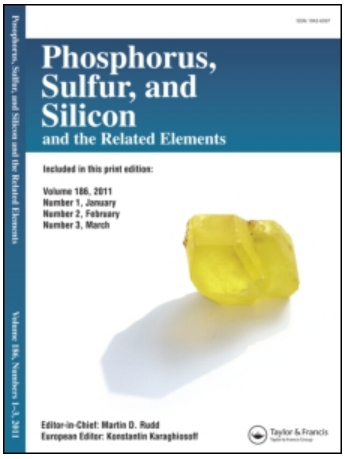

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SYNTHESIS, REACTIONS AND SPECTRAL PROPERTIES OF 3-CHLORO-2,6-DIARYLTETRAHYDRO-4*H*-THIOPYRAN-4-ONES

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SYNTHESIS, REACTIONS AND SPECTRAL PROPERTIES OF 3-CHLORO-2,6-DIARYLTETRAHYDRO-4*H*-THIOPYRAN-4-ONES

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cis-3-Chloro-2,6-diaryltetrahydro-4*H*-thiopyran-4-ones have been synthesised in moderate yields from the addition of hydrogen sulfide to 2-chloro-diarylideneacetone. Their derivatives, sulfones, oximes, sulfone oximes, hydrazones and azines have been prepared. The structure of the above compounds was identified from their spectral characteristics.

Key words: Mass spectra, IR spectra, NMR spectra, sulfones, sulfoxides.

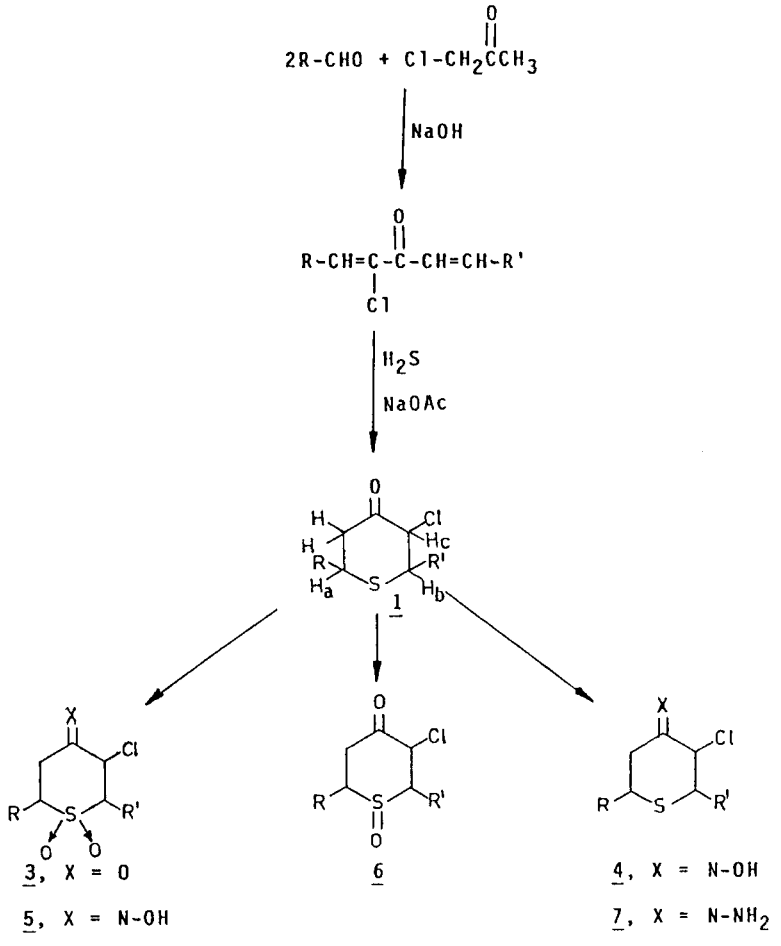
Tetrahydro-4*H*-thiopyran-4-ones and their substituted products are of considerable theoretical interest as well as practical use as precursors of the difficultly available 4*H*-thiopyran-4-ones.[1,2] These are of great importance as intermediates in the synthesis of pyrylium dyes[3] and biologically active compounds.[4]

