286.30)	58.73 58.89	3.52 3.63	9.78 9.93	11.20 11.32	2201 (CN); 1718 (C=O).	7.5–7.0 (m, 4H, arom.), 2.9 (s, 3H, NCH_3), 2.6 (s, 3H, SCH_3).[b]
6	210–212 chloroform	86	$C_9H_7NO_2Br_2$ (320.95)	33.68 33.30	2.20 2.08	4.36 4.19	— —	1690 (C=O), 549 (C—Br).	7.5–7.1 (m, 4H, arom.), 2.9 (s, 3H, NCH_3).[b]
7a	159 methanol	66	$C_{11}H_{12}N_2O_3$ (220.22)	59.99 59.57	5.49 5.33	12.72 12.52	— —	3209 (NH); 1683 (C=O).	10.9–10.7 (br, 1H, NH); 7.5–7.0 (m, 4H, arom.), 3.6–3.1 (m, 4H, $2CH_2$), 2.9 (s, 3H, CH_3).[b]
7b	188 chloroform	58	$C_{11}H_{12}N_2O_2S$ (236.28)	55.91 55.66	5.12 4.95	11.85 11.78	13.57 13.33	3247 (NH); 1684 (C=O).	12.3–12.1 (br, 1H, NH); 7.5–7.0 (m, 4H, arom.), 3.5–3.1 (m, 4H, $2CH_2$), 2.9 (s, 3H, CH_3).[b]
7c	172 ethanol	70	$C_{11}H_{11}NO_3S$ (237.27)	55.68 55.33	4.67 4.49	5.90 5.69	13.51 13.29	1688 (C=O).	7.5–7.0 (m, 4H, arom.), 3.7–3.2 (m, 4H, $2CH_2$), 2.9 (s, 3H, CH_3).[b]

(Continued on next page)

TABLE I Analytical and Spectral Data of the New Compounds (*Continued*)

