Chemistry of Heterocyclic Compounds, Vol. 39, No. 1, 2003

REACTION OF γ-SULTINES WITH ELECTROPHILIC REAGENTS. 1. BROMINATION OF 3,5-DIARYL-1,2-OXATHIOLANE 2-OXIDES

E. V. Grigor'ev and L. G. Saginova

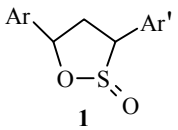
The effects of the nature of the aryl substituents and the reaction conditions on the bromination of 3,5-diaryl-1,2-oxathiolane 2-oxides (γ-sultines) have been studied. The possible mechanisms for the bromination of the γ-sultines are discussed on the basis of the experimental data.

Keywords: 1,3-diaryl-1,3-dibromopropanes, diastereomers, 1,2-oxathiolane 2-oxides (γ-sultines), bromination, diastereoselectivity.

It is known that 1,2-oxathiolane 2-oxides (γ-sultines) have potential bifunctionality and can form 1,3-functional disubstituted propanes as a result of opening the heterocyclic fragment. As is also known [1-3], the most detailed studies concern the ring opening reactions of sultines using nucleophilic reagents. The reaction of 1,2-oxathiolane 2-oxides with electrophilic reagents has been little studied, specifically only the chlorination of some sultines leading to the formation of the corresponding chloro-substituted sulfochlorides has been reported [2, 4, 5].

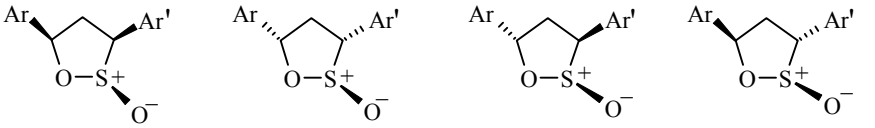
Our work is concerned with a study of the bromination of 3,5-diaryl-1,2-oxathiolane 2-oxides. The chosen subjects for the investigation were 3,5-diphenyl-1,2-oxathiolane 2-oxide (**1a**), 5-(4-methoxyphenyl)-3-phenyl-1,2-oxathiolane 2-oxide (**1b**), and 3,5-bis(4-methoxyphenyl)-1,2-oxathiolane 2-oxide (**1c**). These starting sultines **1a-c** were prepared by the reaction of the corresponding 1,2-diarylcyclopropanes with liquid sulfur dioxide and exist as the four diastereomers *A-D* [6] (see Scheme 1).

Scheme 1



1

a Ar = Ar' = Ph; **b** Ar = 4-MeO–C_6H_4, Ar' = Ph; **c** Ar = Ar' = 4-MeO–C_6H_4

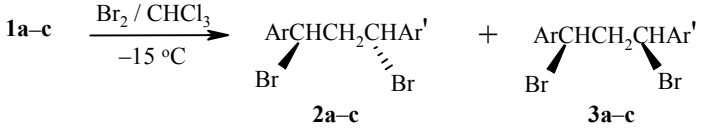


A (2*S**, 3*S**, 5*R**) *B* (2*S**, 3*R**, 5S*) *C* (2*S**, 3*S**, 5*S**) *D* (2*S**, 3*R**, 5*R**)

M. V. Lomonosov State University, Moscow 119899, Russia; e-mail: sag@org.chem.msu.ru, evg@org.chem.msu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 120-125, January, 2003. Original article submitted March 6, 2000.

In this work we have studied both the mixtures of diastereomers *A-D* of the γ-sultines **1a-c** and the pure diastereomer *A* (which predominates in the diastereomer mixtures and can be separated in the pure state).

