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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>

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Online publication date: 16 August 2010

To cite this Article El-Saghier, Ahmed M. M.(2004) 'A NOVEL SYNTHESIS OF SPIRO 1,3-DITHIIN AND SPIRO 1,3-THIAZINE DERIVATIVES UNDER PHASE TRANSFER CATALYSIS (PTC) CONDITIONS', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 179: 7, 1237 — 1250

To link to this Article: DOI: 10.1080/10426500490468065

URL: <http://dx.doi.org/10.1080/10426500490468065>

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A NOVEL SYNTHESIS OF SPIRO 1,3-DITHIIN AND SPIRO 1,3-THIAZINE DERIVATIVES UNDER PHASE TRANSFER CATALYSIS (PTC) CONDITIONS

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(Received April 21, 2003; accepted November 7, 2003)

*Ketene S,S-acetals **1a,b** or ketene N,S-acetals **2a,b** reacts in situ with a variety of ylidenemalononitriles to afford the desired spiro [1,3]dithiin heterocycles **3a,b–11a,b** or spiro[1,3]thiazine heterocycles **12a,b–20a,b**. Treatment of 2-(1-acetyl-2-oxopropylidene)spiro[1,3]thiazine derivatives **13b**, **17d**, and **18d** with malononitrile afforded the corresponding dispiro heterocycles **21**, **22**, and **23**.*

Keywords: Dispiro heterocycles; ketene acetals; spiro-1,3-dithiin; spiro-1,3-thiazine

Dithioacetals can be prepared by condensation of carbonyl compounds with thiols or dithiols in the presence of protic acids, Lewis acids, and some silicon reagents.^{1–9}

Recently, transdithioacetalization of acetals has gained favor as alternative method for the preparation of dithioacetals in which catalysts such as BF₃, OEt₂,¹⁰ Bu₂^tAlS(CH₂)₂SAIBu₂,¹¹ and CoCl₂, Me₃SiCl¹² have been employed. Also, the recent works on dithioacetalization of carbonyl compounds and transdithioacetalization reactions^{8,9,13} introduce compounds that potentially carry a positive halonium ion and can be used as efficient catalysts for both dithioacetalization and transdithioacetalization reactions. The compounds used for that purpose include: 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TABCO),^{14–17} N-bromosuccinimide (NBS), and molecular bromine (Br₂). Cyclic

The author wishes to thank Dr. Jerzy Suwinski and Mr. Mounir Abbas, Institute of Organic Chemistry and Technology, Silesian Technical University, 44-100 Gliwice, Poland, for the empirical calculation.

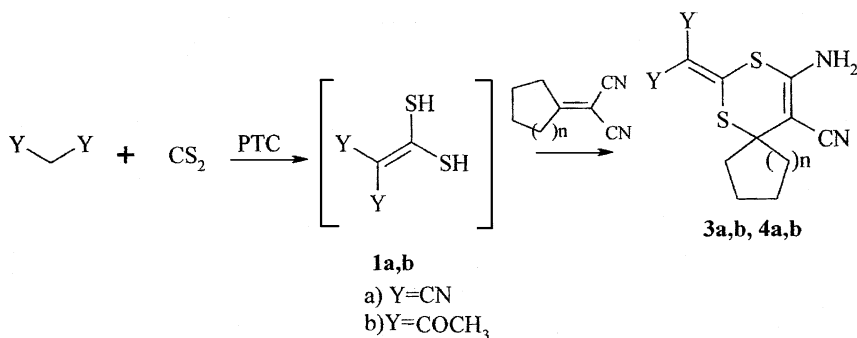
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S,S-acetals for example, 1,3-dithianes and 1,3-dithiolanes, also have found wide synthetic uses as precursors of acyl anion equivalents and as masked methylene group in organic synthesis.^{1-3,18}

DISCUSSION

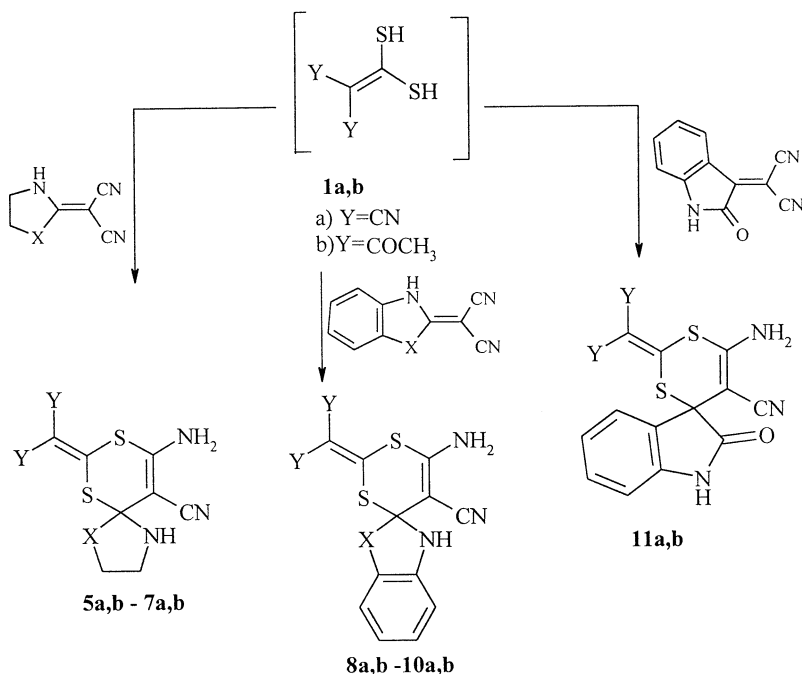
Our recent work on the synthesis of ketene-acetals uses simple phase-transfer catalysis conditions in one-pot reaction, the acetals formed being used in heterocyclic synthesis. In an extension of our previous work on the application of phase transfer catalysis in heterocyclic synthesis via ketene *S,S*- or *N,S*-acetals,¹⁹⁻²⁶ we report here the synthesis of ketene *S,S*-acetals **1a,b** or ketene *N,S*-acetals **2a,b** by reaction of either malonitrile or acetylacetone along with carbon disulfide or phenyl isothiocyanate in 1:1 molar ratio using solid-liquid phase transfer catalysis conditions [dioxane/ K_2CO_3 /tetrabutyl ammonium bromide (TBAB)].