Comp. no.	M.P. (°C) cryst. solvent	Yield (%)	Mole. form. (mol. wt.)	Analytical data cal./found C	H	N	S	IR (cm^{-1})	^{1}H-NMR δ (ppm) a, $CDCl_3$; b, DMSO-d_6
7d	249 DMF	61	$C_{15}H_{12}N_2O_2S$ (284.32)	63.36 63.07	4.25 4.11	9.85 9.58	11.28 10.99	3311 (NH), 1683 (C=O).	11.3–11.1 (br, 1H, NH); 7.5–6.8 (m, 8H, arom.). 2.9 (s, 3H, CH_3).[b]
7e	221 ethanol	59	$C_{15}H_{13}N_3O_2$ (267.27)	67.40 67.06	4.90 4.71	15.72 15.50	— —	3341, 3290 (2 NH), 1685 (C=O).	12.0–11.8 (br, 1H, NH); 9.9–9.7 (br, 1H, NH); 7.5–6.8 (m, 8H, arom.), 2.9 (s, 3H, CH_3).[b]
7f	233 ethanol	68	$C_{10}H_{10}N_4O_2S$ (250.27)	47.99 47.58	4.03 3.83	22.39 22.12	12.81 12.58	3369, 3271, 3211 (NH + NH_2), 1683 (C=O).	10.6–10.4 (br, 1H, NH); 7.5–7.0 (m, 4H, arom.), 5.5–5.2 (br, 2H, NH_2), 2.9 (s, 3H, CH_3).[b]
8a	273–5 ethanol	72	$C_{15}H_{13}NO_4S_2$ (335.39)	53.71 53.51	3.91 3.77	4.17 4.00	19.12 18.99	1702 (C=O), 1689 (CO_{amidic}).	7.5–7.0 (m, 4H, arom.), 2.9 (s, 3H, CH_3), 2.3 (s, 6H, 2 $COCH_3$).[a]
8b	153 ethanol	65	$C_{16}H_{15}NO_5S_2$ (365.41)	52.28 52.00	4.13 4.03	3.83 3.63	17.55 17.31	1736 (C=O_{ester}), 1702 (C=O), 1680 (C=O_{amidic}).	7.5–7.0 (m, 4H, arom.), 4.1 (q, 2H, CH_2), 2.9 (s, 3H, NCH_3), 2.3 (s, 3H, $COCH_3$), 1.3 (t, 3H, CH_3).[a]
8c	227 dioxan	79	$C_{13}H_7N_3O_2S_2$ (301.33)	51.81 51.52	2.34 2.22	13.94 13.59	21.28 21.03	2201 (CN), 1682 (C=O).	7.5–7.0 (m, 4H, arom.), 2.9 (s, 3H, CH_3).[a]
8d	166 ethanol	67	$C_{15}H_{12}N_2O_4S_2$ (348.39)	51.71 51.33	3.47 3.29	8.04 7.90	18.40 18.21	2199 (CN), 1723 (C=O_{ester}), 1681 (C=O_{amidic}).	7.5–7.0 (m, 4H, arom.), 4.1 (q, 2H, CH_2), 2.9 (s, 3H, NCH_3), 1.3 (t, 3H, CH_3).[a]
10	311 $CHCl_3$	72	$C_{12}H_8N_3OBr$ (290.10)	49.68 49.29	2.78 2.63	14.48 14.23	— —	2209 (CN), 549 (C—Br).	7.9 (s, 1H, CH), 7.5–7.0 (m, 4H, arom.), 2.9 (s, 3H, NCH_3).[a]
11	197 ethanol	64	$C_{16}H_{15}N_3O_3S$ (329.36)	58.34 58.66	4.59 4.66	12.76 12.98	9.73 9.88	3321, 3200 (NH_2), 2200 (CN), 1732 (C=O).	7.5–7.0 (m, 5H, arom + CH.), 5.7–5.4 (br, 2H, NH_2), 4.4–4.1 (q, 2H, CH_2), 2.9 (s, 3H, NCH_3), 1.3–1.0 (t, 3H, CH_3).[b]
12a	331 DMF	71	$C_{18}H_{14}N_4O$ (302.32)	71.50 71.22	4.67 4.59	18.53 18.23	— —	3329, 3266 (NH_2), 2197 (CN).	7.4–6.9 (m, 9H, arom.), 5.2–4.9 (br, 2H, NH_2), 2.9 (s, 3H, CH_3).[b]

