

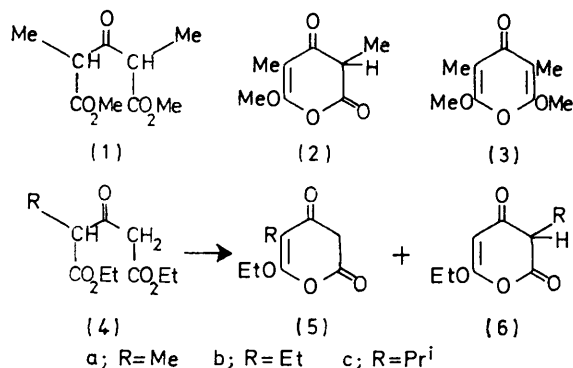
Cyclisation of Esters of Monoalkylacetonedicarboxylic Acids. Isolation of a 4-Oxo-4*H*-pyran-3-sulphonic Acid

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Treatment of diethyl 2-methyl-3-oxopentanedioate or its 2-ethyl analogue with fuming sulphuric acid affords a 4-oxo-4*H*-pyran-3-sulphonic acid. Spectroscopic evidence suggests that these products may be better represented as pyrylium-3-sulphonates or as mixtures of uncharged and dipolar tautomers. The 3-sulphonic acid of 2,6-dimethyl-4*H*-pyran-4-one has also been prepared, but attempts to prepare the 3-sulphonic acid of 2-methoxy-6-methyl-4*H*-pyran-4-one have been unsuccessful.

SCHROETER observed that when dimethyl 2,4-dimethyl-3-oxopentanedioate (1) was treated with cold concentrated sulphuric acid two products were obtained.¹ The major product was originally formulated as a



cyclobutane-1,3-dione but was later shown by Woodward and Small to be the 4*H*-pyran-2,4-dione (2).² The second product was correctly formulated by Schroeter as the 2,6-dimethoxy-4*H*-pyran-4-one (3). Interestingly, Schroeter also observed that when fuming sulphuric acid was used an additional unstable sulphur-containing compound was obtained. More recently Corbella *et al.* have shown that 3-oxopentanedioates (4) are converted into mixtures of isomeric 4*H*-pyran-2,4-diones [(5) and (6)] upon treatment with a 1 : 2 mixture (v/v) of 20% oleum and 96% sulphuric acid.³

As part of a study involving the synthesis of a number of substituted cyclic β -diketones some of these reactions have been reinvestigated. Although it has not been possible to reproduce the results of Corbella, a new product has been isolated whose formation can be accounted for by an extension of the general reaction scheme established by earlier workers.

The esters (4a and b) were prepared by standard methods.⁴ Treatment of either with a 1 : 2 mixture of 20% oleum and concentrated sulphuric acid at 0° gave a crystalline product which contained sulphur. No evidence could be found under these conditions for the formation of the 4*H*-pyran-2,4-diones (5) and (6),

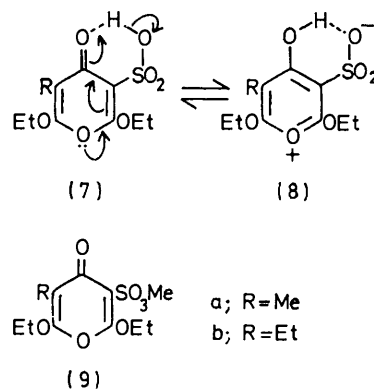
¹ G. Schroeter and C. Stassen, *Ber.*, 1907, **40**, 1604; G. Schroeter, *Ber.*, 1916, **49**, 2697.

² R. B. Woodward and G. Small, *J. Amer. Chem. Soc.*, 1950, **72**, 1297.

