# Adamantane Rearrangements. The Isomerization of Dihydrocedrene to 1-Ethyl-3,5,7-trimethyladamantane

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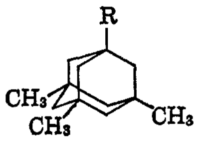
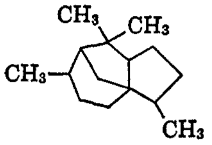
From the time of Friedel[3] it has been known that alkanes undergo extensive changes in the presence of aluminum chloride and similar catalysts.[4] Aschan[5] demonstrated that cyclohexane could be isomerized, in part, to methylcyclopentane. Through the work of Zelinsky and Turova-Pollak,[6] Linstead,[7] and others[4] with condensed bicyclic molecules the potentialities of this reaction became generally known. The number of compounds which subsequently have been rearranged is impressive.[4]

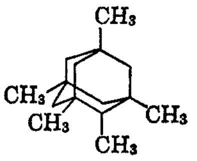
A recent extension of this procedure has been the preparation of a class of compounds possessing basic diamond-like skeletons. Every tricyclic saturated hydrocarbon of ten or more carbon atoms carefully investigated thus far has isomerized to adamantane or to an adamantane homolog when treated with strong Lewis acid catalyst.[8,9] $C_{10}H_{16}$ tricyclics give adamantane,[8] $C_{11}H_{18}$ precursors give 1-methyladamantane, and 1,3-dimethyladamantane is formed from $C_{12}H_{20}$ tricyclanes.[8,9] Perhydrofluorene ($C_{13}H_{22}$) and both perhydroanthracene and perhydrophenanthrene ($C_{14}H_{24}$) undergo a series of transformations with an especially active $AlBr_3$–sludge catalyst system to give end products of greatest thermodynamic stability: 1,3,5-trimethyladamantane (I, R = H) and 1,3,5,7-tetramethyladamantane (I, R = $CH_3$), respectively.[9]



I



II



III

In view of the consistent success of these diamondoid isomerizations,[10] we were intrigued by the possibility that some previous investigator working with a tricycloalkane might have, unwittingly, achieved an adamantane rearrangement. We demonstrate here that this was undoubtedly the case.

In 1938, Prokopets and Boguslavskaya reported the interconversion of isomers of perhydroanthracene and perhydrophenanthrene with $AlCl_3$ at 100°.[11] In view of the results of Schneider's group with these same compounds,[9] it is quite possible that alkyladamantanes were among the products of these reactions,[11] but were undetected. Gas chromatography and other modern methods which facilitate the examination of complex mixtures had, after all, not yet been developed. However, it is not certain that alkyladamantanes were actually obtained by the Russian workers.[11] $AlCl_3$ is often a much less effective catalyst than that employed by Schneider, Warren, and Janoski[9] for these rearrangements. $AlCl_3$ is also variable in its activity depending on its purity and history,[4] and the product mixtures were necessarily too poorly characterized by Prokopets and Boguslavskaya[11] to enable their work to be repeated precisely.

In 1943, Naves, Papazian, and Perrottet[12] reported that the sesquiterpene derivative, dihydrocedrene (II), could be converted to an "isodihydrocedrene" in high yield by the action of $AlCl_3$ for 48 hr at room temperature. At that time the detailed structure of cedrene itself was not known,[13] but its tricyclic nature had been rather firmly established. No structure for "isodihydrocedrene" was proposed, but the product, a liquid, was rather well characterized by its physical properties.[12] We have repeated this reaction, and have monitored its course by gas chromatography. Conversion of dihydrocedrene (II) to a new isomer is remarkably smooth. After 48 hr at room temperature, at the reported conditions,[12] conversion to the new substance is 75%. An additional day at 50° sufficed to complete the reaction, and over 90% yield of a compound, essentially pure, was obtained. It seems likely in view of the ease of this rearrangement that Naves, *et al.*,[12] also had this substance in hand, possibly as the major component of a mixture.

We suspected on thermodynamic grounds[9b,14] that the new isomer was 1-ethyl-3,5,7-trimethyladamantane (I, R = $C_2H_5$), which should be the most stable $C_{15}H_{26}$ tricyclic hydrocarbon.[14] (Other possibilities, such as 1,2,3,5,7-pentamethyladamantane (III) suffer from a plethora of skew butane and axial cyclohexane interactions.) Our structural prediction was quickly verified by the spectral properties of the rearrangement product (see Experimental Section), and the assignment was confirmed by synthesis (Chart I). Since cedrene is readily available and it can easily be hydrogenated, 1-ethyl-3,5,7-trimethyladamantane can now be added to the list of easily obtainable adamantanoid com-

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(2) Investigation, 1963–1964; Ph.D. Thesis, Princeton University, 1965.

