unavoidable experimental uncertainty, it is evident that the four *exo–endo* rate ratios are essentially constant. Certainly, there is no change in the *exo–endo* rate ratio of the magnitude one might have predicted for the major decrease in carbon participation which should have accompanied the introduction of a highly stable tertiary benzylic carbonium center at position 2.

The results are clearly more consistent with the steric explanation than that based on carbon participation. However, we prefer to establish the effect of substituents in the aromatic ring before reaching a final decision.

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Stereochemistry of the Grignard Reagents from *exo*- and *endo*-Norbornyl Chlorides

Sir:

Sauers and Kwiatkowski[1] have recently proposed that the Grignard reagent prepared from *exo*-norbornyl bromide was a rapidly equilibrating mixture of *exo* and *endo* isomers. This postulate was based on the observation that carbonation of the reagent from the *exo*-norbornyl bromide gave a mixture of *exo* and *endo* acids whose ratio depends on the temperature of carbonation. In order to study the nature of the norbornyl Grignard reagent we have examined the proton nmr spectra of the Grignard reagents prepared from both *exo*- and *endo*-norbornyl chlorides as a function of temperature.[2]

The *exo*-norbornyl chloride was prepared by the addition of hydrogen chloride to norbornene[3] while the *endo*-norbornyl chloride was prepared by catalytic hydrogenation of a 10:90 mixture of *exo*- and *endo*-5-chloro-2-norbornenes[4] and then solvolysis of the resulting mixture of chlorides in 80% ethanol–water to remove the *exo* isomer. The Grignard reagents were prepared from triply sublimed magnesium[5] in nmr tubes which had been adapted so that a small rubber serum bottle cap allowed: first, the evacuation of the tube containing the magnesium, and then the addition of the ethyl ether, halide, and an internal standard.[6] After the Grignard had been prepared the tubes were centrifuged so that the excess magnesium and traces of magnesium hydroxide would be trapped in the inside of the serum cap. The spectra were recorded on a Varian A-60 variable temperature nmr spectrometer.

The spectra of the Grignard reagents were identical whether prepared from the *exo* or *endo* chlorides. At 25°, two high-field multiplets were observed, one at τ 9.88 and the other at τ 10.32. If one assigns the low-field multiplet to the hydrogen on the carbon bearing the magnesium atom in the *endo* configuration and the higher field multiplet to the corresponding proton on the *exo* Grignard reagent by analogy with other *exo–endo* pairs of norbornyl compounds, then the difference in position for the *exo* proton of *endo*-norbornyl chloride and the *exo* proton of *endo*-norbornyl Grignard is 4.06 ppm. The difference for the *endo* proton of *exo*-norbornyl chloride and the *endo* proton of *exo*-norbornyl Grignard is 4.14 ppm. This difference in effective magnetic shielding is consistent with the value of 4.19 ppm we have observed in going from ethyl chloride to the corresponding ethyl Grignard reagent, lending support to our assignments. The difference in position of the two norbornyl Grignard high-field multiplets, 0.44 ppm, is also consistent with the corresponding difference for a large number of *exo–endo* pairs of norbornyl compounds, 0.40 to 0.48 ppm.

The integration of the area under each of the high-field multiplets was essentially independent of the temperature, −40 to +80°. The average integration for several different samples of the Grignard reagent prepared from the *endo*-norbornyl chloride indicated 54% *endo* and 46% *exo* norbornyl Grignard. A similar average for the reagent prepared from the *exo* chloride indicated a composition of 53% *endo*- and 47% *exo*-norbornyl Grignard reagents. The addition of up to $^3/_4$ mole of water or carbon dioxide per mole of Grignard did not affect the high-field proton splitting pattern or the relative integrations of these peaks but did lower the absolute area of each. If we accept Sauers' proposal, to explain the varying ratios of products, that carbon dioxide reacts faster with the *exo*-norbornyl Grignard than with the *endo*, then these reagents must reequilibrate before the nmr spectrum is taken after the addition of the water or carbon dioxide. On this basis, the isomerization at room temperature must be relatively rapid on a laboratory time scale, 0.5 hr.

The high-field, τ 10.32, multiplet assigned to the *endo* proton of the *exo*-norbornyl Grignard reagent is very similar to the multiplet of the corresponding proton of *exo*-norbornyl chloride. This τ 10.32 multiplet is the X portion of an AA′MX system. First-order analysis[7,8] yielded the nonzero coupling constants for the spin–spin interactions of J_{AX} = 9.6, $J_{A'X}$ = 7.5, J_{MX} = 2.3 cps. The lower field, τ 9.88, multiplet assigned to the *exo* proton of the *endo*-norbornyl Grignard reagent appears more complex, as does the *exo* proton of *endo*-norbornyl chloride. First-order analysis indicated that this nine-line multiplet (intensities 1,2,2,2,2,2,2,2,1) is the X portion of an ABMNX system where the coupling constants are J_{AX} = 13.2, J_{BX} = 6.6, J_{MX} = 3.3, and J_{NX} = 3.3 cps.

