Tetrahedron. Vol. 27, pp. 4317 to 4322. Pergamon Press 1971. Printed in Great Britain

ASPECTS OF THE 2,3-TRIMETHYLENENORBORNANE-ADAMANTANE REARRANGEMENT

SELECTIVE HALOGENATION OF ADAMANTANE AND 1-METHYLADAMANTANE[1]

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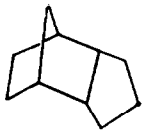
Abstract—Aluminium bromide-catalyzed bromination of either *exo*- or *endo*-2,3-trimethylenenorbornane gives 1,3,6-tribromoadamantane, 1,3,5-tribromoadamantane and 1,2,3,5,6,7-hexabromonaphthalene; intermediate products of the reaction could not be detected. Methods for the selective bridgehead mono- and dichlorination of adamantane and 1-methyladamantane are described. Hydrolysis of 1,3-dichloroadamantane and 5-methyl-1,3-dichloroadamantane with sodium hydroxide at 180° proceeds *via* fragmentation, giving bicyclo[3.3.1]nonane derivatives.

ALTHOUGH several by-products have been isolated and identified and several mechanistic schemes proposed for the aluminium halide-catalyzed rearrangement of *endo*-2,3-trimethylenenorbornane (1) into adamantane,[2,3,4,5] little is known on the experimental side about the intricacies of this reaction beyond the fact that the first step involves the isomerization of **1** into its *exo*-isomer (**2**).[2] The experiments reported in this paper were undertaken initially to explore the possibility of trapping and identifying intermediate products of this rearrangement, and arising from this study we have developed new procedures for the selective chlorination of adamantane and 1-methyladamantane.

The experimental procedure adopted involved the addition of 2,3-trimethylenenorbornane, **1** or **2**, to a solution of $AlBr_3$ in Br_2 at 0°; it was hoped that the rate of rearrangement would be slow at this temperature and that intermediate carbonium ions might be partially trapped through reactions with the solvent. Initial studies revealed that the choice of **1** or **2** made little difference to the outcome of the reaction, consequently, the more readily available isomer **1** was used in the majority of experiments. In a typical experiment the hydrocarbon was added to the Br_2 solution at 0° during 3 hr, and the mixture stirred at 0° for 24 hr, then at room temp. for 24 hr. Work-up as described in the experimental gave three products one of which, easily separated from the others because of its extreme insolubility in cold CCl_4, was assigned the 1,2,3,5,6,7-hexabromonaphthalene structure (**3**) on the following basis. The parent peak in its mass spectrum corresponded to the molecular formula $C_{10}H_2Br_6$ and hydrogenolytic debromination of the compound over Pd afforded naphthalene. The location of the substituents and other structural features of this highly substituted naphthalene derivative were determined by X-ray analysis.[6] Although the isolation of **3** does not illuminate the problem in hand, its mode of formation is interesting. In 1929 Zelinsky and Turova-Pollak[7] reported that *cis*- and *trans*-decalin undergo oxidative bromination with $AlBr_3$ in Br_2, each yielding a hexabromonaphthalene; they did not determine the substitution patterns of the two compounds, but the hexabromide derived from *cis*-decalin is clearly

identical with the 1,2,3,5,6,7-isomer (**3**), m.p. 312°, isolated in the present work. Now the rearrangement of **1** into adamantane also produces small amounts of *trans*-decalin[8], probably *via* the *cis*-isomer as the Russian workers[9] also observed the $AlBr_3$-catalyzed *cis*- to *trans*-decalin isomerization; and under the experimental conditions employed in the present work, oxidative bromination of the *cis*-isomer probably occurs faster than does isomerization.

The remaining two products of the bromination reaction were isolated in 64% yield in the ratio *ca.* 1 : 1, and were easily separated by chromatography over silica gel. The analytical and mass spectrometric data indicated that they were tribromides and direct comparison of one with an authentic sample of 1,3,5-tribromoadamantane (**4**) established its identity.[10] The presence of the adamantane skeleton in the second isomer was



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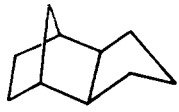

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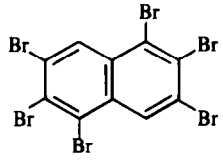

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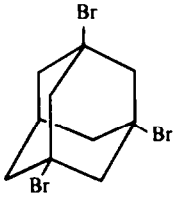