It was found that the γ-sultines **1a-c** react with bromine in chloroform at -15°C to form a mixture of the diastereomers of the corresponding 1,3-diaryl-1,3-dibromopropanes **2a-c** and **3a-c** (see Table 1). The obtained stereochemical results infer different mechanisms for the reaction of the γ-sultines with bromine with the participation of different intermediates. In general terms the reaction of the γ-sultines **1a-c** with bromine can be represented by the following scheme:

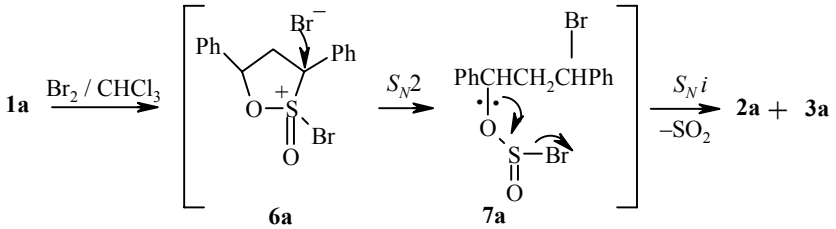


The composition of the reaction mixtures was determined from ^{1}H NMR spectroscopic data. Assignment of the signals for the diastereomers **2** and **3** was carried out on the basis of the fact that the chemical shifts of the diastereotopic protons of the methylene group in the *meso*/*erythro* (*R**, *S**)-isomers **3a-c** differ more markedly than those of the *dl*/*threo* (*R**, *R**)-isomers **2a-c** [7]. The methylene proton signals in compounds **2a-c** appear as the AB part of an ABX_2 (**2a, c**) or ABXY (**2b**) spin systems as a degraded triplet at 2.96 ppm due to the closeness of the chemical shifts of the H_A and H_B protons. In the **3a-c** diastereomers the methylene protons signals appear as an AB-quartet of triplets with chemical shifts 2.92 and 3.24 ppm with J_{AB} = 14.8 Hz (see Experimental).

When carrying out the experiment, specially purified chloroform was not used. The presence of the 1% ethanol in the solvent did not influence the results of the reaction except for the case of the formation of some of the bromoethoxy compounds **4b** and **5b** (see Scheme 3) which were found in addition to the main dibromide reaction products **2b** and **3b** when brominating the sultine **1b** (see Table 1).

Bromination of 3,5-diphenyl-1,2-oxathiolane 2-oxide (**1a**) was carried out both for the separated diastereomer A and also for the mixture of diastereomers *A-D*. It was found that the diastereomer A of sultine **1a** is brominated stereospecifically to form exclusively the *dl*-diastereomer **2a** (Table 1). A study of the bromination of the mixture of diastereomers *A-D* showed that the *A*, *B* diastereomers are markedly more active than *C*, *D*. The composition of the reaction mixtures (Table 1) shows that the *A*, *B* diastereomers give the *dl*-isomer **2a** and *C*, *D* give the *meso* form **3a**. The low yield of compound **3a** is very likely due to the low reactivity of the diastereomers *C*, *D* of sultine **1a**. The stereospecificity of the bromination of the stereoisomers of sultine **1a** can be rationalized in terms of Scheme 2:

Scheme 2



The reaction begins with attack of a bromine cation at the unshared electron pair of the sulfur atom of the sultine to give the cyclic cationic intermediate **6a**. There then occurs an S_N2 nucleophilic attack on the intermediate **6a** by a bromide anion with an inversion of configuration to give the opened structure **7a** which undergoes an S_Ni reaction with retention of the configuration of the carbon atom attacked.

TABLE 1. Results of the Reaction of the γ-Sultines **1a-c** with Bromine in $CHCl_3$–EtOH (1%) at -15°C

Substrate	Diastereomer composition, %	Time, h	Composition of the reaction mixture, %		Stereochemical composition of the reaction mixture, %			
			Reaction products	Substrate **1a**	Reaction products		Substrate	
1a-*A*	100	48	**2a**, 70	30	*dl*,	100	*A*,	100
1a, *A*/*B*/*C*/*D*	44/15/24/17	24	**2a** + **3a**, 45	55	*dl*/*meso*,	95/5	*A*/*B*/*C*/*D*,	14/3/38/45
1a*, *A*/*B*/*C*/*D*	44/14/24/17	48	**2a** + **3a**, 70	30	*dl*/*meso*,	86/14	*C*/*D*,	50/50
1b, *A*/*B*/*C*/*D*	41/21/22/16	2	**2b** + **3b**, 72*[2]		*threo*/*erythro*,	50/50		
1b, *A*/*B*/*C*/*D*	41/21/22/16	2.5	**2b** + **3b**, 77		*threo*/*erythro*,	50/50		
			4b + **5b**, 23		1*R**, 3*R**/1*R**, 3*S**	50/50		
1c, *A*/*B*/*C*/*D*	88/3/7/2	1.5	**2c** + **3c**, 87*[2]		*dl*/*meso*,	50/50		

