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A Convenient Method for the Introduction of 1,3-Dithiolan-2-yl Group into Active Methylene Compounds

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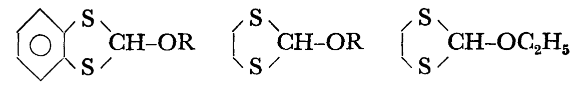
Synopsis. The reaction of 2-ethoxy-1,3-dithiolane with a variety of active methylene compounds in the presence of a zinc chloride catalyst was investigated. By this reaction the introduction of a 1,3-dithiolan-2-yl group into the active methylene compounds was achieved. Some behavior of the 1,3-dithiolan-2-yl derivative of ethyl acetoacetate, which is one of the newly obtained compounds, was also briefly examined.

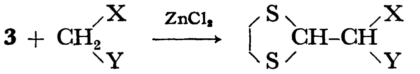
Recently, 2-alkoxy-1,3-benzodithioles (**1**) have become readily available by means of the action of benzyne on carbon disulfide in the presence of alcohols,[1] and their behavior toward carbon nucleophiles has been studied.[2,3]



1 **2** **3**

In contrast, no description of the chemistry of 2-alkoxy-1,3-dithiolanes (**2**), the corresponding saturated system of **1**, is to be found in the literature, except for our own earlier report,[4] which involves the synthesis of 2-ethoxy-1,3-dithiolane (**3**) and its reaction with *n*-BuLi.

We wish now to report the reaction of **3** with a variety of active methylene compounds (**4**), by which the introduction of a 1,3-dithiolan-2-yl group into **4** was conveniently achieved.

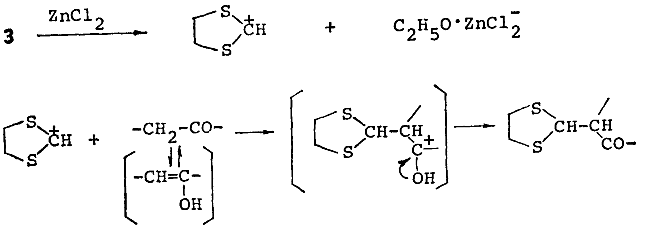


4 **5**

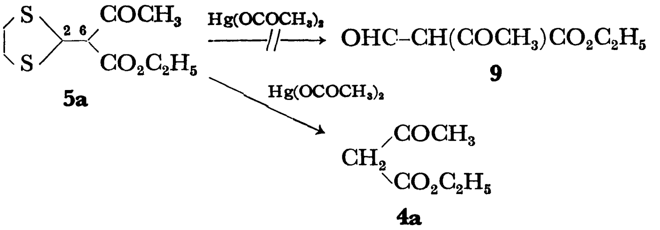
a: $X=COCH_3$, $Y=CO_2C_2H_5$
b: $X=COCH_3$, $Y=CO_2CH_3$
c: $X=Y=CO_2C_2H_5$
d: $X=Y=CO_2CH_3$
e: $X=Y=COCH_3$
f: $X=CN$, $Y=CO_2C_2H_5$
g: $X=COC_6H_5$, $Y=CO_2C_2H_5$

The reaction of **4** with **3** proceeded smoothly without a solvent under the catalytic action of a metal halide such as zinc chloride or iron(III) chloride, and 1,3-dithiolan-2-yl derivatives of **4** (**5**) could be isolated in quite good yields (Table 1).

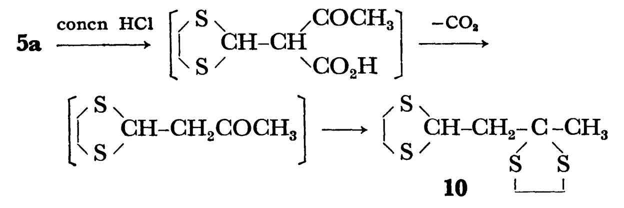
The reaction may involve the initial loss of the exocyclic ethoxyl group of **3** to give the 1,3-dithiolan-2-ium ion and its subsequent attack on the active methylene compound.



