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REACTIONS OF γ-SULTINES WITH ELECTROPHILIC REAGENTS. 2*. BROMINATION OF 3,5-DIARYL-1,2-OXATHIOLANE 2-OXIDES IN THE PRESENCE OF LEWIS ACIDS

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The bromination of 3,5-diaryl-1,2-oxathiolane 2-oxides (γ-sultines) has been studied in the presence of added Lewis acids. It was discovered that γ-sultines with donor substituents react with bromine with ring fission and conjugated addition of the nucleophilic reactant. Possible mechanisms for the reaction are discussed based on the data obtained.

Keywords: 1,3-diaryl-1-bromo-3-ethoxypropane, 1,3-diaryl-1,3-diethoxypropane, diastereomers, Lewis acids, 1,2-oxathiolane 2-oxides (γ-sultines), bromination, diastereoselectivity.

Bromination of 3,5-diaryl-1,2-oxathiolane 2-oxides in chloroform containing 1% ethanol leads to the preferential formation of 1,3-diaryl-1,3-dibromopropanes and an insignificant quantity of the corresponding 1,3-diaryl-1-bromo-3-ethoxypropanes [1].

The present work is devoted to a study of the bromination of 3,3-diaryl-1,2-oxathiolane 2-oxides in chloroform in the presence of Lewis acids. The initial compounds were 3,5-diphenyl-1,2-oxathiolane 2-oxide (**1a**), 5-(4-methoxyphenyl)-3-phenyl-1,2-oxathiolane 2-oxide (**1b**), and 3,5-bis(4-methoxyphenyl)-1,2-oxathiolane 2-oxide (**1c**). The sultines **1a-c**, obtained by the reaction of the appropriate 1,2-diaryl-cyclopropanes with liquid sulfur dioxide, exist as four diastereomers: *A cis*-3,5-diaryl-1,2-oxathiolane (2,3-*cis*)-2-oxide; *B cis*-3,5-diaryl-1,2-oxathiolane (2,3-*trans*)-2-oxide; *C trans*-3,5-diaryl-1,2-oxathiolane (2,3-*cis*)-2-oxide; *D trans*-3,5-diaryl-1,2-oxathiolane (2,3-*trans*)-2-oxide [2].

The γ-sultines **1a-c** were used only as diastereomer *A* in this work.

We discovered that on using equimolar additions of HgO, $AlBr_3$, and $ZnBr_2$ to the bromination of sultines **1a-c** the yield of bromoethoxy substituted compounds was significantly increased (see Table 1). The compositions of the reaction mixtures were determined by ^1H NMR spectra, the assignment of signals of diastereomers **2** and **3** was carried out as described previously in [1]. The preferential formation of bromoethoxypropanes on brominating sultine **1b** may be explained using added $ZnBr_2$ as example.

The role of the additive probably comprises fission of bromide ion from the intermediate **7b** and binding it in a complex, which enables a weak nucleophile such as ethyl alcohol to interact with the resulting carbocation **8b**, preventing competition from the bromide anion. This effect was first discovered when using

* For Part 1 see [1].

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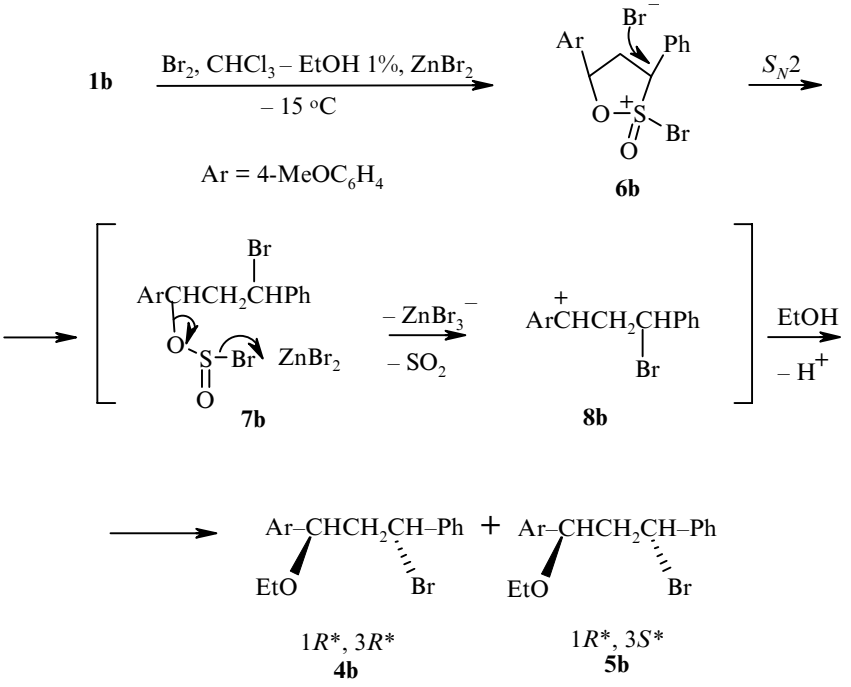


HgO and also on adding $AlBr_3$, but the best results were achieved when using $ZnBr_2$ obtained *in situ* from zinc dust and bromine in chloroform immediately before reaction with the sultine (Table 1).