Cyanoketene *S,S*-acetal **1a** or ketoketene *S,S*-acetal **1b** was then allowed to react in situ with cycloalkylidenemalononitriles using PTC conditions in one-pot reaction to give the desired spiro cycloalkylidene[1,3]dithiin heterocycles **3** ($n = 1$), **4** ($n = 2$) in an excellent yield. Spectral evidence strongly supported the structures, in particular, the signals in the 1H NMR spectrum for the NH_2 groups at δ 6.20 for **3a** ($Y=CN$), δ 6.00 for **3b** ($Y=COCH_3$), δ 6.30 for **4a** ($Y=CN$) and δ 6.10 for **4b** ($Y=COCH_3$).



The reaction mechanism was assumed to proceed via two steps where a preliminary nucleophilic addition of one of the two $-SH$ groups formed to the ethylenic bond followed by cyclization via another nucleophilic attack of the other $-SH$ group to the cyano group.

Also, ketene *S,S*-acetal **1a** or **1b** was allowed to react with a variety of ylidenemalononitrile including: 2-oxazolylidene-, 2-(2,3-dihydrobenzo-[d]oxazolylidene)-, 2-thiazolylidene-, 2-(2,3-dihydrobenzo-[d]thiazolylidene)-, 2-perhydro-2-imidazolylidene-, 2-(2,3-dihydro-1H-benzo[d]-imidazolylidene)-, and 2-(2-oxo-2,3-dihydro-1H-3-indolyiden)-malononitrile in situ using the same PTC conditions to afford the corresponding spiro[1,3]dithiin heterocycles **5a,b-11a,b** (cf. Scheme 1).



SCHEME 1

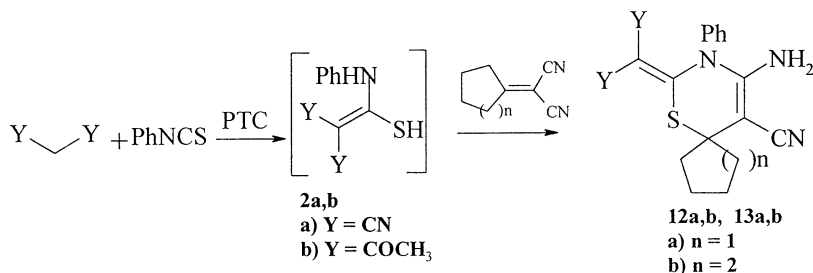
The IR spectra of these compounds showed the appearance of the characteristic bands corresponding to NH₂ group, C=O of the acetyl groups in **5b-11b** and NH₂ groups, CN groups in **5a-11a**. ¹H NMR

TABLE I Spiro 1,3-Dithiin and Spiro 1,3-Thiazine Derivatives

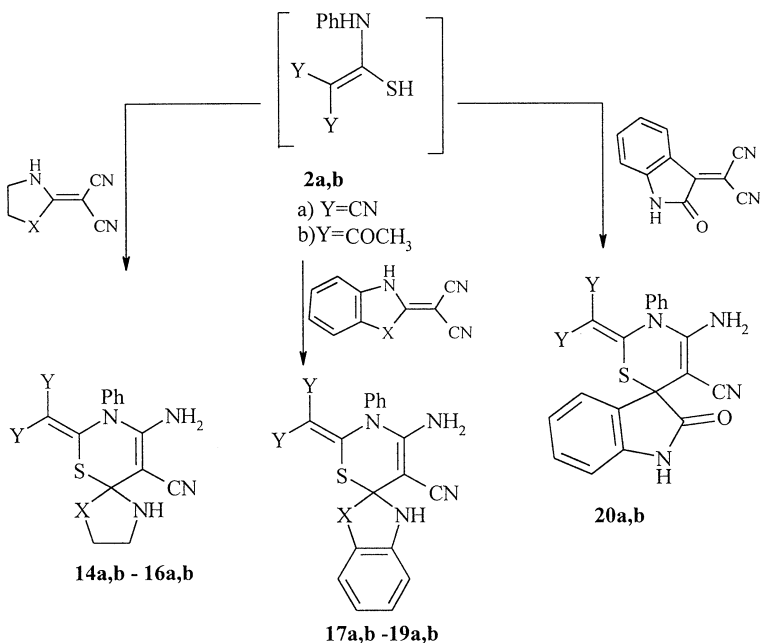
Comp. no.	Y	X	Comp. no.	Y	X
3a, 4a, 11a, 12a, 13a, 20a	CN	—	6a, 9a, 15a, 18a	CN	S
3b, 4b, 11b, 12b, 13b, 20b	COCH ₃	—	6b, 9b, 15b, 18b	COCH ₃	S
5a, 8a, 14a, 17a	CN	O	7a, 10a, 16a, 19a	CN	NH
5b, 8b, 14b, 17b	COCH ₃	O	7b, 10b, 16b, 19b	COCH ₃	NH

