sensitive to steric crowding than the carbonyl carbon.

Conclusions

(1) As was reported for the reaction with water and OH^-, benzylidenemalonodialdehyde (1) displays strong Lewis acidity toward amines. The K_1 values for amine addition to 1 are >100-fold higher than for the addition of the same amines to benzylidene Meldrum's acid (3), another highly electrophilic olefin. The fact that the $K_1(1)/K_1(3)$ ratios of >100 are substantially larger than the corresponding ratios for water or OH^- addition to 1 and 3 (4.33) is attributed to a steric effect that lowers K_1 for amine addition to 3.

(2) β_{nuc}^n for amine addition to 1 is quite small (0.26 for primary amines, 0.18 for the piperidine/morpholine pair), as seems characteristic for reactions of highly electrophilic olefins. This low β_{nuc}^n suggests a transition state with little C–N bond formation and may explain why semicarbazide does not show an enhanced rate constant for nucleophilic attack (α effect).

(3) log k_0 for piperidine and morpholine addition to 1 is 1.2 log units lower than log k_0 for the reaction of 3 with the same amines. This difference reflects the greater resonance contribution to the stability of the carbanionic portion of $T_A^{\pm}$ derived from 1 compared to that in $T_A^{\pm}$ derived from 3. The stronger resonance leads to a stronger k_0-lowering PNS effect.

(4) In contrast to the reaction of piperidine and morpholine with benzylideneacetylacetone (4), no additional PNS effects caused by intramolecular hydrogen bonding or steric effects could be detected in the reaction of 1. The absence of a PNS effect arising from hydrogen bonding is a consequence not only of a weaker intramolecular hydrogen bond than in $T_A^{\pm}$ derived from 4 (smaller $\delta \log K_1^{HB}$ in eq 10) but of a smaller β_{nuc}^n, which reduces $|\alpha_{HB} - \beta_{nuc}^n|$ in eq 10. With respect to the steric PNS effect, the much smaller size of 1 compared to 4 apparently renders it negligible.

(5) log k_0 for the addition of primary amines to 1 is approximately 1.7 log units lower than for the reaction with piperidine and morpholine. This reflects the well-known PNS effect caused by delayed solvation of the incipient ammonium ion.

Experimental Section

Materials. Benzylidenemalonodialdehyde was synthesized by two methods. In the first, the procedure of Arnold, Král, and Dvořák,[2a] which is based on reaction of the trimethinium perchlorate ($(CH_3)_2N{=}CHCH{=}CHN^+(CH_3)_2ClO_4^-$) with benzaldehyde was used. Since the preparation of the trimethinium[45] salt requires the highly toxic phosgene as a reagent, subsequent syntheses followed the method developed by Reichardt et al.[1a,46] ^1H NMR ($CDCl_3$) δ 9.90 (s, 1 H, CHO), 9.75 (s, 1 H, CHO), 7.90 (s, 1 H, vinyl), 6.7–7.25 (m, 5 H, phenyl).

The purification of the amines has been described in previous reports.[11a,47]

Kinetic Runs. The procedures used were similar to ones reported earlier.[9-11] The kinetic experiments were performed on a Durrum-Gibson stopped-flow spectrophotometer, and the absorption spectra were recorded on a 559 Perkin-Elmer spectrophotometer. Rates in the forward direction were monitored at 325 nm; in the water-trap experiments for the determination of k_{-1} the reactions were monitored at 263 nm and in the semicarbazide-trap experiments at 270 nm. pH measurements were performed on mock solutions. The pH meter was calibrated for 50% Me_2SO–50% water with buffers described by Hallé et al.[48]

pK_a of Malonodialdehyde. The pK_a of the enol form of malonodialdehyde was determined spectrophotometrically at 266 nm (λ_{max} of the anion) in acetate buffers ranging in pH from 3.79 to 5.42. A pK_a of 4.33 was obtained.

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Registry No. 1, 82700-43-4; semicarbazide, 57-56-7; cyanomethylamine, 540-61-4; glycine ethyl ester, 459-73-4; glycinamide, 598-41-4; 2-methoxyethylamine, 109-85-3; *n*-butylamine, 109-73-9; morpholine, 110-91-8; piperidine, 110-89-4.

Supplementary Material Available: Kinetic data, Tables S1–S16 (21 pages). Ordering information is given on any current masthead page.

(45) Arnold, Z.; Holy, A. *Collect. Czech. Chem. Commun.* **1965**, *30*, 47.
(46) (a) Reichardt, C.; Yun, K.-Y. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 65.
(47) (a) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (b) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *106*, 2969.
(48) Hallé, J.-C.; Gaboriaud, R.; Schaal, R. *Bull. Soc. Chim. Fr.* **1970**, 2047.

Electronic Control of Face Selection in the Capture of Radicals

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A simple procedure is described which leads to the pure epimeric 2-(5-phenyl)adamantanecarboxylic acids *E*-1 and *Z*-1. Both acids upon treatment with bromine and mercuric oxide in carbon tetrachloride undergo the Hunsdiecker reaction to give the same mixture of *E*- and *Z*- 2-bromo-5-phenyladamantanes 4. 5-Phenyl-2-methyleneadamantane 6 undergoes reaction with bromotrichloromethane to give two diastereomeric adducts. In both instances, the major isomer results from the abstraction of a bromine atom by the *zu* face of the intermediate 5-phenyl-2-adamantyl radicals. The results mesh with other examples of face selection which we have previously ascribed to transition-state hyperconjugation. An additional case (hydride shift in a carbocation) was encountered in this work, as well as one apparent exception: the oxirane formation from adamantanone and sulfonium ylids. That result is attributed to thermodynamic control of the initial addition step.

