The Proton Magnetic Resonance Spectra of Adamantane and Its Derivatives[1]

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The proton magnetic resonance (p.m.r.) spectra of some 50 adamantane derivatives have been obtained at 60 Mc. and assignments of the resonances have been made. P.m.r. is shown to be a quick and effective method for the identification of adamantanes. The value of the vicinal coupling constant, 2.6 c.p.s., is reasonably consistent with the value calculated from the original Karplus equation. Chemical shifts for polysubstituted derivatives may be predicted with considerable accuracy by means of an additivity relationship based on the shifts of monosubstituted compounds.

Although adamantane has been known for 30 years, and numerous derivatives have been prepared,[4] no comprehensive study of the spectral properties of these substances has been reported. The only detailed investigation in the literature is that of Mecke and Spiesecke,[5] who analyzed the infrared spectrum of adamantane itself. Landa has suggested that a band in the infrared at 1017–1038 cm.$^{-1}$ is characteristic of adamantane compounds.[6] However, this band is absent in the infrared spectrum of adamantane itself and some of its simple derivatives, and in others it is so weak as to be of little diagnostic value.[4]

The p.m.r. spectra of but a few adamantane compounds have been reported[7–11] and some of the early investigations, carried out at 40 Mc., gave spectra crude by present standards. We have examined the spectra of nearly 50 adamantane derivatives, of a variety of substitution patterns, with a Varian A-60 instrument. P.m.r. spectroscopy is demonstrated here to be a simple and reliable method for the structural elucidation of these substances. Furthermore, the spectra of 1-substituted adamantanes are of interest in a more general sense, in that the observed chemical shifts and coupling constants are of theoretical importance.

Results

Adamantane.—The p.m.r. spectrum of adamantane in CCl_4 solution (Figure 1) shows a doublet at τ 8.22, with spacing of 1.7 c.p.s. A barely visible shoulder on the low field side of this peak (at about τ 8.12) is probably attributable to the bridgehead hydrogens, which, fortuitously, have nearly the same chemical shift as the methylene protons. In such cases of coincidence, a change of solvent can often induce selective shifts of the resonance positions of protons in different parts of a molecule, thus permitting details obscured under normal conditions to be revealed.[12] Adamantane, a nonpolar molecule, does not respond to such changes of solvent. Spectra taken in benzene, pyridine, and nitrobenzene show little change in appearance or in chemical shift.

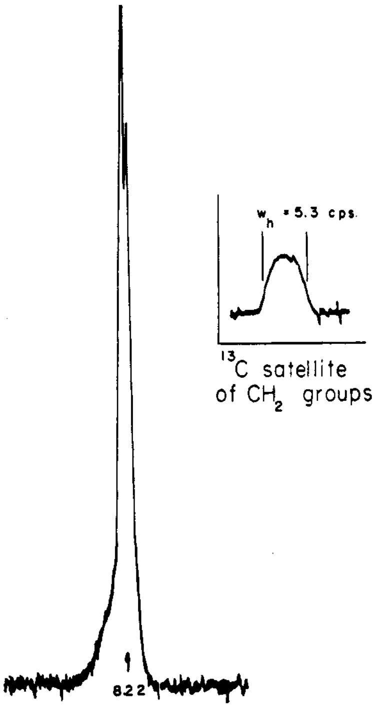

Figure 1.—The p.m.r. spectrum of adamantane.

Examination of the resonances due to ^1H coupling with ^{13}C in natural abundance,[13] with the aid of a time averaging device (CAT),[14] allows an estimate of J_{vic} between the bridgehead and methylene protons. The ^{13}CH resonances (from the CH_2 groups) are broad singlets, $w_h = 5.3$ c.p.s., $J_{^{13}CH} = 120 \pm 1$ c.p.s. A unique J_{vic} cannot be obtained, but clearly, $J_{vic} \leq 5.3/2 = 2.65$ c.p.s.

1-Substituted Adamantanes.—Tables I and III list the chemical shifts and coupling constants for a number of 1-substituted adamantanes. Figure 2 illustrates the spectrum of a typical compound, 1-methyladamantane. The resonances of the protons β, γ, and δ to the substituent are usually well separated, and assignments can readily be made from the chemical shifts, integrated intensities, and peak widths. The three bridgehead protons (γ) give a peak of half the area of those from

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(1) Taken from the Ph.D. Thesis of R.C.F., Princeton University, 1964.

(2) National Science Foundation Predoctoral Fellow, 1963–1964; Allied Chemical Corporation Fellow, 1962–1963.

(3) Alfred P. Sloan Foundation Research Fellow, 1962–1966; J. S. Guggenheim Fellow, 1964–1965; Fulbright Research Fellow, 1964–1965.

(4) For a review, see R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

(5) R. Mecke and R. Spiesecke, *Ber.*, **88**, 1997 (1955).

(6) S. Landa and S. Hala, *Collection Czech. Chem. Commun.*, **24**, 93 (1955).

(7) G. V. D. Tiers, quoted by H. Conroy, *Advan. Org. Chem.*, **2**, 287 (1960).

(8) H. Stetter, M. Schwarz, and A. Hirschorn, *Ber.*, **92**, 1629 (1959).

(9) Dr. G. V. D. Tiers very kindly obtained and interpreted the p.m.r. spectra of a number of adamantane derivatives prepared in an earlier investigation. See R. D. Nicholas, Ph.D. Thesis, Princeton University, 1960; *Dissertation Abstr.*, **22**, 430 (1961); P. von R. Schleyer and R. D. Nicholas, *J. Am. Chem. Soc.*, **83**, 182, 2700 (1961).

(10) H. F. Reinhardt, *J. Org. Chem.*, **27**, 3258 (1962).

(11) K. Gerzon, E. V. Krumkalns, R. L. Brindle, F. J. Marshall, and M. A. Root, *J. Med. Chem.*, **6**, 760 (1963).

(12) *Cf.*, *e.g.*, G. Slomp and F. MacKellar, *J. Am. Chem. Soc.*, **82**, 999 (1960); P. Laszlo and P. von R. Schleyer, *ibid.*, **86**, 1171 (1964).

(13) P. Laszlo, *Sciences*, No. 26, 58 (1963).

(14) L. C. Allen and L. F. Johnson, *J. Am. Chem. Soc.*, **85**, 2668 (1963); P. Laszlo and P. von R. Schleyer, *ibid.*, **85**, 2017 (1963).

