# Adamantane Rearrangements

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## 1 Introduction

The chemistry[1] of diamondoid hydrocarbons is replete with examples of molecular rearrangement, the archetype of which is undoubtedly the aluminium chloride-catalysed transformation of *endo*-tetrahydrodicyclopentadiene (1) into adamantane (2).[2,3] An intriguing aspect of this reaction is perhaps the possibility that there may be literally hundreds of pathways, all accessible under strong Lewis acid catalysis, between precursor and product, and there is the additional practical difficulty that because adamantane is so much more thermodynamically stable than all other isomeric tricyclic hydrocarbons, the detection and isolation of intermediates in what is essentially an equilibrium-controlled process is very difficult by ordinary analytical techniques. These problems notwithstanding, the discovery was highly successful and significant. Not only did it provide an attractive alternative to the earlier method[4] of extracting adamantane from vast



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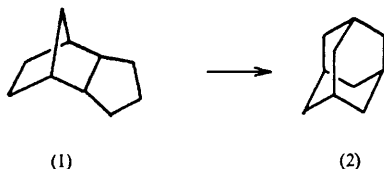
quantities of Czechoslovakian petroleum, or multistage rational synthesis,[5] but it was also the first step towards the realization of a much older idea that diamondoid molecules (and hopefully even diamond itself) could be synthesized by hydrocarbon rearrangement.[6]

[1] This review is concerned mainly with the general types of rearrangement reactions of diamondoid molecules, with particular emphasis on recent thermodynamic and mechanistic aspects. For general articles on adamantane chemistry and synthetic methods see (a) R. C. Fort, jun. and P. von R. Schleyer, *Chem. Rev.*, 1964, **64**, 277; (b) Z. Weidenhoffer and S. Hala, *Sbornik Vys. Sk. Chem.-Technol. Prague, Technol. Paliv.*, 1971, **22**, 5; (c) R. C. Bingham and P. von R. Schleyer, *Fortschr. Chem. Forsch.*, 1971, **18**, 1; (d) V. V. Sevost'yanova, M. M. Krayoshkin, and A. G. Yurchenko, *Russ. Chem. Rev.*, 1970, **39**, 817; (e) E. M. Engler and P. von R. Schleyer, MTP International Review of Science, Organic Chemistry, Series One, Butterworths 1973, vol. 5, p. 239.

[2] P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1957, **79**, 3292.

[3] P. von R. Schleyer and M. M. Donaldson, *J. Amer. Chem. Soc.*, 1960, **82**, 4645.

[4] S. Landa, *Chem. listy*, 1933, **27**, 415.

[5] V. Prelog and R. Seiwerth, *Ber.*, 1941, **74**, 1644.

[6] For a personal account of an attempt to synthesize diamonds by pyrolysis of long-chain hydrocarbons bearing *gem*-dimethyl groups see R. L. Wormell, *Chem. in Britain*, 1970, **6**, 136.

## 2 Rearrangement Catalysts

With conventional aluminium chloride catalysis at 170 °C the yields of adamantane from *endo*-tetrahydrodicyclopentadiene were low (15—20%),[7] and intensive efforts were made to improve the efficiency and selectivity of the process, following no doubt the realization that some derivatives of adamantane might possess beneficial medicinal properties. *endo*-Tetrahydrodicyclopentadiene, the most accessible of all the known $C_{10}$ tricyclic hydrocarbons, could scarcely be improved on as the starting material; consequently, efforts were directed towards modifying the catalyst.

The difficulties with conventional aluminium chloride catalysis (which lately have been largely overcome) are catalyst deactivation and the formation of numerous by-products which complicate the isolation of pure adamantane. Aluminium chloride is insoluble in saturated hydrocarbons and initially isomerization is an interfacial process which can lead rapidly to catalyst deactivation. The extent of by-product formation can be considerable. Schleyer and his co-workers[8] observed hundreds of compounds in the mother liquors from a typical adamantane preparation. Such a multitude of products is perhaps not too surprising considering the mechanism of the rearrangement and its predominant driving force, which is the relief of strain in the precursor; the strongly acidic conditions required to prod the system towards equilibrium by repeatedly forming and re-forming cationic intermediates, and the relatively high temperatures involved, are also the conditions whereby relief of strain in the precursor can also be achieved by fragmentation and disproportionation reactions. Nevertheless, substantial improvements were realized. Replacement of aluminium chloride by boron fluoride–hydrogen fluoride afforded adamantane in 30% yield,[9] and yields of up to 40% were obtained with an aluminium chloride–hydrogen chloride system under 40 atm of hydrogen.[10]

Mixed catalysts of the aluminium halide–hydrogen halide type, often referred to nowadays as 'sludge' catalysts, are by no means recent innovations in hydrocarbon chemistry. In 1929 Zelinsky and Turova-Pollak[11] reported the preparation of a catalytically active liquid from aluminium bromide, hydrogen bromide, and *cis*-decalin. The function of the hydrogen halide in this type of catalyst was not elucidated until several years later. Nenitzescu and Cantuniari[12] observed that cyclohexane did not rearrange into methylcyclopentane when in contact with freshly prepared, anhydrous aluminium chloride, but when water was added rearrangement proceeded rapidly. This, and related observations with certain Friedel–Crafts-type reactions, led to the suggestion that the true co-catalyst was hydrogen chloride and not water, and that the role of the latter was limited to formation of hydrogen chloride by hydrolysis of the Lewis acid, the enhanced

[7] P. von R. Schleyer, M. M. Donaldson, R. D. Nicholas, and C. Cupas, *Org. Synthesis*, 1963, **42**, 8.

[8] Observations quoted in ref. 1*a*.

[9] R. E. Ludwig, U.S. P. 2937211 (*Chem. Abs.*, 1960, **54**, 19540c).

[10] H. Koch and J. Franken, *Brennst. Chem.*, 1961, **42**, 90 (*Chem. Abs.*, 1961, **55**, 21059i).

[11] N. D. Zelinsky and M. B. Turova-Pollak, *Chem. Ber.*, 1929, **62B**, 1658.

[12] C. D. Nenitzescu and I. P. Cantuniari, *Chem. Ber.*, 1933, **66**, 1097.

catalytic activity being due to the production of the conjugate species HAlCl₄, presumed to be an extremely powerful acid.[13] But this suggestion was disproved by Pines and Wackher[14] and by Brown and Pearsall,[15] the latter having failed to detect any indications of compound formation between aluminium chloride and hydrogen chloride over a wide temperature range, and the former by showing that whereas hydrogen chloride alone, in the absence of other substances, did not activate aluminium chloride in the isomerization of n-butane, the presence of as little as 0.01 mol % of olefinic impurities was sufficient to initiate reaction. It is now generally accepted that the true initiators in these isomerizations are species of the type $R^+AlCl_4^-$, generated from the Lewis acid and an alkyl halide formed by addition of the hydrogen halide to traces of olefin present in the alkane, and that activation of aluminium halides by water alone is a distinctly different process.[16]

One of these 'sludge' catalysts, developed by Schneider[17] for rearrangement of various perhydroaromatics into alkyladamantanes, is the product of cleavage of mixed dimethylhexanes by aluminium bromide or chloride in the presence of the corresponding hydrogen halide. The composition of a typical catalyst is 83.98% $AlBr_3$, 6.49% HBr, and 9.53% hydrocarbon.[18] Another version, used by Williams,[19] consists of a mixture of either t-butyl or isobutyl bromide and aluminium bromide. These 'sludge' catalysts are believed to have prolonged lifetimes and, although they are immiscible with alkanes, they are mobile liquids, which facilitates the ease of mixing. Adamantane has been obtained in up to 60% yield using such catalysts.[20] The only report of the use of a water-promoted catalyst[21] claims a substantial improvement in the yield of adamantane when water was added to a mixture of *endo*-tetrahydrodicyclopentadiene and aluminium chloride at 80 °C. Catalysts of the superacid class have also been investigated: fluoroantimonic acid gives a 37.5% conversion into adamantane;[22] chloro-sulphonic acid is also effective though yields are low.[23]

Gas-phase processes received very little attention until recently. Plate *et al.*[24] obtained adamantane in 6—13% yields using an aluminosilicate catalyst at 450—475 °C; numerous acyclic, alicyclic, and aromatic products were also

[13] See C. A. Thomas, 'Anhydrous Aluminium Chloride in Organic Chemistry', Reinhold, New York, 1941.
[14] H. Pines and R. C. Wackher, *J. Amer. Chem. Soc.*, 1946, **68**, 2518.
[15] H. C. Brown and H. W. Pearsall, *J. Amer. Chem. Soc.*, 1951, **73**, 4681.
[16] For an authoritative account of the mechanisms of hydrocarbon rearrangement see C. D. Nenitzescu, in 'Carbonium Ions', ed. G. A. Olah and P. von R. Schleyer, Wiley-Interscience, New York, 1970, Vol. 2, Chap. 13.
[17] A. Schneider, U.S. P. 3128316 (*Chem. Abs.*, 1964, **61**, 4244a); Neth. Patent Appl., 300223 (*Chem. Abs.*, 1966, **64**, 6528s).
[18] A. Schneider, R. W. Warren, and E. J. Janoski, *J. Amer. Chem. Soc.*, 1964, **86**, 5365.
[19] V. Z. Williams, jun., A. B. Thesis, Princeton University, 1965. See also M. J. T. Robinson and H. J. F. Tarratt, *Tetrahedron Letters*, 1968, 5.
[20] H. Hoffmann and C. H. Trottier, U.S. P. 3 457 317 (*Chem. Abs.*, 1969, **71**, 90 924).
[21] R Achard, F. P. 1431816 (*Chem. Abs.*, 1966, **65**, 15250).
[22] J. Olah and G. A. Olah, *Synthesis*, 1973, 488.
[23] A. Karim and M. A. McKervey, unpublished results.
[24] A. F. Plate, Z. K. Nikitina, and T. A. Burtseva, *Neftekhimiya*, 1961, **1**, 599 (*Chem. Abs.*, 1962, **57**, 4938a).

formed, and this line of approach appears not to have been pursued. Within the past few years, however, several solid catalysts capable of isomerizing n-alkanes in the gas phase at low temperatures to near their equilibrium branched-chain isomer distributions have been developed in the petroleum industry.[25] The essential feature of the catalytic activity of these materials is the introduction of chlorine into platinum–alumina by reaction with various chlorinating agents such as carbon tetrachloride or thionyl chloride. Although hydrocarbon isomerization on chlorinated platinum–alumina has customarily been carried out in a hydrogen atmosphere, there are recent indications that the use of hydrogen chloride instead of hydrogen has a markedly beneficial effect on both the activity and longevity of the catalyst. A comparative study[26] of the efficiency of a typical catalyst in the gas-phase isomerization of n-hexane using an atmosphere of hydrogen chloride, hydrogen, and nitrogen, revealed that the hydrogen halide was superior to hydrogen, both of which were vastly superior to nitrogen; in the inert atmosphere the catalyst suffered rapid deactivation due to coking. Several hydrocarbons known to yield adamantanes under conventional aluminium halide catalysis were exposed to chlorinated platinum–alumina in an atmosphere of dry hydrogen chloride and the results (Table 1) revealed a very high selectivity for adamantane production with essentially no by-product formation.[27] The rearrangement of *exo*-tetramethylenenorbornane (4) provided the most dramatic example for, within the limits of detectability, 1- and 2-methyladamantane (6) and (7) were the sole products in quantitative yield. Chlorinated platinum–alumina is also an effective catalyst for liquid-phase isomerization at room temperature when used as a suspension in *o*-dichlorobenzene.[28]

**Table 1**

| | Precursor | | |
| --- | --- | --- | --- |
| | (1) or (3) | (4) | (5) |
| *Products* % | | | |
| Adamantane (2) | 60 | | |
| 1-Methyladamantane (6) | | 98 | |
| 2-Methyladamantane (7) | | 2 | |
| 1,3-Dimethyladamantane (8) | | | 86 |
| 1-Ethyladamantane (9) | | | 7 |
| 1,x-Dimethyladamantane (10) | | | 7 |
| Material recovery | 98—100 | 98—100 | 98—100 |
| Starting material | 39 | — | — |
| By-products | 1 | — | — |

reaction temperature *ca.* 165 °C

[25] For a recent review see J. P. Giannetti, H. G. McIlvreid, and R. T. Sebulsky, *Ind. and Eng. Chem.* (*Process Res. Development*), 1970, **9**, 473.
[26] D. E. Johnston, M. A. McKervey, and J. J. Rooney, unpublished results.
[27] D. E. Johnston, M. A. McKervey, and J. J. Rooney, *J. Amer. Chem. Soc.*, 1971, **93**, 2798.
[28] R. Hamilton, M. A. McKervey, and J. J. Rooney, unpublished results.