³ A. Corbella, P. Garibaldi, G. Jommi, and G. Russo, *Gazzetta*, 1968, **98**, 1096.

although the i.r. spectrum of the crude solid obtained from (4a) contained weak bands at 1745 and 1730 cm⁻¹ which may be due to small amounts of these. Variation of the reaction time and reaction conditions had no effect upon the outcome other than to alter the yield of product. The yield increased when a higher concentration of sulphur trioxide was used (1 : 1 oleum-sulphuric acid), and decreased when the concentration of sulphur trioxide was reduced.

Chemical and spectroscopic evidence indicates that the new products are the 4-oxo-4*H*-pyran-3-sulphonic acids (7). The mass spectrum of (7b) contains a molecular ion at *m/e* 292 (C₁₁H₁₆O₇S). High resolution measurements together with the presence of appropriate metastable peaks in the low resolution spectrum indicate that the molecular ion fragments to yield successively *m/e* 264 (*M* - C₂H₄), 236 (*M* - C₂H₄ - CO/C₂H₄), 208, and 190. A similar fragmentation pattern is observed in the spectrum of (7a). The n.m.r. spectrum of (7b) shows the presence of two ethoxy-groups [τ 5.29 (q), 5.32 (q), 8.48 (t), and 8.50 (t) (all *J* 7 Hz)], and one ethyl



group [τ 7.54 (q) and 8.92 (t) (*J* 7.5 Hz)]. Its i.r. spectrum contains bands between 1260—1150 and 1080—1010 cm⁻¹ characteristic of a sulphonic acid or its salt.⁵ The close similarity between the i.r. and u.v. spectra of (7a and b) and those of a pyrylium salt (Table) suggests that the compounds may be better represented as the pyrylium-3-sulphonates (8). Furthermore since no signal corresponding to the sulphonic acid

⁴ A. Corbella, P. Garibaldi, and G. Jommi, *Chimica e Industria*, 1967, **49**, 634.

⁵ L. J. Bellamy, 'The Infrared Spectra of Complex Molecules,' Methuen, London, 1958, p. 364.

proton can be seen in the n.m.r. spectrum, it seems probable that rapid interconversion of the tautomers (7) and (8) is occurring.

I.r. and u.v. spectra of pyrones and pyrylium salts

Pyran	$\nu_{\max}/\text{cm}^{-1}$	$\lambda_{\max}(\text{EtOH})/(\log_{10}e)$	Ref.
4-MeO-6-Me-2-one	1730, 1710, 1643, 1563 ^a	282 (3.79)	†
	1713, 1702, 1642, 1562 ^b	280 (3.80)	
2-MeO-6-Me-4-one	1680, 1625, 1585 ^a	245 (4.02)	†
	1673, 1627, 1593 ^b	240 (4.11)	
6-Me-2(3H),4-dione	1710, 1652, 1622, 1585, 1533 ^a	285 (3.86)	†
	1717, 1662, 1627, 1588, 1538 ^b	283 (3.78)	
4-R-2,6-Me ₂ cation	1654s, 1575w, 1555s ^{c,d}	—	‡
	—	285 (4.08) ^e	§
(7b)	1640s, 1580w, 1512s ^a	299 (3.93)	
(7a)	1635s, 1570w, 1505s ^a	296 (3.81)	
(13)	1645s, 1555m, 1530m ^a	247 (4.08)	

^a KBr. ^b CHCl₃. ^c Nujol. ^d R = OMe, ^e R = Me.

† E. A. Chandross and P. Yates, *Chem. and Ind.*, 1960, 149.
‡ H. Tsubomura, *J. Chem. Phys.*, 1958, **28**, 355. § A. T. Balaban, V. E. Sahini, and E. Keplinger, *Tetrahedron*, 1960, **9**, 163.

Treatment of a suspension of the sulphonic acid (7a or b) in ether with ethereal diazomethane afforded a monomethyl derivative (9a or b). The n.m.r. spectrum of (9b) contained a three-proton singlet at τ 6.06 in addition to ethoxy- and ethyl signals.