showed the appearance of NH_2 signals for all spiro[1,3]dithiin derivatives **5a,b**–**11a,b** and the appearance of a new signal for $-\text{CH}_3$ referring to acetyl groups in **5b**–**11b** (cf. Tables I and II).

In connection with this basic idea, cyanoketene *N,S*-acetal **2a** and ketoketene *N,S*-acetal **2b** were allowed to react with cycloalkylidenemalononitriles to give the corresponding cycloalkylidene spiro[1,3]thiazine derivatives **12a,b**, **13a,b**.



In the same line for the synthesis of spiro derivatives, the previous ylidenemalononitriles were allowed to react with intermediate **2a** or **2b** to afford the spiro[1,3]thiazine heterocycles **14a,b**–**20a,b** (cf. Scheme 2).



SCHEME 2

TABLE II Analytical and Spectral Data of the Prepared Compounds

Compd. no.	m.p. °C ^a (Crys. solvent)	Yield %	Analytical data calc. L (Found) ^b %				IR (KBr) ν (cm ⁻¹) ^c	¹ H-NMR (DMSO-d ₆) ^d δ (ppm)	
			C	H	N	S			
3a	211–213 ethanol	91	C ₁₂ H ₁₀ N ₄ S ₂ (274.35)	52.53	3.64	20.41	23.37	3460, 3350 (NH ₂), 2986 (CH aliph.), 2220, 2210 (3CN)	6.20–6.00 (br, 2H, NH ₂), 2.30–1.60 (m, 8H, cyclic CH ₂)
3b	235–237 benzene	86	C ₁₄ H ₁₆ N ₂ O ₂ S ₂ (308.41)	54.45	5.18	9.08	20.08	3398, 3280 (NH ₂), 2920 (CH aliph.), 2207 (CN), 1680 (C=O)	6.00–5.80 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃), 2.30–1.60 (m, 8H, cyclic CH ₂)
4a	256–258 ethanol	90	C ₁₃ H ₁₂ N ₄ S ₂ (288.38)	54.14	4.16	19.42	22.23	3463, 3370 (NH ₂), 2970 (CH aliph.), 2218, 2212 (3CN)	6.30–6.00 (br, 2H, NH ₂), 2.30–1.50 (m, 10H, cyclic CH ₂)
4b	198–200 dioxane	82	C ₁₅ H ₁₈ N ₂ O ₂ S ₂ (322.44)	55.82	5.58	8.68	19.88	3418, 3330 (NH ₂), 2910 (CH aliph.), 2221 (CN), 1680 (C=O)	6.10–5.90 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃), 2.30–1.50 (m, 10H, cyclic CH ₂)
5a	269–272 methanol	75	C ₁₀ H ₇ N ₅ OS ₂ (277.31)	43.31	2.52	25.24	23.12	3450, 3345, 3210 (NH, NH ₂), 2930 (CH aliph.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 6.20–6.00 (br, 2H, NH ₂), 3.30–3.00 (d, 4H, 2CH ₂)
5b	244–246 dioxane	77	C ₁₂ H ₁₃ N ₃ O ₃ S ₂ (311.37)	46.28	4.17	13.48	20.59	3460, 3360, 3221 (NH, NH ₂), 2920 (CH aliph.), 2220 (CN), 1680 (C=O)	9.80 (br, 1H, NH), 6.10–5.80 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
6a	239–240 ethanol	76	C ₁₀ H ₇ N ₅ S ₃ (293.37)	40.94	2.38	23.86	32.78	3455, 3345, 3220 (NH, NH ₂), 2930 (CH aliph.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 6.20–6.00 (br, 2H, NH ₂), 3.30–3.00 (d, 4H, 2CH ₂)
6b	227–229 ethanol	79	C ₁₂ H ₁₃ N ₃ O ₂ S ₃ (327.43)	44.02	3.97	12.82	29.94	3460, 3360, 3221 (NH, NH ₂), 2920 (CH aliph.), 2220 (CN), 1680 (C=O)	9.80 (br, 1H, NH), 6.30–6.00 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
7a	312–314 ethanol	65	C ₁₀ H ₈ N ₆ S ₂ (276.33)	43.46	2.89	30.39	23.20	3463, 3380, 3210, 3180 (2NH, NH ₂), 2930 (CH aliph.), 2220, 2210 (3CN)	10.20 (br, 1H, NHO), 9.90 (br, 1H, NH), 6.20–6.00 (br, 2H, NH ₂), 3.30–3.00 (d, 4H, 2CH ₂)

