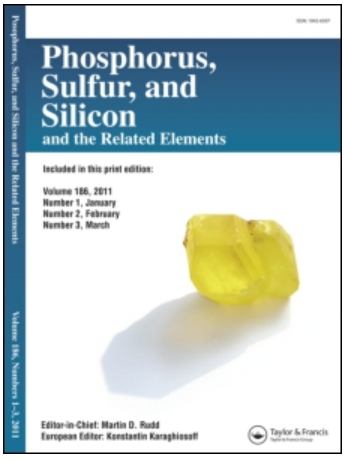


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF POLYFUSED HETEROCYCLIC SYSTEMS DERIVED FROM BIS(AMMONIOTHIO)-2-CYANOACRYLAMIDE

A. A. Sultan[a]; A. M. Soliman[a]; A. K. El-shafei[a]
[a] Chemistry Department, Faculty of Sciences, Sohag, Egypt

To cite this Article Sultan, A. A. , Soliman, A. M. and El-shafei, A. K.(1995) 'SYNTHESIS OF POLYFUSED HETEROCYCLIC SYSTEMS DERIVED FROM BIS(AMMONIOTHIO)-2-CYANOACRYLAMIDE', Phosphorus, Sulfur, and Silicon and the Related Elements, 101: 1, 95 — 102
To link to this Article: DOI: 10.1080/10426509508042504
URL: http://dx.doi.org/10.1080/10426509508042504

Phosphorus, Sulfur, and Silicon, 1995, Vol. 101, pp. 95–102
Reprints available directly from the publisher
Photocopying permitted by license only

SYNTHESIS OF POLYFUSED HETEROCYCLIC SYSTEMS DERIVED FROM BIS(AMMONIOTHIO)-2-CYANOACRYLAMIDE

A. A. SULTAN, A. M. SOLIMAN and A. K. EL-SHAFEI*
Chemistry Department, Faculty of Sciences, Sohag, Egypt

(Received July 27, 1994; in final form November 25, 1994)

Some new functionally substituted 1,3-dithiolo(4,5-b)pyrrolo(2′,3′-e)-4,8-benzoquinones were obtained starting with 1,3-dithiolo(4,5-b)-4,7-benzoquinone derivatives and active methylene reagents. The structure of the obtained new compounds was assigned.

Key words: Bis(ammoniothio)-2-cyanoacrylamide, 1,3-dithiolo(4,5-b)-4,7-benzoquinone, 1,3-dithiolo(4,5-b)pyrrolo(2′,3′-e)-4,8-benzoquinone.

