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RESEARCH ARTICLE

A new method for the synthesis of tetrahydrothiophene-*S*,*S*-dioxide derivatives: the Michael ring closure reaction between halomethyl (*E*)-β-styryl sulfones and CH-acids

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Bromomethyl and chloromethyl (*E*)-β-styryl sulfones enter a Michael ring closure reaction with sodium enolates prepared from dimethyl malonate, malononitrile and ethyl acetoacetate. The condensation results in formation of substituted tetrahydrothiophene-*S*,*S*-dioxides. It is a new instance of α-haloalkyl sulfones transformations, which are not connected with Ramberg–Bäcklund reaction.

Keywords: Halomethyl (*E*)-β-styryl sulfone; Michael ring closure reaction; Tetrahydrothiophene-*S*,*S*-dioxide derivatives; CH-acids

1. Introduction

It is common knowledge that α-haloalkyl sulfones upon interaction with bases are exposed to 1,3-dehydrohalogenation resulting in the formation of episulfones. Extrusion of sulfur dioxide from the latter leads to a preparation of alkenes. These tandem transformations, known as Ramberg–Bäcklund reactions, are widely used in the organic synthesis [1–3]. Alongside that, there are some examples of substituted α-haloalkyl sulfones by processes of 1,5- and 1,6-elimination competing or even in preference to 1,3-dehydrohalogenation. This results in the formation of five- or six-membered cyclic sulfones. In particular, as we showed earlier [4], hydroxyhalogenosulfones **1a**,**b**, if treated with base, besides product Ramberg–Bäcklund reaction **2**, give tricyclic sulfone **3** as result of 1,6-dehydrohalogenation (Scheme 1).

Other earlier examples concern transformations of α-halogenoalkyl-γ′-oxosulfones enolates **4** which may predominantly [5, 6] or exceptionally [7, 8] react in favor of 1,5-dehydrohalogenation with formation of 1,3-oxathiolane-*S*,*S*-dioxide derivatives **5**. Products of 1,3-dehydrohalogenation in this case are unsaturated ketones **6** (Scheme 2).

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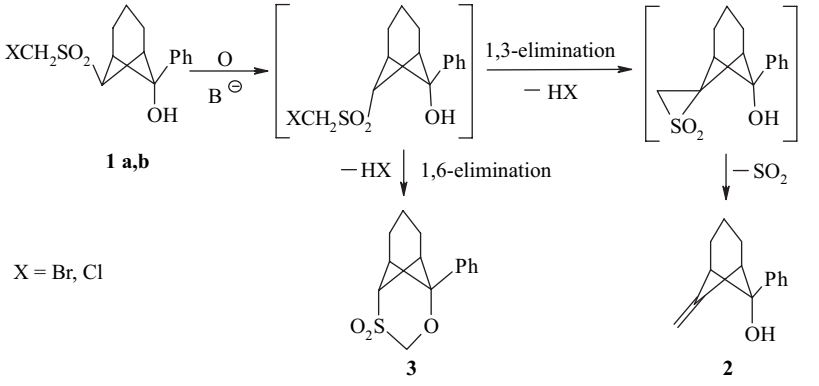
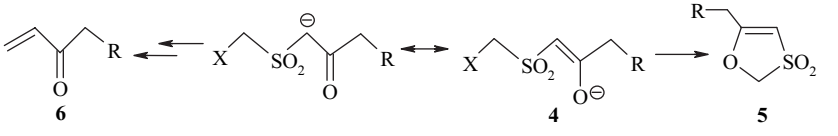
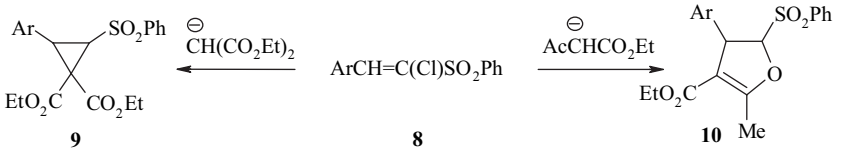