The formation of (7) may involve cyclisation of the ester to yield a 4H-pyran-4-one (10) followed by sulphonation, or sulphonation followed by cyclisation (paths a and b, respectively). There have been no previous reports of the sulphonation of 4H-pyran-4-ones, apart from the isolation of a 1:1 complex of 2,6-dimethyl-4H-pyran-4-one and sulphur trioxide.⁶ However it is accepted that the sulphonation of heteroaromatic compounds such as pyridine⁷ and pyridin-4-one⁸ requires a high temperature and forcing conditions. Shusherina⁹ reports that 3-sulphonation of 5,6-tetramethylene-2H-pyran-2-one (11) and 5,6-dimethyl-2H-pyran-2-one (12) by 34% oleum occurs at 100°. The apparent ease with which (7) is obtained may therefore indicate that the reactivity of the pyranone (10) is considerably enhanced by the presence of the two ethoxy-substituents. In fact the pyranone may be more accurately described as an activated alkene or as an $\alpha\beta$ -unsaturated ketone (both of which undergo ready sulphonation)¹⁰ rather than as an aromatic compound.

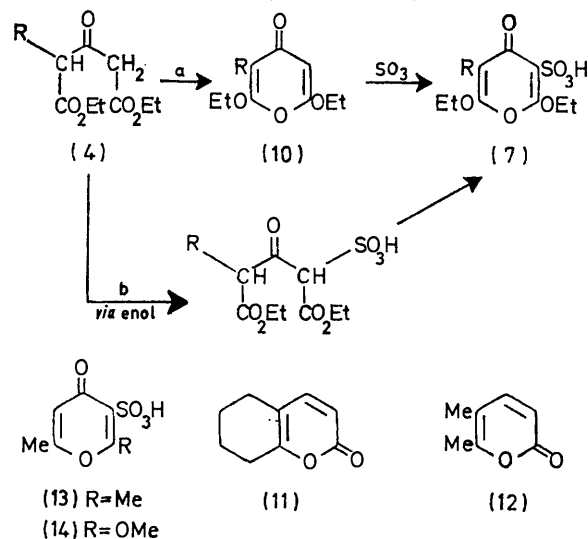
Because of the lack of published data on the sulphonation of 4-pyrones we have investigated the sulphonation of two such compounds in the hope of obtaining some information about the influence of alkoxy-substituents upon the ease of this process. Thus, 2,6-dimethyl-4H-pyran-4-one underwent sulphonation when heated with oleum at 220°, yielding the 3-sulphonic acid (13). How-

⁶ F. Muth, 'Methoden der Organischen Chemie' (Houben-Weyl), 1955, vol. 9, p. 505.

⁷ S. M. McElvain and M. A. Goese, *J. Amer. Chem. Soc.*, 1943, **65**, 2233.

⁸ E. Koenigs and O. Jungfer, *Ber.*, 1924, **57**, 2080.

ever, although 2-methoxy-6-methyl-4H-pyran-4-one reacted with oleum at a much lower temperature (80°), none of the expected sulphonic acid (14) was obtained,



probably owing to the occurrence of competing reactions involving cleavage of the activated pyrone ring or the methyl ether group. Indeed the only pure product isolated was a small amount of 4-methoxy-6-methyl-2H-pyran-2-one. In any event these reactions give us little insight into the mechanism of the cyclisation reaction and neither pathway a nor b can be excluded from consideration at present.

EXPERIMENTAL

I.r. and u.v. spectra were recorded on a Perkin-Elmer Infracord 257 and a Pye Unicam SP 800 spectrophotometer, respectively. N.m.r. spectra were obtained on a Varian HA100 instrument (tetramethylsilane as internal reference) and mass spectra on an A.E.I. MS9 double-focusing instrument (electron beam energy 70 eV; source temperature 250°). Thin-layer chromatograms were run on Silica Gel G in benzene-methanol-acetic acid (10:2:1).

