TABLE I

CALCULATED CHARGES IN ALKOXIDE IONS

	Present work				MINDO,[b]	CNDO/2,[c]
Anion, RO^- [a]	δ_O	δ_R	δ_C	δ_H	δ_O	δ_O
OH^-	−0.658	−0.342		−0.342	−1.08	
CH_3O^-	−0.526	−0.474	−0.161	−0.104	−0.91	−0.68
$C_2H_5O^-$	−0.492	−0.508	−0.114	−0.056	−0.85	−0.67
$C_3H_7O^-$	−0.477	−0.523	−0.093	−0.034	−0.81	−0.66
$C_4H_9O^-$	−0.469	−0.531	−0.081	−0.023		−0.66
$C_5H_{11}O^-$	−0.464	−0.536	−0.074	−0.015		−0.66

[a] The oxygen is assumed to be hybridized with 20% s character in the hydroxide ion and 26.4% s character in the alkoxides. These values are from the 104.5° bond angle in H_2O and the somewhat greater angle (~110°) in alcohols. Under the relaxed steric conditions of the anion, the s character probably changes somewhat. Small changes in s character do not change the results significantly. [b] Reference 5. [c] Reference 6.

than the fluorine atom itself. The results confirmed the earlier arguments of Schubert, *et al.*[8,13]

The experimental work of Brauman and Blair[3] provides striking confirmation of the expectation expressed above. In the negatively charged alkoxide anion (the conjugate base of the acidic alcohol), the negative charge resides predominantly on the oxygen but the ion will be stabilized (*i.e.*, its basicity will be reduced) to the extent that this charge can be delocalized[14] onto the alkyl groups. In this case the electronegativities of the alkyl groups (2.27–2.29) are all *greater* than that of an oxygen atom with a unit negative charge ($\chi_o \leq 0$)[15] and hence absorb electron density from the latter and the larger groups are capable of absorbing a greater amount before becoming saturated. This interpretation is thus essentially the same as that suggested earlier by Schubert, *et al.*,[8] the larger groups are more polarizable and can absorb charge more readily, but may be expressed in terms of electronegativity parameters derived from fundamental *atomic* properties rather than intuitive arguments. The results are given in Table I. It should be noted that these results were obtained using the simplifying assumption of electronegativity equalization.[9–11] The problems and errors inherent in this simplification have been discussed elsewhere[9,16] and attempts have been made to improve the calculations by various means,[17] but it may be said that the *qualitative* trends shown in Table I will not be altered by such attempts to improve the quantitative calculations with the possible exception of the very large groups (*n*-butyl, *tert*-butyl, *n*-pentyl). While the present values can hardly be interpreted as accurate estimates of the real charges, they are internally self-consistent and at least as reasonable as the estimates obtained by more elaborate methods. The very high values of the MINDO estimates (−0.8 to −1.0 on oxygen)[5] and CNDO/2 estimates (−0.67 on oxygen with almost no dependence upon the nature of R)[6,17a] result from the neglect of the effect of forcing large electron densities on a small oxygen atom.[18]

It is apparent that when discussing the inductive effect of groups it will be necessary to consider both inherent electronegativity and relative charge capacity. In some ways, this result is akin to Pearson's suggestions[19] that a hardness–softness factor (the HSAB principle) be considered in addition to inherent strength in acids and bases. However, even here the possibility of confusion can exist. Pearson and Songstad[20] have claimed that the *tert*-butyl group is "harder" than the methyl group and that it is a poorer electron donor (toward electronegative substrates) despite general opinion to the contrary. As can be seen from the above discussion, the *tert*-butyl group is both a better donor and a better acceptor (in appropriate situations) than methyl or hydrogen. If experimental criteria and applications of the HSAB rule indicate that *tert*-butyl is "harder" than methyl, it is apparent that factors other than polarizability must be responsible for "softness." This conclusion has been reached on the basis of other evidence elsewhere.[17,21]

Registry No.—OH^-, 14280-30-9; CH_3O^-, 3315-60-4; $C_2H_5O^-$, 16331-64-9; $C_3H_7O^-$, 26232-83-7; $C_4H_6O^-$, 26232-84-8; $C_5H_{11}O^-$, 26675-02-5.

Acknowledgment.—I should like to thank Professor W. M. Schubert for helpful criticism of this article.

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(13) Unfortunately, ref 8 was unknown to the author in 1965. Although derived independently, Figure 1 of ref 9 provides a quantification of Figure 2 of ref 8 for the electron donating and withdrawing properties of alkyl groups with respect to the hydrogen atom.

(14) The term delocalization is used here to mean simply that all the atoms in the alkoxide ion acquire a negative charge through the inductive effect with no implications of conjugation or hyperconjugation.