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CHART I

$$\begin{tikzcd}
\mathrm{I\ (R = H)}^{9a} \arrow[r, "\mathrm{Br_2}", "(68\%)"'] & \mathrm{I\ (R = Br)}^{a} \arrow[rr, "\mathrm{CH_2{=}CHBr}", "{\mathrm{AlBr_3},\ -60^\circ\ (40\%)}"'] & & \mathrm{I\ (R = CH_2CHBr_2)} \arrow[d, "{\mathrm{NaOH},\ \mathrm{(HOCH_2CH_2)_2O}^{b}}", "(95\%)"'] \\
\mathrm{II} \arrow[rr, "\mathrm{AlCl_3}", "(92.5\%)"'] & & \mathrm{I\ (R = C_2H_5)} & \mathrm{I\ (R = C{\equiv}CH)} \arrow[l, "\mathrm{H_2}"', "(79\%)"]
\end{tikzcd}$$

[a] H. Koch and J. Franken, *Ber.*, **96**, 213 (1963). [b] Following H. Stetter and P. Goebel, *ibid.*, **95**, 1039 (1962).

pounds.[8,9,15] Other tricyclic sesquiterpenes besides cedrene will likely serve as well as starting materials for the preparation of I (R = $C_2H_5$).

## Experimental Section

**Rearrangement of Dihydrocedrene (II) to 1-Ethyl-3,5,7-trimethyladamantane (I, R = $C_2H_5$).**—Cedrene, $[\alpha]^{22}\mathrm{D}$ −84.6° ($CCl_4$) (Aldrich Chemical Co.), was hydrogenated in acetic acid solution with $PtO_2$ to give dihydrocedrene (II), $[\alpha]^{22}\mathrm{D}$ −6.2°.[12] The product showed only one peak on gas chromatography, using a 300-ft capillary column coated with SE-30. To 37 g of II, 18.5 g of powdered $AlCl_3$ was added, and the mixture stirred at room temperature. After 48 hr, gas chromatography showed that the starting material had completely disappeared and five new components had formed. One of these comprised *ca.* 75% of the mixture. The rearrangement was continued for an additional 24 hr at 50°. Analysis now showed that the major component was present in *ca.* a 25-fold excess over a single, second compound. The liquid was decanted from the catalyst and the latter was washed with several portions of petroleum ether (bp 30–60°). The combined organic material was washed with water and then with sodium bicarbonate solution, and dried over anhydrous magnesium sulfate. Distillation yielded 34.2 g (92.5%) of material, homogeneous to gas chromatography, with bp 108.5–110.5° at 12 mm, $n^{21}\mathrm{D}$ 1.4841, $[\alpha]^{22}\mathrm{D}$ −0.03° (neat). Naves, *et al.*,[12] starting with "artificial" cedrene, $[\alpha]\mathrm{D}$ −86.3°, prepared dihydrocedrene, $[\alpha]\mathrm{D}$ −6.2°, and rearranged this to "isodihydrocedrene," bp 90–92° at 1.6 mm, $n^{20}\mathrm{D}$ 1.4831, $[\alpha]\mathrm{D}$ −0.52°. The small, residual optical rotations are probably due to optically active impurities.

*Anal.* Calcd for $C_{15}H_{24}$: C, 87.38; H, 12.62. Found: C, 87.65; H, 12.60.

The structure of the compound was established by analysis of the mass and nmr spectra, in comparison with the behavior of polyalkyladamantanes of known composition. The base peak in the mass spectrum at *m/e* 177 represented loss of the ethyl group. A peak at *m/e* 191 (loss of methyl) was also prominent (16% of base). The parent peak itself at *m/e* 206 was only present in 0.5% abundance. Other peaks with greater than 10% abundance were at *m/e* 121 (45%), 107 (20%), 55 (16%), and 41 (27%). The base peaks of 1-alkyladamantanes are also those formed by loss of the substituent, ethyl groups being lost more readily than methyl.[16] 1-Ethyl-3-methyladamantane and 1-ethyl-3,5-dimethyladamantane gave mass spectral peaks representing parent, loss of methyl, and loss of ethyl in the ratio 3:1:30 for the former compound, and 1:1:10 for the latter.[9a] The similar ratios found here for I (R = $C_2H_5$) were 0.03:1:6.3 and for 1-ethyl-3,5-dimethyladamantane were 0.12:1:17.5 under similar instrumental conditions.

