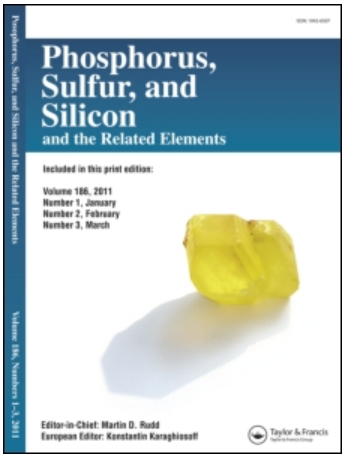


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

MODERN FRIEDEL-CRAFTS CHEMISTRY.XI. CYCLIZATION OF ARYL HALOALKYL SULFONES, ARYLSULFONYLACYL CHLORIDES AND THEIR CORRESPONDING SULFIDES

Aboel-Magd A. Abdel-wahab[a]; Ahmed M. El-khawaga[a]; Maher F. El-zohry[a]; Ali A. Khalaf[a]
[a] Chemistry Department, Faculty of Science, Assist University, Assiut, Egypt

To cite this Article Abdel-wahab, Aboel-Magd A. , El-khawaga, Ahmed M. , El-zohry, Maher F. and Khalaf, Ali A.(1984) 'MODERN FRIEDEL-CRAFTS CHEMISTRY.XI. CYCLIZATION OF ARYL HALOALKYL SULFONES, ARYLSULFONYLACYL CHLORIDES AND THEIR CORRESPONDING SULFIDES', Phosphorus, Sulfur, and Silicon and the Related Elements, 19: 1, 31 — 44
To link to this Article: DOI: 10.1080/03086648408077562
URL: http://dx.doi.org/10.1080/03086648408077562

Phosphorus and Sulfur, 1984, Vol. 19, pp. 31–44
0308-664X/84/1901-0031/$18.50/0

MODERN FRIEDEL–CRAFTS CHEMISTRY. XI. CYCLIZATION OF ARYL HALOALKYL SULFONES, ARYLSULFONYLACYL CHLORIDES AND THEIR CORRESPONDING SULFIDES

ABOEL-MAGD A. ABDEL-WAHAB, AHMED M. EL-KHAWAGA, MAHER F. EL-ZOHRY and ALI A. KHALAF

Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt

(*Received April 4, 1983*)

The sulfone group deactivation for cyclialkylation and cycliacylation reactions in the presence of Friedel–Crafts catalysts was demonstrated in a number of aryl chloroalkylsulfones (**1–8**) and arylsulfonylacyl chlorides (**17a–22a**), respectively. As expected, the corresponding arylchloralkyl sulfides (**9–16**) and arylmercaptoacyl chlorides (**13a–28a**) underwent ring-closure reaction in most cases under the same conditions. The ease of cyclization was governed by the ring size, the stability of the attacking carbocation and the nucleophilicity of the aryl moiety. Also, the behaviour of benzyl sulfones (**29**, **31a**, and **32a**) and sulfides (**33**, **34a** and **36a**) was inconsistent. Noteworthy, the Friedel–Crafts cyclization reaction is thus considered an accessible method for the synthesis of compounds **37–41** and **45**, **51**.

During the last twenty years, Khalaf, Roberts and their coworkers[1–8] published numerous studies on the cyclialkylation and cycliacylation of different classes of organic compounds under the influence of Friedel–Crafts catalysts. One of these studies was aimed essentially at the clarification of the discrepancies and the claims concerning the cyclization of systems deactivated by carbonyl group.[8] On the basis of this study, it was concluded that cyclization of ketones in which the deactivating carbonyl group was directly attached to or conjugated with the aromatic nucleus, at which ring closure is expected to occur, is practically impossible. This conclusion, in addition to our interest in sulfur chemistry,[9,10] prompted us to investigate the cyclialkylation and the cycliacylation reactions on molecules deactivated by groups other than carbonyl group such as sulfone group. For this purpose, a number of aryl haloalkyl sulfones (**1–8**) and arylsulfonylacyl chlorides (**17–22**) were prepared and subjected to Friedel–Crafts conditions as with aryl haloalkyl ketones.[11,12] For comparison, the corresponding aryl haloalkyl sulfides (**9–16**) and arylmercaptoacyl chlorides (**23–28**) were also subjected to reaction under similar conditions.

The desired sulfur compounds were prepared essentially by known literature procedures. Their identities were confirmed by elemental and spectroscopic analysis as well as by comparison with reported literature data (Table I). The cyclization of the compounds of Table I were attempted under various conditions. With reference to Table II, attempted cyclization of phenyl 2-chloroethyl sulfone (**1**), *p*-tolyl 2-chloroethylsulfone (**2**), *p*-chlorophenyl 2-chloroethyl sulfone (**3**), β-naphthyl 2-chloroethyl sulfone (**4**), phenyl 3-chloropropyl sulfone (**6**), *p*-tolyl 3-chloropropyl sulfone (**7**) and *p*-chlorophenyl 3-chloropropyl sulfone (**8**) with $AlCl_3$ in CS_2 at 25°C or at 50°C, $AlCl_3/H_2SO_4$ at 25–90°C or with H_2SO_4 at 90° failed to occur and the starting sulfones were mostly recovered unchanged (85–95%, Table III). Only in the case of the tertiary halosulfone **5** some of *p*-tolyl isobutyl sulfone was formed by