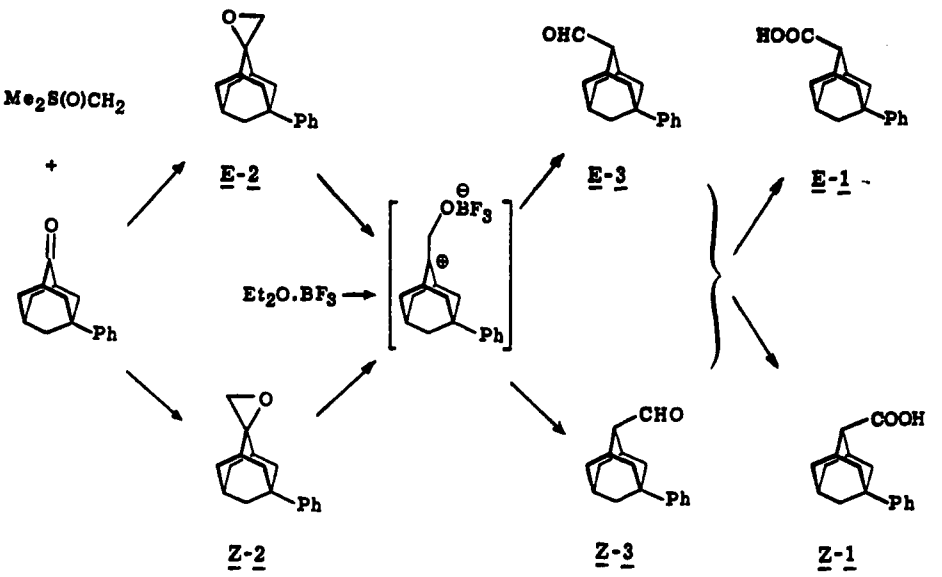
Introduction

Face selections in the addition to trigonal carbon and in the departure of a leaving group from tetragonal carbon are at the heart of stereogenesis and stereodemise. Accordingly, an enormous amount of effort has been devoted to this aspect of stereochemistry, as witness the protracted dispute about the nature of solvolysis mechanisms,[1] and the many theories offered to explain the preference for

(1) For a summary and many references, see: Brown, H. C. *The Nonclassical Ion Problem*; with comments by Schleyer, P. v. R.; Plenum: New York, 1977.

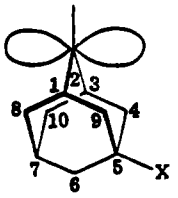
0022-3263/91/1956-2001$02.50/0

Scheme I



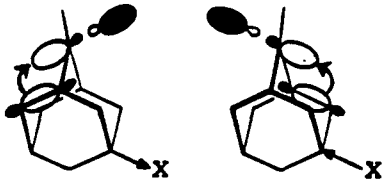
axial nucleophilic attack on rigid cyclohexanones.[2] Fueling these disputes has been the difficulty of separating steric and electronic effects, not least because conformational uncertainty has been part and parcel of most systems employed in studies of this phenomenon.

5-Substituted adamantanones and their derivatives offer an ideal resolution of this dilemma: the basic skeleton is rigid, and the distant substituent in the equatorial 5-position does not affect the chemistry at the trigonal center C_2 in any steric way. Whiting et al.[3] were the first



chemists to make use of this probe, reporting in 1975 that 2-adamantyl esters solvolyze with excess retention of configuration. Soon after, we published papers demonstrating its usefulness[4] in the stereochemical investigation of carbocations,[5] carbanions,[6] and carbenes;[7] these were followed by others on the topics of σ participation in solvolysis,[8] nucleophilic attack on ketones,[8a,9] electrophilic addition to olefins,[10] cycloaddition,[11] sigmatropic shifts,[12] and orbital symmetry.[13]

In all of these studies, we have been able to interpret our observtions in terms of the notion of transition-state hyperconjugation, an idea introduced by Cieplak[14] in 1981 to explain the long-known inclination of nucleophiles to attack cyclohexanones from the axial direction. In this view, the energy of the activated complex in a rection involving a forming or breaking bond is lowered by the delocalization of electrons comprising an antiperiplanar vicinal σ bond into the antibonding component of the bond in transition ($\sigma^{*\ddagger}$). It is obvious that electron-withdrawing substituents in our probes then should favor attack on the *zu* face, whereas σ donors should lead to attack on the *en* face, as observed. It is also obvious that this hypothesis is similar to Winstein's proposal[15] of σ participation in heterolysis, and indeed, we have held[8a] that for carbocations, there is no distinction between the two.



Both Cieplak[16] and we[10] have predicted that radical formation and capture should have the same stereoelec-

(2) For informative recent summaries and lead references, see: (a) Fraser, R. R.; Stanciulescu, M. *J. Am. Chem. Soc.* **1987**, *109*, 1580. (b) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353. (c) Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1988**, *110*, 4074. (d) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447. (e) Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449.

(3) (a) Sinnott, M. L.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1446. (b) Storesund, H. J.; Whiting, M. C. *Ibid.* **1975**, 1452. 1,2-Disubstituted adamantanes had already been applied in a similar vein; see, e.g.: Ree, B. R.; Martin, J. C. *J. Am. Chem. Soc.* **1970**, *92*, 1660. Buss, V.; Gleiter, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 3927. We note here in passing that to avoid confusion, we use the numbering shown above throughout this article even though it is technically wrong in some instances (thus, 2-bromo-5-phenyladamantane is really 4-bromo-1-phenyladamantane, etc.).

(4) le Noble, W. J.; Chiou, D.-M.; Matuszynska, H.; Okaya, Y. *Tetrahedron Lett.* **1977**, 3865.

(5) le Noble, W. J.; Chiou, D.-M.; Okaya, Y. *Tetrahedron Lett.* **1978**, 1961.

(6) le Noble, W. J.; Chiou, D.-M.; Okaya, Y. *J. Am. Chem. Soc.* **1978**, *100*, 7743.

