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ACID-CATALYSED ACYLATIONS OF BICYCLO[3.3.1]NONAN-2,6-DIONES

A NOVEL PREPARATION OF THE ADAMANTANE SKELETON

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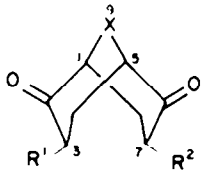
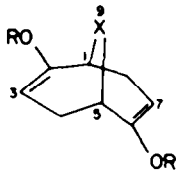
Abstract—The acid-catalysed acylations of bicyclo[3.3.1]nonan-2,6-dione **1** and its 9-thia-2 and 9-oxa-3 analogues with Ac_2O are described. At high acidity, *C*-acylation is favoured over *O*-acylation and for **1** and **2** intramolecular aldol condensation occurs with the formation of adamantanes **18** and **19** and 2-thiaadamantanes **15** and **16**. These results are compared with alternative acylations of **2** using 2-acetoxypropene, $(PhCO)_2O$ and acid halides.

The acid-catalysed acylation, at oxygen and carbon, of active methylene compounds and the thermal rearrangement of enol esters have been reviewed.[1] It is noteworthy that the course of acylation of carbonyl compounds and hence the position of substitution are affected by variations in reaction conditions.





1: X = CH_2; R' = R² = H
2: X = S; R' = R² = H
3: X = O; R' = R² = H
4: X = S; R' = H, R² = Ac
5: X = O; R' = R² = Ac

6: X = CH_2; R = Ac
7: X = S; R = Ac
8: X = O; R = Ac
9: X = S; R = COPh
10: X = S; R = $COCH_2Cl$

The bicyclic dione **1**, which is not expected to enolise by removal of a bridgehead proton, has been shown[2] to react with Ac_2O containing a catalytic quantity of conc. H_2SO_4 (one drop per 30 ml Ac_2O) yielding mainly bisenol acetate **6**, the formation of *C*-acylated products being unreported. We have found that the analogous 9-thiabicyclo[3.3.1]nonan-2,6-dione **2**[3] reacts sluggishly with Ac_2O–H_2SO_4 forming mixtures of mono- and bisenol acetates **11** and **7** accompanied by varying amounts of minor products. A moderate increase in the proportion of **7** was achieved[3] through constant removal by distillation of the acetic acid formed during the reaction and by prolonging reaction time. With *p*-toluenesulphonic acid (*p*-TsOH) as catalyst the acetylation (6 h) was considerably cleaner and furnished mainly **7** (64%) free from the above minor products. A milder acetylation of **2** with 2-acetoxypropene-*p*-TsOH[4] gave a tar-free product which was mainly **11** after 20 h and mainly **7** after 40 h.

During investigations of the Ac_2O–H_2SO_4 treatment of **2**, an increase in the acidity of the reaction medium caused some charring and was found to disfavour *O*-acylation, increasing the proportion of the hitherto minor products.[3] Thus after 24 h at 150° using 21 drops of conc. H_2SO_4 per 30 ml Ac_2O (Table 1) the predominant products were a tricyclic diketoacetate $C_{12}H_{14}O_4S$, m.p. 172–173° and a structurally similar diketoalkene $C_{10}H_{10}O_2S$, m.p. 169–170°. At yet higher acidity (24 drops conc. H_2SO_4 per 30 ml Ac_2O) the alkene was the sole product (Table 1).

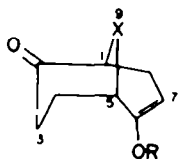
The structures of these tricyclic compounds were deduced by spectroscopic analysis[5,6] and chemical interconversions[3] and are assigned respectively as 6-acetoxy-6-methyl-2-thiaadamantan-4,8-dione **15** and 6-methylene-2-thiaadamantan-4,8-dione **16**. The 2-thiaadamantane skeleton must arise by two sequential condensations, a *C*-acylation to give **4**, followed by an intramolecular aldol condensation. This insertion of the carbonyl carbon of acetic anhydride between the closely placed[8] C-3 and C-7 atoms of a bicyclo[3.3.1]nonane to form **15** is a novel method of creating the adamantane framework.

