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2-THIAADAMANTANES. INTERCONVERSIONS, DEGRADATIONS AND SPECTROSCOPIC ANALYSIS

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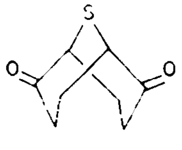
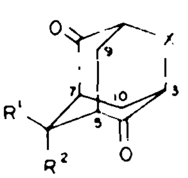
Abstract—Chemical and spectroscopic evidence is presented in proof of structure of the tricyclic products from acid-catalysed acetylation of 9-thiabicyclo[3.3.1]nonan-2,6-dione.

In the acetylation of 9 - thiabicyclo[3.3.1]nonan - 2,6 - dione **1** with Ac_2O–H_2SO_4 the formation in the reaction medium of tricyclic products, acetate, A, and exomethylene compound, B, has been demonstrated.[1,2] Although the nature of the functional groups present in these products was readily deduced the complexity of their NMR spectra did not permit a straightforward assignment of skeletal structure. A and B are established as derivatives of 2-thiaadamantane by the chemical conversions and spectroscopic analysis described below.

Base hydrolysis of acetate A (δCH_3COO 2.0; ν_{CO}(KBr) 1740 cm^{-1}), which possessed a tertiary methyl group (δ 1.62), furnished a diketoalcohol $C_{10}H_{12}O_3S$ **2**, m.p. 265–267° (ν(KBr) 3399 cm^{-1}). Dehydration of **2** with $POCl_3$-pyridine gave a diketoalkene (δ 4.93, s, 2 H), identical in all respects to product, B. Acid treatment of A also led[2] to B. The exomethylene function of B was demonstrated by the formation of a crystalline dibromide **3** (δ^{CH_2Br} 3.8, s, 2 H) in reaction with Br_2/HOAc and a trione $C_9H_8O_4S$ **4** (ν_{CO} 1705 cm^{-1}) on ozonolysis. Thus the partial structure, H_3C–C–OAc for A is established, B differing from A only in the loss of acetic acid from this function.

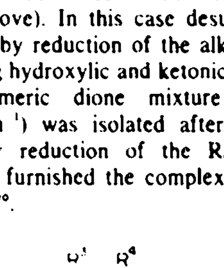


1.

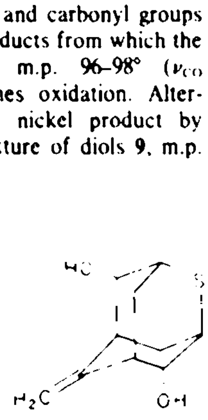


2. X = S; R¹ = Me; R² = OH
3. X = S; R¹ = CH_2Br; R² = Br
4. X = SO; R¹, R² = O
5. X = S; R¹ = Me; R² = OAc
6. X = S; R¹, R² = CH_2

The above ozonolysis also showed the presence of a nuclear thioether bridge which had been oxidised to sulphoxide (ν_{SO} 1025 cm^{-1}). In corroboration a sulphur-free bicyclic diketoalkene **7**, m.p. 70–71° (ν_{CO} 1720 cm^{-1}; δ $C{=}CH_2$ 4.96, s, 2 H) was formed in the reduction of B with acetone-deactivated Raney nickel.[3] Strong carbonyl absorptions of both A and B (e.g. $\nu_{CO}(CCl_4)$ 1729 and 1719 cm^{-1} for A) indicated the presence of two skeletal carbonyl groups. This was confirmed by the reduction of B with $LiAlH_4$ to a diastereomeric mixture of diols **10** from which a racemic modification, m.p. 218–220° (δ^{HCOH} 3.82, m, 2H) was isolated by TLC. Additional support for the skeletal functional groups was obtained in the reduction of B with undeactivated Raney nickel[3] (see above). In this case desulphurisation was accompanied by reduction of the alkene and carbonyl groups yielding hydroxylic and ketonic products from which the enantiomeric dione mixture **8**, m.p. 96–98° (ν_{CO} 1710 cm^{-1}) was isolated after Jones oxidation. Alternatively reduction of the Raney nickel product by $LiAlH_4$ furnished the complex mixture of diols **9**, m.p. 162–167°.



7. R¹, R² = O; R³, R⁴ = CH_2
8. R¹, R² = O; R³ = H; R⁴ = Me
9. R¹ = R³ = H; R² = OH; R⁴ = Me



10.