(Continued on next page)

TABLE II Analytical and Spectral Data of the Prepared Compounds (Continued)

Compd. no.	m.p. °C ^a (Crys. solvent)	Yield %	Analytical data calc. L (Found) ^b %				IR (KBr) ν (cm ^{−1}) ^c	¹ H-NMR (DMSO-d ₆) ^d δ (ppm)	
			C	H	N	S			
7b	324–326 methanol	77	C ₁₂ H ₁₄ N ₄ O ₃ S ₂ (310.38)	46.43 46.62	4.51 4.39	18.04 17.97	20.66 20.54	3460, 3370, 3221, 3177 (2NH, NH ₂), 2980 (CH aliph.), 2218 (CN), 1680 (C=O)	10.20 (br, 1H, NH), 9.80 (br, 1H, NH), 6.10–5.80 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃), 2.90 (br, 1H, NH), 8.00–7.80 (m, 4H, arom.) 6.20–6.00 (br, 2H, NH ₂)
8a	297–299 dioxane	69	C ₁₄ H ₇ N ₅ OS ₂ (325.36)	51.68 51.67	2.15 2.23	21.51 21.33	19.71 19.67	3460, 3365, 3220 (NH, NH ₂), 3050 (CH arom.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 8.00–7.80 (m, 4H, arom.) 6.20–6.00 (br, 2H, NH ₂)
8b	235–237 dioxane	71	C ₁₆ H ₁₃ N ₃ O ₃ S ₂ (359.41)	53.46 53.39	3.62 3.66	11.68 11.71	17.84 18.09	3465, 3370, 3210 (NH, NH ₂), 3080 (CH arom.), 2220 (CN), 1680 (C=O)	9.90 (br, 1H, NH), 8.00–7.70 (m, 4H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
9a	253–255 dioxane	66	C ₁₄ H ₇ N ₅ S ₃ (341.42)	49.25 49.46	2.05 1.99	20.50 20.41	28.17 28.31	3460, 3365, 3220 (NH, NH ₂), 3050 (CH arom.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 8.00–7.80 (m, 4H, arom.), 6.20–6.00 (br, 2H, NH ₂)
9b	282–284 dioxane	72	C ₁₆ H ₁₃ N ₃ O ₃ S ₃ (375.47)	51.12 50.98	3.46 3.55	11.18 11.24	25.62 25.73	3455, 3350, 3210 (NH, NH ₂), 3080 (CH arom.), 2218 (CN), 1680 (C=O)	9.90 (br, 1H, NH), 8.00–7.70 (m, 4H, arom.), 6.30–6.10 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
10a	343–346 methanol	85	C ₁₄ H ₈ N ₆ S ₂ (324.37)	51.83 51.77	2.47 2.53	25.89 25.97	19.77 19.64	3460, 3355, 3220, 3186 (2NH, NH ₂), 3080 (CH arom.), 2220, 2209 (3CN)	10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.00–7.70 (m, 4H, arom.), 6.20–6.00 (br, 2H, NH ₂)
10b	355 ^d dioxane	79	C ₁₆ H ₁₄ N ₄ O ₂ S ₂ (358.43)	53.61 53.66	3.91 3.89	15.62 15.38	17.89 18.01	3465, 3370, 3210, 3180 (2NH, NH ₂), 3080 (CH arom.), 2218 (CN), 1685 (C=O)	10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.00–7.70 (m, 4H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
11a	311–313 benzene	92	C ₁₅ H ₇ N ₅ OS ₂ (337.37)	53.39 53.44	2.07 2.14	20.75 20.39	19.01 19.27	3640, 3360, 3230 (NH, NH ₂), 2220, 2210 (3CN), 1670 (C=O)	10.30 (br, 1H, NH), 8.20–7.80 (m, 4H, arom.), 6.20–6.00 (br, 2H, NH ₂)

