

in benzene solution was achieved only with the coupling constants of opposite signs. The spacings between the lines shown in Fig. 1 at 241.7 and 243.7 cps. and 221.9 and 220.7 cps. (Fig. 1) were reduced to 1.4 and 0.1 cps., respectively, at 40 Mc. With coupling constants of the same sign, the computed spacings for these lines were 0.8 and 0.9 cps., respectively.

On the basis of these results, we believe that the relative signs of J_{AC} and J_{BC} must be taken as being indeed different from J_{AB} . Interestingly, this conclusion could only have been reached by treatment of the spin system as ABC_3 , not as the ABX_3 approximation in which a change in the sign of J_{AB} relative to J_{AC} and J_{BC} does not affect the theoretical spectrum.

The results can be regarded as disquieting in two connections. First, the difference in sign between the geminal and vicinal H-H couplings runs counter to the theoretical predictions of Karplus and Gutowsky¹⁰ for substances with normal bond angles. Second, in analogy with the findings of Castellano and Waugh¹¹ for ABC systems, rather different sets of spin-coupling and chemical-shift parameters were found to give nearly identical theoretical spectra for diethyl sulfite in benzene and each of these corresponds amazingly well to the experimental spectrum at 60 Mc. Indeed, the previously mentioned excellent agreement between theoretical and experimental spectra obtained for acetaldehyde diethyl acetal now has been duplicated with $\nu_B - \nu_A = 9.23$ cps., $\nu_C - \nu_A = 146.3$ cps., $J_{AC} = 9.30$ cps. and J_{AC} equal to $J_{BC} = 7.03$ cps. with J_{AB} opposite in sign to J_{AC} and J_{BC} .

Clearly, caution and judgment must be exercised in use of the iterative method of obtaining spin-spin coupling constants since there seems to be no assurance that a "final" solution is truly unique.^{7b,11}

Acknowledgment.—We are deeply indebted to Dr. Stanley L. Manatt and the Computing Center of the Jet Propulsion Laboratory for the IBM 7090 calculations of the theoretical spectra.

(10) H. S. Gutowsky, M. Karplus and D. M. Grant, *J. Chem. Phys.*, **31**, 1278 (1959); M. Karplus, *ibid.*, **30**, 11 (1959).

(11) S. Castellano and J. S. Waugh, *ibid.*, **34**, 295 (1961).

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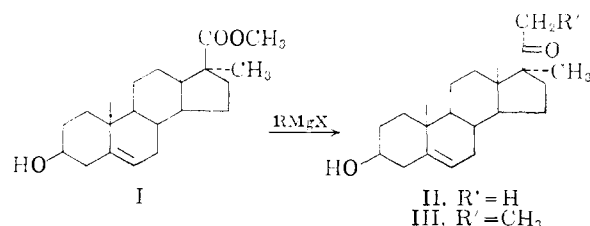
RECEIVED AUGUST 9, 1961

STERICALLY CONTROLLED GRIGNARD REACTIONS. A NEW SIMPLE ROUTE TO 17 α -METHYLATED STEROID ANALOGS

Sir:

We wish to report a convenient new synthesis of 17 α -methylated steroid derivatives which has made possible the preparation of highly active progesterone homologs. When the readily available methyl 3 β -hydroxy-17 α -methyl-5-etenate (I)¹ was refluxed in anisole for one hour in presence of excess methylmagnesium bromide, the corresponding sterically hindered ketone, 17 α -methylpregnenolone II¹ was obtained in 70% yield. The latter substance was converted to the known¹ 17 α -methyl-

(1) Pl. A. Plattner, H. Heusser, P. Th. Herzog, *Helv. Chim. Acta*, **32**, 270 (1949).



progesterone by Oppenauer oxidation. Only about 20% of the "normal" product, the corresponding carbinol 17 α ,20-dimethyl-5-pregnen-3 β ,20-diol, was formed and conveniently separated by chromatography.