TABLE I

Preparation of starting aryl chloroalkyl sulfones and sulfides and arylsulfonyl- and arylmercaptocarboxylic acids

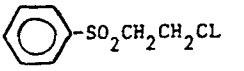
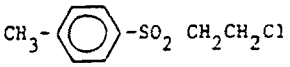
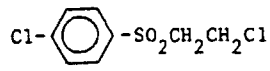
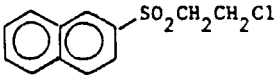
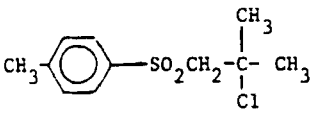
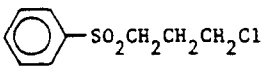
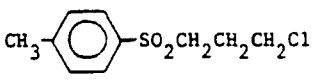
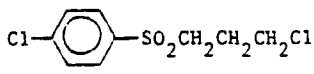
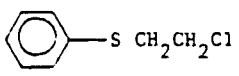
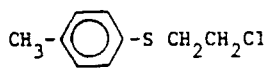
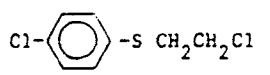
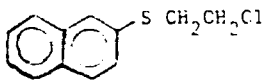
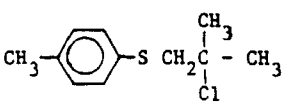
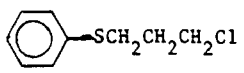
Compound no.	Structural formula	Yield %	M.P. °C (b.p.)	Lit. M.P. °C (b.p)	Ref.
1		85	91	92	21
2		95	70	71	22
3		94	95	96	23
4		60	100	100	23
5		88	(145°C/0.01 mm) 14	(146°C/0.01 mm)	24
6		77	26	26	21
7		78	76	77	21
8		82	68	68	22
9		86	(120°C/15 mm)	(120°C/15 mm)	25
10		75	(140°C/17 mm)	(139–140/17 mm)	26
11		71	33	34	21
12		80	61	62	21
13		68	(93°C/0.01 mm)	(92°C/0.01 mm)	24
14		86	(150°C/16 mm)	(137/13 mm)	27

TABLE I (*Continued*)

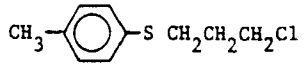
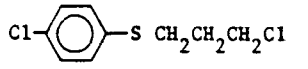
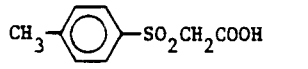
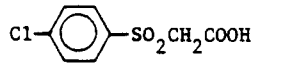
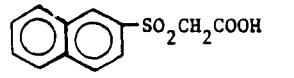
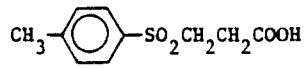
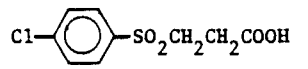
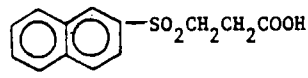
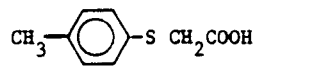
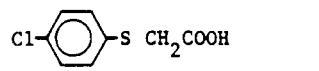
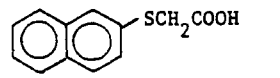
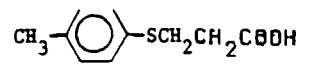
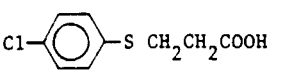
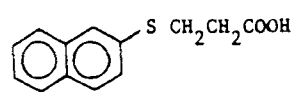
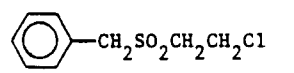
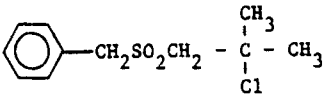
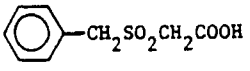
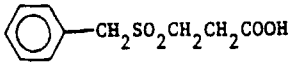
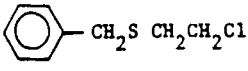
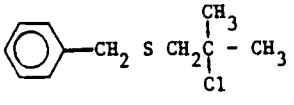
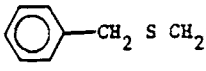
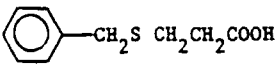
Compound no.	Structural formula	Yield %	M.P. °C (b.p.)	Lit. M.P. °C (b.p)	Ref.
15		94	(119°C/2 mm)	(118°C/2 mm)	28
16		81	(125°C/0.1 mm)	(124°C/0.1 mm)	29
17		75	164	166	30
18		72	138	139	31
19		65	120	104	32
20		73	199	200	30
21		72	142	142–143	31
22		61	135	137	32
23		91	90–91	92	33
24		90	103–105	104	34
25		91	90	89–91	35
26		91	68–69	70	36
27		90	90°C	90–91°C	37
28		94	103	104–105	38
29		78	56	58	39

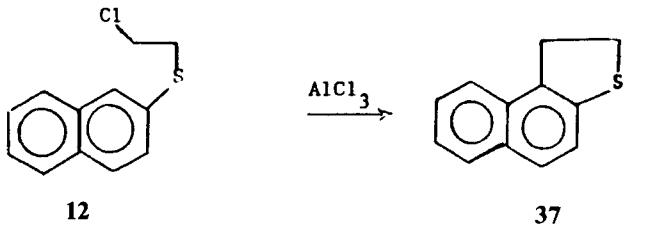
TABLE I (*Continued*)

