Carboxylation of 2-Methyladamantan-2-ol and 2-(1-Adamantyl)ethanol: Evidence for the Intermolecular Nature of Hydride Transfer Reactions in Rearrangements involving Adamantyl Cations

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Three experimental procedures are described for Koch–Haaf carboxylation of 2-methyladamantan-2-ol: at normal concentrations at 0° the major products are 2-methyladamantane-1-carboxylic acid and *syn*- and *anti*-4-methyladamantane-1-carboxylic acid; at normal concentrations at 50° the major product is 3-methyladamantane-1-carboxylic acid; but with high dilution conditions at 0° 2-methyladamantane-2-carboxylic acid is formed exclusively. Carboxylation of 2-(1-adamantyl)ethanol at room temperature with either normal or high dilution conditions gives predominantly 3-ethyladamantane-1-carboxylic acid, whereas at 50° equal amounts of this acid and adamantane-1-carboxylic acid are produced. These rearrangements are interpreted in terms of stereochemical inhibition of intramolecular 1,2-hydride shifts and dilution-controlled intermolecular hydride shifts.

We have described [1] some aspects of the rapid sequence of rearrangements of 2-methyladamantan-2-ol (1a) in 98% sulphuric acid. Initially at low temperatures 2-methyladamantane, 2-methyladamantan-1-ol (2a), and *syn*- and *anti*-4-methyladamantan-1-ol (3a) are formed; at 50° 1-methyladamantane and 3-methyladamantan-1-ol (4a), the product in which methyl and hydroxy-functions have shifted, are obtained; and at still higher

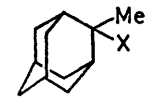
[1] B. D. Cuddy, D. Grant, A. Karim, M. A. McKervey, and E. J. F. Rea, preceding paper.

temperatures with longer reaction times disproportionation and/or oxidation of the presumed intermediate appropriate secondary alcohols leads to 5-methyladamantan-2-one and 1-methyladamantan-2-one.

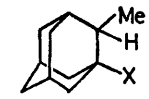
The question now arises as to how best to interpret the mechanism of these rearrangements. We tentatively suggested in a preliminary communication [2] that the 2-methyl-2-adamantyl cation (5) could undergo a series of reversible 1,2-hydride shifts [3] to give the other tertiary cations (6) and (7), leading ultimately to an equilibrium mixture of the alcohols (1a), (2a), and (3a) at low temperatures, and that at 50° the 1,3-alcohol (4a) is the product of a combination of 1,2-hydride shifts and a 1,2-methyl shift. This interpretation is incomplete inasmuch as it does not account for the hydrocarbons formed in the reaction; clearly 1- and 2-methyladamantane are products of disproportionation processes in which the appropriate cations are reduced by intermolecular hydride transfer. Later however the intramolecular hydride shift mechanism was questioned on stereoelectronic grounds.[4,5]

Let us consider the interconversion of the cations (5) and (6), bearing in mind that the relationship which provides maximum orbital overlap at the transition state is one in which the vacant orbital of the cation and the bond to the substituent undergoing migration are coplanar. In acyclic cations a favourable conformation with zero dihedral angle between the C–H bond and the vacant orbital is easily achieved by rotation about the conjoining bond. However, in adamantyl cations rotational conformational changes are precluded and the dihedral angles in the cations (5) and (6) are held rigidly at 90 and 60°, respectively. Consequently, the highly deformed transition state connecting these two cations should be so unfavourable that 1,2-shifts will be either extremely slow relative to the rate of 1,2-shifts in acyclic cations, or possibly even kinetically inaccessible. Similar conclusions were reached independently by Brouwer and Hogeveen [6] from a consideration of the absence of line broadening in the n.m.r. spectrum of the 1-adamantyl cation in antimony pentafluoride-based superacid media. A recent attempt [7] to quantify these obstacles to 1,2-hydride shifts in adamantyl cations gives as a minimum estimate an activation energy of *ca.* 30 kcal mol^{-1} from the observation that in antimony pentafluoride–sulphonyl chloride fluoride at 105° the [3,5,7-$^2H_3$]-1-adamantyl cation exhibits less than 10% tertiary–secondary scrambling. This value is to be compared with an estimated barrier to 1,2-hydride shifts in typical acyclic cations of about 15 kcal mol^{-1}.[6,8]

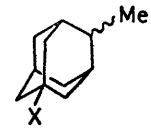
What has just been said about stereochemical inhibition of 1,2-hydride shifts should apply equally well to intramolecular 1,2-methyl shifts in adamantyl cations. Intermolecular methyl shifts must be considered highly unlikely (what appears to be an example of such a shift can be realised by an addition–fragmentation mechanism involving olefinic intermediates [9]); nevertheless, the apparent 1,2-methyl shift is observed experimentally, with the alcohol (1) in sulphuric acid and with 2-methyladmantane in Lewis acids.[10] This aspect of the problem has been elegantly elucidated by Schleyer and his co-workers,[10] who showed through experiments with labelled materials that the apparent 1,2-methyl shift is actually a skeletal reorganisation, probably involving protoadamantyl intermediates,