In order to investigate the possibility of the synthesis of a novel class of compound (**9**) with three different carbonyl groups at the same carbon atom, we examined the reaction of **5a** with mercury(II) acetate[6] under conditions similar to those employed for the cleavage of cyclic ethylene thioacetals.[7] However, the product thus obtained was ethyl acetoacetate, and no trace of **9** was isolated. This means that the reaction proceeded only with an exclusive bond fission between 2-C and 6-C.



On the other hand, the hydrolysis of **5a** with a large excess of boiling conc. HCl for 5—6 h gave a bis(1,3-dithiolan-2-yl) derivative, acetoacetaldehyde bis(ethylene thioacetal) (**10**), in a 48% yield[mp 31—33 °C (hexane) (lit,[8] 30—32 °C)], but formylacetone or its derivative, which seems to be simultaneously obtainable, could not be detected.

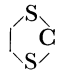
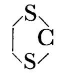


Experimental

Reaction of 2-Ethoxy-1,3-dithiolane (3) with Active Methylene Compounds (4). General Procedure: A mixture of 33 mmol of **3**, 39—40 mmol of an active methylene compound, and *ca.* 15 mmol of a catalyst was stirred at room temperature for 24 h, with the exclusion of any moisture, and then poured into a large quantity of an aqueous sodium carbonate solution. The organic layer was separated, combined with an ethereal extract of the aqueous phase, and dried ($MgSO_4$), and the ether was removed. The oily residue was distilled *in vacuo* to afford the desired product. The product can be purified further by column chromatography if necessary. Only in the case of the reaction with ethyl benzoylacetate, the removal of ether and the excess ethyl benzoylacetate leave a solid residue, which was purified by recrystallization from ethanol.

Reaction of 1,3-Dithiolan-2-yl Derivative of Ethyl Acetoacetate (5a) with Mercury(II) Acetate. To a solution of 5 g (21 mmol) of **5a** in 200 ml of acetone, we added 50 ml of water,

TABLE 1. REACTIONS OF 2-ETHOXY-1,3-DITHIOLANE (**3**) WITH VARIOUS ACTIVE METHYLENE COMPOUNDS (**4**)

Run	Active methylene compound	Catalyst	Products[a] and yields[b] (%)		
1	**4a**	$ZnCl_2$	**5a**[c]	(70),	 $(CH_3)CH_2CO_2C_2H_5$[d] (trace) **6**
2	**4a**	$ZnBr_2$	**5a**[c]	(72),	**6**[d] (trace)
3	**4a**	$AlCl_3$	**5a**[c]	(14),	**6**[d] (39)
4	**4a**	$FeCl_3$	**5a**[c]	(65),	**6**[d] (26)
5	**4b**	$ZnCl_2$	**5b**[e]	(68),	 $(CH_3)CH_2CO_2CH_3$[f] (trace) **7**
6	**4c**	$ZnCl_2$	**5c**[g]	(49)	
7	**4d**	$ZnCl_2$	**5d**[h]	(53)	
8	**4e**	$ZnCl_2$	**5e**[i]	(39),	 $(CH_3)CH_2COCH_3$[j] (trace) **8**
9[k]	**4f**	$ZnCl_2$	**5f**[l]	(24)	
10	**4g**	$ZnCl_2$	**5g**[m]	(60)	