Compound no.	Structural formula	Yield %	M.P. °C (b.p.)	Lit. M.P. °C (b.p)	Ref.
30		87	16	—	—
31		90	139	140	40
32		78	178	177	41
33		77	(115°C/6 mm)	(114°C/6 mm)	39
34		68	(130°C/4 mm)	—	—
35		93	61	62–63	42
36		88	81	82	41

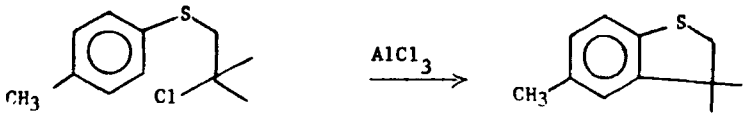
[a]All these compounds (**1–36**) gave correct elemental analysis for C, H, S and halogen.

hydride exchange[13] mechanism (Table II). As with aryl haloalkyl ketones, the failure to effect the closure of sulfones **1–8** is undoubtedly due to the stronger sulfone deactivation.[14] Accordingly, we examined the cyclization behaviour of the corresponding sulfides (**9–16**) and also the benzyl haloalkyl sulfones (**29** and **30**) in which such conjugative sulfone deactivation was eliminated. As expected, most sulfides underwent cyclization to the corresponding cyclic sulfides (Entries 1–6, Table II). However, the ease of closure depended upon factors such as ring size, stability of attacking carbocation and nucleophilicity of the aryl moiety. For example, whereas sulfides **9**, **10**, and **11** failed to undergo 5-membered ring closures to the corresponding benzothiophenes, β-naphthyl 2-chloroethyl (**12**) gave, but to a small extent, 1,2-dihydronaphtho [2,1-b]thiophene (**38**, 11%). This is due to the reactivity of the naphthyl group as compared with *p*-chlorophenyl in **11**, phenyl in **9** to *p*-tolyl in **10**. Also, the facile closure of the tertiary chloroalkyl *p*-tolylsulfide (**13**) to 2,3-dihydro-3,3,5-trimethylbenzothiophene (**38**, 88%) is the result of the stability of the intermediate tertiary carbocation. The failure to cyclize sulfides **9**, **10** and **11** may be due to the known difficulty of primary closure to 5-membered ring.

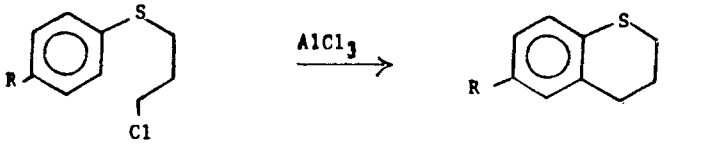
The results of Table II, in the light of the recent work of Khalaf and Roberts,[2–7,13,15–18] indicates great similarities between the behaviour of aryl haloalkyl sulfides and the structurally related arylhaloalkanes.



12 37



13 38



R = H (14)
= CH_3 (15)
= Cl (16)

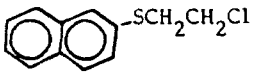
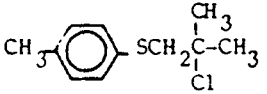
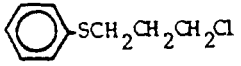
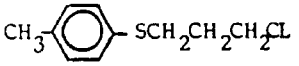
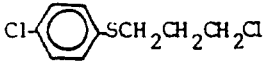
R = H (39)
= CH_3 (40)
= Cl (41)

As in cyclialkylation reactions, cycliacylation reactions have been shown to be retarded by carbonyl deactivation.[8] This part of the work was carried out to investigate the deactivation effect of the sulfone group on the ring closures of arylsulfonylacyl chlorides. Accordingly, arylsulfonylcarboxylic acid (**17–22**) were preapred (Table **I**) and the corresponding arylsulfonylacyl chlorides (**17a–22a**) were subjected to one or more different Friedel–Crafts conditions. As evident from Table III, attempts to cyclize **17a–21a** in the presence of $AlCl_3$ in CS_2 at room or reflux temperatures were unsuccessful and the corresponding acids (**17–21**) were recovered (Table III). However, because of naphthyl group compound **22a** underwent closure to 5,6-benzothiochromanone-*S*,*S*-dioxide (**42**) to the extent 33% upon treatment with $AlCl_3$ in CS_2 at reflux temperature. Also, in the presence of strong $AlCl_3/H_2SO_4$ catalyst **20a** and **21a** underwent 6-membered ring acylation to 6-methyl thiochromanone-*S*,*S*-dioxide (**43**, 20%) and 6-chlorothiochromanone-*S*,*S*-dioxide (**44**, 17%), respectively (Entries 12, 15, Table III).

On the contrary to sulfones (**17a–22a**) the corresponding sulfides (**23a–28a**) were successfully cyclized. For example, **23a**, **24a**, **26a**, **27a**, and **28a** gave upon treatment with $AlCl_3$ catalyst 2,3-dihydro-3-keto-5-methylbenzothiophene (**45**, 40%), 2,3-dihydro-3-keto-5-chlorobenzothiophene (**46**, 42%), 6-methylthiochromanone (**47**, 89%), 6-chlorothiochromanone (**48**, 85%) and 5,6-benzothiochromanone (**49**, 93%), respectively. The only exception is the case of **25a** which gave only black polymer (Entries 18–26, Table III).