TABLE 1. Interaction of Diastereomers *A* of γ-Sultines **1a-c** with Bromine in $CHCl_3$–EtOH (1%) in the Presence of Additives at -15°C

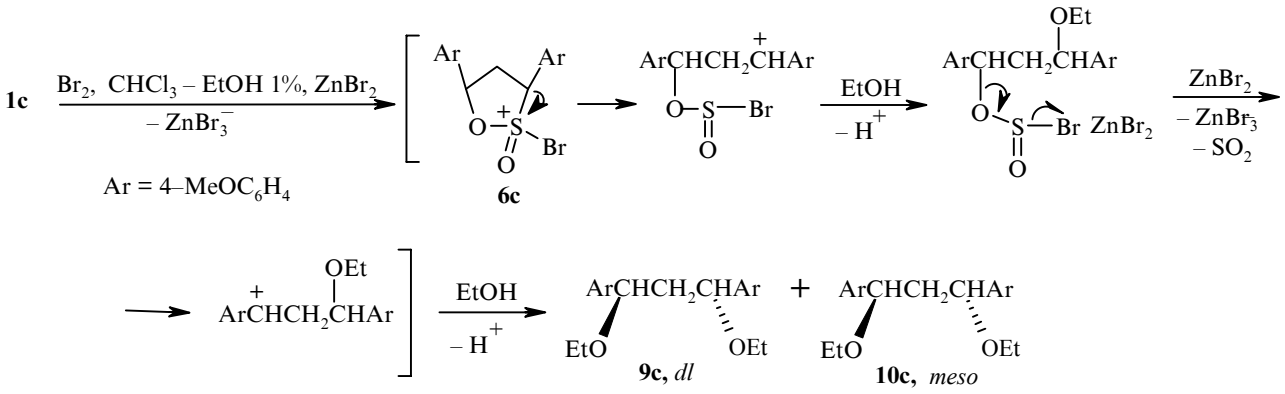
Substrate	Additive	Time, h	Composition of reaction mixture		Stereochemical composition of reaction mixture	
			Reaction products	Substrate	Reaction products	Substrate
1a*	$ZnBr_2$	24	**2a**, 46% **4a**+**5a**, 28%	**1a**, 26%	*dl*, 100% 1*R**,3*R**/1*R**,3*S** = = 44/56	*A*, 100%
1b	HgO	2	**2b**+**3b**, 13% **4b**+**5b**, 87%		*threo/erythro* = 50/50 1*R**,3*R**/1*R**,3*S** = = 50/50	
	HgO	3	**4b**+**5b**, 90%*[2]		1*R**,3*R**/1*R**,3*S** = = 33/67	
	$AlBr_3$	24	**2b**+**3b**, 9% **4b**+**5b**, 80%	**1b**, 11%	*threo/erythro* = 43/67 1*R**,3*R**/1*R**,3*S** = = 50/50*[3]	
	$ZnBr_2$	1.5	**4b**+**5b**, 100%		1*R**,3*R**/1*R**,3*S** = = 33/67	
	$ZnBr_2$	1	**4b**+**5b**, 58%	**1b**, 42%	1*R**,3*R**/1*R**,3*S** = = 36/64	*A*/*B*/*C*/*D* = = 54/21/18/7
1c	$ZnBr_2$*[4]	1.5	**10c**+**11c**, 95%*[2]		*dl/meso* = 50/50	

* Reaction was carried out at +20°C.
*[2] Yield of substance isolated.
*[3] Diastereomeric composition not determined.
*[4] Twofold excess of $ZnBr_2$ used.

On carrying out the reaction in the presence of additives the main product in a series of experiments was a mixture of diastereomers of 1-bromo-3-ethoxy-3-(4-methoxyphenyl)-1-phenylpropane (**4b, 5b**) with admixture of 1,3-dibromo-1-(4-methoxyphenyl)-3-phenylpropanes (**2b, 3b**). The molar ratio of diastereomers **4b** and **5b** varied from 1:1 to 1:2. The generally detected predominant formation of the (*R**,*S**) diastereomer **5b** may be explained in the following way. Conversion of intermediate **6b** into **7b** occurs with inversion of configuration at the $C_{(3)}$ atom, then on forming carbocation **8b** contact ion pair appears and attack of ethanol takes place predominantly from the rear with inversion of the configuration of the $C_{(5)}$ atom of the sultine. On putting diastereomer *A* (2*S**,3*S**,5*R**) of sultine **1b** into the reaction inversion of the configuration of the $C_{(3)}$ and $C_{(5)}$ atoms leads to the formation of the (*R**,*S**)-diastereomer **5b** (see Table 1).

