Functionalization and Cleavage of Adamantane with Lead Tetra-acetate; the Formation of $2(3 \rightarrow 4)$ abeo-Adamantane † from Adamantane

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Two different oxidative reactions of the adamantane nucleus with lead tetra-acetate are described. With adamantane and 2-adamantan-1-ylethanol in acetic acid sequential introduction of acetate groups at the bridgehead position occurs. In the presence of iodine, adamantan-1-ol affords tricyclo[4,3,1,03,8]decan-4-one via a bicyclo[3,3,1]nonanone.

DURING studies directed toward the synthesis of 1,2disubstituted adamantane derivatives, the ether (2) was obtained by treating 2-adamantan-1-ylethanol (1) with lead tetra-acetate.⁴ It has since been found that when acetic acid is used as solvent there is no cyclization. Instead acetylation of the hydroxy-group occurs, followed by acetoxylation at the bridgehead positions. Adamantane itself has been found to undergo similar sequential bridgehead functionalization, but adamantan-1-ol gave an intractable mixture.

Presumably a radical mechanism is operative in the cyclization, whereas hydride abstraction occurs in the acetic acid. To our knowledge this is the first clear example of lead tetra-acetate acting as a hydride abstractor.

Stetter and his co-workers prepared the methylene ketone (12) by a multi-step synthesis.⁵ Since this compound can be used to prepare a variety of 1,3disubstituted adamantanes, a more simple synthesis was sought. In the ester (11), expected to be the intermediate formed by the action of lead tetra-acetate on adamantan-1-ol, all the thickened bonds are coplanar. It was thus hoped that this ester would cleave in the manner shown (broken arrows) to give (12).

When adamantan-1-ol was treated with lead tetraacetate and iodine in benzene at 60° (without iodine no reaction occurred), the iodine intervened in the desired cleavage, and the iodo-ketone (13) was obtained. The structure of this iodo-compound is demonstrated by its n.m.r. spectrum (solution in deuteriochloroform; 60 MHz). This exhibits a relatively sharp two-proton doublet centred at τ 7.0 (J ca. 7 Hz), due to CH₂I, and a broad high-field triplet centred at τ 9.1, arising from the two axial hydrogens H_E lying in the shielding zone of the carbonyl group. The triplet character of this signal is as expected for these protons, which are geminally coupled to protons H_F , with trans diaxial coupling to H_{G} and minor coupling to H_{H} . Only the conformation shown would give rise to these signals.



The iodo-ketone decomposed on prolonged heating in benzene to the ketone (14).[‡] This transition was more

¹ R. B. Vogt, Tetrahedron Letters, 1968, 1575.

² J. E. Baldwin and W. D. Foglesong, J. Amer. Chem. Soc., 1968, 90, 4303.

³ IUPAC-IUB 1967 Revised Tentative Rules for Steroids Nomenclature, Biochim. Biophys. Acta, 1968, 164, 453. ⁴ W. H. W. Lunn, W. D. Podmore, and S. S. Szinai, J. Chem.

Soc. (C), 1968, 1657.
⁵ H. Stetter and P. Tacke, Chem. Ber., 1963, 96, 694.

⁶ M. L. Sinnott, H. J. Storesund, and M. C. Whiting, Chem. Comm., 1969, 1000.

 $[\]dagger$ In previous reports tricyclo[4,3,1,0^{3,8}]decane has been called isoadamantane 1 and protoadamantane.² We prefer the name $2(3 \rightarrow 4)$ abeo-adamantane, using the nomenclature accepted for steroids.³ This name not only relates the compound to adamantane, as desired, but is descriptive of the structure.

[‡] While this paper was in preparation a synthesis of the ketone (14) was reported,⁶ though the evidence for its structure was not definitive. The complex shape of the carbonyl peak in the i.r. spectrum of this ketone in carbon tetrachloride was also noted by us (ν_{max} . 1715 and 1722sh cm.⁻¹).

smoothly effected by heating in pyridine or methanolic sodium hydrogen carbonate.

(pyridine)

(13)

(14)



and in the spectrum of a solution in [2H₆]benzene it is clearly evident as a one-proton sextet centered at τ 7.34. This corresponds to the X portion of an ABX system in which coupling constants J_{MN} , J_{MO} , and J_{MP} are ca. 7.0, 8.0, and 3.5 Hz, respectively.

The small (11 Hz) shielding of H_M in benzene as compared to deuteriochloroform is reasonable since this proton is equatorial and α to the carbonyl group (see Figure).⁷ In the case of adamantanone (17), the two protons H_R give a broad signal at τ 7.46 and 7.53 in deuteriochloroform and in benzene, respectively, a shielding of 7 Hz. *

A broad single-proton triplet is present in the n.m.r. spectrum (100 MHz) of the 2,4-dinitrophenylhydrazone (15a) derived from (14); the characteristics of the signal are again in accord with the structure shown. The parent ion in the mass spectrum of this derivative lies at m/e 378, in agreement with the formula $C_{20}H_{18}N_4O_4$.

