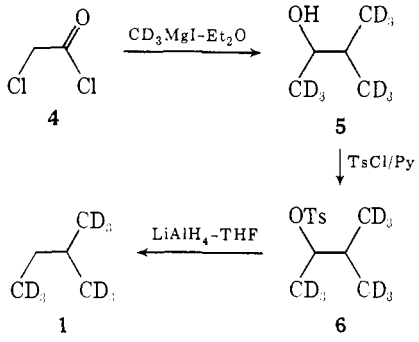
Scheme I



2-Methyl-3-butanol-d_9 (5). 2-Methyl-3-butanol-d_9 (**5**) was prepared using a procedure similar to that reported by Huston, Jackson, and Spero[26] for the undeuterated compound. The apparatus, which consisted of a 500-ml three-necked flask fitted with a Hofmann condenser, dropping funnel, nitrogen intake, and drying tubes, was dried in an oven for several hours, and flushed with dry nitrogen after assembly. Reagent grade magnesium turnings, 5.20 g (0.214 mol), and a small quantity of methyl-d_3 iodide (Stohler, 99.5% D) were added. The mixture was stirred vigorously and the remaining methyl-d_3 iodide (30 g total or 0.211 mol), dissolved in 100 ml of anhydrous ether, was added dropwise over a 1.5-hr period. Following the addition, the mixture was stirred for an additional 0.5 hr. Chloroacetyl chloride, 5.96 g (0.0527 mol), was dissolved in 100 ml of anhydrous ether, and added dropwise to the Grignard over a 1-hr interval so as to maintain a mild reflux. The ether was removed by distillation and the residue heated for 2 days at 95–100°.

The tarry residue was hydrolyzed by addition of ice, 100 ml of ether, and concentrated hydrochloric acid until the mixture was just acidic. The aqueous phase was extracted ten times with about 300 ml of ether, and the ether was dried over anhydrous potassium carbonate and sodium sulfate, and filtered. The filtrate was distilled slowly through a vacuum-jacketed Vigreux column. Several fractions were collected and analyzed by glc. The final two fractions (2.80 g, 55% theory), bp 94–112° (lit. bp 112° (734 mm)), were suitable for the next reaction. The undecoupled nmr spectrum of **5** exhibits three broad signals at δ 1.6 (C–H β to OH), 2.1 (C–H α to OH), and 3.5 (OH), with the expected integration ratio 1:1:1.

Methyl-3-butanol-d_9 Tosylate (6). To a stirred solution of 2.35 g (0.0242 mol) of **5** in 20 ml of dry reagent grade pyridine which was cooled in an ice bath was added dropwise a solution of 9.25 g (0.0484 mol) of *p*-toluenesulfonyl chloride in 20 ml of pyridine. Pyridinium chloride crystallized out after about 15 min. The reaction mixture was sealed in a flask and left for 2 days at 7°. After this time, the mixture was poured over ice and concentrated hydrochloric acid added until the resultant mixture was distinctly acid. The product was extracted three times with ether, and the combined ether extracts were washed with 5% hydrochloric acid and water and then dried over a mixture of anhydrous potassium carbonate and sodium sulfate. After filtration, the ether was removed on a rotary evaporator, and the residue was dissolved in pentane. The pentane was distilled and the process was repeated until no water droplets were observed in the distillate. The dry tosylate (**6**) was recrystallized three times from pentane, yield 5.36 g (88.5%), mp 20–21°. The undecoupled nmr spectrum of **6** exhibits an AB quartet centered at δ 7.6 (aromatic), a broad doublet at 4.5 (H α to –OTs), a singlet at 2.4 (aromatic methyl), and a multiplet at 1.8 (H β to –OTs), with the expected integration ratio 4:1:3:1.

2-Methylbutane-d_9 (1). Reagent grade tetrahydrofuran (30 ml) was distilled from lithium aluminum hydride into a dry three-necked 100-ml flask. The flask was fitted with a condenser and a pressure-equalizing dropping funnel with an intake for dry nitrogen. Lithium aluminum hydride, 2.0 g (0.052 mol), was added slowly through a powder funnel. The stirred mixture was heated in an oil bath at 65–70°, and 3.0 g (0.012 mol) of three times recrystallized **5** dissolved in 20 ml of dried tetrahydrofuran was added dropwise. The vaporized hydrocarbon, **1**, was conducted through a micro purification train connected to the generating apparatus, consisting of bromine water (to remove 2-methyl-2-butene which was previously detected by glpc), sodium thiosulfate solution, and two ethylene glycol bubblers (to remove tetrahydrofuran solvent), and a tube of Drierite. Purified **1** was conducted finally through a finely drawn polyethylene tube into a constricted nmr tube immersed in a Dry Ice–2-propanol bath. A previous undeuterated sample, prepared and purified in the same way, was found by glpc to be pure.

Acknowledgment. The authors are grateful to the National Science Foundation for Grant No. GP-3815 which provided support for this work.

(26) R. C. Huston, R. I. Jackson, and G. B. Spero, *J. Amer. Chem. Soc.*, **63**, 1459 (1941).

Stereochemical Control of Reductions. III. An Approach to Group Haptophilicities[1]

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Contribution from the Department of Chemistry, Rutgers University, Newark, New Jersey 07102. *Received January 15, 1973*

Abstract: The tetrahydrofluorene system **1**, angularly substituted with a series of functional groups R, has been catalytically hydrogenated over a palladium catalyst. For each functional group the percentage of cis isomer in the product is taken as a measure of that group's tendency, termed haptophilicity, to be bound to the catalyst surface during olefin reduction and thereby to enforce addition of hydrogen from its own side of the molecule. The nature of haptophilic activity and its correlation with various measures of group electronic characteristics and size are discussed.

Since the work of Linstead on the reduction of phenanthrenes,[3] many of the stereochemical aspects of heterogeneous catalytic hydrogenation have been made comprehensible in terms of the approach, fit, and binding of the reducible molecule to the surface of the catalyst.[4] These concepts have been applied with particular success to molecules whose geometry or substituents present severe steric hindrance to this

(1) (a) Abstracted in part from the Ph.D. Thesis of R. E. N. (b) Part II: H. W. Thompson and R. E. Naipawer, *J. Org. Chem.*, **37**, 1307 (1972).

