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REACTIONS OF γ-SULTINES WITH ELECTROPHILIC REAGENTS. 3*. CHLORINATION OF 3,5-DIARYL-1,2-OXATHIOLANE 2-OXIDES

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The influence of the nature of the aryl substituents and the reaction conditions for the chlorination of 3,5-diphenyl-1,2-oxathiolane 2-oxide and 3,5-bis(4-methoxyphenyl)-1,2-oxathiolane 2-oxide have been studied. Possible mechanisms for the chlorination of γ-sultines are discussed.

Keywords: 1,3-diaryl-1,3-dichloropropanes, diastereomers, 3-chloro-1,3-diphenylpropanesulfonyl chloride, 1,2-oxathiolane 2-oxides (γ-sultines), diastereoselectivity, chlorination.

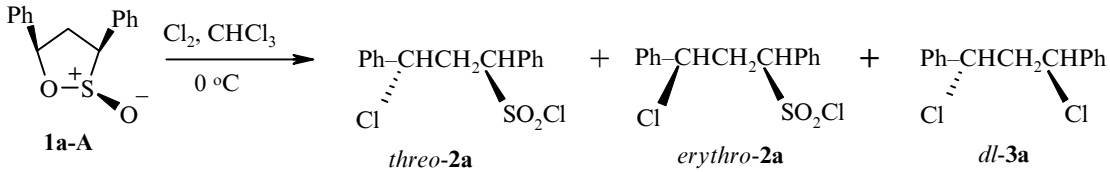
There are practically no studies of the chlorination of γ-sultines. A study of the bromination of 3,5-diaryl-1,2-oxathiolane 2-oxides, which occurred stereospecifically to give high yields of 1,3-diaryl-1,3-dibromopropanes, has been reported [1, 2]. Chlorination has been reported for only a few sultines: the products were chlorine substituted sulfonyl chlorides [3-5].

In the present work the chlorination of 3,5-diaryl-1,2-oxathiolane 2-oxides was studied. The compounds studied were 3,5-diphenyl-1,2-oxathiolane 2-oxide (**1a**) and 3,5-bis(4-methoxyphenyl)-1,2-oxathiolane 2-oxide (**1b**). The chlorinating agents used were a saturated solution of chlorine in chloroform and sulfuryl chloride. The reactions were monitored by TLC. The quantitative composition of the reaction mixtures was analysed by ^{1}H NMR spectroscopy.

γ-Sultines **1a**,**b** are known to exist as the four diastereomers **A-D** [2]. The sultine **1a** used in this study was either the individual diastereomer **A**, having the *cis,cis* configuration of the five-membered ring [6], or the mixture of the diastereomers **A-D**, whereas the sultine **1b** was used only as a mixture of the diastereomers **A-D**.

Reaction of the diastereomer **A** of compound **1a** with chlorine led to the formation in 90% yield of a mixture of the diastereomers of the sulfonyl chloride **2a** (*threo-erythro*, 88:12) and 10% of the *dl*-form of the dichloride **3a** (Scheme 1, Table 1).

Scheme 1



1a-A *threo*-**2a** *erythro*-**2a** *dl*-**3a**

* For paper 2 see [1].

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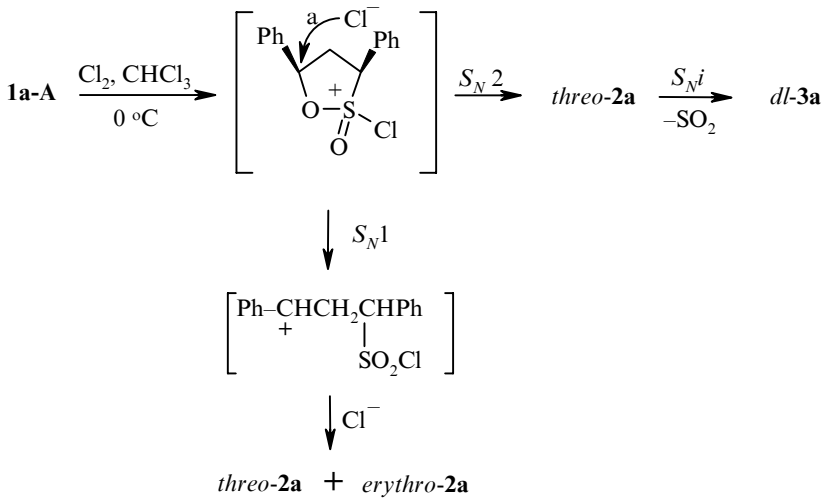
The sulfonyl chloride **2a** proved to be an unstable compound: after keeping the reaction mixture in chloroform solution for a month at 0°C it consisted of 91% of the diastereomer *dl*-**3a** and 9% of a mixture of the diastereomers of **2a** (*threo-erythro*, 63:37). Chlorination of a mixture of the diastereomers **A-D** of sultine **1a** under analogous conditions gave 95% of a mixture of diastereomers of **2a** (*threo-erythro*, 80:20) and 5% of the *dl*-diastereomer of **3a**. It can be concluded from these results that chlorination of the sultine **1a** occurs stereospecifically and can be expressed by Scheme 2.