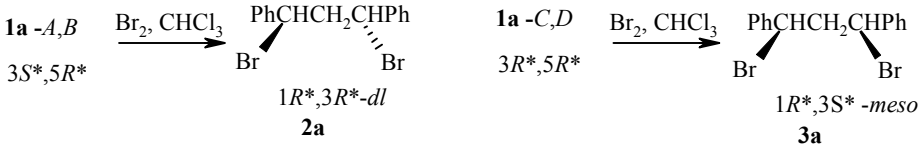
* Twofold excess of bromine used, reaction carried out at 20°C.
*[2] Yield of separated compound.

TABLE 2. ^{1}H NMR Spectra of Compounds **2a-c**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)			
	CH_2	CH_3O, s	CHBr	H arom.
2a	2.96 (2H, t, ^3J = 7.2)	—	5.22 (2H, t, ^3J = 7.2)	7.3-7.5 (10 H, m)
3a	2.92; 3.24* (2H, $^2J_{AB}$ = 14.8)	—	4.91 (2H, t, $^3J_{AX}$ = $^3J_{BX}$ = 7.2)	7.3-7.5 (10 H, m)
2b	2.96; 2.97*[2] (2H, $^2J_{AB}$ = 14.0)	3.83 (3H)	5.19; 5.20*[3] (2H, $^3J_{AX}$ = $^3J_{BY}$ = 6.4; $^3J_{AY}$ = $^3J_{BX}$ = 8.1)	6.90 (2H, d ,^3J = 8.8); 7.3-7.4 (7H, m)
3b	2.92; 3.24*[2] (2H, $^2J_{AB}$ = 14.7)	3.83 (3H)	4.88 (1H, dd, $^3J_{AX}$ = 6.7, $^3J_{BX}$ = 8.2); 4.95 (1H, t, $^3J_{AY}$ = $^3J_{BY}$ = 7.5)	6.90 (2H, d, ^3J = 8.8); 7.3-7.4 (7H, m)
2c	2.97 (2H, t, ^3J = 7.2)	3.81 (6H)	5.17 (2H, t, ^3J = 7.2)	6.88 (4H, d, ^3J = 8.8); 7.32 (4H, d, ^3J = 8.8)
3c	2.90; 3.23* (2H, $^2J_{AB}$ = 14.8)	3.82 (6H)	4.93 (2H, dd, $^3J_{AX}$ = 7.0, $^3J_{BX}$ = 8.0)	6.89 (4H, d, ^3J = 8.8); 7.32 (4H, d, ^3J = 8.8)

* AB- part of the ABX_2 spin system.
*[2] AB- part of the ABXY spin system.
*[3] XY- part of the ABXY spin system.

Hence, bearing in mind the inversion of configuration of atom $C_{(3)}$ of the sultine and its retention at atom $C_{(5)}$ the bromination of the diastereomers *A*, *B* of sultine **1a** stereospecifically leads to the formation of the *dl*-isomer **2a** whereas the *C*, *D* diastereoisomers form the *meso* isomer **3a** and this can be illustrated using the following scheme:



The low activity of the *C*, *D* diastereomers of sultine **1a** with a *trans* configuration of the phenyl groups (see Scheme 1) can be explained by the fact that, in the limiting stage of the reaction (attack of the bromide anion at atom $C_{(3)}$ of the cyclic cation intermediate **6a** (see Scheme 2)) the approach of the nucleophile on either side of the ring is hindered by the steric effect of one of the phenyl groups whereas this can be avoided in the case of the *A*, *B* diastereomers with *cis*-arranged phenyl substituents.

The stereospecificity of the bromination of sultine **1a** allows one to exclude from consideration the possible formation of 1,2-diphenylcyclopropane as intermediate in this reaction. It is known that bromination of the latter under analogous conditions always leads to the formation of a mixture of the diastereomers **2a** and **3a** [8].