TABLE I

CHEMICAL SHIFTS IN 1-SUBSTITUTED ADAMANTANES[a] (τ)

Substituent X	β-H	γ-H	δ-H	Other features
F	8.17	7.80	8.38	
Cl	7.89[b]	7.89[b]	8.30	
Br	7.70	7.92	8.27	
I	7.37	8.03	8.14	
NH_2	8.45	7.96	8.38	NH_2, 9.05
$NHCOCH_3$	7.95[b]	7.95[b]	8.31	NH, 3.57; CH_3, 8.16
OH	8.36[b]	7.88	8.36[b]	OH, 8.0–8.7
OCH_2CH_2OH	8.33	7.85	8.26	CH_2, *ca.* 7.42
$OCOC_6H_4NO_2$-*p*	7.73[b]	7.73[b]	8.23	Ar, 1.81[c]
CH_3	8.52	8.08	8.32	CH_3, 9.21
C_2H_5	8.50	8.00	8.26	CH_3, 9.21; CH_2, 8.98
$(CH_3)_2CH$	8.48	8.00	8.31	CH_3, 9.20; CH, *ca.* 8.9
CH_2OH	8.50	8.01	8.29	CH_2, 6.89
CH_2OCOCH_3	8.46	8.01	8.29	CH_2, 6.37; CH_3, 8.00
$CH_2OSO_2C_6H_4CH_3$-*p*	8.48	8.01	8.29	CH_2, 6.50; Ar, 2.46[c]
$CH_2OSO_2C_6H_4NO_2$-*p*	8.49	8.00	8.29	CH_2, 6.38; Ar, 1.72[c]
CH_2Cl	8.40	7.96	8.29	CH_2, 6.80
$CH(OH)C_6H_5$	8.4–8.5[b]	8.1	8.4–8.5[b]	CH, 5.90; Ar, 2.78
$C(CH_3)_2OH$	8.46[b]	8.17	8.46[b]	CH_3, 9.00
$C(CH_3)_2Br$	8.41	8.13	8.31	CH_3, 8.35
$C(CH_3)=CH_2$	8.4–8.5[b]	8.17	8.4–8.5[b]	CH_3, 8.4–8.5; $=CH_2$, 5.69
CH_2CH_2Br	8.54	8.17	8.40	CH_2Br, 6.85; Ad–CH_2, *ca.* 8.2
C_6H_5	8.10	7.96	8.25	Ar, 2.89
p-$C_6H_4OCH_3$	8.15	7.96	8.23	OCH_3, 6.33; Ar, 2.90, 3.32
COOH	8.06	7.97	8.26	
$COOCH_3$	8.12	8.01	8.29	CH_3, 6.40

[a] In CCl_4 solution. [b] Unresolved resonances. [c] Center of aromatic quartet.

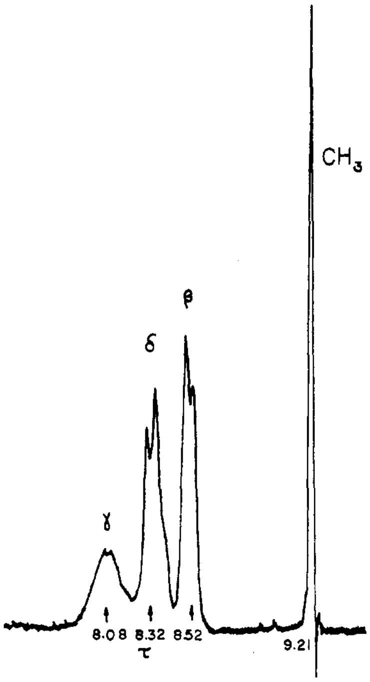

Figure 2.—The p.m.r. spectrum of 1-methyladamantane.

the β and δ protons. Ordinarily, the chemical shifts of the δ hydrogens, farthest from the substituent, are displaced the least from the value (τ 8.22) found for the methylene protons of adamantane itself. Although there are in fact two sorts of δ protons, these invariably fall together in all spectra we have observed. However, as a consequence of this nonequivalence, the composite δ peak is broader (typically w_h = *ca.* 8 c.p.s.) and more complex than the β hydrogen peak which most often is a doublet of w_h = 5.3 c.p.s. (Table III). The bridgehead proton resonances appear as a featureless, broad (w_h = *ca.* 10 c.p.s.) band. Finally, adamantane derivatives show a very precise chemical shift additivity relationship (see below), which can be used to check assignments. Naturally, when the β and δ resonances fall close to one another, the assignments (Table I) are less secure than usual.

Particularly striking are the large variations in chemical shift with changes of the 1-substituent. The positions of the β protons vary over 1.17 p.p.m., but the ranges for the γ (0.37 p.p.m.) and δ (0.24 p.p.m.) positions are less, as expected. The substituent shifts are correlated (see Discussion) by various measures of substituent electronegativity, such as E_R and σ^*. Interestingly, the slopes of these correlation lines alternate positive and negative for the successive (β, γ, and δ) positions; halogens give a separate correlation from the other substituents.[15,16]

In view of the significant chemical shift variations induced by the substituents, it is not surprising to find compounds for which the resonances of the β, γ, and δ protons are not well separated. In 1-chloroadamantane (Figure 3), the β and γ protons give a single peak in CCl_4 solution, while, in 1-hydroxyadamantane (Figure 4), it is the β and δ resonances which overlap. Other examples of such conjunction may be found in Table I. Selective solvent shifts are spectacularly effective in these instances (Table II) in separating the various resonances. For this purpose, benzene is superior to dimethylaniline, nitrobenzene, or pyridine. Surprisingly, the β protons, closest to the substituent,

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(15) This has been observed previously; *e.g.*, H. Spiesecke and W. G. Schneider, *J. Chem. Phys.*, **35**, 722 (1961).

(16) G. S. Reddy and J. H. Goldstein [*ibid.*, **36**, 2644 (1962)] have used the variation of the halogens from a plot of $J_{^{13}CH}$ *vs.* δ to assign values for X_M, the magnetic anisotropy of the CX bond.

