spectra identical with an authentic sample[17,18]. Progesterone (12) was obtained in 40% overall yield by a similar reaction sequence from 5α-pregnane-3,6,20-trione.

1, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ O; $R_4 = $ H; $\Delta^{9(11)}$

2, $R_1 = R_3 = $ O; $R_2 = H_2$; $R_4 = $![]---H; $\Delta^{4(5)}$

3, $R_1 = R_3 = R_4 = $ O; $R_2 = H_2$; $\Delta^{4(5)}$

4, $R_1 = R_3 = $ O; $R_2 = H_2$; $R_4 = $ H; $\Delta^{4(5)}$ and $\Delta^{9(11)}$

5, $R_1 = R_2 = R_3 = $ O; $R_4 = $ H; $\Delta^{9(11)}$

6, $R_1 = $![]---H; $R_2 = $ H; $R_3 = $ O; $R_4 = H_2$; $\Delta^{5(6)}$

7, $R_1 = $![]---OMe; $R_2 = R_3 = $ O; $R_4 = $ H; $\Delta^{9(11)}$

8, $R_1 = $![]---OMe; $R_2 = $![]---H; $R_3 = $ O; $R_4 = $ H; $\Delta^{9(11)}$

9, $R_1 = $![]---OMe; $R_2 = $![]—H; $R_3 = $ O; $R_4 = $ H; $\Delta^{9(11)}$

10, $R_1 = R_3 = $ O; $R_2 = $![]---H; $R_4 = $ H; $\Delta^{9(11)}$

11, $R_1 = R_3 = $ O; $R_2 = H_2$; $R_4 = $ H; $\Delta^{4(5)}$ and $\Delta^{9(11)}$

12, $R_1 = R_3 = $ O; $R_2 = R_4 = H_2$; $\Delta^{4(5)}$

13, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ (ethylene ketal); $R_4 = H_2$

13a, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ (ethylene ketal); $R_4 = H_2$

14, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ O; $R_4 = H_2$

15, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ O; $R_4 = $ H; $\Delta^{9(11)}$

16, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ O; $R_4 = H_2$; $\Delta^{14(15)}$

17, $R_1 = $![]---H; $R_2 = $![]—H; $R_3 = $ O; $R_4 = H_2$; $\Delta^{14(15)}$

The recently published procedure for remote group functionalization[19] suggested a simple synthesis of the starfish sterol 1 as a final step in its structure proof. The 20-ethylene ketal[20] of pregnenolone acetate (6) was treated with diborane in THF followed by alkaline hydrogen peroxide oxidation to give, in 60% yield, 13

(17) C. W. Shoppee and T. Reichstein, Helv. Chim. Acta, 24, 351 (1941).
(18) L. H. Knox, E. Velarde, S. Berger, D. Cuadriello, and A. D. Cross, J. Org. Chem., 29, 2187 (1964).
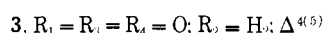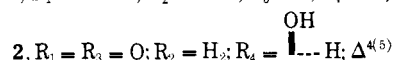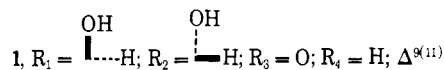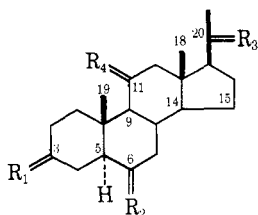(19) R. Breslow, J. A. Dale, P. Kalicky, S. Y. Liu, and W. N. Washburn, J. Amer. Chem. Soc., 94, 3276 (1972).
(20) W. J. Adams, D. K. Patel, V. Petrow, I. A. Stuart-Webb, and B. Sturgeon, J. Chem. Soc., 4490 (1956).