(7) le Noble, W. J.; Chiou, D.-M.; Okaya, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3244.

(8) (a) Cheung, C. K.; Tseng, L. T.; Lin, M.-h.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598; **1987**, *109*, 7239. (b) Lin, M.-h.; Cheung, C. K.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 6562. (c) Xie, M.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 3839. (d) Adcock, W.; Coope, J.; Shiner, V. J.; Trout, N. A. *J. Org. Chem.* **1990**, *55*, 1411.

(9) (a) Li, H.; le Noble, W. J. *Tetrahedron Lett.* **1990**, *31*, 4391. (b) Lin, M.-h.; Silver, J. E.; le Noble, W. J. *J. Org. Chem.* **1988**, *53*, 5155. (c) Xie, M.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 3836.

(10) Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874.

(11) (a) Chung, W.-S.; Turro, N. J.; Srivastava, S.; Li, H.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 7882. (b) Chung, W.-S.; Turro, N. J.; Silver, J.; le Noble, W. J. *J. Am. Chem. Soc.* **1990**, *112*, 1202.

(12) (a) Lin, M.-h.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 997. (b) Lin, M.-h.; Watson, W. H.; Kashyap, R. P.; le Noble, W. J. *J. Org. Chem.* **1990**, *55*, 3597.

(13) Lin, M.-h.; Boyd, M. K.; le Noble, W. J. *J. Am. Chem. Soc.* **1989**, *111*, 8746.

(14) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.

(15) Winstein, S.; Trifan, D. *J. Am. Chem. Soc.* **1952**, *74*, 1147, 1154.

(16) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1987**, *109*, 5875.

tronic bias as the other reactions already mentioned, although it is also clear that this prejudice, if it exists at all, will not be as strong as in cationic processes.[17] We describe here the results of our research concerning this question. Two reactions were employed to generate the 2-adamantyl radicals: the Hunsdiecker decarboxylation, and the free-radical addition of bromotrichloromethane.

Results and Discussion

The Hunsdiecker reaction of silver or mercuric carboxylates with bromine to give the corresponding bromide, carbon dioxide, and silver bromide is well-known[18] to take place via free radicals. Indeed, the reaction occurs with loss of configuration;[19] thus, Eliel reported[20] the formation of identical mixtures from *cis*- and *trans*-4-*tert*-butylcyclohexanecarboxylic acids. The 1- and 2-adamantanecarboxylic acids have also been studied by Tabushi.[21] Our own results with the 2-isomer differ somewhat from his in that we did not encounter any chloroadamantane products resulting from chlorine abstraction from the carbon tetrachloride medium. This may be due to our use of red mercuric oxide, as recommended by Cristol,[22] rather than the difficult-to-dry silver salt; in any case, since the differences did not interfere with our planned study, we did not pursue them. Our yields of 2-bromoadamantane were 60%.

The Koch–Haaf approach we used to obtain the 2-carboxylic acid parent compound proved unsuitable for the unknown 5-phenyl derivatives because of sulfonation, and we followed Farcasiu's route[23] instead (Scheme I); this offered the additional advantage of allowing us to test two subsidiary addition reactions the stereochemistry of which had not yet been examined with our adamantyl probe. The first of these is the methylene transfer. Cook[24] and Corey[25] have each recorded an example of a ketone reacting with dimethyl sulfonium and sulfoxonium methylide to give oxiranes of opposite configuration; however, in our case, essentially the same mixture of *E*- and *Z*-**2** was obtained as shown by NMR.[26] We expected the *E* isomer to be the major one, in accord with all of our previous experience, and to confirm this, we applied two highly effective NMR tools to the mixture (which we could enrich but not separate): the ^{13}C NMR additivity method, in which the chemical shifts of all carbon atoms in both isomers are calculated from the values of the corresponding atoms in adamantane, 1-phenyladamantane, and the parent oxirane,[27] and the shift reagent method, which probes the location of the oxygen atom by measurements of the chemical shift changes in response to the addition of small amounts of $Eu(fod)_3$. Both approaches showed to our surprise that the *Z* isomer was in fact the principal product; the methylene had been added to the *en* face by a preference of 58:42, based on CH_2O integration (these hydrogen atoms were assigned on the basis of spectra of enriched mixtures). Consistent with this finding were the following observations. *m*-Chloroperbenzoic acid oxidation of 5-phenyl-2-methyleneadamantane, expected to give predominantly the *Z* isomer of **2**, does indeed produce a mixture of which the NMR spectra were almost identical with that obtained with the sulfur ylids (*E*/*Z* = 42:58). Secondly, the sulfoxonium ylid also gives primarily the *Z* isomer when it is made to react with 5-fluoroadamantan-2-one;[28] the configurations of those compounds had already been proved several years ago.[10] This is the first example we have encountered in which transition-state hyperconjugation does not predict the major isomer correctly. The cause of this exception is undoubtedly the reversibility of the initial, configuration-determining step; Johnson has garnered strong evidence[29] for this supposition. It appears that the thermodynamic preference in this case is opposite to the kinetic one because the former leaves two donor–acceptor pairs of single bonds in antiperiplanar positions.[30] One feature that remains unexplained is that while only dimethyl sulfoxonium methylide reacts with thermodynamic control in the Cook and Corey examples, both reagents do so in our case.[31]

The next step in Scheme I, the acid-catalyzed rearrangement of the oxiranes to give the corresponding aldehydes, gave us the chance to study a 1,2-hydride shift with our probe. Since the aldehydes are not very stable, the mixtures were examined by NMR (aldehyde proton ratio is 59:41) and then at once converted into the carboxylic acids by Jones oxidation; the overall yield in the sequence from ketone to acids is more than 80%. The configurations of the acids and their methyl esters were determined once again by means of the ^{13}C additivity and shift reagent methods; both ^{13}C and ^{1}H NMR integration led to an *E*/*Z* ratio of 58:42. The original and enriched (in *Z* isomer) oxirane mixtures gave the same result. Remarkably, it proved possible in this case to separate the isomeric acids by a simple precipitation procedure; the sodium salt of the major isomer is quite insoluble in water. This makes *E*- and *Z*-**1** probably the most easily accessible pair of epimers in the series of 2,5-disubstituted adamantanes available in pure form to date. The weights of the analytically pure isomers thus isolated (92% from a mixture) agreed with the NMR result, at 55:45. The major isomer (*E*) is the one expected on the basis of the incursion of transition-state hyperconjugation in the hydride shift.