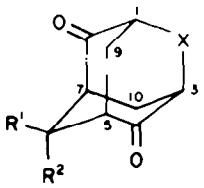
The intermediacy of the *C*-acylated dione **4** remains experimentally unsupported, as it was not directly isolable and its presence in the product mixture could not

Table 1. Treatment of diones **1**, **2** and **3** with conc. H_2SO_4/Ac_2O

Dione	H_2SO_4 (drops/30 ml Ac_2O)	Reaction Time (h)	*O*-Acylated products†	*C*-Acylated products†
1	15.0	6	**6** (18%)	**18** (20%); **19** (31%)
2	0.5	10	**11** (60%); **7** (30%)	—
2	1.2	24	**11** (16%); **7** (64%)	—
2	5.0	6	**11** (18%); **7** (45%)	**15** (28%)
2	21.0	24	**7** (0.7%)	**15** (20.5%); **16** (9.1%)
2	24.0	24	—	**16** (26%)
3	18.75	6	**8** (25%)	**5** (11%)

†Yields refer to purified material.



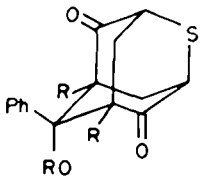


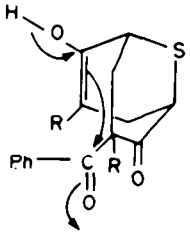
11: X = S; R = Ac
12: X = S; R = COPh
13: X = S; R = $COCH_2Cl$
14: X = S; R = H

15: X = S; R' = CH_3; R^2 = OAc
16: X = S; R',R^2 = CH_2
17: X = S; R' = CH_2Br; R^2 = $OCOCH_2Br$
18: X = CH_2; R' = CH_3; R^2 = OAc
19: X = CH_2; R',R^2 = CH_2

(Systematic numbering for **15** to **17** only)

be inferred by NMR. In contrast the analogous reaction of 9-oxabicyclo[3.3.1]nonan-2,6-dione **3**[9] with Ac_2O–H_2SO_4 furnished the doubly *C*-acetylated bicyclic dione **5** m.p. 154–156° as well as bisenol acetate **8** m.p. 89–91°. The formation of **4** is also supported by the isolation of a single tricyclic product **20**, m.p. 232–234°, bearing bridgehead acyl substituents, in the acid-catalysed treatment of **2** with excess $(PhCO)_2O$. An attempt to generate a *C*-acyl bicyclic precursor of **20** by reducing the ratio of anhydride to substrate to 2:1 furnished only mono- and bisenol benzoates **12** and **9** in good yield.





20: R = COPh

21: R = COPh

Reflux of **2** with acyl halides in presence of H_2SO_4 catalyst furnished products of either *O*-acylation or *C*-acylation. Acetyl chloride (b.p. 51°) gave no reaction but alkene **16** was formed in low yield when the reaction mixture was distilled allowing the temperature to rise. Chloroacetyl chloride (b.p. 107°) produced the unstable acetates **13** and **10** whereas *C*-acylation-cyclisation to the sensitive dibromide **17** occurred with bromoacetyl bromide (b.p. 150°). With benzoyl chloride at 170° **12** and **9** were formed.

In the formation of the tricyclic skeleton, as in **15**, the new carbon bridge is created through *C*-acetylation [Scheme 1] of the enol **14** or more probably[1] its acetate **11** with the anhydride-acid complex **22**. Ring closure of the transient 1,3-dicarbonyl intermediate **4** is effected by acid-catalysed intramolecular aldol condensation involving the newly inserted 3-acetyl group which is *endo* in one tautomeric form **4b**, the driving force for cyclisation being the attainment of the strain-free adamantane framework.

This *C*-acylation pathway is favoured at high acidity (Table 1) whereas only enol esters **7** and **11** are formed at low acid concentration. At intermediate acidity (*ca.* 5 drops conc. H_2SO_4/30 ml Ac_2O, Table 1) the proportions of **7** and **15** are thermodynamically controlled[10] as is shown by the conversion of **7** to a mixture of **11**, **15** and **16** (trace) on treatment with Ac_2O–H_2SO_4. However, the cyclisation, **4** → **15**, is in fact irreversible since subjection of **15** to the acylation conditions (Table 2) afforded **16** but no bicyclic products.

