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THE π-ROUTE TO 2,4-SUBSTITUTED ADAMANTANES

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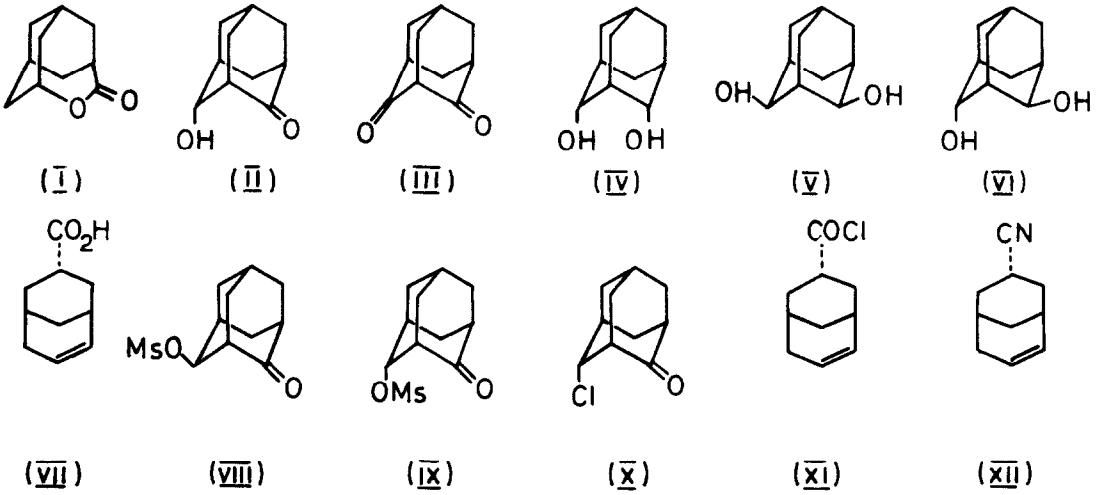
During a study of adamantane rearrangements it was observed that 4-oxohomoadamantan-5-one (I) (1) undergoes a smooth rearrangement in 50% sulphuric acid *via* a mechanism which exemplifies the π-route to 2,4-disubstituted adamantanes. The lactone, obtained in 96% yield by oxidation of adamantanone (2) with hydrogen peroxide-selenium dioxide in hot t-butanol, was heated in 50% sulphuric acid at 90° for 5 hr. The product was a 1:6 mixture of (I) and 4^{a}-hydroxyadamantan-2-one (II), m.p. 316-320°, (65% yield); i.r. (KBr): 3400, 1720, and 1710 cm^{-1}; n.m.r. (100 MHz, $CDCl_3$) τ : 5.72 (1H, C-4), 7.35 (1H, C-3), 7.53 (1H, C-1), and 7.63-8.20 (10H). Additional evidence for the location of the hydroxyl group was obtained by oxidation with chromic acid in acetone to the known adamantane-2,4-dione (III) (3). The n.m.r. spectrum of (II) indicated the presence of a single stereoisomer and this was confirmed by capillary g.l.p.c. analysis of the corresponding trifluoroacetate. The configuration at C-4 was assigned as follows. Reduction of (II) with lithium aluminium hydride gave two diols (ratio 19:1). The n.m.r. spectrum of the major diol contained a single low field absorption for the protons on C-2 and C-4 suggesting that this product was one of the two possible symmetrical adamantane-2,4-diols (IV) and (V), and the i.r. spectrum (4.10^{-3}M CCl_4) exhibited a strong absorption at 3540 cm^{-1} due to intramolecular hydrogen bonding. Of the two diols (IV) and (V) only the former has the correct configuration for intramolecular hydrogen bonding. It follows, therefore, that the hydroxy-ketone and its major reduction product have the configurations shown in (II) and (IV), respectively. Reduction of adamantane-2,4-dione with lithium aluminium hydride gave all three adamantane diols in yields of 45% (IV) 16% (V), and 39% (VI).

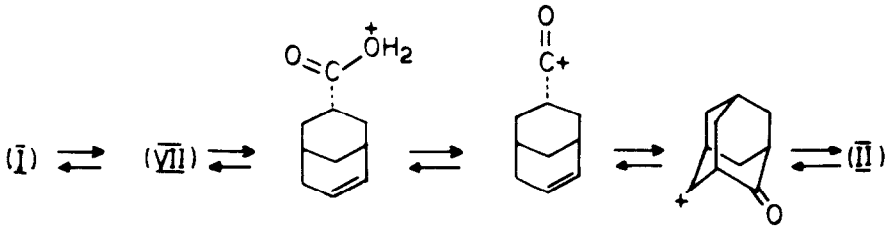


(I) (II) (III) (IV) (V) (VI)

(VII) (VIII) (IX) (X) (XI) (XII)

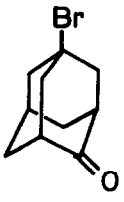
We can now comment on the configuration of the 4-substituted adamantan-2-one prepared by Sasaki et al.(4). These authors found that treatment of adamantanone with sodium azide in methanesulphonic acid gave 4-methylsulphonyloxyadamantan-2-one and the suggestion was made that the product results from a direct substitution reaction on adamantanone. Although the configuration at C-4 was not established, the observation that the product could be converted into bicyclo[3.3.1]non-2-ene-7-carboxylic acid (VII) (1) on treatment with potassium hydroxide suggests that the mesylate group is equatorial as in (VIII) since this is exactly the configuration which permits fragmentation of the adamantane skeleton. The physical and spectral data for 4^{a}-methylsulphonyloxyadamantan-2-one (IX), obtained from (II) and the acid chloride, now show this to be the case : mesylate (IX), m.p. 106-107°, was distinctly different from mesylate (VIII), m.p. 73-75°.