The Hunsdiecker reaction is portrayed in Scheme II. The reaction was carried out under mild conditions (half hour at 40 °C in carbon tetrachloride), at first with an unenriched mixture of *E*- and *Z*-**1**, and this produced a mixture of three compounds. It was established by means of GC–mass spectrometry that they were isomers with composition $C_{10}H_{19}Br$, the parent peaks consisting of doublets with *m*/*z* values of 290 and 292 Da. The GC traces were similar to the HPLC record[32] in that they show

(17) Bartlett, P. D.; McBride, J. M. *J. Am. Chem. Soc.* **1965**, *87*, 1727.
(18) Johnson, R. G.; Ingham, R. K. *Chem. Rev.* **1956**, *56*, 219.
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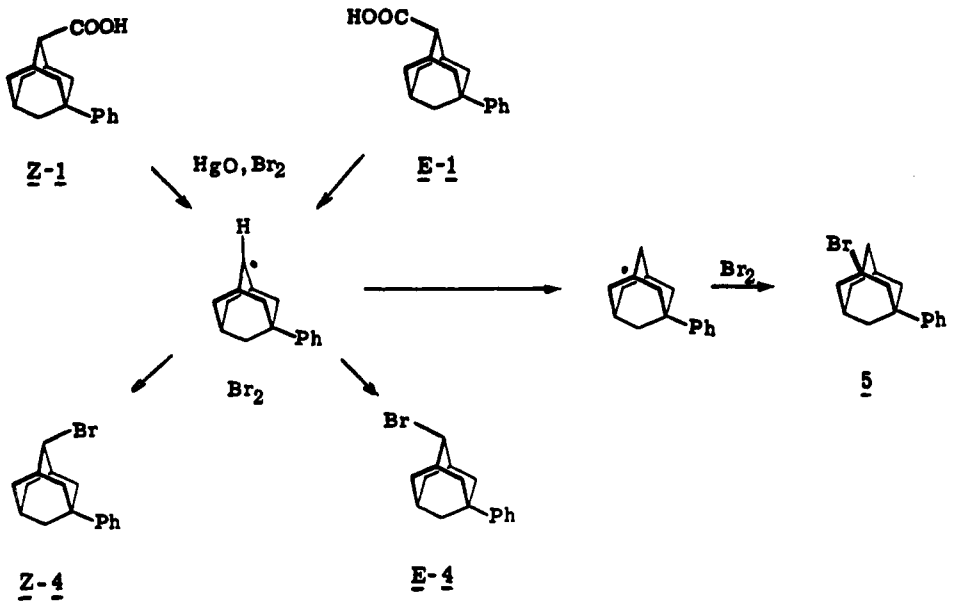
(21) Tabushi, I.; Aoyama, Y.; Kojo, S.; Hamuro, J.; Yoshida, Z. *J. Am. Chem. Soc.* **1972**, *94*, 1177.
(22) Cristol, S. J.; Douglass, J. R.; Firth, W. C.; Krall, R. E. *J. Org. Chem.* **1962**, *27*, 2711.
(23) Farcasiu, D. *Synthesis* **1972**, 615.
(24) Cook, C. E.; Corley, R. C.; Wall, M. E. *Tetrahedron Lett.* **1965**, 891.
(25) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
(26) This finding is reminiscent of an earlier one[9b] in which two alkylating agents reported to exhibit highly different face selectivities vis-a-vis ketones gave exactly the same ratio of products with 5-fluoroadamantanone.
(27) Srivastava, S.; Cheung, C. K.; le Noble, W. J. *Magn. Reson. Chem.* **1985**, *23*, 232.
(28) We thank Mr. A. Mukherjee for this experiment.
(29) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424.
(30) The equilibrium preference for (*Z*)- over (*E*)-2-phenyladamantan-5-ol[5a] and that of (*Z*)- over (*E*)-2-phenyl-2-(tosyloxy)-5-fluoroadamantane (Lin, M.-h. Ph.D. Thesis, Stony Brook, 1987) are other examples of this.
(31) The *E*/*Z* ratios were 44:56 and 41:59 with the sulfonium and sulfoxonium ylids, respectively. One perhaps unlikely possibility that was considered was that of metathesis of the ylid and carbonyl functions, followed by addition of oxygen to the olefin; however, an experiment with ^{17}O-enriched adamantanone ruled it out (see the Experimental Section).
(32) We are indebted to Mr. J. E. Silver of Schering-Plough Corp. for this experiment.

