

Abnormal Hypoiodite Reactions of 2-Substituted Adamantan-2-ols: Novel Routes to 4-Oxahomo- and 2-Oxa-adamantanes

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Summary 5-Substituted 4-oxahomoadamantanes are formed in the reaction of 2-substituted adamantan-2-ols with lead tetra-acetate and iodine; novel routes to 1-substituted 2-oxa-adamantanes are reported, and the mechanisms of these reactions are discussed.

WE reported recently¹ that treatment of adamantan-1-ol with lead tetra-acetate and iodine yielded an iodoketone whose structure was consistent with the intermediacy of the 1-adamantyloxy-radical. Likewise, thermolysis of 2-substituted adamantan-2-ol hypoiodites furnished bicyclic chloroketones expected from the β -scission of the t-alkoxy-radicals. In contrast, however, only 'abnormal' products

were isolated in the hypoiodite reactions [*i.e.* Pb(OAc)₄/I₂] of 2-substituted adamantan-2-ols.

The reaction of 2-methyladamantan-2-ol (I) with Pb(OAc)₄/I₂ in C₆H₆ (80°, 1.5h) yielded a yellow crystalline di-iodoether (C₁₁H₁₆I₂O),[†] m.p. 149–151° (32–52%). This compound, which had an unusually high density (*d*¹⁷ 2.26), had the following spectroscopic properties [i.r. ν (CCl₄) 1582 (ϵ 78), 1262, 1185 (ϵ 450), 1108, 1035 (ϵ 271), 582, 530, and 455 cm⁻¹; 220 MHz n.m.r. τ (CDCl₃) 5.37 (1H, m, separation between outer lines 12.5 Hz), 6.15 (1H, m, separation between outer lines 15.2 Hz), and 7.94–8.41 (14H, complex m); *m/e* (*M*⁺) 418]. The data are consistent[‡] with the assigned structure (II), 5-iodo-5-iodo-methyl-4-oxahomoadamantane, and confirmatory evidence

[†] Satisfactory micro-analyses were obtained for all new compounds.

[‡] The 1582 cm⁻¹ absorption is probably a combination band. The absence of a low field signal for the -CH₂I protons arises because they lie predominantly within the *shielding* zone of the ether oxygen atom. Courtauld Molecular Models indicate a strong preference for this type of conformation. In (IV) and (IVa) the expected downfield shifts for the -CH₂X resonances were observed.

was obtained from chemical degradative studies. The formation of (III), (IV), (IVa), (V), and (IX) confirms the substitution pattern about positions 4 and 5 of the oxahomoadamantane system in (II), and the assignments are in complete accord with the spectroscopic data *e.g.* [(III); i.r. ν (CCl_4) 3100w, 1612s ($\text{O}=\text{C}=\text{C}$), 1278s, 1177s, 1140s, and 1042s cm^{-1} ; 100 MHz n.m.r. τ (CCl_4) 5.32 (1H, s, =CH), 5.48 (1H, m, separation between outer lines 14 Hz, 3-H), 7.00 (1H, m, separation between outer lines 18 Hz, 6-H), and 7.9–8.5 (12H, complex m); m/e (M^+) 290]. The total structure of (III), and by analogy that of (II) follows from the sequence (III) \rightarrow (V) \rightarrow (VII) since (V) and (VII) were prepared by an unambiguous route from the known compound 4-oxahomoadamantan-5-one (VIII).²

The di-iodoether (II) was rapidly decomposed by conc. HCl with loss of iodine to give (IV). However, with 0.67N-HCl in dimethylformamide at 105° the product was methyl 2-oxa-adamant-1-yl ketone (VI; 60%), b.p. 65–70° (bath)/0.01 mm; i.r. ν (CCl_4) 1708 cm^{-1} ; 100 MHz n.m.r. τ (CCl_4) 5.90 (1H, m, 3-H), 7.82 (2H, m, 5-H and 7-H), 7.94 (3H, s, CH_3), and 8.0–8.5 (10H, complex m); m/e (M^+) 180 (45%) and 137 (100%).