TABLE II

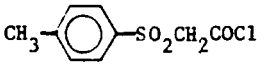
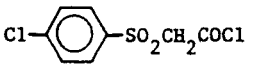
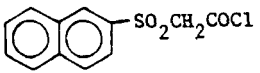
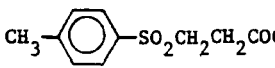
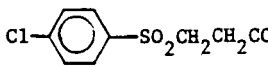
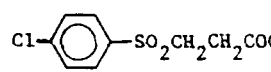
Reactions of aryl haloalkyl sulfones and sulfides with Friedel–Crafts catalysts[a]

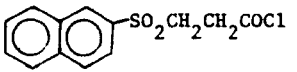
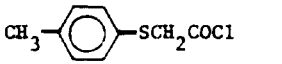
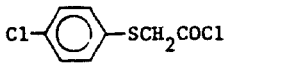
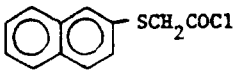
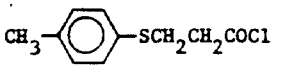
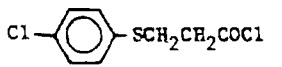
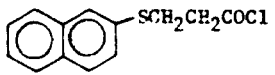
Entry no.	Starting material	Reaction Conditions				Product composition (%)
		Catalyst	Solvent	Temp. °C	Time h	
1		$AlCl_3$	CS_2	Reflux	3	1,2-Dihydronaphtho[2,1-b]thiophene (11), ethyl 2-naphthyl sulfide (22) and starting material (50)
2		"	"	RT	3	2,3-Dihydro-3,3,5-trimethylbenzothiophene (64), isobutyl *p*-tolyl sulfide (36)
3	"	"	"	Reflux	3	2,3-Dihydro-3,3,5-trimethylbenzothiophene (88), isobutyl *p*-tolyl sulfide (12)
4		"	"	"	3	Thiochroman (65), phenyl *n*-propyl sulfide (20), starting material (trace)
5		"	"	"	3	6-methylthiochroman (60), *n*-propyl *p*-tolyl sulfide (15), *p*-thiocresol (10)
6		"	"	"	3	6-Chlorothiochroman (60), *n*-propyl *p*-tolyl sulfide (20), *p*-chlorothiophenol (5)

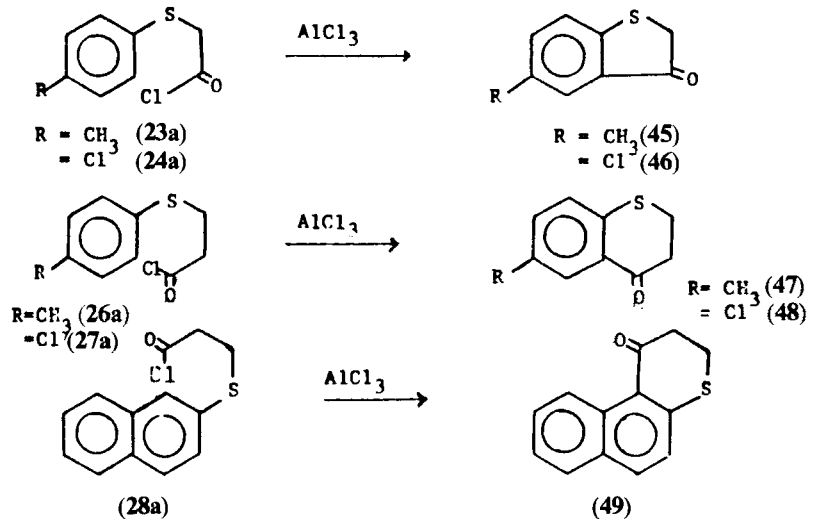
[a]Attempted cyclization of sulfones **1–8** (using Methods B, C and D), sulfides **9–12** (method B at RT and reflux temperature) and **14–16** (Method B at RT) afforded the starting materials unreacted (85%–95%). In addition, sulfone **6** and sulfides **9–11** (Method B at reflux temperature) gave also *p*-tolyl isobutyl sulfone (trace), ethyl phenyl sulfide (6%), ethyl *p*-tolyl sulfide (8%) and ethyl *p*-chlorophenyl sulfide (9%), respectively.

TABLE III

Reactions of arylsulfonyl- and arylmercaptoacyl chlorides with Friedel–Crafts catalysts