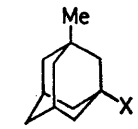
(1) a; X = OH
b; X = CO_2H



(2) a; X = OH
b; X = CO_2H



(3) a; X = OH
b, X = CO_2H



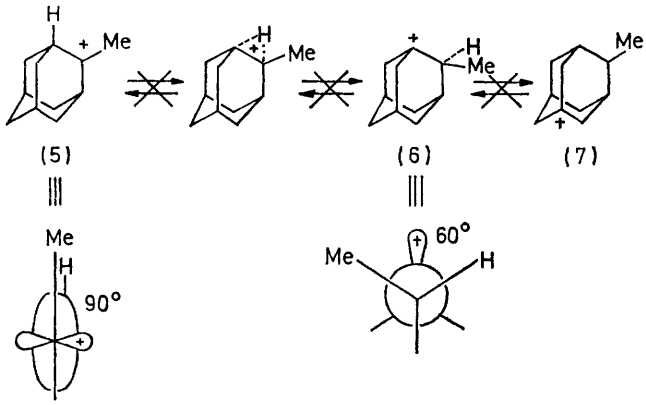
(4) a; X = OH
b; X = CO_2H

throughout which the methyl substituent always remains bonded to the same carbon atom. Thus, despite the fact that, relative to adamantane, protoadamantyl derivatives are of high energy,[11] they are still preferable to the highly distorted transition state associated with a 1,2-methyl shift.

We now wish to demonstrate that the hydride transfer reactions which interconnect cations (5), (6), and (7) are, in fact, intermolecular, since they can be inhibited by the use of conditions of sufficiently high dilution. Intramolecular hydride shifts are necessarily first-order in substrate and should be concentration-independent, but intermolecular hydride shifts, being second-order, should be highly concentration-dependent. Similar studies with different substrates have been conducted independently by Schleyer and Schlatmann

[2] M. A. McKervey, J. R. Alford, J. F. McGarrity, and E. J. F. Rea, *Tetrahedron Letters*, 1968, 5165; see also ref. 3.
[3] *Cf.* H. W. Geluk and J. L. M. A. Schlatmann, *Tetrahedron*, 1968, **24**, 5361.
[4] P. Von R. Schleyer, *Angew. Chem. Internat. Edn.*, 1968, **8**, 529.
[5] P. von R. Schleyer, L. K. M. Lam, D. J. Raber, J. L. Fry, M. A. McKervey, J. R. Alford, B. D. Cuddy, V. G. Keizer, H. W. Geluk, and L. J. M. A. Schlatmann, *J. Amer. Chem. Soc.*, 1970, **92**, 5246; see also J. Burkhard, J. Vais, and S. Landa, *Z. Chem.*, 1969, **9**, 29.
[6] D. M. Brouwer and H. Hogeveen, *Rec. Trav. chim.*, 1970, **89**, 211.
[7] P. Vogel, M. Saunders, W. Thielecke, and P. von R. Schleyer, *Tetrahedron Letters*, 1971, 1429.
[8] M. Saunders and J. Rosenfeld, *J. Amer. Chem. Soc.*, 1969, **91**, 7756; M. Saunders, M. H. Jaffe, and P. Vogel, *ibid.*, 1971, **93**, 2558; R. E. Leone and P. von R. Schleyer, *Angew. Chem. Internat. Edn.*, 1970, **9**, 860.
[9] R. E. Moore, R. W. Warren, and A. Schneider, *Amer. Chem. Soc., Div. Petrol. Chem. Prep.*, 1970, **15**, B43; E. I. Bagrii, T. Yu Frid, and P. I. Sanin, *Izvest. Akad Nauk S.S.S.R., Ser. khim.*, 1970, 498 (*Chem. Abs.*, 1970, **73**, 3513).
[10] Z. Majerski, P. von R. Schleyer, and A. P. Wolf, *J. Amer. Chem. Soc.*, 1970, **92**, 5731.
[11] Z. Majerski, S. H. Liggero, P. von R. Schleyer, and A. P. Wolf, *Chem. Comm.*, 1970, 1596.

and their respective collaborators, and a preliminary account of their results and those of the experiments to be described here has been published.[5,12,13] At



the outset the high rate at which alcohols (1a), (2a), and (3a) reach equilibrium in sulphuric acid was considered to be an obstacle to dilution studies. We discovered, however, that while the corresponding carboxylic acids (1b), (2b), and (3b) also equilibrate in sulphuric acid *via* a mechanism which must have the same essential feature, *i.e.* hydride transfer, they do so much more slowly than do the alcohols under similar conditions. In fact, when the sulphuric acid contains carbon monoxide (from added formic acid) in high concentration relative to the carboxylic acid these rearrangements are almost totally inhibited (see later). Accordingly, we examined in some detail the Koch–Haaf carboxylation [14] of the alcohols (1a), (2a), and (3a).