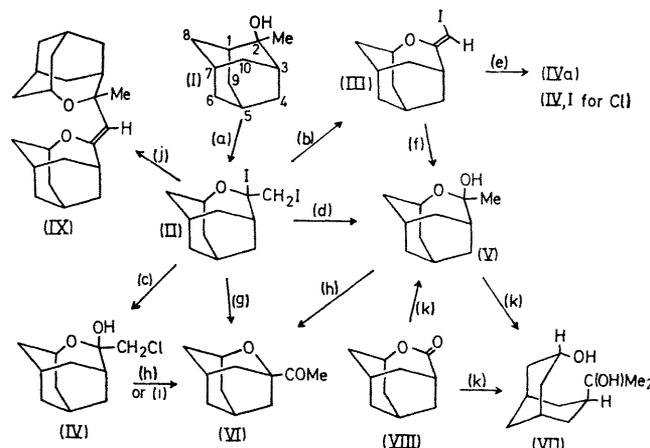
The ketone (VI) was also obtained from both (IV) and (V) by the action of aq. $\text{HCl}-\text{HCONMe}_2-\text{I}_2$. Iodine was essential to the conversion (V) \rightarrow (VI), but in the case (IV) \rightarrow (VI) sodium iodide was an adequate substitute (halogen generated *in situ*). G.l.c. analysis indicated that (IV) was a by-product in the conversion (II) \rightarrow (VI) and that the hemiacetal (V) was the kinetically significant intermediate in each case. The phenyl analogue of (V), (Ph for Me),[§] which was the product isolated from the reaction of 2-phenyladamantan-2-ol[¶] with $\text{Pb}(\text{OAc})_4/\text{I}_2$, was likewise converted by aq. $\text{HCl}-\text{HCONMe}_2-\text{I}_2$ into 2-oxa-adamant-1-yl phenyl ketone (55%).

The formation of the oxa-adamantyl ketones can be rationalised as follows: (i) formation of hemiacetals (V) through elimination reactions followed by addition of water across the reactive vinyl-ether double bond; (ii) acid-catalysed ring fission to 3-hydroxybicyclo[3,3,1]non-7-yl ketones; (iii) acid-catalysed iodination at C-7, the most substituted position α to the $\text{C}=\text{O}$ function;³ (iv) intramolecular $\text{S}_{\text{N}}2$ displacement of I^- by the *endo*-hydroxy-group at C-3.

The change (II) \rightarrow (VI) and the various corollary transformations, which includes the relay (VIII) \rightarrow (V) \rightarrow (VI), appear to be novel methods for ring contraction and may be capable of more general application.

It is most likely that the di-iodoether (II) is not the primary reaction product in the oxidation, but rather the mono-iodoether 5-iodo-5-methyl-4-oxahomoadamantane (IIa), otherwise the corresponding oxidation of (I), (Ph for Me) would fail. The conversion (IIa) \rightarrow (II) could occur

in one of two ways: (a) the elimination of HI to give (III), (=CH₂ for =CHI) followed by the addition of iodine across the reactive double bond, or (b) direct oxidative iodination of the methyl group, a process for which there is a reasonable analogy.⁴ Although no distinct choice between (a) and



SCHEME. Reagents: (a) $\text{Pb}(\text{OAc})_4 + \text{I}_2$; (b) Bu^tOK in Me_2SO ; (c) CHCl_3 soln. + conc. HCl; (d) Bu^n_3SnH in Et_2O , aqueous work-up; (e) silica gel; (f) PtO_2/H_2 in EtOH ; aqueous work-up; (g) dil. HCl in HCONMe_2 at 105°; (h) dil. HCl + I_2 in HCONMe_2 at 105°; (i) dil. HCl + NaI in HCONMe_2 at 105°, trace AcOH; (j) Zn in Et_2O , trace AcOH; (k) MeMgI in Et_2O .

(b) can be made at present, experiments indicate that elimination of HI as in (a) can occur readily. Thus, reaction of (I), (Et for Me)⁵ with $\text{Pb}(\text{OAc})_4/\text{I}_2$ yielded the methyl homologue of (III), (=CMeI for =CHI); all attempts to isolate a di-iodoether failed although it must have been formed.

The more general question of whether these 'abnormal' hypiodite reactions (and related processes) proceed by way of free radical intermediates (as is currently accepted⁶) is under investigation. Preliminary results indicate a rather more complex involvement of the lead species than is normally assumed. For example, the thermolysis of the hypochlorite of (I)¹ yielded (II) when conducted in the presence of iodine and lead tetra-acetate. The readily isolable compound (II) could not be detected when iodine was the sole additive. The precise function of the iodine is also obscure since the oxidation of (I) by lead tetra-acetate alone proceeded extremely slowly, and then only furnished a mixture of products.

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§ Formed by hydrolysis of the corresponding reactive mono-iodoether in the aqueous work-up.

¶ Prepared from adamantan-2-one and phenylmagnesium bromide, m.p. 80.5–81° (71%).

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³ For example see E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart, and Winston, New York, 1959, p. 383.

⁴ Y. Yukawa and M. Sakai, *Bull. Chem. Soc. Japan*, 1966, 39, 827.

⁵ S. Landa, J. Vais, and J. Burkhard, *Coll. Czech. Chem. Comm.*, 1967, 32, 570.

⁶ For example see K. Heusler and J. Kalvoda, *Angew. Chem. Internat. Edn.*, 1964, 3, 525.