On hydrolysis with KOH in aqueous MeOH (see above), A underwent deacetylation with retro-aldol cleavage to give **1** confirming that the 9 - thiabicyclo[3.3.1]nonan - 2,6 - dione nucleus is contained in the skeletal framework of A and B. From the above chemical properties A and B are assigned the structures **5** and **6** respectively.

The proton NMR spectra of A and B exhibited broad overlapped skeletal resonances in the δ 2.6–3.5 region and conveyed at first sight limited evidence for the tricyclic nucleus of structures **5** and **6**.

In spectra of B recorded in the presence of $Eu(fod)_3$ the skeletal signals became resolved (Fig. 1A) into four mutually coupled two-proton multiplets, the coincidence of the two ABCD systems arising through the presence of a C_2 symmetry axis. The large observed coupling constant of 13 Hz was attributed to the geminal splitting of the C-9 methylene protons. From molecular models the dihedral angles which H_a^9 form with H^1 and H^5 are approximately equal (i.e. *ca.* 55°), consistent with the observed vicinal couplings of 4 Hz.[4] Dihedral angles of *ca.* 65° which H_b^9 forms with H^1 and H^5 give rise to the two observed vicinal 3 Hz couplings.[4] From NMDR experiments assignment is made of the methylene protons on C-9 (and C-10) as δ 2.63 and 2.83 for H_a and δ 3.03 and 3.23 for H_b (Fig. 1B) but clear differentiation between the methine protons, H^1 and H^5 is not possible. Unique assignment of the latter was achieved by cor-

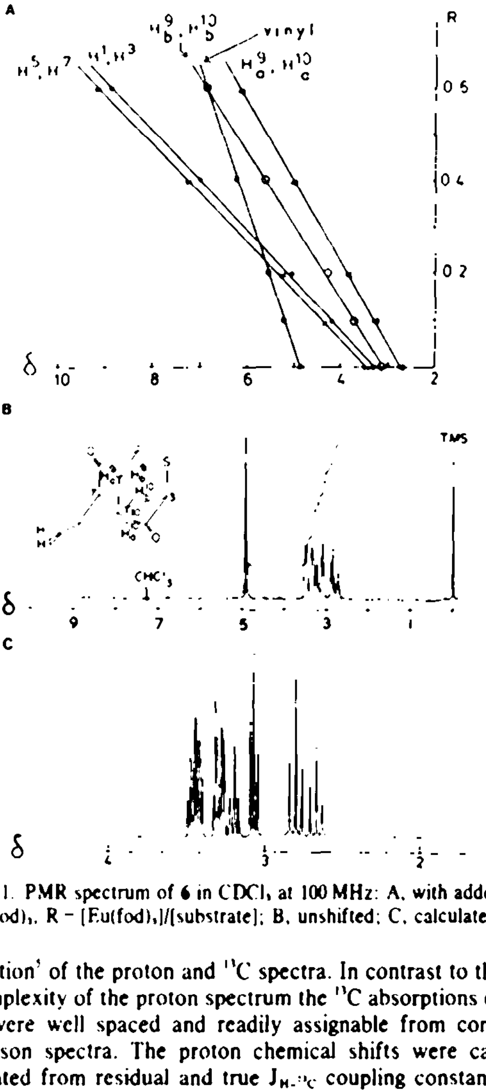


Fig. 1. PMR spectrum of **6** in CDCl$_3$ at 100 MHz: A, with added Eu(fod)$_3$, R = [Eu(fod)$_3$]/[substrate]; B, unshifted; C, calculated.

relation[5] of the proton and ^{13}C spectra. In contrast to the complexity of the proton spectrum the ^{13}C absorptions of B were well spaced and readily assignable from comparison spectra. The proton chemical shifts were calculated from residual and true $J_{H-^{13}C}$ coupling constants in the assigned off-resonance and gated decoupled ^{13}C spectra. From this comparison the methine absorptions due to H^1 and H^3 occur at δ 3.26 and those at δ 3.46 correspond to the protons on C-5 and C-7. From the observed chemical shifts and coupling constant values of B the NMR spectrum (Fig. 1C) calculated using the computer programme UEA ITR is found to be closely similar to the observed spectrum (Fig. 1B). This supports the assignment of B as **6** containing the required ABCD system as interpreted above.