It should be mentioned that in reactions of diastereomer *A* of sultine **1b** unreacted substrate isolated from the reaction mixture was an equilibrium mixture of diastereomers *A*-*D* (Table 1). The isomerization of 3,5-diaryl-1,2-oxathiolane 2-oxides in the presence of Lewis acids, probably proceeding through the formation of open carbocationic intermediates, was described previously in [2].

As was assumed previously in [1], bromination of sultine **1c** proceeds with the sequential formation of two carbocations, which makes possible the introduction of two nucleophilic substituents. This was confirmed on brominating sultine **1c** in chloroform solution in the presence of a twofold excess of $ZnBr_2$, as a result of which an equimolar mixture of the diastereomers of diethoxy-substituted compounds **9c** and **10c** was isolated in 95% yield.



It was also shown that bromination of diphenylsultine **1a**-*A* in chloroform containing ethanol (1%) in the presence of $ZnBr_2$ leads to the formation of 46% *dl*-dibromide **2a** and 28% of an equimolar mixture of the diastereomers of 1-bromo-3-ethoxy-1,3-diphenylpropane.

It is therefore possible to assume that in the presence of $ZnBr_2$ the bromination of sultine **1a** may proceed partially through the formation of a carbocationic intermediate.

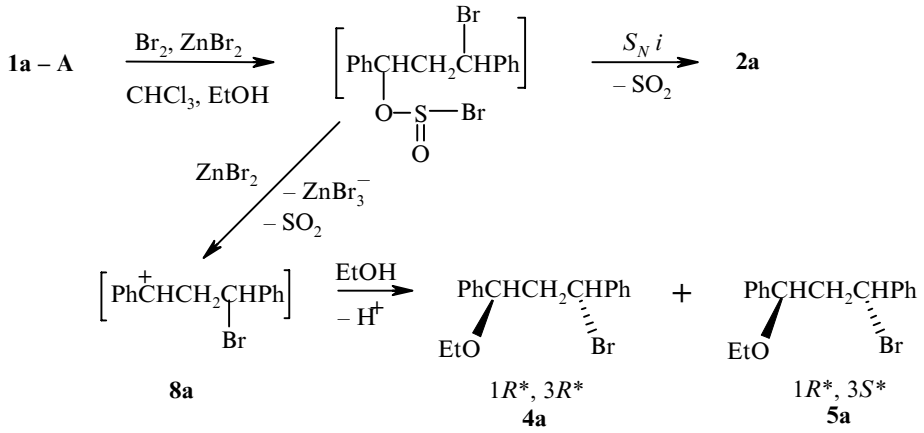


TABLE 2. ^{1}H NMR Spectra of Compounds **4a,b**, **5a,b**, **10c**, and **11c**

Compound	Chemical shifts, δ, ppm (coupling constants, *J*, Hz)						
	CH_3 (t, ^3J = 7.0)	CH_2	CH_2O	CH_3O	CHO, dd	CHBr, dd	H arom.
4a	1.24 (3H)	2.42 (2H, m)	3.30-3.50* (2H, m)	—	4.62 (1H, ^3J = 3.6, ^3J = 9.6)	5.34 (1H, ^3J = 4.0, ^3J = 7.2)	7.3-7.5 (10H, m)
5a	1.19 (3H)	2.43*[2] (2H, m)	3.30-3.50 (2H, m)	—	4.12 (1H, ^3J = 2.4, ^3J = 9.6)	5.05 (1H, ^3J = 3.2, ^3J = 9.6)	7.3-7.5 (10H, m)
4b	1.23 (3H)	2.45 (2H, m)	3.40; 3.46*[2] (2H, $^2J_{AB}$ = 9.2, ^3J = 7.0)	3.82 (3H, s)	4.55 (1H, ^3J = 3.8, ^3J = 9.5)	5.33 (1H, ^3J = 4.1, ^3J = 10.4)	6.92 (2H, d); 7.27 (2H, d, ^3J = 8.8); 7.3-7.5 (5H, m)
5b	1.15 (3H)	2.45; 2.84*[3] (2H, $^2J_{AB}$ = 14.0)	3.13; 3.30*[2] (2H, $^2J_{AB}$ = 9.4, ^3J = 7.0)	3.81 (3H, s)	4.06 (1H, $^3J_{AM}$ = 5.6, $^3J_{BM}$ = 8.2)	5.02 (1H, $^3J_{AX}$ = 8.0, $^3J_{BX}$ = 7.4)	6.90 (2H, d); 7.22 (2H, d, ^3J = 8.8); 7.3-7.5 (5H, m)
10c	1.19 (6H)	1.96 (2H, dd, ^3J = 6.2, ^3J = 7.4)	3.32; 3.43*[4] ($^2J_{AB}$ = 9.4, ^3J = 7.0)	3.79 (6H, s)	4.48 (2H, ^3J = 6.2, ^3J = 7.4)	—	6.87 (4H, d); 7.24 (4H, d, ^3J = 8.8)
11c	1.14 (6H)	1.80; 2.43*[4] ($^2J_{AB}$ = 13.6)	3.19; 3.28*[2] ($^2J_{AB}$ = 9.4, ^3J = 7.0)	3.81 (6H, s)	4.11 (2H, $^3J_{AX}$ = 6.8, $^3J_{BX}$ = 7.8)	—	6.86 (4H, d); 7.18 (4H, d, ^3J = 8.8)