The latter observation also indicates that **16** does not arise directly from a bicyclic precursor but is the product of elimination of CH_3CO_2H from **15**. The adamantane **15** was slowly converted to **16** when heated with a catalytic quantity of H_2SO_4 in an inert solvent (1,2-dimethoxyethane or 1,4-dioxan) (Table 2) but was unchanged after pyrolysis at temperatures between 150° and 220°. Compound **16** itself was inert to Ac_2O–H_2SO_4. Thus the elimination step, **15** → **16** [Scheme 1], is an irreversible, acid-catalysed process (most probably E-1,[11] *via* the tertiary carbonium ion **23** favoured in the polar medium) rather than a pyrolytic *cis*-elimination.[5]

Table 2. Treatment of **15** with conc. H_2SO_4

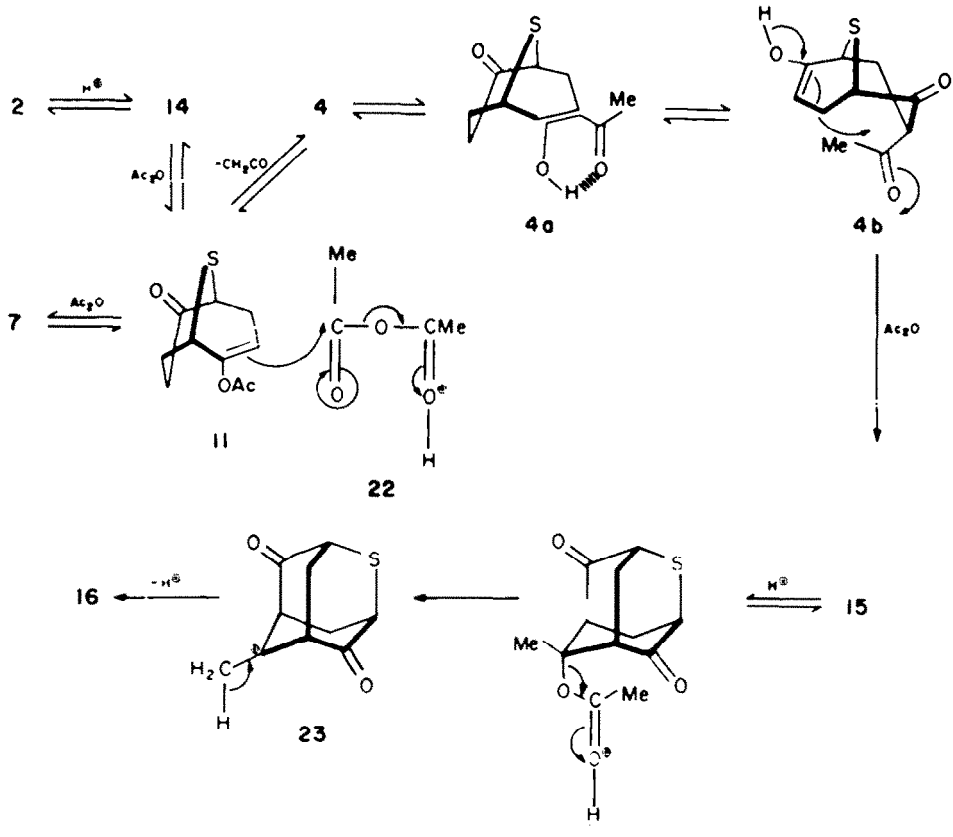
Solvent	Reaction time (h)	Proportion **15**:**16**
Ac_2O	4	1:4
$(CH_2OMe)_2$	2	9:1
1,4-Dioxan	4	4:1

In the reaction of **2** with $(PhCO)_2O$–H_2SO_4, tricyclic benzoate **20** arises by intramolecular aldol condensation of the triply *C*-acylated intermediate **21**, *C*-acylation after ring closure being unlikely since enolisation in the tricyclic skeleton would place double bonds in unfavourable bridgehead locations.

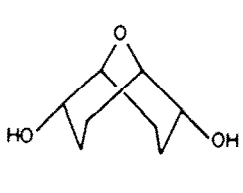
Since *C*-acylations as well as *O*-acylations have been encountered in reactions of 9-heterobicyclo[3.3.1]nona-2,6-diones **2** and **3** with anhydrides, the absence of *C*-acyl or tricyclic products in the reported[2] acetylation of the 9-methano analogue **1** would seem incongruous. However, it was found that a slight modification of the described[2] procedure, employing (*vide supra*) increased amount of acid (15 drops conc. H_2SO_4 per 30 ml Ac_2O) furnished three products of which bisenol acetate **6**,[2] m.p. 77–79°, was the minor (18%). The major products (Table 1) were in fact 4 - methyleneadamantan - 2,6 - dione **19**[12] (31%) m.p. 160–162° and 4 - acetoxy - 4 - methyladamantan - 2,6 - dione **18** (20%) m.p. 124–126°, arising by the *C*-acylation-cyclisation process established above.