SCHEME 1



SCHEME 2

In each of the considered cases, cyclization of α-haloalkyl sulfones was carried out by means of C−O bond formation. At the same time it should be acknowledged that α-haloalkyl sulfones, containing a CH-acid fragment in the γ'- or δ'-positions also will be capable of 1,5- or 1,6-dehydrohalogenation with formation of C−C bond. Our assumption is that Michael adducts of halomethyl (*E*)-β-styryl sulfones **7a** or **7b** with CH-acid enolate could be the necessary precursor for realization of 1,5-cyclization. In this case, established examples of sulfonyl substituted cyclopropanes **9** and 2-sulfonyl substituted dihydrofurans **10**, both formed in the Michael Ring Closure reaction (MRCR) of β-(α-chlorostyryl) sulfones **8** with sodium malonate and sodium ethyl acetoacetate held out hope for a favorable outcome [9] (Scheme 3). In much the same fashion, alkyl α-bromovinyl sulfones, interacting with primary amines in DMSO in aza-MRCR, transform into 2-sulfonyl aziridines [10].



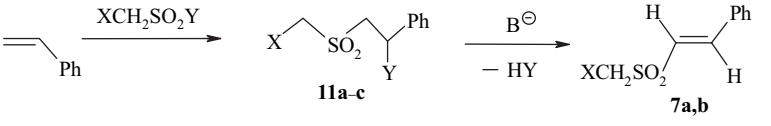
SCHEME 3

In the present work we report successful synthesis of tetrahydrothiophene derivatives in the MRCR using substrates **7a**,**b** and some CH-acids enolates.

2. Results and discussion

Halomethyl sulfones **7a** and **7b**, which were chosen as initial compounds, are described in the literature. Bromide **7a** was obtained from styrene by means of photochemical addition of

bromomethane sulfonyl bromide and subsequent 1,2-dehydrobromination of dibromide **11a** in full accordance with the published procedure [11]. Reproduction of **7b** chloride synthesis according to the Asscher-and-Vofsi method [12] from styrene and chloromethane sulfonyl chloride through intermediate dichloride **11c** resulted in a rather low yield of the desired product. We managed to increase the yield of unsaturated sulfone **7b** by means of photochemical reaction of styrene and chloromethane sulfonyl bromide and subsequent selective 1,2-dehydrobromination of **11b** by analogy to the literature [11] (Scheme 4). In the present work the spectral characteristics of halogenated sulfones **7b**, **11b** and **11c** are reported for the first time.

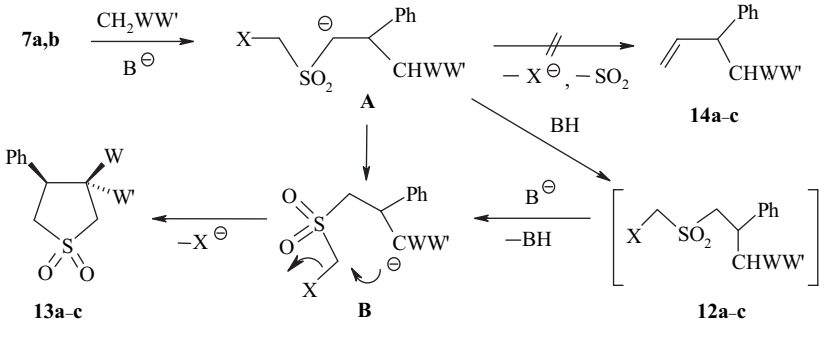


X = Br (**7a, 11a**), Cl (**7b, 11b,c**); Y = Br (**11a,b**), Cl (**11c**)