|     |     |     |     |
| --- | --- | --- | --- |
| (3) | (4) | (5) | (6) |



|     |     |     |     |
| --- | --- | --- | --- |
| (7) | (8) | (9) | (10) |
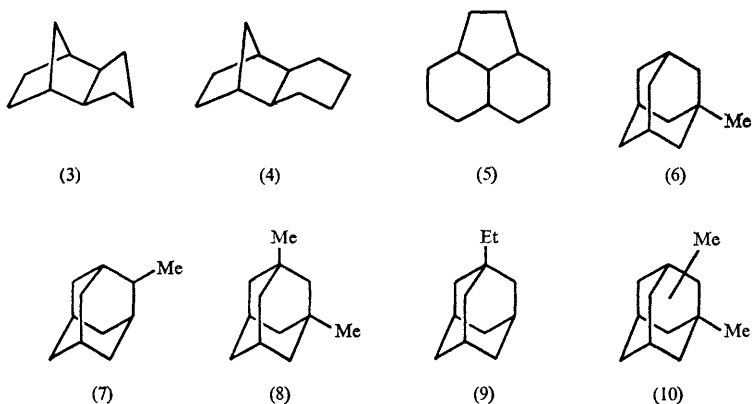
## 3 Adamantane Rearrangements Exemplified

Apart from *endo-* and *exo-*tetrahydrodicyclopentadiene there are several other known $C_{10}$ tricycloalkanes: twistane (11),[29] tricyclo[5,2,1,0^{4,10}]decane (12),[30] protoadamantane (13),[31] *exo-*1,2-trimethylenenorbornane (14),[32] and 2,6-tri-methylenenorbornane (15).[32] As expected, they all rearrange to adamantane under aluminium halide catalysis, the most ready case being that of protoadamantane, which has been observed to rearrange in the gas phase on metal(0) catalysts such as palladium, platinum, and rhodium at temperatures as low as 150 °C,[33] as well as in concentrated sulphuric acid and in liquid bromine.[34]



|      |      |      |      |      |
| ---- | ---- | ---- | ---- | ---- |
| (11) | (12) | (13) | (14) | (15) |
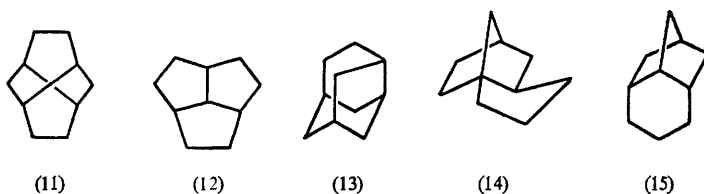
An important aspect of the rearrangement route to diamondoid hydrocarbons is the degree to which it is capable of extension. Two examples involving $C_{11}$ and $C_{12}$ precursors are included in Table 1 and just a few of the very many discovered since 1956 are summarized in Scheme 1. Far less obvious precursors have also

[29] H. W. Whitlock and M. W. Siefken, *J. Amer. Chem. Soc.*, 1968, **90**, 4929; see also M. Tichy, L. Kniezo, and J. Hapala, *Tetrahedron Letters*, 1972, 699.

[30] L. A. Paquette, G. V. Meehan, and S. J. Marshall, *J. Amer. Chem. Soc.*, 1968, **90**, 6779.

[31] B. R. Vogt, *Tetrahedron Letters*, 1968, 1575; J. E. Baldwin and W. D. Fogelsong, *J. Amer. Chem. Soc.*, 1968, **90**, 4303.

[32] E. M. Engler, M. Farcasiu, A. Sevin, J. M. Cense, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1973, **95**, 5769.

[33] H. A. Quinn, J. H. V. Graham, M. A. McKervey, and J. J. Rooney, *J. Catalysis*, 1972, **26**, 333; M. A. McKervey, J. J. Rooney and N. G. Samman, *ibid.*, 1973, **30**, 330.

[34] A. Karim and M. A. McKervey, *J.C.S. Perkin I*, in the press.
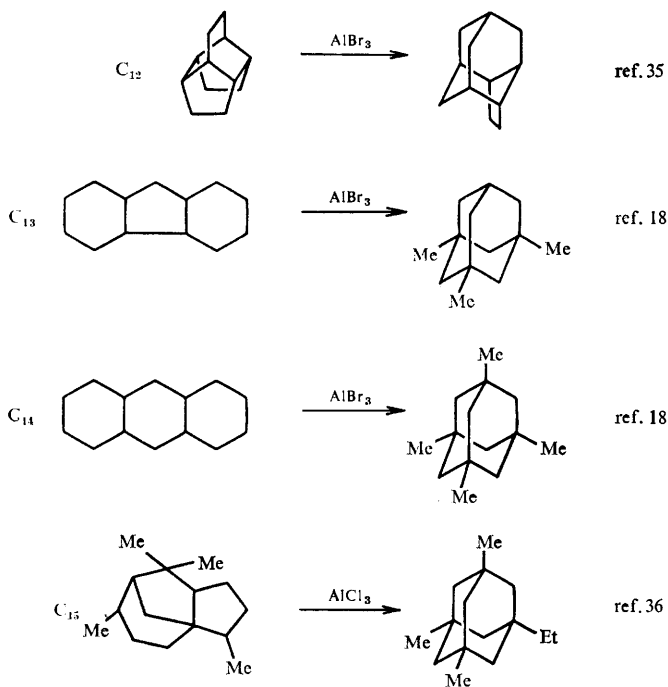
**Scheme 1**

been used. Cholesterol, nujol, abietic acid, camphene, caryophyllene, and squalene all yield small amounts of alkyladamantanes on treatment with aluminium halides.[37] None of these substances is isomeric with its diamondoid product and disproportionation processes must occur prior to or during rearrangement. Ideally, the hydrocarbon precursor should be isomeric with the product and it is desirable, though by no means essential, that it should possess a moderate degree of strain. The importance of choice of precursor is nicely illustrated by developments in the chemistry of diamantane (16), the second homologue of the diamondoid series. Schleyer and his co-workers[38] discovered that diamantane could be obtained by rearrangement of the [2 + 2]norbornene photodimer (17) in yields of 1—10% depending on which stereoisomer of the dimer was employed. Fragmentation and disproportionation reactions predominated with this precursor, no doubt because of the presence of the highly strained cyclobutane ring, and tetracycle (18) was the major product. Later work[39] showed that diamantane

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[35] Unpublished observation quoted in ref. 1c. This compound has also been found in Czechoslovakian petroleum, S. Hala and S. Landa, *Angew. Chem.*, 1966, **78**, 1060.

[36] P. von R. Schleyer, G. J. Gleicher, and C. A. Cupas, *J. Org. Chem.*, 1966, **31**, 2014.

[37] M. Nomura, P. von R. Schleyer, and A. A. Arz, *J. Amer. Chem. Soc.*, 1967, **89**, 3657.
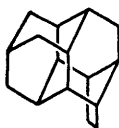
[38] C. A. Cupas, V. Z. Williams, jun., P. von R. Schleyer, and D. J. Trecker, *J. Amer. Chem. Soc.*, 1965, **87**, 617.

[39] T. M. Gund, V. Z. Williams, jun., E. Osawa, and P. von R. Schleyer, *Tetrahedron Letters*, 1970, 3877.

could be obtained in 30% yield from the pentacycle (19); however, this precursor is not readily available. Much greater improvements were realized using the norbornadiene dimer, Binor-S (20), whose tetrahydro-derivative (structure unknown), readily obtained by catalytic hydrogenolysis of the cyclopropane rings, is isomeric with diamantane. With aluminium bromide as the catalyst in carbon disulphide tetrahydrobinor-S furnished diamantane in 65% yield;[39] with aluminium chloride in dichloromethane the yield was 82%.[40] The rearrangement route has also been used to synthesize triamantane (21), the third member of the diamondoid series, from the polycycle (22).[41] Thus far, tetramantane, for which there are three possible structural isomers, (23)—(25), has not been synthesized by any route. An attempt to isomerize polycycle (26) into tetramantane produced hydrocarbon (27) instead.[42] Since tetramantane is almost certainly more thermodynamically stable than (27), the structure of which incorporates the norbornane skeleton, the reasons for the failure of this route must be kinetic not thermodynamic. Several other interesting polycyclic hydrocarbons possessing irregular
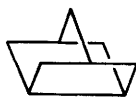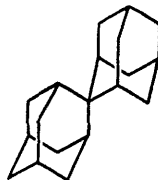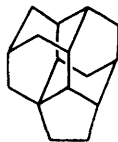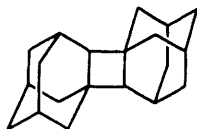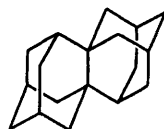


ref.43    ref.44    ref.45



ref.44    ref.46    ref.47

[40] T. Courtney, D. E. Johnston, M. A. McKervey, and J. J. Rooney, *J.C.S. Perkin I*, 1972, 2691.

[41] V. Z. Williams, jun., P. von R. Schleyer, G. J. Gleicher, and L. B. Rodewald, *J. Amer. Chem. Soc.*, 1966, **88**, 3862.

[42] P. von R. Schleyer, E. Osawa, and G. B. Drew, *J. Amer. Chem. Soc.*, 1968, **90**, 5034.

[43] B. R. Vogt and J. R. E. Hoover, *Tetrahedron Letters*, 1967, 2841; P. von R. Schleyer and E. Wiskott, *ibid.*, p. 2845; A. Nickon, G. D. Pandit, and R. O. Williams, *ibid.*, p. 2851.

[44] S. T. Rao, M. Sundaralingam, E. Osawa, E. Wiskott, and P. von R. Schleyer, *Chem. Comm.*, 1970, 861.

[45] E. Boelma, J. Strating, and H. Wynberg, *Tetrahedron Letters*, 1972, 1175; W. D. Graham and P. von R. Schleyer, *ibid.*, p. 1179.
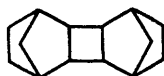
[46] D. Grant, M. A. McKervey, J. J. Rooney, N. G. Samman, and G. Step, *J.C.S. Chem. Comm.*, 1972, 1186; D. Lenoir, *Tetrahedron Letters*, 1972, 4049.

[47] W. D. Graham, P. von R. Schleyer, E. W. Hagaman, and E. Wenkert, *J. Amer. Chem. Soc.*, 1973, **95**, 5785.
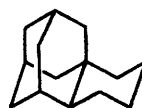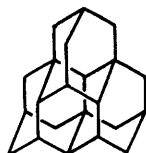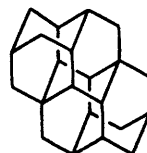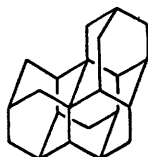
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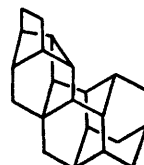
(20)

(21)

(22)

(23)

(24)

(25)

(26)

(27)

structures related to adamantane have also been synthesized, though not all by the rearrangement route. Some of them are shown here.

In a few instances, techniques have been developed which permit the rearrangement of suitable hydrocarbons into adamantanes with concomitant introduction of one or more functional groups. Kovacic and Roskos[48] found that treatment of *endo*-tetrahydrodicyclopentadiene (1) with aluminium chloride in dichloromethane containing trichloroamine furnished 1-aminoadamantane (28) in high yield; interestingly, apart from acting as the functionalization agent, trichloroamine appeared to have a markedly beneficial effect on the ease and selectivity of the rearrangement step. The technique has also been applied to halogenation.

[48] P. Kovacic and P. D. Roskos, *J. Amer. Chem. Soc.*, 1969, 91, 6457.

For example, treatment of (1) with aluminium bromide in bromine solution at 0 °C yielded a 1:1 mixture of tribromides (29) and (30); at −15 °C, isomer (29) was the main product.[49] Other examples include the synthesis of 1-chloro-3-methyladamantane (31) from tetramethylenenorbornane (4) using aluminium chloride–acetyl chloride and of 1,3-dichloro-5-methyladamantane (32) from the same precursor using aluminium chloride–paraformaldehyde.[49] These reagent combinations have proved particularly useful in diamantane methodology.