Entry no.	Starting material	Reaction Conditions: Catalyst	Solvent	Temp. °C	Time h	Product composition (%)
1		$AlCl_3$	CS_2	RT	3	*p*-Tolylsulfonylacetic acid (88)
2	"	"	"	Reflux	3	" (85)
3	"	$AlCl_3/H_2SO_4$	25–90	25–90	4	" (70) Black polymer (20)
4		$AlCl_3$	CS_2	RT	3	*p*-Chlorophenylsulfonylacetic acid (95)
5	"	"	"	Reflux	3	" (93)
6	"	$AlCl_3/H_2SO_4$	"	25–90	4	" (70) Unidentified polymer (22)
7		$AlCl_3$	"	RT	3	2-Naphthylsulfonylacetic acid (85)
8	"	"	"	Reflux	3	" (80)
9	"	$AlCl_3/H_2SO_4$	"	25–90	4	" (70) Black polymer (26)
10		$AlCl_3$	"	RT	3	*p*-Tolylsulfonylpropionic acid (85)
11	"	"	"	Reflux	3	" (80)
12	"	$AlCl_3/H_2SO_4$	"	25–90	4	" (50) 6-Methylthiochromanone-S,S-dioxide (20)
13		$AlCl_3$	"	RT	3	*p*-Chlorophenylsulfonylpropionic acid (81)
14		$AlCl_3$	CS_2	Reflux	3	*p*-Chlorophenylsulfonylpropionic acid (78)
15	"	$AlCl_3/H_2SO_4$	"	25–90	4	" (50) 6-Chlorothiochromanone-S,S-dioxide (17)

16		$AlCl_3$	"	RT	3	2-Naphthylsulfonylpropionic acid (89)
17	"	"	"	Reflux	3	" (46) 5,6-Benzothiochromanone-S,S-dioxide (33)
18		$AlCl_3/CH_3NO_2$	CS_2	RT	3	2,3-Dihydro-3-keto-5-methylbenzothiophene (40) Black polymer (40)
19	"	$AlCl_3$	"	RT	3	2,3-Dihydro-3-keto-5-methylbenzothiophene (40) Black polymer (60)
20		$AlCl_3/CH_3NO_2$	"	RT	3	2,3-Dihydro-3-keto-5-chlorobenzothiophene (42) Black polymer (46)
21	"	$AlCl_3$	"	RT	3	2,3-Dihydro-3-keto-5-chlorobenzothiophene (25) Black polymer (71)
22		$AlCl_3/CH_3NO_2$	"	RT	3	Black resinous material (90)
23	"	"	"	RT	3	" (88)
24		$AlCl_3$	"	RT	3	6-Methylthiochromanone (89)
25		"	"	RT	3	6-Chlorothiochromanone (85)
26		"	"	RT	3	5,6-Benzothiochromanone (93)



The behaviour of benzyl sulfides and sulfones was inconsistent. Whereas benzyl 2-chloro-2-methylpropyl sulfide (**34**) and benzylmercaptoacetyl chloride (**35a**) underwent cyclization to 4,4-dimethyl isothiochroman (**50**, 80%) and isothiochroman-4-one (**51**, 63%), respectively, benzyl 2-chloroethyl sulfone (**29**), benzyl 2-chloro-2-methylpropyl sulfone (**30**), benzyl 2-chloroethyl sulfide (**33**), benzylsulfonylacetyl chloride (**31a**), β-(benzylsulfonyl)propionyl chloride (**32a**) and β-(benzylmercapto)propionyl chloride (**36a**) gave only a high melting point polymeric materials. No satisfactory explanation is currently available for this inconsistency.

In conclusion, the results of this paper, beside their mechanistic importance, demonstrated that Friedel–Crafts ring closure reactions offer an accessible method for the synthesis of **37–41** and **45–51**.

EXPERIMENTAL

All melting points were uncorrected and were determined on a Kofler melting point apparatus. GLC analysis were conducted on a Pye-Unicam series 105 gas chromotograph using 5′ × 1/8″ column packed with 10% SE 30 over chromosorb at temperatures specified in each case and nitrogen flow rate 60 mL/min. Chromatographic separation was carried out also using 100 × 2 cm glass columns packed with neutral alumina or silica gel as well as 15 × 5 cm glass plates covered with thin film of silica gel. IR spectra were obtained using a Pye-Unicam SP 200 G spectrophotometer. UV spectra were recorded using Pye-Unicam SP-800 spectrophotometer. NMR spectra were carried out in $CDCl_3$ and CCl_4 using EM-360 60 Hz and EM-390 90 Hz NMR spectrophotometers.

Starting materials

Aryl chloroalkyl sulfides (**9–16, 33–34**): were prepared either by the alkylation of the thiols (thiophenol, *p*-thiocresol, *p*-chlorothiophenol, 2-mercaptonaphthalene and benzyl thiol) with chlorohydrins (ethylene-chlorohydrin, 2-hydroxy-2-methylchloropropane and 3-hydroxychloropropane) followed by reaction with thionyl chloride or by direct alkylation of thiols with dichloroalkanes (1,2-dichloroethane and 1,3-dichloropropane) as reported before.[19]

Arylmercaptocarboxylic acids (**23–28, 35–36**): were prepared similarly via alkylation of the previous thiols with 2-chloroacetic acid or with 3-chloropropionic acid.

Arylchloroalkyl sulfones (**1–8, 29–30**) and arylsulfonylcarboxylic acids (**17–22, 31–32**): Oxidation of **9–16, 33–34** and **23–28, 35–36** with hydrogen peroxide in acetic acid[20] gave the corresponding sulfones **1–8, 29–30** and **17–22, 31–32**, respectively. Results, physical properties and references are indicated in Table I.

Arylmercaptoacyl chlorides (**13a–28a, 35a–36a**) and arylsulfonylacyl chlorides (**17a–22a, 31a–32a**) were prepared after reflux of 0.2 mol of the corresponding acid in 0.22 mol thionyl chloride followed by evaporation of the excess thionyl chloride using rotatory evaporator. The product showed only one spot on TLC and correct elemental analysis.