SCHEME 4

It was discovered that bromide **7a** reacts with double excess of dimethyl malonate and sodium methoxide in methanol in a sealed glass tube (67 h, 60 °C). The resultant substance was not the expected Michael adduct **12a**, but the product of its 1,5-cyclization–tetrahydrothiophene derivative **13a** (yield 55%). The formation of the latter in protic medium presumably follow the path: **A** → **12a** → **B** → **13a**. The result of the reaction is controlled by the higher stability of anion **B** in comparison with anion **A**, *cf.* [9], as well as by the thermodynamic benefit of formation of unstrained five-membered cyclic sulfone **13a**. An even higher yield of sulfone **13a** (76%) was obtained as a result of interaction between bromide **7a** and dimethyl malonate in an aprotic solvent (THF, 20 h, 20 °C) when sodium hydride was used as the base. In this case it can be assumed that intramolecular transfer of a proton into anion **A** with the formation of anion **B** is possible without participation of Michael adduct **12a**. Tetrahydrothiophene derivative **13a** was obtained with the use of sulfone **7b** in NaH–THF system as well. In this case the yield of product **13a** turned out to be less (55%) (Scheme 5).

Similarly the reaction between compound **7a** and malononitrile in NaH–THF system has resulted in a satisfactory yield (69.5%) of the cyclic sulfone **13b**. The interaction between



W = W' = CO2Me (**a**); W = W' = CN (**b**); W = CO2Et, W' = COMe (**c**)

SCHEME 5

unsaturated sulfone **7a** and ethyl acetoacetate under the same conditions eventually yielded cyclic sulfone **13c** in the form of a single diastereoisomer (yield based on reacted alkene **7a** comprises 61.2%). It is obvious that in these cases the conversion of bromide **7a** into products **13b**,**c** takes place by means of transfer of anion **A** to anion **B**-by-passing Michael adduct **12b**,**c**.

^{1}H and ^{13}C NMR spectra, as well as IR spectra are in complete accordance with the structures attributed to the compounds **13a**–**c**. Comparison of ^{1}H NMR spectra of compounds **13a** and **13c** allows one to assign the configuration of **13c** as one where the CO_2Et and Ph groups are in *cis*-position to each other. Such a configurational assignment is based on both the existing differences in chemical shifts of CO_2Me group protons and ethoxycarbonyl group methylenic protons (∼0.45 ppm), and the observation of a difference in chemical shifts of protons of two methoxycarbonyl groups in **13a** (0.44 ppm), most likely caused by shielding effect of phenyl on the opposite CO_2Me group. It is suggested that in the assigned configuration for **13c**, the chemical shift of the diastereotopic protons of the fragment OCH_2 should resonate near 3.90 ppm, and this is indeed observed. None of the examples of halomethyl sulfones **7a**,**b** chemistry described herein proceed to form alkenes **14a**–**c**, products that may be expected under the Ramberg–Bäcklund reaction. Thus, the condensation that we carried out should be considered as MRCR of halomethyl β-styryl sulfones yielding tetrahydrothiophene-*S*,*S*-dioxide derivatives.

3. Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 (300.130 and 75.468 MHz respectively) spectrometer in $CDCl_3$ using TMS as an internal standard (δ, ppm). IR spectra were measured by a Fourier Spectrometer InfraLum FT-02 (KBr pellets). Analytical TLC was performed by Silufol UV–254 plates, eluent: hexane – ethyl ether, 1:2, developer: iodine. Column chromatography was performed on silica gel L 40/100 μ, eluent light petroleum ether–ethyl ether, 2:1. bromomethyl (*E*)-2-phenylethenyl sulfone **7a**, mp 136–137 °C ($CHCl_3$), was prepared according to the literature procedure [11].

3.1 *Chloromethyl 2-bromo-2-phenylethyl sulfone 11b*

Sulfone **11b** with the yield of 69% was prepared from styrene and chloromethane sulfonyl bromide [6] according to the procedure [11] described for the sulfone **11a**. Colorless crystals (mp 97–98 °C from $CHCl_3$). ^{1}H NMR δ (ppm): 7.47–7.53 (m, 2H) and 7.38–7.47 (m, 3H), $H_{arom.}$; 5.40 (dd, J = 6.2 and 8.8 Hz, 1H), C<u>H</u>Br; 4.20 (dd, J = 8.8 and 15.4 Hz, 1H) and 4.02 (ddd, J = 0.9, 6.2 and 15.4 Hz, 1H), CH_2; 4.30 (dd, J = 0.9 and 12.3 Hz, 1H) and 3.57 (d, J = 12.3 Hz, 1H), C<u>H$_2$</u>Cl. ^{13}C NMR δ (ppm): 138.6, 130.3, 129.7 and 128.1, $C_{arom.}$; 57.9; 56.8; 43.5 (C<u>H</u>Br). IR ν (cm^{-1}): 447m, 503m, 700v.s, 766m, 868s, 913m, 1112s, 1140v.s, 1318m, 1340s. Calcd (%) for $C_9H_{10}BrClO_2S$ (297.597): C, 36.32; H, 3.39. Found: C, 36.44; H, 3.45.