Not only are the relative intensities of the two high-field multiplets constant when the temperature is varied, but there was no indication of broadening of the multiplets as the temperature was lowered or raised. This can be interpreted as evidence that the *exo* and *endo* forms of the Grignard reagent are not rapidly isomerizing on an nmr time scale. This is in agreement with Roberts' conclusions for secondary Gri-

(1) R. R. Sauers and G. T. Kwiatkowski, *J. Org. Chem.*, **27**, 4049 (1962).
(2) E. A. Hill has recently published a related study (*ibid.*, **31**, 20 (1966)).
(3) L. Schmerling, *J. Am. Chem. Soc.*, **68**, 195 (1946).
(4) J. D. Roberts, W. Bennett, and R. Armstrong, *ibid.*, **72**, 3329 (1950).
(5) We are grateful to the Dow Chemical Co. for a generous gift of triply sublimed magnesium used in these investigations.
(6) The τ values were calculated using the methyl proton of toluene at τ 7.67 as the internal standard inasmuch as tetramethylsilane interfered with the measurements.
(7) P. L. Corio, *Chem. Rev.*, **60**, 363 (1960).
(8) Coupling constants were measured on a Varian HA-100 spectrometer. We are indebted to Dr. D. Hollis for running these spectra.

gnards,[9] based on the nonequivalence of methyl groups somewhat distant from the carbon atom bearing the magnesium atom. From the width of the lines we can estimate that the *exo–endo* isomerization reaction half-life time is greater than 0.5 sec.

Acknowledgment. We are grateful for support of this research by a Frederick Gardner Cottrell Grant from the Research Corporation.

(9) G. M. Whitesides and J. D. Roberts, *J. Am. Chem. Soc.*, 87, 4878 (1965).

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Characterization of Functional Groups by Nuclear Magnetic Resonance. I. Classification of Alcohols from the Fluorine-19 Spectra of Trifluoroacetates[1]

Sir:

We wish to describe an nmr scheme for classification of hydroxyl compounds which in our hands has generally proved to be more reliable and informative than other recently described nmr techniques.[2]

Because a number of functional groups can be acetylated, we initially considered that the acetate group might be a useful nmr probe for classification purposes. Unfortunately, the differences in chemical shift between acetate groups of isomeric alcohols are only a few cycles/second and provide no dependable scheme for classification. The fact that ^{19}F chemical shifts are in general about an order of magnitude larger than ^{1}H chemical shifts for a given structural perturbation suggested to us that ^{19}F nmr chemical shifts of the trifluoroacetyl derivatives of alcohols and perhaps amino, mercapto, and phenolic functional groups might provide reliable classification schemes.

Study of the ^{19}F nmr spectra of the trifluoroacetate (TFA) esters of a large number of alcohols revealed that the TFA groups give sharp ^{19}F signals and that the order of shielding is always primary < secondary < tertiary. Figure 1a illustrates this for a mixture of these three classes of alcohols.[3,5] Figures 1b, c, and d show results for mixtures of alcohols, illustrating the general nature of substituent effects on the chemical shift of the TFA group.[6] Figure 1d illustrates a rather