(2) NASA Predoctoral Trainee, 1966–1967.

(3) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levene, and R. R. Whetstone, *J. Amer. Chem. Soc.*, **64**, 1985 (1942), and following articles.

(4) (a) R. L. Burwell, Jr., *Chem. Rev.*, **57**, 895 (1957); (b) S. Siegel, *Advan. Catal. Relat. Subj.*, **16**, 123 (1966).

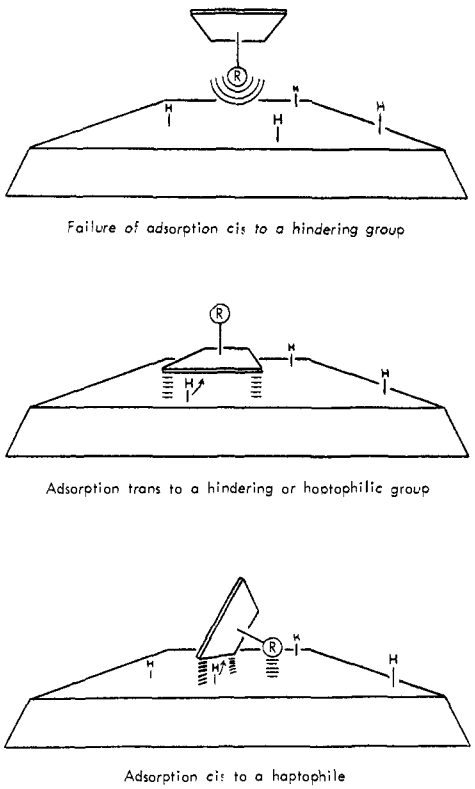


Figure 1.

approach or fit.[5] More recently, we[6] and others[7-9] have reported instances in which the presence in the reducible molecule of certain groups, notably hydroxyl, has produced hydrogenation stereochemistry opposite that predicted on the basis of purely steric effects.[10] The most definitive examples of such behavior have been observed in compounds which are generally planar (so as to provide a good fit to the catalyst surface) except for a single group projecting angularly from the molecular plane (such as to provide unambiguous steric hindrance to approach from one side;[7,8] see Figure 1). When this angular group is or contains hydroxyl (or in some instances methoxyl[8b]) it is often found that heterogeneous catalytic hydrogenation leads to introduction of hydrogen cis instead of trans with respect to the angular group.[11] In such cases it is difficult to resist the interpretation that some type of attractive (haptophilic[12]) interaction has bound the hydroxyl group to the catalyst surface during reduction so as to enforce addition of hydrogen from the same side in spite of the group's hindrance. While it is possible that this represents some previously unobserved force at work at the catalyst surface, we have found it more reasonable to view this haptophilicity as part of the spectrum of attractive interactions already known to exist between metal catalyst surfaces and other molecular or atomic species. These known attractive interactions include the binding of multiply bonded functional groups to the catalyst surface immediately prior to and during transferral of hydrogen to them, termed chemisorption.[13] They also include the usually stronger, often irreversible interaction called poisoning observed between various transition metal catalysts and certain species containing unshared electron pairs, notably divalent sulfur, mercury and its salts, etc.[14] While still imperfectly understood in detail, these phenomena are at least familiar ones whose mechanisms are believed to be understood in a general way as being due to bond formation between electron-donor atoms and empty or half-filled surface orbitals of the metal catalyst. In this context, the haptophilicity of hydroxyl groups toward transition metal catalysts can be viewed as similar in type to these two kinds of attractive interactions and would presumably lie between the two energetically. Since hydrogenation–chemisorption probably involves the rehybridization of a π bond, while poisoning (as well as hydrogenolysis–chemisorption) involves donation of unshared pairs, this haptophilicity may be closer in type to poisoning and can be conceived of as a weak and hence reversible version of catalyst poisoning. Once this view is adopted, it is evident that the same phenomenon might be observable for functional groups other than hydroxyl, depending on the availability of unshared pairs of electrons on the haptophilic group.

Our success in demonstrating and assessing this effect for hydroxyl in the tetrahydrofluorene system[6] encouraged us to undertake a study of the above proposition. We hoped thereby to determine the haptophilic tendencies of a variety of functional groups and thence to understand better the exact mechanism of and requisites for haptophilic intervention in heterogeneous catalytic hydrogenation.

Clearly the ideal system for such a study would provide a reducible double bond in a situation where haptophilic activity would lead to one isomer while dependence of the reaction on only "ordinary," hindering forces would lead to another. The system should also provide for holding constant all factors which might affect stereochemistry beside the one being cor-

(5) (a) H. I. Hadler, *Experientia*, **11**, 175 (1955); (b) J. R. Lewis and C. W. Shoppee, *J. Chem. Soc.*, 1365 (1955); (c) C. W. Shoppee, B. A. Agashe, and G. H. R. Summers, *ibid.*, 3107 (1957); (d) W. Cocker, P. V. R. Shannon, and P. A. Staniland, *J. Chem. Soc. C*, 41 (1966); (e) K. Hanaya, *Bull. Chem. Soc. Jap.*, **43**, 442 (1970).

(6) H. W. Thompson, *J. Org. Chem.*, **36**, 2577 (1971).

(7) (a) L. S. Minckler, A. S. Hussey, and R. H. Baker, *J. Amer. Chem. Soc.*, **78**, 1009 (1956); (b) W. G. Dauben, J. W. McFarland, and J. B. Rogan, *J. Org. Chem.*, **26**, 297 (1961), and references cited therein.

(8) (a) T. J. Howard, *Chem. Ind. (London)*, 1899 (1963); (b) T. J. Howard, *Recl. Trav. Chim. Pays-Bas*, **83**, 992 (1964); (c) S. Mitsui, Y. Senda, and H. Saito, *Bull. Chem. Soc. Jap.*, **39**, 694 (1966); (d) T. J. Howard and B. Morley, *Chem. Ind. (London)*, 73 (1967).

(9) (a) M. C. Dart and H. B. Henbest, *J. Chem. Soc.*, 3563 (1960); (b) S. Nishimura and K. Mori, *Bull. Chem. Soc. Jap.*, **36**, 318 (1963); (c) J. E. McMurry, *Tetrahedron Lett.*, 3731 (1970); (d) G. Brieger, D. L. Hachey, and D. Ciarimitaro, *J. Org. Chem.*, **34**, 220 (1969).