[m/e 363 (M+ − CH₃); mp 205–207° (needles from aqueous methanol); $[\alpha]^{22}$D (CHCl₃) +29.5°; λ_{max} (KBr) 3400 cm⁻¹; nmr (60 MHz, CDCl₃) C-18 CH₃, 0.76 (s, 3 H), C-19 CH₃, 0.82 (s, 3 H), C-21 CH₃, 1.26 (s, 3 H), carbinol methines, 3.13–4.00 (c, 2 H) shifted to 4.40–5.0 in the diacetate 13a, cyclic ethylene ketal methylene, 3.90 (c, 4 H)], which on acetylation furnished the diacetate 13a [mp 165–167° (needles from aqueous methanol); $[\alpha]^{21}$D (CHCl₃) +31.01°; λ_{max} (KBr) 1717–1735 cm⁻¹]. Treatment of 13a with iodobenzene dichloride yielded a crude product containing the 9α-chloro derivative which was directly dehydrochlorinated with silver perchlorate in acetone. Preparative thin layer chromatography of the resulting mixture (50% yield) on 20% AgNO₃ impregnated silica gel led to three products. In order of elution these were 5α-pregnane-3β,6α-diol-20-one diacetate (14) (30%, identical with a sample prepared from its ketal 13a); 5α-pregn-9(11)-ene-3β,6α-diol-20-one diacetate (15) [37%, identical (gc, ir, nmr, and mass spectra) with natural[1] starfish genin diacetate]; and 16 [33%, M+ 416 (100%); nmr (60 MHz, CDCl₃) C-18 CH₃, 0.85 (s, 3 H), C-19 CH₃, 0.90 (s, 3 H), C-21 CH₃, 2.13 (s, 3 H), two acetates, 2.03 (s, 6 H), two acetate methines, 4.40–5.0 (c, 2 H), and an olefinic proton, 5.13 (c, 1 H)]. Hydrolysis of 15 provided 1 [identical in all respects with the natural[1] starfish genin, $[\alpha]^{21}$D (CHCl₃) +98.7°[1c] which on subsequent oxidation gave the known triketone 5. Saponification of the Δ^{14} isomer 16 led to 17 [mp 198–200° (needles from aqueous ethanol); M+ 332 (100%); nmr (100 MHz, CDCl₃) C-18 CH₃, 0.85 (s, 3 H), C-19 CH₃, 0.87 (s, 3 H), C-21 CH₃, 2.16 (s, 3 H), 17α-H, 2.90 (c, 1 H), two carbinol methines, 3.40–3.80 (c, 2 H), and an olefinic proton, 5.19 (c, 1 H)]. The mass spectrum of 17 displayed important peaks at m/e 317 (M+ − CH₃), 314 (M+ − H₂O), 299 (314 − CH₃), 289 (M+ − C₂H₃O), 281 (299 − H₂O), 271 (314 − C₂H₃O), 253 (271 − H₂O), 95 (C₇H₁₁), and 43 (C₂H₃O). The nmr chemical shifts for the C-18 methyl group and the absence of ring D cleavage[21] in its mass spectrum firmly established the position of the double bond.

(21) L. Tökes, G. Jones, and C. Djerassi, J. Amer. Chem. Soc., 90, 5465 (1968); C. Djerassi, Pure Appl. Chem., 21, 205 (1970).
(22) Visiting Postdoctoral Scholar from the University of West Florida, Pensacola, Fla. 32504.

Jerome E. Gurst,[22] Younus M. Sheikh, Carl Djerassi*

Department of Chemistry, Stanford University
Stanford, California 94305
Received October 26, 1972

On Steric Attraction

Sir:

In certain exothermic association reactions there may be an electronic factor favoring formation of the sterically more hindered product. Consider the progress of a model reaction—the recombination of an ethyl cation with an ethyl anion. One likely approach, 1, is sterically unhindered, leading to an anti conformation of butane. Another possible approach, 2, leads to the higher energy eclipsed conformation.
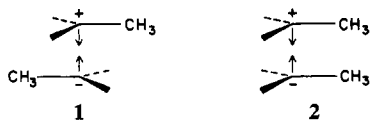
The primary interaction between a cation and an anion is that between the acceptor orbital of the cation, its lowest unoccupied molecular orbital (LUMO), and the highest occupied molecular orbital (HOMO), the donor orbital, of the anion. The LUMO of the ethyl cation and the HOMO of the ethyl anion have the same shape.[1] Hyperconjugative mixing of CH_3 σ and σ^* orbitals of local π symmetry into the carbocation or anion p orbital[2] produces a modified LUMO or HOMO, **3**. The important feature here is delocalization of the
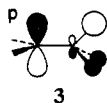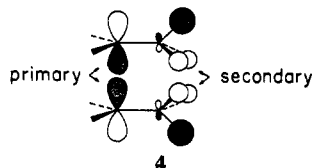
p orbital, with a significant out-of-phase contribution on the methyl hydrogens.[3] When the donor and acceptor approach in conformation **2**, the primary bonding mixing of the p orbitals is reinforced by a secondary, stabilizing interaction of just those sterically encumbered methyl group hydrogens. This is shown in **4**.

The secondary, attractive interaction is important only in the region of distant approach. As the C–C separation diminishes, the rapidly rising closed shell repulsions of interacting occupied CH_3 levels[5] take over and destabilize the eclipsed approach.

The presence of this secondary stabilizing interaction, which had nothing to do with the attractive region of the van der Waals potential or London dispersion forces, has been confirmed in extended Hückel calculations on some model systems. The argument is not dependent on the hypothesis of heterolytic attack, but can be just as well derived for recombining ethyl radicals. The general conclusion is reached that *in highly exothermic association reactions, where the transition state occurs at large separation of reaction partners, the activation energy for the path leading to the sterically more hindered product may be lower.*[6,7]

(1) The carbanion is here assumed to be locally planar. Its likely pyramidalization does not affect the argument.

(2) R. Hoffmann, L. Radom, J. A. Pople, P. v. R. Schleyer, W. J. Hehre, and L. Salem, *J. Amer. Chem. Soc.*, **94**, 6221 (1972), and references therein.

(3) The usual rules of orbital interaction, derived from perturbation theory, apply here (see ref 4). p mixes into itself the σ CH_3 orbital of π symmetry in an antibonding way and the corresponding σ^* orbital in a bonding way. Approximate cancellation at methyl group carbon and reinforcement at the hydrogens follow.

(4) R. Hoffmann, *Accounts Chem. Res.*, **4**, 1 (1971); E. Heilbronner and H. Bock, "Das HMO-Modell und Seine Anwendung," Verlag Chemie, Weinheim, 1968; K. Fukui, *Fortschr. Chem. Forsch.*, **15**, 1 (1970).

(5) J. P. Lowe, *J. Amer. Chem. Soc.*, **92**, 3799 (1970); R. Hoffmann, *Pure Appl. Chem.*, **24**, 567 (1970).
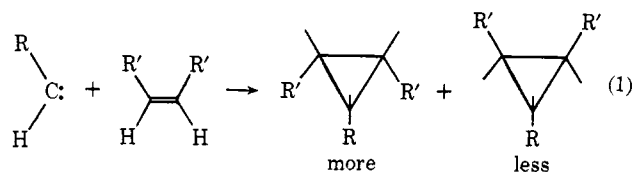
(6) The result is formally similar to the Ingold postulate (C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, p 827), but the rationale is very different. See also G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955); M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **34**, 11 (1938).