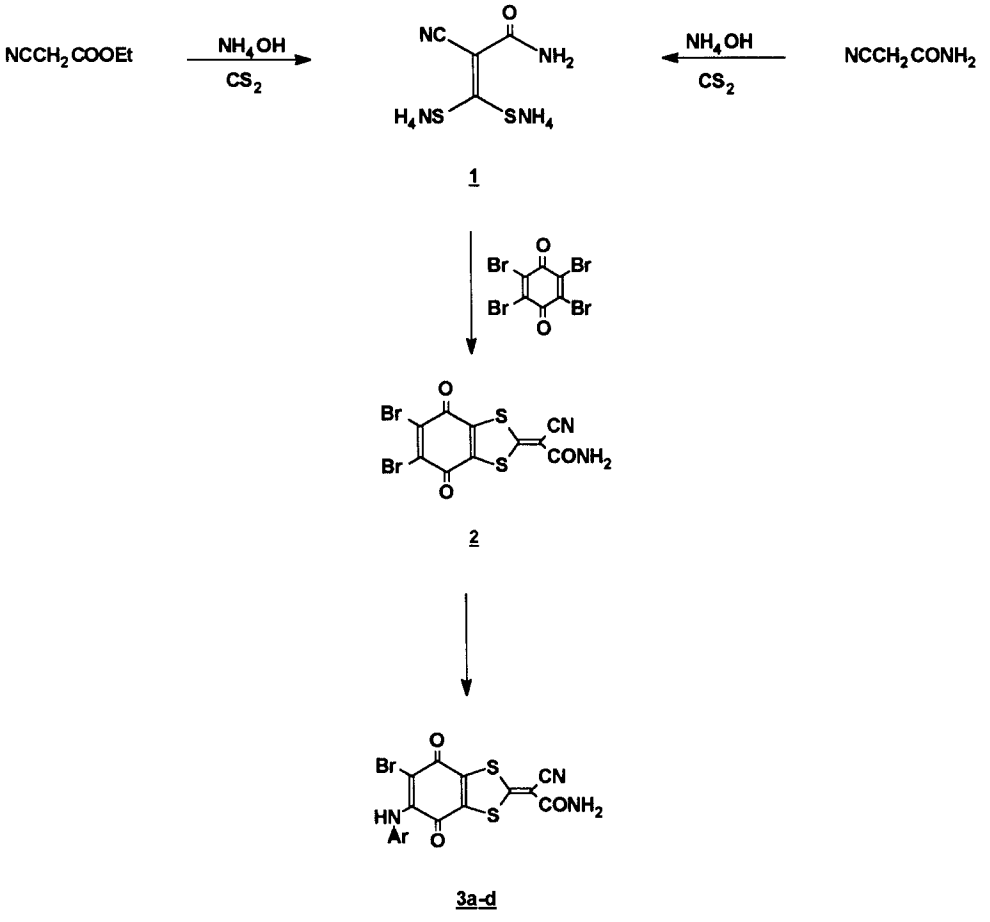
INTRODUCTION

The reported activity of α-oxoketene gem-thiols as precursors in the synthesis of many sulfur heterocycles,[1–7] has prompted us to use bis(ammoniothio)-2-cyanoacrylamide[8] 1 as a building block for the synthesis of polyfused heterocycles containing pyrrole, benzoquinone and 1,3-dithiolane nuclei.

RESULTS AND DISCUSSION

Compound 1 was obtained from reaction of either ethylcyanoacetate or cyanoacetamide with CS_2 and ammonia. The stirring of compound 1 with tetrabromo-1,4-benzoquinone at r.t. in aqueous ethanol gave the corresponding product 5,6-dibromo-2-(2′-cyanoacrylamide)-1,3-dithiolo (4,5-b)-4,7-benzoquinone 2 which was then allowed to react with a series of primary aromatic amines including: aniline, *p*-toluidine, anisidine and *p*-nitroaniline in refluxing ethanol to give the dehydrobrominated products: *viz*, 6-arylamino-5-bromo-2-(2′-cyanoacrylamide)-1,3-dithiolo(4,5-b)-4,7-benzoquinone derivatives 3a–d, cf. Scheme I.

A series of active methylene compounds including malononitrile, ethylcyanoacetate, diethylmalonate, acetoacetic esters and acetylacetone were allowed to react with arylamine derivatives 3a–d in DMF in presence of an equivalent amount of triethylamine. The reaction mixture was refluxed over different periods of time (2–5 hrs, cf. Table I) to give the corresponding polyfused ring systems cf. Scheme II. In each case, the reaction mechanism involves a vinylic substitution of bromine atom in benzoquinone *via* an addition/elimination process. Subsequent cyclization



SCHEME I

gave the expected triheterocyclic ring systems. Thus, the reaction of 3a–d with malononitrile or ethylcyanoacetate gave 6-amino-7-arylamino-5-cyano-2(2′-cyanoacrylamide)-1,3-dithiolo(4,5-b)pyrrolo (2′,3′-e)-4,8-benzoquinone 4a–d or 6-amino-7-arylamino-5-carbethoxy-2-(2′-cyanoacrylamide)-1,3-dithiolo(4,5-b)pyrrolo-(2′,3′-e)-4,8-benzoquinone 5a–d, respectively, *via* HBr elimination followed by a nucleophilic addition of HN-Ar atom at the cyano function and tautomerism. With diethylmalonate or ethylacetoacetate, the reaction mechanism involves elimination of HBr molecule followed by a nucleophilic addition to the carbonyl group with loss of ethanol molecule to give 7-arylamino-5-carbethoxy-2-(2′-cyanoacrylamide)-6-hydroxy-1,3-dithiolo(4,5-b)pyrrolo(2′,3′-e)-4,8-benzoquinone 6a–d or 5-acetyl-7-arylamino-2-(2′-cyanoacrylamide)-6-hydroxy-1,3-dithiolo(4,5-b)pyrrolo(2′,3′e)-4,8-benzoquinone 7a–d, respectively. The reaction of 3a–d with acetylacetone gave 5-acetyl-7-arylamino-2-(2-cyanoacrylamide)-6-methyl-1,3-dithiolo(4,5-b)pyrrolo(2,3-