Three carboxylation procedures were employed: (i) a solution of the alcohol in 98% formic acid was added during 1·5 h to 98% sulphuric acid at 2—5°; (ii) similar to (i) except that a two-phase system of sulphuric acid and carbon tetrachloride was used; and (iii) a solution of the alcohol in 98% sulphuric acid was kept at 50° for 3 min then cooled in an ice-bath and treated with 98% formic acid. In each case the reaction was quenched with ice and the products were isolated and purified as their potassium salts. The results obtained were strikingly different with the three procedures (entries 1—3 in the Table): the product from (i) was a mixture of isomeric methyladamantanecarboxylic acids; that from (ii) was essentially pure 2-methyladamantane-2-carboxylic acid (1b), m.p. 148—149°; and the product from (iii) was identical with 3-methyladamantane-1-carboxylic acid (4b) synthesised alternatively by carboxylation of 1-bromo-3-methyladamantane.

The sharp singlet at τ 8·65 in the n.m.r. spectrum of the unrearranged acid (1b) established the character of the methyl substituent, and the two-proton singlet at τ 6·40 in the spectrum of the alcohol (8), derived from the acid (1b) by lithium aluminium hydride reduction, indicated that the carboxy-group was tertiary. The n.m.r. spectrum of the mixture of acids obtained by procedure (i) exhibited three doublets between τ 8·90 and 9·03, in addition to the singlet due to the small amount of the acid (1b) present, and g.l.c. analysis of the methyl esters revealed the presence of four components, the least abundant of which corresponded in retention time with the methyl ester of acid (1b). We noted subsequently that by allowing the reaction mixture to reach room temperature during several hours before quenching with ice the unrearranged acid (1b) could be almost completely eliminated from the mixture of acids obtained with procedure (i).

				Product distribution (%) [a]					
Reaction	Alcohol	Procedure	Yield (%)	(1b)	(2b)	(3b)[b]	(4b)	(10)	(11)
1	(1a)	(i)	95	6	56	38			
2	(1a)	(ii)	90	>97					
3	(1a)	(iii)	25				>97		
4	(2a)	(i)	92	8	60	32			
5	(2a)	(ii)	88		>97				
6	(3a)	(i)	93	7	29	64			
7	(3a)	(ii)	83			97			
8	(9a)	(i)	31					90	
9	(9a)	(ii)	20					70	30
10	(9a)	(iii)	60					50	

[a] By n.m.r. analysis of the acids and g.l.c. analysis of the methyl esters. [b] The *syn–anti* ratio was *ca.* 1 : 1 in each case.

In view of the behaviour of 2-methyladamantan-2-ol in sulphuric acid in the absence of carbon monoxide, it appeared likely that the mixture of acids obtained with procedure (i) contained the 1,2-isomer (2b) and the *syn*- and *anti*-1,4-isomers (3b). Fractional crystallisation of this mixture from aqueous methanol gave the preponderant isomer, 2-methyladamantane-1-carboxylic acid (2b), m.p. 134·5—136·0°, in 35% yield. The structural assignment is based on the presence in the n.m.r. spectrum of a single doublet for the methyl substituent at τ 9·03 and on the results of carboxylation of 2-methyladamantan-1-ol (2a): use of procedure (ii) gave acid (2b) of >97% isomeric purity whereas with procedure (i) the carboxylation proceeded with 40% rearrangement (reactions 5 and 4). The remaining acids were identified as *syn*- and *anti*-4-methyladamantane-1-carboxylic acid (3b), synthesised by carboxylation of a 1 : 1 mixture of alcohols (3a). Use of procedure (ii) (reaction 7) gave a crystalline product, m.p. 65—70°, whose n.m.r. spectrum displayed two doublets

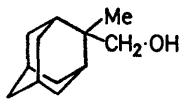
[12] D. J. Raber, R. C. Fort, jun., E. Wiskott, C. W. Woodworth, P. von R. Schleyer, J. Weber, and H. Stetter, *Tetrahedron*, 1971, **27**, 3.

[13] H. W. Geluk and J. L. M. A. Schlatmann, *Amer. Chem. Soc., Div. Petrol. Chem. Prep.*, 1970, **15**, B40.

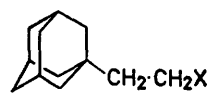
[14] H. Koch and W. Haaf, *Annalen*, 1958, **618**, 251.