Scheme II

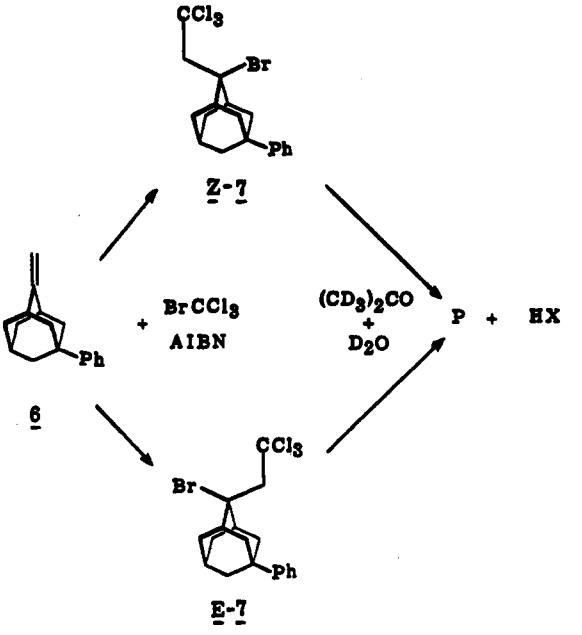


two major peaks, closely spaced but with a base-line separation, and a third minor one with considerably longer retention time. This minor component, amounting to 19% by GC and 24% by HPLC, is presumed to be the 1-bromo-3-phenyladamantane (**5**). The other two isomers were present in the ratio of 58:42 (GC) or 59:41 (HPLC). The results were the same when pure *E*-**1** was employed; with pure *Z*-**1**, a ratio of 62:38 was obtained. It is clear that the products are formed effectively from a common intermediate.[33]

We were unable to separate the isomers on a larger scale, but the ^{13}C NMR spectrum of the mixture could be analyzed satisfactorily in terms of the chemical shifts calculated by means of the additivity method; all 14 signals of the adamantyl skeleton of *E*- and *Z*-**4** and a few of the 10 of **5** were located. Integration of the ^{13}C NMR spectrum was then studied with a program designed to avoid NOE problems.[34] It should be noted that the two C_2 and the two C_6 signals cannot be differentiated by the additivity calculation since the predicted chemical shifts are necessarily the same; however, the $C_{4,9}$ and $C_{8,10}$ signals can be so predicted. All four signal pairs are in the ratio of 43:57, and the *Z* isomer is predominant. Thus, the 2-adamantyl radical preferentially captures the bromine atom at the *zu* face as expected on the basis of transition-state hyperconjugation.

We began our stereochemical study of the free-radical addition of $BrCCl_3$ with scouting experiments which showed that the product from methyleneadamantane is quite sensitive to thermal elimination; thus, if *tert*-butyl peroxide is used as the initiator at 105 °C, the product is exclusively 2-(2,2,2-trichloroethylidene)adamantane. If benzoyl peroxide is used at 80 °C, this is a minor product (20%), appearing together with 80% 2-bromo-2-(2,2,2-trichloroethyl)adamantane, and if AIBN is employed at 60–62 °C, the latter product is virtually the only one after 4–5 h (>95%), at which time the starting material is completely consumed. The starting olefin, the desired

Scheme III



addition product, and the elimination product are easily recognized in the ^1H NMR by their signals at δ 4.5, 3.8, and 6.3, respectively.

The reaction with 5-phenyl-2-methyleneadamantane **6** at 60–62 °C is essentially complete after 10 h and gives rise to a clean mixture of adducts. The trichloroethyl proton signals appear as well-separated signals at δ 3.716 and 3.759, in a 36:64 ratio (Scheme III). None of the methods we have applied earlier to ascertain the configurations were usable in this instance: attempts at chromatographic separation or even enrichment failed, there is no basic atom to complex with shift reagents, and chemical shift additivity cannot be used when the signals in the parent adduct cannot be assigned independently. Fortunately, we could make use of the previously noted instability of the adducts to elimination. On the basis of our earlier work[8] on 2-adamantyl cation capture and formation, the *Z* adduct should undergo elimination much faster than the *E* isomer. Indeed, when a sample of the original product mixture is dissolved in 5:1 $(CD_3)_2CO$ and D_2O (V/V), the signal which is initially the major one quickly diminishes compared to

(33) The 2-adamantyl radical is planar; 2-substituents in some instances render the radical pyramidal. For a discussion, see: Kira, M.; Akiyama, M.; Ichinose, M.; Sakurai, H. *J. Am. Chem. Soc.* **1989**, *111*, 8256.

(34) Harris, R. K. *Nuclear Magnetic Resonance Spectroscopy. A Physiochemical View*; Longman: Burnt Hill, Harlow, Essex, England, 1983; p 113.

the minor methylene signal, and it has completely vanished when the minor isomer is still plainly present. By comparing these two peaks with others in the spectrum, we can estimate that the rate ratio is roughly 10;[35] the major reaction of the 2-(2,2,2-trichloroethyl)adamantyl radical has again occurred at the *zu* face. We conclude that, like other reactions studied before, radical capture favors that face which has the most electron rich bond antiperiplanar to the newly forming bond.

Experimental Section

General. All NMR spectra were taken with our QE 300 instrument in $CDCl_3$ unless otherwise noted. 2-Adamantanecarboxylic acid was prepared from 2-adamantanol by means of a Koch–Haaf procedure in 91% yield as described by McKervey.[36] ^1H NMR: δ 11 (OH, bs, 1 H), 2.67 (C_2H, s, 1 H), 2.35 ($H_{1,3}$, s, 2 H), 1.97–1.67 (m, 12 H). ^{13}C NMR: δ 181.25 (COOH), 49.43 (C_2), 38.10 ($C_{8,10}$), 37.26 (C_6), 33.53 ($C_{4,9}$), 29.33 ($C_{1,3}$), 27.35 ($C_{5,7}$). The ^{13}C data agree with a literature listing.[37] 2-Methyleneadamantane was prepared as described elsewhere.[10]