TABLE 1

Physical and analytical data of the prepared compounds

Comp. No.	React. Time	M.P(°C) (Cryst.Solv.)	Yield %	Mol.Formula (m.Wt.)	Analytical data (Cal./Found %) C	H	N	S	Br
2	2h.	186 (Ethanol)	80	$C_{10}H_2N_2O_3S_2Br_2$ (422.11)	28.45 28.38	0.48 0.93	6.63 6.12	15.19 15.23	37.87 37.34
3a	1h.	202 (Dioxane)	67	$C_{16}H_8N_3O_3S_2Br$ (434.15)	44.23 44.28	1.86 1.32	9.68 9.18	14.77 15.12	13.41 19.20
3b	1h.	280 (Ethanol)	66	$C_{17}H_{10}N_3O_3S_2Br$ (448.17)	45.52 46.22	2.25 2.65	9.38 9.93	14.31 14.92	17.83 18.32
3c	45min.	300 (Ethanol)	69	$C_{17}H_{10}N_3O_4S_2Br$ (464.17)	43.95 43.32	2.17 1.82	9.05 8.82	13.82 13.35	17.22 17.98
3d	45min.	165 ($CHCl_3$)	67	$C_{16}H_7N_4O_5S_2Br$ (479.15)	40.07 39.85	1.47 1.97	11.69 11.05	13.38 13.91	16.68 17.11
4a	4h.	339 (DMF)	66	$C_{19}H_9N_5O_3S_2$ (419.26)	54.39 54.93	2.16 1.75	16.71 16.24	15.30 15.94	
4b	4h.	321 (Ethanol)	73	$C_{20}H_{11}N_5O_3S_2$ (433.28)	55.40 55.86	2.56 2.06	16.17 15.89	14.80 14.33	
4c	4h.	305 (DMF)	75	$C_{20}H_{11}N_5O_4S_2$ (449.28)	53.42 52.97	2.47 2.96	15.59 15.08	14.27 13.89	
4d	4h.	265 (Dioxane)	70	$C_{19}H_8N_6O_5S_2$ (464.26)	49.11 49.67	1.74 1.45	18.1 18.53	13.81 14.21	
5a	3h.	307 (DMF)	66	$C_{21}H_{14}N_4O_5S_2$ (466.30)	54.05 54.63	3.03 2.77	12.02 12.54	13.75 13.23	
5b	4h.	305 (Ethanol)	68	$C_{22}H_{16}N_4O_5S_2$ (480.31)	54.97 55.12	3.36 3.87	11.67 11.24	13.35 13.81	
5c	5h.	308 (Ethanol)	75	$C_{22}H_{16}N_4O_6S_2$ (496.31)	53.20 53.86	3.25 2.79	11.29 11.76	12.92 12.64	
5d	4h.	235 (DMF)	73	$C_{21}H_{13}N_5O_7S_2$ (511.30)	49.29 49.64	2.56 2.08	13.70 13.21	12.54 11.98	
6a	3h.	308 (Dioxane)	70	$C_{21}H_{13}N_3O_6S_2$ (467.28)	53.93 54.34	2.80 2.56	8.99 8.19	13.72 14.02	

TABLE I (*Continued*)