The effect we discuss here, which may loosely be called steric attraction, is essentially quantum mechanical and tied to the phases of the interacting wave functions. This point may be reinforced by the following further conclusions, which can easily be derived. In the system **5**, where a double bond is inserted between
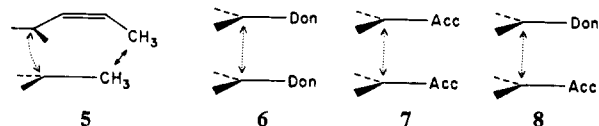
the sterically active CH_3 group and the addition center, the secondary interaction will be destabilizing, repulsive. If the CH_3 group in the model system is replaced by good π donors and acceptors it can be shown that the secondary interaction is stabilizing in **6** and **7**, but destabilizing in **8**. Thus whether the secondary interaction is attractive or repulsive depends on the number of electrons involved—clearly we have at hand still another manifestation of orbital symmetry control.[8,9]

One manifestation of this effect may be the remarkable contrathermodynamic stereoselectivity in the addition of unsymmetrical carbenes to cis-substituted olefins[10,11] (eq 1). The donor in this case is the ethylene π

$$
\begin{array}{c}
\text{R} \\
\diagdown \\
\text{C:} \\
\diagup \\
\text{H}
\end{array}
+
\begin{array}{c}
\text{R}' \quad \text{R}' \\
\diagup \quad \diagdown \\
\text{H} \quad \quad \text{H}
\end{array}
\rightarrow
\underset{\text{more}}{\text{R}'\text{—}\triangle\text{—R}'}
+
\underset{\text{less}}{\text{R}'\text{—}\triangle\text{—R}'} \quad (1)
$$

orbital and the acceptor is the empty p orbital of the carbene.[12] The secondary interaction hypothesis can also rationalize the reversed addition selectivity of carbenes substituted by π acceptors.[10d] There are alternative explanations of the stereoselectivity of carbene addition invoking dispersion forces or secondary electrostatic interactions,[10,13] and perhaps all of these factors combine to give the observed contrathermodynamic stereoselectivity. The secondary electrostatic explanation, for example, is well suited to explain the substituent-selectivity trends observed with aryl and heteroatomic carbenes,[10d] and could be superimposed on the fundamental attraction described here.

There are a number of other kinetically controlled reactions in which steric attraction may be important.[14]

(7) In very low activation energy reactions we expect the effect will be primarily dynamic; that is, the product distribution will be determined by the shape of the potential energy surface. See also P. S. Skell and M. S. Cholod, *J. Amer. Chem. Soc.*, **91**, 7131 (1969).

(8) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969), and references therein.

(9) Some of the ideas outlined here were anticipated by R. Hoffmann and R. A. Olofson, *J. Amer. Chem. Soc.*, **88**, 943 (1966). They are also implicit in the independent work of N. D. Epiotis, *ibid.*, in press, and in part in R. Sustmann and G. Binsch, *Mol. Phys.*, **20**, 9 (1971).

(10) (a) G. L. Closs, R. A. Moss, and J. J. Coyle, *J. Amer. Chem. Soc.*, **84**, 4985 (1962); (b) G. L. Closs and R. A. Moss, *ibid.*, **86**, 4042 (1964); (c) G. L. Closs, *Top. Stereochem.*, **3**, 193 (1968); (d) a comprehensive summary of the work in this area is given by R. A. Moss in "Selective Organic Transformations," Vol. I, B. S. Thyagarajan, Ed., Wiley, New York, N. Y., 1970, p 35ff.

(11) An explanation similar to ours has been given by T. Fueno, S. Nagase, K. Tatsumi, and K. Yamaguchi, *Theor. Chim. Acta*, **26**, 43 (1972).

(12) P. S. Skell and A. Y. Garner, *J. Amer. Chem. Soc.*, **78**, 3409 (1956); R. Hoffmann, *ibid.*, **90**, 1475 (1968).

(13) U. Schöllkopf quoted in *Chem. Eng. News*, 42 (August 5, 1963); U. Schöllkopf, A. Lerch, and J. Paust, *Chem. Ber.*, **96**, 2266 (1963); U. Schöllkopf, G. J. Lehmann, J. Paust, and H.-D. Härtl, *ibid.*, **97**, 1527 (1964).