The introduction of a donor substituent at the $C_{(5)}$ position of the γ-sultine **1b** enables a change in the mechanism of the bromination in such a way that the intermediate **7b** (see Scheme 3) is able to split off a bromide anion and sulfur dioxide to form the stabilized carbocation **8b** which can then react with bromide anion to give an equimolar mixture of the diastereomers **2b** and **3b**.

In principle, carbocation **8b** can react with other (including weak) nucleophiles and this can explain the formation of minor amounts of the compounds **4b** and **5b** in the presence of the 1% ethanol in the chloroform (Table 1).

Scheme 3

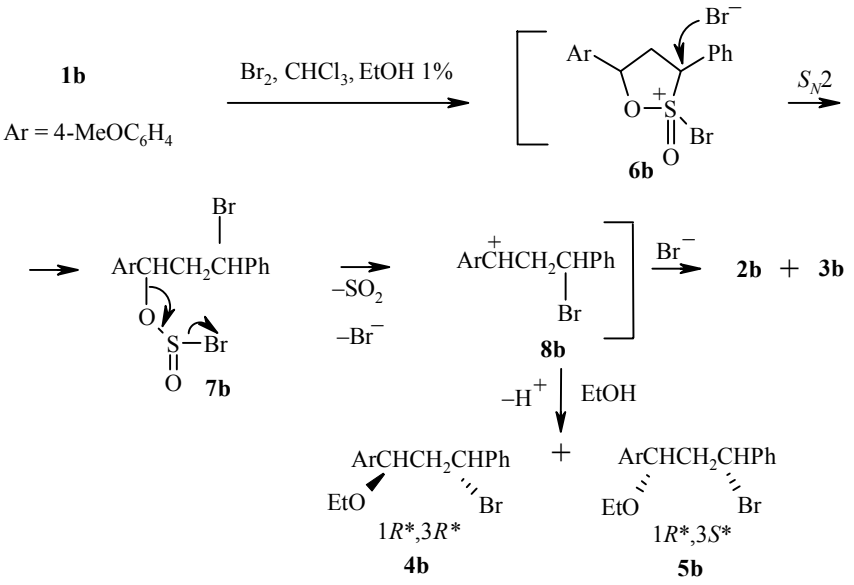
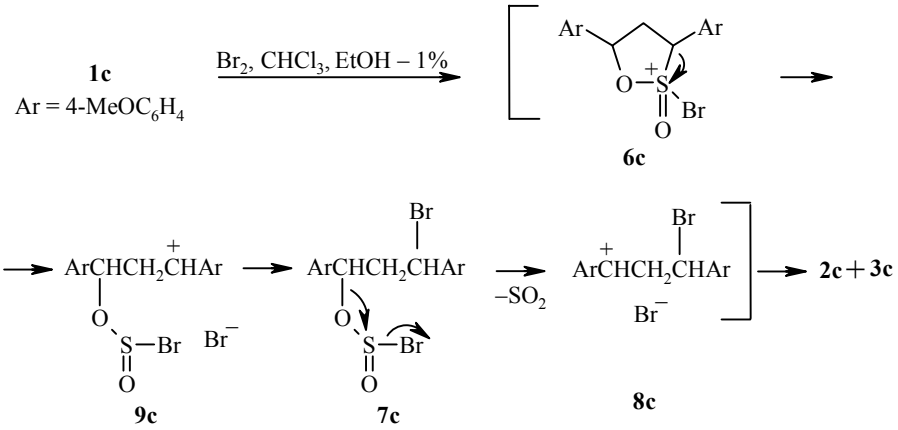


TABLE 3. ^{13}C NMR Spectra of Compounds **2a-c** and **3a-c**

Compound	Chemical shifts, δ, ppm				
	CH_2	CHBr	CH_3O	CH arom.	C arom.
2a	49.11	52.97	—	127.32; 128.67; 128.86	140.77
3a	48.94	51.77	—	127.28; 128.61; 128.77	140.18
2b	49.23	52.91; 53.17	55.29	114.18; 127.32	132.31; 132.93
3b	49.10	51.97; 52.12	55.29	127.37; 128.64; 128.71; 128.83	140.35; 140.82; 159.70; 159.72
2c	49.29	53.17	55.27	114.17	132.42; 132.92;
3c	49.19	52.35	55.27	128.64; 128.65	159.70; 159.72