Comp. No.	React. Time	M.P(°C) (Cryst.Solv.)	Yield %	Mol.Formula (m.Wt.)	Analytical data (Cal./Found %) C	H	N	S	Br
6b	4h.	302 (DMF)	71	$C_{22}H_{15}N_3O_6S_2$ (481.30)	54.86 55.12	3.14 3.53	8.73 9.02	13.32 13.97	
6c	4h.	305 (Methanol)	68	$C_{22}H_{15}N_3O_7S_2$ (497.30)	53.09 52.86	3.04 3.45	8.45 8.88	12.90 12.34	
6d	5h.	238 (DMF)	72	$C_{21}H_{12}N_4O_8S_2$ (512.28)	49.20 48.86	2.36 2.84	10.94 10.43	12.52 12.07	
7a	3h.	305 (DMF)	73	$C_{20}H_{11}N_3O_5S_2$ (437.26)	54.89 55.08	2.54 2.11	9.61 10.03	14.67 14.98	
7b	5h.	298 (DMF)	75	$C_{21}H_{13}N_3O_5S_2$ (451.28)	55.85 55.54	2.90 2.45	9.31 9.87	14.21 13.97	
7c	4h.	279 (Ethanol)	65	$C_{21}H_{13}N_3O_6S_2$ (467.28)	53.93 54.23	2.80 2.34	8.99 9.27	13.72 13.94	
7d	5h.	233 (DMF)	70	$C_{20}H_{10}N_4O_7S_2$ (482.26)	49.77 49.33	2.09 2.35	11.62 12.01	13.30 12.98	
8a	4h.	320 (Benzene)	68	$C_{21}H_{13}N_3O_4S_2$ (435.28)	57.90 57.45	3.01 3.33	9.65 9.23	14.73 15.18	
8b	4h.	318 (DMF)	67	$C_{22}H_{15}N_3O_4S_2$ (449.30)	58.76 58.43	3.37 2.97	9.35 9.85	14.27 13.98	
8c	5h.	300 ($CHCl_3$)	74	$C_{22}H_{15}N_3O_5S_2$ (465.30)	56.74 56.34	3.25 2.97	9.03 9.34	13.78 13.45	
8d	4h.	205 (DMF)	72	$C_{21}H_{12}N_4O_6S_2$ (480.28)	52.47 52.89	2.52 2.13	11.67 12.08	13.35 13.64	

e)-4,8-benzoquinone 8a–d *via* HBr elimination followed by a nucleophilic addition to the carbonyl group with loss of water molecule and cyclization.

The structure of the obtained products was assigned both by elemental analyses, IR and ^{1}H-NMR spectra. The IR spectra of compounds 4a–d–8a–d revealed the NH_2 group absorptions around 3400 Cm^{-1} and 3280 Cm^{-1}, the CN group absorptions around 2200 Cm^{-1} and the carbonyl groups around 1650 Cm^{-1}. ^{1}H-NMR spectra of these compounds showed a broad band around 6.50 ppm corresponding to $CONH_2$ protons.