The proton NMR spectra of A shifted with Eu(dpm)$_3$ were poorly resolved; consequently, analysis was made of the Eu(fod)$_3$-shifted spectra of the corresponding alcohol **2**. These showed skeletal resonances (e.g. see Fig. 2) in the form of eight partly resolved, one-proton multiplets arising from two non-coincident (no C_2 axis present) ABCD systems. The observed coupling constants and measured dihedral angles being similar to the values for alkene, B, indicate a close structural relationship and support the assignment of this alcohol as **2**. It follows that acetate A has structure **5**.

EXPERIMENTAL

For general experimental details see preceding paper.[2]

2-Thiaadamantane-4,6,8-trione-2-oxide **4**. An oxygen–ozone mixture was bubbled for 2 h through a solution of **6** (45 mg, 0.23 mmol) in methyl acetate (AR, 50 ml) at 70°. The deep blue solution decolourised on standing. Zinc (20 mg, 0.3 mmol) and AcOH (AR, 1 drop) were added to the reaction solution at room temperature and the suspension magnetically stirred overnight. Filtration, concentration and preparative TLC in CHCl$_3$ gave **4** as cubes (10 mg, 20%), decomp. *ca.* 120°. (Found: 212.01434. $C_9H_8O_4S$ requires: 212.01432); ν_{max} (KBr) 2950, 2920, 2850, 1705, 1115, 1070, 1025 and 940 cm^{-1}; δ (d_6-Me$_2$CO) 2.56, 2.83, 3.27 and 3.53 (all m, 4 H; C-9 and C-10 CH$_2$), 3.3 (m, 2 H; C-5 and C-7 CH), 3.96 (m, 2 H; C-1 and C-3 CH); mass spectral peaks at *m/e* 212 (M$^+$), 186 and 164.

6-Bromo-6-bromomethyl-2-thiaadamantan-4,8-dione **3**. A solution of bromine (84 mg, 0.52 mmol) in Me$_2$CO (AR, 3 ml) was added dropwise to a magnetically stirred solution of **6** (100 mg, 0.51 mmol) in Me$_2$CO (2 ml). Stirring was continued for 30 min, CHCl$_3$ was added and the solution washed with aq Na$_2$CO$_3$, water, dried (MgSO$_4$) and evaporated to give crude dibromide **3** (160 mg, 90%). Crystallisation from CHCl$_3$-petroleum spirit furnished plates, m.p. 189.5–190.5°. (Found: C, 34.20; H, 3.05. $C_{10}H_{10}O_2SBr_2$ requires: C, 33.92; H, 2.83%); ν_{max} (KBr) 3000, 2960, 2920, 1712, 1314, 1280, 1220, 979, 963, 923 and 670 cm^{-1}; δ 2.93 (m, 2 H; C-9 and C-10 CH), 3.26–3.5 (m, 6 H; C-1, C-3, C-5, C-7, C-9 and C-10 CH), 3.8 (m, 2 H; CH$_2$ Br); mass spectral peaks at *m/e* 354 (M$^+$), 274, 245, 218, 194 and 165.

6-Methylene-2-thiaadamantan-4,8-diol **10**. A solution of **6** (133 mg, 0.68 mmol) in anhydrous Et$_2$O (10 ml) was added dropwise to a magnetically stirred suspension of LiAlH$_4$ (52 mg, 1.37 mmol) in anhydrous Et$_2$O (20 ml). Stirring was continued for 2 h. Saturated aq Na$_2$SO$_4$ was added dropwise and the suspension filtered. The filtrate on TLC in CHCl$_3$ gave two bands. The major band contained diol **10** which sublimed in vacuum (0.03 mm Hg) as plates (65 mg, 48%), m.p. 218–220°. (Found: C, 60.32; H, 7.14. $C_{10}H_{14}O_2S$ requires: C, 60.59; H, 7.12%); ν_{max} (KBr) 3360, 3080, 2945, 2920, 2895, 2850, 1655, 1432, 1348, 1271, 1073, 1050, 1030,