(15) A *negative* electronegativity, like a negative pH, is an extremely unlikely, though possible situation. The meaning of this value is that oxygen *cannot* contain a total unit negative charge while coexisting in a covalent bond with *any* other atom or group of atoms.

(16) R. Ferreira, *J. Phys. Chem.*, **68**, 2240 (1964); G. Klopman, *J. Amer. Chem. Soc.*, **86**, 1463 (1964); J. E. Huheey, *J. Phys. Chem.*, **70**, 2086 (1966).

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(17a) NOTE ADDED IN PROOF.—Similar results have recently been obtained by R. B. Hermann, *J. Amer. Chem. Soc.*, **92**, 5298 (1970)

(18) For discussions of the relation between effective charge and Coulomb integrals in terms of fixed (*i.e.*, ionization potential) electronegativity *vs.* variable orbital electronegativity, see G. Doggett, *Theor. Chim. Acta*, **15**, 344 (1969), and references therein.

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Preparation of Bridgehead Alkyl Derivatives by Grignard Coupling

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We have developed a simple, high yield way to convert adamantane-type bridgehead bromides to the cor-

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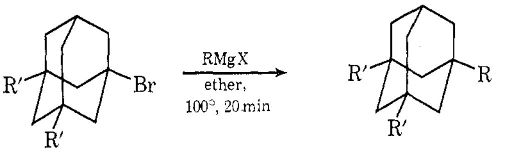
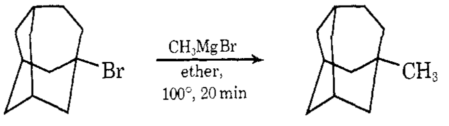
responding methyl (or other alkyl) derivatives. Diamondoid hydrocarbons can often be prepared by rearrangement[1-3] and functional groups added subsequently.[2] One of the most useful methods is ionic bromination, which exhibits a strong preference for bridgehead substitution.[2,4] However, conversion of, *e.g.*, 1-bromoadamantane to 1-methyladamantane according to literature procedures, was a cumbersome, four-step process involving preparation and then reduction of the corresponding carboxylic acid.[5] Direct quaternization of tertiary carbons is not generally very satisfactory. For example, Wurtz coupling reactions have been used to prepare 1-ethyl- and 1-propyladamantane, but the yields were very poor.[6] Grignard reagents are known to react with *tert*-halides, but low yields of alkanes are expected.[7]

Nevertheless, when 1-adamantyl bromide (Ia) was heated in an aerosol pressure bottle with excess CH_3MgBr in ether for only 20 min at 100°, 1-methyladamantane (IIa) was obtained in 83% yield. (More conventional reaction conditions using higher boiling solvents gave unsatisfactory results.) As Table I reveals, this is quite a useful, general procedure for bridgehead methylation. We have applied the reaction not only in the adamantane series, but also to the synthesis of two new compounds, 3-methylhomoadamantane (IV) and 1-methyldiamantane (VI).[8]

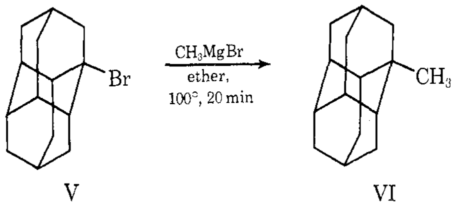


Ia, R' = H
b, R' = CH_3

IIa, R = CH_3; R' = H
b, R = R' = CH_3
c, R = C_2H_5; R' = H
d, R = *tert*-C_4H_8; R' = H
e, R = $CH_2C_6H_5$; R' = H



III IV



V VI

The utility of the procedure was further illustrated by the preparation of 1-methyladamantane (IIa) labeled in the methyl group with ^{13}C and separately with ^{14}C. In these cases it was not possible to use the optimum conditions (large excess of Grignard reagent), but the yields were still satisfactory (64%). It was demonstrated in both instances that no rearrangement occurred; the isotopic labels were found to be exclusively in the methyl groups. The Kuhn–Roth oxidation[9] of 1-methyladamantane-methyl-^{14}C (specific activity 0.34 nCi/mg C) yielded acetic acid isolated as the thallous salt[10] (specific activity 1.83 nCi/mg C). This corresponds to 97.1% of the activity in the starting 1-methyladamantane. The Schmidt degradation of the TlOAc gave inactive CO_2 and methylamine with all of the activity. The mass spectrum of 1-methyladamantane-methyl-^{13}C exhibited the same (M + 1)/M ratio 136/135 (corresponding to adamantyl-^{13}C/adamantyl) as unlabeled 1-methyladamantane. This confirms the suggestion that alkyladamantanes cleave preferentially by loss of the alkyl substituents.[11]

The methylation yields with the bridgehead bromides, Ia, Ib, III, and V, are much better than those reported in the literature for other *tert*-alkyl halides.[7] This provides another instance where the chemistry at the bridgehead of polycyclic bridged ring systems is much cleaner due to the inhibition of competing reactions.[2,17] Ordinary *tert*-halides give elimination byproducts with Grignard reagents;[7] elimination is not possible with adamantane and the other bridged ring systems studied; and yields of coupling products are enhanced as the result.