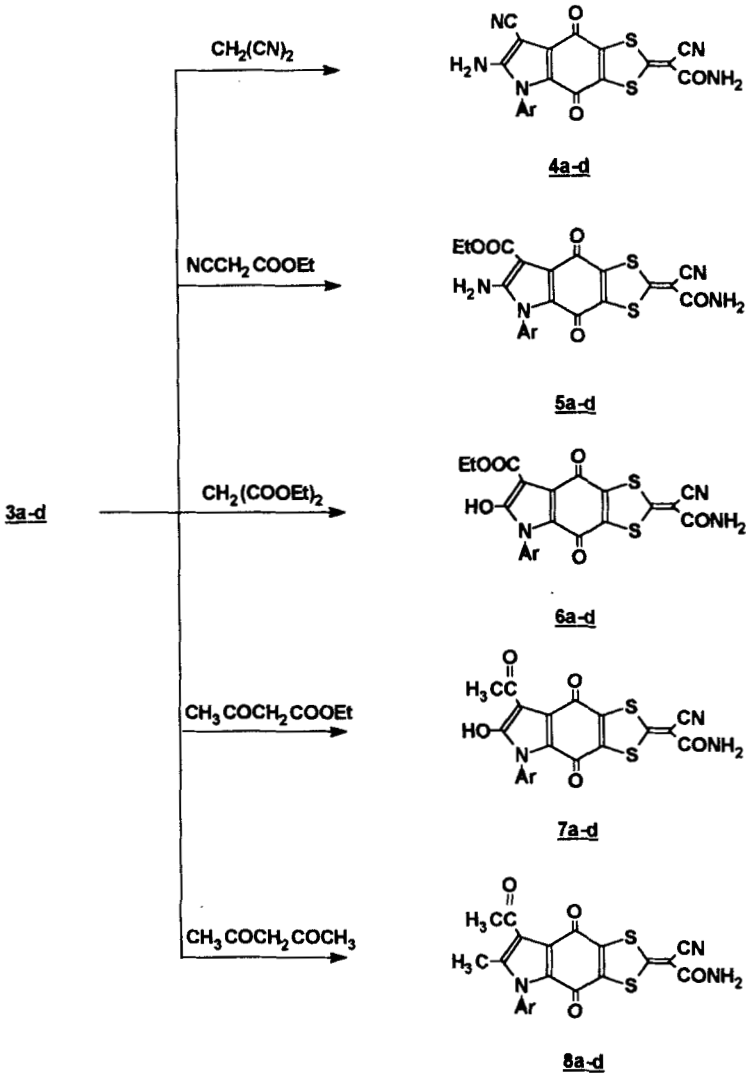
TABLE II

IR and ^{1}H-NMR spectra of the prepared compounds

Comp. No.	IR(KBr) ν(cm^{-1})	^{1}H-NMR(DMSO-d_6) δ(ppm)
2	3409,3339(NH_2),2209(CN),1678(C=O), 1650(C=O).	6.40(br,2H,$CONH_2$).
3a	3400,3310(NH_2),3231(NH),2209(CN), 1680(C=O),1640(C=O).	8.90(br,1H,NH),8.10-7.90(m,5H, arom.),6.35(br,2H,$CONH_2$).
3b	3408,3310(NH_2),3238(NH),2918,2853 (CH,aliph.),2210(CN),1670(C=O), 1635(C=O).	8.80(br,1H,NH),7.90-7.80(m,4H, arom.),6.30(br,2H,$CONH_2$),1.30(s, 3H,CH_3).
3c	3409,3305(NH_2),3227(NH),2910,2839 (CH,aliph.),2209(CN),1684(C=O), 1647(C=O).	8.85(br,1H,NH),8.00-7.90(m,4H, arom.),6.20(br,2H,$CONH_2$),3.90(s, 3H,CH_3).
3d	3408,3300(NH_2),3200(NH),2207(CN), 1680(C=O),1635(C=O).	8.95 (br,1H,NH), 7.90-7.67 (m,4H, arom.),6.40(br,2H,$CONH_2$).
4a	3441,3335,3290,3110(2NH_2),2210 (CN),1690(C=O),1650(C=O).	8.10-8.00(m,5H,arom.),7.60(br, 2H,NH_2),6.90(br,2H,$CONH_2$).
4b	3440,3330,3285,3197(2NH_2),2955, 2889(CH,aliph.),2208(CN),1690, 1637(C=O).	7.90-7.75(m,4H,arom.),7.50(br,2H, NH_2),6.55(br,2H,$CONH_2$),1.20(s,3H, CH_3).
4c	3443,3320,3198,3101(2NH_2),2900, 2842(CH,aliph.),2209(CN),1686, 1652(C=O).	8.20-8.05(m,4H,arom.),7.40(br,2H, NH_2),6.45(br,2H,$CONH_2$),3.93(s,3H, OCH_3).
4d	3435,3320,3280,3190(2NH_2),2207 (CN),1690,1640(C=O).	7.90-7.82(m,4H,arom.),7.45(br,2H, NH_2),6.35(br,2H,$CONH_2$).
5a	3410,3300,3231,3110(2NH_2),2910, 2885(CH,aliph.),2199(CN),1687 (C=O),1652(C=O).	7.95-7.85(m,5H,arom.),7.50(br, 2H,NH_2),6.45(br,2H,$CONH_2$),4.10-3.95(q,2H,CH_2),1.50-1.15(t,3H,CH_3).
5b	3439,3330,3290,3184(2NH_2),2990, 2980(CH,aliph.),2210(CN),1687, 1645(C=O).	7.85-7.45(m,4H,arom.),7.40(br,2H, NH_2),6.54(br,2H,$CONH_2$),4.50-4.15 (q,2H,CH_2),1.50(t,3H,CH_3),1.25 (s,3H,CH_3).
5c	3450,3330,3210,3185(2NH_2),2915, 2851(CH,aliph.),2215(CN),1680, 1640(C=O).	8.05-7.85(m,4H,arom.),7.35(br,2H, NH_2),6.50(br,2H,$CONH_2$),4.35-4.22 (q,2H,CH_2),3.90(s,3H,OCH_3),1.45 (t,3H,CH_3).
5d	3438,3320,3270,1197(2NH_2),2890, 2870(CH,aliph.),2210(CN),1680, 1635(C=O).	8.00-7.80(m,4H,arom.),7.35(br,2H, NH_2),6.25(br,2H,$CONH_2$),4.13-3.95 (q,2H,CH_2),1.50(t,3H,CH_3).