EXPERIMENTAL

Preparative TLC was performed on glass plates (20 × 20 cm^2 or 20 cm × 1 m) spread with Merck Kieselgel G or HF_{254} (1 mm thick). Column chromatography was carried out on neutral Al_2O_3



Scheme 1.



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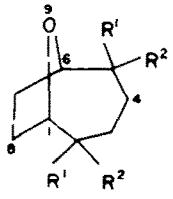

25: R¹ = H; R² = OH(endo)
26: R¹,R² = O

(Woelm, Gd I). Mps. were recorded on a Kofler hot-stage apparatus and are uncorrected. Petroleum spirit was of b.p. 60–80°. Dioxan was purified by percolation through Al_2O_3. PMR spectra were recorded on Varian T-60 or HA-100 instruments on solutions in $CDCl_3$ with TMS as internal reference. Mass spectra were measured on an AEI MS12 spectrometer. IR spectra were run on Perkin-Elmer 257 or 225 spectrometers on solutions in CCl_4 or on pressed discs (KBr). UV spectra were obtained on a Unicam SP800 instrument on solutions in Ar MeOH. Pyrolyses and acid-catalysed equilibrations were carried out in thick-walled Pyrex tubes, flushed with N_2, sealed under vacuum and heated in a Gallenkamp sublimation block.

Preparation of substrates. The synthesis of diones 1[7] and 2[7] have been reported.

Dione 3 has been prepared[8] by oxidation of diol 24, separated by repeated fractional crystallisation of the derived acetates from a mixture[11] of 24 and 25. A convenient method is given below for the synthesis of 3 in higher yield by acid hydrolysis of 8, the major product of reaction of dione mixture 3 and 26 with Ac_2O–*p*-TsOH.

Jones reagent (8N, 18 ml) was added to a solution of diol mixture 24 and 25[11] in acetone (100 ml). After stirring for 0.5 h at room temperature, the solution was neutralised with aq $NaHCO_3$ and continuously extracted with EtOAc for 2 days. Removal of solvent gave diones 3 and 26 which were eluted as a 2:1 (by NMR) mixture, colourless oil (2.21 g, 47%), from TLC in benzene–EtOAc (2:1).

A solution of this dione mixture (1.04 g; 6.76 mmol) and *p*-TsOH (20 mg) in Ac_2O (25 ml) was refluxed for 42 h. Removal of Ac_2O (distillation and co-distillation with benzene) and extraction with Et_2O gave a brown oil (1.39 g) which was chromatographed (TLC) in benzene–EtOAc (3:1). The major band furnished bisenol acetate 8 (830 mg; 52%) which sublimed (85° at 0.03 mmHg) as needles, m.p. 89–91°. (Found: C, 60.34; H, 5.77. $C_{12}H_{14}O_3$ requires: C, 60.50; H, 5.92%); $\nu_{max.}$(KBr) 1758 cm^{-1}; $\nu_{max.}$ (CCl_4) 1765 cm^{-1} (ϵ 440, $\Delta\nu^{\frac{1}{2}}$ 31 cm^{-1}); δ 2.11 (s, 6H; CH_3), 1.85–2.90 (m, 4H; CH_2), 4.39 (m, 2H; C-1 and C-5 CH), 5.52 (m, 2H; olefinic); mass spectral peaks at *m/e* 238 (M^+), 196, 154, 136, 126, 97, 83, 70, 55 and 43.

A mixture of 8 (800 mg, 3.36 mmol) and 2M aq HCl (25 ml) was refluxed for 16 h. The cooled reaction mixture was neutralised with aq $NaHCO_3$ and continuously extracted with EtOAc for 6 h. Removal of solvent and crystallisation of the residue from Et_2O–petroleum spirit afforded dione 3 (437 mg, 84%), m.p. 53–55° (lit.[8] m.p. 54–55°).

Reaction of diones 1, 2 *and* 3 *with* Ac_2O–H_2SO_4. Details of reaction times, acidity and appropriate yields of *O*-acylated and *C*-acylated products are given in Table 1. In all cases the Ac_2O was replenished after 3 h and at later reaction times as required.