Analogously, the 5 α ,6 α epoxide obtained by peracetic acid treatment of I, m.p. 170–171°, $[\alpha]_D - 67.2$, gave in similar yields 3 β ,5 α -dihydroxy-6 β ,17 α -dimethylpregnan-20-one, m.p. 188–192°, which was directly oxidized by chromic acid to the 3,20-dione, m.p. 230–233°, and converted by methanolic sodium hydroxide to 6 α ,17-dimethylprogesterone, m.p. 137–140°, $[\alpha]_D + 90.5$, λ_{max} 239 m μ , $\log \epsilon$ 4.2. The latter substance, and the corresponding 6-dehydro derivative, m.p. 143–146°, $[\alpha]_D + 87.1$, λ_{max} 292 m μ , $\log \epsilon$ 4.4, obtained by chloranil dehydrogenation, were orally at least as active, in the Clauberg test, as 19-nor-17 α -ethynyltestosterone, and twenty times more active than 17 α -methylprogesterone.

NOTE ADDED IN PROOF.—6,17-Dimethyl-6-dehydroprogesterone is as active orally as 6 α -methyl-17-acetoxypregesterone. It is devoid of any androgenic properties.

Treatment of I with ethylmagnesium iodide in anisole gave 17 α ,21-dimethylpregnenolone III, m.p. 145–148°, with no detectable amount of carbinol being formed. Oppenauer oxidation gave 17 α ,21-dimethylprogesterone, m.p. 157–159°, $[\alpha]_D + 107.7$, λ_{max} 241 m μ , $\log \epsilon$ 4.2² in 70% over-all yield. Further transformations of these methylated steroids together with a report on their 6-halogenated derivatives³ will be presented in a more detailed paper.

(2) All rotations in 1% chloroform solution. All new compounds had satisfactory elemental analysis. We are indebted to Dr. G. Papineau-Couture and his associates for the analytical data and to Drs. C. Chappel and C. Revesz for the bioassays.

(3) Prepared by Dr. Y. Lefebvre of these laboratories.

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RECEIVED SEPTEMBER 20, 1961

INERTIAL EFFECTS OF SUBSTITUENTS ON HOT ATOM CAPTURE¹

Sir:

Hot hydrogen atoms can replace hydrogen and other atoms and groups with high collision efficiency.² The course of these reactions has been shown to be largely controlled by steric factors.² However certain results, particularly on alkyl replacement, have not found explanation. This letter reports a remarkable new effect in the hot hydrogen displacement of halogen atoms from

(1) Studies supported by the U. S. Atomic Energy Commission. Contribution No. 1681 from the Sterling Chemistry Laboratory.

(2) D. Urech and R. Wolfgang, *J. Am. Chem. Soc.*, **83**, 2982 (1961). This paper contains references to the earlier literature.

halomethanes. Its interpretation involves recognition of factors that appear to control hot atom substitution of heavy atoms and groups.

High kinetic energy (hot) hydrogen in the form of tritium recoiling from the $\text{He}^3(n,p)\text{T}$ nuclear process was allowed to react with the various fluoro-, chloro- and bromomethanes. The techniques of carrying out such reaction, the suppression of competing thermal processes and the analysis of the tritium-containing products have been described previously.²

The most significant results on the fluoro-methane series are summarized in the table. While replacement of F by T is quite probable in CH_3F , it is much less so in CH_2F_2 , and almost non-existent in CHF_3 and in CF_4 . By contrast replacement of H by T changes much less within this series. Exactly parallel trends appear in the chloro- and bromomethanes.

TABLE I

SINGLE ATOM DISPLACEMENT BY HOT TRITIUM IN FLUORO-METHANES

Reacting fluoro-carbon	Displacement of H		Displacement of F		
	Product	Yield, %*	Product	Yield, %*	
CH_4	CH_3T	28.0	7.0	
CH_3F	CH_2FT	12.7	4.2	CH_3T	5.3
CH_2F_2	CHF_2T	5.8	2.9	CH_2FT	1.6
CHF_3	CF_2T	2.9	2.9	CHF_2T	0.7
CF_4	CF_3T	0.3

* Relative to total T reacting.