The reaction of 3,5-bis(4-methoxyphenyl)-1,2-oxathiolane 2-oxide (**1c**) as a mixture of diastereomers *A-D* with bromine in chloroform with an admixture of ethanol leads to the formation of the 1,3-dibromo-1,3-bis(4-methoxyphenyl)propane as an equimolar mixture of *dl*- and *meso*-diastereomers **2c** and **3c** in quantitative yield. The reaction very likely occurs *via* formation of the stabilized carbocation **9c** at the stage of opening of the cyclic intermediate **6c**:



Hence it has shown that the nature of the substrate significantly affects the mechanism of bromination of γ-sultines and this leads to a fundamental difference in the stereochemical outcome.

EXPERIMENTAL

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were obtained on a Varian VXR 400 instrument using $CDCl_3$ at 30°C (see Tables 2 and 3).

3,5-Diaryl-1,2-oxathiolane 2-Oxides 1a-c were synthesized by reacting the corresponding 1,2-diarylcyclopropanes with sulfur dioxide according to the methods reported in [9, 10].

Bromination of 3,5-Diaryl-1,2-oxathiolane 2-Oxides. (General Method). A solution of bromine (0.3 mmol) in chloroform (15 ml) was added over 1 h with stirring to a solution of the sultine (0.3 mmol) in chloroform (15 ml) cooled to -15°C. After the completion of the addition of the bromine the mixture was stirred at -15°C for the time indicated in Table 1. It was then poured into water, the organic layer separated and washed with Na_2SO_3 solution to the disappearance of color, then twice with water, and dried over $CaCl_2$.

***dl*-1,3-Dibromo-1,3-diphenylpropane (2a).** Yield 70% as beige colored crystals; mp 113-114°C (decomp., $CHCl_3$–pentane). The ^1H NMR spectrum corresponded to that in [8].

***threo/erythro*-1,3-Dibromo-1-(4-methoxyphenyl)-3-phenylpropane (2b, 3b).** Yield 72% as beige crystals; mp 89-90°C ($CHCl_3$–pentane). Found, %: C 50.00; H 4.24. $C_{16}H_{16}Br_2O$. Calculated, %: C 50.03; H 4.20.

***dl/meso*-1,3-Dibromo-1,3-bis(4-methoxyphenyl)propane (2c, 3c).** Yield 87% as gray-violet colored crystals; mp 93°C ($CHCl_3$–pentane). Found, %: C 50.39; H 4.60. $C_{17}H_{18}Br_2O_2$. Calculated, %: C 49.30; H 4.38.

REFERENCES

1. J. F.King, P. de Mayo, C. L. McIntosh, K. Piers, and D. J. H. Smith, *Can. J. Chem.*, **48**, 3704 (1970).
2. J. F. King, A. Hawson, B. L. Huston, L. J. Danks, and J. Komery, *Can. J. Chem.*, **49**, 943 (1971).
3. F. Jung, N. K. Sharma, and T. Durst, *J. Amer. Chem. Soc.* **95**, 3420 (1973).
4. N. K. Sharma, F. de Reinach-Hirtzbach, and T. Durst, *Can. J. Chem.*, **54**, 3012 (1976).
5. R. M. J. Liskamp, H. J. M. Zeegers, and H. C. J. Ottenheijm, *J. Org. Chem.*, **46**, 5408 (1981).
6. E. V. Grigor'ev, A. V. Yatsenko, N. V. Novozhilov, L. G. Saginova, and V. S. Petrosyan, *Moscow State University Reports, Series 2, Khimiya,* **34**, 87 (1993).
7. V. M. Potapov, *Stereokhimiya*, Khimiya, Moscow (1988), p. 124.
8. R. T. LaLonde, P. B. Ferrara, and A. D. Debboli, *J. Org. Chem.*, **37**, 1094 (1972).
9. O. B. Bondarenko, A. V. Buevich, T. I. Voevodskaya, L. G. Saginova, and Yu. S. Shabarov, *Zh. Org. Khim.*, **24**, 1937 (1988).
10. N. V. Novozhilov, E. V. Grigor'ev, L. G. Saginova, and V. S. Petrosyan, *Moscow State University Reports, Series 2, Khimiya*, **33**, 502 (1992).