The rate-determining step of the Ramberg–Bäcklund rearrangement[15] and related cyclopropane forming addition–eliminations[16] may present such cases. In the former reaction an intramolecular SN2 displacement leads to episulfone formation, with the less stable product preferentially formed. Here again reasonable alternative rationalizations have been proposed.[15,17]

(14) Several such reactions have been discussed by M. Schlosser, who stresses a fundamental contrathermodynamic trend in carbon–carbon linking reactions: *Bull. Soc. Chim. Fr.*, 455 (1971); *Top. Stereochem.*, 5, 1 (1970).

(15) N. P. Neureiter and F. G. Bordwell, *J. Amer. Chem. Soc.*, 85, 1209 (1963); N. P. Neureiter, *ibid.*, 88, 558 (1966). Reviewed by F. G. Bordwell in "Organosulfur Chemistry," M. J. Janssen, Ed., Interscience, New York, N. Y., 1967, p 271, and by L. A. Paquette in "Mechanisms of Molecular Migrations," Vol. 1, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., 1968, p 121.

(16) L. L. McCoy, *J. Amer. Chem. Soc.*, 80, 6568 (1960); 82, 6416 (1962); 84, 2246 (1964); M. Mousseron, R. Fraise, R. Jacquier, and G. Bonavent, *C. R. Acad. Sci.*, 248, 1465 (1959).

(17) L. A. Paquette, *Accounts Chem. Res.*, 1, 211 (1968); D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, p 253

(18) Fellow of the Alfred P. Sloan Foundation.

Roald Hoffmann*

Department of Chemistry, Cornell University
Ithaca, New York 14850

Charles C. Levin

Department of Chemistry, Smith College
Northampton, Massachusetts 01060

Robert A. Moss[18]

Wright Laboratory, School of Chemistry
Rutgers University, The State University of New Jersey
New Brunswick, New Jersey 08903

A Direct Proton Magnetic Resonance Study of Hydrogen Bond Formation of Organic Lewis Acids with Triethylamine

Sir:

The concept of the hydrogen bond has been widely applied to many chemical and biological systems, and consequently it has been the object of extensive discussion and review.[1] Several workers recently determined thermodynamic quantities for hydrogen bond formation in numerous Lewis acid–base mixtures by calorimetric,[2–7] infrared,[2,3,5,6,8–10] and fluorine-19 nmr[9–12] techniques. The enthalpies and equilibrium

(1) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman, San Francisco, Calif., 1960.

(2) E. M. Arnett, T. S. S. R. Murty, P. v. R. Schleyer, and L. Joris, *J. Amer. Chem. Soc.*, 89, 5955 (1967).

(3) E. M. Arnett, L. Joris, E. Mitchell, T. S. A. R. Murty, T. M. Gorrie, and P. v. R. Schleyer, *ibid.*, 92, 2365 (1970).

(4) E. M. Arnett and E. J. Mitchell, *ibid.*, 93, 4052 (1971).

(5) K. F. Purcell, J. A. Stikeleather, and S. D. Brunk, *ibid.*, 91, 4019 (1969).

(6) R. S. Drago, N. O'Bryan, and G. C. Vogel, *ibid.*, 92, 3924 (1970).

(7) R. S. Drago, G. C. Vogel, and T. E. Needham, *ibid.*, 93, 6014 (1971).

(8) D. F. DeTar and R. W. Novak, *ibid.*, 92, 1361 (1970).

(9) J. Mitsky, L. Joris, and R. W. Taft, *ibid.*, 94, 3442 (1972).

