Synthesis of 5-Aryl-4,6-bis[alkoxycarbonyl]-1,3-dithiane 1,1,3,3-Tetroxides

V. BALIAH, S. PREMA

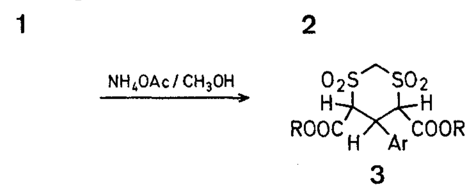
Department of Chemistry, Annamalai University, Annamalainagar - 608002, India

C. B. JAWAHARSINGH, KN. CHOCKALINGAM, R. JEYARAMAN*

Department of Chemistry, The American College, Madurai - 625002, India

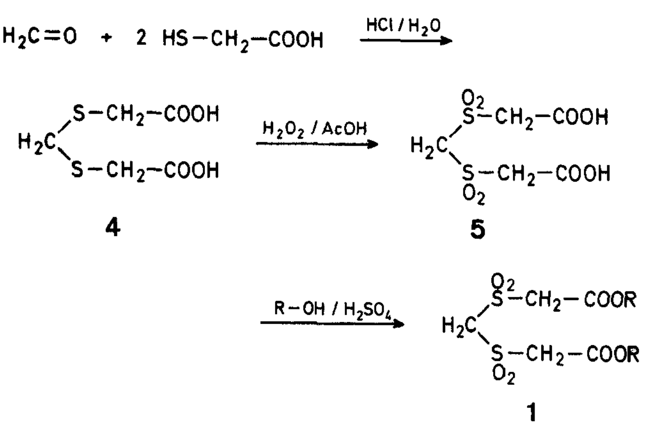
Many 1,3-dithianes have been synthesized and their use in the synthesis of new products has been widely studied[1,2]. Most of the 1,3-dithianes were obtained from propane-1,3-dithiol[3] and aldehydes or ketones and therefore possess substituents at the 2-position only. Fewer 1,3-dithianes are known which have substituents at other positions[4,5]. We report here a new facile synthesis of 5-aryl-4,6-bis[alkoxycarbonyl]-1,3-dithiane 1,1,3,3-tetroxides via a condensation process.

Dimethyl or diethyl methylene-bis-sulfonylacetate (**1**) was condensed with aromatic aldehydes (**2**) in the presence of ammonium acetate in ethanol to yield the 1,3-dithiane 1,1,3,3-tetroxides (**3**). Although the reaction was performed in a manner analogous to that used for the preparation of 1,4-thiazines[6,7] with the expectation of obtaining eight-membered rings, *only six-membered ring compounds were formed because of their greater stability and ease of formation.*



*The structures of the new compounds **3** were established on the basis of microanalyses, mass-, I.R.-, and ^{1}H-N.M.R.-spectral data.*

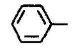
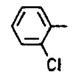
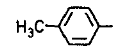
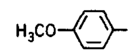
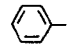
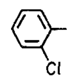
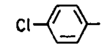
The starting materials **1** were prepared from formaldehyde and mercaptoacetic acid by a three-step sequence using modified known procedures, the yields of **1** being better than those reported in the literature[8].



Methylenedithiodiacetic Acid (4):

To a mixture of paraformaldehyde (30 g, 75 ml of 40% solution, 1 mol) and mercaptoacetic acid (184 g, 205 ml of 90% solution, 2 mol) is added concentrated hydrochloric acid (10 ml), the mixture is stirred at 40-50 °C for 2 h and at 90-100 °C for 2 h, and is then kept in a refrigerator for 2 days. The crystalline product is isolated by suction and recrystallized from water; yield: 145-150 g (75-80%); m.p. 128-130 °C (Ref.[9], m.p. 128.5-129.5 °C).

Table 1. 5-Aryl-4,6-bis[alkoxycarbonyl]-1,3-dithiane 1,1,3,3-Tetroxides **(3)**

3	R	Ar	Solvent[a]	Yield [%]	m.p. [°C]	Molecular formula[b]
a	CH_3		methanol	30-35	180-181°	$C_{14}H_{16}O_8S_2$ (376.4)
b	CH_3		methanol	40-45	183-184°	$C_{14}H_{15}ClO_8S_2$ (410.8)
c	CH_3		methanol	30-35	175-176°	$C_{15}H_{18}O_8S_2$ (390.4)
d	CH_3		methanol	30-35	157-160°	$C_{15}H_{18}O_9S_2$ (406.4)
e	C_2H_5		ethanol	35-40	155-156°	$C_{16}H_{20}O_8S_2$ (404.4)
f	C_2H_5		ethanol	35-40	151-152°	$C_{16}H_{19}ClO_8S_2$ (438.9)
g	C_2H_5		ethanol	30-35	178-180°	$C_{16}H_{19}ClO_8S_2$ (438.9)

[a] Solvent used in reaction and for recrystallization.

[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.21; H, ±0.20.