5-Phenyl-2-adamantanespirooxirane (2). Sodium hydride (50.9 mg, 2.12 mM) in the form of a 50% dispersion in mineral oil was washed three times with pentane, and dimethyl sulfoxide (10 mL, dried over CaH_2) and solid trimethyl sulfoxonium iodide (Aldrich, 220 mg, 0.99 mM) were added. Fifteen minutes after hydrogen evolution ceased, the flask was cooled to room temperature, and 5-phenyladamantan-2-one[8a] (200 mg, 0.88 mM) was added in small portions. The mixture was stirred at room temperature for 1 h and then at 55 °C for 1.5 h, cooled to room temperature, and poured into ice–water (20 mL). Extraction with hexane gave a crude mixture (190 mg, 89%) that was analyzed by means of ^1H and ^{13}C NMR. It was purified by flash column chromatography (silica gel, ethyl acetate–hexane) and crystallization (hexane) to give a white solid (155 mg, 73%) with a narrow melting range (58–59 °C). By collecting very small fractions in a chromatographic separation, it was possible to enrich the major isomer up to 80%. The assignment of configuration and analysis are described in the text. ^1H NMR: δ 7.39–7.19 (m, ArH), 2.71 (s, CH_2O, *Z*-**2**), 2.69 (s, CH_2O, *E*-**2**), 2.28–1.57 (m). ^{13}C NMR [where applicable, calculated chemical shifts and sensitivity to $Eu(fod)_3$ (in arbitrary units, valid for this experiment alone) are given in parentheses] *E*-**2**: δ 149.54 (C_i), 128.13 (C_m), 125.81 (C_p), 124.81 (C_o), 64.12 (C_2, 63.31, 61.23), 54.84 (CH_2O, 61.62), 42.58 (C_6, 42.12, 5.55), 42.32 ($C_{4,9}$, 41.90, 6.33), 36.11 ($C_{1,3}$, 36.24, 21.40), 35.63 (C_5, 34.45, 7.17), 34.14 ($C_{8,10}$, 33.81, 10.30), 27.55 (C_7, 27.48, 5.53).

Z-**2**: δ 149.82 (C_i), 128.14 (C_m), 125.73 (C_p), 124.79 (C_o), 63.69 (C_2, 63.31, 41.83), 54.49 (CH_2O, 41.74), 42.58 (C_6, 42.12, 3.79), 40.54 ($C_{4,9}$, 40.11, 7.27), 36.36 ($C_{1,3}$, 36.24, 14.66), 35.89 ($C_{8,10}$, 35.60, 4.54), 35.36 (C_5, 34.45, 5.54), 27.69 (C_7, 27.48, 5.05).

The known parent compound was also prepared by this route.[23] ^1H NMR: δ 2.63 (CH_2O, s, 2 H), 2.05–1.73 (m, 12 H), 1.39 ($H_{1,3}$, bs, 2 H). ^{13}C NMR (relative $Eu(fod)_3$ sensitivities in parentheses): δ 64.41 (C_2, 50.66), 54.65 (CH_2O, 50.26), 36.92 (C_6, 4.36), 36.70 ($C_{8,10}$, 4.96), 35.74 ($C_{1,3}$, 17.59), 34.91 ($C_{4,9}$, 8.31), 26.98 (C_7, 5.89), 26.85 (C_5, 6.39).

Search for Oxygen Scrambling.[31] Adamantanone (100 mg, H_2O–^{17}O (5%, 0.2 mL, also contains substantial amount of ^{18}O) and THF (0.5 mL) were sealed together in a thick-walled vessel, and the tube was heated in refluxing THF for 1 week. The labeled adamantanone was converted into the spirooxirane as described above. Comparison of the ^{17}O NMR spectra in $CHCl_3$ solution by means of an MSL 400-MHz spectrometer showed that the compounds had comparable ^{17}O contents. Analysis of the M, M + 1, and M + 2 peaks of the mass spectra showed that no ^{17}O loss had occurred at all during the epoxidation. Adamantanone: M + 1, 20.1%, M + 2, 29.4%. Oxirane: M + 1, 22.4%, M + 2, 29.5%. It was also found that dimethylsulfone does not oxidize **6**.

5-Phenyl-2-adamantanecarboxylic Acid (1). A solution of the unenriched mixture of oxiranes **2** (180 mg, 0.75 mM) in dry benzene (distilled from sodium, 15 mL) was treated with freshly distilled boron trifluoride etherate (64 mg, 0.45 mM) in a separatory funnel at room temperature for 1 min; cold water was added, and the organic layer was worked up in the usual way to afford 5-phenyl-2-adamantanecarboxaldehydes **3** as a viscous liquid. TLC (ethyl acetate–hexane) gave a single spot. ^1H NMR: δ 9.81 (s), 9.74 (s), 7.35–7.17 (m), 2.59 (s), 2.45 (bs), 2.18–1.64 (m). ^{13}C NMR: δ 205.29, 150.06, 149.97, 128.19, 125.82, 124.77, 55.84, 55.64, 43.26, 42.62, 42.55, 38.94, 36.88, 36.23, 32.61, 28.73, 28.59, 28.12. Several batches of crude mixture were combined (443 mg, 1.85 mM), dissolved in acetone (50 mL) and treated with Jones' reagent (10 mL, 8 N CrO_3) with stirring at 15–20 °C for 5 min and then at room temperature for 3 h. Deposits forming on the side of the flask were occasionally rinsed back in with acetone. The solution was poured into water (40 mL) and extracted with chloroform. Further workup as usual furnished crude **1** (412 mg, 87%), melting over the range 149–157 °C. Treatment of this solid with 1 N NaOH (60 mL) at 50 °C for 30 min followed by filtration while still warm, acidification (concentrated HCl) of the solution, and extraction with chloroform led to *Z*-**1** (175 mg, 42%); similar treatment of the insoluble solid gave *E*-**1** (205 mg, 50%). Both isomers were crystallized from chloroform–hexane. *E*-**1**: mp 184–5 °C. ^1H NMR: δ 11.5 (bs, 1 H), 7.33–7.16 (m, 5 H), 2.73 (s, 1 H), 2.56 (s, 2 H), 2.09–1.94 (m, 9 H), 1.69–1.65 (m, 2 H). ^{13}C NMR (where applicable, calculated values in parentheses): δ 180.98 (COOH), 150.08 (C_i), 128.18 (C_m), 125.79 (C_p), 124.81 (C_o), 48.83 (C_2, 48.50), 43.45 ($C_{4,9}$, 43.40), 42.95 (C_6, 42.60), 35.64 (C_5, 35.10), 32.72 ($C_{8,10}$, 32.60), 29.98 ($C_{1,3}$, 30.00), 28.01 (C_7, 28.00). Anal. Calcd: C, 79.65; H, 7.86. Found: C, 79.30; H, 7.98.