3.2 *Chloromethyl 2-chloro-2-phenylethyl sulfone 11c*

The compound **11c** was prepared by Asscher-and-Vofsi method [12] from styrene and chloromethane sulfonyl chloride with the yield of 58%. Colorless crystals (mp 84–85 °C from CCl_4). ^{1}H NMR δ (ppm): 7.32–7.55 (m, 5H), $H_{arom.}$; 5.40 (dd, J = 5.5 and 8.0 Hz, 1H), C<u>H</u>Ph; 4.50 (d, J = 12.2 Hz, 1H) and 3.92 (d, J = 12.2 Hz, 1H), CH_2Cl; 4.04 (dd, J = 8.0 and 12.0 Hz, 1H) and 3.82 (dd, J = 5.6 and 12.0 Hz, 1H), CH_2. ^{13}C NMR δ (ppm): 137.7,

129.7, 129.2 and 127.1, $C_{arom.}$; 57.2; 56.5; 54.9. IR ν (cm^{-1}): 455s, 507m, 708v.s, 769s, 868s, 1112m, 1140v.s (SO_2, ν_s), 1279m, 1320m, 1340s (SO_2, ν_{as}). Calcd (%) for $C_9H_{10}Cl_2O_2S$ (253.146): C, 42.70; H, 3.98. Found: C, 42.61; H, 3.93.

3.3 *Chloromethyl (E)-2-phenylethenyl sulfone 7b*

The chlorosulfone **7b** with the yield of 82% was prepared according to the procedure [11] described for sulfone **7a** by dehydrobromination of dihalide **11b** under the action of Na_2CO_3 in aqueous dioxane (20 h, 20 °C). Dehydrochloration of the dichloride **11c** with Et_3N in benzene (1 h, 20 °C) according to the procedure [12] resulted in **7b** with the yield of 71%. Colorless crystals (mp 99–100 °C from $CHCl_3$); lit. [12]: mp 103–104 °C (benzene). ^{1}H NMR δ (ppm): ^{1}H NMR δ (ppm): 7.43–7.60 (m, 5H), $H_{arom.}$; 7.72 (d, J = 16.0 Hz, 1H) and 6.92 (d, J = 16.0 Hz, 1H), C<u>H</u>SO_2 and C<u>H</u>Ph); 4.53 (s, 2H), CH_2Cl. ^{13}C NMR δ (ppm): 148.4 and 121.1, C=C; 131.9, 131.7, 129.2 and 128.9, $C_{arom.}$; 57.7 (CH_2). IR ν (cm^{-1}): 481s, 618m, 744s, 973m, 1133v.s (SO_2, ν_s), 1307s (SO_2, ν_{as}), 1392m, 1622m (C=$C_{olefin.}$), 3014w, 3071w. Calcd (%) for $C_9H_9ClO_2S$ (216.685): C, 49.89; H, 4.19. Found: C, 50.12; H, 4.23.

3.4 *Dimethyl 1,1-dioxo-4-phenyltetrahydro-3H-1λ^6-thiophene-3,3-dicarboxylate 13a*