(28)  (29)  (30)



(31)  (4)  (32)
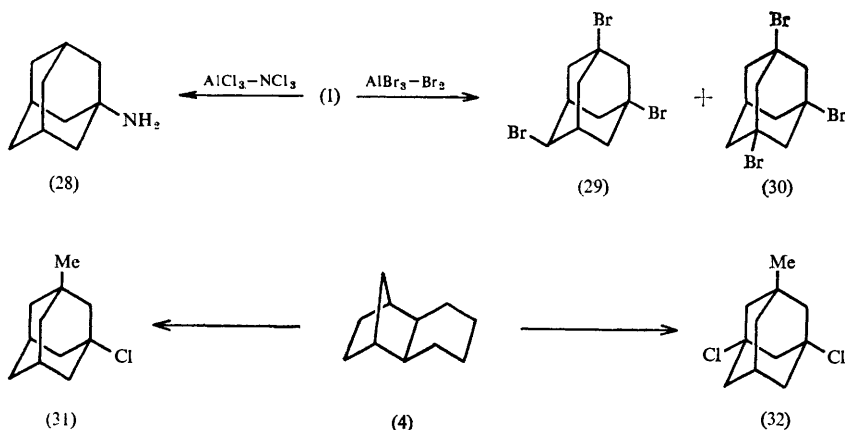
With aluminium chloride–acetyl chloride, tetrahydrobinor-S furnished in high yield a 1:1 mixture of the apical and zonal chlorides (33) and (34), whereas with aluminium chloride–paraformaldehyde, three dichlorides (35)—(37) were produced.[40,50] At −15 °C in chlorosulphonic acid, tetrahydrobinor-S furnished the diapical dichloride (35) in high yield.[51] In this reaction, chlorosulphonic acid acts as solvent, catalyst, and functionalization agent.



(33)  (34)  (35)  (36)  (37)
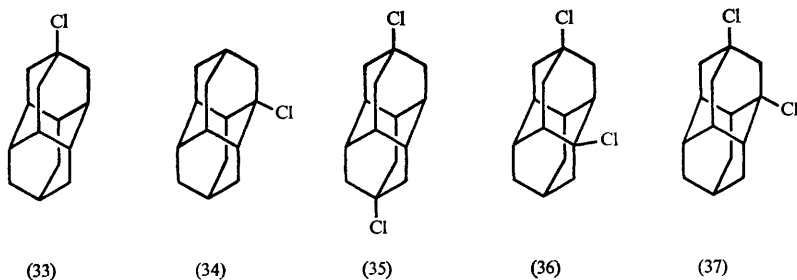
[49] H. Hamill, A. Karim, and M. A. McKervey, *Tetrahedron*, 1971, 27, 4317.
[50] D. Faulkner, R. A. Glendinning, D. E. Johnston, and M. A. McKervey, *Tetrahedron Letters*, 1971, 1671.
[51] F. Blaney, D. E. Johnston, J. J. Rooney, and M. A. McKervey, *Tetrahedron Letters*, in the press.

### 4 Mechanistic and Thermodynamic Aspects

Adamantane has been vividly described by Whitlock and Siefken[29] as '. . . a bottomless pit into which rearranging molecules may irreversibly fall'. This description is not strictly accurate inasmuch as it is now known from studies with labelled materials that adamantane undergoes degenerate skeletal change[52] and that under conditions of kinetic control the 2-adamantyl cation rearranges in part to the 4-protoadamantyl cation.[53] Nevertheless, it does highlight some of the problems involved in attempting to unravel the intricacies of the rearrangement route which is obviously complex, probably involving a multistep series of rearranging cations, and about which, at least on the experimental side, very little is known.

Although there is still a great scarcity of reliable experimental thermochemical data in this area, there can be no doubt that adamantane is by far the most thermodynamically stable of all the tricyclodecanes. Comparison of the experimental enthalpies of formation of *endo*-tetrahydrodicyclopentadiene ($-14.4$ kcal mol$^{-1}$)[54] and adamantane ($-30.6$ kcal mol$^{-1}$)[54,55] reveals that the enthalpy of isomerization is $-16.2$ kcal mol$^{-1}$: the precursor contains the highly strained norbornyl system (calculated strain energy[56,57] of *ca.* 17 kcal mol$^{-1}$) and it is the relief of this strain which probably provides the major thermodynamic driving force for rearrangement. The high thermodynamic stability of adamantane is associated with the high degree of branching in the system and the nearly 'ideal' diamondoid topology. This is not to say, however, that adamantane is a completely strain-free system. Molecular mechanics calculations, conducted independently by two groups[56,57] indicate that adamantane has a strain energy of 6—7 kcal mol$^{-1}$. The precise origins of this strain are still uncertain: whereas Schleyer's calculations[56] indicate that it can be accounted for mainly in terms of C $\cdots$ C non-bonding repulsions, those of Allinger[57] suggest that it arises largely from an excessive number of H $\cdots$ H repulsions. Despite the use of different types of non-bonding potential function, both sets of calculations predict that diamantane (16) should have a larger strain energy than adamantane. The experimental enthalpy of formation of diamantane[58] bears this out when allowance is made for the enthalpies of plastically crystalline transitions above 25 °C.[59]

Although many of the precursors used in adamantane synthesis do indeed

[52] Z. Majerski, S. H. Liggero, P. von R. Schleyer, and A. P. Wolf, *Chem. Comm.*, 1970, 1596.

[53] M. L. Sinnott, H. J. Storesund, and M. C. Whiting, *Chem. Comm.*, 1969, 1000.

[54] R. H. Boyd, S. N. Sanwal, S. Shary-Tehrany, and D. McNally, *J. Phys. Chem.*, 1971, 75, 1264.

[55] R. S. Butler, A. S. Carson, P. G. Laye, and W. V. Steele, *J. Chem. Thermodynamics*, 1971, 3, 277.

[56] E M. Engler, J. D. Andose, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1973, 95, 8005, and references therein.

[57] N. L. Allinger, M. T. Tribble, M. A. Miller, and D. N. Wertz, *J. Amer. Chem. Soc.*, 1971, 93, 1637.

[58] A. S. Carson, P. G. Laye, W. V. Steele, D. E. Johnston, and M. A. McKervey, *J. Chem. Thermodynamics*, 1971, 3, 915.

[59] T. Clark, D. E. Johnston, H. Mackle, M. A. McKervey, and J. J. Rooney, *J.C.S. Chem. Comm.*, 1972, 1042; T. Clark, H. Mackle, M. A. McKervey and J. J. Rooney, *J.C.S. Faraday I*, 1974, 70, 1279.

possess substantial amounts of strain energy, it is now apparent that the thermo-dynamic urge for rearrangement does not necessarily require an overall relief of strain. This idea has been demonstrated very convincingly by Schneider *et al.*,[60] who studied the conversion of relatively strain-free perhydroaromatics into poly-alkyladamantanes. Starting with a mixture of isomeric perhydrophenanthrenes (38) and an aluminium bromide sludge catalyst at 0 °C, these workers observed the formation of a transient equilibrium at which *trans,syn,trans*-perhydro-anthracene (39) predominated. At higher temperatures, further equilibration produced 2e-methylperhydrophenalene (40) (and isomers thereof not included in



(38) mixture of isomers

(39)

25°C

less stable isomers

(40)

Et

Me \`/ \`Me

(41)

Me

Me \`/ \`Me

Me

(42)
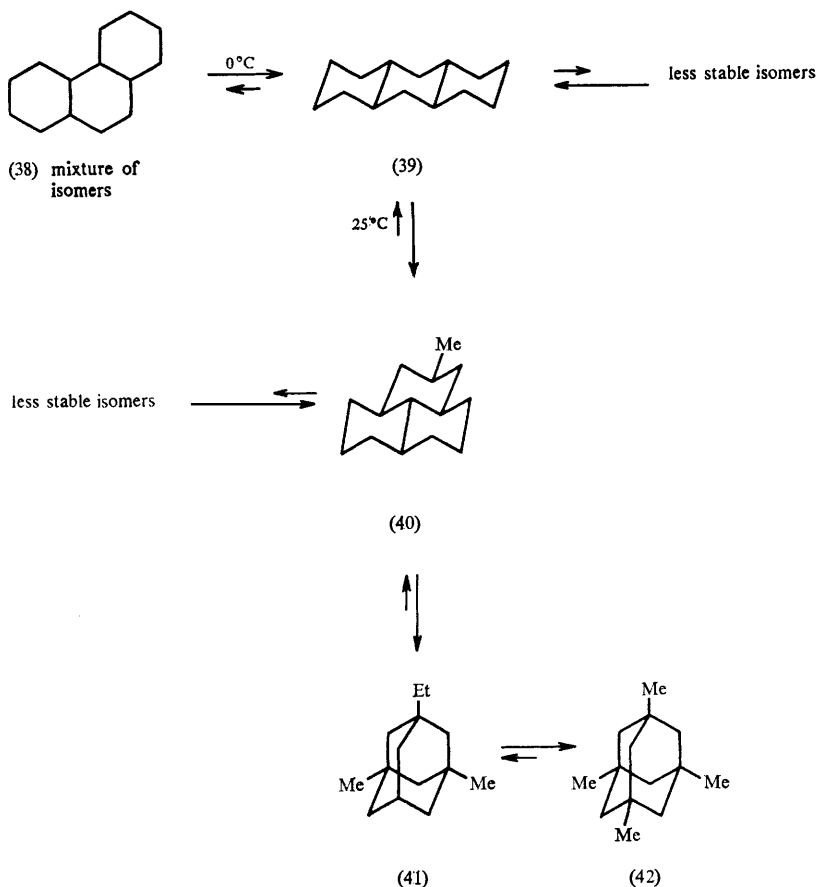
**Scheme 2**

[60] A. Schneider, R. W. Warren, and E. J. Janoski, *J. Org. Chem.*, 1966, **31**, 1617.

Scheme 2), 1,3-dimethyl-5-ethyladamantane (41), and ultimately 1,3,5,7-tetra-methyladamantane (42). By combining the various equilibria relating to isomer (39) the equilibrium concentrations at 25 °C were calculated to be 0.0006% (39), 0.008% (40), 6.0% (41), and 94% (42); the enthalpy change (39) → (42) was estimated by conformational analysis to be − 10.8 kcal mol⁻¹, in good agreement with that calculated by molecular mechanics.[56,57] The thermodynamic driving force for this sequence cannot be relief of strain in (39), which is composed of nearly strain-free cyclohexane rings in the energetically favourable *trans,syn,trans* arrangement; furthermore, molecular mechanics calculations indicate that isomers (39) and (42) are about equally strained to the extent of *ca.* 2 kcal mol⁻¹. It appears, therefore, that the thermodynamic driving force is provided by the increase in chain branching accompanying each successive step of the rearrangement and the concomitant accumulation of quaternary carbon atoms.

Acid-catalysed rearrangement of hydrocarbons is thought to occur *via* the following sequence: formation of cations by intermolecular hydride transfer; rearrangement, single or multiple, of the cations; saturation of the cations by hydride transfer; and, in heterogeneous reactions, distribution of the products between the acid and hydrocarbon phases. The problem of defining the mechanistic relationship of tetrahydrodicyclopentadiene to adamantane is not a simple one. It does not follow, for example, that the shortest pathway between the two skeletons should be particularly relevant to the actual pathway followed, nor indeed that there should even be a single pathway; Whitlock and Siefken[29] have counted no less than 2897 possibilities, employing only 1,2-alkyl shifts and treating each pathway as a sequential interconversion of carbon skeletons each
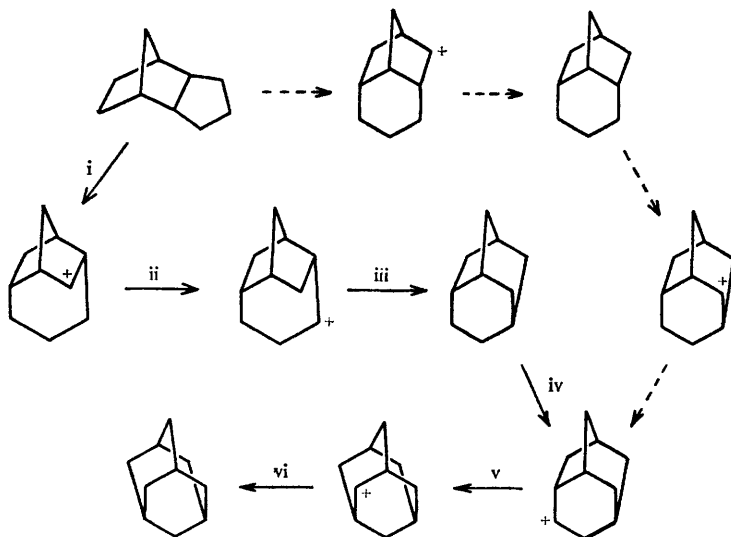


**Scheme 3**

of which is a set of cations and parent hydrocarbons and which is not encountered more than once in the sequence.

The first comment on the mechanism of the rearrangement route was that of Schleyer and Donaldson,[3] who intended it as an illustration of what could be involved rather than as a firm commitment to any particular pathway. The mechanism (solid arrows in Scheme 3) commences with hydride abstraction from either *endo-* or *exo-*(1) (the two are interconvertible under aluminium halide catalysis) and proceeds *via* a 2,6-alkyl shift for which there is no direct precedent in norbornane chemistry. The remaining steps involve transposition of inter-mediate cationic centres (steps ii and iv), probably *via* intermolecular hydride transfer, 1,2-alkyl shifts (steps iii and v), and finally hydride capture (step vi). A slightly different route (broken arrows in Scheme 3), involving a 1,4-alkyl shift (also without precedent in norbornane chemistry) was suggested later by Russian workers.[61] Schleyer and Nicholas[62] investigated the rearrangement of six methyl-substituted tetrahydrodicyclopentadienes, the idea being that the substituent, acting as a positional label, might provide a clue to the mechanism.