Z-**1**: mp 190–1 °C. ^1H NMR: δ 11.8 (bs, 1 H), 7.33–7.17 (m, 5 H), 2.69 (s, 1 H), 2.57 (s, 2 H), 2.07–1.78 (m, 11 H); ^{13}C NMR: δ 180.98 (COOH), 150.39 (C_i), 128.18 (C_m), 125.74 (C_p), 124.81 (C_o), 48.56 (C_2, 48.50), 43.09 (C_6, 42.60), 38.88 ($C_{4,9}$, 38.90), 37.12 ($C_{8,10}$, 37.10), 35.56 (C_5, 35.10), 30.07 ($C_{1,3}$, 30.00), 28.12 (C_7, 28.00). Anal. Calcd: C, 79.65; H, 7.86. Found: C, 79.45; H, 8.03.

The (*E*)-methyl ester was prepared with diazomethane; the effects of $Eu(fod)_3$ on the carbon resonances were meausred and used to assign the signals. The shifts so obtained were compared with those calculated on the basis of the parent ester.[37] *E* ester, ^1H NMR: δ 7.4–7.2 (m, 5 H), 3.72 (s, 3 H), 2.65 (s, 1 H), 2.54 (s, 2 H), 2.1–1.6 (m, 11 H). ^{13}C NMR (where applicable, calculated values and $Eu(fod)_3$-induced shifts given in parentheses): δ 174.75 (COOMe), 150.13 (C_i), 128.13 (C_m), 125.70 (C_p), 124.75 (C_o), 51.43 ($COOCH_3$, 16.72), 48.85 (C_2, 48.50, 17.01), 43.43 ($C_{4,9}$, 43.50, 3.56), 42.97 (C_6, 42.80, 2.44), 35.61 (C_5, 35.40, 3.02), 32.68 ($C_{8,10}$, 32.40, 7.38), 30.09 ($C_{1,3}$, 30.30, 10.63), 28.00 (C_7, 28.30, 4.52) (calculated for the *Z* ester: $C_{4,9}$, 38.90 and $C_{8,10}$, 37.20).

Hunsdiecker Reactions. General Procedure. A sample of 2-adamantanecarboxylic acid (25 mg, 0.14 mM) was mixed with red mercuric oxide (38 mg, 0.17 mM) in 2 mL of CCl_4 and stirred at 40 °C for 50 min. A 1% solution of bromine in CCl_4 (0.01 mL) was added in one lot. The mixture was stirred at 40 °C for an additional 30 min, cooled to room temperature, diluted with CCl_4 (10 mL), and filtered; the filtrate was worked up to give a crude product shown to be 2-adamantyl bromide by comparison with an authentic sample (^1H and ^{13}C NMR). The yield was 60%. Application of this procedure to *E*- and *Z*-**1** as well as a mixture of the two gave essentially identical mixtures. These mixtures were analyzed by means of HPLC (Waters 990, 80/20 methanol–water, flow rate 1 mL/min at 900 psi) to give three peaks at 16.2, 17.2, and 20.6 min in the ratio 43.2:30.1:17.6 and by means of capillary GC (J & W scientific, DB 1701, 30-m column, T program: 100 °C for 2 min, then increasing at 5 °C/min until 250 °C) to give three peaks at 31.4, 31.6, and 37.0 min in the ratio 23.7:16.9:13.1, respectively. ^1H NMR: δ 7.30–7.21 (m, 5 H), 4.69 (s, 1 H), 2.67–1.65 (13 H). ^{13}C NMR: δ 149.86, 149.16, 128.17, 125.88, 125.79, 124.74, 124.69, 62.56 (C_2, *E*), 62.20 (C_2, *Z*), 43.87 ($C_{4,9}$, *E*), 43.47 (C_6, *E*), 43.15 (C_6, *Z*), 37.71 ($C_{8,10}$, *Z*), 37.05 ($C_{4,9}$, *Z*), 36.61 ($C_{1,3}$, *E*, *Z*), 35.74 (C_5, *E*), 35.20 (C_5, *Z*), 30.76 ($C_{8,10}$, *E*), 28.08 (C_7, *E*), 27.45 (C_7, *Z*). Calcd shifts: *E*-**4**, 44.00 ($C_{4,9}$), 30.60

(35) It was noted that the vinyl region shows the growth of three singlets rather than the one implied by Scheme III: two nearly equally intense peaks at δ 6.452 and 6.465, and a third at δ 6.290. The former two slowly give way to the latter.

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($C_{8,10}$); *Z*-**4**, 36.90 ($C_{4,9}$), 37.70 ($C_{8,10}$). The analysis was done by ^{13}C NMR integration of an oxygen-saturated $CDCl_3$ solution by means of the 1PDNA pulse sequence with delay time of 36 s; 1500 transients were taken.[34] The *E*/*Z* peak ratios were 43:57 based on C_2, 44:56 based on C_6, 42:58 with $C_{4,9}$, and 43.5:56.5 with $C_{8,10}$.