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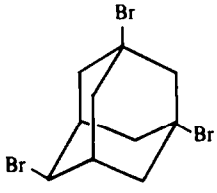

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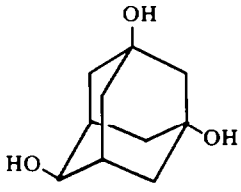

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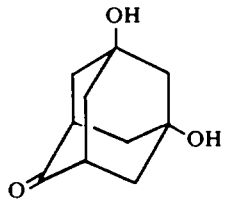

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established by hydrogenolytic debromination over Pd and the one-proton signal in the NMR spectrum of this tribromide at 5·53 τ indicated that one of the Br atoms was attached to a non-bridgehead position. Hydrolysis employing $AgSO_4$ in H_2SO_4 gave a triol, m.p. 310–312°, whose NMR spectrum (DMSO) displayed a doublet at 5·48 τ for the proton of the secondary OH group and two one proton singlets at 5·60 and 5·64 τ for the protons of the tertiary OH groups. Oxidation of the triol with chromic acid in acetone gave a keto-diol which was assigned structure **7** since the NMR spectrum (DMSO) contained a singlet at 5·40 τ for the protons of both tertiary OH groups in addition to a broad two-proton singlet at 7·64 τ attributable to the protons alpha to the carbonyl group. Accordingly, the tribromide and the triol were assigned structures **5** and **6**, respectively.

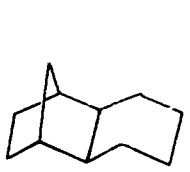
In summary, the $AlBr_3$-catalyzed rearrangement of **1** into adamantane in Br_2 solution proceeds readily at 0° without apparent intermediates inasmuch as glpc analysis of the mixture revealed only starting material and the two tribromides (**4**) and (**5**) at intermediate times. It has recently been suggested[11] that adamantane is so much more stable than all other isomeric C_{10} hydrocarbons that under equilibrium conditions, such as obtain

with $AlBr_3$, the concentration of isomeric structures intermediate between **1** and adamantane will be so low as to be practically undetectable by glpc techniques.

The rearrangement proceeded smoothly though slowly to completion even at −15° (the lower limit due to the mixture freezing) but at this temp. one detail of the process became apparent; namely, the temperature dependence of the relative amounts of **4** and **5** produced. By monitoring the reaction at −15° it was discovered that only the 1,3,6-isomer was present after 4 hr; after 7 hr the 1,3,5-isomer was being produced in trace amounts, but owing to the difficulty in maintaining this temperature for long periods the following procedure was adopted. The starting material was added to the Br_2 solution at −12 to −15° during 3 hr, the mixture was stirred at −12° for 5 to 7 hr, and then at −7° for 48 hr. Work-up gave a mixture of **4** and **5** in the ratio 1 : 2·5 from which pure **5** could be obtained in 39% yield by fractional crystallization from ether–light petroleum.

Although the results of these bromination reactions do not provide anything factual about the mechanism of rearrangement of 2,3-trimethylenenorbornane into adamantane, a number of points of interest arise. Firstly, they give the qualitative impression that Br_2, far from suppressing the rearrangement, has a beneficial effect in that the reaction proceeds readily at or below 0° with relatively little of the harmful side reactions leading to fragmentation that have been encountered at higher temperatures in the absence of a solvent; indeed, the yields of adamantane in brominated form are quite high relative to the yields recorded for rearrangement of **1** by other techniques.[5,12] In this respect, the solubility of the catalyst in Br_2 may be an important factor. Kovacic and Roskos[13] have observed similar beneficial effects in the amination of **1** with $AlCl_3$-trichloramine. Secondly, tribromide **5** provides a direct synthetic entry into the formerly unreported 1,3,6-trisubstituted adamantane series. The fact that **5** is produced in the reaction is interesting because the $AlBr_3$-catalyzed bromination of adamantane is known to yield the 1,3,5-isomer (**4**) exclusively.[10] Hence the reaction leading to **5** must involve bromination of the starting material or of an intermediate in the rearrangement which, however, continues on to the adamantane stage. A separate experiment in which **5** was treated with $AlBr_3$ in Br_2 at room temp. for 24 hr established that **4** was not produced by rearrangement of **5** during the reaction.