This phenomenon may be understood by considering the reactive collision in detail. Hot hydrogen displacement of a hydrogen atom has been discussed previously: The impinging hot atom approaches in a direction approximately normal to the C-H bond and, on collision, ejects the bound hydrogen with a velocity comparable to that of its own approach. It can thus occupy the same position held by the ejected atom and be bound by the existing orbital (see Fig. 1, AI-AIII). Variations in probability of C-H bond displacement (as in Table I) can be accounted for on the basis of steric hindrance to approach by neighboring atoms or groups.²

A model of hot hydrogen displacement of a fluorine atom cannot be as simple. The hot atom approaching the C-F bond at an approximately normal angle can on collision break it, largely by displacing the binding electrons, thus greatly weakening the bond, and also by imparting a major fraction of its momentum to the fluorine. However, the comparatively large inertial mass of the fluorine causes it to move out only slowly, thus preventing the incident hydrogen from immediately occupying its position in space (see Fig. 1, BI-BII). As a result, the hot hydrogen will be far off the tetrahedral angle for sp^3 binding and is only very weakly bound to the carbon. It would therefore tend to recoil from this position of high potential energy and be captured by the fluorine or escape as a free atom. The C-T bond can, however, be strengthened and the tritium retained as the whole molecule turns, thus reestablishing tetrahedral binding.³ Such

(3) Contrary to a possible intuitive impression, significant rotation of the CH_3 "away" from the tritium is not induced by the collision

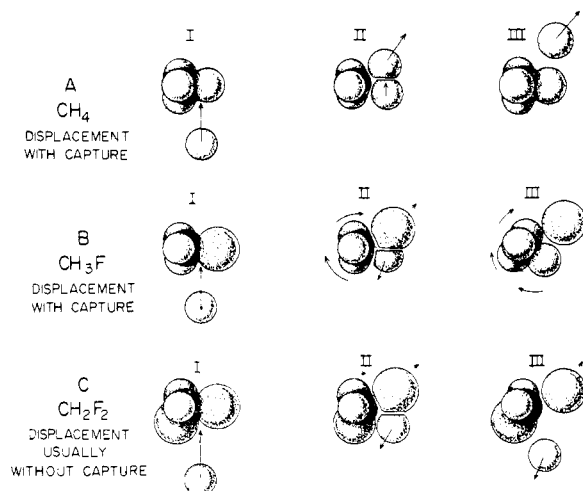


Fig. 1.—Effect of substituent mass on orbital availability for hot atom capture: results of hot hydrogen attack on substituted methanes. The length of the arrows represents relative velocity. Possible capture by the fluorine atom is not indicated.

rotation must be completed in the order of 10^{-14} sec.—the time required for a 1 e.v. T atom to move 1 Å. The corresponding rotational energy of a CH_3 group is a few e.v.—an energy that becomes available by forming a strong C-T bond. Actually this rotation also can be described as a restoring bending motion of the CH_3 relative to the T. A coupling mechanism for inducing rapid rotation therefore exists and the T atom can be captured on fluorine displacement in CH_3F (see Fig. 1, BIII).⁴ This is confirmed by the data.

By contrast if the residual group has heavy substituents in addition to that being displaced its much greater moment of inertia will preclude rapid rotation to strengthen the C-T bond (see Fig. 1, CI-CIII). Such rotation would require of the order of tens of e.v. and there is no efficient mechanism of providing this much energy. As a result attack on a C-F bond in CH_2F_2 , CHF_3 and CF_4 is unlikely to result in capture of the hot atom by the fluoromethyl group. The low efficiency of halogen displacement in all polysubstituted methanes thus follows naturally.