Cyclization procedures

The cyclization behaviour of the starting materials (**1–36**) was examined through five general procedures (A, B, C, D and E) using $AlCl_3/CH_3NO_2$ at 25°C, $AlCl_3$ at 25°C at 25°C or 50°C, $AlCl_3/H_2SO_4$ 25–90°C, H_2SO_4 at 90°C and $FeCl_3$ at 25°C catalysts, respectively.

A Using $AlCl_3/CH_3NO_2$ as catalyst. A 100 ml 3-necked flask equipped with thermometer, dropping funnel, reflux condenser capped with calcium chloride tube and magnetic stirrer was charged with 0.04 mol of anhydrous $AlCl_3$, 0.04 mol of nitromethane and subsequently 50 ml of CS_2 solvent. To this mixture was added dropwise 0.01 mol of the compound to be investigated. The reaction, mixture was allowed to stir for three hours at room temperature, then decomposed with cold 5% hydrochloric acid solution. The organic layer was separated, washed with water, with 5% sodium bicarbonate solution, again with water, dried over magnesium sulfate and filtered. The solvent was distilled using rotatory evaporator and the residue was identified. In some cases a solid was precipitated after decomposition with hydrochloric acid. Therefore, the solid was filtered, washed with water, recrystallized from the proper solvent and identified. In other cases, the acidic products were extracted with 5% Na_2CO_3 solution and recovered with hydrochloric acid.

B Using $AlCl_3$ as catalyst. As in procedure A without the addition of nitromethane.

C Using $AlCl_3/H_2SO_4$ as catalyst. After stirring of a mixture of 0.02 mol of anhydrous $AlCl_3$, 50 ml CS_2 and 0.005 mol of the investigated compound for three hours at room temperature, as described before, the CS_2 solvent was removed at reduced pressure and 10 ml of conc. H_2SO_4 was added to the oily complex.

The reaction mixture was heated for one hour at 90°C while stirring cooled, diluted with water and extracted with ether. The ether extracts was treated as in Procedure A.

D Using H_2SO_4 as catalyst. To 0.005 mol of the investigated sulfone (or sulphide) there was added 10 ml of 96% H_2SO_4 over a period of 5 minutes. The reaction mixture was stirred at 90°C for one hour (became dark in colour) and decomposed by pouring onto ice. The products were separated as before.

E Using $FeCl_3$ as catalyst. The same procedure was again applied as in Method A except that $AlCl_3/CH_3NO_2$ catalyst was replaced by $FeCl_3$ catalyst. Only cyclization of **33** was attempted under these conditions.

Data concerning reaction conditions (catalyst, solvent, temperature and reaction period), yield and composition of the final products are summarized in Tables II, III and IV.

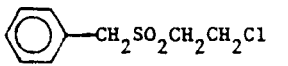
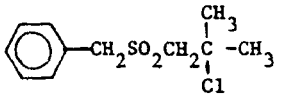
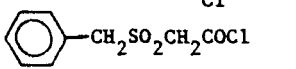
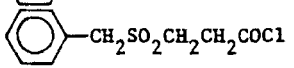
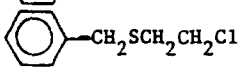
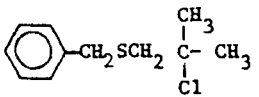
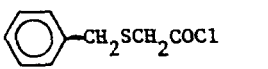
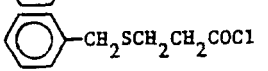
Attempted cyclialkylation of arylchloroalkyl sulfones **1–8**. The cyclialkylation of **1–8** was attempted using Methods B (at room and reflux temperatures), C and D. In all cases, the starting materials were recovered almost quantitatively as confirmed by mp, mmp, elemental analysis, GLC and spectroscopic data (85–95%, Table II). Only, attempted cyclization of **5** using Method B at reflux temperature gave in addition a trace of *p*-tolyl isobutyl sulfone, mp 78°C, mmp 79°C and lit.[43] mp 79°C.

Attempted cyclialkylation of aryl chloroalkyl sulfides (**9–11**). Treatment of **9–11** with $AlCl_3$ catalyst (Method B) at room temperature afforded the starting material unreacted (85%–95%, Table II). Using Method B at reflux temperature, GLC analysis using authentic samples showed in addition to the starting sulfide, the formation of ethyl phenyl sulfide (6%), ethyl *p*-tolyl sulfide (8%), and ethyl *p*-chlorphenyl sulfide (9%), respectively.

Attempted cyclialkylation of **12** *using Method B.* At room temperature, the starting sulfide **12** was recovered in 90%. However, application of Method B at reflux temperature and analysis of the crude product (**19**), using column chlormatogram packed with silica gel showed that the reaction products are: ethyl 2-naphthyl sulfide (22%) eluted with pet. ether–benzene mixture (4 : 1), mp, mmp 16°C, lit.[44] mp 16°C; the starting sulfide (**12**, 50%) was eluted with pet. ether–benzene mixture (1 : 1), mp, mmp, lit.[23] 62°C and 1,2-dihydronaphtho [2,1-b]thiophene (**37**, 11%) was eluted with benzene–ether mixture (4 : 1), mp 78°C (methanol), mmp 78°C and lit.[45] mp 78–79°C. (Entry 1, Table II).