The results of these bromination experiments suggested that it might be generally possible and frequently convenient to effect the rearrangement of suitable hydrocarbons into adamantanes with the introduction of functional groups in essentially a single operation. Kovacic and Rostos[13] have used this approach to prepare several aminoadamantanes from tricyclic precursors and trichloramine-$AlCl_3$; it has recently been applied successfully to the functionalization of diamantane directly from tetrahydro-Binor S,[14] and in work with chiral adamantanes[15] when a convenient preparation of 3-methyladamantane-1-carboxylic acid was required we were able to dispense with the isolation and tedious purification of 1-methyladamantane[16] by using the following procedure. A solution of *exo*-2,3-tetramethylenenorbornane (**8**)[17] in CH_2Cl_2 containing $AlCl_3$ was refluxed while monitoring by glpc. After 15 min. the mixture contained about equal amounts of 1- and 2-methyladamantane, **9** and **10**, but after 2 hr the 1-Me compound was the preponderant isomer (~98%). The mixture was cooled to 0° and AcCl and $AlCl_3$ added. Distillation of the crude product gave 3-methyl-1-chloroadamantane (**11**) in high yield. Carboxylation of **11** using the Koch–Haaf procedure gave the acid (**12**). Adaption of the rearrangement-functionalization procedure to the introduction of two Cl substituents was unexpectedly easy: if instead of AcCl paraformaldehyde and additional $AlCl_3$



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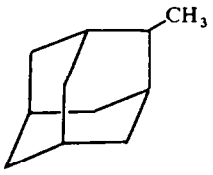

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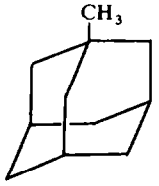

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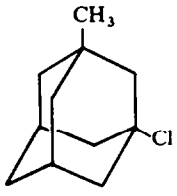

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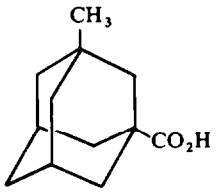

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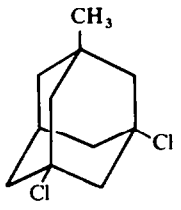

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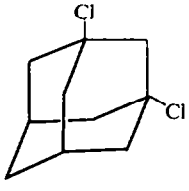

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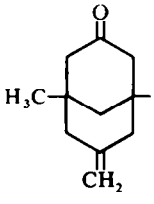

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were added to the CH_2Cl_2 solution, the product obtained in 74% yield was 5-methyl-1,3-dichloroadamantane (**13**), m.p. 45–46°. Application of the dichlorination procedure to adamantane itself gave 1,3-dichloroadamantane (**14**) in high yield. Dichlorides (**13**) and (**14**) are useful synthetic intermediates for 3,7-difunctionalized bicyclo[3.3.1]nonanes since on treatment with NaOH in aqueous THF at 180° they underwent fragmentation, yielding the olefinic-ketones **15**[15] and **16**[18,19] respectively.

EXPERIMENTAL

M.ps were determined in sealed capillary tubes. IR spectral data relate to KBr discs. NMR spectra were measured at 100 MHz with TMS as internal standard. Mass spectrometric data were obtained with an A.E.I. MS 902 spectrometer, with an ionizing beam of 70 e.v. Light petroleum had b.p. 40–60°. The drying agent employed was $MgSO_4$. Glpc refers to analysis on a 2 m column packed with Versamid 930 on Chromosorb W (5% w/w).

Bromination of endo-2,3-*trimethylenenorbornane* (**1**). (a) The hydrocarbon (5 g) was added to a stirred solution of $AlBr_3$ (10 g) in Br_2 (50 ml) at 0° during 3 hr; the mixture was stirred at 0° for 24 hr, and then at room temp. for 24 hr, after which it was poured onto ice and CCl_4 added with stirring. Aqueous sodium disulphite was added and the mixture filtered, yielding 1,2,3,5,6,7-*hexabromonaphthalene* (6·4 g, 29%), m.p. 312° (from toluene) (lit.,[7] m.p. 312°), *m/e* (M^+) 602.