(10) However, see (a) P. B. Russell, *J. Chem. Soc.*, 1771 (1954); (b) T. G. Halsall, W. J. Rodewald, and D. Willis, *Proc. Chem. Soc., London*, 231 (1958); (c) T. G. Halsall, W. J. Rodewald, and D. Willis, *J. Chem. Soc.*, 2798 (1959); (d) M. G. McComble, H. B. Henbest, and W. R. Jackson, *J. Chem. Soc. C*, 2467 (1967); (e) S. J. Daum, P. E. Shaw, and R. L. Clarke, *J. Org. Chem.*, **32**, 1427 (1967); (f) B. Franzus, W. C. Baird, Jr., E. I. Snyder, and J. H. Surridge, *ibid.*, **32**, 2845 (1967); (g) W. C. Baird, Jr., B. Franzus, and J. H. Surridge, *ibid.*, **34**, 2944 (1969).

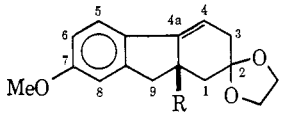
(11) It will be assumed here that pairs of hydrogens are always added cis with respect to each other; the terms cis and trans will therefore be used in this context to describe stereochemistry with respect to the angular group R; see G. V. Smith and J. A. Roth, *J. Amer. Chem. Soc.*, **88**, 3879 (1966).

(12) From ἅπτω = I attach or fasten myself to; φιλέω-ᾰ = I love; loving to grasp or cling. The word is not found in classical Greek, nor does it occur among the writers of the Renaissance, nor anywhere else.

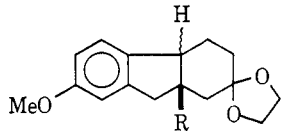
(13) (a) I. Horiuti and M. Polanyi, *Trans. Faraday Soc.*, **30**, 1164 (1934); (b) G. C. Bond, "Catalysis by Metals," Academic Press, New York, N. Y., 1962, pp 229 ff, 467 ff; (c) G. C. Bond and P. B. Wells, *Advan. Catal. Relat. Subj.*, **15**, 91 (1964).

(14) (a) Reference 13b, pp 99–100; (b) E. B. Maxted, *Advan. Catal. Relat. Subj.*, **3**, 129 (1951); (c) P. N. Rylander, "Catalytic Hydrogenation over Platinum Metals," Academic Press, New York, N. Y., 1967.

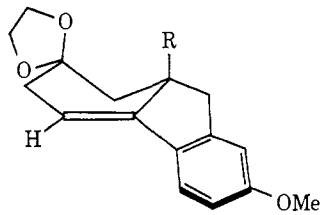
related with haptophilicity. However, such an ultimate degree of independence of variables is simply not possible, since substituting even one atom for another inevitably changes polarities, bonding angles, atomic volumes, and thence conformations. Nevertheless, we believed that with the tetrahydrofluorene compounds **1** and the hydrogenation conditions previously described[6] we had a system which could give useful data. In addition, our system offered the advantages of easy availability, good crystallinity coupled with sufficiently low molecular weight to allow vpc analysis, stability of the position of the double bond, the possibility of no more than two isomers, plus, most importantly, a demonstrated sensitivity to haptophilic effects.



1



2 = trans; **3** = cis



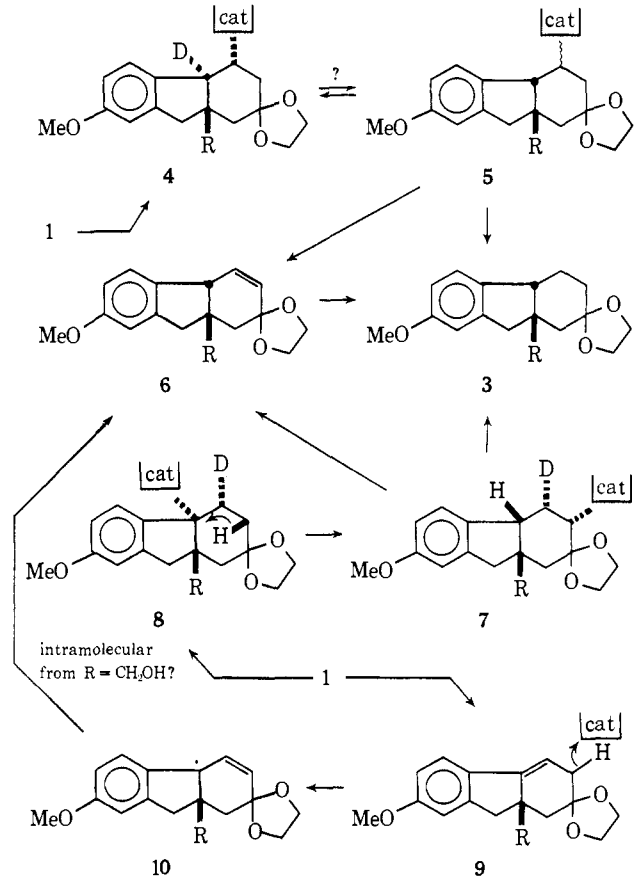
Results of Hydrogenations and Control Reactions. We have therefore examined the hydrogenation of compound **1**, substituted with a series of functional groups R, which vary in polarity, size, shape, etc.[1b] Hydrogenations were carried out in 2-methoxyethanol as solvent and utilizing a 5% palladium/carbon catalyst under the standardized conditions previously described[6] (see Experimental Section). The cis–trans ratios of the products were determined by several techniques, often in combination, including nmr, vpc, and fractional crystallization. These results and the analytical methods employed are summarized in Table II.