2,6-Diethoxy-5-ethyl-4-oxo-4H-pyran-3-sulphonic Acid (7b).—Diethyl 2-ethyl-3-oxopentanedioate⁴ (192 mg) was added dropwise at 0° during 30 min to a stirred mixture of 20% oleum (0.16 ml) and conc. sulphuric acid (0.32 ml). The mixture was allowed slowly to warm to room temperature and stirred overnight. The acidic solution was dropped onto crushed ice (3 g) with swirling; the white precipitate was filtered off, washed with a little cold water, and dried (P₂O₅). The solid (79 mg) was purified by dissolving it in saturated aqueous sodium carbonate (0.5 ml), extracting the solution with chloroform (2 × 0.5 ml), and acidifying the aqueous layer with conc. hydrochloric acid (4 drops). The solid was filtered off, washed with water, dried, and recrystallised from nitromethane-ether; m.p. 160–161°, R_F 0.12, ν_{\max} (KBr) 3600–2200, 1640, 1580, 1512, 1455, 1407, 1377, 1347, 1292, 1260, 1190, 1164, 1043, 990, 918, 843, 765, and 690 cm⁻¹, τ (CDCl₃) 5.29 (2H, q, *J* 7 Hz), 5.32 (2H, q, *J* 7 Hz), 7.54 (2H, q, *J* 7.5 Hz), 8.48 (3H, t, *J* 7 Hz),

⁹ N. P. Shusherina, N. D. Dmitrieva, A. G. Shil'nikova, and R. Ya. Levina, *Vesta. Mosh. Univ., Ser. II. Khim.*, 1964, **19**, 60 (*Chem. Abs.*, 1965, **62**, 9094h).

¹⁰ E. E. Gilbert, 'Sulphonation and Related Reactions,' Interscience, New York, 1965, p. 55.

8.50 (3H, t, J 7 Hz), and 8.92 (3H, t, J 7.5 Hz), λ_{\max} (EtOH) 223 (log ϵ 3.93), 237 (3.71), 257 (3.67), and 299 (3.93) nm. λ_{\max} (EtOH-NaOH) 228 (3.50) and 295 (4.06) nm (Found: C, 44.9; H, 5.5. $C_{11}H_{16}O_7S$ requires C, 45.1; H, 5.8%).

2,6-Diethoxy-5-methyl-4-oxo-4H-pyran-3-sulphonic Acid (7a).—This was prepared in the same way (yield of crude solid, 206 mg from 480 mg of ester); m.p. 153—155° (from acetone), R_F 0.11, ν_{\max} (KBr) 3600—2200, 1635, 1570, 1505, 1468, 1438, 1400, 1382, 1342, 1266, 1201, 1169, 1139, 1004, 970, 900, 840, 755, and 690 cm^{-1} , λ_{\max} (EtOH) 212 (log ϵ 4.32) and 296 (3.81) nm, λ_{\max} (EtOH-NaOH) 224 (3.67) and 293 nm (3.97) (Found: C, 43.0; H, 5.0. $C_{10}H_{14}O_7S$ requires C, 43.2; H, 5.05%).

Cyclisation by Use of Higher Concentration of Sulphur Trioxide.—The ester (493 mg) was added dropwise at 0° during 30 min to a stirred mixture of 20% oleum (1.13 g) and conc. sulphuric acid (0.944 g). The mixture was allowed to warm slowly to room temperature and stirred overnight. Work-up as before gave a crude solid (184 mg) which on purification afforded (7b) (102 mg), m.p. 160—161°.

Cyclisation by Use of a Lower Concentration of Sulphur Trioxide.—A similar reaction of the ester (200 mg) with 20% oleum (0.05 ml) and conc. sulphuric acid (0.42 ml) gave a crude solid (11 mg) whose i.r. spectrum indicated that it was a 2-pyrone. Purification afforded 5 mg of solid shown by t.l.c. to consist of two components (R_F 0.49 and 0.43).