TABLE IV

Reactions of benzyl sulfones and sulfides with Friedel–Crafts catalysts

Entry no.	Starting material	Reaction Conditions: Catalyst	Solvent	Temp. °C	Time h	Production composition (%)
1		$AlCl_3/CH_3NO_2$	CS_2	RT	3	Unidentified polymer (88)
2	"	$AlCl_3$	"	"	3	" (90)
3		"	"	"	3	" (89)
4		"	"	"	3	" (92)
5		"	"	"	3	" (95)
6		$AlCl_3/CH_3NO_2$	CS_2	"	3	" (92)
7	"	$AlCl_3$	"	"	3	" (90)
8	"	$FeCl_3$	"	"	3	" (85)
9		$AlCl_3$	CS_2	"	3	4-Dimethylisothiochroman (70) Benzyl isopropyl sulfide (15) Polymer (10)
10	"	"	"	Reflux	3	4-Dimethylisothiochroman (80) Polymer (15)
11		$AlCl_3$	"	RT	3	Isothiochroman-4-one (63) Polymer (20)
12		$AlCl_3/CH_3NO_2$	CS_2	"	3	Unidentified polymer (90)
13	"	$AlCl_3$	"	"	3	" (85)

Cyclialkylation of **13** *using Method B.*

(a) At room temperature: GLC analysis at 170°C showed two compounds and their isolation was performed using column chromatogram packed with silica gel: *iso*butyl *p*-tolyl sulfide (36%) was eluted with benzene–ether mixture (3 : 2) and oxidized to the corresponding *iso*butyl *p*-tolyl sulfone mp and mmp 78°C, lit.[43] mp 79; and 2,3-dihydro-3,3,5-trimethylbenzothiophene (**38**, 64%) was eluted with benzene–ether mixture (1 : 4) and oxidized to 2,3-dihydro-3,3,5-trimethylbenzothiophene-*S,S*-dioxide, mp 122–124°C. Elemental analysis for $C_{11}H_{14}O_2S$, calculated: S, 15.23%; found: S, 15.10%. IR absorption showed ν_{SO_2} at 1150 cm^{-1}.[46] NMR ($CDCl_3$): δ 7.1 (m, 3 H, aromatic), δ 3.2 (S, 2 H, CH_2), δ = 2.6 (S, 3 H, CH_3 to aromatic) and δ 1.7 (S, 6 E, gem dimethyl). Entry 2, Table II.

(b) At reflux temperature: also, *iso*butyl *p*-tolyl sulfide and 2,3-dihydro-3,3,5-trimethylbenzothiophene (**37**) were formed in 12% and 88%, respectively (Entry 3, Table II).

Attempted cyclization of **14** *using Method B*

(a) At room temperature: the starting material was recovered in 96%.

(b) At reflux temperature: GLC analysis revealed, using authentic samples, the presence of phenyl propyl sulfide (20%), trace of the starting **14** and thiochroman (**39**, 65%). Separation of the mixture was accomplished using silica gel column chromatogram. Thiochroman was converted into thiochroman *S,S*-dioxide, mp 88°C, lit.[47] mp 88.5°C. Elemental analysis for $C_9H_{10}O_2S$, calculated: S, 17.58%, found: S, 17.55% (Entry 4, Table II).

Attempted cyclization of **15** *using Method B*

(a) At room temperature: the starting sulfide **15** was recovered in 95%.

(b) At reflux temperature: GLC analysis using authentic samples showed the presence of *p*-thiocresol (9%), *n*-propyl *p*-tolyl sulfide (15%) and 6-methylthiochroman (**40**, 60%). Also, **40** was eluted with benzene from silica gel column chromatogram and oxidized with H_2O_2/CH_3COOH to 6-methylthiochroman-*S,S*-dioxide, mp 80°C, lit.[48] mp 81°C. Elemental analysis for $C_{10}H_{12}O_2S$, calculated: S, 16.32%; found: S, 16.51% (Entry 5, Table II).

Attempted cyclization of **16** *using Method B*

(a) At room temperature: the starting sulfide **16** was recovered in 90%.

(b) At reflux temperature: using GLC analysis and authentic samples the reaction products were identified as *p*-chlorothiophenol (5%), *p*-chlorphenyl 4-propyl sulfide (20%) and 6-chlorothiochroman (**41**, 60%). Furthermore, **41** was also eluted with benzene from silica gel column chromatogram and oxidized to its -*S,S*-dioxide, mp 143°C, lit.[48] mp 139–144°C. Elemental analysis for $C_9H_9ClO_2S$, calculated: S, 14.78%; Cl, 16.39; found: S, 14.91%; Cl, 14.88%. (Entry 6, Table II).

Attempted cyclization of **17a–19a**. Using Methods B and C, the precursor acids **17**, **18** and **19**, respectively, were regenerated from the alkaline extract. Their melting points were not depressed upon admixing with authentic sample of **17**, **18** and **19**. (Entries 1–9, Table III).

Attempted cyclization of **20a**. Using Method B at room or reflux temperature, **20** was recovered. Method C gave only 50% of **20** and 6-methylthiochromanone-*S,S*-dioxide (**43**, 20%), mp and mmp 162°C, lit.[30] mp 163°C (Entries 10–13, Table III).