For each functional group R a control reduction was run on the minor product isomer to establish its stability to the reaction conditions. None of the products was found to be epimerizable under these conditions, and even when a 33-fold increase of catalyst was employed in one instance (**2**, R = COOMe), no equilibration was detectable,[15] although the cis epimer is known to be the more stable in this system.[1b]

One of the presumed advantages for the use of the tetrahydrofluorene system **1** was the positional stability of its double bond, since olefin migrations are commonly encountered in catalytic hydrogenations particularly with palladium catalysts.[16] In the absence of careful studies, usually employing deuterium, such migrations render mechanistic interpretation of results moot, as products, rather than arising directly from starting materials, may be derived from unanticipated intermediates not isolable or even detectable because of low concentration or high reactivity, and stereochemistry may be the result of equilibrations prior to the actual olefin-saturation steps. Equilibration, at least in our hexahydrofluorenes, is known to favor the cis ring juncture,[1b] and the results which we are attributing to an "anomalous," haptophilic pathway involve predominantly cis isomers. Therefore, in spite of the small quantities of catalyst employed, which should disfavor many such reactions,[17] the most interesting of our results might be explainable by an isomerization proceeding through some catalyst-associated state. Many of our substituent functional groups, those to which we have assigned low haptophilicities, produced preponderances of trans material on hydrogenation, so it is clear that equilibration paths cannot be followed for all our R groups. However, a selective process of this sort might be responsible for the high percentages of cis isomer observed with some of the R groups. Consequently, we have carried out under our reaction conditions the catalytic deuteration of compounds **1**, R = CH_2OH (95% cis), and R = COOMe (15% cis), representing respectively groups of high and low haptophilicity.

Some of the most likely paths leading to cis products from trans-adsorbed intermediates are shown in Scheme I. Isomerizations proceeding through steps

Scheme I

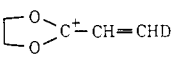
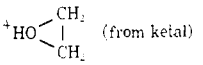
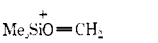
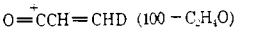


(15) H. W. Thompson and R. R. Muccino, *J. Amer. Chem. Soc.*, **94**, 1183 (1972).

(16) See H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1971, pp 20–28, for leading references.

(17) (a) H. O. House, R. G. Carlson, H. Müller, A. W. Noltes, and C. D. Slater, *J. Amer. Chem. Soc.*, **84**, 2614 (1962); (b) J.-F. Sauvage, R. H. Baker, and A. S. Hussey, *ibid.*, **83**, 3874 (1961).

Table I.[a] Principal Mass Spectral Peaks for Undeuterated and Deuterated 3, R = CH_2OSiMe_3

Undeuterated		Deuterated		Deuterium	
m/e	% of base	m/e	% of base	incorp.	Fragment[b]
186	(100.0)	187	(100.0)	d_1	A
73	(51.0)	73	(59.9)	d_0	Me_3Si^+
260	(42.4)	261	(51.0)	d_1	B
99	(37.1)	100	(44.2)	d_1	
75	(23.5)	75	(23.4)	d_0	Me_2SiOH^+
272	(19.6)	188	(22.8)	d_1	C
187	(19.0)	273	(18.3)	d_1	D
171	(17.7)	172	(16.1)	d_1	E
55	(13.7)	45	(13.9)	d_0	 (from ketal)
115	(12.9)	103	(13.2)	d_0	
103	(12.4)	160	(13.1)	d_1	F
158	(12.0)	159	(13.0)	d_1	G
45	(11.7)	56	(12.6)	d_1	 (100 − C_2H_4O)
159	(11.2)	116	(12.1)	d_1	H

[a] The mass spectra of both undeuterated and deuterated 2, R = CH_2OSiMe_3, are similar to those of 3, R = CH_2OSiMe_3, with few important differences. The five most populous peaks, for example, are the same five as shown here, although in a different order. [b] See Scheme II.

1-4-5-6-3 and possibly **1-9-10-6-3** should result in incorporation of excess deuterium. Those proceeding by way of **1-8-7-3** or **1-8-7-6-3**, and possibly **1-9-10-6-3**, involving intramolecular hydrogen transfers,[18] would introduce only two deuteriums per molecule, but at C-3 and C-4 instead of C-4 and C-4a. Only a sequence such as **1-4-5-3** provides the required isomerization with incorporation of only two deuteriums at the normally expected positions. However, step **4-5** is not a detailed mechanism, and more fully elaborated versions of this step either involve $\Delta^{3,4}$ species or are quite implausible.

Our deuteration results and their interpretation are as follows. Compound **1**, R = COOMe, was catalytically deuterated and the pure trans product isolated as described.[6] The molecular ion peaks in its mass spectrum show principally d_2 species, with the ratio of these peaks indicating no more than about 8% d_3 species. A control deuteration of **2**, R = COOMe-d_0, indicated that little or none of this excess deuterium was introduced by exchange into the saturated product. The minor cis product is not preparatively separable in pure form from hydrogenation mixtures; its analysis was therefore carried out by vapor phase chromatography–mass spectrometry coupling techniques (vpc–ms), which did not indicate clearly any greater population of d_3 species in the cis product. Whatever the source of this relatively small amount of excess deuterium, therefore, it is evidently not an important factor in the process which determines product stereochemistry.

(18) (a) G. V. Smith and J. R. Swoap, *J. Org. Chem.*, **31**, 3904 (1966); (b) G. V. Smith and J. F. Deany, *J. Catal.*, **5**, 152 (1966).