(ratio *ca.* 1 : 1) at τ 8·90 and 9·00. This isomer ratio was confirmed by g.l.c. analysis of the methyl esters. Use of procedure (i), on the other hand, gave 36% rearrangement (reaction 6).

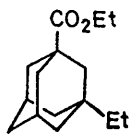
Shortly after this work had been completed the Koch–Haaf carboxylation of 2-methyladamantan-2-ol was reported by Vais, Burkhard, and Landa [15] who apparently employed procedure (i) with normal reagent concentrations. Although there is generally good agreement between their conclusions and ours concerning the nature and distribution of the major products of the reaction, one point of disagreement is their



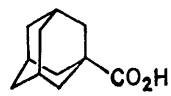
(8)



(9) a; X = OH
b; X = CO_2H
c; X = OTs
d; X = CN
e; X = H

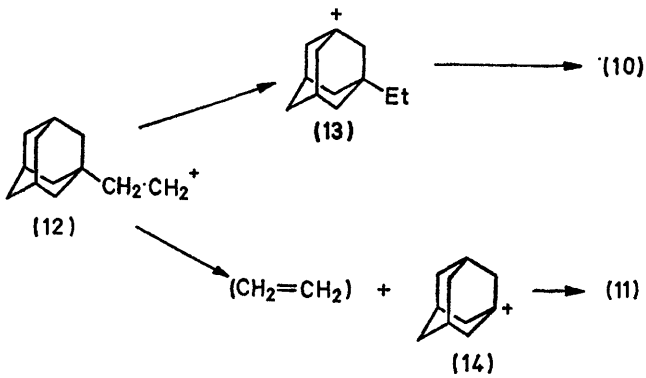


(10)



(11)

observation that minor amounts of ethylideneadamantane are also formed. This olefin is an unlikely product of such a reaction since it should be also prone to protonation and carboxylation, giving ethyladamantanecarboxylic acids. In our opinion ethylideneadamantane is not formed in the carboxylation reaction; rather it results from a neopentyl-type rearrangement during the subsequent sequence of chemical transformations used by Landa and his co-workers to facilitate identification of the primary products of the reaction.



The final three entries in the Table relate to carboxylation of 2-(1-adamantyl)ethanol (9a).[16,17] Although this alcohol gave low yields of acids, presumably because of its primary character, the results obtained helped to illuminate further the mechanism of these hydride transfer reactions. For comparative purposes, the unrearranged acid (9b), which would be expected from 'normal' carboxylation of alcohol (9a), was synthesised by an alternative route. The tosylate (9c) was exposed to sodium cyanide in dimethyl sulphoxide at 70° to give the nitrile (9d), which was then hydrolysed to the acid with hot concentrated hydrochloric acid. Employing procedure (i) at room temperature alcohol (9a) gave an acidic product (31%) containing several minor components (10%) and one major component (90%) which was clearly not the unrearranged acid (9b), nor was this acid one of the minor components. The mass spectrum of the preponderant product exhibited a strong $M - 29$ fragment indicative of the presence of an ethyl group, and the n.m.r. spectrum contained a five-line pattern at τ 8·70—9·40 characteristic of a bridgehead ethyl substituent; the remaining n.m.r. absorptions were similar to those in the spectrum of the acid (4b).[18] On this basis the compound was assigned the 3-ethyladamantane-1-carboxylic acid structure (10), and confirmatory evidence was obtained by preparing this acid from 1-ethyladamantane (9e) [19] as described in the Experimental section. Carboxylation of 2-(1-adamantyl)ethanol (9a) by procedure (ii) at room temperature gave an acidic product (20%) composed of the acid (10) (70%) and adamantane-1-carboxylic acid (11) (30%), whereas use of procedure (iii) gave equal amounts of these two acids in 60% yield.

In summary, we believe that the evidence of disproportionation products mentioned earlier and the carboxylation results obtained with the alcohols (1a), (2a), and (3a), taken together, establish the intermolecular nature of these hydride transfer processes. At the normal reagent concentrations of procedure (i) bimolecular rearrangement of the cations (5)—(7) competes successfully with capture of these ions by carbon monoxide; with the relatively high carbon monoxide concentrations employed the latter reaction becomes essentially irreversible at or near 0°. However, when carbon tetrachloride is incorporated into the system in procedure (ii) as a co-solvent immiscible with sulphuric acid the conditions approach those of a high dilution experiment, since in this modification the alcohol is dispersed in the carbon tetrachloride (upper) layer whence it slowly diffuses into the sulphuric acid layer. A much lower substrate concentration in sulphuric acid results and bimolecular rearrangement is inhibited. In the carboxylation of adamantan-2-ol [5] a similar effect can be achieved without adding carbon tetrachloride by using a very large relative amount of sulphuric acid (1000 ml per g alcohol).