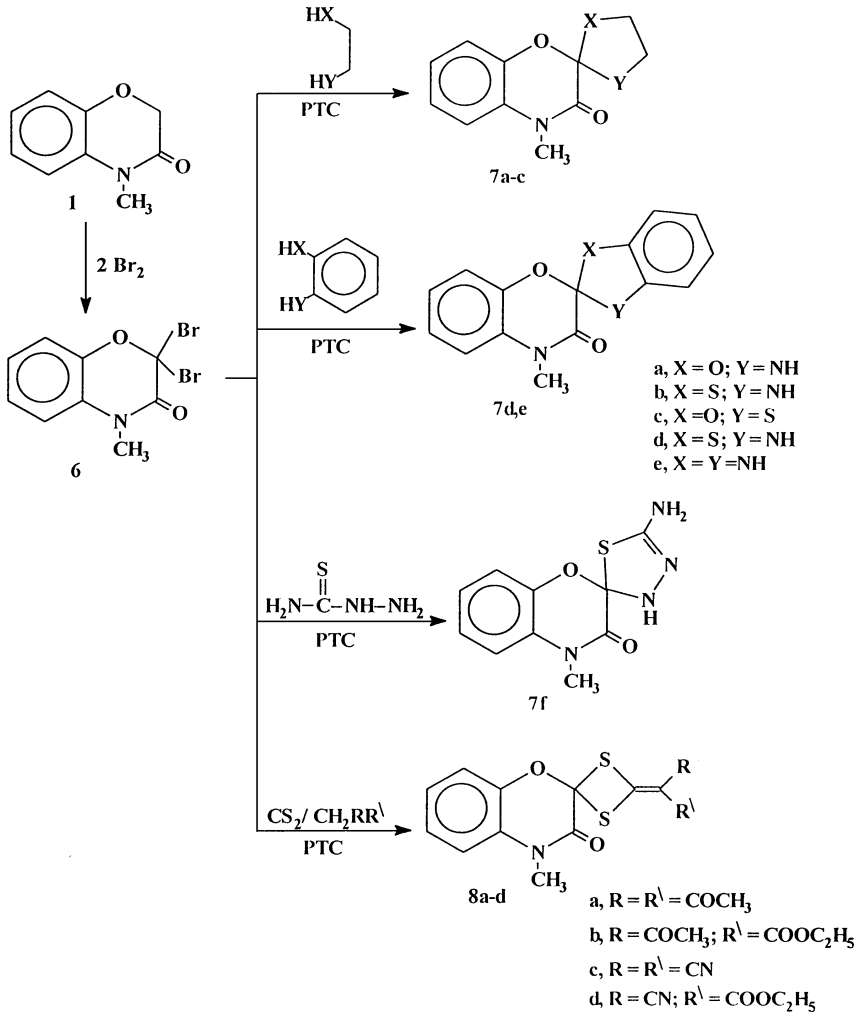
12b	229 ethanol	69	$C_{19}H_{16}N_4O$ (316.34)	72.13 71.77	5.09 4.98	17.71 17.43	— —	3322, 3241 (NH_2), 2199 (CN).	7.5–7.0 (m, 9H, arom.), 5.4–5.0 (br, 2H, NH_2), 3.8 (S, 2H, CH_2), 2.9 (s, 3H, CH_3).[b]
14a	239 ethanol	79	$C_{16}H_{15}NO_4S_2$ (349.41)	54.99 54.66	4.33 4.31	4.01 3.98	18.35 18.11	1707 (C=O), 1681 (CO_{amidic}).	7.5–7.0 (m, 4H, arom.), 3.8 (s, 2H, CH_2), 2.9 (s, 3H, CH_3), 2.1 (s, 6 H, 2 CH_3).[a]
14b	198 ethanol	68	$C_{16}H_{14}N_2O_4S_2$ (362.41)	53.02 52.61	3.89 3.77	7.73 7.55	17.69 17.36	2201 (CN), 1734 (C=O), 1680 (C=O_{amidic}).	7.5–7.0 (m, 4H, arom.), 4.4–4.1 (q, 2H, OCH_2), 4.0 (s, 2H, SCH_2), 2.9 (s, 3H, CH_3), 1.6–1.0 (t, 6H, 2CH_3).[a]
14c	273–5 ethanol	70	$C_{14}H_9N_3O_2S_2$ (315.36)	53.32 52.95	2.88 2.70	13.32 13.17	20.33 20.09	2203 (CN), 1680 (C=O_{amidic}).	7.5–7.0 (m, 4H, arom.), 3.9 (s, 2H, CH_2), 2.9 (s, 3H, CH_3).[a]
15	287 dioxan	82	$C_{13}H_9N_3O_2$ (239.22)	65.26 64.83	3.79 3.62	17.56 17.36	— —	2209 (CN), 1683 (C=O_{amidic}).	8.65 (d, 1H, CH), 8.30 (d, 1H, =CH), 7.5–7.0 (m, 4H, arom.), 2.9 (s, 3H, CH_3).[a]
16a	317 dioxan	84	$C_{18}H_{17}N_3O_4$ (339.34)	63.70 63.34	5.05 4.89	12.38 12.20	— —	3211, 3143 (NH_2), 2199 (CN), 1705 (C=O), 1680 (C=O_{amidic}).	7.5–7.0 (m, 4H, arom.), 5.4–5.1 (br, 2H, NH_2), 3.2 (S, 2H, CH_2), 2.9 (s, 3H, NCH_3), 2.1 (s, 6H, 2CH_3).[a]
16b	206 ethanol	63	$C_{19}H_{19}N_3O_5$ (369.36)	61.78 61.38	5.18 5.00	11.38 11.20	— —	3211, 3143 (NH_2), 2198 (CN), 1745 (CO_{ester}), 1700 (CO), 1680 (CO_{amidic}).	7.5–6.9 (m, 4H, arom.), 5.6–5.3 (br. 2H, NH_2), 4.4–4.1 (q, 2H, OCH_2), 3.2 (S, 2H, CH_2), 2.9 (s, 3H, NCH_3), 2.4 (s, 3H, $COCH_3$), 1.5–1.0 (t, 3H, CH_3).[a]
16c	188 ethanol	59	$C_{20}H_{21}N_3O_6$ (399.39)	60.14 59.78	5.30 5.11	10.52 10.27	— —	3311, 3250 (NH_2), 2200 (CN), 1733 (CO), 1680 (CO_{amidic}).	7.5–7.0 (m, 4H, arom.), 5.4–5.1 (br, 2H, NH_2), 4.4–4.1 (q, 4H, 2 OCH_2), 3.2 (S, 2H, CH_2), 2.9 (s, 3H, NCH_3), 1.5–1.0 (t, 6H, 2CH_3).[a]