(a) *Specimen procedure.* 2 (2.445 g, 14.4 mmol), Ac_2O (20 ml) and conc H_2SO_4 (AR; 14 drops) were heated at 150–160° (bath temp.) for 3 h allowing acetic acid to distil (stillhead temperature 115–116°). Further Ac_2O (20 ml) was added and the reflux continued for 21 h. The reaction mixture was concentrated and purged by azeotropic distillation with benzene. The dark residue was extracted with boiling petroleum spirit and then with boiling Et_2O. The petroleum extract contained mainly 15 which recrystallised from $CHCl_3$–petroleum spirit as needles (261 mg, 7%), m.p. 172–173° (Found: C, 56.62; H, 5.49. $C_{12}H_{14}O_4S$ requires: C, 56.69; H, 5.55%); $\nu_{max.}$ (KBr) 1740, 1712, 1238, 1102, 988 and 971 cm^{-1}; $\nu_{max.}$ (CCl_4) 1752 (ϵ 710, $\Delta\nu^{\frac{1}{2}}$ 13 cm^{-1}), 1729 (ϵ 560, $\Delta\nu^{\frac{1}{2}}$ 20 cm^{-1}) and 1719 cm^{-1} (ϵ 480, $\Delta\nu^{\frac{1}{2}}$ 13 cm^{-1}); δ 1.62 (s,

3H; CH_3), 2.0 (s, 3H; CH_3CO_2–), 2.90 (m, *ca.* 4H; C-9 and C-10 CH_2), 3.20 (m, *ca.* 2H; C-5 and C-7 CH), 3.36 (m, *ca.* 2H; C-1 and C-3 CH); mass spectral peaks at *m/e* 254 (M^+), 212, 194, 179, 166 and 133. The Et_2O extract furnished a mixture of **7**, **15** and **16** which were separated by TLC using $CHCl_3$ as solvent. The most mobile component was **16** which crystallised from $CHCl_3$–petroleum spirit as broad needles (254 mg, 9.1%), m.p. 169–170°. (Found: C, 61.94; H, 5.32. $C_{10}H_{10}O_2S$ requires: C, 61.85; H, 5.19%): ν_{max} (CCl_4) 1723, 905 cm^{-1}; δ 2.63 and 2.83 (both m, 2H; C-9 and C-10 CH), 3.03 and 3.23 (both m, 2H; C-9 and C-10 CH), 3.26 (m, 2H; C-1 and C-3 CH), 3.46 (m, 2H; C-5 and C-7 CH), 4.93 (s, 2H; olefinic); mass spectral peaks at *m/e* 194 (M^+), 166, 138, 123, 111, 105, 91 and 77.

The middle band contained **7** (28 mg, 0.7%), m.p. 106–107° (lit.[1] m.p. 107–107.5°). The least mobile component was **15** (495 mg, 13.5%).

(b) *Dione* **3** (220 mg, 1.4 mmol) reacted as above with Ac_2O (8 ml) and conc H_2SO_4 (5 drops) for 6 h. Preparative TLC of the combined Et_2O and petroleum extracts using EtOAc/benzene (1:3) as solvent gave **5** (R_f *ca.* 0.6), which sublimed (110° at 0.03 mmHg) as needles (36 mg, 11%), m.p. 154–156°. (Found: C, 60.25; H, 5.93. $C_{12}H_{14}O_3$ requires: C, 60.5; H, 5.92%); ν_{max} (KBr) *ca.* 1600 cm^{-1} (broad, complex); δ2.05 (s, 6H; CH_3), 2.35 (s, 2H; *enol* H), 2.66 (d, 2H; J 1.5 Hz; C-4 and C-8 H-*exo*), 2.83 (d, 2H; J 6 Hz; C-4 and C-8 H-*endo*), 4.53 (dd, 2H; J 6 and 1.5 Hz; C-1 and C-5 CH); mass spectral peaks at *m/e* 238 (M^+), 164, 121, 93, 65 and 43; and **8** (R_f *ca.* 0.4) (83 mg, 25%).