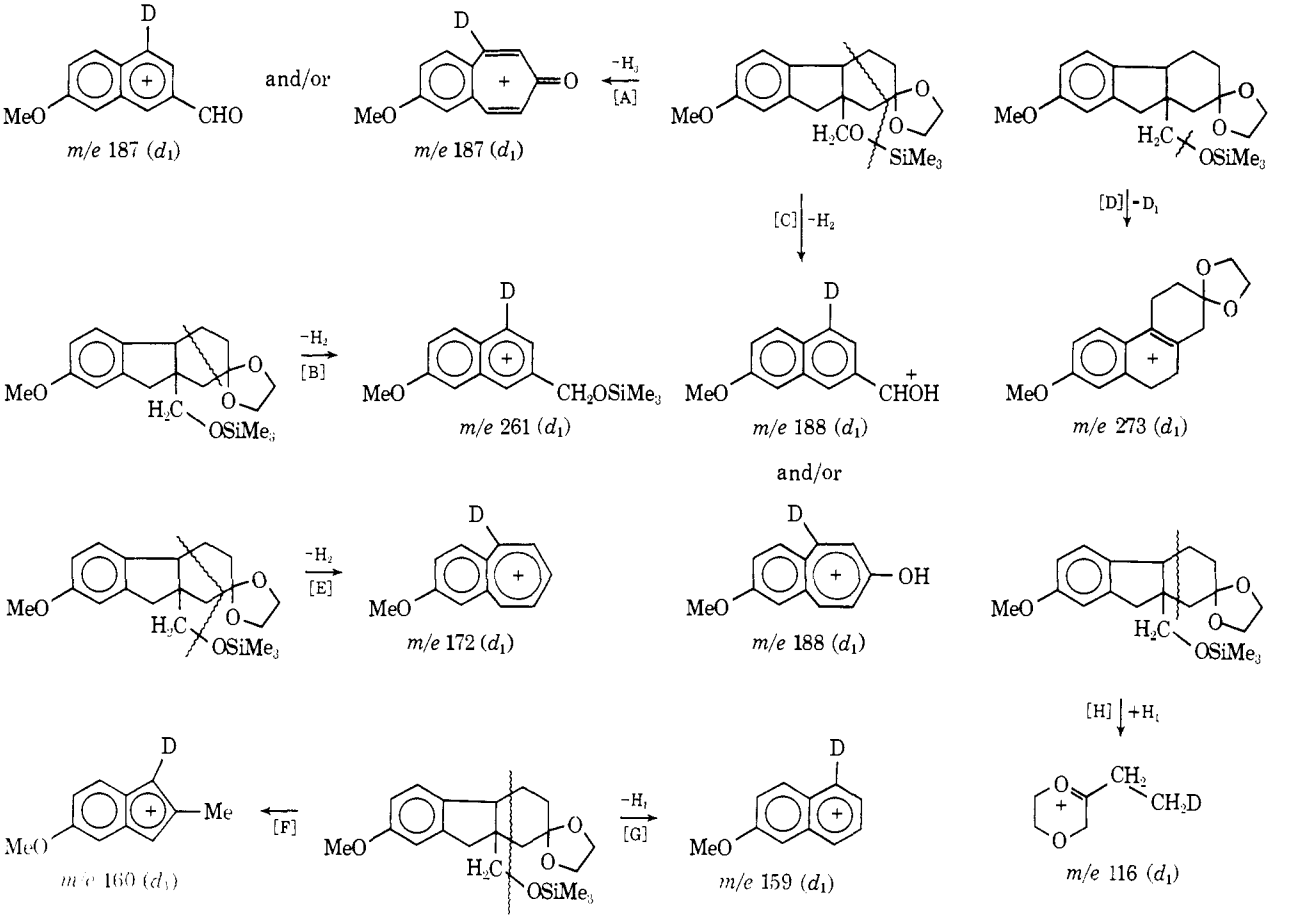
Previous results indicated that the cis and trans products from catalytic deuteration of **1**, R = CH_2OH, could best be separated by vpc as their trimethylsilyl ethers.[6] These derivatives were therefore subjected to vpc–ms and led to spectra considerably simpler than those from the carbomethoxy compounds, presumably as a result of the increased effectiveness of fragmentations in the 9a substituent in relation to the various competing processes.[19] This and the ketal fragmentation are in fact so efficient that no peaks with m/e greater than M − 90 (M − $C_3H_{10}OSi$) were consistently observable for either isomer.

Although total deuterium incorporation could not be directly assessed since molecular ion peaks were unobservable, specific fragmentations could be confidently assigned to all major peaks in both isomers, and these allowed not only good assessment of the total number of deuterium atoms but confirmation of their positions as well. Since either a radical or cation is particularly well stabilized at C-4a, most fragmentations involved cleavage of either the C-4–C-4a or the C-4a–D bond and most observable peaks therefore represented d_1 species. A few d_2 peaks (of low intensity) could be found, but no peaks were assignable to d_3 species.

The occurrence of isomerizations or equilibrations during deuteration should increase the d_2 component of those fragments containing C-3, since excess deuterium is most likely to appear there (Scheme I). The pertinent peaks in the nondeuterated compound are

(19) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

Scheme II



m/e 99, 115, and 272 (Table I and Scheme II). When intensities were compared in deuterated and undeuterated **3**, R = CH_2OSiMe_3, the first two of these peaks yielded values of 14.5 and 43%, respectively, for the maximum population of d_2 species present. However, these values are known to be high because of the presence of interfering adjacent peaks (see Experimental Section for peaks and intensities). Because of freedom from such complications, the most valuable of these peaks for assessing excess deuterium content is that at *m/e* 272 (d_0), which gives a maximum value for d_2 species of 5.2%. This deuteration therefore appears to proceed even more cleanly than that of the trans-producing carbomethoxy compound and shows very clearly that the stereochemistry which we attribute to haptophilic effects is not the result of olefin isomerization or similar processes prior to complete saturation. The major peaks (>10% of base) for compound **3**, R = CH_2OSiMe_3, are shown in descending order together with their probable assignments in Table I and Scheme II.

Discussion

A useful haptophilicity series should ideally assign to each functional group a number which could be used in all situations to predict the ratio of products from hydrogenation. Whether the numbers in Table II represent such a series obviously remains to be assessed. Equally desirable would be a method of deriving haptophilicities from other functional group parameters which have already been measured. In theory, a group's haptophilic effectiveness, *i.e.*, in inducing addition of hydrogen cis with respect to itself, would be expected to increase with increasing ability to donate electrons toward the catalyst surface and to decrease with increasing bulk. This may be expressed in a general way as

$$\mathbf{H} = f(E) - f(S) \qquad (1)$$

where **H** is the haptophilicity and E and S simply represent some known or measurable electronic and steric terms which describe the properties involved.

In Table II we have shown for the groups studied, along with the gross haptophilicities expressed simply as percentage of cis isomer observed, several of the standard measures of electron-concentrating or -donating ability[20,21] and bulk with which we have attempted correlations.

These are: (1) the dipole moments (μ) of the corresponding methyl compounds;[22] (2) the group electronegativities (χ);[20,23] (3) the group basicities (givenas

(20) It should be noted that several measures of electron-donating ability, such as σ values and probably χ, would seem *a priori* unsuitable for use as E since they indicate ability of a group to release or withdraw electrons only toward or from its point of attachment. They may be thought of as concerned with release at the functional group's roots, while we desire a measure of ability to release electrons toward or at the branches of the group.

(21) For some other quantities not listed here, see C. Reichardt, *Angew. Chem., Int. Ed. Engl.*, **4**, 29 (1965); R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 556.