SCHEME 1

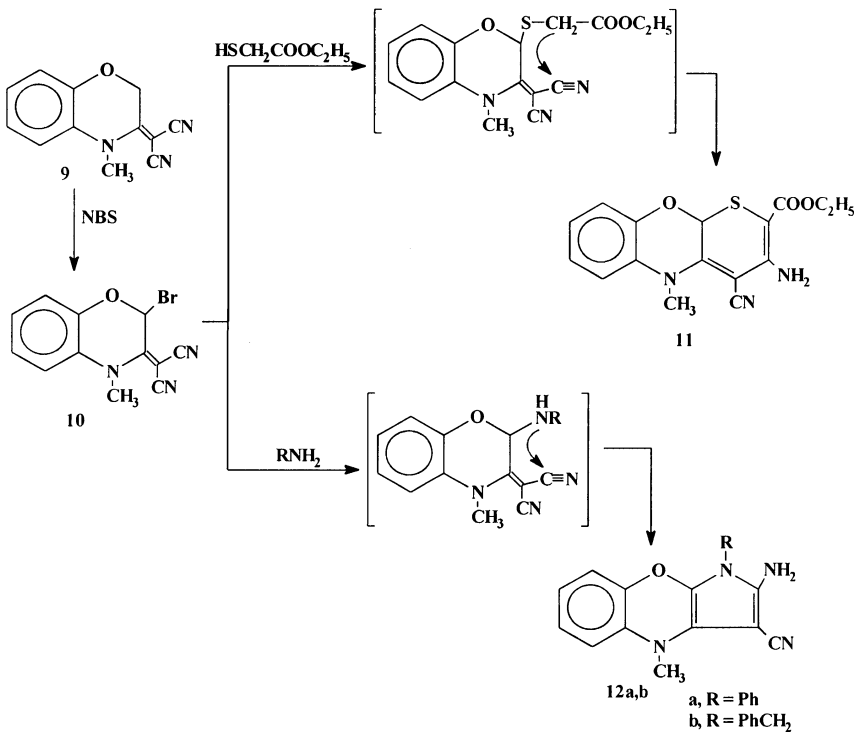
yielded the 2-bromo derivative **10** (*cf.* Scheme 3). Compound **10** was allowed to react with ethyl thioglycolate in DMF to afford the fused thiopyrano[2,3-b]-1,4-benzoxazine derivative **11**. While treatment of compound **10** with aniline of benzylamine yielded pyrrolo[2,3-b]-1,4-benzoxazine derivatives **12a**,**b**, respectively (*cf.* Scheme 3, Table I).

2-(1-Ethoxymethyliden)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-3-one.[10] **13** was obtained by reacting compound **1** with triethylorthoformate. Compound **13** was allowed to react with CS_2 and different



SCHEME 2

reactive methylene compounds, namely acetylacetone, ethyl cyanoacetate or malononitrile under solid-liquid phase-transfer catalysis conditions [dioxan/K_2CO_3/tetrabutyl-ammonium bromide (TBAB)] to yield the corresponding spiro dithiolane derivatives **14a–c**, respectively (*cf.* Scheme 4). The spectral data of compounds **14a–c** were in agreement with the proposed structures (*cf.* Table I). Moreover, the reaction of compound **13** with malononitrile in refluxing acetic anhydride gave