(43)                          (7)                          (6)
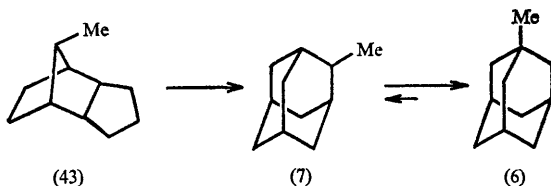
For example, if the mechanism i—vi (Scheme 3) is valid, the 7-methyl isomer (43) should produce 2-methyladamantane (7) on rearrangement. But this idea was thwarted by the discovery that (43), and the other isomers studied, produced a mixture of 1- and 2-methyladamantane, and that under the rearrangement conditions the products interconvert, eventually producing a preponderance of the bridgehead isomer (*ca.* 98% at equilibrium at 25 °C).[63]

The most illuminating comments on the mechanism of the rearrangement route are those of Whitlock and Siefken.[29] These workers found that rearrangement of twistane (11) into adamantane is a much readier process than is that of *endo-*tetrahydrodicyclopentadiene (1), suggesting that twistane is 'nearer' to adaman-tane than is (1). However, rather than examine individual mechanisms on an *ad hoc* basis, they proposed that because of the sheer complexity of the problem, such rearrangements can be classified and interpreted in terms of random pro-cesses. Using a general mathematical model the idea of 'nearness' was developed within a tricyclodecane map or graph, the most recent version[32] of which is reproduced with a slight modification in Scheme 4. The basis set of rearranging structures was defined as all the possible tricyclodecanes excluding isomers with

[61] O. A. Aref'ev, N. S. Vorob'eva, V. I. Epishev, and A. A. Petrov, *Neftekhimiya*, 1971, **11**, 32.
[62] P. von R. Schleyer and R. D. Nicholas, *Tetrahedron Letters*, 1961, 305.
[63] E. M. Engler, K. R. Blanchard, and P. von R. Schleyer, *J.C.S. Chem. Comm.*, 1972, 1210.

alkyl substituents or three- or four-membered rings. Implicit in the graph as originally defined is that all members of the basis set are of equal energy and all rate constants are unity. The single interconverting operation was taken to be a 1,2-cationic shift which represents the only route by which each member of the



(44)          (45)          (46)
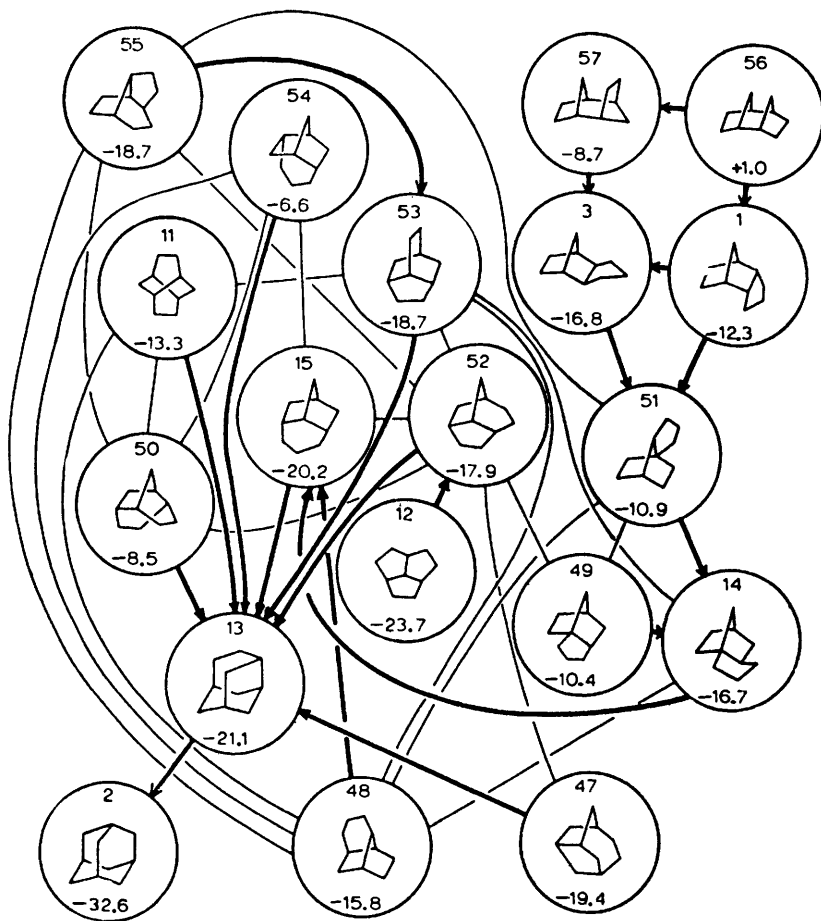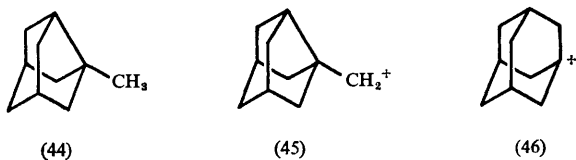


**Scheme 4** $\Delta H°_f$ in kcal mol$^{-1}$

basis set is allowed to undergo rearrangement of the type $R^1H \rightleftharpoons R^{1+} \rightleftharpoons R^{2+} \rightleftharpoons R^2H$ *etc.* in all possible ways, provided that the intermediate cations are secondary or tertiary in character, not primary. Thus $C_{10}H_{16}$ structures of type (44) were excluded from the basis set even though conditions which simulate the formation of the primary cation (45) (*e.g.* solvolysis of the primary tosylate) do lead to complete rearrangement to the 1-adamantyl cation (46).[64] The justification for omitting processes involving or simulating the formation of primary cations in the aluminium chloride-catalysed isomerization of hydrocarbons was that such processes are not normally competitive in rate with those involving the more substituted cations.

A member of the basis set was transformed into a cation simply by designating any secondary or tertiary carbon atom as the site of reactivity. Application of the interconverting operation produced a new cation which was allowed if its parent hydrocarbon belonged to the basis set. This process was then repeated with the aid of a computer to include all 1,2-shifts of all secondary or tertiary cations of all members of the basis set, thus defining the rearrangement possibilities. What emerges from this treatment is that adamantane and (1) are indeed far apart on the graph, that of the total of 2897 possible routes between the two the shortest (five steps) can be realized in ten different ways, and that when the structures are this far apart the percentage contribution of any one route should then be very small. In contrast, there is one two-step route, $(11) \rightarrow (13) \rightarrow (2)$, between twistane and adamantane, though here again there are no less than 2196 more circuitous routes. The probability of the two-step route is only 1/32 on a random walk basis.

Whitlock and Siefken were able to modify the graph considerably by placing an additional restriction on the interconverting operation. It is known that some bridgehead positions, notably those of bicyclo[2,2,1]heptane (a recurring structural unit in the tricyclodecane graph), yield tertiary cations of very high energy. When those bridgehead positions judged to be 'bad' sites for tertiary cations were disallowed the graph split in two, isolating structures (14), (49), (51), (1), (3), (56), and (57) from the others. In other words, *endo-* or *exo-*tetrahydrodicyclopentadiene cannot now transverse the graph to adamantane without the intervention of a bridgehead cation whereas this obstacle does not arise with twistane. This, the authors suggest, is a physically more convincing explanation of the difference in ease of rearrangement of (1) and (11). Similarly, isomer (12)[30] rearranges to adamantane under very mild conditions: the two are only three steps apart on the graph and the formation of a bridgehead cationic intermediate is not required. If the restriction on bridgehead cations is eased slightly so as to allow the intervention of ion (58) then the shortest pathway between (1) and adamantane *via* 1,2-shifts is $(1) \rightarrow (51) \rightarrow (14) \rightarrow (15) \rightarrow (13) \rightarrow (2)$.

In constructing the tricyclodecane graph Whitlock and Siefken made the simplifying assumption that all members of the basis set are of equal energy. This is certainly not the case with isomers (1) and (2) (the only pair whose

[64] P. von R. Schleyer and E. Wiskott, *Tetrahedron Letters*, 1967, 2845.

experimental enthalpies of formation are known) and any equality of stability among the others must be considered fortuitous. Schleyer and his co-workers[32] have introduced a considerable degree of chemical reality into the graph by including the calculated enthalpies of formation of all 19 isomers. The enthalpies of transition states connecting structures of this magnitude are not yet accessible by molecular mechanics calculations but they can be approximated by the calculated enthalpies $\Delta\Delta H_t$ (relative to the t-butyl cation) of the presumed secondary and tertiary cationic intermediates. The data reveal that several of the isomers, *viz.* (49), (50), (54), (56), and (57), are of very high energy, while structures (56), (57), and (12) are dead ends mechanistically. The data confirm that the five-step route (Scheme 5) proposed by Whitlock and Siefken is indeed the most favourable, though the first step is actually endothermic, and that the cationic intermediates indicated are those with the most favourable $\Delta\Delta H_t$ values. The efficacy of this route has received some experimental support. To avoid the endothermic 'bottleneck' step (1) → (51), Schleyer and his co-workers[32] studied the rearrangement of (14) to adamantane under very mild conditions and observed the transient formation of the intermediates (15) and (13). Similar studies with *endo*- and *exo*-tetrahydrodicyclopentadiene using chlorinated platinum–alumina as the catalyst as a suspension in chloroform revealed the presence of minute amounts of intermediates; thus far, however, none has been identified.[65]
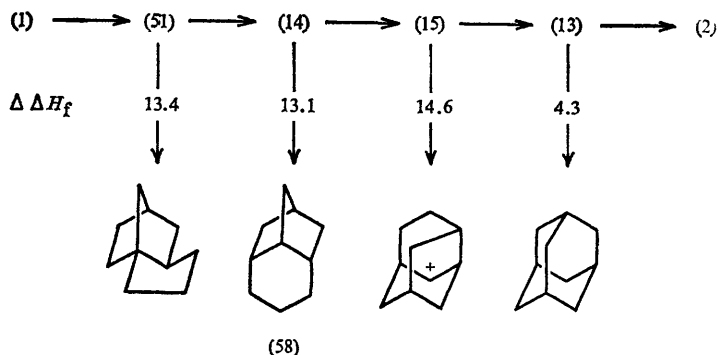


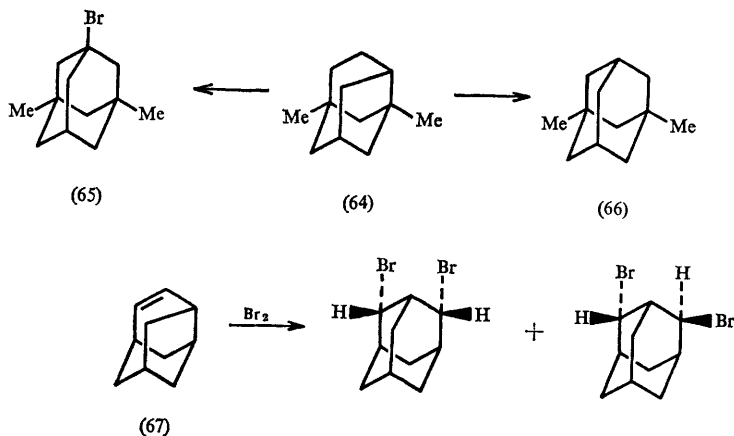**Scheme 5** $\Delta\Delta H_t$ in kcal mol$^{-1}$

Further support for the proposed pathway comes from a solvolytic study of the tosylate (59).[66] In aqueous acetone this derivative of isomer (14) undergoes complete rearrangement to alcohol (60) which, on exposure to sulphuric acid, yields 1-adamantanol (61). Similarly, Whitlock and Siefken[29] found that treatment of 2-anisyl-2-twistanol (62) with sulphuric acid causes rearrangement to the protoadamantyl derivative (63).

[65] R. Hamilton, M. A. McKervey, and J. J. Rooney, unpublished results.
[66] E. J. Corey and R. S. Glass, *J. Amer. Chem. Soc.*, 1967, **89**, 2600.