Table II

Solvent Shifts[a] for 1-Substituted Adamantanes

Substituent	Solvent	ΔH_β	ΔH_γ	ΔH_δ	Other
F	Benzene	0	16	16	
Cl	Benzene	5	20	19	
	$C_6H_5N(CH_3)_2$	8	21	18	
	Pyridine	2	11	11	
	$C_6H_5NO_2$	1	8	6	
Br	Benzene	3	21	19	
	Pyridine	0	12	10	
	$C_6H_5NO_2$	2	8	7	
I	Benzene	8	21	20	
OPNB	Benzene	6	17	16	
OH	Benzene	4	12	14	
	Pyridine	−14	2	6	
	$C_6H_5NO_2$	−6	6	6	
$NHCOCH_3$	Benzene	1	3	8	CH_3, 18
$C(CH_3)_2Br$	Benzene	4	2	0	CH_3, 2
$C(CH_3){=}CH_2$	Benzene	0	0	0	$=CH_2$, −30

[a] Relative to CCl_4; the variations in chemical shifts relative to TMS internal standard (in c.p.s.) are taken as positive when the resonances move upfield, and negative when they move downfield from their positions in CCl_4 solution.

Table III

Coupling Constants in 1-Substituted Adamantanes

1-Substituent	$J_{\beta\gamma}$, c.p.s.	w_h, β protons, c.p.s.
F	2.7 ($J_{H_\beta F}$ 5.5)	...
Br	2.5	5.2
I	2.5	5.0
NH_2	2.7	...
CH_3	2.6	5.3
CH_2OH	2.5	5.3
CH_2OCOCH_3	2.5	5.3
CH_2OTs	2.6	5.3
CH_2Cl	2.6	...
CH_2CH_2Br	2.6	...
C_6H_5	2.5	5.3
Average	2.6 ± 0.1	5.3 ± 0.2

are affected least in chemical shift by a change in solvent (Table II). We plan further investigations into these interesting solvent effects.

There is a dearth of observable splitting in adamantane spectra. Most peaks are rather broad singlets, w_h = 5–10 c.p.s. In those instances where coupling is discernible (Table III), all J's are identical, 2.6 ± 0.2 c.p.s. Within the precision of measurement, agreement with the value estimated for adamantane itself is very good.[17] We regard our result as a maximum value; the actual J_{vic} may be somewhat less than 2.6 c.p.s.

2-Substituted Adamantanes.—The spectra of 2-substituted adamantanes (Table IV) are the least informative of those examined, but differences from the spectra of the 1-substituted adamantanes are quite sufficient to distinguish between compounds of the two types. Most of the protons in a 2-substituted adamantane give rise to general absorption in the τ 8.0–8.5 region, usually with a prominent peak near 8.22, the resonance position of adamantane. The only singular and readily identifiable features are the protons on the 2-substituent itself, if any, the 2-proton if the compound is secondary, and the two adjacent bridgehead protons. This "fuzziness" is a consequence of the low

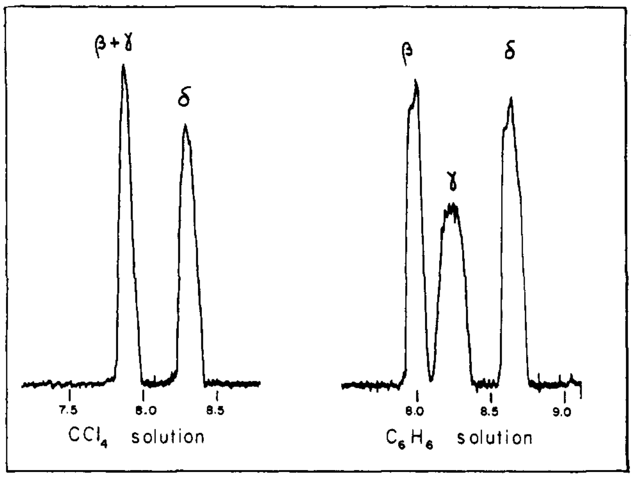


Figure 3.—Solvent effect on the spectrum of 1-chloroadamantane.

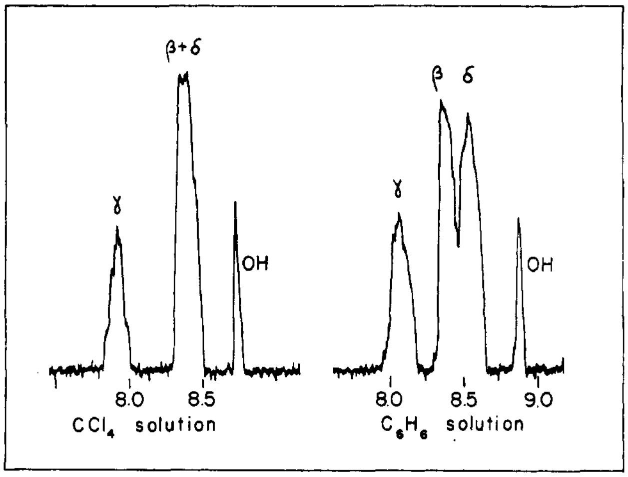
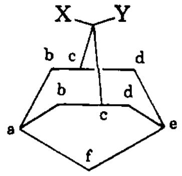


Figure 4.—Solvent effect on the spectrum of 1-hydroxyadamantane.

Table IV

Chemical Shifts in 2-Substituted Adamantanes



X	Y	Features of the nucleus	Other
CH_3	OH	H_c = 7.9; others 8.25 and 8.69	CH_3, 8.69
H	OH	H_c = 8.0; H_X = 6.20; others 8.09–8.70, sharp peak at 8.20	
X = Y = CH_2		H_c = 7.52; others 8.12	$=CH_2$, 5.52
H[a]	CH_3	~8.20	CH_3, 8.96
X = Y = O[a]		H_c = 7.59; others 8.00	

[a] 40-Mc. spectrum.[9]

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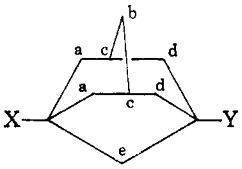
[17] O. Jardetsky (private communication) has argued that the peak separations, which we have reported in Table III, do not represent the true coupling constants, since the lines do not split to the base line even with the best resolution available. In such cases, according to Jardetsky, the separation of the overlapping lines is smaller than the separation between the centers of the lines, and the latter better reflects the true coupling constant. Jardetsky estimates the value of J in 1-bromoadamantane to be 3.0 c.p.s., after correction for overlap. We agree that care should be exercised in reporting values of J, when these are small and are derived from incompletely resolved lines. We believe, however, that the smaller value of J (2.6 c.p.s.) is preferable in the adamantane series. We observe consistently (Table III) not only a constancy of peak separation, but also a constancy of line width, w_h = 5.3 ± 0.3 c.p.s., corresponding to a doublet with J = 2.65 ± 0.2 c.p.s. We feel that the agreement of this value with that derived for adamantane itself is particularly significant. Were the degree of overlap an important factor, we would not expect this close and consistent correspondence.