a) Satisfactory elemental analyses were obtained for all new compounds. b) Yields were based upon **3**, and referred to isolated ones. c) Bp 137.5—139.5 °C/2 mmHg. NMR ($CDCl_3$): δ 1.30 (t, 3H), 2.30 (s, 3H), 3.23 (s, 4H), 3.87 (d, 1H), 4.22 (q, 2H), 5.04 (d, 1H). d) The structure proposed for **6** is in agreement with the results of elemental analysis, the mass spectra, and the NMR spectroscopic data. Bp 99—103 °C/1.5 mmHg (lit,[5] 86 °C/0.1 mmHg. NMR ($CDCl_3$): δ 1.28 (t, 3H), 1.93 (s, 3H), 3.04 (s, 2H), 3.36 (s, 4H), 4.18 (q, 2H). e) Bp 136.5—139.5 °C/2 mmHg. NMR ($CDCl_3$): δ 2.30 (s, 3H), 3.24 (s, 4H), 3.78 (s, 3H), 3.91 (d, 1H), 5.06 (d, 1H). f) The structure proposed for **7** is in agreement with the results of elemental analysis, the mass spectra, and the NMR spectroscopic data. Bp 94—97 °C/2 mmHg. NMR ($CDCl_3$): δ 1.90 (s, 3H), 3.03 (s, 2H), 3.35 (s, 4H), 3.69 (s, 3H). g) Bp 138—139 °C/1.5 mmHg. NMR ($CDCl_3$): δ 1.24 (t, 3H), 3.23 (s, 4H), 3.62 (d, 1H), 4.23 (q, 2H), 5.03 (d, 1H). h) Bp 137—138 °C/2 mmHg. NMR ($CDCl_3$): δ 3.26 (s, 4H), 3.67 (d, 1H), 3.79 (s, 3H), 5.03 (d, 1H). i) Purified by column chromatography on silica gel (eluent 50% ether–50% hexane). Mp 50—52.5 °C (ethanol). NMR ($CDCl_3$): δ 2.26 (s, 3H), 3.28 (s, 4H), 4.06 (d, 1H), 5.16 (d, 1H). j) The structure proposed for **8** is in agreement with the results of elemental analysis, the mass spectra, and the NMR spectroscopic data. Bp 142—145 °C/18 mmHg. NMR ($CDCl_3$): δ 1.86 (s, 3H), 2.17 (s, 3H), 3.20 (s, 2H), 3.32 (s, 4H). k) The reaction was performed at 90—100 °C for 8 h. l) Bp 140—142 °C/2 mmHg. NMR ($CDCl_3$): δ 1.30 (t, 3H), 3.38 (broad s, 4H), 4.07 (d, 1H), 4.32 (q, 2H), 5.07 (d, 1H). m) Mp 46—49 °C (ethanol). NMR ($CDCl_3$): δ 1.16 (t, 3H), 3.21 (s, 4H), 4.19 (q, 2H), 4.74 (d, 1H), 5.41 (d, 1H), 7.40—8.33 (m, aromatic 5H).

15 g (47 mmol) of mercury(II) acetate, and 15 g (87 mmol) of cadmium carbonate.[9] This mixture was stirred for 72 h at an ambient temperature, and then the mixture was filtered. After the removal of acetone from the filtrate, the residue was taken up in ether. The evaporation of the solvent under reduced pressure afforded 0.96 g (35%) of ethyl acetoacetate.

References

1) J. Nakayama, *Synthesis*, **1975**, 38.

2) J. Nakayama, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 540.

3) S. Ncube, A. Pelter, and K. Smith, *Tetrahedron Lett.*, **1977**, 255.

4) S. Tanimoto, T. Miyake, and M. Okano, *Bull. Inst. Chem. Res. Kyoto Univ.*, in press.

5) J. F. Harris, Jr., U. S. Patent 2839445; *Chem. Abstr.*, **52**, 17289 (1958).

6) By the employment of mercury(II) chloride an unidentified white solid was isolated.

7) G. P. Pollini, A. Barco, M. Anastasia, and G. Traverso, *Chem. Abstr.*, **69**, 58862y (1968).

8) R. H. Shapiro, T. E. McEntee Jr., and D. L. Coffen, *Tetrahedron*, **24**, 2809 (1968).

9) Under similar conditions, but with cadmium carbonate omitted, almost the same yield of ethyl acetoacetate was obtained; *i.e.*, the cadmium carbonate is not essential to the reaction.