TsO

(59)

OH

(60)

OH

(61)

OH

R

(62)   R = p-CH$_2$OC$_6$H$_4$   (63)

OH
R
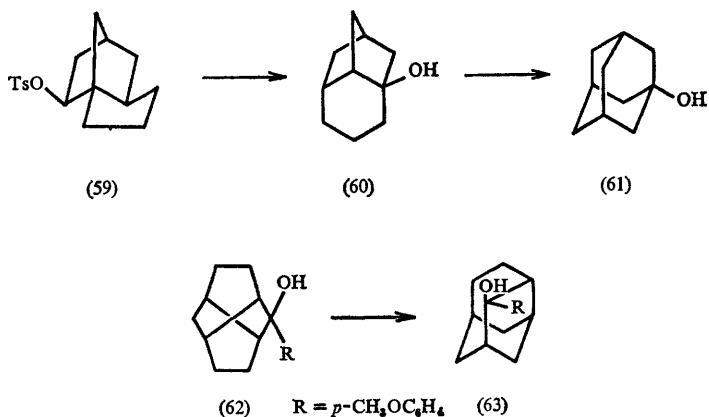
Protoadamantane plays a crucial role in the tricyclodecane graph for it represents the only direct exit to adamantane, and, as expected, the protoadamantane to adamantane rearrangement occurs with remarkable ease. In the hydrocarbon series, catalysis has been observed with such diverse reagents as the aluminium halides,[67] sulphuric acid,[23] bromine [e.g. (64) → (65)],[34] palladium, platinum, and rhodium [e.g. (64) → (66)],[68] and with functionalized derivatives the rearrangement has been widely used as a synthetic route to substituted adamantanes which are otherwise difficult to prepare. The reaction of protoadamantene (67) with bromine provides an illustrative example;[69,70] others are summarized in Scheme 6.

Br

Me                    Me

(65)

Me                    Me

(64)

Me                    Me

(66)
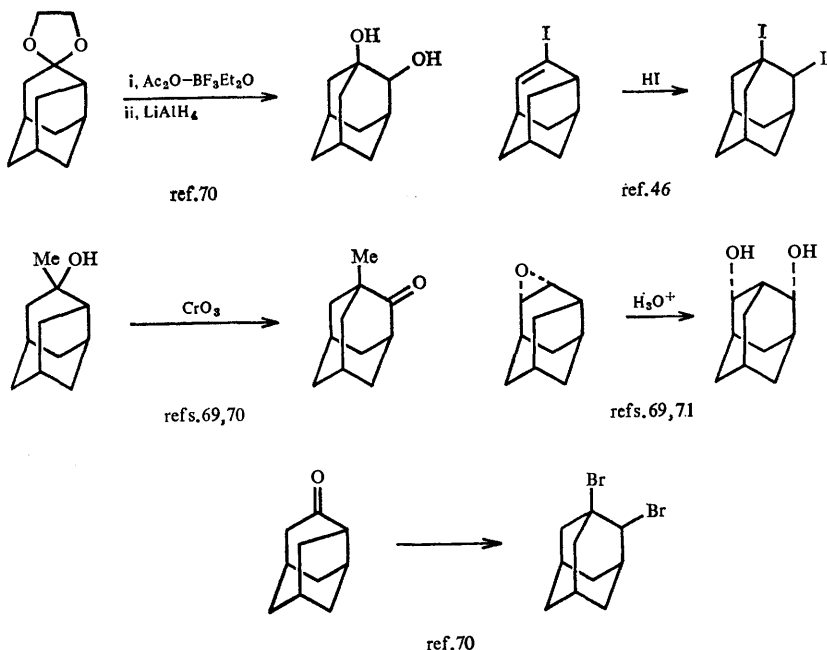
(67)

Br₂

Br   Br
H          H

+

Br   H
H          Br

[67] D. Lenoir and P. von R. Schleyer, *Chem. Comm.*, 1970, 941; see also L. A. Spurlock and K. P. Clark, *J. Amer. Chem. Soc.*, 1970, **92**, 3829.
[68] J. McIlfatrick, M. A. McKervey, and J. J. Rooney, unpublished results.
[69] D. Lenoir, R. Glaser, P. Mison, and P. von R. Schleyer, *J. Org. Chem.*, 1971, **36**, 1821.
[70] B. D. Cuddy, D. Grant, and M. A. McKervey, *J. Chem. Soc.* (C), 1971, 3173.

ref.70                                    ref.46

refs.69,70                              refs.69,71

ref.70

**Scheme 6**

## 5 Rearrangements involving the Peripheral Shift of Substituents

A notable feature of the chemistry of a variety of substituted adamantanes is the ease with which they undergo acid-catalysed peripheral shifts of the type shown.



Two general situations have been recognized depending on the nature of the substituent, one intramolecular (for alkyl and aryladamantanes) and the other intermolecular (for hydroxy- and halogeno-adamantanes), and there is now general agreement that the intramolecular route does not involve a simple 1,2-cationic shift of the substituent.

Geluk and Schlatmann[72] found that exposure of 1-adamantanol (61) to 96% sulphuric acid at 70 °C affords good yields of adamantanone, and subsequent

[71] J. Boyd and K. H. Overton, *J.C.S. Perkin I*, 1972, 2533.
[72] H. W. Geluk and J. L. M. A. Schlatmann, *Tetrahedron Letters*, 1968, 5361, 5369.

experiments revealed that 1-adamantanol exists at equilibrium with 2-adaman-tanol (68) in 96% sulphuric acid, the secondary isomer amounting to *ca.* 2% of the mixture at 25 °C. On this evidence it was suggested that the ketone is formed by disproportionation and/or direct oxidation of the secondary alcohol and that equilibration of the alcohols is established *via* a reversible intramolecular 1,2-hydride shift involving the secondary and tertiary adamantyl cations. Somewhat similar, though more complex, behaviour was observed with 2-methyl-2-adamantanol (69)[73] in 98% sulphuric acid: at 0 °C an equilibrium is established with isomers (70) and (71); at 50 °C isomer (72), in which both hydroxy and methyl functions have shifted, is the main product; and at still higher temper-atures disproportionation and/or oxidation leads ultimately to the ketones (73) and (74).[74,75]
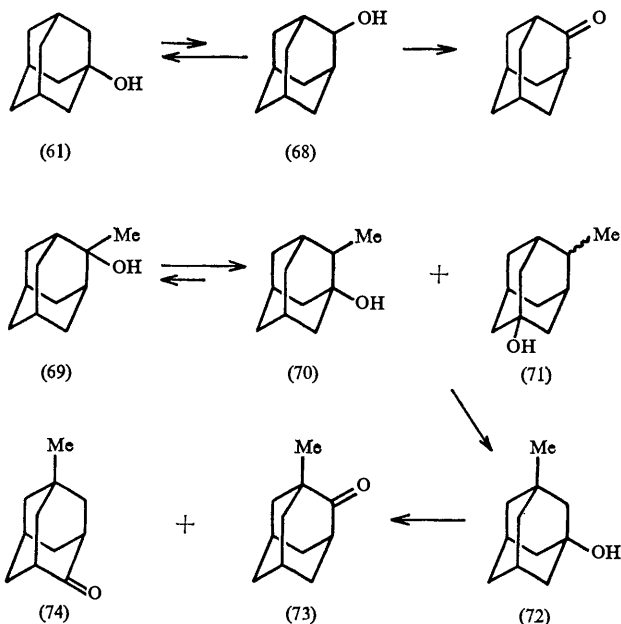


The validity of the intramolecular 1,2-hydride shift mechanism has been questioned on stereoelectronic grounds.[76] Consider the interconversion of the
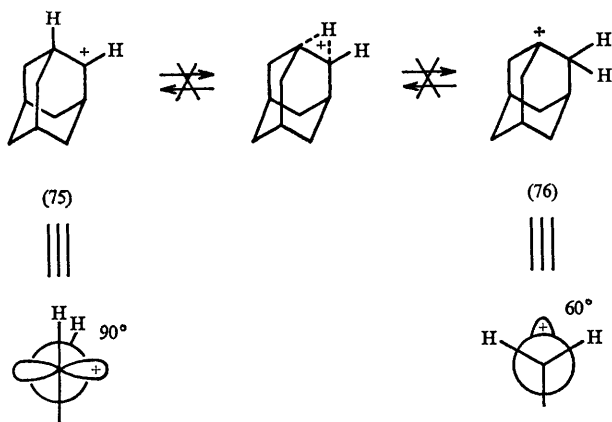
[73] B. D. Cuddy, D. Grant, A. Karim, M. A. McKervey, and E. J. F. Rea, *J.C.S. Perkin I*, 1972, 2701.
[74] H. W. Geluk and J. L. M. A. Schlatmann, *Rec. Trav. chim.*, 1969, **88**, 13.
[75] J. A. Bone, J. R. Pritt, and M. C. Whiting, *J.C.S. Perkin I*, 1972, 2644.
[76] P. von R. Schleyer, *Angew. Chem.*, 1969, **81**, 539; 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 J. L. M. A. Schlatmann, *J. Amer. Chem. Soc.*, 1970, **92**, 5246.

(75)                                    (76)

secondary and tertiary adamantyl cations (75) and (76) by such a mechanism, bearing in mind that the arrangement which provides maximum orbital overlap at the transition state is one in which the vacant orbital of the cation and the C—H bond undergoing migration are co-planar. In acyclic cations the favourable conformation with zero dihedral angle between the C—H bond and the vacant orbital is easily achieved by rotation about the conjoining bond, but in adamantyl cations rotational changes of this type are precluded and the dihedral angles in ions (75) and (76) are rigidly held at 90° and 60°, respectively. Consequently, the highly deformed transition states connecting the secondary and tertiary cations should be so unfavourable that the rate of a 1,2-hydride shift will be extremely low relative to that in an acyclic system. An attempt to quantify this obstacle to a 1,2-hydride shift in adamantyl cations gives, as a minimum estimate, an activation energy of *ca.* 30 kcal mol$^{-1}$ from the observation that the [3,5,7-$^2$H$_3$]adamantyl cation in SbF$_5$-SO$_2$ClF at 105 °C exhibits <10% tertiary-secondary interconversion.[77,78] This value is about twice that estimated for a 1,2-hydride shift in a typical acyclic cation.

A clue to the mechanism of these peripheral rearrangements emerged from dilution studies which indicated that they are in fact intermolecular since they can be inhibited by the use of sufficiently dilute reaction conditions. Intramolecular hydride shifts are necessarily first-order in substrate and should be concentration independent, but intermolecular shifts, being second-order, should be concentration dependent. Landa *et al.*[79] observed that treatment of 2-adamantanol (68) with sulphuric acid–formic acid (Koch–Haaf carboxylation conditions) gave largely the unrearranged acid (77) whereas Schleyer *et al.*,[76] employing an apparently similar procedure, found the product to be largely the

[77] D. M. Brouwer and H. Hogeveen, *Rec. Trav. chim.*, 1970, **89**, 211.
[78] P. Vogel, M. Saunders, W. Thielecke, and P. von R. Schleyer, *Tetrahedron Letters*, 1971, 1429.
[79] S. Landa, J. Burkhard, and J. Vais, *Z. Chem.*, 1967, **7**, 388.

rearranged acid (78). The cause of this discrepancy was found to lie not in the SO$_3$ content of the medium but rather in the total volume of sulphuric acid employed in the two experiments: at relatively high concentrations of the alcohol in sulphuric acid rearrangement occurs, whereas use of high-dilution conditions suppresses rearrangement. In the absence of formic acid, interconversion of alcohols (61) and (68) is also concentration dependent; at a concentration of 0.08 mol l$^{-1}$ a solution of either isomer in 96% sulphuric acid reaches equilibrium within seconds; at 0.0004 mol l$^{-1}$ isomerization is not observed.[76,80] High-dilution conditions can be simulated by the use of an immiscible cosolvent. For example, carboxylation of 2-methyl-2-adamantanol (69) in a two-phase mixture of carbon tetrachloride–sulphuric acid yields essentially pure 2-methyl-2-adamantanecarboxylic acid[76,81] whereas with normal reagent concentrations



(77)    (68)    (78)

(79)

(78) 30%
(81) 70%

(80)    (81)
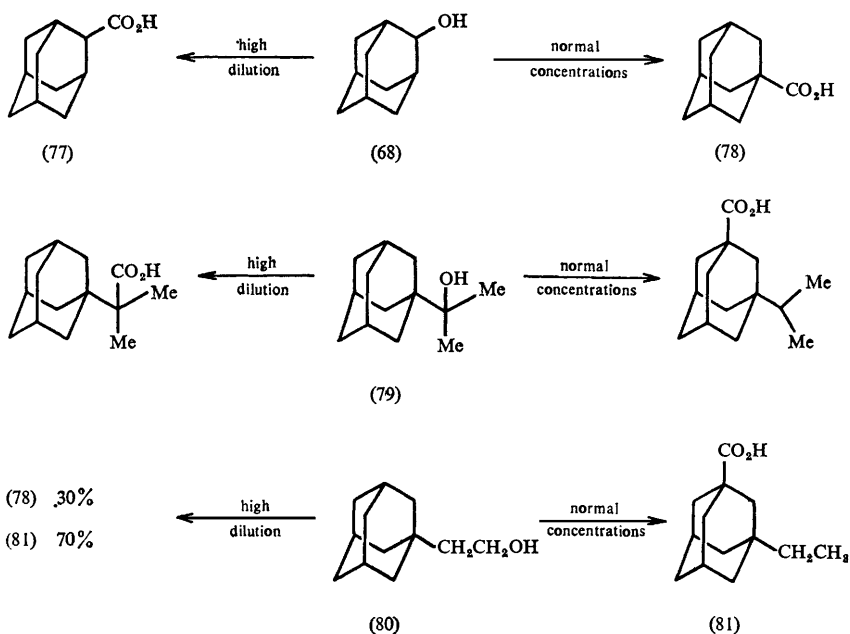
carboxylation proceeds with rearrangement, yielding acids derived from alcohols (70) and (71).[81,82] In the two-phase modification slow diffusion of the alcohol from the carbon tetrachloride into the sulphuric acid layer achieves the conditions of high dilution. Dilution studies indicate that the rearrangements which occur during Koch–Haaf carboxylation of alcohols (79)[83] and (80)[81] are also inter-
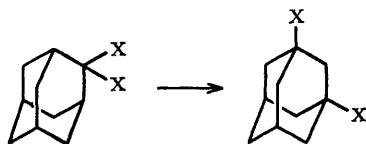
[80] H. W. Geluk and J. L. M. A. Schlatmann, *Rec. Trav. chim.*, 1971, **90**, 516.
[81] J. R. Alford, B. D. Cuddy, D. Grant, and M. A. McKervey, *J.C.S. Perkin I*, 1972, 2707.
[82] J. Vais, J. Burkhard, and S. Landa, *Z. Chem.*, 1969, **9**, 268.
[83] D. J. Raber, R. C. Fort, E. Wiskott, C. W. Woodworth, P. von R. Schleyer, J. Weber, and H. Stetter, *Tetrahedron*, 1971, **27**, 3.