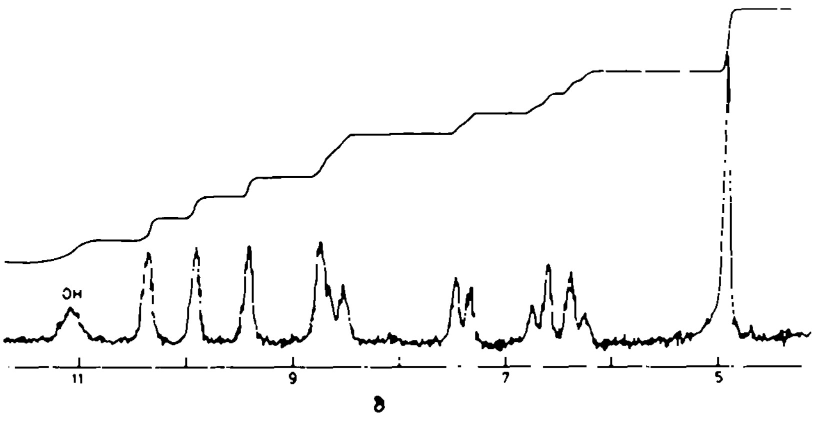


Fig. 2. PMR spectrum of **2** at 100 MHz in CDCl$_3$ with added shift reagent; [Eu(fod)$_3$]/[Substrate] = 0.85.

960, 950, 910, 890, 744 and 713 cm^{-1}; δ 1.77, 1.89, 2.71 and 2.83 (all m, 4 H; C-9 and C-10 CH_2), 2.6 (m, 2 H; C-1 and C-3 CH), 2.71 (m, 2 H; C-5 and C-7 CH), 3.13 (s, 2 H; hydroxyl), 3.8 (m, 2 H; C-4 and C-8 CH), 4.8 (s, 2 H: olefinic); mass spectral peaks at *m/e* 198 (M^+), 169 and 151.

This separated portion of the product represents only one of the three possible enantiomeric pairs of diols. This sharp melting product shows zero specific rotation in $CHCl_3$, gives a single sharp peak (ret. time 11.4 min) on GLC (TMS ether, 1% OV1 on Gaschrom Q, 4 ft column) and shows both PMR (*vide supra*) and ^{13}CMR spectra, characteristic of a single compound.

Treatment of **6** *with undeactivated Raney nickel.* **6** (70 mg, 0.36 mmol), excess Raney nickel and 95% ethanol (20 ml) were reflexed for 15 min. After filtration the nickel was washed with hot EtOH and the combined extracts concentrated. The residue, a complex mixture of diols and hydroxyketones, remained unchanged after refluxing the EtOH with excess Raney nickel for a further h. To simplify the product mixture reduction ($LiAlH_4$) and oxidation (Jones reagent) were carried out as in the two subsequent sections.

9-*Methylbicylo*[3.3.1]*nonan*-2,6-*diol* **9**. Reduction of the above mixture (50 mg) with $LiAlH_4$ (23 mg, 0.6 mmol) followed the same procedure as used in the formation of **10** from **6** (*vide supra*). Sublimation (120°, 0.2 mm Hg) of the crude product gave **9** as plates (35 mg, 57%), m.p. 162–167°. Analytical TLC in EtOAc showed **9** to be a mixture of diastereoismers. (Found: C, 70.77; H, 10.46. $C_{10}H_{18}O_2$ requires: C, 70.54; H, 10.66%); ν_{max}(KBr) 3280, 2930, 2875, 1455, 1084, 1060, 1032, 1022, 1005, 971 and 960 cm^{-1}; δ 0.96–1.36 (m, 4 H; C-9 CH and CH_3), 1.46 (s, 2 H; hydroxyl), 1.4–1.9 (m, 10 H; C-3, C-4, C-7 and C-8 CH_2, C-1 and C-5 CH), 3.7–4.1 (m, 2 H; C-2) and C-6 CH); mass spectral peaks at *m/e* 170 (M^+), 152, 134 and 119.

