A CONVENIENT SYNTHESIS OF ETHYL SULPHONYLACETATES

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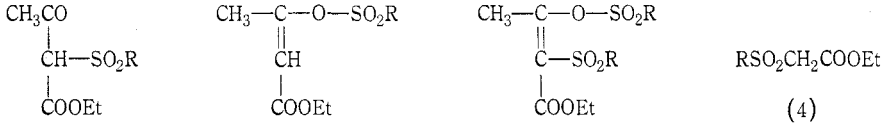
As part of a project utilizing compounds containing a methylene group activated by a sulphone substituent, the reaction of sulphonyl chlorides with the sodio derivative of ethyl acetoacetate was of interest as a potential source of intermediates for further synthesis.

Earlier workers[1,2] failed to obtain the expected sulphonyl derivative when *p*-toluenesulphonyl chloride was made to react with the sodium salt of ethyl acetoacetate. However, Böhme and Fischer[3] succeeded in obtaining sulphonyl derivatives when *aliphatic* sulphonyl chlorides were employed. When they carried out the reaction in ether using methanesulphonyl chloride two products were isolated: the expected methanesulphonyl derivative (1; R = Me) and a further product (2; R = Me) formed by substitution on the oxygen atom of the enol form of ethyl acetoacetate. In ethanol, the methanesulphonyl derivative (1; R = Me) was again formed, together with a dimethanesulphonyl derivative (3; R = Me) in which substitution on both oxygen and carbon had occurred.[3]



(1) (2) (3) (4)

The reaction of methanesulphonyl chloride with the sodio derivative of ethyl acetoacetate in ethanol was initially reinvestigated, but, in view of the poor yields (18–24% of total products) previously obtained,[3] the reaction time was extended from 15 min[3] to 48 hr. Distillation of the crude product gave only one major component which was readily formulated as ethyl methanesulphonylacetate (4; R = Me) from analytical and n.m.r. data. The only recognizable by-product was unchanged ethyl acetoacetate and no evidence for the products previously reported[3] could be found.

The formation of ethyl sulphonylacetates under these conditions was shown to be quite general when the reaction was successfully extended to arylsulphonyl

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[1] Kohler, E. P., and MacDonald, M. B., *Am. chem. J.*, 1899, **22**, 227.

[2] Findeisen, T. von, *J. prakt. Chem.*, 1906, **65**, 529.

[3] Böhme, H., and Fischer, H., *Ber. dt. chem. Ges.*, 1943, **76B**, 92.

chlorides. The product yields and physical data of the compounds prepared are recorded in Tables 1 and 2 and compared with literature data.[3–8]

The reaction presumably involves formation of the expected sulphonyl compound (1), followed by ketonic hydrolysis in the reaction medium. The facile hydrolysis of the methanesulphonyl derivative (1; R = Me) with water or alkali to give methanesulphonylacetic acid[3] provides evidence for this mechanism.

TABLE 1

YIELDS, BOILING POINTS, AND ANALYSES OF ETHYL SULPHONYLACETATES RSO_2CH_2COOEt

R	Yield (%)	Boiling Points (°C/mm) This Work	Literature	Found (%) C	H	Calc. (%) C	H
Methyl	51	111–113/0·2	122/0·8	36·5	6·1	36·2	6·1
Ethyl	56	110–111/0·1	110/0·3,[4] 101–104/0·6[5]	40·2	6·6	40·0	6·7
Phenyl	53	134–135/0·01	[a]	52·6	5·3	52·6	5·3
p-Tolyl	46	140–142/0·05	149/0·2[5b]	54·6	5·9	54·5	5·8
p-Chlorophenyl	45	150–152/0·1	160–170/2,[7] 172/12[8]	45·5	4·2	45·7	4·2
p-Bromophenyl	41	154–156/0·05[c]	[c]	39·2	3·6	39·1	3·6
2-Thienyl	41	138–139/0·01	—	41·3	4·4	41·0	4·3
p-Anisyl	51	183–184/0·03[d]	154/0·002[5]	48·6	5·5	48·8	5·7

[a] M.p. 41–42°.[6] [b] M.p. 31–32°.[5] [c] M.p. this work 45–47°, lit.[9] 52° (reported to contain one mole of water of crystallization). [d] Some decomposition occurred.