(22) (a) C. P. Smyth in "Technique of Organic Chemistry," Vol. 1, Part 3, A. Weissberger, Ed., Interscience, New York, N. Y., 1960, p 2602; (b) A. L. McClellan, "Tables of Experimental Dipole Moments," W. H. Freeman, San Francisco, Calif., 1963.

(23) (a) J. E. Huheey, *J. Phys. Chem.*, **69**, 3284 (1965); (b) J. E. Huheey, *ibid.*, 70, 2086 (1966); (c) J. K. Wilmshurst, *Can. J. Chem.*, **35**, 937 (1957); (d) P. R. Wells, *Progr. Phys. Org. Chem.*, **6**, 111 (1968).

Table II. Comparison of H with Other Functional Group Parameters

Group	Analytical method	% cis	% trans	μ, D	χ	pK_a	P	M_D	V_s	V_r
CH_2OH[a]	Vpc[d]	95 ± 2	5 ± 2	1.7	3.65[e]	−2.2	71	7.24	79	300
CHO[b]	Vpc, nmr	93 ± 2	7 ± 2	2.5	2.90	−8	65	5.73	56	110
CN	Vpc	75 ± 1	25 ± 1	3.6	3.20	−10	66	6.46	46	46
CHNOH[c]	Nmr, cryst.	65 ± 2	35 ± 2	0.9	(2.95)[f]	+1.8	91	8.98	88	320
COONa	Vpc, nmr	55 ± 2	45 ± 2		2.95[g]	(+4.8)[h]				
COOLi	Vpc, nmr	23 ± 1	77 ± 1		2.95[g]	(+4.8)[h]				
COOH	Vpc, nmr	18 ± 2	82 ± 2	1.7	2.85	−6.1	75	7.25	74	295
COOMe[a]	Vpc, nmr	15 ± 1	85 ± 1	1.9	2.75	−6.3	119	12.0	121	790
COMe	Nmr	14 ± 2	86 ± 2	2.7	2.70	−7.2	104	10.4	102	345
$CONH_2$	Cryst.	10 ± 2	90 ± 2	3.7	(2.95)[f]	−1	92	9.15	87	315

[a] Reference 6. [b] The isolated product consisted of *ca.* 75% aldehydes in the indicated ratio, the remainder being the reduced hydroxymethyl compounds. As the ratio of reduced aldehydes, which was observed over the course of reaction, did not change appreciably, it is inferred that the rate of carbonyl reduction of the saturated aldehydes either is very low or in about the same ratio for cis and trans as their production. Data from control reactions suggest the latter. [c] The stereochemistry of this oxime is assumed to be anti because of the high degree of substitution and hindrance about C-9a. [d] This vpc analysis was carried out on the silyl ethers. [e] This is the value associated with OH. It is used in place of the value for CH_2OH because for our purposes OH is the only active portion of the group and we wish to use χ not as a measure of the group's ability to withdraw electrons from C-9a, but as a measure of the group's ability to concentrate electrons at its extremity. [f] These values were derived from the tables correlating χ with nmr shifts in ref 23d. The oxime value is an average of those for syn and anti acetaldoxime. [g] Values given in ref 23b for carboxylate independent of cation. [h] By definition.

pK_a for the conjugate acids of the corresponding methyl compounds[24]); (4) the group parachors (P);[25] (5) the group molar refractivities (M_D);[26] (6) the static or simple volumes of Fisher–Hirschfelder–Taylor models of the groups (symbolized by V_s and normalized to CHO = 56 for easy comparison with P and M_D and for closest correspondence with $10M_D$ for all groups except CN); (7) the volumes swept out by the same models assuming complete and rapid rotation about all single bonds (symbolized by V_r and normalized to CN = 46 for comparison with V_s).[27] The quantity V_r is in actuality an upper limit for the true rotated volume. While models of **1** clearly indicate restricted rotation for some of the groups R, it is not possible to determine exactly how much rotation is allowed; thus the true rotated volumes for these groups will fall between V_s and V_r. (Note, however, that the *order* of sizes is identical for V_s and V_r and hence is likely to be the same for the true rotated volumes.) It may also be observed that, when appropriately normalized, the quantity V_s correlates quite closely (*ca.* ±3% on average) with molar refractivity for all groups except CN, and with parachor for all except CN and CHO.

Examination of Table II shows that the gross haptophilicities do not correlate very closely with any single one of the steric or electronic measures given and correlate very badly with μ and pK_a in particular. The correlation with χ is fair except for the reversal of CHO and CN and the essentially identical electronegativities of CHO (93% cis) and COOH (18% cis). The correlation with measures of bulk is only general; while several individual groups are out of place in the P and M_D series, the existence of a broad trend is evident, in which the smaller groups have higher haptophilicities. The correlation with V_s and V_r is less impressive.

Several examples illustrate the apparent dependence of H, however, on both steric and electronic factors. By all our measures CHO and COMe are quite similar electronically; however, their haptophilicities are very different. That this may be attributed to steric factors is suggested by the large differences in all our measures of bulk. The complementary case is illustrated by CH_2OH and COOH, which, according to all our steric measures, are quite similar in size (and which are, moreover, nearly the same shape). While the dipole moments are of no value in explaining the large difference in haptophilicity for these two groups, both χ and pK_a values predict that CH_2OH should be the more haptophilic, as it is by a large factor.

Comparison of results for carboxyl and carboxylates is instructive. Because of the small size of lithium ions[28] and the partly covalent nature of the Li–O bonds,[29] a lithium carboxylate is expected to be a tight pair, probably about the same size as COOH, but should have greater electron density on oxygen. This is borne out in the hydrogenation results. The much greater H for the sodium carboxylate suggests that the greater density and availability of electrons on oxygen in the more ionic sodium compound[29] more than compensates for the greatly increased bulk of the cation. We interpet this one as strongly supporting the dependence of haptophilicity on available electron density.

We have had only slight success at a combined electronic-steric correlation; one utilizing P, χ, and H, and developed as a nomogram but shown here in equation form (eq 2), works quite well for CH_2OH, CN, COMe, and COOMe, but the remaining groups (COOH, CHO) for which we have good values of both P and χ do not fit the relationship. It may be that even the apparent fit for CH_2OH, CN, COMe, and COOMe is fortuitous since χ is intended as a measure

(24) E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 223 (1963).