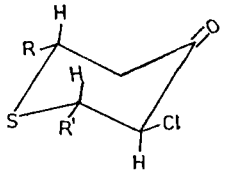
In the course of synthesizing new substituted tetrahydro-4*H*-thiopyran-4-ones, *cis*-3-chloro-2,6-diaryltetrahydro-4*H*-thiopyran-4-ones have been prepared. As described earlier 2,6-diaryltetrahydro-4*H*-thiopyran-4-ones were generally synthesized from the addition of hydrogen sulfide to diarylideneacetone.[5] Similarly, *cis*-3-chloro-2,6-diphenyl-**1a**, *cis*-3-chloro-2-phenyl-6-*p*-tolyl-**1b**, and *cis*-3-chloro-2,6-di-*p*-tolyl-**1c** tetrahydro-4*H*-thiopyran-4-ones were formed from the addition of hydrogen sulfide to 2-chloro-dibenzylideneacetone, 2-chloro-benzylidene-*p*-tolylideneacetone, and 2-chloro-di-*p*-tolylideneacetone, respectively, which were prepared from the condensation of the corresponding substituted aldehydes and chloroacetone (Scheme I).

Generally, six-membered heterocyclic rings are known to be mostly in the chair conformation.[6] Sulfur heterocycles also demonstrate the chair conformation for the heterocyclic ring from their conformational studies.[7] Assuming a chair conformation for the 3-chlorotetrahydro-4*H*-thiopyran ring the two aryl groups in 2,6-diaryl derivatives as well as the chlorine substitutent may be expected to occupy the less hindered equatorial positions as shown in **2** (Scheme I).

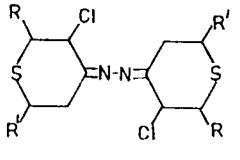
The infrared spectra of **1a–c** (Table I) showed a strong carbonyl absorption at 1705–1728 cm^{-1}. Their ^1H NMR spectra clearly indicates that these compounds are present as *cis* isomers (Table II). The methylene protons on C-5 appeared as a multiplet at δ 2.82-3.20 and the benzylic proton on C-6 as a double of doublets at δ 4.00–4.38 ($J_{6,5ax}$ = 12.1–13.8 Hz; $J_{6,5eq}$ = 2.2–4.2 Hz). The benzylic proton on C-2 appeared as a doublet at δ 3.98–4.42 ($J_{2,3ax}$ = 11.9–14.0 Hz). These ^1H NMR data (Table II) demonstrate the equatorial conformation[8,9] of the diaryl groups and the chlorine substituent in the C-3 position, as shown in **2** (Scheme I).

Further weight was added to the structure of 3-chlorotetrahydrothiopyranes **1a–c** through the study of their electron impact mass spectra. These compounds gave a





2



7b, c

	R	R'
a,	C_6H_5	C_6H_5
b,	C_6H_5	p-$CH_3C_6H_4$
c,	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$

SCHEME I

TABLE I

Infrared spectral data (cm^{-1}) of *cis*-3-chloro-2,6-diaryl-tetrahydro-4*H*-thiopyran-4-ones and their derivatives

	CO	SO_2	SO	C=N	OH
1_a	1718				
1_b	1728				
1_c	1705				
3_a		1138,1318,1340			
3_b		1130,1322,1332			
3_c		1132,1316,1330			
4_a				1618	3318
4_b				1610	3220
4_c				1642	3384
5_a		1140,1312,1344		1628	3380
5_b		1152,1318,1346		1658	3435
5_c		1150,1324,1340		1636	3400
6_a	1708		1040		
6_b	1722		1062		
6_c	1730		1068		

moderately intense molecular ion peak followed by chlorine lost and subsequent fragmentations characteristic of 2,6-diaryl tetrahydrothiopyranes.[10] (c.f. Experimental).