TABLE II (*Continued*)

Comp. No.	IR(KBr) ν(cm^{-1})	^{1}H-NMR(DMSO-d$_6$) δ(ppm)
6a	3450(OH),3347,3231(NH_2),2933,2900 (CH,aliph.),2207(CN),1740,1658, 1637(C=O).	9.55(br,1H,OH),7.95-7.92(m,5H, arom.),6.30(br,2H,$CONH_2$),4.40-4.10(q,2H,CH_2),1.50-1.35(t,3H,CH_3).
6b	3445(OH),3310,3195(NH_2),2900,2870 (CH,aliph.),2210(CN),1730,1685, 1638(C=O).	9.70(br,1H,OH),8.00-7.87(m,4H, arom.),6.43(br,2H,$CONH_2$),4.50-4.39(q,2H,CH_2),1.43-1.32(t,3H,CH_3), 1.24(s,3H,CH_3).
6c	3452(OH),3348,3233(NH_2),2933,2898 (CH,aliph.),2210(CN),1735,1683, 1642(C=O).	9.65(br,1H,OH),8.10-7.97(m,4H, arom.),6.35(br,2H,$CONH_2$),4.20-4.12(q,2H,CH_2),3.85(s,3H,OCH_3), 1.35(t,3H,CH_3).
6d	3460(OH),3346,3248(NH_2),2938,2887 (CH,aliph.),2212(CN),1730,1680, 1639(C=O).	9.55(br,1H,OH),8.11-7.96(m,4H, arom.),6.30(br,2H,$CONH_2$),4.15-3.98(q,2H,CH_2),1.40(t,3H,CH_3).
7a	3460(OH),3350,3245(NH_2),2900,2890 (CH,aliph.),2208(CN),1684,1658, 1637(C=O).	9.60(br,1H,NH),8.00-7.90(m,5H, arom.),6.20(br,2H,$CONH_2$),3.60(s, 3H,CH_3).
7b	3440(OH),3315,3200(NH_2),2885,2870 (CH,aliph.),2207(CN),1682,1657, 1635(C=O).	**9.50(br,1H,OH),8.00-7.86(m,4H, arom.),6.10(br,2H,$CONH_2$),3.53 (s,3H,CH_3),1.30(s,3H,CH_3).**
7c	3455(OH),3350,3245(NH_2),2910,2890 (CH,aliph.),2205(CN),1680,1655, 1635(C=O).	9.60(br,1H,OH),8.15-7.95(m,4H, arom),6.25(br,2H,$CONH_2$),4.03 (s,3H,OCH_3),3.50(s,3H,CH_3).
7d	3460(OH),3355,3256(NH_2),2900,2878 CH,aliph.),2210(CN),1683,1657, 1639(C=O).	9.53(br,1H,OH),8.11-7.48(m,4H, arom.),6.33(br,2H,$CONH_2$),3.10 (s,3H,CH_3).
8a	3335,3220(NH_2),2995,2880(CH, aliph.),2209(CN),1680,1660,1635 (C=O).	8.00-7.34(m,5H,arom.),6.30(br,2H, $CONH_2$),3.55(s,3H,CH_3),1.18(s,3H, CH_3).
8b	3320,3190(NH_2),2910,2885(CH, aliph.),2211(CN),1680,1658,1637 (C=O).	7.95-7.80(m,4H,arom.),6.15(br,2H, $CONH_2$),3.65(s,3H,CH_3),1.20-1.10 (m,3H,2CH_3).
8c	3330,3225(NH_2),2995,2880(CH, aliph.),2210(CN),1690,1660,1640 (C=O).	8.11-7.97(m,4H,arom.),6.25(br,2H, $CONH_2$),3.95(s,3H,CH_3),3.80(s,3H, CH_3),1.30(s,3H,CH_3).
8d	3335,3228(NH_2),2989,2870(CH, aliph.),2207(CN),1687,1646,1637 (C=O).	8.00-7.87(m,4H,arom),6.30(br,2H, $CONH_2$),3.75(s,3H,CH_3),1.30(s,3H, CH_3).