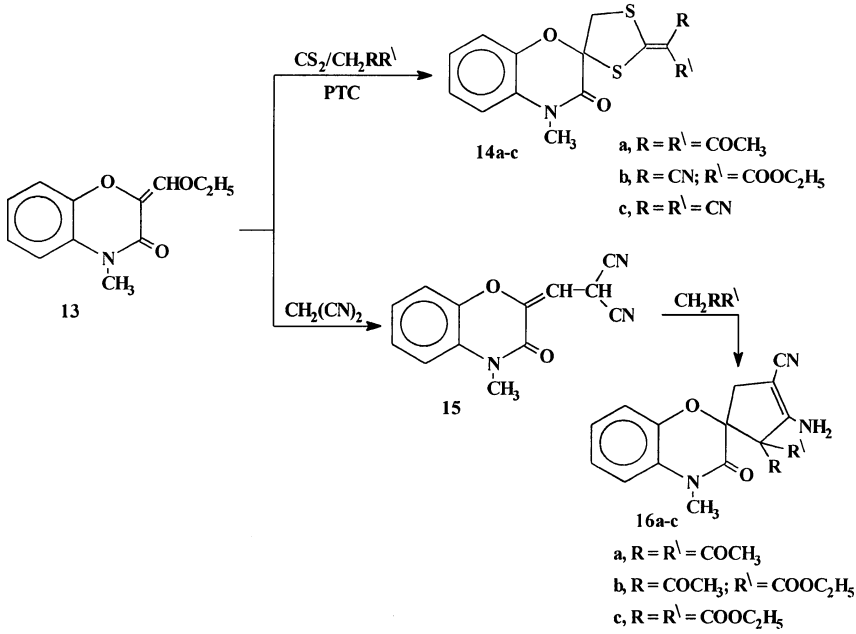


SCHEME 3

the corresponding 2-(4-methyl-3-oxo–3,4-dihydro-2H-1,4-benzoxazin-2-ylidenmethyl)malononitrile **15**. The IR spectra showed an absorption band at 2209 cm^{-1} for CN groups and the ^{1}H-NMR spectra revealed the disappearance of the ethoxy group and the presence of two peaks at 8.30 and 8.65 ppm due to =CH– and $CH(CN)_2$, respectively (*cf.* Table I). Compound **15** was proved to be an excellent precursor for the synthesis of spiro cyclopentene derivatives **16a–c** when reacted with acetylacetone, ethyl acetoacetate, or diethyl malonate, respectively (*cf.* Scheme 4). The IR spectra showed the presence of NH_2 and CN groups in addition to CO group and the ^{1}H-NMR spectra were in agreement with the proposed structures (*cf.* Table I).

Experimental

All melting points are uncorrected. IR spectra (cm^{-1}) were recorded on a Nicolet, 710 FT-IR Spectrophotometer in KBr pellets, ^{1}H-NMR



SCHEME 4

spectra were recorded at 60 MHz on a Varian A-60 Spectrophotometer using TMS as an internal reference standard. Elemental analyses were carried out on an elemental analyzer, model 240 C. All compounds were checked for purity on TLC plates.

Synthesis of Compounds 2a,b and 3a,b—General Procedure

A mixture of compound **1** (0.01 mol), CS_2 (0.012 mol), anhydrous potassium carbonate (3 g), a catalytic amount of TBAB, and dioxan (20 ml) was stirred for 20 minutes at 40°C. To the reaction mixture was added ethyl chloroacetate or bromomalononitrile (0.01 mol). The reaction mixture was stirred for 6 h at 65°C. The dioxan layer was separated by filtration, washed thoroughly with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The solid residue was crystallized from the suitable solvent to give compound **2a**,**b**, respectively. The solid potassium carbonate was dissolved in distilled water (50 ml). The separated solid was collected by filtration and crystallized from the proper solvent where compounds **3a**,**b** were obtained (*cf.* Scheme 1, Table I).