The model formulated provides an explanation of the earlier and unexplained observation² that recoil tritium attack on a C-C bond invariably results in the favored capture of the hot hydrogen by the simpler radical. Thus neopentane yields eight times as much CH_3T as $(\text{CH}_3)_3\text{CT}$.² On rupture of the C-C bond the smaller group can rotate more rapidly to establish a strong bond and is thus favored in the competition for capture of the hot atom. A critical experiment was carried out on $\text{H}_3\text{C-CF}_3$ to test this hypothesis as against two itself. If in colliding with the C-F bond, a 5 e.v. T atom yields half its momentum to the carbon, the C atom thus acquires approximately 0.3 e.v. Nearly all this energy is translational, less than 0.1 e.v. being in rotation about the center of mass of the CH_3 . This is insignificant on the time scale of the collision and negligible compared to the restoring bending force if a C-T bond is formed.

(4) The tritium atom (Fig. B1, 2) will also tend to insert by directly pushing apart the C and F atoms. This vibrational stretching relaxation is too slow to be very effective; the inertial effects are therefore considered to be primarily, though not purely, rotational.

others.² An explanation based on steric obstruction would predict a ratio $\text{CH}_3\text{T}/\text{CF}_3\text{T}$ smaller than that of $\text{CH}_3\text{T}/\text{C}(\text{CH}_3)_3\text{T}$ from neopentane; and one based on bond strength would predict that $\text{CH}_3\text{T}/\text{CF}_3\text{T}$ be unity since the strengths of the $\text{CH}_3\text{-T}$ and $\text{CF}_3\text{-T}$ bonds are virtually equal. The experiments showed a ratio $\text{CH}_3\text{T}/\text{CF}_3\text{T}$ in excess of twenty, confirming the present model.

Competition for capture of the hot atom is thus controlled by the same factor in attack on both C-C and C-X bonds: The availability of a strong bonding orbital within the time of collision, where this is governed by the inertia of the substituents on the central atoms. This principle should be completely general for hot atom reactions but has no counterpart in thermal processes.

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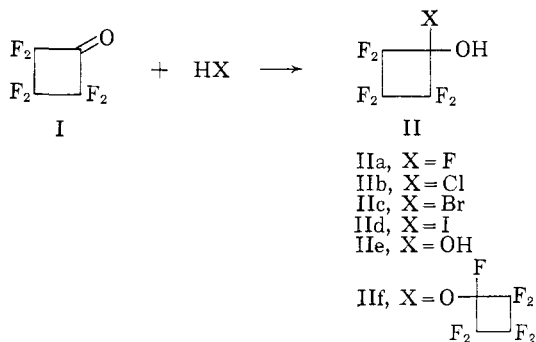
ROBERT ODUM
RICHARD WOLFGANG

NEW HAVEN, CONNECTICUT
RECEIVED SEPTEMBER 16, 1961

α -HALOALCOHOLS

Sir:

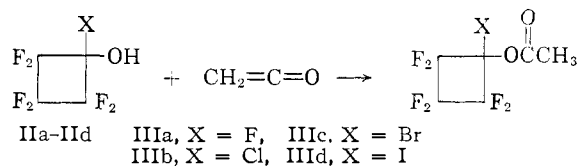
We wish to report the first preparation and *isolation* of certain α -haloalcohols in pure form, and to describe some studies of hydrogen bonding in these systems. Hexafluorocyclobutanone (I), an



extraordinarily reactive ketone,^{1a} reacts rapidly at low temperatures with hydrogen halides^{1b} to give the distillable α -haloalcohols IIa-IId in high yields. Thus, equimolar quantities of I and hydrogen fluoride were condensed in an evacuated Monel vessel at -195° . After allowing the mixture to warm to $+20^\circ$, distillation in a nitrogen atmosphere through a thoroughly dry glass column gave a 75% yield of heptafluorocyclobutanol (IIa), b.p. $57\text{--}58^\circ$ (some dec.); b.p. 6° (85 mm.); Found: C, 24.6, 24.6; H, 0.7, 0.7; infrared O-H stretching absorption at 3550 and 3450 cm^{-1} (shoulder); H^1 n.m.r., singlet at 5.52τ (internal reference). IIa reacts vigorously and quantitatively with water to liberate HF and form hexafluorocyclobutanone hydrate (IIe),¹ also accessible *via* the addition of water to I. When two equivalents of I were combined with one equivalent of hydrogen fluoride as described above, an 80% yield of the hemiketal II f, b.p. -21° (0.05 mm.), was obtained. *Anal.* Found: C, 25.7; H, 0.5; F, 65.6; infrared O-H stretching absorption at 3570 (sharp) and 3340 cm^{-1}

(1) (a) D. C. England, *J. Am. Chem. Soc.*, **83**, 2205 (1961). (b) S. Andreades and D. C. England, Abstracts, 140th Meeting of the American Chemical Society, September, 1961, p. 14-M.