The suggested cleavage mechanism, for which there is a precedent,⁸ together with the evidence for the structures of the products, seems sufficient to confirm the course of the reactions. In particular the extraordinarily highfield resonance of protons H_E in (13) and the presence of

the unique proton H_M in (14) appear to defy any other explanation.

 $2(3\rightarrow 4)$ abeo-Adamantane (16) has been previously synthesized; ^{2,9} it appeared desirable to prepare it from



(14). Attempts to prepare the hydrazone of (14) by Barton's procedure 10 (suggested to minimize the formation of azine) led, in fact, only to the recovery of azine (15b). At this point attempts to reduce (14) to (16) were not pursued since the derivation of the structure of the ketone is based on grounds which are probably more secure than those used to arrive at the structure of (16).

EXPERIMENTAL

Treatment of 2-Adamantan-1-vlethanol with Lead Tetraacetate in Glacial Acetic Acid.-(a) The alcohol (0.9 g.), lead tetra-acetate (3.01 g., 1.35 mol.), and glacial acetic acid (10 ml.) were refluxed with stirring for 2.5 hr., after which time the mixture gave a negative starch-iodide test. The mixture was cooled, poured into ice-water, and extracted with ether. The extract was washed with water and then dilute sodium hydrogen carbonate, dried (MgSO₄), and evaporated to give an oil, which was chromatographed on Grace-Davison silica gel (45 g.). Benzene eluted 2adamantan-1-ylethyl acetate (3) as an oil (0.56 g.), homogeneous according to t.l.c. (Found: C, 75.4; H, 10.25; Ac, 18.7. $C_{14}H_{22}O_2$ requires C, 75.65; H, 9.95; Ac, 19·35%), 7 8·60 (2H, t, J ca. 7·5 Hz), 8·4 (12H, m), 8·06 (3H, m), 7.98 (3H, sharp s), and 5.88 (2H, t, J ca. 7.5 Hz).

Benzene-ethyl acetate (9:1) eluted 2-(3-acetoxyadamantan-1-yl)ethyl acetate (4) as an oil (1.11 g.), homogeneous according to t.l.c. (Found: C, 68.75; H, 8.8; Ac, 30.7. $C_{16}H_{24}O_4$ requires C, 68.55; H, 8.65; Ac, 30.7%), τ 8.5 (8H, m, including t centered at τ 8.48, J ca. 7.5 Hz), 8.0 (14H, m, including two sharp acetate signals at τ 8.04 and 7.98), and 5.86 (2H, t, J ca. 7.5 Hz).

(b) The alcohol (2.52 g.), lead tetra-acetate (19.84 g., 3.4 mol.), and acetic acid (75 ml.) were refluxed with stirring for 5.5 hr., then processed and chromatographed as in (a) on silica gel (100 g.). Benzene eluted pure diacetate (4) (0.24 g.). Benzene-ethyl acetate (19:1 and 9:1)eluted a single (t.l.c.) product as an oil (2.73 g.), 2-(3,5-

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¹⁰ D. H. R. Barton, R. E. O'Brien, and S. Sternhell, J. Chem. Soc., 1962, 470.

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^{*} The n.m.r. spectra of adamantanone in deuteriochloroform and hexadeuteriobenzene both consist of three peaks: τ (CDCl₃) 8.07 (2H), 7.96 (10H), and 7.46 (2H); τ (C₆D₆) 8.48 (4H), 8.33 (8H), and 7.53 (2H). These data conform with the shielding behaviour of benzene in collision complexes with ketones de-scribed by Bhacca and Williams.⁷ The two protons which are observed in the middle signal for the solution in deuteriochloroform and in the high-field signal for the solution in hexadenterio benzene, are presumably those labelled H₈ in the Figure.

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diacetoxyadamantan-1-yl)ethyl acetate (5) (Found: C, 63·45; H, 8·0; Ac, 37·49. $C_{18}H_{26}O_6$ requires C, 63·9; H, 7·75; Ac, 38·15), τ 8·5 (4H, m, including t centered at 8·40, J ca. 7·5 Hz), 8·0 (19H, m with two sharp acetate signals at 8·04 and 7·98), 7·7 (1H, m), 7·55br (2H), s), and 5·85 (2H, t, J ca. 7·5 Hz).