Oxidation of 3-chlorotetrahydrothiopyranes **1a–c** with hydrogen peroxide gave the respective sulfones **3a–c**. The reaction of 3-chlorotetrahydrothiopyranes **1a–c** as well as the sulfones **3a–c** with hydroxylamine hydrochloride gave the corresponding oximes **4a–c** and sulfone oximes **5a–c**, respectively (Scheme I). The infrared spectra of the oximes **4** and sulfone oximes **5** (Table I) showed C=N absorptions at 1610–1658 cm^{-1} as well as a broad hydroxyl absorptions at 3220–3435 cm^{-1}. Moreover, the sulfones **3** and **5** showed three bands in the ranges 1130–1152, 1312–1324 and 1330–1346 cm^{-1} characteristic for the SO_2 group.

The ^1H NMR spectra (Table II) of the oximes **4** was almost similar to the ^1H NMR spectra of the parent chlorotetrahydrothiopyranes **1** except for the up field shift in the resonance of the C-3 and C-5 protons. Moreover, an exchangeable OH proton was observed at δ 7.98–8.62. On the other hand, the ^1H NMR spectra of the sulfones **3** and the sulfone oximes **5** showed beside other characteristic (Table II) a down field shift in the resonance of C-2 and C-6 protons (δ 4.62–4.86) relative to the parent chlorotetrahydrothiopyranes due to the deshielding effect of the sulfone group.

Further confirmation of the structure of the sulfones, oximes and sulfone oximes was obtained by study of their electron impact mass spectra. The fragmentation patterns were similar to the parent compounds. However, it is observed that for the sulfones **3** and sulfone oximes **5**, no molecular ion peaks were detected, the highest

TABLE II

^{1}H NMR spectra (δ) of 3-chloro-2,6-diaryltetrahydro-4*H*-thiopyran-4-ones and their derivatives in $CDCl_3$ (**a**)

	CH_2 (m)	CH_a (dd)	CH_b (d)	CH_c (d)	Ar-H (m)	Others
1_a	2.88	4.20	3.98	4.46	7.36	
1_b	3.20	4.00	4.42	4.52	7.16	2.36 (s, CH_3)
1_c	2.82	4.38	4.22	4.42	7.22	2.34 (s, 2 CH_3)
3_a	3.62	4.60	4.66	4.82	7.21	
3_b	3.60	4.62	4.82	4.64	7.26	2.38 (s, CH_3)
3_c	3.76	4.74	4.86	4.72	7.18	2.36 (s, 2 CH_3)
4_a	2.62	3.88	3.80	4.02	7.28	8.32 (s, 2 OH)*
4_b	2.76	3.92	3.92	4.22	7.32	2.36 (s, CH_3), 8.62 (s, OH)*
4_c	2.70	4.20	4.00	4.12	7.18	2.40 (s, 2 CH_3), 7.98 (s, OH)*
5_a	3.10	4.62	4.68	4.26	7.22	11.38 (s, OH)*
5_b	3.22	4.74	4.86	4.32	7.36	2.38 (s, CH_3), 11.22 (s, OH)*
5_c	3.12	4.66	4.72	4.28	7.18	2.32 (s, 2 CH_3), 11.06 (s, OH)*
6_a	2.62	4.12	4.22	4.40	7.22	
6_b	2.70	4.02	4.32	4.44	7.28	2.30 (s, CH_3)
6_c	2.78	4.19	4.30	4.62	7.36	2.34 (s, 2 CH_3)
7_a	2.82	4.00	4.20	4.26	7.24	4.96 (s, NH_2)*

* Exchangeable with D_2O.

mass peak always corresponding to elimination of sulfur dioxide molecule from the molecular ion (M-SO_2).

On the other hand, oxidation of *cis*-3-chlorotetrahydrothiopyran-4-ones **1a–c** with bromine water gave the corresponding sulfoxides **6a–c** (Scheme I). The structure of these sulfoxides was determined by studying their spectral characteristics in addition to their elemental analyses (Tables I–III).