3.4.1 Method A. Dimethyl malonate (1.0 g, 7.6 mmol) and compound **7a** (1.0 g, 3.8 mmol) were added to the solution of sodium methylate in methanol, which was prepared from dissolving sodium (0.175 g, 7.6 mmol) in dry methanol (8 ml). The mixture was heated at 60 °C for 67 h in a sealed glass tube. Then methanol was removed under water aspirator vacuum, and water (30 ml) was added to the residue. The crude solid product was filtered off, washed with water and a small amount of ether, and then air-dried. Recrystallization ($CHCl_3$–CCl_4) gave 0.65 g (55%) of compound **13a**, colorless crystals (mp 130–131 °C). ^{1}H NMR δ (ppm): 7.38 (br. s, 5H), $H_{arom.}$; 4.66 (t, J = 7.3 Hz, 1H), H^4; 4.05 (d, J = 14 Hz, 1H) and 3.67 (d, J = 14 Hz, 1H), H^2; 3.86 (s, 3H), *trans*-CO_2Me and 3.42 (s, 3H), *cis*-CO_2Me; 3.60–3.71 (m, 2H) H^5. ^{13}C NMR δ (ppm): 168.4 and 166.8 (OC=O); 136.1, 128.7, 128.4 and 128.2, $C_{arom.}$; 61.6 (C^3), 56.5, 55.6, 54.3, 53.5, 45.6. IR ν (cm^{-1}): 706m, 789m, 3012w, 1120s (SO_2, ν_s), 1146m, 1236m, 1310s (SO_2, ν_{as}), 1434m, 1728v.s (C=O), 1747s (C=O), 2960w. Calcd (%) for $C_{14}H_{16}O_6S$ (312.339): C, 53.84; H, 5.16. Found: C, 53.79; H, 5.24.

3.4.2 Method B. Sodium hydride (0.17 g of 60% suspension in mineral oil, 4.2 mmol) was freed of mineral oil by washing and decanting with hexane. The system was evacuated to remove the solvent and the vacuum was broken by introduction of argon and subsequent addition of THF (5 ml). Dimethyl malonate (0.5 g, 3.8 mmol) in THF (10 ml) was added dropwise at 5 °C for 10 min at stirring. The stirring was continued for 1 h at 20 °C. After dropwise addition of compound **7a** (1.0 g, 3.8 mmol) in THF (10 ml), stirring was continued at 20 °C for 20 h. The mixture was quenched with water (250 ml) and neutralized with aqueous HCl (1:1). The crude solid product was filtered off, washed with water and air-dried. Recrystallization ($CHCl_3$–CCl_4) gave 0.9 g (76%) of compound **13a**, colorless crystals (mp 129–130 °C).

3.4.3 Method C. To the solution, which was prepared from dimethyl malonate (0.57 g, 3.8 mmol) and NaH (0.17 g of 60% suspension in mineral oil, 4.2 mmol) in THF (15 ml), the sulfone **7b** (0.82 g, 3.8 mmol) was added at 20 °C. The reaction mixture was stirred at room temperature for 24 h and was worked up as stated above. The resulting product was purified on a silica gel column to give 0.64 g (54%) compound **13a** (mp 129–130 °C).

3.5 *1,1-Dioxo-4-phenyltetrahydro-3H-1λ⁶-thiophene-3,3-dicarbonitrile 13b*

The compound **12b** was prepared according to the method *B* from sulfone **7a** and malononitrile with the yield of 69.5% (mp 236–237 °C from dioxane–ether). ^{1}H NMR in CD_3SOCD_3 δ (ppm): 7.55–7.64 (m, 2H) and 7.45–7.55 (3H), $H_{arom.}$; 4.65 (dd, J = 8.0 and 12.6 Hz, 1H), H^4; 4.59 (d, J = 13.1, 1H) and 4.34 (d, J = 13.1, 1H), H^2; 4.06 (dd, J = 8.0 and 13.8 Hz, 1H) and 3.98 (dd, J = 12.6 and 13.8 Hz, 1H), H^5. ^{13}C NMR in CD_3SOCD_3 δ (ppm): 132.8, 130.6, 129.9 and 129.5, $C_{arom.}$; 113.6 and 113.2 (CN); 58.5; 53.0 (C^3); 48.6, 40.4. IR ν (cm^{-1}): 529s, 700s, 770m, 1140v.s (SO_2, ν_s), 1231m, 1262s, 1306s (SO_2, ν_{as}), 1339s, 2253w (CN), 2967m, 3029m. Calcd (%) for $C_{12}H_{10}N_2O_2S$ (246.286): C, 58.52; H, 4.09; N, 11.37. Found: C, 58.54; H, 4.09; N, 11.32.