The behaviour of 2-(1-adamantyl)ethanol (9a) on carboxylation supports this interpretation. The very

[15] J. Vais, J. Burkhard, and S. Landa, *Z. Chem.*, 1969, **9**, 268.
[16] M. A. McKervey, *Chem. and Ind.*, 1967, 1791.
[17] W. H. W. Lunn, W. D. Podmore, and S. S. Szinai, *Chem. Comm.*, 1968, 1657.
[18] *Cf.* R. C. Fort, jun., and P. von R. Schleyer, *J. Org. Chem.*, 1965, **30**, 789.
[19] R. W. Warren, A. Schneider, and E. J. Janoski, *Appl. Spectroscopy*, 1968, **22**, 115.

high energy 2-(1-adamantyl)ethyl cation (12) is reduced by intermolecular hydride transfer much more rapidly than it can react with carbon monoxide and the major acidic product is that derived from reaction of the much more stable 3-ethyl-1-adamantyl cation (13) with carbon monoxide. Although none of the minor acidic products was identified, it is conceivable that they all arise through carboxylation of cations produced by a 1,2-hydride shift in the cation (12) with subsequent ring expansion to homoadamantane intermediates. The possibility that the acid (9b) might be an unstable intermediate in the formation of the acid (10) was excluded by showing that the acid (9b) was stable under the reaction conditions. On the other hand, an increase in the dilution of the reagents (reaction 9) renders bimolecular reduction of the cation (12) less likely and there is competition between this pathway and a unimolecular one whereby cation (12) fragments into ethylene (which presumably undergoes further reactions) and the much more stable 1-adamantyl cation (14) which then combines with carbon monoxide.

Finally we comment on the product distributions obtained by procedure (i) with the alcohols (1a), (2a), and (3a). These isomers interconvert rapidly in sulphuric acid and for steric reasons the 1,4-isomers (3a) predominate at equilibrium at 0°. Analogously, the 1,4-isomers (3b) should be thermodynamically the most stable of the corresponding carboxylic acids, but this is not apparent from the carboxylation data which indicate that each alcohol gives a different product distribution; it could be confirmed however by equilibration experiments with the individual isomers (1b) and (2b). As already indicated there is virtually no isomerisation of these acids in sulphuric acid at 0° when formic acid is also present, but when formic acid is omitted equilibrium ratios could be obtained within 1 h at room temperature.* For example, a solution of isomerically pure acid (1b) in 98% sulphuric acid at 20° yielded after 15 min a mixture of acids (2b) and (3b) in the ratio 2 : 1, but after 1 h an equilibrium ratio of 1 : 3 was obtained. A similar result was obtained with the pure 1,2-isomer (2b). When these solutions were kept for longer periods (up to 20 h) substantial amounts of the 1,3-isomer (4b) were produced, although the isomer ratio [(2b) : (3b)] remained constant at 1 : 3. Comparison of this equilibrium ratio with the carboxylation data shows that when these two acids are formed from 2-methyladamantan-2-ol there is a kinetic preference for the 2-methyl-1-adamantyl cation, just as was observed in the bromination of 2-methyladamantane.[1]

EXPERIMENTAL

M.p.s were determined for samples sealed in capillary tubes. G.l.c. refers to analysis on (A) a 20 m column coated with fluorosilicone oil or (B) a 2 m column packed with diethylene glycol succinate (20% w/w) on Chromosorb W. ^{1}H N.m.r. spectra were measured at 100 MHz with tetramethylsilane as internal standard; the integrated peak areas are in accord with the structural assignments. Mass spectrometric data were obtained with an A.E.I. MS902 spectrometer with an ionising beam energy of 70 eV. Light petroleum had b.p. 40—60°. The drying agent employed was magnesium sulphate.

Preparation of Methyladamantanols.—2-Methyladamantan-2-ol (1a) was obtained from adamantanone and methylmagnesium bromide. 2-Methyladamantan-1-ol (2a) and a 1 : 1 mixture of *syn*- and *anti*-4-methyladamantan-1-ol (3a) were prepared from 2-methyladamantane as described in the preceding paper.[1]

General Carboxylation Methods.—Procedure (i). A solution of the alcohol (0·4 g) in 98% formic acid (5 ml) was added during 1·5 h with stirring to 98% sulphuric acid (50 ml) kept at 2—5° in an ice-bath throughout the addition. Stirring was continued for 1 h at this temperature and the solution was then poured on ice (300 g) and extracted with carbon tetrachloride (3 × 100 ml). The extract was shaken with N-potassium hydroxide (3 × 80 ml) and the alkaline solution was subsequently washed with dichloromethane and made strongly acidic with 5N-hydrochloric acid. The precipitated acid was taken up in dichloromethane, and the solution was washed with water and dried. Evaporation of the solvent gave the acid.