(25) (a) S. Sugden, "The Parachor and Valency," Rutledge, London, 1929; (b) O. R. Quayle, *Chem. Rev.*, **53**, 439 (1953); (c) T. Isemura in "Handbook of Organic Structural Analysis," Y. Yukawa, Ed., W. A. Benjamin, New York, N. Y., 1965, p 466.

(26) K. Fajans in "Technique of Organic Chemistry," Vol. 1, Part 2, A. Weissberger, Ed., Interscience, New York, N. Y., 1960, pp 1169–1211.

(27) The quantity V_r has been corrected by excluding all volume swept out "behind" the group's point of attachment but including as swept-out volume any inaccessible voids left by the rotations. Again, by analogy, only branches above ground are counted in the volume but space under the overhanging branches is also included.

(28) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 505 ff.

(29) Y. Koga and R. Matsuura, *Mem. Fac. Sci. Kyushu Univ., Ser. C*, **4**, 1 (1961); *Chem. Abstr.*, **63**, 3171 (1965).

of a group's ability to withdraw or concentrate electrons along its bond of attachment rather than of ability to donate electrons to an external acceptor.[23d]

$$\mathbf{H} + 13 = (210 - P)(2.5)(\chi - 2.5)/(\chi - 1.7)(1.9) \quad (2)$$

It is by no means even certain that any such detailed correlation with other parameters can be reasonably expected. The measures of group bulk we have employed, for example, are crude ones which take no account of the shape or orientation of the group involved. Two out of many examples will suffice. All our measures of bulk agree that CN is smaller than CH_2OH, yet because CN is linear while CH_2OH is bent, when these groups are substituted into system **1**, the orbitals containing the unshared electrons which we presume to be involved in haptophilic bonding will be *farther* from carbon 9a in the nitrile by about 0.3–0.4 Å. Again, while we have based our calculation of V_r, for obvious reasons, on the anti aldoxime, syn and anti relationships are not distinguished in the calculations leading to values for P, M_D, and V_s. Yet the syn isomer, with its more exposed nitrogen, should have very different properties of electron donation to an external surface than the anti. The foregoing and similar considerations, concerning the exact angles at which individual molecular geometries will allow the required orbitals to contact an external surface, make it dubious that any all-inclusive system can be found for correlating **H** with other group parameters.

The question then remains whether the numbers which we call **H**, the per cent cis isomer found for each R group in system **1**, can predict with any accuracy the relative production of cis and trans isomers in another system or under other experimental conditions. It may be instead that the dependence on such nearly inassessable factors as the exact angular relationship and distance between the orbitals of the haptophile and of the olefin is so critical as to make each case unique.

In this context, assessment of the value of **1** as a model should take recognition of several features, besides the nature of the R group, which must contribute to the complex of factors controlling the stereochemistry of hydrogenation. The C-2 ketal oxygen, for example, probably provides a supplementary haptophilic site, which, because of the possbilities for hydrogen bonding and steric interaction with some of the R groups, may vary in haptophilic effectiveness as conformational changes involving C-2 take place. In addition, the solvent[31] we have used is one which is capable of hydrogen bonding in varying degrees with all of our R groups, and such solvation could drastically alter the effective bulk or electron-donating ability of a group in comparison with our estimations. Such factors are an indication of the lack of ideality of the system comprising **1** and our experimental conditions, and we have been forced, while recognizing their existence, to disregard these possibilities for lack of any way of assessing them. However, a haptophilic series which is useful for prediction in real systems must likewise be derivable from real systems. We therefore wish to offer our data as an initial approach to group haptophilicities, providing a series which will be subject to further refinement, modification, and expansion as results from other systems become available.

The ultimate utility of such a series is improved predictability and control of stereochemistry in heterogeneous catalytic hydrogenation. In terms of such control, the haptophilic order presented here has a number of obvious practical implications concerning the order in which steps should be performed in a reaction sequence and the possibility of masking, unmasking, or changing the form of groups prior to hydrogenation to achieve a desired stereochemical result.

(30) For some recent discussions, with leading references, of the role of solvent in determining stereochemistry, see ref 5d and S. Nishimura, M. Shimahara, and M. Shiota, *J. Org. Chem.*, **31**, 2394 (1966).

Experimental Section[31]

Procedure for Hydrogenations. Hydrogenations were carried out with a low-pressure apparatus at 1 atm (76 ± 2 cm) and room temperature (25 ± 2°) using Matheson Coleman and Bell "Chromatoquality" 2-methoxyethanol and 5% palladium on carbon (lot No. 11-333) supplied by Engelhard Industries, Newark, N. J., in the ratio 33 mg of catalyst and 16 ml of solvent per mmol of olefin. In the cases of CHO, $CONH_2$, and COMe the catalyst ratio was changed to 66 mg/mmol in order to shorten reaction times and avoid by-product formation.

To a flask containing a Teflon-covered magnetic stirring bar and the appropriate quantity of catalyst was added a solution of 0.30–0.50 mmol of the olefin in 2-methoxyethanol. The flask was then alternately evacuated and filled with hydrogen several times to remove all air. The final charge of hydrogen was adjusted to *ca.* 1 atm with a mercury leveling bulb and rapid stirring was begun. When at least the theoretical quantity of hydrogen had been absorbed and uptake had ceased, the product was isolated by filtration (catalyst washed with additional solvent) and removal of all solvent under vacuum. The residue was sublimed or distilled in a micro-sublimation apparatus at *ca.* 0.01 mm and the cold-finger weighed immediately before and after removal of the sublimate. Recovered yields were 97–99% except in the case of CHO (87%), which had been stopped several times and isolated for analysis before continuing the hydrogenation. In the case of the metal carboxylates, the residue from concentration was dissolved in 50 ml of water and this solution was acidified to pH 3–4 with saturated aqueous oxalic acid before extraction three times with CH_2Cl_2. These combined extracts were then dried, concentrated, and sublimed as described above (yields 90–98%).

Analysis of Product Mixtures. The entire volatile product from each sublimation was washed from the cold-finger with $CDCl_3$, and this solution was concentrated and used directly for nmr and vpc analyses.[31] Vpc detector responses were calibrated with known isomer mixtures similar in composition to those being analyzed. Results for the oxime were obtained by fractional crystallization of the highly insoluble trans isomer and nmr analysis of the remaining liquors. Results for the amide were obtained by fractional crytallizations from Et_2O and from Et_2O–CH_2Cl_2.