TABLE V

CHEMICAL SHIFTS IN 1,3-DISUBSTITUTED ADAMANTANES (τ)[a]



X	Y	H_a	H_b	H_c	H_d	H_e	Other
CH_3	CH_3	8.63 (8.62)	8.46 (8.42)	8.02 (8.04)	8.63 (8.62)	8.84 (8.82)	CH_3's, 9.20
CH_3	Br	8.52 (8.57)	8.37 (8.37)	7.85 (7.88)	7.78 (7.80)	7.92 (8.00)	CH_3, 9.13
CH_3	Cl	8.59 (8.50)	8.41 (8.40)	7.89 (7.85)	7.97 (7.99)	8.17 (8.19)	CH_3, 9.12
CH_3	OH	8.61 (8.66)	8.41 (8.36)	7.88 (7.84)	8.41 (8.41)	8.61 (8.61)	CH_3, 9.14; OH, 6.84
CH_3	$OCOC_6H_4NO_2$-*p*	8.52 (8.52)	8.36 (8.32)	7.75 (7.75)	7.80 (7.78)	8.04 (8.02)	CH_3, 9.09; AR, 1.82
CH_3CH_2	Br	8.56 (8.55)	8.38 (8.31)	7.80 (7.80)	7.80 (7.74)	8.01 (7.98)	CH_3, 9.21; CH_2, 9.08
$(CH_3)_2CH$	Br	8.46 (8.53)	8.31 (8.36)	7.69 (7.80)	7.69 (7.79)	7.88 (7.96)	CH_3's, 9.14; CH, ~8.9
$(CH_3)_2CH$	OH	8.55 (8.62)	8.45 (8.95)	7.92 (7.76)	8.45 (8.40)	8.45 (8.57)	CH_3's, 9.19; CH, ~8.9
Br	Br	7.71 (7.75)	8.39 (8.32)	7.71 (7.72)	7.71 (7.75)	7.18 (7.18)	
Benzene solution solvent shifts[b]		+20 (19)	+37 (38)	+41 (42)	+20 (19)	+3 (3)	

[a] Values in parentheses are predicted on the basis of additivity (see text). [b] Cycles per second from CCl_4 values.

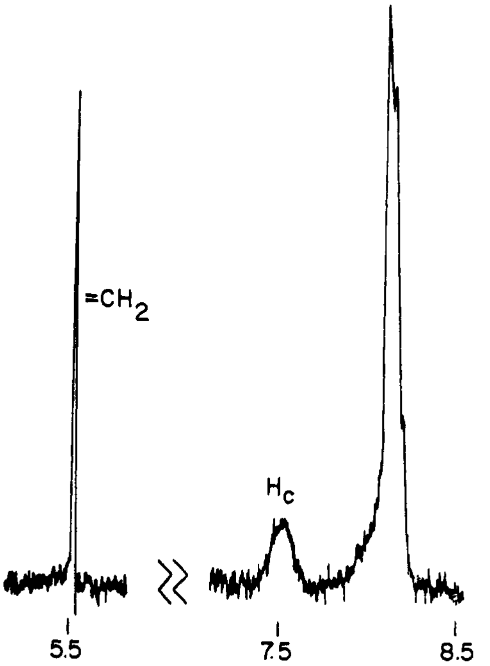


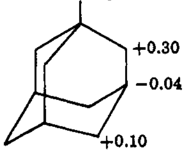
Figure 5.—The p.m.r. spectrum of 2-methyleneadamantane.

symmetry of these compounds. A compound like 2-methyleneadamantane (Figure 5) has five different kinds of aliphatic protons, while 2-hydroxyadamantane (Figure 6) has eight (excluding the hydroxyl and the C*H*OH).

The vinyl resonance of 2-methyleneadamantane, τ 5.52, is somewhat higher than usual; compare isobutene, 5.40[7]; methylenecyclobutane, 5.30[18]; methylenecyclopentane, 5.18[18]; and methylenecyclohexane, 5.45.[18] The methyl resonance of 2-methyladamantane at τ 8.96 is appreciably lower than that of 1-methyladamantane, 9.25.

1,3-Disubstituted Adamantanes.—Because of the high symmetry of the adamantane system, spectra of 1,3-disubstituted compounds are not so complicated as might be expected. If the two substituents are identical, four different kinds of protons can be discerned in the p.m.r. spectrum; if the substituents are different, five kinds. (Actually, the protons of several of the methylene groups are nonequivalent, but in practice the resonances cannot be separated.) In most cases (Figure 7 and Table V), the observable resonances are separated cleanly, and may be assigned from their chemical shifts and relative areas. 1,3-Dibromoadamantane gives only three peaks in CCl_4 solution, due to coalescence of the bridgehead proton resonances with one of the methylene peaks; changing to benzene as solvent once again is effective in separating these features (Figure 8).

Chemical shifts in the adamantane series display an amazingly consistent additivity; each substituent added to a bridgehead influences the resonance frequencies of the various protons in the molecule independent of whatever other substituents may be present. This additivity is illustrated below for 1,3-dimethyladamantane (II). In 1-methyladamantane (I), the β protons absorb at τ 8.52, or 0.30 p.p.m. to higher field than the methylene protons of adamantane. The δ protons, at τ 8.32, are shifted 0.10 p.p.m. If we take τ 8.12 as the absorption of the bridgehead protons in adamantane, those of 1-methyladamantane (τ 8.08) are shifted −0.04 p.p.m. The effect of the 1-methyl is summarized in I.



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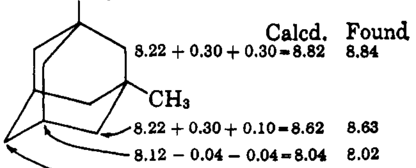

II

The chemical shifts of the four different kinds of adamantoid protons in 1,3-dimethyladamantane (II) can easily be calculated by considering their relationship to each of the substituents. II illustrates the method, which can be extended with equally good accuracy to 1,3,5-trisubstituted adamantanes (Table VII), and, for the few cases we have studied, to 1,3,5,7-tetrasubstituted derivatives. The calculated chemical shifts are given in parentheses in Tables V and VII for

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(18) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "Varian High Resolution N.m.r. Spectra Catalog," Vol. I, Varian Associates, Palo Alto, Calif., 1962.