11b	298–300 acetone	89	$C_{17}H_{13}N_3O_3S_2$ (371.42)	54.97 55.12	3.50 3.56	11.31 11.42	17.26 17.31	3640, 3350, 3210 (NH, NH ₂), 2216 (CN), 1680, 1660 (C=O)	9.80 (br, 1H, NH), 8.00–7.80 (m, 4H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
12a	215–217 ethanol	91	$C_{18}H_{15}N_5S$ (333.41)	64.71 64.67	4.49 4.59	20.09 19.96	9.96 10.11	3460, 3350 (NH ₂), 2986 (CH aliph.), 2220, 2210 (3CN)	8.20–7.80 (m, 5H, arom), 6.20–6.00 (br, 2H, NH ₂), 2.30–1.60 (m, 8H, cyclic CH ₂)
12b	208–210 methanol	88	$C_{20}H_{21}N_3O_2S$ (367.46)	65.37 65.44	5.71 5.62	11.43 11.57	8.72 8.65	3398, 3280 (NH ₂), 2920 (CH aliph.), 2207 (CN), 1680 (C=O)	8.20–7.80 (m, 5H, arom), 6.00–5.80 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃), 2.30–1.60 (m, 8H, cyclic CH ₂)
13a	221–223 ethanol	89	$C_{19}H_{17}N_5S$ (347.43)	65.68 65.77	4.89 5.10	20.15 20.23	9.21 9.11	3463, 3370 (NH ₂), 2970 (CH aliph.), 2218, 2212 (3CN)	8.20–7.80 (m, 5H, arom), 6.30–6.00 (br, 2H, NH ₂), 2.30–1.50 (m, 10H, cyclic CH ₂)
13b	218–219 ethanol	93	$C_{21}H_{23}N_3O_2S$ (381.49)	66.11 65.97	6.03 5.99	11.01 10.96	8.40 8.55	3418, 3330 (NH ₂), 2910 (CH aliph.), 2221 (CN), 1680 (C=O)	8.20–7.80 (m, 5H, arom), 6.10–5.90 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃), 2.30–1.50 (m, 10H, cyclic CH ₂)
14a	257–259 dioxane	78	$C_{16}H_{12}N_6OS$ (336.37)	57.13 57.33	3.57 3.66	24.97 25.12	9.51 9.59	3450, 3345, 3210 (NH, NH, NH ₂), 2930 (CH aliph.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 8.20–7.80 (m, 5H, arom), 6.20–6.00 (br, 2H, NH ₂), 3.30–3.00 (d, 4H, 2CH ₂)
14b	231–233 benzene	84	$C_{18}H_{18}N_4O_3S$ (370.42)	58.36 58.45	4.86 4.91	15.12 15.23	8.65 8.81	3460, 3360, 3221 (NH, NH ₂), 2920 (CH aliph.), 2220 (CN), 1680 (C=O)	9.80 (br, 1H, NH), 8.20–7.80 (m, 5H, arom), 6.10–5.80 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
15a	199–200 ethanol	87	$C_{16}H_{12}N_6S_2$ (352.43)	54.52 54.61	3.40 3.52	23.83 23.77	18.19 18.34	3450, 3345, 3210 (NH, NH ₂), 2930 (CH aliph.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 8.20–7.80 (m, 5H, arom), 6.20–6.00 (br, 2H, NH ₂), 3.30–3.00 (d, 4H, 2CH ₂)
15b	186–188 ethanol	79	$C_{18}H_{18}N_4O_2S_2$ (386.48)	55.93 56.12	4.66 4.81	14.48 14.56	16.59 16.66	3460, 3360, 3221 (NH, NH ₂), 2920 (CH aliph.), 2220 (CN), 1680 (C=O)	9.80 (br, 1H, NH), 8.20–7.80 (m, 5H, arom.), 6.10–5.80 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃)

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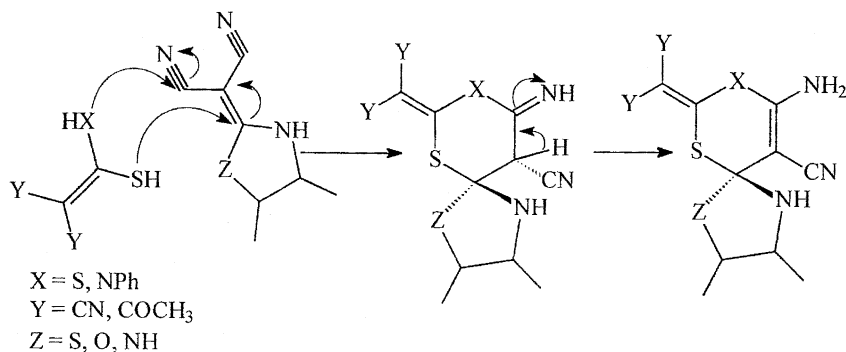
TABLE II Analytical and Spectral Data of the Prepared Compounds (Continued)