2-Bromo-2-(2,2,2-trichloroethyl)adamantane. Treatment of methyleneadamantane (1 equiv), dissolved in bromotrichloromethane (10 equiv), with di-*tert*-butyl peroxide (0.3 equiv) at 105 °C for 4 h gave a product the ^1H NMR spectrum of which showed that no starting olefin was left (δ 4.50) and that the product (CH_2CCl_3, δ 3.72) had virtually completely decomposed by elimination: the three single peaks observed at δ 6.20–6.25 suggest that the allylic halide products are capable of allylic rearrangement and/or halide exchange. If benzoyl peroxide was substituted (0.06 equiv) and the reaction done at 80 °C for 3–4 h, the ^1H NMR showed the addition to be complete and that only 20% of the adduct had decomposed; use of AIBN (0.05 equiv) at 60–62 °C for 5 h gave rise to fairly pure adduct with a melting range of 32–47 °C. ^1H NMR: δ 3.72 (s, 2 H), 2.71 (s, 1 H), 2.67 (s, 1 H), 2.43 (s, 2 H), 2.28 (s, 1 H), 2.23 (s, 1 H), 2.0–1.7 (m, 8 H). ^{13}C NMR: δ 97.67 (CCl_3), 77.80 (C_2), 61.78 (CH_2CCl_3), 39.69 ($C_{1,3}$), 39.20 (C_6), 34.94 ($C_{8,10}$), 34.69 ($C_{4,9}$), 26.83 ($C_{5,7}$).

2-Methylene-5-phenyladamantane (6). The procedure is similar to Olah's.[38] Methyl triphenylphosphonium bromide (1.89 g, 5.3 mM), dried over P_2O_5 at 85 °C overnight, was covered with ether (25 mL) freshly distilled from sodium benzophenone ketyl and treated with *n*-butyllithium (2.4 M in hexane, 2.2 mL, 5.3 mM) with stirring under nitrogen. The salt dissolved in a half hour to give a brick-red solution. 5-Phenyladamantanone (1 g, 4.4 mM) in ether (20 mL) was added in 15 min at room temperature; then, the mixture was refluxed for 20 h. After the addition of water (40 mL) and filtration to remove the phosphine oxide, the usual workup furnished 1.22 g of a viscous liquid which solidified after chromatography (silica gel, hexane). Yield: 0.95 g (96%). Mp: 28–29 °C. ^1H NMR: δ 7.36–7.15 (m, 5 H), 4.58 (s, 2 H), 2.65 (s, 2 H), 2.2–1.8 (m, 11 H). ^{13}C NMR: δ 156.87 (C_2), 150.10 (C_i), 128.12 (C_m), 125.65 (C_p), 124.84 (C_o), 101.42 (=CH_2), 44.89 ($C_{4,9}$), 42.65 (C_6), 39.27 ($C_{1,3}$), 38.71 ($C_{8,10}$), 36.38 (C_5), 28.89 (C_7). High resolution MS: calcd 224.1565, found 224.1564.

2-Bromo-5-phenyl-2-(2,2,2-trichloroethyl)adamantanes (7). Treatment of olefin **6** with $BrCCl_3$ and initiator AIBN as described above (10 h) gave a viscous, liquid product essentially free of olefins. ^1H NMR: δ 7.39–7.21 (m), 3.76 (s), 3.72 (s), 2.93–1.82 (m). ^{13}C NMR: δ 149.10, 148.69, 128.34, 128.20, 126.10, 125.89, 124.77, 124.55, 97.61, 97.45, 76.45, 76.36, 61.70, 61.47, 45.50, 44.46, 40.51, 40.42, 40.08, 39.62, 35.39, 35.30, 34.16, 33.87, 27.45, 27.40. The CH_2CCl_3 peaks at δ 3.76 and 3.72 were in a 64:36 ratio. Dissolution of the mixture in acetone-d_6–D_2O (5:1, v/v) and monitoring of these peaks at 21 °C showed that the major peak at δ 3.76 vanished roughly 10 times faster than the minor one; it was gone after 24 h, at which point the 3.72 peak was at about 30% of its original intensity. Three signals grew in simultaneously at δ ~6.5; their relative intensities change, and after 4 days only one was left, at δ 6.30.

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Supplementary Material Available: Calculated and observed chemical ^{13}C shifts of *E*- and *Z*-**2** and their dependence on added shift reagent and the ^{13}C spectra of mixtures of *E*- and *Z*-**2** and of *E*- and *Z*-**7** (3 pages). Ordering information is given on any current masthead page.

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Stereochemistry of Nucleophilic Addition to Several Rigid, Sterically Unbiased 7-Norbornanones

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A stereochemical investigation is reported of the reactions of lithium aluminum hydride (LAH) and of methyllithium with three sterically unbiased, rigid ketones: tetracyclo[7.4.0.0^{2,7}.0^{6,10}]trideca-3,12-dien-8-one (**2**), pentacyclo[6.5.0.0^{4,12}.0^{5,10}.0^{9,13}]tridecan-11-one (**3**), and pentacyclo[6.5.0.0^{4,12}.0^{5,10}.0^{9,13}]trideca-2,6-dien-11-one (**4**). Various proton NMR techniques were brought to bear upon the dual problems of characterization and analysis of the mixtures of epimeric alcohols obtained. The results can be interpreted in terms of transition-state hyperconjugation. A comparison with literature data on other endo-substituted 7-norbornanones points up the need, in studies of electronically controlled face selection, for probes that not only have sterically equivalent faces but are also conformationally rigid.

Introduction

Face selection in additions to trigonal carbon is at the heart of stereogenesis, and much attention has been lavished on it.[1] A multitude of factors can influence it; they include steric effects, conformations of the flanking groups, complexation of reagents, deviations from planarity, product stability, and electronic effects. Studies of these factors have usually depended on choices of substrates, the faces of which are equivalent, as much as possible, with respect to each of the other effects. Cyclic and polycyclic ketones and their reactions with reducing and alkylating agents have therefore been prominent in these studies. We presently report our results observed in the LAH reduction and methylation with MeLi of several 7-norbornanones and compare them with others known to have been stud-

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