Other alkyl groups besides methyl may also be introduced, but the yields are not so good (Table I).[12-16] With the higher Grignard reagents, the coupling reaction must compete with Grignard reduction, and considerable adamantane is formed as by-product. When Ia was treated with *tert*-butylmagnesium bromide, only adamantane (the reduction product) was formed (84% yield). However, reasonable yields of 1-ethyladamantane (IIc) and 1-benzyladamantane (IIe) were achieved.

We believe the alkylation method reported here has considerable potential, especially with polycyclic "cage" molecules.

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TABLE I
PRODUCTS OF THE COUPLING REACTION OF 1-BROMOADAMANTANES WITH GRIGNARD REAGENTS

Starting material	Grignard reagent, *M* (ethyl ether soln)	Molar ratio, RMgX/I	Coupling product, yield	Yield of adamantane[h]
Ia	CH_3MgBr, 3	3.2	IIa, 83%[a]	
Ia	CH_3MgI, 1.5	1.5	IIa, 70%[b]	
Ib	CH_3MgBr, 3	3.7	IIb, 92%[c]	
Ia	C_2H_5MgBr, 2	7.2	IIc, 39%[d]	36%[g]
Ia	*tert*-C_4H_9MgBr, 2	5.4	IId, 0%[e]	84%
Ia	$C_6H_5CH_2MgBr$, 2	2.0	IIe, 38%[f]	48%[g]
III[k]	CH_3MgBr, 3	3.5	IV, 87%[i]	
V[l]	CH_3MgBr, 3	3.5	VI, 90%[j]	

[a] Mp 102–103° (lit.[5a] mp 103°). [b] Mp 101–103°. 1-Iodoadamantane was formed in *ca.* 10% yield, mp 74–76° (lit.[12] mp 75.3–76.4°). [c] Bp 82° (13 mm) [lit.[5b] bp 88–89.5° (19 mm)]. [d] Separated by glc; nmr spectrum identical with literature.[3] [e] For a method of preparation of IId, see ref 13. [f] Mp 42–44° (lit.[14] mp 43–44°). [g] Yields by glc. [h] Reduction product; see text. [i] Mp 109–111°. [j] Mp 215–218°. See ref 8. [k] Reference 15. [l] Reference 16.

Experimental Section

General Procedure.—A high pressure aerosol glass bottle (Fischer and Porter Co.) was charged with 10 mm of the bromoadamantane (Ia or Ib[18]) and the quantities of the Grignard reagents are given in Table I. (It is important to use concentrated reagents. Lower yields are obtained with lower concentrations.) In the case of CH_3MgBr, commercial (Arapahoe Chemicals) reagent was used; otherwise the Grignard solutions in ethyl ether were prepared in the usual manner. The bottle was flushed with nitrogen and closed tightly. The reaction mixture was stirred magnetically while being heated in an oil bath at 90–100°. After about 10 min of heating, a white precipitate typically was observed; the total heating time was 20–30 min. After cooling, 20 ml of pentane was added and the excess Grignard reagent destroyed by cautious addition of 2% aqueous HCl at 0°. The layers were separated; the aqueous one was extracted with three 10-ml portions of pentane. The combined organic solutions were washed with 20 ml of 10% aqueous K_2CO_3, two 20-ml portions of water, and then dried over Na_2SO_4. After evaporation of the solvent through a Vigreux column, the product was isolated in an appropriate manner: sublimation *in vacuo* (IIa), distillation *in vacuo* (IIb), or preparative gas chromatography (20 ft × 0.25 in. 15% Carbowax 20M at 177°) (IIc and IIe). Table I provides further details. The identity of the products was confirmed by nmr and mass spectroscopy.[11,12]

Summary of Other Experiments. A. Refluxing Solvents.—Reaction of Ia with excess methylmagnesium bromide in refluxing ether solution gave only 13% IIa after 5 hr and 20% after 18 hr. If the ethyl ether was replaced by adding tetrahydrofuran and distilling off the lower boiling solvent, no IIa was observed after 50 min. A similar experiment employing dioxane in place of tetrahydrofuran led to the formation of a precipitate; refluxing this heterogenous mixture (after removal of ethyl ether) gave only 16% IIa in addition to unreacted starting material.