Table VI

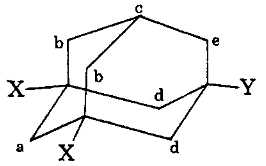
1-Substituent Shifts in Carbon Tetrachloride Solution[a]

	1-Substituent								
	F	Cl	Br	I	CH_3	C_2H_5	i-C_3H_7	OH	OPNB[b]
β-Protons	−0.05	−0.33	−0.52	−0.85	+0.30	+0.28	+0.26	+0.09	−0.49
γ-Protons	−0.32	−0.23	−0.20	−0.09	−0.04	−0.12	−0.12	−0.24	−0.49
δ-Protons	+0.16	+0.08	+0.05	+0.08	+0.10	+0.04	+0.09	+0.14	+0.01

[a] Shifts to higher field are positive, to lower field negative; values are given in parts per million. [b] OPNB = $OCOC_6H_4NO_2$-*p*.

Table VII

Chemical Shifts in 1,3,5-Trisubstituted Adamantanes (τ)



X	Y	H_a	H_b	H_c	H_d	H_e	Other
CH_3	Cl	8.81 (8.90)	8.64 (8.70)	7.82 (7.81)	8.22 (8.29)	8.06 (8.09)	CH_3's, 9.10
CH_3	Br	8.79 (8.87)	8.61 (8.67)	7.70 (7.74)	8.02 (8.12)	7.88 (7.90)	CH_3's, 9.12
CH_3	OH	(8.96)	(8.76)	(7.80)	(8.71)	(8.51)	
CH_3	$OCOC_6H_4NO_2$-*p*	8.78 (8.82)	8.59 (8.62)	7.70 (7.71)	8.10 (8.12)	7.87 (7.92)	CH_3's, 9.08
Br	Br	7.21 (7.23)	7.73 (7.80)	7.65 (7.52)	7.21 (7.23)	7.73 (7.80)	
Benzene solvent shifts[a]		+21 (25)	+38 (41)	+62 (63)	+21 (25)	+38 (41)	
CH_3	CH_3	8.90 (8.92)	8.71 (8.72)	7.98 (8.00)	8.90 (8.92)	8.71 (8.72)	CH_3's, 9.20

[a] Given in cycles per second from CCl_4 values.

ready comparison with the experimentally observed ones. Table VI summarizes the 1-substituent shifts.

As in the case of monosubstituted adamantanes, a lack of clear cut splitting is apparent in the spectra of 1,2-disubstituted adamantanes. The peaks are rather broad, w_h = 4–10 c.p.s. In part, this is due to the nonequivalence of the protons in certain of the methylene groups, notably H_a and H_d (Table V) if the substituents X and Y are the same, and in addition H_b if they are not. However, even the isolated methylene, H_e, with identical protons, shows some broadening (w_h = *ca.* 4 c.p.s.)

1,3,5-Trisubstituted Adamantanes.—When all three substituents in a 1,3,5-trisubstituted derivative are the same, three peaks are found in the p.m.r. spectrum. If two different substituents are present, five peaks are seen (Figure 9 and Table VII). If all three groups are different, seven peaks should be observable; we have not, however, examined any compounds of this type. In the compounds listed in Table VII, only the lone bridgehead proton of 1,3,5-tribromoadamantane does not give rise to a well-separated signal; in this case, benzene again is effective in shifting the resonances selectively. It is noteworthy that these benzene solvent shifts, like the chemical shifts themselves, are additive. Using the data of Table II, the benzene solvent shifts of 1,3-dibromoadamantane and 1,3,5-tribromoadamantane protons can be calculated (Tables V and VII). Agreement with the experimentally measured values is excellent.

Splitting again is absent in the spectra of these compounds, but the peaks are somewhat less broad (w_h = 3–7 c.p.s., under resolution which gives a TMS line of w_h = 1.6 c.p.s.) than in previous instances.

1,3,5,7-Tetrasubstituted Adamantanes.—1,3,5,7-Tetrabromoadamantane gives a single sharp line at τ 7.28 (calculated from additivity, τ 7.28) since all protons are equivalent. The sharpness of the line, w_h = 1.4 c.p.s., contrasts with the relatively broad lines obtained (*vide supra*) for less fully substituted adamantanes. The methylene groups of tetramethyladamantane (kindly supplied by Dr. A. Schneider) give a sharp line at τ 8.99 (calculated from additivity, 9.02), while trimethylbromoadamantane has resonances at τ 9.13(CH_3), 8.88 (8.97), and 8.12 (8.20).

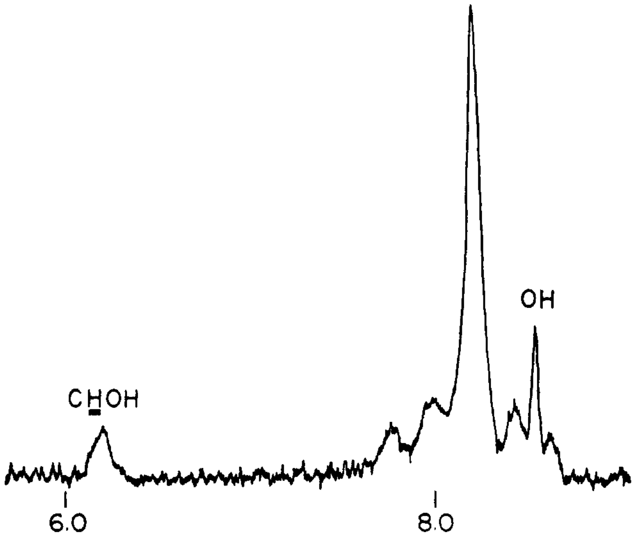


Figure 6.—The p.m.r. spectrum of 2-hydroxyadamantane.