(82) X = Cl or Br

molecular in character. Similar kinds of rearrangement, catalysed by aluminium halides, are observed with 2,2-dichloro- and 2,2-dibromo-adamantane (82),[73] and although the 1-adamantyl cation does not exhibit tertiary–secondary interconversion in SbF$_5$-based super-acids, deuterium labelling studies indicate that intermolecular tertiary–tertiary exchange does occur in these media also.[29]

What has just been said about stereoelectronic inhibition of intramolecular 1,2-hydride shifts in adamantyl cations should apply equally well to intramolecular 1,2-alkyl shifts. Intermolecular shifts of alkyl substituents must be considered highly unlikely (what appears to be an example[75,84] probably proceeds by an addition–fragmentation mechanism involving olefinic intermediates). Nevertheless, the apparent 1,2-methyl shift is observed experimentally, with 1- and 2-methyladamantane catalysed by aluminium bromide, and with 2-methyl-2-adamantanol (69) in sulphuric acid. This aspect of the problem was elucidated through experiments with labelled materials. When 2-methyl[2-$^{14}$C]adamantane (83)[85] was exposed to aluminium bromide the product was 1-methyl[1-$^{14}$C]-adamantane (84) with *ca.* 90% of the starting activity in the 1-position and none in the methyl group. Specifically labelled adamantane itself, when similarly treated, exhibited scrambling of the carbon atoms (degenerate isomerization).[52] These results establish that the methyl group, in moving from the 2-position to the 1-position, remains attached to the same skeletal carbon atom, thereby eliminating any significant contribution from a 1,2-methyl shift mechanism. The most likely alternative consistent with the fate of the labelled atom appears to be a skeletal reorganization involving an adamantane → protoadamantane → adamantane rearrangement of the type summarized in Scheme 7. What is significant about these changes is the suggestion that adamantane can 'climb out' of the Whitlock and Siefken 'bottomless pit' to the much more strained protoadamantyl system. In fact substantial inferential information is available to support the general validity of Scheme 7. In the first place, Whiting and his co-workers[53] found that acetolysis of 2-adamantyl tosylate (85; R = H) gives, in addition to 2-adamantyl acetate, 0.5% of 4-protoadamantyl acetate. Secondly, the position of the deuterium label in the products of solvolysis of 4-*endo*-[4-$^2$H]-protoadamantyl tosylate (86)[67] in aqueous acetone suggests the intervention of a degenerate protoadamantane akin to that indicated in Scheme 7. As expected, cation-stabilizing substituents facilitate the protoadamantane → adamantane rearrangement in, for example, solvolysis of 1-methyl-2-adamantyl tosylate

[84] R. E. Moore, R. W. Warren, and A. Schneider, *Amer. Chem. Soc. Div. Petrol. Chem. Prep.*, 1970, **15**, B43.

[85] Z. Majerski, P. von R. Schleyer, and A. P. Wolf, *J. Amer. Chem. Soc.*, 1970, **92**, 5731.

**Scheme 7** ● = ¹⁴C



R = H, 0.5%

R = Me, 30%

(85)



(86)
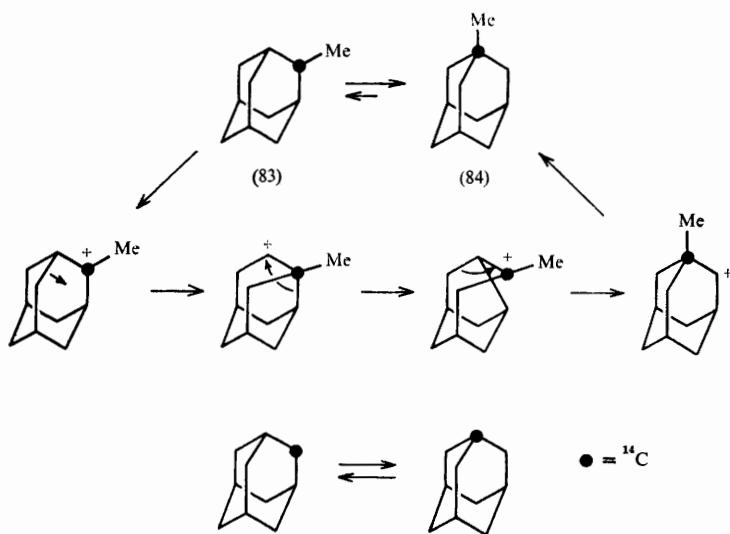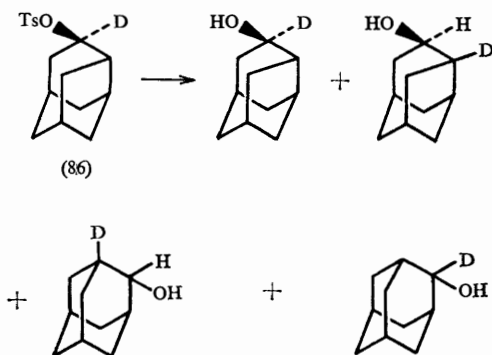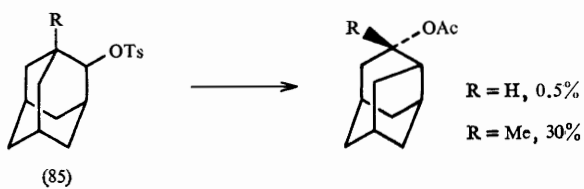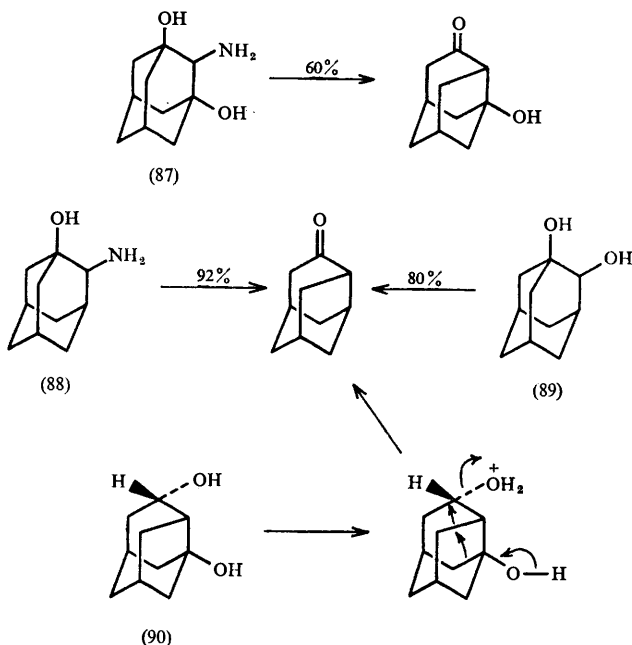
(85; R = Me),[67] deamination of amino-alcohols (87)[86] and (88),[67] and pinacol rearrangement of diol (89)[70] in dilute sulphuric acid. The transformation of diol (90) into 4-protoadamantanone under acid catalysis probably proceeds *via* a protoadamantane → adamantane → protoadamantane rearrangement.[86] A more involved case of the peripheral shift of substituents, presumably involving both intermolecular hydride transfers and protoadamantyl intermediates, is cycliz-ation–rearrangement of alcohol (91) in concentrated sulphuric acid.[87] Proto-adamantyl intermediates have been invoked to explain the formation of tri-bromides (92) and (93) in the reaction of 2-methyladamantane with bromine;[88] the reaction of adamantylideneadamantane (94) with chlorine may proceed *via* a similar mechanism.[89]

Apart from the dichotomy of mechanism of these various peripheral re-arrangements of substituted adamantanes one common feature does emerge: the preference for bridgehead substitution at equilibrium. In analysing the thermodynamics of these equilibria it is useful to compare the topologies of a 1- and 2-substituted adamantane (Scheme 8) with those of a monosubstituted cyclohexane. One can visualize the former as formal analogues (denoted by the heavy lines) of the latter, *i.e.* the adamantane isomers resemble the axial and

[86] J. R. Alford and M. A. McKervey, *Chem. Comm.*, 1970, 615.
[87] F. Blaney, D. Faulkner, M. A. McKervey, and G. Step, *J.C.S. Perkin I*, 1972, 2697.
[88] J. R. Alford, D. Grant, and M. A. McKervey, *J. Chem. Soc. (C)*, 1971, 880.
[89] J. H. Wieringa, J. Strating, and H. Wynberg, *Tetrahedron Letters*, 1970, 4579.

(91)



(92)          (93)



(94)
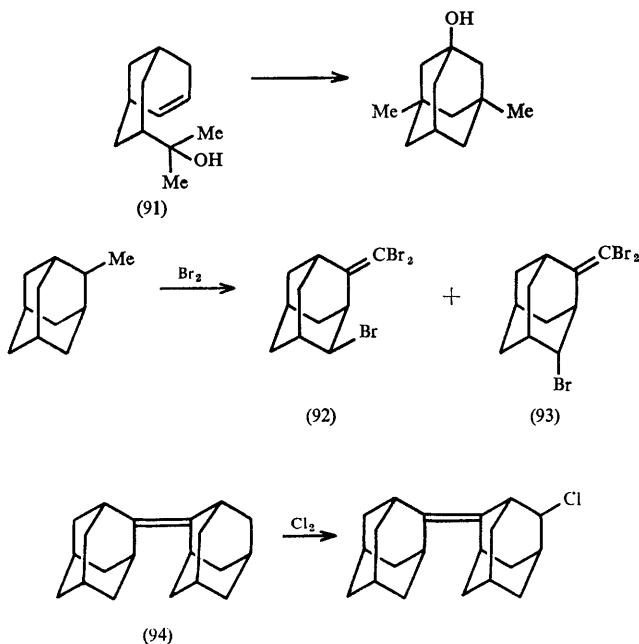
equatorial conformers of a monosubstituted cyclohexane. On this basis alone, in the absence of other factors, 1-substituted adamantanes should be preferred at equilibrium. However, this comparison requires some qualification. Firstly, the adamantane equilibrium is complicated by the fact that an 'axial' secondary component (96a) is in equilibrium with an 'equatorial' tertiary component (96e) so that the enthalpy change needs to be corrected to allow for the change in substitution pattern if it is to be compared directly with the enthalpy change associated with (95). Secondly, there should exist a substantial difference in flexibility between the two systems: an axially substituted cyclohexane can adopt a somewhat flattened geometry in which the most favourable balance between the various forms of strain is achieved whereas the rigidity of the adamantane skeleton should preclude any comparable flattening of its constituent rings. The problem of the change in substitution pattern in equilibrium (96) does not arise in the comparable case of the 1- and 4-substituted diamantanes (97a) and (97e); both are now bridgehead derivatives, and differences in flexibility notwithstanding, the suggestion has been made that diamantyl derivatives should provide good models for studying some aspects of conformational change in substituted cyclohexanes.[91] Equilibrium (97) is in fact a three-component system if the secondary isomer (97s) is included, but with some of the systems to be discussed here the concentration of (97s) at equilibrium at ordinary temperatures is very small and the data (Table 2) have been treated as if the equilibrium consisted only of isomers (97a) and (97e).
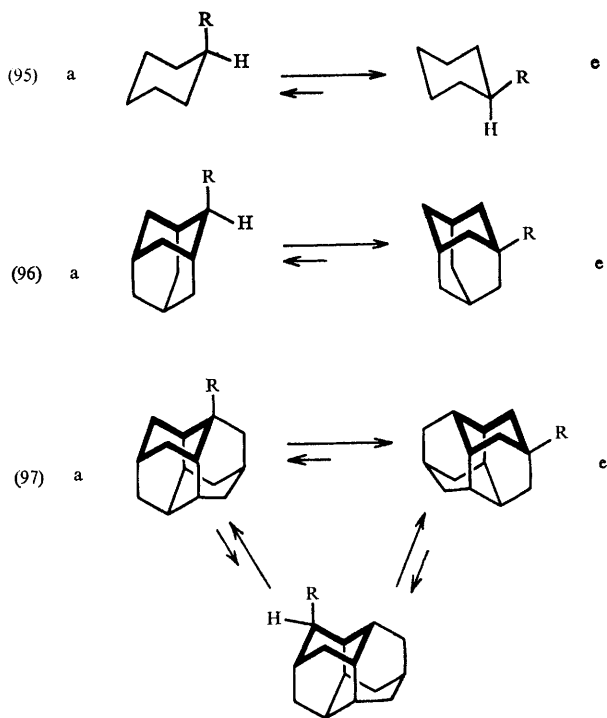
**Scheme 8**