Attempted cyclization of **21a**. The acid **21** was recovered from Method B. Method C gave in addition to **21** (50%) 6-chlorothiochromanone-*S,S*-dioxide (**44**, 17%), mp 154°C (aqueous acetone, 2 : 1), lit.[49] mp 155°C. Elemental analysis for $C_9H_7SO_3Cl$, calculated: S, 16.45%, Cl, 18.25%; found, S, 15.96%, Cl, 18.38% (Entries 13–15, Table III).

Attempted cyclization of **22a**. **22** was recovered in 89% upon treatment of **22a** with Method B at room temperature whereas 5,6-benzothiochromanone-*S,S*-dioxide (**42**, 33%) was formed, in addition to **22** (46%), at reflux temperature, **42** was melted at 149°C, lit.[50] mp 150°C. Elemental analysis for $C_{13}H_{10}SO_3$, calculated: S, 13.00; found: S, 13.12% (Entries 16–17, Table III).

Cyclization of **23a**. Method A produced 2,3-dihydro-3-keto-5-methylbenzothiophene (**45**, 40%) and uncrystallizable black polymer (40%). Method B, at room temperature gave also **45** in only 25% and the black polymer in 60%. **45** was melted at 85°C (methanol), mmp 86°C and lit.[51] mp 87°C (Entries 18, 19, Table III).

Cyclization of **24a**. 2,3-dihydro-3-keto-5-chlorobenzothiophene[46] was formed upon applying Method A in 42% and from Method B in 25%. A black polymer was also separated in both cases (40%, 60%, respectively). Mp of **46** was 99°C (pet. ether, 60–80°C), mmp and lit.[52] mp 100°C (Entries 20, 21, Table III).

Attempted cyclization of **25a**. Method A and Method B gave only unidentified black polymer.

Cyclization of **26a**. Method B gave 6-methylthiochromanone (**47**, 89%), mp 40°C, lit.[36] mp 41°C. Also, **47** was oxidized to **43** using H_2O_2/ACOH,[53] mp and mmp 162°C, lit.[30] mp 163°C (Entry, 24, Table III).

Cyclization of **27a**. 6-chlorothiochromanone (**48**, 85%) was formed by using method B, mp 66°C, lit.[48] mp 67°C. Oxidation of **48** with H_2O_2/ACOH gave **44**, mp and mmp 154°C, lit.[49] mp 155°C (Entry 25, Table III).

Cyclization of **28a**. 5,6-benzothiochromanone (**49**) was isolated in 93% yield using Method B, mp 68°C, lit.[38] mp 68–69°C. Oxidation[53] of **49** gave 5,6-benzothiochromanone-*S*,*S*-dioxide (**42**), mp, mmp 149°C, lit.[50] mp 150°C (Entry 26, Table III).

Attempted cyclization of **29**. Treatment of **29** with Method A and with Method B gave a high melting point (charrs above 360°C) polymer insoluble in the common solvent (ethanol, ether, acetone, chloroform, acetic acid or benzene), Entries 1, 2, Table IV.

Attempted cyclization of **30**. Method B afforded a high melting point polymer (charrs above 360°C) insoluble in the common solvent (Entry 3, Table IV).

Attempted cyclization of **31**. A high melting point polymer (charrs above 360°C) insoluble in the common solvent was obtained from Method B (Entry 4, Table IV).

Attempted cyclization of **32**. A polymer of high melting point (charrs above 360°C) was obtained from Method B (Entry 5, Table IV).

Attempted cyclization of **33**. Cyclization of **33** using Methods A, B and E gave a high melting point polymer (charrs above 360°C) insoluble in common solvents (Entries 6–8, Table IV).

Cyclization of **34**. Method B (at room temperature) gave benzyl isopropyl sulfide (15%), 4-dimethylisothiochroman (**50**, 70%) and a high melting point polymer (charrs above 360°C) while this method at reflux temperature gave only **50** (80%) and a polymer (15). Benzyl isopropyl sulfide was eluted with, from silica gel column chromatogram, pet. ether (60–80)–benzene mixture (3 : 2) and identified using authentic sample and GLC technique. Also, **50** was eluted with benzene and oxidized[53] to 4-dimethylisothiochroman-*S*,*S*-dioxide, mp 152°C, lit.[20] mp 150–154°C. Elemental analysis for $C_{11}H_{14}O_2S$, calculated: S, 15.23%; found: S, 15.51%; ir spectra showed absorption at 1150 cm^{-1} (ν_{SO_2}) and NMR ($CDCl_3$), δ 7.3 (m, 4 H, phenyl), δ 4.3 (S, 2 H, CH_2, α to aromatic), δ 3.3 (S, 2 H, CH_2 β to aromatic) and δ 1.8 (S, 6 H, gem dimethyl). (Entries 9, 10, Table IV).

Cyclization of **35a**. Method B, at room temperature, gave isothiochroman-4-one (**51**, 63%), mp, mmp 60°C, lit.[42] mp 61°C. Also, a high melting point polymer (charrs above 360°C) was obtained in 20% (Entry 11, Table IV).

Attempted cyclization of **36a**. Methods A and B gave only a polymeric materials (charrs above 360°C) insoluble in the common solvents.

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