Scheme 2



It follows from these schemes that the predominant formation of the *threo*-diastereomer of the sulfonyl chloride **2a** probably occurs *via* an S_N2 mechanism with inversion of the configuration of atom $C_{(5)}$ of the cyclic cationic intermediate, formed as a result of electrophilic attack by chlorine on the unshared electron pairs of the sulfur atom. Formation by the $S_N1$mechanism is considerably less likely because it requires the formation of the weakly stabilised benzyl carbocation. Subsequent decomposition of the *threo*-**2a** diastereomer occurs stereoselectively to give the *dl*-diastereomer of the dichloride **3a** exclusively. Since the unstable sulfonyl chloride cannot be isolated in the pure form, it was converted into the corresponding sulfonamide **4a** by reaction

TABLE 1. Results of the Interaction of the γ-Sultines **1a,b** with Chlorine in $CHCl_3$ at 0°C

Substrate, diastereomeric composition, %	Time, h	Composition of the reaction mixture, %	Stereochemical composition of the reaction mixture, %
1a-A	168	**2a**, 91 **3a**, 9	**2a**, *threo-erythro*, 88:12 **3a**, *dl* 100
1a, **A–B–C–D**, 54:17:20:9	168	**2a**, 95 **3a**, 5	**2a**, *threo-erythro*, 80:20 **3a**, *dl* 100
1b,* **A–B–C–D**, 57:18:18:7	5	**3b**, 51*[2]	**3b**, *dl–meso*, 56:44
1b,*[3] **A–B–C–D**, 57:18:18:7	24	**3b**, 100	**3b**, *dl–meso*, 56:44

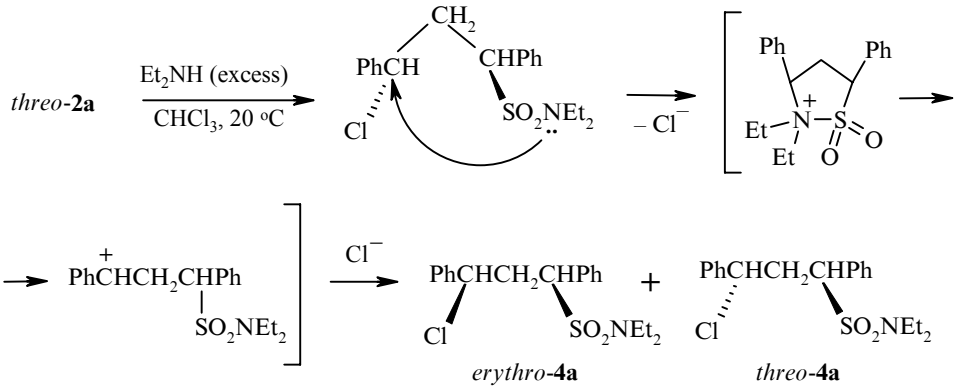
* Reaction carried out at -10°C.

*[2] The reaction mixture contained 49% of sultine **1b**, **A:B:C:D** 64:11:17:8 .

*[3] A two fold excess of SO_2Cl_2 was used as chlorinating agent.