Procedure (ii). The experiment was performed as for procedure (i) with the same quantities except that the formic acid solution was added to a two-phase system composed of carbon tetrachloride (100 ml) and 98% sulphuric acid (50 ml).

Procedure (iii). To 98% sulphuric acid (50 ml) held at 50° in a constant-temperature bath was added 2-methyladamantan-2-ol (0·4 g) in one portion. The solution was stirred rapidly for 3 min, then cooled in an ice-bath and treated with 98% formic acid (5 ml) dropwise with stirring during 5 min. After a further 10 min the mixture was poured on ice and the product was isolated as described under procedure (i). Several recrystallisations from aqueous methanol gave 3-methyladamantane-1-carboxylic acid (4b) (0·12 g, 25%), m.p. 93—96° (lit.,[21] 96—98°), identified by comparison (i.r. and n.m.r.) with an authentic sample prepared from 1-bromo-3-methyladamantane.[22]

The products obtained by these three procedures were each analysed directly by n.m.r. spectroscopy. A portion of each product was also treated with diazomethane in ether and the resulting methyl esters were analysed by g.l.c. analysis on column (A) at 140°; the isomer distributions were obtained from the integrated areas of the g.l.c. traces and from the integrated peak areas for the various methyl groups in the n.m.r. spectra. The isomer distributions in the Table refer to the crude acids before purification by crystallisation.

2-Methyladamantane-2-carboxylic Acid (1b).—Carboxylation of 2-methyladamantan-2-ol (1a) by procedure (ii) gave the *acid* (90%), m.p. 148—149° (from aqueous methanol) (Found: C, 74·0; H, 9·5. $C_{12}H_{18}O_2$ requires C, 74·25; H, 9·25%), τ (CCl_4) 8·65 (3H, s, Me), 7·85—8·50

* For a recent discussion on the rate constants for the equilibrium $R^+ + CO \rightleftharpoons R{-}\overset{+}{C}{=}O$ in strongly acidic solutions, see ref. 20.

[20] H. Hogeveen, F. Baardman, and C. F. Roobeek, *Rec. Trav. chim.*, 1970, **89**, 227.

[21] H. Koch and J. Franken, *Chem. Ber.*, 1963, **96**, 213.

[22] K. Gerzon, E. V. Krumkalns, R. L. Brindle, F. J. Marshall, and M. A. Root, *J. Medicin. Chem.*, 1963, **6**, 763.

(14H, m, skeletal H), and −0·50 to 0·00br (1H, CO_2H). G.l.c. analysis of the methyl ester of the *crude* acid showed an isomeric purity of >97%. The carboxylation of 2-methyladamantan-2-ol by procedure (ii) on much larger scales gave the pure acid with an average yield of 90%.

2-Methyladamantane-1-carboxylic Acid (2b).—Carboxylation of 2-methyladamantan-1-ol (2a) by procedure (ii) gave the *acid* (88%), m.p. 134·5—136·0° (from aqueous methanol) (Found: C, 73·8; H, 9·05. $C_{12}H_{18}O_2$ requires C, 74·25; H, 9·25%), τ (CCl_4) 9·03 (3H, d, Me), 7·90—8·60 (14H, m, skeletal H), and −0·50 to 0·00br (1H, CO_2H). G.l.c. analysis of the methyl ester of the *crude* product gave an isomeric purity of >97%.

syn- *and* anti-*4-Methyladamantane-1-carboxylic Acid* (3b).—Carboxylation of a 1 : 1 mixture of *syn-* and *anti-*4-methyladamantan-1-ol (3a) by procedure (ii) gave the acid mixture (83%), m.p. 65—70° (from aqueous methanol) (Found: C, 74·2; H, 9·15. Calc. for $C_{12}H_{18}O_2$: C, 74·25; H, 9·25%), τ (CCl_4) 8·90 (d) and 9·00 (d) (3H, ratio *ca.* 1 : 1, *syn-* and *anti-*Me), 7·80—8·60 (14H, m, skeletal H), and −0·50 to 0·00br (1H, CO_2H). G.l.c. analysis of the methyl esters showed the two isomers (>97%) in the ratio *ca.* 1 : 1.

2-Methyladamantane-1-carboxylic Acid (2b) *by Carboxylation of 2-Methyladamantan-2-ol* [*Procedure* (i)].—A solution of the alcohol (2·0 g) in 98% formic acid (8 ml) was added dropwise with stirring to 98% sulphuric acid (50 ml) at 2—5° during 1·5 h. The mixture was then allowed to warm to room temperature and poured on ice. The product, isolated as in procedure (i), was a crystalline solid (2·1 g, 88%), m.p. 75—110°. Analysis by n.m.r. indicated the presence of acids (2b) (major) and (3b) (minor). Fractional crystallisation of the mixture from aqueous methanol gave the pure 1,2-acid, m.p. 131—132°, in 35% yield.