(c) *Dione* **1** (510 mg, 3.35 mmol) reacted as above with Ac_2O (8 ml) and conc. H_2SO_4 (4 drops) for 6 h. Preparative TLC of the combined Et_2O and petroleum extracts using EtOAc/hexane (3:7) as solvent (double elution) gave in order of decreasing mobility **6** which crystallised from Et_2O–petroleum spirit as prisms (139 mg, 18%), m.p. 77–79° (lit.[2] m.p. 78–79°); ν_{max} (KBr) 1743 cm^{-1}; δ 1.92 (m, 2H; C-9 CH_2), 2.12 (s, 6H; CH_3), 2.28 (m, 4H; C-4 and C-8 CH_2), 2.56 (m, 2H; C-1 and C-5 CH), 5.37 (m, 2H; olefinic); **19** which crystallised from $CHCl_3$–hexane as needles (181 mg, 31%), m.p. 160–162° (lit.[12] m.p. 163–164°); **18** which crystallised from $CHCl_3$–petroleum spirit as needles (162 mg, 20%), m.p. 124–126° (sealed tube). (Found: C, 66.32; H, 6.81. $C_{11}H_{16}O_4$ requires: C, 66.08; H, 6.83%); ν_{max} (KBr) 1720 cm^{-1}; ν_{max} (CCl_4) 1750 (ϵ^* 560, $\Delta\nu^*_{1/2}$ 24 cm^{-1}) and 1724 cm^{-1} (ϵ^* 820, $\Delta\nu^*_{1/2}$ 28 cm^{-1}); δ 1.62 (s, 3H; CH_3), 2.04 (s, 3H; CH_3CO_2–), 1.80–2.60 (broad m, 6H; CH_2), 2.70 (m, 2H; C-1 and C-7 CH), 3.25 (m, 2H; C-3 and C-5 CH); mass spectral peaks at *m/e* 236 (M^+) 194, 176, 148, 120, 108, 99, 55 and 43.

Reaction of dione **2** *with* Ac_2O–*p*-TsOH. **2** (2.14 g, 12.6 mmol), Ac_2O (25 ml) and *p*-TsOH (10 mg) were refluxed (oil bath temp. 150°) for 3 h. During the following 3 h acetic acid was allowed to distil while the Ac_2O was replenished as required. Removal of Ac_2O as above and extraction with petroleum spirit gave a yellow gum (2.41 g) which solidified on standing. Recrystallisation from Et_2O/petroleum spirit gave **7** (1.46 g, 46%). The mother liquor (950 mg) contained **7** and **11** in the ratio (by NMR) of 5:3.

Reaction of dione **2** *with* 2-*acetoxypropene*-p-*TsOH*

(a) A solution of **2** (100.4 mg, 0.59 mmol) and *p*-TsOH (2.5 mg) in 2-acetoxypropene (1.2 ml, 11.5 mmol) was refluxed (bath temp. 115°) for 20 h, allowing acetone to distil. The reaction solution in EtOAc was washed with aq $NaHCO_3$, brine, and dried ($MgSO_4$). Removal of solvent furnished a red-brown oil (145 mg) which was fractionated into two components by preparative TLC using Et_2O–petroleum spirit (7:3) as solvent. The more polar constituent (20 mg) was unreacted **2**. The more mobile component (82 mg, 82% based on **2** consumed) was **11** which recrystallised from $CHCl_3$–petroleum spirit as needles, m.p. 88–90.5°. (Found: C, 56.67; H, 5.56. $C_{10}H_{12}O_3S$ requires: C, 56.6; H, 5.7%); ν_{max} (CCl_4) 1763, 1710, 1369, 1205, 1195 and 1100 cm^{-1}; δ 2.16 (s, 3H; CH_3), 2.40–2.90 (m, 6H; CH_2), 3.20 (m, 1H; C-1 CH), 3.46 (m, 1H; C-5 CH), 5.60 (t, 1H; J 4 Hz; olefinic); mass spectral peaks at *m/e* 212 (M^+) and 170.

(b) Dione **2** (202 mg, 1.19 mmol), *p*-TsOH (16 mg) and 2-acetoxy-propene (5.2 ml) were refluxed as above for 15 h. 2-Acetoxy-propene (5.2 ml) and *p*-TsOH (16 mg) were added and reflux continued for 25 h. Volatiles were removed by raising the bath temperature and after cooling the reaction mixture was extracted as before. The residual brown oil, which solidified on standing, was purified by filtration through a column (9 cm × 8 mm) of Al_2O_3. Fractions eluted with $CHCl_3$–Et_2O 1:9 to 1:4 consisted of **7** (61 mg, 20%). Fractions eluted with $CHCl_3$–Et_2O 2:3 to 7:3 contained a mixture of **7** and **11**. Preparative TLC of this mixture using Et_2O–petroleum spirit (3:2) as solvent furnished a further portion of **7** (180 mg, 59.6%).