**Table 2** *Isomerization enthalpies* $(-\Delta H°)$ *for equilibria* (95), (96), *and* (97). *Data in* kcal mol$^{-1}$

| Group R | (97) a ⇌ e | (97) s ⇌ a | (97) s ⇌ e | (96) a ⇌ e | (95) a ⇌ e | Diamantyl: cyclohexyl ratio |
|---|---|---|---|---|---|---|
| OH | 1.1 | — | — | — | 1.10 | 1.00 |
| Cl | 0.68 | — | — | — | 0.52 | 1.29 |
| Br | 0.60 | — | — | — | 0.45 | 1.33 |
| CH$_3$(gas) | 2.14 | 0.64 | 2.70 | 2.77 | 1.90 | 1.14 |
| CH$_3$(sol) | 2.00 | 0.47 | 2.54 | 2.63,3.37 | 1.70 | 1.18 |
| CH$_3$CH$_2$(gas) | 2.21 | 0.41 | 2.62 | — | — | — |
| CH$_3$CH$_2$(sol) | 2.20 | 0.39 | 2.59 | — | 1.80 | 1.22 |

Schleyer and his co-workers[63] have studied the temperature dependence of equilibrium (96) in solution for the case where R is methyl using aluminium bromide catalysis. More recently, the methyladamantanes have also been examined over wide temperature ranges both in solution and in the gas-phase using

chlorinated platinum–alumina as the catalyst.[90] In the diamantyl series five systems have been examined: the alcohols in 98 % sulphuric acid,[91] the chlorides[92] and bromides[40] in dichloro- and dibromo-methane containing the appropriate aluminium halide, and the methyl[93] and ethyl[90] derivatives in solution and in the gas phase using chlorinated platinum–alumina. Although mechanistic studies have not been performed with the diamantyl isomerizations it is reasonable to assume that the alcohols, chlorides, and bromides rearrange *via* intermolecular hydride transfer while protodiamantyl intermediates are probably involved with the methyl and ethyl cases. In comparing the data (Table 2) for the adamantyl and diamantyl systems with those from the literature for the cyclohexane system[94] it is preferable to use enthalpy changes rather than free energy changes. Thus although the $-\Delta H°$ data included for (95a $\rightleftharpoons$ e) are not the familiar '*A* values' usually quoted, the differences between the two sets of data are very slight because with simple substituents the entropy change ($\Delta S°$) associated with (95 a$\rightleftharpoons$ e) is very small: chlorocyclohexane has a $-\Delta H°$ value of 0.52 kcal mol$^{-1}$ [95] and, at $-80$ °C, a $-\Delta G°$ value of 0.53 kcal mol$^{-1}$.[96] On the other hand, entropy differences have a considerable effect on the position of equilibrium in the diamantyl and adamantyl systems. The behaviour of the isomeric tertiary chlorodiamantanes (97a $\rightleftharpoons$ e, R = Cl) is illustrative. The enthalpy change ($-\Delta H°$) favours the e-isomer by 0.68 kcal mol$^{-1}$ yet, at equilibrium at 17 °C, the two isomers are of equal thermodynamic stability and, above 17 °C, the a-isomer is actually the more thermodynamically stable of the two. However, the experimental entropy change ($\Delta S°$) is 2.2 cal deg$^{-1}$ mol$^{-1}$ in favour of the a-isomer and symmetry differences between the isomers appear to be responsible: isomer (97a) has $C_s$ symmetry whereas isomer (97e) has $C_{3v}$ symmetry, and consequently the entropy change due to symmetry should be $R \ln 3$ or 2.2 cal deg$^{-1}$ mol$^{-1}$, in complete agreement with the measured value. The entropy change for the other members of the tertiary diamantyl series are ($\Delta S°$ in cal deg$^{-1}$ mol$^{-1}$) R = OH (3.4), Br (1.6), CH$_3$ (gas) (1.2), CH$_3$ (sol) (1.53), CH$_3$CH$_2$ (gas) (2.64), CH$_3$CH$_2$ (sol) (2.57). In the case of methyladamantane the entropy difference due to symmetry should also be 2.2 cal deg$^{-1}$ mol$^{-1}$; the experimental value in solution is 3.0 cal deg$^{-1}$ mol$^{-1}$.[63]

The main points to emerge from the data in Table 2 are (i) in the diamantyl and adamantyl series the isomerization enthalpies ($-\Delta H°$) all favour the e-isomer; (ii) excluding the alcohols, which may be complicated by solvent effects, the isomerization enthalpies in the diamantyl series are larger than those in the corresponding cyclohexyl series, though only slightly so: the diamantyl:cyclo-

[90] R. Hamilton, M. A. McKervey, and J. J. Rooney, unpublished observations.
[91] D. E. Johnston, M. A. McKervey, and J. J. Rooney, *J.C.S. Chem. Comm.*, 1972, 29.
[92] M. A. McKervey, D. E. Johnston, and J. J. Rooney, *Tetrahedron Letters*, 1972, 1547.
[93] R. Hamilton, D. E. Johnston, M. A. McKervey, and J. J. Rooney, *J.C.S. Chem. Comm.*, 1972, 1209.
[94] J. A. Hirsch, in 'Topics in Stereochemistry', ed. N.L. Allinger and E. L. Eliel, Interscience, New York, 1967, Vol. 1, p. 199.
[95] J. Reisse, in 'Conformational Analysis, Scope and Present Limitations', ed. G. Chiurdoglu, Academic Press, New York, 1971, p. 219.
[96] F. R. Jensen, C. H. Bushweller, and B. H. Beck, *J. Amer. Chem. Soc.*, 1969, 91, 344.

hexyl ratios fall in the range 1.14—1.33; (iii) $-\Delta H°$ for chlorodiamantane is greater than that for bromodiamantane as is found with chloro- and bromocyclohexane; and (iv) the tertiary methyl- and ethyl-diamantane isomerization enthalpies are about equal, as is the case with methyl- and ethyl-cyclohexane in solution[94] (ethylcyclohexane appears not to have been measured in the gas phase). Thus, in general, there is a good correlation between the data for diamantane derivatives and those for monosubstituted cyclohexanes. The change in substitution pattern associated with the shift of the substituent in isomerizations (97s ⇌ e) and (96a ⇌ e) is such that it results in the largest isomerization enthalpies observed. However, there is a discrepancy between the two independently determined $-\Delta H°$ values for methyladamantane in solution. Whereas Engler *et al.*[63] obtained a value of 3.37 kcal mol$^{-1}$ for methyladamantane in the temperature range 35—70 °C, more recent work[90] yields values almost identical with those for the methyldiamantane isomerizations, 2.63 kcal mol$^{-1}$ in solution in the temperature range 50—179 °C and 2.77 kcal mol$^{-1}$ in the gas phase in the temperature range 143—250 °C. When corrected for the change in substitution type by subtracting 0.7 kcal mol$^{-1}$, Engler's value indicates a substantial enhancement of axial methyl strain in 2-methyladamantane, contrary to that found by Hamilton. Molecular mechanics calculations have been applied to the problem, and the data for the methyladamantanes and methyldiamantanes predict an enhancement of axial strain,[56] but any detailed analysis must await the measurement of the heats of formation of the various isomers. The general impression given by the data in Table 2 is that, for the substituents listed, the isomerization enthalpies measured with diamantane and adamantane are only slightly larger than those with cyclohexane, despite the differences in flexibility between the two systems. It is interesting to note in this connection that a recent *X*-ray structure determination of 2-iodoadamantane reveals that the axial substituent does not cause any significant skeletal distortions.[97]

There is one exception to the preference for bridgehead substitution at equilibrium. It involves the isomeric biadamantanes (98) and (99) whose equilibration has been studied as a function of temperature.[98] At 60 °C the 2,2'-isomer (99) is the main component (70%). The derived thermodynamic parameters are $\Delta G° = -0.51$ kcal mol$^{-1}$, $\Delta H° = 1.11$ kcal mol$^{-1}$, and $\Delta S° = 5.4$ cal deg$^{-1}$ mol$^{-1}$. The dominant factor controlling the position of equilibrium is the appreciable entropy change in favour of (99) and the experimental $\Delta S°$ is in excellent agreement with the value (5.3 cal deg$^{-1}$ mol$^{-1}$) calculated from the difference in symmetry numbers ($R \ln 3 = 2.2$ cal deg$^{-1}$ mol$^{-1}$) and the change in substitution type (3.1 cal deg$^{-1}$ mol$^{-1}$) between (98) and (99). The peripheral shift of a phenyl substituent in adamantane[99] and in diamantane[90] has also been observed, but thermodynamic data are not available. Two other types of peripheral shift have been observed: the axial–equatorial change in the keto-alcohol (100) and keto-

[97] G. H. Wahl, jun., R. L. Greene, and J. Bordner, *J.C.S. Chem. Comm.*, 1973, 927.
[98] J. Slutsky, E. M. Engler, and P. von R. Schleyer, *J.C.S. Chem. Comm.*, 1973, 685.
[99] A. C. Udding, J. Strating, and H. Wynberg, *Tetrahedron Letters*, 1968, 1345; J. K. Chakrabarti, M. R. J. Jolley, and A. Todd, *ibid.*, 1974, p. 391.

(98)          (99)
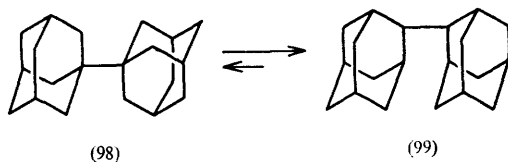
mesylate (101)[100,101] in sulphuric acid and methanesulphonic acid, respectively, and a specific 1,3-hydride shift in the unsaturated alcohol (102).[102] The latter type of hydride shift is not observed in the solvolysis of [2-$^2$H]adamantyl tosylate.[53]



(100)   X = OH
(101)   X = OMs

      (102)
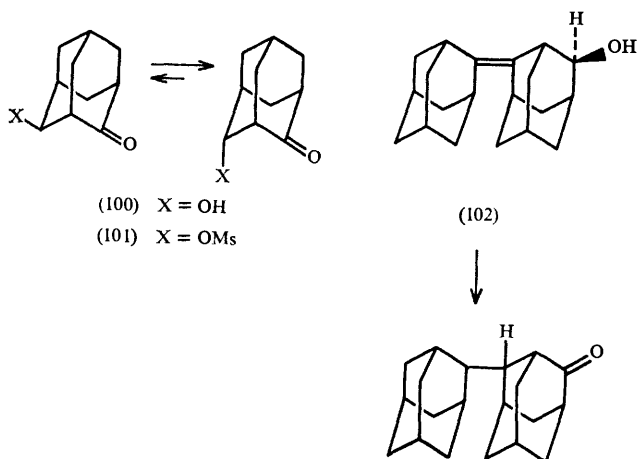
## 6 Further Skeletal Rearrangements