The nmr spectrum of I (R = $C_2H_5$) would be expected to be similar to the two-peak spectrum of tetramethyladamantane, I (R = $CH_3$), which has methyl resonances at $\tau$ 9.20 and methylene resonances at $\tau$ 8.99.[17] The two major nmr peaks of I (R = $C_2H_5$) had almost the same chemical shifts ($\tau$ 8.99 and 9.19), but, as anticipated, the area of the methylene proton peak was greater. The ethyl group appeared as a rather diffuse multiplet; this feature was also expected, since ethyladamantane derivatives showed $A_2B_3$ and not simple $A_2X_3$ patterns.[9]

**1-Bromo-3,5,7-trimethyladamantane (I, R = Br).**—1,3,5-Trimethyladamantane I (R = H) was brominated after the literature procedure.[18a] From 7.5 g of I (R = H) 7.9 g (68%) of I (R = Br), mp 100.5–101.5°, was obtained: lit.[18a] mp 101–102°.

**1-(2′,2′-Dibromoethyl)-3,5,7-trimethyladamantane (I, R = $CH_2CHBr_2$).**—The procedure used was based on similar reactions described for adamantyl bromide.[18b] I (R = Br), 7.0 g, in 15 ml of vinyl bromide was cooled to −60° in a Dry Ice–acetone bath. A total of 3.0 g of aluminum bromide was added carefully. After 3 hr the suspension was poured intoa beaker containing 30 ml of ether and 30 ml of water. The organic layer was separated and the aqueous layer extracted with several portions of ether. The combined ether layers were washed with water, saturated sodium carbonate, and water, and dried over calcium chloride. Distillation yielded 4.0 g (40%) of I (R = $CH_2CHBr_2$), bp 130–135° at 0.5 mm.

*Anal.* Calcd for $C_{15}H_{24}Br_2$: C, 49.45; H, 6.59; Br, 43.96. Found: C, 49.71; H, 6.68; Br, 43.52.

The nmr showed a triplet centered at $\tau$ 4.20 (-C*H*$Br_2$), a doublet at $\tau$ 7.46 (side chain $CH_2$), two singlets at $\tau$ 8.80 and $\tau$ 8.94 for the two types of ring $CH_2$ groups, and a singlet at $\tau$ 9.17 for the methyl groups. The peak area ratios were 1:2:6:6:9, as expected for I (R = $CH_2CHBr_2$).

**1-Ethynyl-3,5,7-trimethyladamantane (I, R = HC≡C).**—The dehydrohalogenation of 3.0 g of I (R = $CH_2CHBr_2$) was carried out in a refluxing solution of 3 g of sodium hydroxide in 15 ml of diethylene glycol.[18b] After 12-hr reaction time, 30 ml of water was added and the organic material was extracted with petroleum ether. The organic material was washed twice with water and dried over calcium chloride. Distillation gave 1.6 g of I (R = HC≡C), bp *ca.* 90–29° at 10 mm. The nmr spectrum showed a singlet ethynyl resonance at $\tau$ 8.11, two $CH_2$ singlets at $\tau$ 8.56 and $\tau$ 8.94, and a methyl singlet at $\tau$ 9.17. The area ratio was 1:6:6:9. An infrared spectrum of the compound showed strong ≡C—H absorption at 3307 $cm^{-1}$ and a -C≡C- peak of moderate intensity at 2100 $cm^{-1}$. This was hydrogenated directly.

**1-Ethyl-3,5,7-trimethyladamantane (I, R = $C_2H_5$).**—Using palladium on charcoal as catalyst, 1.5 g of I (R = HC≡C) was hydrogenated for 8 hr in ether solvent. After filtration of the catalyst, distillation gave 1.2 g (79%) of I (R = $C_2H_5$), bp *ca.* 94–95° at 10 mm. A careful comparison established the identity of this material with that prepared from II by rearrangement. Both materials had identical infrared and nmr spectra, and both eluted on the capillary gas chromatograph with the same retention time, singly or when mixed together.

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(15) A methyl-substituted perhydroanthracene has also been shown to rearrange to 1-ethyl-3,5,7-trimethyladamantane.[9b]

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(17) R. C. Fort, Jr., and P. von R. Schleyer, *J. Org. Chem.*, **30**, 789 (1965).

(18) See Chart I: (a) ref *a*; (b) ref *b*.

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## Steroids. V. 2β-Carboxy-A-norcholestane[1]

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The subject of this Note is the synthesis of 2β-carboxy-A-norcholestane (5) and several of its transformation products, and the presentation of evidence in support of the stereochemistry of acid **5**.

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(1) Part IV of this series: M. P. Cava and B. R. Vogt, *J. Org. Chem.*, **30**, 3775 (1965).

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