TABLE 2

N.M.R. SPECTRA (δ VALUES) OF RSO_2CH_2COOEt

R	SO_2CH_2 (s)	Ethyl CH_2 (q)	Ethyl CH_3 (t)	ArH (m)	Others
Methyl	4·05	4·25	1·3		CH_3SO_2 s 3·1
Ethyl	4·0	4·25	1·3		$CH_3CH_2SO_2$ t 1·4
					$CH_3CH_2SO_2$ q 3·3
Phenyl	4·1	4·05	1·1	7·3–8·05 (5H)	
p-Tolyl	4·05	4·1	1·15	7·2–7·9 (4H)	tolyl CH_3 2·4
p-Chlorophenyl	4·2	4·1	1·15	7·4–8·0 (4H)	
p-Bromophenyl	4·15	4·1	1·15	7·55–7·95 (4H)	
2-Thienyl	4·2	4·1	1·15	7·05–7·85 (3H)	
p-Anisyl	4·05	4·1	1·15	6·9–7·9 (4H)	OCH_3 3·8

The method described above provides a convenient one-step synthesis of ethyl sulphonylacetates from readily available materials. Previously, these compounds have been prepared in two or more steps, either by condensation of the sodium salt of the appropriate thiol with chloroacetic acid (or ethyl chloroacetate) followed by

[4] Rothstein, E., *J. chem. Soc.*, 1937, 309.

[5] Leusen, A. M. van, and Strating, J., *Recl Trav. chim. Pays-Bas*, 1965, **84**, 140.

[6] Otto, R., *J. prakt. Chem.*, 1884, **30**, 343.

[7] Gerstenfeld, M., Zwieten, P. A. van, and Huisman, H. O., *Recl Trav. chim. Pays-Bas*, 1963, **82**, 275.

[8] Thuiller, J., Rumpf, P., and Thuiller, G., Belg. Pat. 644,520 (*Chem. Abstr.*, 1965, **63**, 14767).

[9] Troeger, J., and Budde, C., *J. prakt. Chem.*, 1902, [2] **66**, 146.

oxidation with peroxides and esterification,[4,5,8] or by reaction of the sodium salt of the appropriate sulphinic acid with ethyl chloroacetate.[5–7,9]

Experimental

Analyses were performed by the Australian Microanalytical Service, Melbourne. The n.m.r. spectra were obtained on a Varian A60 spectrometer with tetramethylsilane as internal reference for the deuterochloroform solutions. All the sulphonyl chlorides were commercially available with the exception of thiophene-2-sulphonyl chloride, which was prepared by the method of Cymerman-Craig *et al.*[10]

Sodium (0·32 mol) was dissolved in absolute ethanol (500 ml), ethyl acetoacetate (0·3 mol) was added and the solution boiled gently under reflux for 15 min. The sulphonyl chloride (0·3 mol) was then added and the mixture was boiled under reflux with stirring for 48 hr. The mixture was cooled and the precipitated sodium chloride removed by filtration and washed well with ice-cold ethanol. The ethanol was removed in vacuum and water (500 ml) was added to the oily residue. The crude product was extracted with chloroform (3×150 ml) and the combined extracts were washed with water and dried ($MgSO_4$). The chloroform was evaporated and the residual oil distilled under reduced pressure. The forerun in each case was mainly ethyl acetoacetate identified by comparison of the infrared spectra with that of an authentic sample. The boiling points and yields of the compounds prepared are recorded in Table 1.

Acknowledgment

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[10] Cymerman-Craig, J., Vaughan, G. N., and Warburton, W. K., *J. chem. Soc.*, 1956, 4114.