(shoulder). Reaction of IIa with ketene occurs exothermically to give 24% of heptafluorocyclobutyl acetate (IIIa), b.p. $99\text{--}101^\circ$. *Anal.* Found: C, 30.1; H, 1.4; F, 55.2.



In a similar manner, the alcohols IIb-IId were prepared by the addition of the appropriate hydrogen halide to I in 73-90% yields and these alcohols were converted to the corresponding acetate IIIb-III d in 38-81% yields. Consistent elemental analyses, infrared, F^{19} and H^1 n.m.r. spectra were obtained for all of the products described.²

In the absence of moisture, all of the alcohols were reasonably stable on storage except IId which slowly liberated iodine. At elevated temperatures, the equilibrium becomes unfavorable and the alcohols revert to some extent to ketone and hydrogen halide. This is a particular problem with IIa in glass apparatus since prolonged heating will consume HF (shifting the equilibrium to the left) and reaction of HF with glass produces water which also attacks the alcohol.

Ketones and hydrogen halides ordinarily do not give stable addition compounds.^{3,4} Vorländer obtained some unstable ketone-hydrogen halide complexes³ but the presence or absence of alcohol or ketone functions in these materials was not established. In general, 1,1-halohydrins cannot be isolated in pure form because of the rapid establishment of the addition-elimination equilibrium.⁶ For example, 2-chloro-2-propanol cannot be isolated from an acetone-HCl mixture⁵ although 1:1 and 1:2 acetone:HF nondescript complexes were reported in 1883.⁶

Previous attempts to prepare perfluorinated α -fluoroalcohols have been unsuccessful,^{7,8} although one example of an α -fluoroalcohol, monofluoromethanol, has been reported.⁹

Neither ring strain factors nor fluorine substitution adjacent to the carbonyl function, *alone*, can account for the stability of these α -haloalcohols relative to the ketones since neither α -fluorocyclo-

(2) Difficulties were encountered in obtaining good analytical values for IId. These data will appear in a future publication.

(3) D. Vorländer, *Ann.*, **341**, 15 (1905).

(4) W. Hückel, "Theoretical Principles of Organic Chemistry," Vol. I, Elsevier Publishing Co., New York, N. Y., 1955, p. 582.

(5) D. J. Cram and G. S. Hammond, "Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 269.

(6) M. Londolf, *Bull. Soc. Chim.*, **40**, 302 (1883).

(7) (a) J. Banus, H. J. Emeleus and R. N. Haszeldine, *J. Chem. Soc.*, 60 (1951). For example, attempts to prepare the primary CF_3OH from CF_3I produced fluoroform: $\text{CF}_3\text{I} + \text{KOH} \rightarrow \text{CF}_3\text{H} + \text{KOI}$. (b) R. N. Haszeldine and H. J. Emeleus, *Research*, **1**, 715 (1948). (c) R. N. Haszeldine and A. G. Sharpe, "Fluorine and Its Compounds," Methuen and Co., Ltd., London, 1951, p. 92. (d) W. H. Pearson in J. H. Simons, "Fluorine Chemistry," Vol. I, Academic Press, Inc., New York, N. Y., 1950, p. 483.

(8) A. M. Lovelace, D. A. Rausch and W. Postelnek, "Aliphatic Fluorine Compounds," Reinhold Publishing Corp., New York, N. Y., 1958, p. 137.

(9) Gy. Olah and A. Pavlati, *Acta Chim. Acad. Sci., Hungary*, **3**, 203 (1953), report a reduction in ether