Table 2. ^{1}H-N.M.R. ($CDCl_3$/TMS) Spectral Data of Compounds **2b, d, f**[a]; δ [ppm]

2	$COOC\underline{H}_3$ or $COOC\underline{H}_2C\underline{H}_3$	$Ar-OC\underline{H}_3$	$C\underline{H}-Ar$	$SO_2-C\underline{H}_2-SO_2$ ax	$SO_2-C\underline{H}_2-SO_2$ eq	$C\underline{H}-COOR$	H_{arom}
b	3.65 (s)	—	4.3 (m)	4.55, 4.65 (2d, J=13 and 3 Hz)	5.00, 5.15 (2d, J=13 and 3 Hz)	5.25, 5.50 (2d, J=14 Hz)	6.8-7.6 (m)
d	3.7, 3.8 (2s)	3.6 (s)	4.1-4.4 (m)	4.4-4.6 (m)	4.4-4.6 (m)	5.15, 5.4 (2d, J=14 Hz)	6.8-7.2 (dd)
f	0.8-1.1 (t); 3.9-4.3 (q)	—	3.9-4.3 (m)	4.55, 4.75 (2d, J=13 and 3 Hz)	4.85, 5.10 (2d, J=13 and 2 Hz)	5.25, 5.45 (2d, J=14 Hz)	6.9-7.5 (m)

[a] Compounds **2a, c, e, g** are not sufficiently soluble in $CDCl_3$. Their spectra show prominent signals only.

Methylene-bis-sulfonylacetic Acid (5):

To a stirred solution of methylenedithiodiacetic acid (**4**; 19.6 g, 0.1 mol) in acetic acid (50-80 ml), 30% hydrogen peroxide (85 ml, 0.75 mol) is added in small portions while the temperature of the mixture is kept at 20-30 °C. After the addition is complete the mixture is heated on a steam bath with stirring for 30 min, and then cooled to 0 °C for one day. The needle-like crystals of **5** are isolated and recrystallized from ethanol; yield: 22-23 g (85-90%); m.p. 212-214 °C (Ref.[10], m.p. 209-210 °C).

Dimethyl Methylene-bis-sulfonylacetate (1, R = CH_3):

Concentrated sulfuric acid (5 ml) is added to a solution of methylene-bis-sulfonylacetic acid (**5**; 26 g, 0.1 mol) in absolute methanol (500 ml) and the mixture is heated to reflux for 5 h. Part of the solvent is then evaporated in vacuo and the residue is poured onto crushed ice (500 g). The solid which separates is isolated by suction, washed with water, and recrystallized from methanol/ethyl acetate; yield: 26 g (90%); m.p. 92-94 °C (Ref.[11], m.p. 90-94 °C).

Diethyl Methylene-bis-sulfonylacetate (**1**, R = C_2H_5) is prepared in an analogous manner; yield: 85%; m.p. 72-74 °C (Ref.[11], m.p. 73-74 °C).

5-Aryl-4,6-bis[alkoxycarbonyl]-1,3-dithiane 1,1,3,3-Tetroxides (3); General Procedure:

A mixture of the dialkyl methylene-bis-sulfonylacetate (**1**; 0.1 mol), the aromatic aldehyde (**2**; 0.2 mol), ammonium acetate (12 g, 0.15 mol), and methanol or ethanol (200-400 ml) is heated under reflux for 6 h. The solvent is stripped off partially and ice-cold water (100 ml) is

0039-7881/81/1232-0995 $ 03.00

added. The solid which separates is isolated by suction and recrystallized from methanol or ethanol.

This work was carried out with the financial support from the University Grants Commission, New Delhi and the Research and Development Committee of the American College. The authors thank the Director, Central Drug Research Institute, Lucknow, for recording the ^{1}H-N.M.R. and mass spectra.

Received: March 3, 1981
(Revised form: June 11, 1981)

---

* Address for correspondence: Department of Chemistry, Clemson University, Clemson, South Carolina 29631, U.S.A.

[1] E. J. Corey, D. Seebach, *Angew. Chem.* **77**, 1134 (1965); *Angew. Chem. Int. Ed. Engl.* **4**, 1075 (1965).

[2] D. Seebach, *Synthesis* **1969**, 17.

[3] E. L. Eliel, V. S. Rao, F. G. Riddell, *J. Am. Chem. Soc.* **98**, 3583 (1976).

[4] E. L. Eliel, A. A. Hartmann, A. G. Abatjoglou, *J. Am. Chem. Soc.* **96**, 1807 (1974).

[5] Y. Y. Samitov et al., *Zh. Org. Khim.* **10**, 648 (1974); *C. A.* **80**, 132652 (1974).

[6] V. Baliah, T. Rangarajan, *J. Chem. Soc.* **1954**, 3068.

[7] V. Baliah, T. Rangarajan, *J. Org. Chem.* **26**, 969 (1961).

[8] T. P. Ahern, H. O. Fong, R. F. Langler, P. M. Mason, *Can. J. Chem.* **58**, 878 (1980).

[9] B. Holmberg, K. Mattison, *Justus Liebigs Ann. Chem.* **353**, 123 (1907).

[10] W. A. W. Cummings, *J. Chem. Soc.* **1958**, 2058.

[11] L. A. Paquette, R. W. Mouser, *J. Am. Chem. Soc.* **93**, 944 (1971).

0039-7881/81/1232-0996 $ 03.00