The rearrangement of (I) into (II) is reversible in 50% sulphuric acid and the mechanism, which can be interpreted as shown in the scheme, illustrates the π-route to substituted adamantanes. Acid (VII) also gave (I) and (II) in the ratio 1:6 when treated with

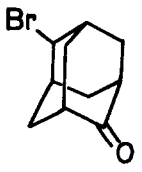


50% sulphuric acid. In 80% sulphuric acid, with added carbon tetrachloride, the rearrangement of (I) gave 4^{a}-chloroadamantan-2-one (X), m.p. 207-209°, in 58% yield. (X) was also produced when the acid chloride (XI), obtained from (VII) and oxalyl chloride, was treated with boron trifluoride etherate in diglyme.

In fact the conversion of adamantanone into the keto-mesylate (VIII) is also an example of the π-route to substituted adamantanes and is not a direct substitution reaction as was suggested by Sasaki et al. (4). Korsloot and Keizer (5) reached this conclusion as a result of their study of the Beckmann rearrangement of adamantanone oxime in 96% sulphuric acid, a reaction which proceeds by ring fission and recyclisation giving (II) and its equatorial isomer, and we have obtained direct evidence on this point. Treatment of adamantanone with sodium azide in methanesulphonic acid at 0° for $1\frac{1}{2}$ minutes afforded, in addition to (VIII), 15% of the unsaturated nitrile (XII) (5). This compound is an intermediate in the reaction since further treatment with methanesulphonic acid alone produced (VIII) in high yield. The formation of (VIII) is, therefore, an example of a Schmidt fragmentation-cyclisation reaction and is not a direct substitution reaction with the ketone. Nevertheless, it is possible to effect such a reaction with adamantanone although the conditions required contrast greatly with those necessary for a similar reaction with adamantane. Conditions under which the hydrocarbon gives 1-bromoadamantane in high yield leave the ketone unchanged. With aluminium bromide catalysis, however, and a reaction time of 10 days, bromination does occur giving 5-bromoadamantan-2-one (XIII) (6) in 90% yield. A second product (2%) was identified as 6-bromoadamantan-2-one (XIV), m.p. 187-189°, on the basis of the spectral data and on conversion via 6-hydroxyadamantan-2-one (XV) into adamantane-2,6-dione (XVI) (7).



(XIII)



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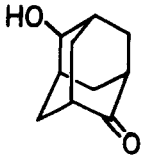
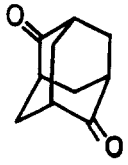


(XV)



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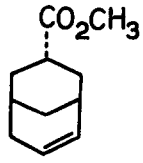
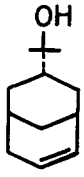


(XVII)



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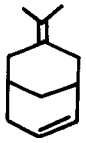
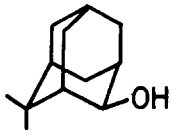
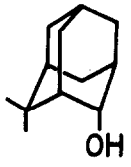


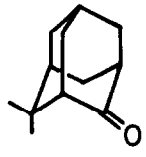
(XIX)



(XX)



(XXI)



(XXII)

Finally we wish to illustrate the extension of the π-route to 2,4-trisubstituted adamantanes. Exposure of alcohol (XVIII), m.p. 56.5-58°, prepared from the unsaturated ester (XVII) and methylmagnesium iodide, to hot formic acid for 2 hr. gave the diene (XIX)(1%) and a mixture of saturated formates (82%). Hydrolysis of the formates gave the alcohols (XX) (86%) and (XXI) (14%), and subsequent oxidation gave 4,4-dimethyladamantan-2-one (XXII), m.p. 174-175°; i.r. (KBr): 1720 and 1710 cm^{-1}; n.m.r. ($CDCl_3$) τ : 9.09 (3H,s), 8.76 (3H,s), and 7.48-8.55 (12H, m). Wolff-Kishner reduction of (XXII) gave 2,2-dimethyladamantane, m.p. 143-144° (8). The stereochemistry of the cyclisation reaction was determined as follows. Lithium aluminium hydride reduction of (XXII) afforded in high yield a single alcohol, m.p. 194-196°, which on the basis of steric approach control was assigned the axial configuration (XXI). Similarly, the preponderance of (XX) in the cyclised products can reasonably be explained on the grounds that addition of formic acid to the 4,4-dimethyl-2-adamantyl cation occurs preferentially from the less hindered equatorial side. The dichotomy of behaviour with the earlier cyclisations, i.e. formation of the equatorial mesylate (VIII) from (XII) in methanesulphonic acid and the axial alcohol (II) from (VII) in 50% sulphuric acid, still requires an explanation (9) (10).

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(3) A.C. Udding, J. Strating, and H. Wynberg, Tetrahedron Letters, 1345 (1968); we thank Professor Wynberg for providing us with the spectral data for adamantane-2,4-dione.

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(9) All new compounds gave satisfactory analytical and spectral values.

(10) We thank the Northern Ireland Ministry of Education for a postgraduate grant to D.F.