The organic layer of filtrate and $CHCl_3$ extracts (2 × 50 ml) of the aqueous layer were combined and

washed with H_2O, dried and concentrated, yielding a mixture of tribromides (9·4 g, 64%). Glpc analysis at 220° showed two components in the ratio *ca.* 1 : 1. The product in light petroleum was placed on a column of silica gel. Elution with light petroleum gave a crystalline solid which on recrystallization from EtOH afforded 1,3,5-*tribromoadamantane* (3·1 g, 23%), m.p. 122–126° (lit.,[10] m.p. 126–127°). Further elution with light petroleum-$CHCl_3$ (4 : 1) gave the second component, recrystallization from EtOH gave 1,3,6-*tribromoadamantane* (3·4 g, 24%), m.p. 169–170°, (Found: C, 32·38; H, 3·69; Br, 64·30, *m/e* (M^+) 373·85200. $C_{10}H_{13}Br_3$ requires: C, 32·18; H, 3·48; Br, 64·34%, *m/e* (M^+) 373·85195), τ ($CDCl_3$) 5·53 (1H, m, >CHBr), 7·15 (2H, s, C—3) and 7·00–7·95 (1OH, M, remaining adamantyl).

(b) The hydrocarbon (10 g) was added to a stirred solution of $AlBr_3$ (20 g) in Br_2 (90 ml) at −12° to −15° over 4 hr; the mixture was stirred at −12° for 5 hr and then at −7° for 48 hr. Work-up as described under (a) gave the hexabromide (16·6 g) and a 1 : 2·5 mixture of tribromides **4** and **5**. Fractional crystallization from EtOH gave the 1,3,6-isomer (**5**) (10·6 g, 39%) of 97–98% purity, m.p. 168–170°.

Hydrogenolysis of 1,2,3,5,6,7-*hexabromonaphthalene* (**3**). A mixture of the hexabromide (1 g), KOH (2·5 g) and 5% Pd/C (0·5 g) in MeOH (100 ml) was exposed to H_2 at atmospheric pressure. When H_2 uptake had ceased the solution was filtered and the filtrate diluted with Et_2O (100 ml), washed with H_2O and dried. Removal of solvent yielded white solid (0·23 g). Sublimation at 50° yielded naphthalene, m.p. 78–80° (lit.,[21] m.p. 80·3°). A m.m.p. showed no depression.

Hydrogenolysis of 1,3,6-*tribromoadamantane* (**5**). Hydrogenolysis of the tribromide, exactly as described above for hexabromonaphthalene, gave adamantane, identified by comparison (m.p. and IR) with an authentic sample.

1,3,6-*Trihydroxyadamantane* (**6**). A mixture of 1,3,6-tribromoadamantane (18 g), $AgSO_4$ (36 g), 98% H_2SO_4 (108 ml) and H_2O (36 ml) was stirred at 100° for 3 hr. The cooled mixture was neutralized with KOH and was evaporated to dryness *in vacuo*. Continuous extraction of the residue with hot EtOH for 24 hr followed by concentration of the extract gave a solid. Two crystallizations from dioxan and one from MeOH gave the *triol* (2·2 g, 25%), m.p. 310–312°, τ (CD_3SOCD_3) 5·48 (1H, d, C-6 OH), 5·60 (1H, s, OH), 5·64 (1H, s, OH) and 7·96–8·90 (12H, remaining adamantyl). Satisfactory analytical data were not obtained.

1,3-*Dihydroxyadamantan*-6-*one* (**7**). The triol (1 g) in acetone (50 ml) was treated dropwise with 8N chromic acid until the first permanent red colour appeared. The mixture was stirred overnight and then treated with anhyd. K_2CO_3. The solids were removed by filtration and the filtrate concentrated. Sublimation of the residue at 180°/2 mm yielded the *dihydroxy-ketone* (0·6 g, 61%), m.p. > 350° (from CCl_4) (Found: C, 65·80; H, 3·94 $C_{10}H_{14}O_3$ requires: C, 65·94; H, 8·79%), τ (CD_3SOCD_3) 5·40 (2H, s, OH's), 7·64 (2H, broad s, C-5 and C-7), 8·14 (2H, s, C-2) and 8·5 (8H, d, remaining adamantyl), ν_{max} 3350, 1715 and 1725 cm^{-1}.

Rearrangement of exo-2,3-*tetramethylenenorbornane* (**8**).[17] (a) A mixture of $AlCl_3$ (10 g) and the hydrocarbon (2 g) in CH_2Cl_2 (50 ml) was refluxed with moisture excluded while monitoring by glpc at 120° samples withdrawn at 5 min intervals. After 2 hr the product was found to be > 98% 1-methyladamantane by glpc co-injection.