9-*Methylbicyclo*[3.3.1]*nonan*-2,6-*dione* **8**. Jones reagent (8 N, 0.12 ml) was added dropwise to a magnetically stirred solution of the above mixture (35 mg) in Me_2CO (AR, 6 ml). Stirring was continued for 30 min. The solution was concentrated, water added and extracted with EtOAc. The combined extracts, washed with water, brine, dried ($MgSO_4$) and evaporated furnished crude dione **8** (23 mg, 67%). Purification by TLC in $CHCl_3$, decolourisation with charcoal and sublimation (120°, 0.35 mm Hg) gave plates, m.p. 96–98°. (Found: C, 72.29; H, 8.50. $C_{10}H_{14}O_2$ requires: C, 72.26; H, 8.49%); ν_{max} (KBr) 2960, 2940, 2900, 2880, 1705, 1440, 1305, 1230, 770 and 740 cm^{-1}; ν_{max} (CCl_4) 1710 cm^{-1} (ϵ^* 703, $\Delta\nu_{1/2}^*$ 25 cm^{-1}); δ 1.05 (d, 3 H; J 7 Hz; CH_3), 0.9–1.3 (m, 1 H; C-9 CH), 1.95–2.2 (m, 4 H; C-4 and C-8 CH_2), 2.3–2.7 (m, 6 H; C-3 and C-7 CH_2, C-1 and C-5 CH); mass spectral peaks at *m/e* 166 (M^+), 138, 123 and 112.

9-*Methylenebicyclo*[3.3.1]*nonan*-2,6-*dione* 7. Raney nickel was deactivated by refluxing with Me_2CO for 1 h. The Me_2CO was decanted and the Raney nickel washed with 95% EtOH. **6** (70 mg, 0.36 mmol), 95% EtOH (20 ml) and excess deactivated Raney nickel were refluxed for 15 min. Work up (*vide supra*) furnished a solid which separated into two bands on TLC in EtOAc-petroleum spirit (1:1). The upper band was unreacted **6**. The lower band on extraction and sublimation (0.3 mm Hg) furnished 7 as plates (20 mg, 78%), m.p. 70–71°. (Found: C, 73.37; H, 7.46. $C_{10}H_{12}O_2$ requires: C, 73.14; H, 7.37%); ν_{max} (KBr) 3090, 2955, 2938, 2867, 1705, 1660, 1450, 1440, 1318, 1230, 1220 and 930 cm^{-1}; ν_{max} (CCl_4) 1720 cm^{-1} (ϵ^* 800, $\Delta\nu_{1/2}^*$ 20 cm^{-1}); δ 1.8–2.2 (m, 4 H; C-4 and C-8 CH_2), 2.3–2.7 (m, 4 H; C-3 and C-7 CH_2), 3.33 (t, 2 H; J 5 Hz; C-1 and C-5 CH), 4.96 (s, 2 H; olefinic); mass spectral peaks at *m/e* 164 (M^+), 136, 122, 108, 94 and 79.

Reflux of **6** with Me_2CO-deactivated Raney nickel for 45 min gave a complex product mixture from which 7, **8** and **9** were isolated by TLC.

6-*Hydroxy*-6-*methyl*-2-*thiaadamantan*-4,8-*dione* 2. A suspension of **5** (66 mg; 0.26 mmol) in 3 M NaOH (50 ml) was allowed to stand at room temperature for 65 h, the solution developing a brown colour. The reaction mixture was neutralised with dil HCl and extracted with EtOAc (2 × 50 ml). The combined EtOAc extracts were dried ($MgSO_4$), evaporated and sublimed (130°, 0.02 mm Hg) furnishing 2 as flakes (51 mg, 95%), m.p. 265–267°. (Found: C, 56.76; H, 5.79. $C_{10}H_{12}O_3S$ requires: C, 56.60; H, 5.70%); ν_{max} (KBr) 3399, 2940, 1718, 1295, 1156, 1109, 971 and 944 cm^{-1}; ν_{max} (CCl_4) 3606, 1729 and 1723 cm^{-1}; δ 1.38 (s, 3 H, CH_3), 2.3 (s, 1 H; hydroxyl), 2.7–3.1 (m, *ca* 5 H; C-5 and C-7 CH, C-9 and C-10 CH_2 (3 H)), 3.1–3.35 (m, *ca* 3 H; C-1 and C-3 CH, C-9 and C-10 CH_2 (1 H)) mass spectral peaks at *m/e* 212 (M^+), 179, 151, 137, 126, 113, 97 and 85.

Treatment of **5** *with KOH in aq MeOH.* A solution of **5** (670 mg; 2.6 mmol), KOH (1.4 g, 25 mmol) in MeOH (10 ml) and water (10 ml) was stirred at room temperature for 65 h. After neutralisation and extraction as above the oily product mixture (393 mg) separated into two components on TLC in EtOAc–$CHCl_3$ (1:9). The upper band gave **1** (288 mg, 65%) and the lower contained 2 (74 mg, 13%).

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