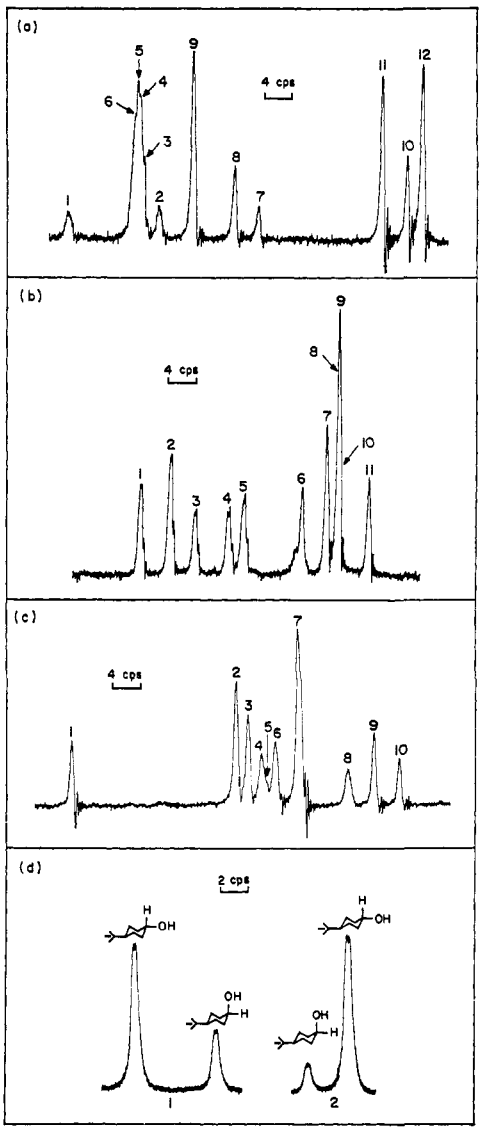

Figure 1. ^{19}F nmr spectra of the trifluoroacetates of some hydroxyl compounds; chemical shifts in parts per million (±0.01) from 10% internal $CFCl_3$ given in parentheses; chemical shifts of overlapping signals determined from more highly resolved spectra of ester mixtures with fewer components. Increasing field to right: (a) 1, CH_3OH (74.21); 2, CH_3CH_2OH (74.43); 3, $CH_3CH_2CH_2OH$ (74.40); 4, $CH_3CH_2CH_2CH_2OH$ (74.39); 5, $(CH_3)_2CHCH_2OH$ (74.38); 6, $(CH_3)_3CCH_2OH$ (74.37); 7, $CH_3CHOHCH_3$ (74.68); 8, $CH_3CHOHCH_2CH_3$ (74.62); 9, $CH_3CH_2CHOHCH_2CH_3$ (74.52); 10, $(CH_3)_3COH$ (75.05); 11, $(CH_3)_2(CH_3CH_2)COH$ (74.99); 12, CF_3CO_2H (75.08) (20% ester mixture in dimethyl sulfoxide). (b) 1, $CH{\equiv}CCH_2OH$ (74.95); 2, $C_6H_5CH_2OH$ (75.02); 3, $CH_2{=}CHCH_2OH$ (75.08); 4, $(CH_3)_3CCH_2OH$ (75.17); 5, $CH_3CH_2CH_2OH$ (75.20); 6, lanosterol (75.35); 7, cholesterol (75.41); 8, cyclopentanol (75.43); 9, cyclohexanol (75.44); 10, cycloheptanol (75.45); 11, $CH_3CHOHCH_3$ (75.52) (15% ester mixture in methylene chloride). (c) 1, C_6H_5OH (73.85); 2, CH_2OHCH_2OH (74.27); 3, $CH_2OHCH_2CH_2OH$ (74.30); 4, $CH_3CHOHCH_2OH$ (74.33); 5, CHF_2CH_2OH (74.34); 6, CF_3CH_2OH (74.37); 7, CH_3CH_2OH (74.43); 8, $CH_3CHOHCH_2OH$ (74.55); 9, $CH_3CHOHCH_2CH_3$ (74.62); 10, $CH_3CHOHCH_3$ (74.68) (20% ester mixture in dimethyl sulfoxide). (d) From two different mixtures of 4-*t*-butylcyclohexanols: 1, *trans* isomer (74.99), *cis* isomer (75.09) (5% in dimethyl sulfoxide); 2, *cis* isomer (76.28), *trans* isomer (76.32) (5% in pentane).

(1) This paper presents results of one phase of research carried out at the Jet Propulsion Laboratory, California Institute of Technology, under Contract No. NAS7-100, sponsored by the National Aeronautics and Space Administration.

(2) See, for example: (a) O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1256 (1964); (b) A. Mathias, *Anal. Chim. Acta*, **31**, 598 (1964); (c) V. W. Goodlett, *Anal. Chem.*, 37, 431 (1965).

(3) All ^{19}F spectra shown here were taken at 56.4 Mc with a Varian HR instrument equipped with the field-frequency lock system described previously.[4] The lock signal was derived from 5 to 10% added 1,1,2,2,-tetrafluoro-1,2-dibromoethane. Other spectra were recorded with a Varian A-56/60.

(4) D. D. Elleman, S. L. Manatt, and C. D. Pearce, *J. Chem. Phys.*, **42**, 650 (1965).

(5) The TFA's were prepared by direct addition of trifluoroacetic anhydride to the alcohols or to the alcohols in an inert solvent followed by removal of excess anhydride and the acid formed either by vacuum or by extraction with dilute aqueous bicarbonate followed by drying. Reaction of primary and secondary alcohols is complete in several minutes. Tertiary and some polyhydroxyl compounds require longer and perhaps more than one treatment with anhydride to achieve complete reaction.

(6) A single electronegative substituent β to the hydroxyl group causes a downfield shift as might be expected on purely inductive grounds (see Figure 1c); the fact that the TFA of 1,1-difluoroethanol is at lower field than that of 1,1,1-trifluoroethanol indicates that simple inductive arguments are invalid here.