Compd. no.	m.p. °C ^a (Crys. solvent)	Yield %	Analytical data calc. L (Found) ^b %				IR (KBr) ν (cm ⁻¹) ^c	¹ H-NMR (DMSO-d ₆) ^d δ (ppm)	
			C	H	N	S			
16a	345–347 dioxane	89	C ₁₆ H ₁₃ N ₇ S (335.38)	57.29	3.87	29.22	9.56	3450, 3345, 3210, 3186 (2NH, NH ₂), 2930 (CH aliph.), 2220, 2210 (3CN)	10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.0–7.70 (m, 5H, arom.), 6.20–6.00 (br, 2H, NH ₂), 3.30–3.00 (d, 4H, 2CH ₂)
				57.46	4.01	29.37	9.67		10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.0–7.80 (m, 5H, arom.), 6.10–5.80 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
16b	315–318 acetone/water	79	C ₁₈ H ₁₉ N ₅ O ₂ S (369.44)	58.51	5.14	18.95	8.68	3460, 3360, 3221, 3180 (2NH, NH ₂), 2920 (CH aliph.), 2220 (CN), 1680 (C=O)	10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.0–7.80 (m, 5H, arom.), 6.10–5.80 (br, 2H, NH ₂), 3.40–3.00 (d, 4H, 2CH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
				58.43	5.24	19.05	8.72		9.90 (br, 1H, NH), 8.30–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
17a	266–268 dioxane	69	C ₂₀ H ₁₂ N ₆ OS (384.41)	62.49	3.12	21.85	8.32	3460, 3365, 3220 (NH, NH ₂), 3050 (CH arom.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 8.30–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
				62.54	3.23	21.94	8.51		9.90 (br, 1H, NH), 8.30–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
17b	243–245 benzene	66	C ₂₂ H ₁₈ N ₄ O ₃ S (418.46)	63.14	4.30	13.38	7.66	3465, 3370, 3210 (NH, NH ₂), 3080 (CH arom.), 2220 (CN), 1680 (C=O)	9.90 (br, 1H, NH), 8.30–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
				63.31	4.45	13.45	7.87		9.90 (br, 1H, NH), 8.30–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
18a	256–259 dioxane	81	C ₂₀ H ₁₂ N ₆ S ₂ (400.47)	59.97	2.99	20.97	16.01	3460, 3365, 3220 (NH, NH ₂), 3050 (CH arom.), 2220, 2210 (3CN)	9.90 (br, 1H, NH), 8.30–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
				60.22	3.14	21.17	16.31		9.90 (br, 1H, NH), 8.30–7.70 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
18b	233–235 benzene	69	C ₂₂ H ₁₈ N ₄ O ₂ S ₂ (434.53)	60.81	4.14	12.88	14.76	3465, 3370, 3210 (NH, NH ₂), 3080 (CH arom.), 2220 (CN), 1680 (C=O)	9.90 (br, 1H, NH), 8.30–7.70 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
				60.67	4.23	12.97	14.54		10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.00–7.70 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
19a	356 ^d acetone	66	C ₂₀ H ₁₃ N ₇ S (383.43)	62.48	3.38	25.49	8.34	3460, 3365, 3220, 3175 (2NH, NH ₂), 3050 (CH arom.), 2220, 2210 (3CN)	10.20 (br, 1H, NH), 9.90 (br, 1H, NH), 8.00–7.70 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
				62.57	3.41	25.55	8.43		

19b	346–348 ^d acetone	73	C ₂₂ H ₁₉ N ₅ O ₂ S 417.48	63.28 63.37	4.55 4.76	16.77 16.92	7.68 7.75	3465, 3370, 3210, 3190 (2NH, NH ₂), 3080 (CH arom.), 2220 (CN), 1680 (C=O)	9.90 (br, 1H, NH), 8.00–7.70 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
20a	325–327 benzene	88	C ₂₁ H ₁₂ N ₆ OS (369.42)	63.62 68.83	3.03 2.97	21.19 20.96	8.09 8.12	3640, 3360, 3230 (NH, NH ₂), 2220, 2210 (3CN), 1670 (C=O)	10.30 (br, 1H, NH), 8.20–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂)
20b	336–338 dioxane	76	C ₂₃ H ₁₈ N ₄ O ₃ S (430.48)	64.17 64.33	4.18 4.13	13.01 12.17	7.45 7.60	3640, 3350, 3210 (NH, NH ₂), 2216 (CN), 1680, 1660 (C=O)	9.80 (br, 1H, NH), 8.10–7.80 (m, 9H, arom.), 6.20–6.00 (br, 2H, NH ₂), 2.60–2.40 (s, 6H, 2CH ₃)
21	288–290 ethanol	77	C ₂₂ H ₂₃ N ₅ OS (405.51)	65.16 65.34	5.67 5.84	17.26 17.35	7.91 8.10	3450, 3350, 3210 (2NH ₂), 3050 (CH arom.), 2860 (CH aliph.), 2220, 2216 (2CN)	8.00–7.60 (m, 5H, arom.) 6.50–6.30 (br, 2H, NH ₂), 6.00–5.80 (br, 2H, NH ₂), 5.20 (s, 1H, =CH), 2.50 (s, 3H, CH ₃), 2.30–1.60 (m, 10H, cyclic CH ₂), 10.10 (br, 1H, NH), 8.00–7.50 (m, 9H, arom.), 6.50–6.30 (br, 2H, NH ₂), 6.00–5.80 (br, 2H, NH ₂), 5.20 (s, 1H, =CH), 2.50 (s, 3H, CH ₃), 2.30–1.60 (m, 10H, cyclic CH ₂)
22	312–314 ethanol	69	C ₂₃ H ₁₈ N ₆ O ₂ S (442.49)	62.43 62.11	4.06 3.90	18.98 19.08	7.24 7.35	3450, 3350, 3210 (NH, 2NH ₂), 3050 (CH arom.), 2860 (CH aliph.), 2220, 2216 (2CN)	10.10 (br, 1H, NH), 8.00–7.50 (m, 9H, arom.), 6.50–6.30 (br, 2H, NH ₂), 6.00–5.80 (br, 2H, NH ₂), 5.20 (s, 1H, =CH), 2.50 (s, 3H, CH ₃), 2.30–1.60 (m, 10H, cyclic CH ₂)
23	334–336 ethanol	81	C ₂₃ H ₁₈ N ₆ OS ₂ (458.55)	60.24 60.33	3.93 4.09	18.32 18.44	13.98 14.24	3450, 3350, 3210 (NH, 2NH ₂), 3050 (CH arom.), 2860 (CH aliph.), 2220, 2216 (2CN)	10.20 (br, 1H, NH), 8.00–7.40 (m, 9H, arom.), 6.50–6.30 (br, 2H, NH ₂), 6.00–5.80 (br, 2H, NH ₂), 5.20 (s, 1H, =CH), 2.50 (s, 3H, CH ₃)