(10) R. W. Taft, D. Gurka, L. Joris, P. v. R. Schleyer, and J. W. Rakshys, *ibid.*, 91, 4801 (1969).
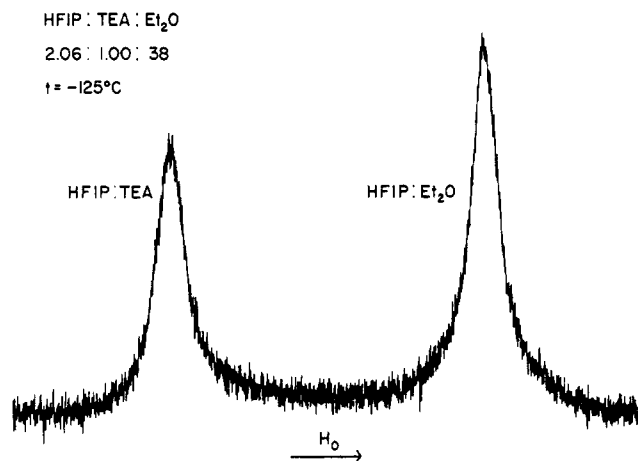

Figure 1. The proton magnetic resonance spectrum of the hydroxyl group of 1,1,1,3,3,3-hexafluoroisopropyl alcohol (HFIP) in a mixture of this compound with triethylamine (TEA) in excess diethyl ether (Et$_2$O). The spectrum was recorded on a Varian HA-100 nmr spectrometer. The species responsible for the signals and the mole ratios of all components are shown in the diagram.

constants for hydrogen bond formation which they measured now provide a more quantitative basis for discussion of this process. For other acid–base systems, it has been demonstrated in these laboratories that at temperatures in the range of $-100°$, ligand and proton exchange can be slowed sufficiently to permit the observation of separate pmr signals for bulk ligand and ligand molecules bound to diamagnetic cations[13–15] and the boron trihalides.[16–18] We have extended this method to acid–base systems in dilute solution and now wish to report the direct observation of a pmr signal for hydrogen nuclei involved in a hydrogen bond. This contrasts with the usual chemical shift studies of exchange averaged pmr signals.

The alcohol portion of the room temperature pmr spectrum of a 1,1,1,3,3,3-hexafluoroisopropyl alcohol (HFIP)–triethylamine (TEA) mixture in a large excess of ether consists of a hydroxyl group singlet positioned ~7 ppm downfield from TMS and a multiple pattern for the 2-carbon hydrogen, split by the six fluorine neighbors. As the sample is cooled, the hydroxyl signal shifts far downfield, broadens extensively, even disappearing into the base line, and below $-110°$, it separates into two distinct peaks. The hydroxyl group signals for one of these mixtures, recorded at $-125°$ on a Varian HA-100 spectrometer, are shown in Figure 1. Analogous spectra were obtained with all solutions listed in Table I. Since the presence of water is precluded by the drying and purification procedures,[19] the two signals in Figure 1 can be attributed to the hy-

(11) D. Gurka, R. W. Taft, L. Joris, and P. v. R. Schleyer, *ibid.*, 89, 5957 (1967).

(12) D. Gurka and R. W. Taft, *ibid.*, 91, 4794 (1969).

(13) A. Fratiello, R. E. Lee, V. M. Nishida, and R. E. Schuster, *J. Chem. Phys.*, 47, 4951 (1967).

(14) A. Fratiello, R. E. Lee, V. M. Nishida, and R. E. Schuster, *ibid.*, 48, 3705 (1968).

(15) A. Fratiello, R. E. Lee, V. M. Nishida, and R. E. Schuster, *Inorg. Chem.*, 10, 2552 (1971).

(16) A. Fratiello, T. P. Onak, and R. E. Schuster, *J. Amer. Chem. Soc.*, 90, 1194 (1968).

(17) A. Fratiello and R. E. Schuster, *Inorg. Chem.*, 11, 11 (1972).

(18) A. Fratiello and R. E. Schuster, *J. Org. Chem.*, 37, 2237 (1972).

(19) PFP was sublimed, the other reagents were dried over CaH$_2$ or CaSO$_4$, and all samples were prepared *in vacuo*.