3.6 *Ethyl t-3-acetyl-1,1-dioxo-4-phenyltetrahydro-1H-1λ⁶-thiophene-c-3-carboxylate 13c*

Sodium hydride (0.18 g of 60% suspension in mineral oil, 4.6 mmol) was washed and dried as in the preceding run: ethyl acetoacetate (0.54 g, 4.2 mmol) was added in THF (10 ml) dropwise at 5 °C for 10 min at stirring, and the resulting solution was stirred at 45 °C for 3 h. Then the solution was cooled and the sulfone **7a** (1.0 g, 3.8 mmol) in THF (10 ml) was added to it and the stirring was continued for 20 h at room temperature. The reaction mixture was worked up as stated above. The crude solid product (0.81 g) was purified on a silica gel column to get the unconvereted sulfone **7a** (0.2 g) and the compound **12c** (0.58 g, 49%). Colorless crystals (mp 145–146 °C from hexane–ether). ^{1}H NMR δ (ppm): 7.34 (br. s, 5H), $H_{arom.}$; 4.66 (t, J = 7.6 Hz, 1H), H^4; 4.09 (d, J = 14.3 Hz, 1H) and 3.48 (d, J = 14.3 Hz, 1H), H^2; 3.98 (dq, J = 7.6 and 10.9 Hz, 1H) and 3.78 (dq, J = 7.6 and 10.9 Hz, 1H), OCH_2; 3.61 (d, J = 7.6 Hz, 2H), H^5; 2.25 (s, 3H), COMe; 1.01 (t, J = 7.6 Hz, 3H), Me. ^{13}C NMR δ (ppm): 198.4 (C=O); 166.8 (OC=O); 136.5, 128.6, 128.3 and 128.2, $C_{arom.}$; 67.3 (C^3); 62.6 (OCH_2); 56.0, 54.2, 26.3 (COMe), 44.1, 13.3 (Me). IR ν (cm^{-1}): 702m, 1124s, 1155s (SO_2, ν_s), 1248s, 1309s (SO_2, ν_{as}), 1330s, 1368w, 1712v.s (C=O), 1734m (C=O), 3002w. Calcd (%) for $C_{15}H_{18}O_5S$ (310.366): C, 58.05; H, 5.85. Found: C, 58.11; H, 5.82.

References

[1] L.A. Paquette. *Org. React.*, **25**, 1 (1977).
[2] R.J.K. Taylor, G. Casy. *Org. React.*, **62**, 357 (2003).
[3] E. Block, H.R. Jeon, D. Putman, S.Z. Zhang. *Tetrahedron*, **60**, 7525 (2004).
[4] V.A. Vasin, E.V. Romanova, S.G. Kostryukov, V.V. Razin. *Mendeleev Commun.*, 122 (1998).
[5] E. Block, M. Aslam, R. Iyer, J. Hutchinson. *J. Org. Chem.*, **49**, 3664 (1984).
[6] E. Block, M. Aslam, V. Eswarakrishnan, K. Gebreyes, J. Hutchinson, R. Iyer, J.A. Laffitte, A. Wall. *J. Amer. Chem. Soc.*, **108**, 4568 (1986).
[7] K. Dickoré. *Liebigs Ann. Chem.*, **671**, 135 (1964).
[8] U. Jacobsson, T. Norin. *J. Org. Chem.*, **39**, 2722 (1974).
[9] I. Yamamoto, T. Sakai, K. Ohta, K. Matsuzaki, K. Fukuyama. *J. Chem. Soc., Perkin Trans. PT. 1.*, 2785 (1985).
[10] J.M. Gaillot, R. Vessiere. *Can. J. Chem.*, **55**, 3190 (1977).
[11] V. A.Vasin, I.Yu. Bolusheva, V.V. Razin. *Sulfur Lett.*, **26**, 101 (2003).
[12] M. Asscher, D. Vofsi. *J. Chem. Soc. C.*, 4962 (1964).