Synthesis of Compound 4

An equimolecular mixture (0.01 mol) of compound **1** and cyanoketene-S,S-diacetals in n-butanol (60 ml) was refluxed until the evolution MeSH ceased (∼32 hr). The reaction mixture was concentrated, cooled, and the precipitate was collected by filtration, washed with pet. ether 40–60°C, and crystallized from the proper solvent.

Synthesis of Compounds 5

A solution of compound **4** (0.005 mol) in ethanol (20 ml) was treated with HCl (10 ml, 5%). The reaction mixture was refluxed for 2 h and then poured into an ice-water mixture (80 ml). The precipitate was collected by filtration and crystallized from the proper solvent.

Synthesis of Compound 6

A solution of compound **4** (0,005 mol) in chloroform (25 ml) was added dropwise to a solution of bromine (0.04 mol) in chloroform (25 ml) with stirring over 45 minutes. The reaction mixture was stirred for an additional 2 h. The solvent was evaporated *in vacuo*. The residual solid was crystallized from a suitable solvent.

Synthesis of Compounds 7a–f—General Procedure

A mixture of compound **6** (0.005 mol), the desired amino compound (0.005 mol), anhydrous potassium carbonate (3 g), a catalytic amount of TBAB, and dry dioxan (30 ml) was stirred for 3 h. The reaction mixture was filtered off, and the filtrate was evaporated *in vacuo*. The residual solid was washed with water, triturated with petroleum ether (60–80°C) and crystallized from a suitable solvent.

Synthesis of Compounds 8a–d—General Procedure

A mixture of the reactive methylene compound (0.02 mol), CS_2 (0.02 mol), anhydrous potassium carbonate (5 g), a catalytic amount of TBAB, and chloroform (50 ml) was stirred for 15 min at 60°C. To the formed dianionic ambident was added compound **6** (0.02 mol). The reaction mixture was stirred for 2 h, then filtered off, and the organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated *in vacuo*. The residue was triturated with petroleum ether (60–80°C) and crystallized from a suitable solvent.

Synthesis of Compound 10

To a stirred solution of compound **9** (0.01 mole) in chloroform (30 ml), freshly recrystallized and dried N-bromosuccinimide (0.01 mole) was added. Stirring was completed to 24 h at 70°C. After cooling the precipitated product was collected and recrystallized from a suitable solvent (*cf.* Table I).

Synthesis of Compound 11

An equimolecular amount (0.01 mole) of compound **10** and methyl thioglycolate in dimethylformamide (30 ml) was refluxed for 7 h, after cooling the reaction mixture was poured into cold water. The precipitate was collected by filtration and crystallized from a suitable solvent (*cf.* Table I).

Synthesis of Compounds 12a,b—General Procedure

A mixture of compound **9** (0.01 mole) and the desired amino compound (0.01 mole) was refluxed in dimethylformamide (20 ml) for 5 h. The reaction mixture was poured into cold water. The precipitated solid was collected by filtration and crystallized from a suitable solvent (*cf.* Table I).

Synthesis of Compounds 14a–c—General Procedure

A mixture of the reactive methylene compound (0.02 mol), CS_2 (0.02 mol), anhydrous potassium carbonate (3 g), a catalytic amount of TBAB, and dioxan (50 ml) was stirred for 40 min at 60°C. To the formed dianionic ambident was added compound **13** (0.02 mol). The reaction mixture was stirred for 6 h at 50°C, filtered, and the organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated *in vacuo*. The solid residue was crystallized from a suitable solvent (*cf.* Table I).

Synthesis of Compound 15

An equimolecular amount (0.03 mol) of compound **13** and malononitrile in acetic anhydride (30 ml) was refluxed for 4 h. The reaction mixture was poured into ice cold water. The precipitate was collected by filtration and crystallized from a suitable solvent (*cf.* Table I).

Synthesis of Compound 16a–c—General Procedure

To a solution of compound **15** (0.005 mol) in absolute ethanol (30 ml) was added the reactive methylene compound (0.005 mol) and a catalytic amount of piperidine. The reaction mixture was refluxed for 3 h. The solvent was evaporated *in vacuo*. The separated solid was washed with water, triturated with petroleum ether (60–80°C) and crystallized from a suitable solvent (*cf.* Table I).

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