In less efficacious reactions where **11** and **7** are produced in approximately equal quantities, closeness of TLC mobility prevents clean separation. The proportion of **7** may be increased by retreatment under the above conditions. Alternatively conc. H_2SO_4 may be used as catalyst as follows. A **7**–**11** mixture (972 mg) in 2-acetoxypropene (25 ml) containing 3 drops conc. H_2SO_4 was refluxed for 13 h. Work-up as above followed by preparative TLC in Et_2O–petroleum spirit (1:1) yielded **7** (544 mg).

Reaction of dione **2** *with* $(PhCO)_2O$–H_2SO_4

(a) A magnetically stirred solution of **2** (250 mg, 1.47 mmol), $(PhCO)_2O$ (10 ml) and conc. H_2SO_4 (5 drops) was heated at 160° (bath temp.) for 5 h, the benzoic acid formed being distilled out under reduced pressure (30 mmHg). The solution was concentrated (155°; 1 mmHg) and the red residue extracted with boiling petroleum spirit and then ether. The petroleum and ether extracts, identical on analytical TLC, were combined, evaporated and refluxed with aq Na_2CO_3 (10% w/v) for 2 h. The solution was extracted with $CHCl_3$ and the extract washed with water and dried ($MgSO_4$). The yellow semi-solid obtained on removal of solvent gave one major band on preparative TLC in $CHCl_3$. Recrystallisation from $CHCl_3$–petroleum spirit using decolourising charcoal furnished **20** as needles (100 mg, 11.6%), m.p. 232–234°. (Found: C, 73.64; H, 4.51. $C_{34}H_{26}O_4S$ requires: C, 73.71; H, 4.47%); ν_{max} (KBr) 1730, 1660, 1600 and 1260 cm^{-1}; λ_{max} 242 (log ϵ 4.63), 255 (4.45) and 279 nm (4.17); δ3.15 (d, 4H; C-9 and C-10 CH_2), 4.06 (t, 2H; C-1 and C-3 CH), 7.40 and 7.88 (both m, 20H; aromatic); mass spectral peaks at *m/e* 586 (M^+), 558, 481, 464, 377, 360 and 343.

(b) A solution of **2** (250 mg, 1.47 mmol), $(PhCO)_2O$ (0.6 ml, 3.15 mmol) and conc. H_2SO_4 (0.3 drop) was heated at 165° for 5 h, in an evacuated pyrolysis tube. Work up as in (a) (10 min reflux with aq Na_2CO_3) followed by preparative TLC in $CHCl_3$ gave starting material and two products. Compound **2** (45 mg) was contained in the band of lowest R_f. The uppermost band furnished **9** which was decolourised with activated charcoal and crystallised from $CHCl_3$–petroleum spirit as plates (105 mg, 18.9%), m.p 189–190°. (Found: C, 69.60; H, 4.87. $C_{22}H_{18}O_4S$ requires: C, 69.83; H, 4.80%); ν_{max} (KBr) 1733, 1724, 1681, 1600, 1255, 1100 and 700 cm^{-1}; ν_{max} ($CHCl_3$) 1728 cm^{-1} (ϵ^* 186, $\Delta\nu^*_{1/2}$ 30 cm^{-1}); λ_{max} 233 (log ϵ 4.35) and 281 nm (3.21); δ 2.76 (t, 4H; C-4 and C-8 CH_2), 3.66 (t, 2H; C-1 and C-5 CH), 5.66 (t, 2H; J 4 Hz; olefinic), 7.55 (m, 6H; aromatic), 8.15 (dd, 4H; J 8 and 2 Hz; aromatic); mass spectral peaks at *m/e* 378 (M^+), 257, 151, 105 and 77.

The middle band contained **12** which was decolourised and recrystallised from ether–petroleum spirit as needles (150 mg, 54.7%), m.p. 75–76°. (Found: C, 65.39; H, 5.27. $C_{15}H_{14}O_3S$ requires: C, 65.69; H 5.15%); ν_{max} (KBr) 1730, 1725, 1705, 1600, 1255, 1105 and 695 cm^{-1}; ν_{max} (CCl_4) 1738 (ϵ^* 270, $\Delta\nu^*_{1/2}$ 15 cm^{-1}) and 1709 cm^{-1} (ϵ^* 307, $\Delta\nu^*_{1/2}$ 15 cm^{-1}); λ_{max} 232 (log ϵ 4.26) and 282 nm (3.47); δ2.3–3.0 (m, 6H; C-3, C-4 and C-8 CH_2), 3.36 (m, 1H; C-1 CH), 3.53 (m, 1H; C-5 CH), 5.8 (t, 1H; J 4 Hz; olefinic) 7.53 (m, 3H; aromatic), 8.10 (dd, 2H; J 7 and 2 Hz; aromatic); mass spectral peaks at *m/e* 274 (M^+), 153, 105 and 77.