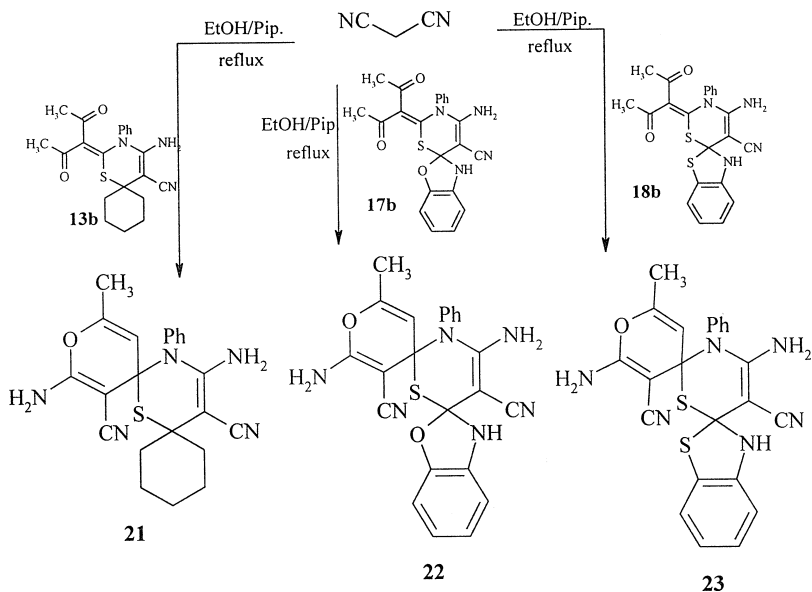
^aUncorrected.^bSatisfactory microanalysis obtained C; +0.35, H; +0.4, N; +0.2.^cMeasured on a Nicolet 710 FT-IR spectrometer.^dMeasured by a Varian EM 360L spectrometer at 60 MHz using TMS as internal standard and DMSO d₆ as a solvent.

The reaction mechanism was assumed to go through cycloaddition reaction where a nucleophilic attack of the $-SH$ group of compound **1** or **2** to the ethylenic bond followed by a nucleophilic attack of the $-XH$ group to the cyano group and cyclization. Here we have a chiral center formed through the addition of the thioc or dithioc acid to the double bond of ketene acetals. The overall yield as an inseparable mixture of the possible regioisomeric adducts is generally good. The 1H -NMR spectrum of these adducts shown only one set of signals. Also, the semi-empirical calculation made by Suwinski group to compare between the energy barriers for the six derivatives of ketene acetals containing heteroatoms (oxazole, thiazole, and pyrazole nuclei) by MOPAC2000 calculation, they found that the reactivity of the three types of nuclei is on the following order thiazole > oxazole > pyrazole.



Treatment of 2-(1-acetyl-2-oxopropylidene)spiro[1,3]thiazine derivatives **13a**, **17d**, and **18d** with malononitrile in refluxing ethanol containing piperidine for about 2 h, where dispiro heterocycles **21–23**, were precipitated. The reaction pathway was assumed to follow a preliminary hydrolysis of one of the two acetyl groups followed by a nucleophilic addition malononitrile at the ethylenic bond with subsequent cyclization (cf. Scheme 3).

The IR and 1H NMR data of all dispiro derivatives **21–23** are in accordance with its structure, where showed the following absorption bands in its ir spectrum, 3450, 3350, 3210 cm^{-1} for 2 NH_2 , 2220, 2210 cm^{-1} for 2CN groups and absence of the characteristic bands of $C=O$ from the starting materials **13b**, **17b**, and **18b** referring to the deacylation and cyclization. The 1H NMR displays four signals appeared as broad bands between δ 6.50–6.30 (2H, NH_2), δ 6.00–5.80 (2H, NH_2), singlets at δ 5.20 (1H, $=CH$) for the ethylenic hydrogen of γ -pyrane ring



SCHEME 3

and singlets at δ 2.10 (3H, CH₃) for methyl groups. The olefinic signal was located at δ 5.20 (1H, =CH), its high-field position points to *E*-configuration around the chiral atom bearing the pyrane ring²⁷ (cf. Tables I and II).

The deacylation of one of the acetyl groups for ketene-acetals using methanol and a catalytic amount of sodium methoxide were reported by Huang et al.²⁸ Also, we reported in a previous work²³ the synthesis of spiro compounds using ketoketene-acetals and active methylene in one-pot reaction and we provide the reaction experimentally in two step reactions where, hydrolysis of one of the two acetyl group using ethanol/piperidine or methanol/MeONa which was separated and allowed to react with the active methylene in the second step to give the same products.

EXPERIMENTAL

All melting points were determined on a Gallenkamp apparatus and were uncorrected. IR spectra were recorded on a Nicolet 710 FT-IR spectrophotometer using the KBr disc technique. ¹H NMR spectra were measured on a Varian EM 360L, 60 MHz NMR

spectrometer in a suitable deuterated solvent, using TMS as internal standard. Elemental analyses were performed on a Perkin-Elmer 240 C microanalyzer.