Discussion

Structure Determination.—As a method for determining the substitution pattern of an adamantane, proton magnetic resonance is without peer. The relatively large chemical shift differences and the absence of splitting combine to make interpretation a simple "first-order" process. In those instances where overlap of resonances complicates the normal spectrum, recourse to benzene as solvent spreads the lines and greatly facilitates assignment of the resonances. The

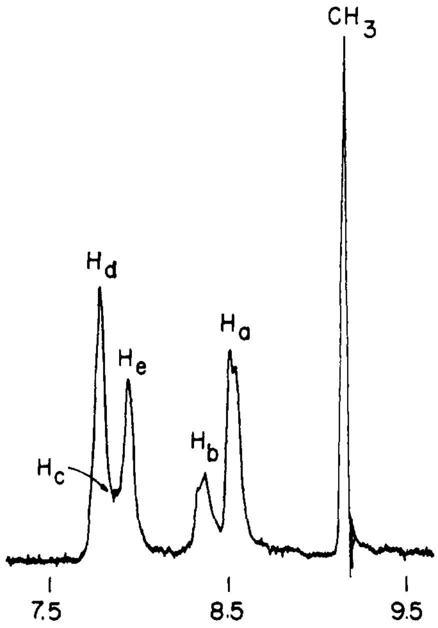


Figure 7.—The p.m.r. spectrum of 1-bromo-3-methyladamantane.

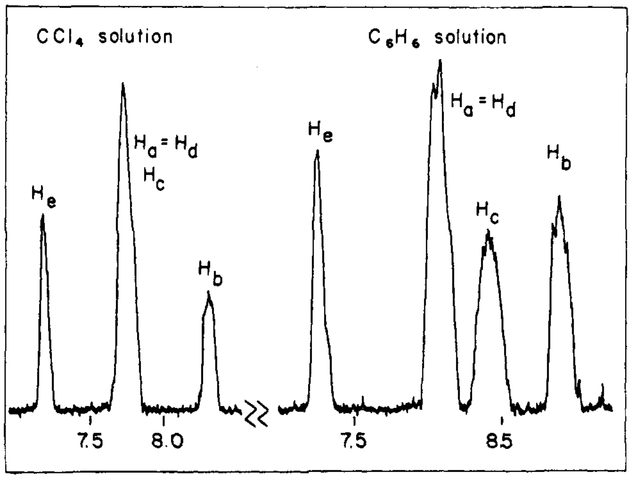


Figure 8.—Solvent effects on the spectrum of 1,3-dibromoadamantane.

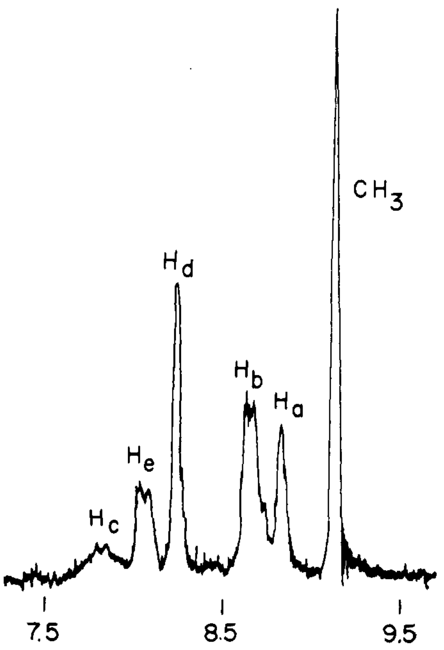


Figure 9.—The p.m.r. spectrum of 1-chloro-3,5-dimethyladamantane.

lack of comprehensive infrared data[19] enhances the diagnostic value of p.m.r. in adamantane structure determination

Coupling.—The adamantane skeleton is extremely rigid; all bonds are held firmly in a skew arrangement, and the dihedral angle between vicinal protons is fixed at 60°. No substituent can affect this angle significantly, for the molecular framework will not permit distortion; nor are 1-substituents expected to exert appreciable electronegativity effects on coupling constants, for a bridgehead substituent is at the least three bonds removed from any proton in the molecule. Finally, in adamantanes, all bond angles are expected to be tetrahedral and all bond lengths normal.[20,21]

Admantane and its simple derivatives thus offer the opportunity of testing the Karplus equation,[22] which relates J_{vic} and dihedral angle, in the absence of all complicating effects.[23] Karplus recently[23] has warned that, in addition to dihedral angle, electronegativities of substituents, bond lengths, and the other bond angles of the fragment under consideration should be expected to influence vicinal coupling constants. *All of these factors are virtually absent in adamantanes.*

We may compare, then, the observed J_{vic} for adamantanes, 2.6 ± 0.2 c.p.s., with the value predicted by the Karplus equation, 1.8 c.p.s. The agreement is reasonable; $J = 2.6$ c.p.s. corresponds to a dihedral angle of 54°. One may conclude that the Karplus treatment well represents the angular dependence of vicinal J's. The numerous recent proposals[24-30] for increasing the values of the constants in the Karplus equation most probably represent attempts to include empirically the effects noted above. As such, they are extremely valuable aids to the practicing organic chemist, but should not be considered to detract from the accuracy of the original Karplus equation.

It is of interest to enquire into the paucity of observable splitting in adamantane derivatives. One would expect, from a first-order analysis, that the β hydrogens in a monosubstituted adamantane would appear as a clean doublet, of J about 1–3 c.p.s. The δ hydrogens, which are nonequivalent, should give an AB quartet with further splitting by the two adjacent bridgehead protons, while the bridgehead would give

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(19) We are currently examining the infrared spectra of the adamantanes prepared in this investigation for features which may be useful in structure determination. In addition, we are initiating a survey of the mass spectral properties of these compounds.

(20) G. Giacomelli and G. Illuminati, *Ric. Sci.*, **15**, 559 (1945); *cf. Chem. Abstr.*, **40**, 6929 (1946); *Gazz. chim. ital.*, **75**, 246 (1945).

(21) W. Nowacki, *Helv. Chim. Acta*, **28**, 1233 (1945); W. Nowacki and K. W. Hedberg, *J. Am. Chem. Soc.*, **70**, 1497 (1948).

(22) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); H. Conroy, *Advan. Org. Chem.*, **2**, 31 (1960).

(23) M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).

(24) O. D. Jardetsky, *ibid.*, **83**, 2919 (1961).

(25) R. U. Lemieux, *Can. J. Chem.*, **39**, 116 (1961).

(26) R. W. Lenz and J. P. Heeschen, *J. Polymer Sci.*, **51**, 247 (1961).

(27) R. J. Abraham and K. L. McLauchlan, *Mol. Phys.*, **5**, 513 (1962).

(28) N. J. Leonard and R. A. Laursen, *J. Am. Chem. Soc.*, **85**, 2027 (1963).