The reaction of 3-chloro-2,6-diphenyltetrahydro-4*H*-thiopyran-4-one **1a** with hydrazine hydrate gave the corresponding hydrazone **7a**. The reaction of 3-chlorotetrahydrothiopyranes **1b,c** with hydrazine hydrate afforded the respective azines **7b,c**. The ^{1}H NMR spectra of the azines **7b,c** displayed a similar pattern of ^{1}H NMR spectra of the parent chlorotetrahydrothiopyranes **1b,c**. The electron impact mass spectra of the azines **7b,c** showed a strong molecular ion peak followed by N—N bond fission (M/2) confirming their azine structure.

EXPERIMENTAL

Microanalyses were performed by the Microanalytical Unit, Cairo University, Cairo. Infrared spectra were measured with a Unicam SP 1025 spectrophotometer for potassium bromide pellets. The ^{1}H NMR spectra were recorded on a Varian EM-390 MHz and a Bruker 270 MHz spectrometers using TMS as internal standard. Mass spectra were recorded at 70 eV with an AEI MS-9 spectrometer coupled to a

TABLE III

Analytical data of *cis*-3-chloro-2,6-diaryltetrahydro-4*H*-thiopyran-4-ones and their derivatives

Compd.	mp (°C)	Yield (%)	Molecular formula	Analysis Calcd (Found)				
				C	H	N	S	X
1a	126	52	$C_{17}H_{15}ClOS$	67.4 (67.2	5.0 4.95		10.6 10.9	11.7 11.6)
1b	138	71	$C_{18}H_{17}ClOS$	68.2 (68.0	5.4 5.1		10.1 10.3	11.2 11.3)
1c	152	70	$C_{19}H_{19}ClOS$	69.0 (69.1	5.8 5.6		9.7 9.5	10.7 10.9)
3a	186	61	$C_{17}H_{15}ClO_3S$	61.0 (60.8	4.5 4.7		9.6 9.4	10.6 10.9)
3b	211	68	$C_{18}H_{17}ClO_3S$	62.0 (62.2	4.9 4.7		9.1 9.2	10.2 10.2)
3c	226	72	$C_{19}H_{19}ClO_3S$	62.9 (62.6	5.2 5.1		8.8 8.9	9.8 10.0)
4a	196	63	$C_{17}H_{16}NClOS$	64.3 (64.1	5.0 5.3	4.4 4.2	10.1 10.3	11.2 11.5)
4b	202	58	$C_{18}H_{18}NClOS$	65.2 (65.3	5.4 5.3	4.2 4.4	9.7 9.6	10.7 10.5)
4c	181	66	$C_{19}H_{20}NClOS$	66.0 (65.8	5.8 5.6	4.1 4.3	9.3 9.5	10.3 10.1)
5a	242	52	$C_{17}H_{16}NClO_3S$	58.4 (58.2	4.6 4.4	4.0 4.2	9.2 9.5	10.2 10.0)
5b	218	58	$C_{18}H_{18}NClO_3S$	59.4 (59.2	5.0 5.3	3.9 3.7	8.8 8.6	9.8 9.9)
5c	268	61	$C_{19}H_{20}NClO_3S$	60.4 (60.1	5.3 5.2	3.7 3.6	8.5 8.7	9.4 9.3)
6a	212	66	$C_{17}H_{17}N_2ClS$	64.5 (64.7	5.4 5.3	8.8 8.6	10.1 10.2	11.2 11.4)
7c	278	53	$C_{38}H_{38}N_2Cl_2S_2$	69.4 (69.1	5.8 5.6	4.3 4.2	9.7 9.7	10.8 10.9)

DS-50 Data system using a direct insertion probe for introduction of samples. Melting points were determined on a Kofler Block and are uncorrected.

2-Chlorodiarylideneactone

To a cold solution of sodium hydroxide (25 g) in water (250 ml) and ethanol (200 ml), one-half of previously prepared mixture of pure aldehyde (0.25 mol) and chloroacetone (0.12 mol) was added. Aflocculent precipitate forms in 2–3 minutes. After 15 minutes the remainder of aldehyde chloroacetone mixture was added. The stirring is continued for a further 30 minutes. The precipitated 2-chlorodiarylideneacetone (71–79% yield) was filtered and washed with water and crystallized from ethanol as yellow needles. IR (cm^{-1}) 1625–1638 (CO); ^{1}HNMR(δ) 7.32–7.98 (m, Ar), 6.56–6.62 (d, 1H) 6.22–6.36 (s, 1H), 5.62–5.88 (d, 1H).