2-Hydroxymethyl-2-methyladamantane (8).—A solution of 2-methyladamantane-2-carboxylic acid (2·0 g) in dry ether (25 ml) was added dropwise during 20 min to a stirred slurry of lithium aluminium hydride (3·0 g) in dry ether (30 ml); the mixture was heated under reflux for 72 h, cooled, treated cautiously with 5% sulphuric acid, and then poured into cold 5% sulphuric acid (200 ml). The ether layer and ethereal extracts of the aqueous layer (5 × 50 ml) were combined, washed with water, and dried. Evaporation left a white solid (1·7 g, 91%). Recrystallisation from light petroleum gave the *alcohol*, m.p. 162—163° (Found: C, 80·3; H, 11·3. $C_{12}H_{20}O$ requires C, 80·0; H, 11·1%), τ (CCl_4) 8·95 (3H, s, Me), 7·82—8·60 (14H, m, skeletal H), 7·79 (1H, s, OH, exchanged with D_2O), and 6·42 (2H, s, CH_2).

1-Adamantylacetic Acid.—The acid, prepared [23] from adamantan-1-ol and 1,1-dichloroethylene, had m.p. 137—138° (lit.,[23] 135—136°).

2-(1-Adamantyl)ethanol (9a).—A solution of 1-adamantylacetic acid (14·3 g) in ether (300 ml) was added dropwise with stirring to a solution of lithium aluminium hydride (3·5 g) in ether (50 ml). The mixture was stirred at room temperature overnight and excess of hydride was then removed by the dropwise addition of 5% sulphuric acid. When precipitation was complete, the mixture was filtered and the solid residue washed with ether. The combined ethereal solutions were washed with water and dried. Evaporation gave the alcohol (12·2 g, 92%), m.p. 74—76° (after sublimation at 100° and 0·5 mmHg) (lit.,[17] 76—78°).

Carboxylation of 2-(1-Adamantyl)ethanol.—Procedure (i). The alcohol (3·0 g) was dissolved with heating in 98% formic acid (15 ml) and added dropwise with stirring to 98% sulphuric acid (150 ml) at 20° during 1 h. The mixture was stirred for an additional 1 h at 20° and then was poured on ice and extracted with ether (4 × 50 ml). The extract was shaken with N-potassium hydroxide (4 × 50 ml). The alkaline extract was made strongly acidic with concentrated hydrochloric acid and extracted with ether (4 × 50 ml). The ethereal extract was dried and concentrated, to give an oil (1·1 g, 31%). A portion of the product was treated with diazomethane in ether and examined by g.l.c. on column (B) at 160°, which showed one major component (90%) and several minor components (10%). The major product was isolated by fractional crystallisation of the mixture from aqueous methanol. The material was identical (m.p., i.r. and n.m.r. spectra) with authentic 3-ethyladamantane-1-carboxylic acid (10) prepared as described later.

Procedure (ii). The experiment was performed as in procedure (i) with the same quantities except that the formic acid solution was added to a two-phase system composed of carbon tetrachloride (500 ml) and sulphuric acid (150 ml). The acidic products (0·7 g, 20%) consisted of 3-ethyladamantane-1-carboxylic acid (70%) and adamantane-1-carboxylic acid (30%) as shown by g.l.c. analysis of the methyl esters.

Procedure (iii). The alcohol (1·0 g) was added to 98% sulphuric acid (50 ml) at 50° and the solution was stirred for 3 min and then cooled in an ice-bath. Formic acid (5 ml) was added during 1 h with stirring and after an additional 1 h at 0° the solution was poured on ice. Work-up as in procedure (i) gave an acidic product (0·7 g, 60%) which was composed of 3-ethyladamantane-1-carboxylic acid (50%) and adamantane-1-carboxylic acid (50%).

2-(1-Adamantyl)ethyl Toluene-p-sulphonate (9c).—To a solution of 2-(1-adamantyl)ethanol (5·0 g) in pyridine (50 ml) at 0° was added toluene-*p*-sulphonyl chloride (6·0 g) with stirring. After 24 h at 0°, the solution was diluted with cold water (200 ml) and extracted with ether (3 × 50 ml). The extract was washed with N-hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water and dried. Evaporation gave the tosylate (7·0 g, 79%) as an oil which was used without further purification.