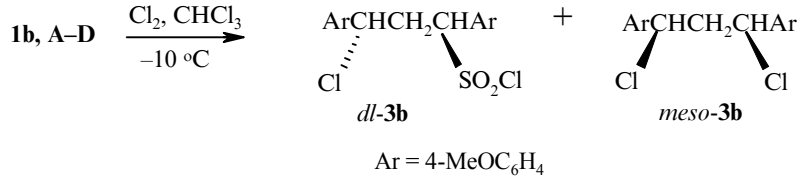
with diethylamine to confirm the structure. It should be noted that the sulfonyl chloride starting material **2a** consisted of an 80:20 mixture of the *threo-erythro* diastereomers, whereas the sulfonamide **4a** obtained consisted of a 1:1 (equimolar) mixture of the *threo-erythro* diastereomers, which can be explained by Scheme 3.

Scheme 3



As a result of chlorination of a diastereomeric mixture of the sultine 3,5-bis(4-methoxyphenyl)-1,2-oxathiolane 2-oxide (**1b**, **A-D**) with a solution of chlorine at -10°C for 5 h a reaction mixture was obtained which consisted of 51% of an equimolar mixture of the *dl*- and *meso*-diastereomers of the dichloride **3b** and 49% of a mixture of diastereomers of the starting material, sultine **1b** (see Scheme 4 and Table 1).

Scheme 4



Further treatment of the reaction mixture with a solution of chlorine in chloroform produced a complex mixture of 1,3-diaryl-1,3-dichloropropanes with chlorine-substituted aromatic substituents and products of destruction.

When sulfuryl chloride was used in the chlorination reaction sultine **1a** did not react, but, in contrast, sultine **1b** reacted readily to give a mixture of the diastereomers of dichloride **3b**. To obtain a maximum yield it was necessary to use a two-fold excess of sulfuryl chloride (see Table 1). The reaction probably occurs according to Scheme 5.

The reaction is very similar to that described above for the chlorination of sultine **1a**. Sulfuryl chloride evidently serves as a source of the electrophile chlorine in the absence of a radical initiator, as data from [5, 7, 8] on the interaction of sulfuryl chloride with sulfoxides indicate. In distinction from sultine **1a**, the subsequent conversion of the cyclic cationic intermediate occurs via the formation of stabilised open chain anisyl carbocations which give rise to a mixture of diastereomers of compound **3b**. The sulfonyl chloride **2b** was not observed in this reaction which may be linked either to its instability with rapid loss of the sulfo group to give compound **3b** (Scheme 5), or with the possibility of the reaction shown in Scheme 6 with a different direction of opening of the cyclic intermediate analogous to the bromination of sultine **1b** [2].

TABLE 2. ^{1}H NMR Spectra of Compounds **2a**, **3a**,**b**, and **4a**

Compound	Chemical shifts, δ, ppm (coupling constants, *J*, Hz)				
	CH_2	CHCl	CHS	Et_2N	CH_{Ar}
2a-*threo*	3.16, 3.37* (2H, $^2J_{AB}$ = 14.0)	4.76 (1H, dd, $^3J_{AM}$ = 9.4, $^3J_{BM}$ = 6.2)	4.43 (1H, dd, $^3J_{AX}$ = 4.8, $^3J_{BX}$ = 10.0)	—	7.2-7.6 (10H, m)
2a-*erythro*	2.93, 3.28* (2H, $^2J_{AB}$ = 14.4)	5.20 (1H, dd, $^3J_{AM}$ = 11.4, $^3J_{BM}$ = 3.0)	4.53 (1H, dd, $^3J_{AX}$ = 3.2, $^3J_{BX}$ = 11.6)	—	7.2-7.6 (10H, m)
4a-*threo*	2.95, 3.17* (2H, $^2J_{AB}$ = 14.0)	4.83 (1H, dd, $^3J_{AX}$ = 8.8, $^3J_{BX}$ = 6.8)	3.87 (1H, dd, $^3J_{AM}$ = 5.2, $^3J_{BM}$ = 9.2)	0.95 (6H, t, ^3J = 7.0); 2.88 (4H, q, ^3J = 7.0)	7.2-7.7 (10H, m)
4a-*erythro*	2.76, 3.07*[2] (2H, $^2J_{AB}$ = 14.0)	4.49 (1H, dd, $^3J_{AX}$ = 11.2, $^3J_{BX}$ = 3.2); 4.50 (1H, dd, $^3J_{AY}$ = 3.6, $^3J_{BY}$ = 11.2)		1.03 (6H, t, ^3J = 7.0); 3.00 (4H, q, ^3J = 7.0)	7.2-7.7 (10H, m)
3a-*dl*	2.7 (2H, dd)	5.25 (2H, dd, ^3J = 6.4, ^3J = 8.0)	—	—	7.2-7.6 (10H, m)
3b-*dl**[3]	2.77 (2H, t)	5.22 (2H, t, ^3J = 7.0)	—	—	6.94 (8H, d); 7.35 (4H, d); 7.36 (4H, d, ^3J = 8.8)
3b-*meso**[3]	2.74, 3.04*[4] (2H, $^2J_{AB}$ = 14.0)	4.87 (2H, dd, $^3J_{AX}$ = 8.0, $^3J_{BX}$ = 6.8)	—	—	

