SULFOLANYLATION OF MALONIC ACID DERIVATIVES

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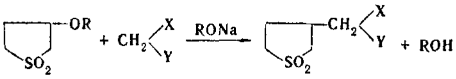
β-Alkoxysulfolanes in the presence of equimolar amounts of sodium ethoxide react with malonic acid derivatives in which the hydrogen atom of the methylene group is activated by CN, COOR, $CONH_2$, and SO_2R substituents to give compounds that are identical to the products of the reaction with 2-sulfolene. A possible scheme for the reaction is proposed on the basis of the experimental data and the PMR spectra.

We have previously [1-4] established that sulfolanyl ethers in the presence of catalytic amounts of bases, hydroxides, alkali-metal alkoxides, or Triton B readily undergo exchange with alcohols, mercaptans, and amines. In the present paper it is demonstrated that β-alkoxysulfolanes in the presence of equimolar amounts of sodium ethoxide react via a similar scheme with malonic acid derivatives in which the hydrogen atom of the methylene group is activated by strong electron-acceptor substituents such as $C\equiv N$, COOR, $CONH_2$, and $SO_2C_6H_5$.



The reaction was accomplished by refluxing equimolar amounts of 3-ethoxysulfolane, malonic acid derivatives, and sodium ethoxide in absolute alcohol for 6-8 h. The same compounds were obtained under similar conditions in the reaction with 2-sulfolene (Table 1).

The sulfolanylation of compounds that contain an active hydrogen by means of 2- and 3-sulfolenes is well-known [5]. The corresponding derivatives of malonic and cyanoacetic esters and nitroparaffins are isolated. However, Argyle and co-workers [5] were unable to add malonodinitrile, cyanamide, and malonodiamide to either 3-sulfolene or 2-sulfolene. We have accomplished these reactions with both ethoxysulfolane and 2-sulfolene and have shown that the purity of the starting materials, particularly the presence of moisture in the reagents, has a great effect on the yields of sulfolanylation products.

On the basis of the data obtained and also considering the known [2,3,6] capacity of sulfolanyl ethers for splitting out a molecule of alcohol to give 2-sulfolene, we assume that the reaction described above is accomplished via a cleavage–addition mechanism. The increased lability of the hydrogen atom in the 2 position of β-alkoxysulfolanes as compared with sulfolane, which we detected by PMR spectroscopy, is evidence in favor of this assumption and against a scheme involving direct nucleophilic substitution.

Thus, in the PMR spectrum of β-methoxysulfolane in 0.006 N NaOD in D_2O, the integral intensity of the group of signals that characterizes the protons in the 2 and 5 positions is reduced as compared with the integral intensity of the same protons in H_2O and D_2O solutions without added alkali. The relatively low accuracy in the measurement of the integral intensity of the signals (10-15% of the measured value) and the superimposition of the peak of the methoxy group on the multiplet of the protons in the 2 and 5 positions do not make it possible to assert that exchange of two hydrogen atoms in D_2O+NaOD reaches equilibrium dur-

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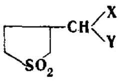
TABLE 1



Compound	X	Y	Mp, °C	Empirical formula	S, %		IR spectrum, ν, cm^{-1}					Yield, %	
					found	calc.	$\nu_{SO_2}^{as}$	$\nu_{SO_2}^{s}$	ν_{CN}	ν_{CO}	ν_{NH}	meth.A	meth.B
I	CN	CN	145	$C_7H_8N_2O_2S$	17,3 17,3	17,4	1135	1330	2278			90	63
II	CN	$COOC_2H_5$	*	$C_9H_{13}NO_4$†			1135	1320	2270	1765		85	—
III	CN	$CONH_2$	146^5				1130	1320	2265	1705	3360 3460 1625 (δ_{NH_2})	19	18
IV	$COOC_2H_5$	$COOC_2H_5$	63^5				1140	1325		1695		75	64
V	$CONH_2$	$CONH_2$	260^5				1130	1330		1755	3415 3460 1620 (δ_{NH_2})	89	54
VI	$C_6H_5SO_2$	$COOCH_3$	160	$C_{13}H_{16}O_6S_2$	19,1 19,2	19,3	1130	1330		1755		36	39

*Bp 190-192° (0.02 mm).

†Found: C 47.1, 47.6; H 5.7, 5.6; N 6.4, 6.5%. Calculated: C 46.7; H 5.7; N 6.1%.

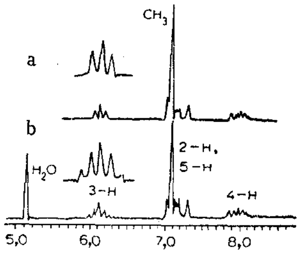
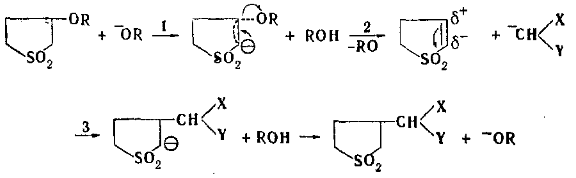


Fig. 1. PMR spectrum of 3-methoxysulfolane in pyridine–D_2O: a) with added NaOD; b) without NaOD.

ing the course of the experiment. However, there is no doubt that more than one hydrogen atom is replaced by deuterium. The decrease in intensity of the indicated signal is accompanied by a decrease in the multiplicity and width of the signal of the hydrogen in the 3 position,* while the signal of the hydrogen atom in the 4 position undergoes no change in either its form or intensity (Fig. 1). Consequently, only the hydrogen in the 2 position participates in the exchange, which is in agreement with the assumption of the intermediate formation of 2-sulfolene.

On the basis of the above, the following scheme can be proposed for the reaction described above:



The addition of the carbanion of a malonic acid derivative in step 3 can probably be explained by its higher nucleophilicity as compared with the ethoxide ion [7], although the basicity of the latter is greater than that of the former by a factor of 500 [8]. However, if less reactive carbanions, for example those formed from diethyl methylmalonate, acetoacetic ester, and acetylacetone, are used, " substitution" products cannot be isolated in the reaction with ethoxysulfolane, and the addition of ethanol to the double bond [5] predominates in the reaction with 2-sulfolene. The decrease in the activity of methylene compounds in the reaction with 2-sulfolene [5] and ethoxysulfolane in general agrees with the increase in their acidities [9] and with the literature data [10] on the nucleophilicity of carbanions in the Michael reaction.

The reaction described in this paper is a convenient method for the preparation of sulfolanylmalonic derivatives, which are possible monomers and modifying agents [11]. In contrast to the previously proposed sulfolanylating agents [5,12], particularly 3-sulfolene, ethoxysulfolane makes it possible to obtain the target products in higher yields and is considerably more accessible than 2-sulfolene and halosulfolanes.

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*The quintet with a width of 16 Hz is converted to a triplet with a width of 7.5 Hz, while the intensity of the signal remains constant.

EXPERIMENTAL

The PMR spectra were recorded with a Varian-60A spectrometer at 20-40°.

Sulfolanylation Products (I-VI). A. A solution of the sodium derivative of malonic acid was added to an equimolar amount of 3-ethoxysulfolane in absolute alcohol, and the mixture was refluxed with stirring for 8 h. The reaction products were isolated from the acidified (with hydrochloric acid) solution by crystallization or extraction with subsequent vacuum distillation.

B. The products were obtained from the sodium derivative of malonic acid and an equimolar amount of 2-sulfolene in absolute ethanol under similar conditions.

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