Reaction of dione **2** *with acyl halides*

(a) A solution of **2** (200 mg, 1.18 mmol), AcCl (10 ml) and conc. H_2SO_4 (4 drops) was refluxed for 6 h. AcCl was distilled using a Bunsen burner. The resulting tar was extracted with ether and the extract washed with aq $NaHCO_3$, water, dried ($MgSO_4$) and evaporated to give **16** (15 mg, 6.6%).

(b) A solution of **2** (160 mg, 0.94 mmol), PhCOCl (6 ml) and conc. H_2SO_4 (4 drops) was heated at 170° (bath temp.) for 6 h. PhCOCl was distilled (140°, 30 mm Hg) and the resulting tar extracted with petroleum spirit and with ether. The combined

extracts after removal of solvent were refluxed with water for 1 h. Extraction of the hydrolysate with $CHCl_3$ and washing of the extract as in (a) gave a mixture of **12** and **9** which were separated by preparative TLC in Et_2O–petroleum spirit (1:1) (20 mg, 8% and 36 mg, 10% respectively).

(c) A solution of **2** (216 mg, 1.27 mmol), $BrCH_2COBr$ (5 ml) and conc. H_2SO_4 (4 drops) was refluxed for 6 h. $BrCH_2COBr$ was distilled (30 mm Hg) and the resulting tar extracted with petroleum spirit and with ether. Work up of the combined extracts as in (a) gave **17** a yellow oily solid (310 mg, 69%), δ 2.7–3.9 (m, *ca.* 8H; skeletal), 3.9–4.2 (m, *ca.* 4H; CH_2Br). This product decomposed on attempted purification by preparative TLC.

(d) A solution of **2** (200 mg, 1.18 mmol), $ClCH_2COCl$ (10 ml) and conc. H_2SO_4 (8 drops) was refluxed for 9 h. $ClCH_2COCl$ was distilled (30 mmHg) and the resulting gum worked up as in (a) yielding a 1:1 mixture of **10** and **13** as a yellow oil (150 mg), δ 2.60 (m, 10H; CH_2), 3.43 (m, 4H; CH), 4.16 (m, 6H; CH_2Cl), 5.55 (t, 2H; J 4 Hz; olefinic), 5.73 (t, 1H; J 4 Hz; olefinic). Both products decomposed on attempted separation by preparative TLC.

Reaction of **7** *and* **16** *with* Ac_2O–H_2SO_4

(a) **7** (100 mg, 0.39 mmol) was heated in a pyrolysis tube at 160° for 5 h with 0.1 ml of a solution of conc. H_2SO_4 (2 drops) in Ac_2O (5 ml). The tarry residue obtained on removal of Ac_2O by co-distillation with benzene was chromatographed (TLC) in $CHCl_3$–petroleum spirit (4:1) and furnished **7** (28 mg, 28%), **11** (26 mg, 31%) and **15** (15 mg, 15%), yields in this case referring to unpurified material. A trace of **16** (δ 4.93) was detected in the PMR spectrum of the crude product mixture.

(b) **16** (15 mg, 0.077 mmol) was heated as above with 0.6 ml of the Ac_2O–H_2SO_4 solution. The crystalline residue obtained on extraction with $CHCl_3$ and removal of Ac_2O as above was unconverted starting material.

Acid treatments of **15**. Treatment of **15** (20 mg samples) with a solution (0.6 ml) of conc. H_2SO_4 (12 drops) in solvent (30 ml) at 155° in sealed tubes was carried out 3 times (see Table 2). The reaction in Ac_2O was worked up as for **16** (*vide supra*). With $(CH_2OMe)_2$ and 1,4-dioxan as solvents the reaction mixtures were extracted with ether (2 × 25 ml), the organic layer being washed with water (2 × 25 ml), dried and evaporated. In all cases the product was a mixture of **15** and **16** in proportion estimated from NMR integration.

Pyrolyses of **15**. Samples of **15** were pyrolysed in sealed tubes at four different temperatures, viz. 150°, 165°, 180° and 220° for 2–4 h. On cooling the tubes were washed out with hot $CHCl_3$. In all cases removal of solvent furnished unreacted **15**.

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