* Signals were partially overlapped by the lines of other compounds.

*[2] AB portion of ABX_3 system.

*[3] AB portion of ABMX system.

*[4] AB portion of ABX_2 system.

TABLE 3. ^{13}C NMR Spectra of Compounds **4b**, **5b**, **10c**, and **11c**

Compound	Chemical shifts, δ, ppm.							
	CH_3	CH_2	CHBr	CH_3O	CH_2O	CHO	CH arom.	C arom.
4b	15.27	48.16	52.80	55.19	64.11	8.92	113.81, 127.32, 127.69, 128.24, 128.60	134.00, 142.19, 159.15
5b	15.23	48.22	51.50	55.19	63.73	79.27	113.87, 127.43, 127.76, 128.33, 128.64	133.30, 141.48, 159.25
10c + **11c**	15.43, 15.52	46.43, 47.50	—	55.34	63.76, 64.07	77.65, 78.73	113.81, 127.87, 128.11	134.51, 135.28, 158.99, 159.11

EXPERIMENTAL

The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained on a Varian VXR 400 instrument in $CDCl_3$ at 30°C. The mass spectra were measured on a Hewlett-Packard Engine GC-MS chromatomass spectrometer at an energy of ionizing electrons of 70 eV.

3,5-Diaryl-1,2-oxathiolane 2-Oxides 1a-c were obtained by the interaction of the appropriate 1,2-diarylcyclopropanes with sulfur dioxide by the procedure of [3,4].

Bromination of 3,5-Diaryl-1,2-oxathiolane 2-Oxides (1a-c) (General Procedure). A. HgO or $AlBr_3$ (0.3 mmol) was added to a solution of sultine (0.3 mmol) in chloroform (15 ml) containing 1% ethanol and the mixture cooled to -15°C. A solution of bromine (0.3 mmol) in chloroform (10 ml) was added with stirring during 1 h. The mixture was stirred at -15°C for the time indicated in Table 1, then poured into water and ice. The organic layer was separated, washed with 10% Na_2SO_3 solution until colorless, then twice with water, and dried over $CaCl_2$.

B. A mixture of zinc dust (0.15 mmol) and chloroform (5 ml) containing 1% ethanol was cooled to -15°C. A solution of sultine (0.15 mmol) in chloroform (10 ml) was added with stirring during 15 min. After this the reaction mixture was stirred at -15°C for the time given in Table 1. The mixture was then treated as described in procedure A.

(1*R,3*R**)/(1*R**,3*S**)-1-Bromo-3-ethoxy-3-(4-methoxyphenyl)-1-phenylpropane (4b/5b).** Yield 90% (by A using HgO) or 100% (by B). Cream colored crystals; mp 127-130°C (decomp.) (CCl_4–pentane). Found, %: C 61.33; H 6.43. $C_{18}H_{21}BrO_2$. Calculated, %: C 61.90; H 6.06. Data of ^1H and ^{13}C NMR spectra are given in Tables 2 and 3.

***dl/meso*-1,3-Diethoxy-1,3-bis(4-methoxyphenyl)propane (9c/10c).** B. Yield 95% (twofold excess of $ZnBr_2$). Mass spectrum, *m/z* (I_{rel}, %): 344 [M^+] (4), 298 (20), 165 (100), 137 (36), 109 (13), 95 (7), 77 (7). Data of ^1H and ^{13}C NMR spectra are given in Tables 2 and 3.

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