Ring expansion of one cyclohexane ring of the adamantane skeleton by a single methylene group produces the homoadamantane system. This type of change has been brought about in a variety of ways, typically those simulating the formation of the primary 1-adamantylmethyl cation (103), which rearranges to the more stable tertiary 3-homoadamantyl cation (104). This expansion leads to an overall increase in ring strain [homoadamantane (105) is more strained than 1-methyl-adamantene by *ca.* 10 kcal mol$^{-1}$],[56] and there are several instances where product compositions reflect the operation of either kinetic or thermodynamic control. On exposure to aluminium bromide, both homoadamantane[103] and 4-homo-
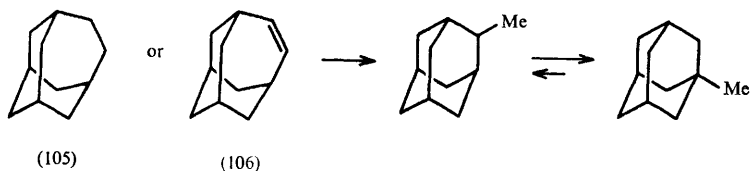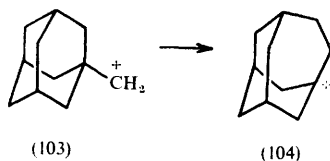
[100] D. Faulkner and M. A. McKervey, *J. Chem. Soc. (C)*, 1971, 3906.
[101] T. Sasaki, S. Eguchi, and T. Toru, *Tetrahedron Letters*, 1971, 1109.
[102] E. Boelma, J. H. Wieringa, H. Wynberg, and J. Strating, *Tetrahedron Letters*, 1973, 2377.
[103] Unpublished results quoted in ref. 1c,

(103)    (104)



(105)    (106)

adamantene[104] (106) rearrange (the latter *via* disproportionation) into 2-methyl-adamantane within minutes, and in a subsequent slower reaction peripheral shift of the methyl group yields 1-methyladamantane. Two of the earliest examples of kinetic control involve deamination of amine (107)[105] and Koch–Haaf carboxy-



(107)



(108)



(111)    (109)    (110)



(113)    (112)    (114)
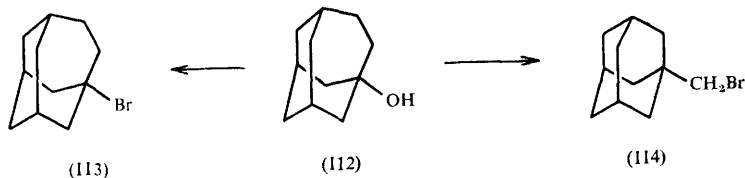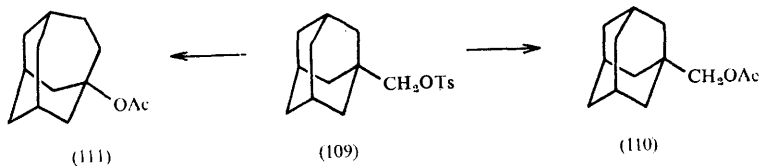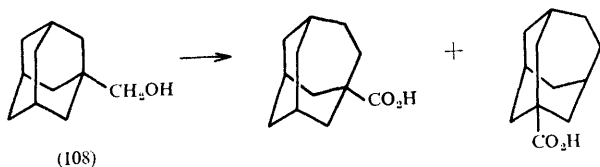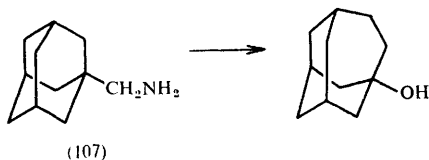
[104] Z. Majerski and K. Mlinaric, *J.C.S. Chem. Comm.*, 1972, 1030.
[105] H. Stetter and P. Goebel, *Chem. Ber.*, 1963, **96**, 550.

lation of alcohol (108),[105] both of which yield homoadamantane derivatives almost exclusively. On the other hand, acetolysis of tosylate (109) in the absence of a buffer yields the unrearranged acetate (110); in the presence of sodium acetate the product is largely 3-homoadamantyl acetate (111).[106] Similar effects are involved in the reaction of 3-homoadamantanol (112) with hydrogen bromide in acetic acid: at 25 °C 3-homoadamantyl bromide (113), the product of kinetic control, is formed; at 125 °C the product is 1-bromomethyladamantane (114).[105] Although the 1-adamantylmethyl cation is formulated above as the primary species (103), there is evidence that C—C single bond participation occurs in the ionization of some 1-adamantyl carbinyl derivatives. Thus acetolysis of the chiral deuteriated tosylate (115) proceeds with complete retention of configuration in both acetates (116) and (117), suggesting the intervention of the bridged ion intermediate (118).[107] Synthetically useful examples of the adamantane → homoadamantane rearrangement include the preparation of 4-homoadamantanone



(115)        (116)        (117)        (118)



(120)        (119)        (121)
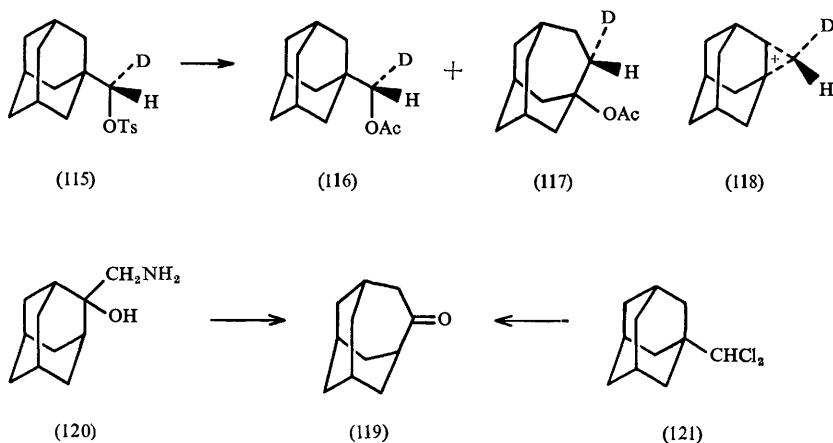
(119) by reaction of diazomethane with adamantanone,[108] deamination of aminoalcohol (120) with nitrous acid,[109] or hydrolysis of dichloride (121) in phosphoric acid.[110]

Ring expansions have also been observed in situations where the intervention of a vinyl cation is simulated at the expansion terminus. The 1-adamantyl cation adds to acetylene in sulphuric acid, forming the vinyl cation (122).[111,112] This cation

[106] J. E. Norlander, S. P. Jindal, P. von R. Schleyer, R. C. Fort, jun., J. J. Harper, and R. D. Nicholas, *J. Amer. Chem. Soc.*, 1966, **88**, 4475.
[107] S. H. Liggero, R. Sustmann, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1969, **91**, 4571.
[108] (a) P. von R. Schleyer, E. Funke, and S. H. Liggero, *J. Amer. Chem. Soc.*, 1969, **91**, 3965; (b) R. M. Black and G. B. Gill, *J. Chem. Soc. (C)*, 1970, 671.
[109] (a) J. E. Norlander, F. Y. H. Wu, and S. P. Jindal, *J. Amer. Chem. Soc.*, 1969, **91**, 2962; (b) J. L. M. A. Schlatmann, J. G. Korsloot, and J. Schut, *Tetrahedron*, 1970, **26**, 949.
[110] I. Tabushi, Z. Yoshida, and N. Takahashi, *J. Amer. Chem. Soc.*, 1970, **92**, 6672.
[111] T. Sasaki, S. Eguchi, and T. Toru, *Chem. Comm.*, 1968, 780.
[112] K. Bott, *Chem. Comm.*, 1969, 1350.

is rapidly trapped by sulphuric acid, giving an intermediate sulphate which is the precursor of 1-adamantylacetaldehyde (123) or of 1-methylhomoadamantan-2-one (124), depending on the amount of water present.[113] Although the ketone can be formally envisaged as the product of rearrangement of cation (122) into cation (125), with the subsequent changes indicated, there is evidence that it arises *via* hydrolysis of an intermediate sulphate and that the rearrangement is a synchronous process.[113] Ketone (124) can also be obtained by treatment of 1-adamantylacetylene[112] with sulphuric acid and by solvolysis of the vinyl triflate (126).[114] The final step in all of these routes leading to ketone (124) involves the conversion of one homoadamantane skeleton into another and deuterium-labelling studies have shown that this type of change occurs degenerately with the parent 4-homoadamantyl cation in solvolytic reactions.[108a,109a]



(122)   (123)   (124)   (126)

(125)
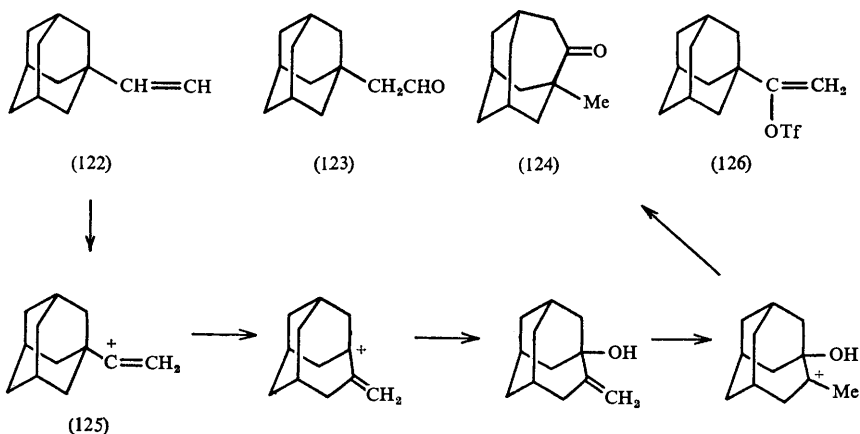
There are now several examples of the adamantane → homoadamantane rearrangement in heterocyclic derivatives. Treatment of *NN*-dichloro-1-amino-adamantane (127) with aluminium chloride generates the 1-adamantyl nitrenium ion (128), which rearranges to the azahomoadamantane system (129).[115] On the other hand, exposure of lactone (130) to 50% sulphuric acid produces keto-alcohol (131).[100] Beckmann rearrangement of adamantanone oxime in phosphoric acid yields the lactam (132);[116] in hydrochloric acid–acetonitrile substantial amounts of the unsaturated nitrile (133) are also formed.[117] There is now general agreement that the nitrile (133) is the reactive intermediate in the Schmidt reaction of adamantanone in methanesulphonic acid, which yields the keto-mesy-

[113] D. R. Kell and F. J. McQuillin, *Chem. Comm.*, 1970, 599.
[114] M. A. Imhoff, R. H. Summerville, P. von R. Schleyer, A. G. Martinez, M. Hanack, T. E. Dueber, and P. J. Stang, *J. Amer. Chem. Soc.*, 1970, **92**, 3802.
[115] P. Kovacic, J. Liu, E. M. Levi, and P. D. Roskos, *J. Amer. Chem. Soc.*, 1971, **93**, 5801.
[116] J. G. Korsloot, V. G. Keizer, and J. L. M. A. Schlatmann, *Rec. Trav. chim.*, 1969, **88**, 447.
[117] J G. Korsloot and U. G. Keizer, *Tetrahedron Letters*, 1969, 3517.

(127)          (128)          (129)



(130)          (131)



(132)          (133)          (134)
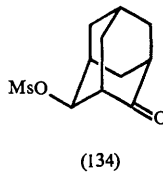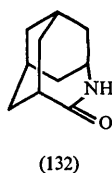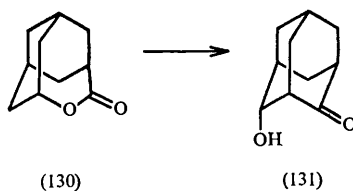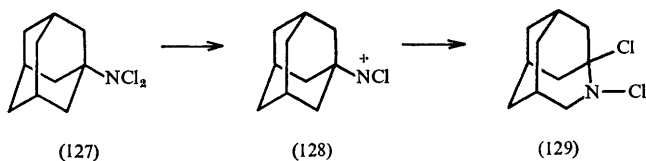
late (134).[100,118,119] Two interesting pyrolytic rearrangements have been discovered At 500 °C 4-homoadamantyl acetate (111) yields 4-methyleneprotoadamantane (135) and 3-vinylnoradamantane (136),[120] and 4-protoadamantene is the major product of pyrolysis of 2-adamantyl mesylate (137).[71] There are two synthetically useful radical rearrangements of adamantane derivatives: on exposure to lead tetra-acetate–iodine 1-adamantanol yields the iodo-ketone (138) which is readily converted by base into 4-protoadamantanone;[121,122] similarly, pyrolysis of 2-methyl-2-adamantyl hypochlorite yields the chloro-ketone (140), which recyclizes to the noradamantane methyl ketone (141).[122]

[118] T. Sasaki, S. Eguchi, and T. Toru, *J. Org. Chem.*, 1970, **35**, 4109.
[119] R. M. Black and G. B. Gill, *J. Chem. Soc.* (*C*), 1970, 671.
[120] B. L. Adams and P. Kovacic, *J.C.S. Chem. Comm.*, 1972, 1310.
[121] W. H. W. Lunn, *J. Chem. Soc.* (*C*), 1970, 2124.
[122] R. M. Black and G. B. Gill, *Chem. Comm.*, 1970, 972.

(135)    +    (136)

(137)

OH    O    I    (138)    O

(139) Me OCl    (140) Cl COMe    (141) COMe