Methyl 2,6-Diethoxy-5-ethyl-4-oxo-4H-pyran-3-sulphonate (9b).—To a stirred suspension of the sulphonic acid (8b) (60 mg) in ether (10 ml) at 0°, ethereal diazomethane (50 ml) was added dropwise during 1 h. The mixture was allowed to warm to room temperature and stirred overnight. The solution was shown by t.l.c. to contain only a trace of starting material, and a new product, R_F 0.71. It was filtered and evaporated to yield a white solid which was recrystallised from ether; m.p. 84—85°, τ ($CDCl_3$) 5.54 (2H, q, J 7 Hz), 5.71 (2H, q, J 7 Hz), 6.06 (3H, s), 7.67 (2H, q, J 7 Hz), 8.52 (3H, t, J 7 Hz), 8.59 (3H, t, J 7 Hz), and 8.99 (3H, t, J 7 Hz).

Methyl 2,6-Diethoxy-5-methyl-4-oxo-4H-pyran-3-sulphon-

ate (9a).—This was prepared in the same way. Recrystallisation from ether gave white needles (22 mg from 40 mg of acid), m.p. 95—96°, λ_{\max} (EtOH) 213 nm (log ϵ 4.53), λ_{\max} (EtOH-NaOH) 222 (4.28) and 238 (4.05) nm (Found: C, 45.2; H, 5.3. $C_{11}H_{16}O_7S$ requires C, 45.2; H, 5.5%).

2,6-Dimethyl-4-oxo-4H-pyran-3-sulphonic Acid (13).—2,6-Dimethyl-4H-pyran-4-one (1 g) was added to 20% oleum (5 ml). Mercury(II) sulphate (25 mg) was added and the mixture heated at 220° for 24 h. The acidic solution was dripped onto crushed ice (25 g) with swirling, brought to pH 7 with barium carbonate, and filtered. The filtrate was extracted with chloroform (3 \times 50 ml). Evaporation of this extract left starting material (273 mg), identified by t.l.c. The sulphonic acid was obtained from the filtrate by elution through an ion-exchange column (Amberlite IR 120) as a brown oil which crystallised upon addition of ethanol to give a white solid (113 mg), m.p. 222—224° (from ethanol) (Found: C, 41.05; H, 3.95; S, 15.75. $C_7H_8O_5S$ requires C, 41.1; H, 3.95; S, 15.7%). R_F 0.12 (starting material 0.46), τ (D_2O) 3.78 (1H, s), 7.38 (3H, s), and 7.74 (3H, s), ν_{\max} (KBr) 3500—2200, 1645, 1555, 1530, 1465, 1336, 1264, 1206, 1192, 1173, 1083, 1016, 980, 928, 898, 695, and 685 cm^{-1} , λ_{\max} (EtOH) 213 (log ϵ 4.06) and 247 (4.08) nm.

Attempted Sulphonation of 2-Methoxy-6-methyl-4H-pyran-4-one.—The pyranone ¹¹ (180 mg) was added to 20% oleum (3 ml) and the mixture was heated at 80° for 24 h. The acidic solution was dripped onto crushed ice (5 g) with swirling, brought to pH 7 with barium carbonate, and filtered. The filtrate was extracted with chloroform (20 ml). The extract was dried ($MgSO_4$), filtered, and evaporated to leave a white solid (22 mg) whose i.r. spectrum was identical with that of 2-methoxy-6-methyl-2H-pyran-2-one. The aqueous filtrate was eluted through an ion-exchange column (Amberlite IR 120) to give a light brown oil. Addition of benzene followed by evaporation left a sticky solid (93 mg), which contained at least two components, but resisted, or was decomposed by, all attempts at purification.

[3/2081 Received, 10th October, 1973]

¹¹ H. Nakata, *Bull. Chem. Soc. Japan*, 1960, **33**, 1688.