Procedure for Control Reactions. For the control reaction for each functional group, the minor hydrogenation product (0.22–0.66 mmol) was subjected to the same conditions as the corresponding olefin had been with respect to ratio of catalyst and solvent and length of reaction time. Material was isolated as described above (98–100% recoveries) and compared with starting materials by nmr. In no instance was evidence for isomerization found.

The control reaction of the trans carbomethoxy compound, employing a massive quantity of catalyst, has been described elsewhere.[15]

Deuterations. Carbomethoxy Substituent. With the procedure and conditions described above for H_2, compound **1**, R = COOMe,

(31) Nmr spectra were taken using a Varian A-60 or A-60A spectrometer and solutions in CCl_4 or $CDCl_3$ ($SiMe_4$ and/or CH_2Cl_2 internal standards). Vapor-phase chromatographic (vpc) analyses were carried out on a 0.125 × 18 in. column packed with 20% UCW-98 on Gas-Chrom Q and/or a 0.125 in. × 8 ft column packed with 3% OV-1 on Gas-Chrom Q and using an Aerograph Model 1720 or a Beckman Model GC-5 instrument; vpc–ms analyses were carried out with the above vpc equipment and a Perkin-Elmer Model 270 low resolution mass spectrometer at an ionization potential of 70 eV.

Table III

—Undeuterated— m/e	(%)	—Deuterated— m/e	(%)
98	(<1.0)		
99	(37.1)	99	(<1.0)
100	(5.8)	100	(44.2)
101	(3.0)	101	(7.5)
102	(<1.0)	102	(<1.0)
114	(<1.0)		
115	(12.9)	115	(<1.0)
116	(3.8)	116	(12.1)
117	(<1.0)	117	(9.1)
118	(<1.0)	118	(2.2)
271	(<1.0)		
272	(19.6)	272	(<1.0)
273	(<1.0)	273	(18.3)
274	(1.4)	274	(<1.0)
275	(<1.0)	275	(<1.0)

was reduced with deuterium gas (99.5% D). Filtration and concentration provided material recrystallized from ether–hexane to yield the pure deuterated trans carbomethoxy compound, mp 145–148°,[6] whose mass spectrum had molecular ion peaks at *m/e* 318 (2.3% of base), 319 (4.5), 320 (12.8), and 321 (4.5). Molecular ion peaks for the corresponding undeuterated material appeared at *m/e* 318 (16.5), 319 (4.0), 320, and 321 (<1.0%). When undeuterated **2**, R = COOMe, was treated as described above with D_2 and Pd/C, then recovered and purified, its molecular ion peak intensities were *m/e* 318 (18.0), 319 (4.0), 320, and 321 (<1.0).

The liquors from crystallization of the deuterated trans carbomethoxy material, which were relatively rich in the cis product, were subjected to vpc–ms; compound **3**, R = COOMe, from this source gave a mass spectrum whose molecular ion distribution was similar to that of **2**, R = COOMe.

Hydroxymethyl Substituent. Compound **1**, R = CH_2OH, was deuterated catalytically using the procedure and conditions described above. The product was filtered, concentrated *in vacuo*, and trimethylsilylated directly for vpc–ms. The major mass spectral peaks and their intensities for both the undeuterated and deuterated cis product are shown in Table I. In addition, the following peaks and intensities for fragments containing C-3, shown in Table III, are of particular value in assessing the extent of deuterium incorporation.

Mass spectra of the undeuterated and deuterated trans products, **2**, R = CH_2OSiMe_3, were obtained from the same preparations and had major mass spectral peaks similar to those of **3**, R = CH_2OSiMe_3, and indicating a similarly small extent of excess deuterium incorporation.

An entire undeuterated hydrogenation mixture containing both **2** and **3**, R = CH_2OH, was treated with D_2 as described above. When reisolated and trimethylsilylated, this material was subjected to vpc–ms and gave spectra indicating negligible deuterium incorporation.

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Alkylation of Tertiary Alkyl Halides with Trialkylaluminums. A Model for Initiation and Termination in Cationic Polymerizations

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Abstract: The alkylation of *tert*-butyl halide with trimethylaluminum, a reaction which quantitatively and rapidly yields neopentane, can be viewed as a model for cationic polymerization initiation and termination. In an attempt to gain insight into the mechanism of these reactions, we have examined the effect of methyl chloride, methyl bromide, methyl iodide, and cyclopentane solvents on the rate of alkylation of *tert*-butyl chloride, bromide, and iodide with trimethylaluminum in the temperature range +50 to −80°. The reactivity of *tert*-butyl halides toward alkylation was found to decrease in the order *t*-BuCl > *t*-BuBr > *t*-BuI. The nature of the solvent also exerts a significant influence, the rates of alkylation decreasing in the order MeCl > MeBr > MeI ≫ cyclopentane. While the individual rates were significantly different, the activation energies calculated for the alkylation of *tert*-butyl halides with trimethylaluminum were found to be constant both in the three methyl halide solvents (10–11.5 kcal/mol) and in cyclopentane (15–16.5 kcal/mol). A mechanism consistent with these observations has been proposed. The stereochemistry of alkylation has been investigated by the reaction of optically active α-phenethyl chloride with triethylaluminum. The significance of these results for the understanding of the mechanism of initiation and termination of cationic polymerization is discussed.

In a previous publication[2] we reported the facile, quantitative reaction of *tert*-alkyl chlorides with trialkylaluminums in MeCl solvent at −78° to produce quarternary carbon compounds (eq 1). The reaction

$$RCl + R_3'Al \longrightarrow RR' + R_2'AlCl \quad (1)$$

was proposed to involve the intermediacy of a carbenium ion–counteranion pair (*e.g.*, *t*-Bu^+ Me_3AlCl^-). The same *tert*-butyl cation–counteranion pair has also been invoked to explain the initiation of cationic polymer-

(1) (a) Taken in part from the Masters Thesis of N. V. D., submitted to the University of Akron, December 1972; (b) Postdoctoral research associate.

(2) J. P. Kennedy, *J. Org. Chem.*, **35**, 532 (1970).