(b) The reaction was repeated using the hydrocarbon (5 g), $AlCl_3$ (25 g) and CH_2Cl_2 (125 ml. After 30 min the mixture was poured onto ice and the organic layer and CH_2Cl_2 extracts (2 × 50 ml) of the aqueous layer were combined and washed with sat. $NaHCO_3$ aq. and dried. Removal of solvent gave a solid (5·1 g) shown by glpc at 120° to contain 1-methyladamantane (50%), 2-methyladamantane (40%) and starting material (10%). A sample of 2-methyladamantane isolated by prep. glpc had m.p. 143–145° (lit.,[22] m.p. 144–146°).

3-*Methyl*-1-*chloroadamantane* (**11**). A mixture of **8** (15 g), $AlCl_3$ (15 g) and CH_2Cl_2 (75 ml) was heated under reflux for 2 hr, and then cooled to 0°. AcCl (9 g) and $AlCl_3$ (12 g) were added and the mixture stirred at 0° for 8 hr, poured onto ice and the organic layer and CH_2Cl_2 extracts (3 × 100 ml) of the aqueous layer combined and washed with sat. $NaHCO_3$ aq. dried and concentrated. Distillation of the residue gave the *chloride* (15·5 g, 84%) b.p. 90–91°/3 mm, m.p. 39–41° (lit.,[23] m.p. 36–38°).

3-*Methyl*-1-*adamantanecarboxylic acid* (**12**). 98% Formic acid (8·5 ml) and a solution of the chloride (**11**) (4·5 g) in CCl_4 (8·5 ml) were added simultaneously with stirring to 98% H_2SO_4 (120 ml) at 4°. The mixture attained room temperature in 2 hr and then poured onto ice. The organic layer and $CHCl_3$ extracts (3 × 40 ml) of the aqueous layer were combined and shaken with 2N NaOH (3 × 30 ml). The alkaline solution was made strongly acidic by the addition of 2N H_2SO_4, and the precipitated product collected. Crystallization from MeOH–H_2O gave the *acid* (3·6 g), 76%), m.p. 96–97° (lit.,[24] m.p. 96–98°).

5-*Methyl*-1,3-*dichloroadamantane* (**13**). A mixture of *exo*-tetramethylene norbornane (5 g), $AlCl_3$ (8 g) and CH_2Cl_2 (50 ml) was heated under reflux for 2 hr and then cooled to 0°. Paraformaldehyde (5 g) was added over 20 min with stirring and after 1 hr at 0° $AlCl_3$ (8 g) and more paraformaldehyde (5 g) were

added. The mixture was stirred at 0° for 3 hr and then poured onto ice. The organic layer and CH_2Cl_2 extracts (2 × 50 ml) of the aqueous layer were washed with sat. $NaHCO_3$ aq. dried and concentrated. The solid residue was sublimed at 50°/0·4 mm, yielding the *dichloride* (5·4 g, 74%), m.p. 45–46° (from EtOH) (Found: C, 60·50; H, 7·59; Cl, 32·61 $C_{11}H_{16}Cl_2$ requires: C, 60·29; H, 7·36; Cl, 32·55%), τ ($CDCl_3$) 7·57 (2H, s, C-2) 7·64 (1H, m, C-7), 7·99–8·59 (10H, m, remaining adamantyl) and 9·00 (3H, s, Me); *m/e* (M^+) 220 and 218.

1-*Methyl*-3-*methylenebicyclo*[3.3.1]*nonan*-7-*one* (**15**). A solution of 5-methyl-1,3-dichloroadamantane (10 g) and 1N NaOH (300 ml) in dioxan (300 ml) was heated in a stainless steel autoclave at 180° for 70 hr. The cooled solution was diluted with H_2O (250 ml) and the mixture extracted with Et_2O (5 × 100 ml). The ethereal extracts were washed with H_2O (4 × 200 ml) and dried. Removal of solvent gave starting material and product. The mixture was placed on a column of alumina. Elution with light petroleum-ether (3 : 1) gave starting material. Further elution with light petroleum-ether (1 : 1) gave the *keto-olefin* (5 g, 67%) as a liquid of *ca.* 98% purity, identical IR and retention time on glpc) with an authentic sample.[15]