(29) R. U. Lemiux, J. D. Stevens, and R. D. Fraser, *Can. J. Chem.*, **40**, 1955 (1962).

(30) R. U. Lemiux and J. W. Lown, *ibid.*, **42**, 893 (1964).

a septuplet from coupling with three methylene groups. In fact, both the β and δ proton rarely show any splitting, and the bridgeheads *always* appear as a broad, unresolved hump.

Virtual coupling[31] and/or long-range coupling,[32] may be invoked to explain the "washing out" of ordinary coupling. Virtual coupling will occur in a group of neighboring protons if one of the spins be so strongly coupled to some of the others that it behaves as a set of N spin $^1/_2$ nuclei rather than a single spin $^1/_2$ nucleus. Another nucleus, outside this group, but coupled to the first, will then "see" a set of N spins, instead of the single one predicted by first-order rules.[31] Virtual coupling may result in "extra" splitting, or simply line broadening, depending upon the relative ν's and J's. In a monosubstituted adamantane, one may envisage the two sets of methylene protons being coupled to each other through the agency of the bridgehead protons, and their resonances consequently being broadened. We feel, however, that virtual coupling probably is not occurring in our adamantane systems, which would be borderline cases at best.

Long-range coupling[32] may also be operative in adamantanes. A moment's examination of a model demonstrates that both the protons of the methylene groups and those at the bridgeheads lie in the "W" arrangement (Figure 10) which has been implicated[32] in most long-range couplings over four bonds in saturated systems. Since most long-range couplings are less than 2 c.p.s. in magnitude, line broadening could easily result from the operation of this phenomenon. Such coupling could also broaden lines in di- and trisubstituted compounds, but should vanish in a symmetrically tetrasubstituted compound, since all methylenes are then equivalent.[33]

Chemical Shifts.—It is interesting that the chemical shifts of 1-substituted adamantanes may be correlated by virtually *any* measure of substituent electronegativity—for example, E_R (Cavanaugh and Daily[34]), σ^* (Taft,[35] illustrated in Figure 11), or μ_G (group dipole moment[36]). There are some large deviations (*e.g.*, phenyl), but on the whole the correlations are as good as those observed in other cases.[37] A separate line is required for halogen substituents.

Such a difference between halogens and other substituents has previously been noted,[15,16] and is usually attributed to the anisotropy of the carbon–halogen bond (the deviation of the phenyl substituent might likewise be explained by anisotropy). However, that any measure of substituent electronegativity should correlate chemical shifts is disturbing, if anisotropy is allowed a part. While E_R may be faulted as an electronegativity measure on the basis of its having been determined by p.m.r. measurements, certainly σ^* and μ_G values are not influenced by anisotropy.

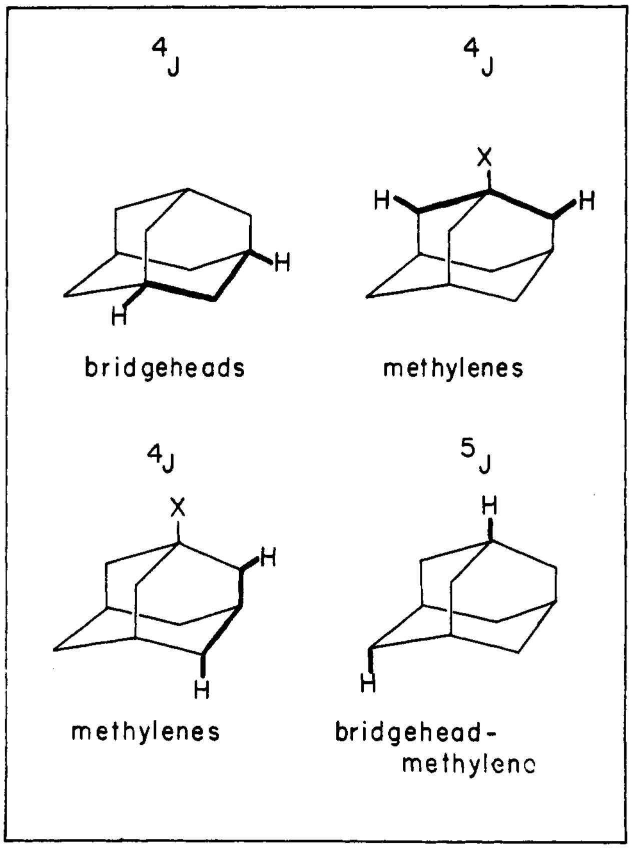

Figure 10.—Possible long-range couplings with adamantanes.

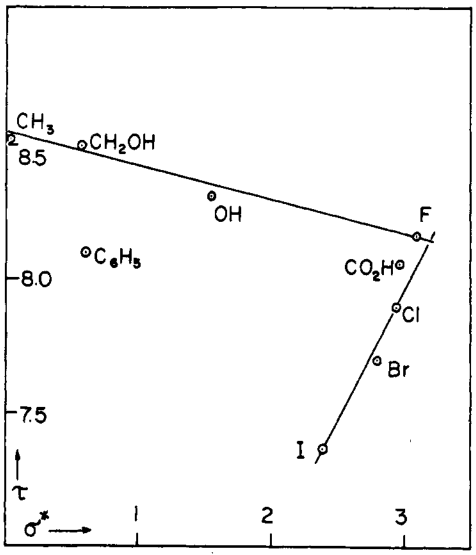

Figure 11.—Chemical shifts of β protons, 1-substituted adamantanes.

Cavanaugh and Daily[34] have argued on similar grounds that anisotropy effects are unimportant, and have introduced a C–C "bond shift" to aid their correlations. While our results allow no choice between these two interpretations, we feel that their reasonable interpretation requires some participation (*vide infra*) of C–X bond anisotropy. Electrostatic field effects[38] are also likely contributors to the observed shifts. Perhaps a quantitative evaluation of inductive and anisotropic effects in a variety of systems of fixed

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[31] J. I. Musher and E. J. Corey, *Tetrahedron*, **18**, 791 (1962).

[32] Reviews: S. Sternhell, *Rev. Pure Appl. Chem.*, **14**, 15 (1964); E. Garbisch, *J. Am. Chem. Soc.*, **84**, 5561 (1964).

[33] A double resonance experiment, performed by Dr. L. B. Rodewald, suggests that such coupling in bromoadamantane is of the order of 0.2 c.p.s. We plan to use double resonance in an extensive study of possible long-range couplings in adamantanes, to be reported subsequently.

