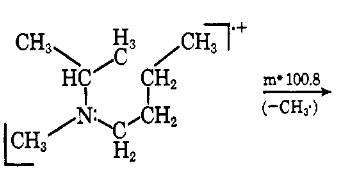
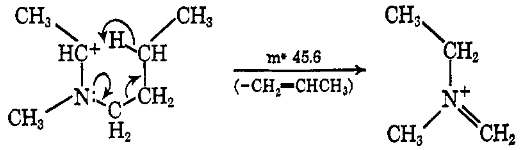


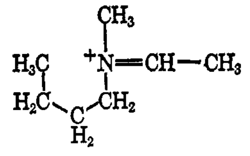
VII, *m/e* 129



VIII, *m/e* 114

severe crowding of the two carbon-bound hydrogens will occur during the transformation).

Hydrogen transfer reactions in the π-bonded conformer of VIII (VIIIa) are fundamentally different than hydrogen transfer reactions in radical cations. Electrocyclic processes which involve only the nitrogen end of the π bond are impossible because the nitrogen valence is saturated. Hydrogen transfer reactions that involve only the nitrogen center in VIIIa should be simply internal displacement reactions. The optimum size for cyclic transition states in these cases will depend more upon geometric factors than electronic factors. The nonspecificity of hydrogen transfer reactions in ions like VIIIa[21] is in accord with this view. Even-electron ions may be qualitatively dealt with as vibrationally excited protonated molecules. If the NBMO which contains the unshared pair in the molecule extends over the entire framework in excited vibrational states, proton mobility should be fairly high in even-electron ions, as has been observed.



VIIIa

Experimental Section

The mass spectra of hexahelicene and related compounds were determined by use of the direct inlet system on an A.E.I. MS-902 double-focusing mass spectrometer with the emission adjusted to 70 eV.

Acknowledgments. It is a pleasure to acknowledge useful discussions with Professors M. J. S. Dewar and M. S. Newman. Professor Newman has also supplied samples of all of the hydrocarbons we have examined. Mr. C. R. Weisenberger provided very able assistance with the mass spectrometer. The mass spectrometer was purchased with a grant from the National Science Foundation. The National Institutes of Health has generously supported our work.

Stereochemistry of the Reactions of 4-Substituted Cyclohexyl Radicals

Frederick R. Jensen, Laird H. Gale, and James E. Rodgers

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received March 25, 1968*

Abstract: The Hunsdiecker reaction with either *cis*- or *trans*-4-alkylcyclohexanecarboxylic acids (alkyl = methyl or *t*-butyl) or the bromine cleavage of *cis*- or *trans*-4-*t*-butylcyclohexylmercuric bromides yields a near-statistical distribution of bromides. In contrast, the sulfuryl chloride cleavage of either *cis*- or *trans*-4-*t*-butylcyclohexylmercuric chlorides yields a *cis:trans* distribution of 70:30. These isomer ratios and values in the literature from cyclohexyl and 2-norbornyl derivatives correspond well with distributions expected on the basis that torsional strain is the controlling factor. Reactions which tend more toward statistical isomer distributions are those which have low heats of reaction and which are expected to have only small structure development in their transition states. Reactions which have more bond formation in their transition states tend to give the products (axial-cyclohexyl or *exo*-norbornyl) which arise from pathways having smaller torsional strain.

Product studies of the halogen transfer reactions of 4-substituted cyclohexyl radicals provide valuable insight into the stereochemistry of atom transfer reactions. The results reported in the literature suggest that a variety of stereochemical outcomes are possible depending on the nature of the atom transfer reagent.[1-5] In the present study the Hunsdiecker reaction has been reinvestigated at a much lower temperature than used previously,[1] with both *cis*- and *trans*-4-methyl- and *cis*- and *trans*-4-*t*-butylcyclohexanecarboxylic acids. In addition, the radical halogen cleavage of alkylmercuric halides[5] has been extended to *cis*- and *trans*-4-*t*-butylcyclohexylmercuric halides. Consideration of the stereochemical results of these reactions plus the data in the literature has resulted in a unifying explanation for the diverse stereochemical product distributions obtained from halogen transfer reactions of 4-substituted cyclohexyl and 2-norbornyl radicals.

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(1) E. L. Eliel and R. V. Acharya, *J. Org. Chem.*, **24**, 151 (1959).

(2) F. D. Greene, C. Chu, and J. Walia, *ibid.*, **29**, 1285 (1964).

(3) F. D. Greene, C. Chu, and J. Walia, *J. Am. Chem. Soc.*, **84**, 2463 (1962).

(4) H. H. Lau and H. Hart, *ibid.*, **81**, 4897 (1959).

(5) F. R. Jensen and L. H. Gale, *ibid.*, **82**, 148 (1960).