Treatment of Adamantane with Lead Tetra-acetate in Glacial Acetic Acid.—(a) Adamantane (2.72 g.), lead tetraacetate (9.32 g., 1.05 mol.), and acetic acid (12 ml.) were refluxed with stirring for 1.75 hr. Complete dissolution was achieved after the first 0.5 hr., and it was necessary during the first part of the reaction to scrape adamantane from the condenser walls back into the reaction mixture. After being cooled and filtered to remove unchanged adamantane (0.3 g.), the mixture was processed as before; silica gel (180 g.) was used for the chromatography.

Benzene eluted a single (t.l.c.) liquid compound (1.59 g.), 1-acetoxyadamantane (7) (Found: C, 74.4; H, 9.45; Ac, 21.95. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.35; Ac, 22.15%), τ 8.33br (6H, s), 8.06 (3H, sharp s), and 7.90br (9H, s). Benzene-ethyl acetate (19:1) eluted another single (t.l.c.) product (0.57 g.), 1,3-diacetoxyadamantane (8) (Found: C, 66.35; H, 8.05; Ac, 33.95. $C_{14}H_{20}O_4$ requires C, 66.65; H, 8.0; Ac, 34.05%), τ 8.42 (2H, m), 8.06 (6H, sharp s), 7.95 and 7.91 (8H), 7.73br (2H, m), and 7.56br (2H, s). No other pure material was recovered.

(b) Adamantane (4.08 g.), lead tetra-acetate (28.78 g., 2.20 mol.), and acetic acid (35 ml.) were refluxed with stirring for 2.5 hr., then processed as in (a); silica gel (400 g.) was used for the chromatography. Benzene eluted the monoacetate (7) (1.04 g.) followed by the diacetate (8) (2.36 g.).

(c) Adamantane (2.72 g.), lead tetra-acetate (29.2 g., 3.3 mol.), and acetic acid (40 ml.) were refluxed with stirring for 3.5 hr. and processed as before; the mixture was chromatographed on silica gel (300 g.). Benzene eluted the diacetate (8) (1.53 g.), and benzene–ethyl acetate (19:1) pure 1,3,5-triacetoxyadamantane (9) (1.52 g.), m.p. 45—46° (Found: C, 62.25; H, 7.4; Ac, 42.2. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.15; Ac, 41.5%), τ 8.0 (15H, 2 peaks, one at 8.06 being intense) and 7.54 (7H, small shoulder at base due to the single bridgehead proton). Later fractions produced only mixtures.

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7-Iodomethylbicyclo[3,3,1]nonan-3-one (13).—Adamantan-1-ol (10·1 g.), lead tetra-acetate (32·6 g., 1·1 mol.), and iodine (18·64 g., 1·1 mol.) were stirred in dry benzene (200 ml.) at 60° for 80 min. The cooled mixture was filtered, and the solid was washed with benzene and then ether. The filtrate and washings were washed with aqueous sodium hydrogen sulphite until colourless, then with water, and then with dilute sodium hydrogen carbonate solution, and dried (MgSO₄). Evaporation at 50° gave an oil which was crystallized from methanol at -70° to give the *iodo-ketone* (8·3 g.), m.p. 78—79° (Found: C, 43·3; H, 5·75; I, 45·1; O, 6·05. C₁₀H₁₅IO requires C, 43·2; H, 5·45; I, 45·1; O, 5·75%), τ 7·00 (2H, d) and 9·10br (2H, t).

 $Tricyclo[4,3,1,0^{3,8}] decan-4-one (14).$ The iodo-ketone (13) (12·0 g.) was stirred in pyridine (12 ml.) at 55° for 4 hr., cooled, and poured into ice-water. The resulting solid was collected and recrystallized from methanol-water to provide the *ketone* (14) (4·6 g.), m.p. 210—212° (Found: C, 79·75; H, 9·35. C₁₀H₁₄O requires C, 79·95; H, 9·4%). The 2,4dinitrophenylhydrazone (15a) had m.p. 195—196° (from ethanol-chloroform) (Found: C, 58·25; H, 5·9; N, 16·85. C₁₆H₁₈N₄O₄ requires C, 58·15, H, 5·5; N, 16·95%).

Azine (15b) from Tricyclo[4,3,1,0^{3,8}]decan-4-one.—The ketone (1·25 g.) was stirred in a mixture of ethanol (10 ml.) and triethylamine (2 ml.), and hydrazine (54·4%; 5 ml.) was added. This mixture was stirred under reflux for 2 hr. and then poured, with stirring, on crushed ice. Extraction with ether, washing the extract with several volumes of saturated sodium chloride solution, and removal of the ether by distillation through a Vigreaux column provided a white, solid residue. Recrystallization from methanol gave pure azine (0·52 g.), m.p. 311—313°; a second crop (0·26 g.), m.p. 310—312°, was obtained by diluting the mother liquors with water (Found: C, 80·75; H, 9·55; N, 9·45. C₂₀H₂₈N₂ requires C, 81·05; H, 9·5; N, 9·45%).

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