[34] J. R. Cavanaugh and B. P. Dailey, *J. Chem. Phys.*, **34**, 1099 (1961).

[35] R. W. Taft, "Steric Effects in Organic Chemistry," M. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 615 ff.

[36] C. P. Smyth, "Dielectric Structure and Behavior," McGraw-Hill Book Co., Inc., New York, N. Y., 1955.

[37] For examples and leading references, see P. Laszlo and P. von R. Schleyer, *J. Am. Chem. Soc.*, **85**, 2709 (1963).

[38] A. D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960).

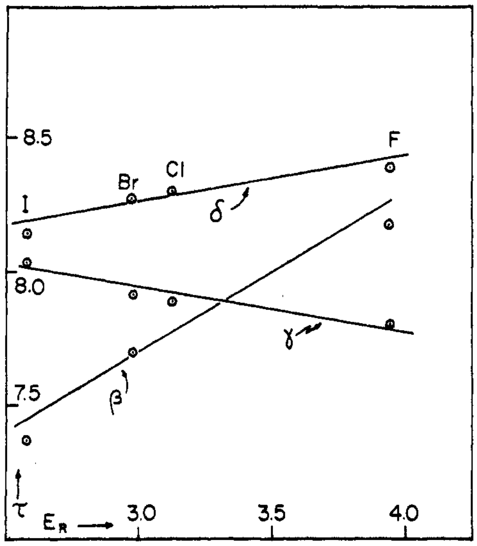

Figure 12.—Alternation of chemical shifts in 1-haloadamantanes

geometry, such as adamantane, will provide a more satisfactory basis for discussion.

Figure 12 illustrates the alternation of chemical shifts in adamantanes; *i.e.*, the β protons of adamantyl fluoride appear at highest field of all the halides, while for the γ protons the reverse is true, and the order reverses once again for the δ protons. This same alternation is observed (but not illustrated) with the correlation lines for other substituents.

A rationalization of this alternation of shifts is difficult, but one may speculate about the interplay of induction and anisotropy, as has been done for the chemical shifts of ethyl derivatives.[15] The α protons of CH_3CH_2Cl, CH_3CH_2Br, and CH_3CH_2I fall to low field of the line determined by the other substituents, and the greatest deviation is found for the most electronegative, Cl. Presumably,[15] the anisotropy contribution to the low-field shift, which should be greatest for iodine, is insufficient to overcome the inductive order.

At the β position in the ethyl series, the inductive effect is considerably attenuated, while the anisotropy shift is nearly the same,[15] and the deviations from the electronegativity plot follow the order of anisotropies.

In the adamantane derivatives, both β and δ shifts appear to be anisotropy controlled, while the γ ones follow an inductive order.

To apply the above argument to the adamantane system, some mechanism is required for making the inductive contribution to the γ shifts once again sufficiently large to determine the slope of the lines. Perhaps the overlap of the rear lobes of bridgehead bond orbitals inside the cage[39] supplies this mechanism. In any event, it is the distinct alternation of chemical shifts which seems to us to argue for the importance of anisotropy, at least in the rigid adamantane system.

The additivity of substituent effects in the adamantane series is interesting also. Such additivity has previously been reported by Shoolery,[40] who deduced a set of substituent constants, and Primas,[41] who likewise produced a group of additive constants. Both of these previous correlations, however, were not applicable to cyclic systems; also, they often failed for tertiary protons. Possibly the inflexible adamantane skeleton is responsible for the success of our predictive correlation.

Experimental

P.m.r. Measurements—All spectra were obtained on a Varian A-60 spectrometer at normal operating temperature (*ca.* 30°). Compounds were examined as *ca.* 10% solutions in reagent CCl_4, benzene, $C_6H_5NO_2$, or pyridine with 1% tetramethylsilane (TMS) as internal standard. Peak positions were read directly from the precalibrated chart paper; calibration was checked frequently against the chemical shift difference (436 c.p.s.) between TMS and $CHCl_3$. We consider chemical shifts accurate to ±2 c.p.s.

Coupling constants were measured with the aid of a transparent scale graduated in millimeters. In most cases, measurements on the normal spectrum were checked on spectra of expanded scale, and are usually the average of J's determined from several spectra. J's are reproducible to ± 0.1 c.p.s.

^{13}C satellite peaks of adamantane were examined with a computer of average transients (CAT) kindly supplied by the Mnemotron Corp., in the manner previously described.[13,14]

Synthetic.—Except as noted below, the adamantane derivatives were prepared by standard methods[4] and purified until their physical properties agreed with those cited in the literature. Satisfactory analyses were obtained on all new compounds or their simple derivatives.

The preparation of ethyl- and isopropyladamantanes and their derivatives will be described in a subsequent publication.

The 2-substituted adamantanes were samples prepared by R. D. Nicholas.[9]

1-Fluoroadamantane.—1-Bromoadamantane (10.0 g., 0.047 mole), 13.4 g. (0.10 mole) of anhydrous silver fluoride, and 100 ml. of dry cyclohexane were heated at reflux, with vigorous stirring, for 24 hr. Care was taken to exclude moisture. Upon completion of the reflux period, the mixture was cooled, and the precipitated silver salts were filtered off and washed thoroughly with warm cyclohexane.

Brief chilling of the solution caused the deposition of 1.5 g. of 1-hydroxyadamantane, identified by n.m.r. and mixture melting point. Removal of the cyclohexane *in vacuo*, and recrystallization of the residue from petroleum ether at −77° gave 4.0 g. (55%) of 1-fluoroadamantane. Sublimation gave material of analytical purity, having m.p. 210–212° dec. (sealed tube).

Anal. Calcd.: C, 77.65; H, 9.74. Found: C, 77.94; H, 9.73.

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(39) Evidence for this phenomenon is summarized in ref. 4; see also, R. C. Fort, Jr., and P. von R. Schleyer, *J. Am. Chem. Soc.*, **86**, 4194 (1964).

(40) J. N. Shoolery, "Technical Information Bulletin," Vol. 2, No. 3, Varian Associates, Palo Alto, Calif., 1959.

(41) L. Primas, quoted by H. Strehlow, "Magnetische Kernresonanz und Chemische Struktur," Dr. Dietrich Steinkopf Verlag, Darmstadt, 1962, p. 33 ff.