Synthesis of Spiro(4-amino-5-cyano-2-ylidene[1,3]dithiin 6:1' Cycloalkanes) 3a,b, 4a,b, Spiro(4-amino-5-cyano-2-ylidene[1,3]dithiin 6:2' Azolidines) 5a,b–7a,b, Spiro(4-amino-5-cyano-2-ylidene[1,3]dithiin 6:2' Bezazoles) 8a,b–10a,b and Spiro(4-amino-5-cyano-2-ylidene[1,3]dithiin 6:3' Imidazoline-2'-ones) 11a,b

General Procedure

An equimolar mixture (0.05 mmol) of malononitrile or acetylacetone and carbon disulfide, tetrabutyl ammonium bromide (TBAB) (0.5 mmol) in 70 ml dioxane was treated with anhydrous K_2CO_3 (7.0 g). The reaction mixture was stirred for 2 h at room temperature. The formed dianionic ambident compounds **1a,b** were then treated with one of the following ylidene malononitriles (0.05 mol), e.g., cyclopentylidene-, cyclohexylidene-, 2-oxazolylidene-, 2-(2,3-dihydrobenzo[d]oxazolylidene-, 2-thiazolylidene-, 2-(2,3-dihydrobenzo[d]thiazolylidene-, 2-perhydro-2-imidazolylidene-, 2-(2,3-dihydro-1H-benzo[d]imidazolylidene- and 2-(2-oxo-2,3-dihydro-1H-3-indolylidene-malononitrile. The reaction mixture was stirred at 70°C for 4 h, filtered, and the solid potassium carbonate layer was dissolved in water and filtered. The filtrate was acidified with acetic acid and the separated solid was crystallized from the appropriate solvent to give compounds **5a,b–11a,b**. The organic layer was evaporated *in vacuo* and the residue was treated with water, filtered and crystallized from the appropriate solvent to give compounds **3a,b** and **4a,b**.

Synthesis of Spiro(4-amino-5-cyano-2-ylidene[1,3]-thiazine 6:1' Cycloalkanes) 3a,b, 4a,b, Spiro(4-amino-5-cyano-2-ylidene[1,3]thiazine 6:2' Azolidines) 5a,b–7a,b, Spiro(4-amino-5-cyano-2-ylidene[1,3]thiazine 6:2' Bezazoles) 8a,b–10a,b and Spiro(4-amino-5-cyano-2-ylidene[1,3]thiazine 6:3' Imidazoline-2'-ones) 11a,b

General Procedure

An equimolar mixture (0.05 mmol) of malononitrile or acetylacetone and phenyl isothiocyanate PhNCS, tetrabutylammonium bromide (TBAB) (0.5 mmol) in 70 ml dioxane was treated with anhydrous K_2CO_3 (7.0 g). The reaction mixture was stirred for 2 h at room temperature. The formed dianionic ambident compounds **2a,b** were then

treated with one of the following ylidenemalononitriles (0.05 mmol), e.g., cyclopentylidene-, cyclohexylidene-, 2-oxazolylidene-, 2-(2,3-dihydrobenzo[d]oxazolylidene-, 2-thiazolylidene-, 2-(2,3-dihydrobenzo[d]thiazolylidene-, 2-perhydro-2-imidazolylidene-, 2-(2,3-dihydro-1H-benzo[d]imidazolylidene- and 2-(2-oxo-2,3-dihydro-1H-3-indolylidene-malononitrile. The reaction mixture was stirred at 70°C for 4 h, filtered, and the solid potassium carbonate layer was dissolved in water and filtered. The filtrate was acidified with acetic acid and the separated solid was crystallized from the appropriate solvent to give compounds **14a,b–20a,b**. The organic layer was evaporated in vacuo and the residue was treated with water, filtered and crystallized from the appropriate solvent to give compounds **12a,b** and **13a,b**.

Synthesis of Dispiro(4,2'-diamino-5,3'-dicyano-6'-methyl-5-phenylpyrane 4':2 [1,3]thiazine 6:1'' Cyclohexane) 21, Dispiro (4,2'-Diamino-5,3'-dicyano-6'-methyl-5-phenylpyrane 4':2 [1,3]thiazine 6:2'' benzoxazole) 22 and Dispiro(4,2'-diamino-5,3'-dicyano-6'-methyl-5-phenylpyrane 4':2 [1,3]thiazine 6:2'' benzthiazole) 23

General Procedure

Malononitrile (0.01 mmol, 0.66 g) and piperidine (1 ml) were added to a stirred suspension of the appropriate spiro[4-amino-2-(1-acetyl-2-oxopropylidene)-5-cyano-3-phenyl[1,3]thiazine 6:1' cyclohexane] **13b** or spiro[4-amino-2-(1-acetyl-2-oxopropylidene)-5-cyano-3-phenyl[1,3]thiazine 6:2' benzoxazole] **17b** or spiro[4-amino-2-(1-acetyl-2-oxopropylidene)-5-cyano-3-phenyl[1,3]thiazine 6:2' benzthiazole] **18b** (0.01 mmol) in (40 ml). The reaction mixture was heated at reflux for 2 h and left to cool. The resulting solid was collected by filtration and recrystallized from the appropriate solvent to give compounds **21** or **22** or **23** respectively.

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