1-3-*Dichloroadamantane* (**14**). Paraformaldehyde (5 g) was added during 20 min to a stirred mixture of adamantane (5 g) and $AlCl_3$ (10 g) in CH_2Cl_2 (30 ml) at 0°. After 1 hr the mixture was allowed to come to room temp. and additional $AlCl_3$ (10 g) and paraformaldehyde (5 g) added. The mixture was stirred for 3 hr and then was poured onto ice. Work-up as described above for 5-methyl-1,3-dichloroadamantane yielded a solid. Sublimation at 100°/4 mm gave the *dichloride* (7·6 g, 90%) of *ca.* 90% purity. Recrystallization from EtOH afforded colourless crystals, m.p. 129–130° (lit.,[25] m.p. 129–130°).

3-*Methylenebicyclo*[3.3.1]*nonan*-7-*one* (**16**). A solution of 1,3-dichloroadamantane (20 g) and 1N NaOH (600 ml) in dioxan (600 ml) was heated in a stainless steel autoclave at 180° for 70 hr. Work-up exactly as described for compound **15** gave the *keto-olefin* (8·1 g, 55%), m.p. 160–163° (lit.,[18] m.p. 162–163°).

REFERENCES

[1] M. A. McKervey, *Am. Chem. Soc., Div. Petrol. Chem. Prepr.* **15**, B37 (1970); M. A. McKervey, D. Grant and H. Hamill, *Tetrahedron Letters* 1975 (1970)

[2] P. von R. Schleyer and M. M. Donaldson, *J. Am. Chem. Soc.* **82**, 4645 (1960)

[3] H. W. Whitlock, Jr., and M. W. Siefken, *Ibid.* **90**, 4929 (1968)

[4] A. Schneider, R. W. Warren and E. J. Janoski, *Trans. New York Academy of Sciences* **30**, 3 (1967)

[5] R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.* **64**, 277 (1964)

[6] We are indebted to Professor G. Ferguson, University of Guelph, Ontario, Canada, for this analysis; the full details will be published elsewhere

[7] N. D. Zelinsky and M. B. Turova-Pollak, *Ber. Dtsch. Chem. Ges.* **62**, 1658 (1929)

[8] H. Koch and J. Franken, *Brennstoff-Chem.* **42**, 90 (1961); *Chem. Abstr.* **55**, 21059 i (1961)

[9] N. D. Zelinsky and M. B. Turova-Pollak, *Ber. Dtsch. Chem. Ges.* **58**, 1292 (1925)

[10] H. Stetter and C. Wulff, *Chem. Ber.* **93**, 1366 (1960)

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

[12] See however D. W. Johnston, M. A. McKervey and J. J. Rooney, *J. Am. Chem. Soc.* **93**, 2798 (1971)

[13] P. Kovacic and P. D. Roskos, *Ibid.* **91**, 6457 (1969)

[14] D. Faulkner, R. A. Glendinning, D. E. Johnston and M. A. McKervey, *Tetrahedron Letters* 1671 (1971)

[15] H. Hamill and M. A. McKervey, *Chem. Comm.* 864 (1969)

[16] P. von R. Schleyer and R. D. Nicholas, *Tetrahedron Letters* **9**, 305 (1961)

[17] K. Alder, J. Mönch and H. Wirtz, *Liebigs Ann.* **627**, 47 (1959)

[18] H. Stetter and P. Tacke, *Chem. Ber.* **96**, 694 (1963)

[19] The fragmentation of 1,3-dibromoadamantane yielding (16) has been described, A. R. Gagneux and R. Meier, *Tetrahedron Letters* 1365 (1969). However, difficulties have been encountered with the preparation of the dibromide,[20] and of the two, the dichloride is now the more accessible.

[20] E. R. Talaty, A. E. Cancienne, Jr., and A. F. Depuy, Jr., *J. Chem. Soc.* (C), 1902 (1968)

[21] *Tables for Identification of Organic Compounds,* (2nd Edition) p. 15. The Chemical Rubber Co., Cleveland, (1964)

[22] P. von R. Schleyer and R. D. Nicholas, *J. Am. Chem. Soc.* **83**, 182 (1961)

[23] H. Stetter and J. Gärtner, *Chem. Ber.* **99**, 925 (1966)

[24] H. Koch and J. Franken, *Ibid.* **96**, 213 (1963)

[25] H. Stetter, M. Krause and W. D. Last, *Ibid.* **102**, 3357 (1969)