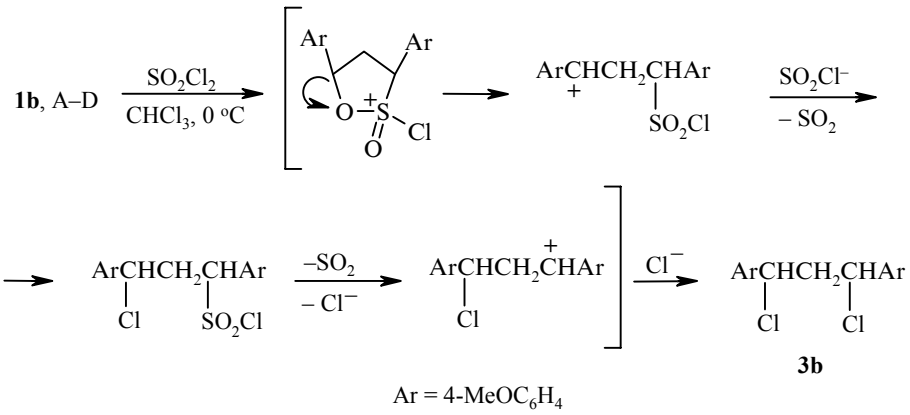
* AB part of an ABMX system.

*[2] AB part of an ABXY system.

*[3] δ(CH_3O) = 3.83 ppm.

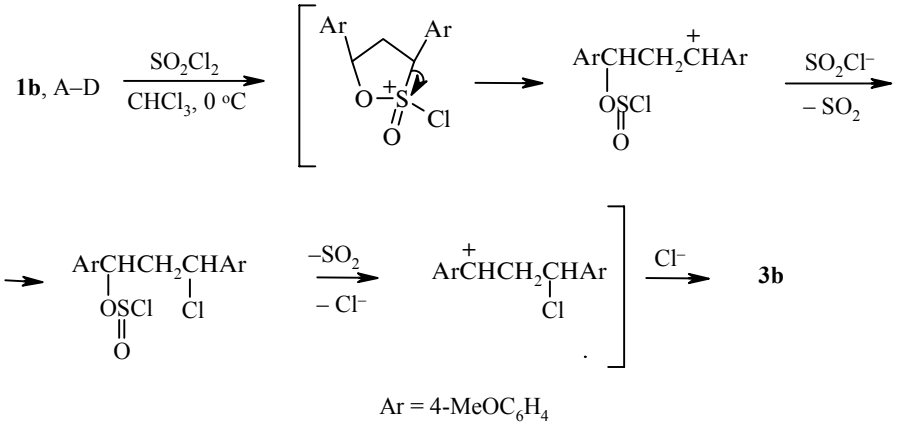
*[4] AB part of an ABX_2 system.