1-Ethyladamantane (9e).—A solution of the crude tosylate (9c) (7·0 g) in dry ether (100 ml) was added dropwise with stirring to a slurry of lithium aluminium hydride (2·0 g) in ether (50 ml). The mixture was stirred for 48 h at room temperature and then treated with cold 5% sulphuric acid until precipitation was complete. The ethereal solution and ethereal washings of the precipitate were washed with water and dried. Evaporation at atmospheric pressure gave an oil which was taken up in light petroleum and passed through a short column of neutral alumina. Elution with light petroleum gave 1-ethyladamantane (2·3 g, 63%) as a liquid. The i.r. and n.m.r. spectral data were in close agreement with the published values.[19]

3-Ethyladamantane-1-carboxylic Acid (10).—A mixture of 1-ethyladamantane (2·15 g) and bromine (25 ml) was heated under reflux for 4·5 h, then cooled, diluted with carbon tetrachloride (150 ml), and poured into water (150 ml). The organic layer was separated, washed with aqueous sodium disulphite and water, and dried. Evapor-

[23] K. Bott, *Chem. Ber.*, 1968, **101**, 564.

ation gave an oil which was passed through a short column of neutral alumina. Elution with light petroleum gave 3-ethyl-1-bromoadamantane (3·0 g, 94%) as an oil which was used without further purification.

The crude bromide (3·0 g) in carbon tetrachloride (5 ml) and 98% formic acid (5 ml) were added simultaneously to 98% sulphuric acid (50 ml) with stirring during 1 h at 2—5°. The mixture was allowed to reach room temperature and then was poured on ice and extracted with carbon tetrachloride (3 × 50 ml). The extract was shaken with N-potassium hydroxide (4 × 60 ml); the alkaline solution was made strongly acidic with concentrated hydrochloric acid and extracted with ether (3 × 50 ml). The extract was washed with water, dried, and concentrated, to yield a white crystalline solid. One recrystallisation from aqueous methanol gave the *acid* (1·6 g, 60%), m.p. 105—107° (Found: C, 74·8; H, 9·8. $C_{13}H_{20}O_2$ requires C, 74·95; H, 9·7%), τ ($CDCl_3$) 8·70—9·30 (5H, m, Et), 7·80—8·65 (14H, m, skeletal H), and 0·00br (1H, CO_2H), *m/e* 208 (M^+, 26%), 180(17), 179(70), 163(50), 136(11), 135(100), 133(18), 93(22), 91(12), and 79(26).

2-(1-*Adamaniyl*)*propionic Acid* (9b).—A solution of the crude tosylate (9c) [from 2-(1-adamantyl)ethanol (2·5 g) and toluene-*p*-sulphonyl chloride (3·0 g)] in dry dimethyl sulphoxide (50 ml) containing sodium cyanide (0·7 g) was heated at 70° with stirring for 4 h. The cooled solution was poured into water and extracted with ether (3 × 50 ml). The extract was washed several times with water, dried, and concentrated, to give the nitrile (9d) (2·5 g) as an oil which slowly crystallised. The entire crude nitrile was hydrolysed with hot concentrated hydrochloric acid under reflux for 4 h. The cooled mixture was poured on ice and the product was isolated as described in procedure (i) to give the acid (2·3 g, 85%), m.p. 145—147° (from aqueous methanol) (lit.,[24] 144—145°), τ ($CDCl_3$) 7·67 (2H, t), 7·90—8·66 (17H, m), and 0·10br (1H, CO_2H).

Rearrangement of the Acids (1b) *and* (2b) *in* 98% *Sulphuric Acid.*—(*a*) To sulphuric acid (25 ml) at 2° was added 98% formic acid (4 ml) with stirring. After 5 min 2-methyladamantane-2-carboxylic acid (0·25 g) was added; the solution was stirred at 2° for 1 h then poured on ice and processed as in procedure (i). The acidic product (95%) was shown by n.m.r. and i.r. spectra to be unrearranged starting material.

(*b*) To sulphuric acid (25 ml) at room temperature was added the acid (1b) (0·25 g) and the solution was stirred for 15 min. The acidic product (88%) was shown by n.m.r. and g.l.c. analysis of the corresponding methyl esters to contain acids (2b) and (3b) in the ratio 2 : 1. Repetition of this reaction for 1 h gave acids (2b) and (3b) in the ratio 1 : 3. When these solutions were kept at room temperatures for longer periods (up to 20 h) substantial amounts of the 1,3-isomer (4b) were produced; the isomer ratio (2b) : (3b) remained 1 : 3.

(*c*) Treatment of 2-methyladamantane-1-carboxylic acid (2b) with sulphuric acid as just described gave the acids (2b) and (3b) in the ratio 1 : 3.

(*d*) A solution of 2-(1-adamantyl)propionic acid (9b) in sulphuric acid at room temperature showed no rearrangement after 1 h.

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[24] L. F. Fieser, M. Z. Nazer, S. Archer, D. A. Berberian, and R. G. Slighter, *J. Medicin. Chem.*, 1967, **10**, 517.