3-Chloro-2,6-diaryltetrahydro-4H-thiopyran-4-ones **1a–e** *(Tables I–III)*

A solution of 2-chlorodiarylideneacetone (0.18 mol) and fused sodium acetate (0.50 mol) in 95% aqueous ethyl alcohol (400 ml) was refluxed for five hours under a stream of hydrogen sulfide gas. The reaction mixture was treated as described earlier[5] and crystallized from benzene-petroleum ether (b.p. 40–60°C) as pale yellow needles. MS: m/z (relative abundance) **1a**: 304 (13), 302 (31), 267 (18), 266 (21), 238

(8), 236 (19), 134 (100), 102 (29), 77 (16); **1b**: 318 (6), 316 (21), 281 (16), 280 (24), 252 (11), 250 (16), 148 (14), 134 (18), 116 (100), 102 (19), 92 (16), 91 (24), 77 (16).

3-Chloro-2,6-diaryltetrahydro-4H-thiopyran-4-one sulfones **3a–c** *(Tables I–III)*

A solution of 2,6-diaryltetrahydro-4*H*-thiopyran-4-ones **1a–c** (0.0018 mol) in glacial acetic acid (10 ml) was kept at room temperature with hydrogen peroxide (30%, 9 ml) for 24 hours. The reaction mixture was treated as described earlier[5] and crystallized from ethanol as colorless needles. MS: m/z (relative abundance) **3a**: ($M^+ - SO_2$) 272 (15), 270 (43), 235 (71), 164 (22), 146 (16), 136 (12), 131 (12), 104 (11), 92 (100), 78 (10); **3b**: ($M^+ - SO_2$) 286 (12), 284 (30), 249 (69), 178 (32), 160 (21), 164 (14), 150 (18), 145 (20), 92 (16), 91 (100).

3-Chloro-2,6-diaryltetrahydro-4H-thiopyran-4-one oximes **4a–c** *and sulfone oximes* **5a–c** *(Tables I–III)*

A solution of 3-chloro-2,6-diaryltetrahydro-4*H*-thiopyran-4-ones **1a–c** or their sulfones **3a–c** (0.0019 mol) in ethanol (30 ml) was refluxed with hydroxylamine hydrochloride (0.0054 mol) and sodium acetate (0.0054 mol) in water (2 ml) for 2–3 hours. The reaction mixture was treated as described earlier[5] to give **4a–c** or **5a–c** which crystallized from benzene-petroleum ether (b.p. 50–70°C) as colorless needles.

3-Chloro-2,6-diaryltetrahydro-4H-thiopyran-4-one sulfoxides **6a–c** *(Tables I–III)*

A solution of 3-chlorotetrahydrothiopyranes **1a–c** (0.0036 mol) in ether (20 ml) was shaken well with bromine water (20 ml, 0.62 g). The ethereal solution after washing with water, drying (Na_2SO_4) and evaporation gave the sulfoxides **6a–c** which crystallized from methanol as pale yellow needles.

3-Chloro-2,6-diphenyltetrahydro-4H-thiopyran-4-one-hydrazone **7a** *and azines* **7b,c**

A solution of 3-chloro-tetrahydro-4*H*-thiopyran-4-ones **1a–c** (0.0036 mol) in ethanol (15 ml) and 99% hydrazine hydrate (2 ml, 0.04 mol) was kept at room temperature for 24 hours. The reaction mixture was treated as described earlier[5] to give the hydrazone **7a** and azines **7b,c** which crystallized from ethanol as needles. MS: m/z (relative abundance) **7c**: M^+ 660 (8), 658 (14), 656 (26), 1/2 M^+ 330 (32), 328 (100).

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