Scheme 5



Ar = 4-$MeOC_6H_4$

Scheme 6



Ar = 4-$MeOC_6H_4$

TABLE 3. ^{13}C NMR Spectra of Compounds **2-4**

Compound	Chemical shifts, δ, ppm				
	CH_2	CHCl	CHS	CH_{Ar}	C_{Ar}
2a- *threo*	40.10	58.75	78.61	127.14, 128.95, 129.31, 129.51, 130.27, 130.82	129.48, 138.62
2a- *erythro*	39.98	59.68	79.58	126.82, 128.76, 129.22, 129.65, 130.29, 130.85	129.50, 137.84
3a-*dl*	49.76	60.90	—	127.14, 128.77, 128.96	140.88
3b-*dl*/*meso**	49.35, 49.36	60.30, 60.81	—	114.15, 114.18, 128.34, 128.35	132.20, 132.82, 159.72, 159.78
4a-*threo*/*erythro**[2]	40.16, 40.55	60.11, 60.72	65.78 66.32	126.91, 127.29, 128.53, 128.76, 128.87, 128.97, 129.00, 129.09, 129.19, 129.28, 129.75, 129.90	132.65, 133.22, 139.84, 140.87

* Signal of the CH_3O group: 55.27 ppm.

*[2] Signals of the Et_2N groups: 14.85 (CH_3), 42.53, 42.63 ppm (CH_2N).

Both reaction directions are equally likely for substrate **1b** and produce the same result. That sultine **1a** does not react with sulfuryl chloride may be explained by the fact that opening of the cyclic intermediate by the S_N1 mechanism does not occur because of the lower stabilisation of the benzyl cation, while the SO_2Cl^- anion is evidently much less nucleophilic than the chloride anion, so that substitution by the S_N2 mechanism is not possible under these conditions.

EXPERIMENTAL

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Varian VXR-400 machine in $CDCl_3$ solution. IR spectra of liquid films were recorded with a UR-20 spectrometer.

Details of the ^1H and ^{13}C NMR spectra of compounds **2-4** are given in Tables 2 and 3.

3,5-Diaryl-1,2-oxathiolane 2-Oxides (1a,b) were synthesized by the reaction of the corresponding 1,2-diarylcyclopropanes with sulfur dioxide by a known method [9, 10].

Chlorination of 3,5-Diaryl-1,2-oxathiolane 2-Oxides (General Method). A saturated solution of chlorine in chloroform was added with stirring to a solution of the sultine (0.3 mmol) in chloroform (15 ml) freed from ethanol impurities (see Table 1). After the reaction had finished (monitored by TLC, Silufol carrier, eluent 4:1:1 CCl_4–$CHCl_3$–ether), the reaction mass was evaporated and the reaction products were analysed.

***threo-erthyro*-3-Chloro-1,3-diphenylsulfonyl Chloride (2a)**, yield 90-95%, unstable, decomposing viscous oil.

***dl*-1,3-Dichloro-1,3-diphenylpropane (3a).** A solution of compound **2a** in chloroform was kept for a month at 20°C. The solvent was then removed to give a yellow oil of the diastereomer *dl*-**3a** with a yield of 90%. The ^1H and ^{13}C NMR spectra were identical to those reported previously [11].

(1*R,3*R**)/(1*R**,3*L**)-N,N-Diethyl-3-chloro-1,3-diphenylpropanesulfonamide (4a).** An excess of diethylamine was added stepwise to a solution of the sulfonyl chloride **2a** in chloroform at 20°C, the mixture was stirred for 5 h, then poured into cold water acidified with hydrochloric acid, extracted with chloroform, washed with water to pH 7, and dried over $CaCl_2$. A yellow mass, 75% yield, was isolated after removal of the solvent. IR spectrum (thin layer): 1335, 1143 (SO_2). Found, %: C 61.42; H 6.65. $C_{19}H_{24}ClNO_2S$. Calculated, %: C 62.37; H 6.61.

***dl/meso*-1,3-Dichloro-1,3-bis(4-methoxyphenyl)propane (3b).** A solution of sulfuryl chloride (0.27 g, 2 mmol) in chloroform was added dropwise to a solution of sultine **1b** (0.3 g, 0.04 mmol) in chloroform cooled to 0°C. The mixture was stirred for a day at 0°C, evaporated, and the residue was recrystallized from 1:10 choroform–pentane, to give grayish white crystals, 95% yield; mp 99-100°C. Found, %: C 63.41; H 5.41. $C_{17}H_{18}Cl_2O_2$. Calculated, %: C 62.78, H 5.58.

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