SCHEME II

EXPERIMENTAL

All melting points were determined on a Kofler melting point apparatus and were uncorrected. IR spectra were obtained on a FT-IR-710 (Nicolet) infrared spectrophotometer. ^{1}H-NMR spectra were obtained on a Varian EM360 A at 60 MHz using TMS as the internal standard. Elemental analyses were carried out on an elemental analyzer model 240C.

Bis(ammoniothio)-2-cyanoacrylamide 1: A mixture of ethylcyanoacetate (12 mg, 0.11 mole), carbon disulfide (16.19, 0.21 mole) and 36 ml of aqueous ammonia (28%) was stirred at r.t. for 8 hrs. The crude product was collected and recrystallized from water-acetone to give light yellow prisms. Yield 40%; m.p. 147–148°C (dec.).

5.6-Dibromo-2-(2-cyanoacrylamide)-1,3-dithiolo-(5,4-b)-4,7-benzoquinone 2: An equimolar mixture (0.02 mole) of tetrabromo-*p*-benzoquinone and compound 1 in ethanol/water (1:2) mixture was stirred for 2 hrs at r.t. The precipitated product was collected and recrystallized from ethanol.

6-Arylamino-5-bromo-2-(2'-cyanoacrylamide)-1,3-dithiolo(4,5-b)-4,7-benzoquinone 3a–d

General method: An equimolar mixture (0.02 mole) of compound 2 and aromatic amine was dissolved in dioxane and was then refluxed over different periods of time (40 min–2 hrs). On cooling the solid product was filtered off and recrystallized from the proper solvent.

Reaction of Compounds 3a–d *with Active Methylene Compounds*

General method for synthesis of compounds 4a–d–8a–d: An equimolar mixture (0.01 mole) of compounds 3a–d and the active methylene compound was dissolved in dimethylformamide and was treated with 0.01 mole of triethylamine. The reaction mixture was refluxed over varying periods of time (2–5 hrs) until a solid was formed. The reaction mixture was cooled and the collected product was filtered off and recrystallized from the proper solvent.

REFERENCES

1. R. Gompper and H. Schaefer, *Chem. Ber.*, **100,** 591 (1967).
2. M. Saquet and A. Thuiller, *Bull. Soc. Chim., France*, 2841 (1967).
3. a) I. Shahak and Y. Sasson, *Tetrahedron Letters*, 4207 (1973); b) L. Jensen, L. Dalgaard and S. O. Lawesson, *Tetrahedron*, **30,** 2413 (1974).
4. A. Thuiller and J. Vialle, *Bull. Soc. Chim., France*, 1398 (1959).
5. R. I. N. Harris and L .T. Oswald, *Aust. J. Chem.*, **27,** 1309 (1974).
6. B. Choshan and S. Smiles, *J. Chem. Soc. Chem. Comm.*, **105,** 1396 (1914).
7. P. T. S. Lous and T. E. Campr, *J. Org. Chem.*, **36,** 4103 (1970).
8. Y. Masataka, N. Masaki, O. Hiroko, I. Tsuneo and Y. Kei-ichi, *J. Org. Chem.*, **47,** 1090 (1982).