When 1-bromoadamantane (Ia) was refluxed with a 4 molar excess of methyllithium in ethyl ether, 1-methyladamantane (IIa) formed very slowly. The yields follow: after 2 days, 7%; 3 days, 14%; 5 days, 20%. The only other compound detected was starting material.

B. Use of $FeCl_3$ in Attempted Preparations of IId.—These reactions were carried out at *ca.* −65°.[19] Three attempts were made: anhydrous $FeCl_3$ (Fisher Scientific Co.) was dissolved in the ether solution of *tert*-C_4H_9MgBr and then Ia in ether added, $FeCl_3$ was added together with Ia to the Grignard solution, and $FeCl_3$ was added to the solution of Ia in the Grignard reagent. In no case did the nmr spectrum of the product show any significant formation of 1-*tert*-butyladamantane (IId).[13]

1-Methyladamantane-methyl-^{14}*C*.—1-Methyladamantane-methyl-^{14}*C* (specific activity 0.34 nCi/mg C) was obtained in 64% yield following the general procedure described above. Grignard reagent, prepared from 5.6 g (32 mmol) of $^{14}CH_3I$ (specific activity 3.80 nCi/mgC) and 730 mg (30 mg-atoms) of magnesium turnings in 20 ml of anhydrous ether, and 1-bromoadamantane (4.3 g, 20 mmol) were stirred at 100° for 30 min, followed by the usual isolation procedure.

The product was subjected to the Kuhn–Roth oxidation following the reported procedure.[9a] The acetic acid (isolated as thallous salt)[10] had a specific activity of 1.83 nCi/mg C. The Schmidt degradation[9b] of the TlOAc gave inactive CO_2 and methylamine which was assayed as *N*-phenyl-*N′*-methylthiourea (specific activity 0.46 nCi/mg C corresponding to 100.5% of the activity in the TlOAc).

1-Methyladamantane-methyl-^{13}*C*.—1-Methyladamantane-methyl-^{13}*C* was prepared as described for 1-methyladamantane-methyl-^{14}*C* using $^{13}CH_3I$ (70% ^{13}C). The (M + 1)/M ratio 151/150 (corresponding to 1-methyladamantane-^{13}*C*/1-methyladamantane) showed 71% of ^{13}C labeled molecules. The (M + 1)/M ratio 136/135 (corresponding to adamantyl-^{13}*C*/adamantyl) was found to be essentially the same as that of unlabeled 1-methyladamantane.

1-Benzyladamantane (**IIe**).—This compound had been prepared in the literature by a different route, but no spectral details were provided.[14] The mass spectrum shows a pattern characteristic of 1-alkyladamantane: the ring signal for the adamantyl cation (*m/e* 135) was the most intense. In addition, a strong molecular ion peak (*m/e* 226) and a strong peak from the benzyl group (*m/e* 91) were observed. Nmr spectrum in $CDCl_3$ showed C_6H_5 (m, δ 7.4–6.9, 5 H), $C_6H_5\mathbf{CH_2}$ (s, 2.39, 2 H), adamantyl bridgehead protons (broad s, 1.9 3 H), adamantyl methylene protons (m, 1.4–1.7, 12 H).

3-Methylhomoadamantane (**IV**).—This compound was prepared from 3-bromohomoadamantane (III)[15] in 87% yield following the general procedure (above): mp 109–111°; nmr (15% in $CDCl_3$) $\mathbf{CH_3}$ (s, δ 0.90, 3 H), the remainder of homoadamantane spectrum[20] appearing in the range δ 1.3–2.2 17 H; mass spectrum *m/e* 149 (base peak, $M^+ - CH_3$), 164 (M^+).

Anal. Calcd for $C_{21}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.46; H, 12.02.

1-Methyldiamantane (**VI**).[8]—1-Methyldiamantane[8] was prepared in 90% yield from 1-bromodiamantane[16] following the general procedure: mp 215–218°; nmr (~15% in $CDCl_3$) $\mathbf{CH_3}$ (s, δ 0.93, 3 H), the remainder of the spectrum, δ 1.25–2.35, 19 H; mass spectrum *m/e* 187 (base peak, $M^+ - 15$), 202 (M^+).

Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96 Found: C, 89.32; H, 11.08.

Registry No.—IIe, 7131-11-5; IV, 26460-75-3; VI, 26460-76-4.

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Anomalous Nitration in the 2,1,3-Benzothiadiazole Series

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Although examples of the replacement of nuclear bromine by a nitro group during nitration of aromatic bromo compounds have been known for several

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