Table I. Product Distribution from the Hunsdiecker Reaction with the Silver Salts of *cis-* and *trans*-4-Methyl- and *cis-* and *trans*-4-*t*-Butylcyclohexanecarboxylic Acids

Silver salt	Type of addition[d]	Temp, °C	Yield, %	Alkyl bromide product distribution, % *cis*	*trans*
trans-4-Methyl	N	0	56	48.0	52.0
trans-4-Methyl	I	0	25	48.3	51.7
cis-4-Methyl[a]	N	0	40	50.9	49.1
cis-4-Methyl	I	0	49	51.0	49.0
trans-4-*t*-Butyl[b]	N	0	57	49.4	50.6
cis-4-*t*-Butyl[b]	N	0	62	55.4	44.6
1:1 mixture[b] 4-*t*-Butyl	N	0	60	52.2	47.8
cis-4-*t*-Butyl	N	−15	62	55.2	44.8
trans-4-*t*-Butyl	N	−15	54	50.1	49.9
cis-4-*t*-Butyl	N	25	55	51.7	48.3
cis-4-*t*-Butyl	N	50	42	48.5	51.5
cis-4-*t*-Butyl	N	75	38	50.3	49.7
trans-4-*t*-Butyl[c]	N	0	67	50.0	50.0
cis-4-*t*-Butyl[c]	N	0	52	56.0	44.0

[a] Average of two experiments. [b] Average of six experiments for each conditions, and an average of the product distribution by nmr with a precision of ±1.5%. [c] Bromine was added all at once. [d] N = normal addition, I = inverse addition.

Results

Hunsdiecker Reaction. *cis-* and *trans*-4-methyl- and *cis-* and *trans*-4-*t*-butylcyclohexanecarboxylic acids were prepared by standard procedures. The silver salts of these acids were prepared and subjected to the Hunsdiecker reaction. The product distributions resulting from the 4-methylcyclohexanecarboxylic acids were determined by infrared analysis employing the intensity of the C–Br equatorial absorption at 14.2 μ and the C–Br axial absorption at 14.6 μ as measures of *trans*-4-methyl- and *cis*-4-methylcyclohexyl bromides, respectively.[6] The product distributions resulting from the 4-*t*-butylcyclohexanecarboxylic acids were determined by nuclear magnetic resonance techniques. The peak areas were found quantitatively, assigning the multiplet at δ 3.88 to *trans*-4-*t*-butylcyclohexyl bromide (axial proton) and the broad singlet at δ 4.59 to *cis*-4-*t*-butylcyclohexyl bromide (equatorial proton). The standards used for calibrating the ir analyses and assigning peaks for the nmr analyses were prepared by the stereospecific cleavage of pure *cis-* and *trans*-4-methyl- and pure *cis-* and *trans*-4-*t*-butylcyclohexylmercuric bromides by bromine in pyridine solution.[5] The results are summarized in Table I.

The product distribution is almost statistical at 0° starting with the silver salts of either *cis*-4-methyl- or *trans*-4-methylcyclohexanecarboxylic acid. The method of reaction, normal or inverse addition, has no effect on the product distribution. The slight reproducible preference for *trans*-bromide from the *trans* acid and *cis*-bromide from the *cis* acid suggests a small degree of retention of configuration. In control experiments it was demonstrated that the more stable *trans* acid could be recovered from the silver salt with no loss of configuration and that the more stable *trans*-4-methylcyclohexyl bromide is not isomerized under the reaction conditions.[7] These control experiments do not eliminate the possibility of selective decomposition of *cis*-4-methylcyclohexyl bromide; however, the reproducibility of the experimental results and the low reaction temperature argue against this.

The silver salts of either *cis-* or *trans*-4-*t*-butylcyclohexanecarboxylic acid also yield nearly statistical product distributions from the Hunsdiecker reaction at 0°, in contrast to Eliel and Acharya's[1] results at 77°. The observed tendency for retention of configuration is greater with the 4-*t*-butyl-substituted acids, the *cis* acid yielding 55.4% *cis*-bromide while the *trans* acid yields 50.6% *trans*-bromide. A 1:1 mixture of the two acids yields a product distribution intermediate between that from either pure acid. The effect of reaction temperature was investigated starting with the silver salts of *cis*-4-*t*-butylcyclohexanecarboxylic acid and, as the temperature is increased, a progressive decrease occurs in the amount of *cis*-bromide in the product. This decrease in *cis*-bromide parallels a general decrease in the over-all alkyl bromide yield from 62 to 38% and probably results from selective decomposition of the *cis*-4-*t*-butylcyclohexyl bromide. A control experiment demonstrated that selective decomposition of *cis*-4-*t*-butylcyclohexyl bromide occurs when a mixture of the *cis-* and *trans*-alkyl bromides is maintained in refluxing carbon tetrachloride for 2 hr.

Halogen Cleavage of Alkylmercuric Halides. Pure samples of *cis-* and of *trans*-4-*t*-butylcyclohexylmercuric bromides were prepared by a general method described previously.[8] Each isomeric mercuric bromide was cleaved with bromine in an inert atmosphere at 0°, reaction conditions which favor the free-radical cleavage.[5] The product distributions of *cis-* and *trans*-4-*t*-butylcyclohexyl bromides were determined by the nmr technique and the results are summarized in Table II. Table II also summarizes the similar results for the bromine cleavage of *cis-* and *trans*-4-methylcyclohexylmercuric bromides.[5] Approximately statistical distributions of *cis-* and *trans*-4-alkylcyclohexyl bromides are obtained from the bromine cleavage of each of the pure 4-alkylcyclohexylmercuric bromides.

Pure *cis-* and *trans*-4-*t*-butylcyclohexylmercuric chlorides were prepared from the corresponding alkylmercuric bromides. The attempted chlorine cleavage of *trans*-4-*t*-butylcyclohexylmercuric chloride gave a low

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(6) D. H. R. Barton, J. E. Page, and C. W. Shoppee, *J. Chem. Soc.*, 331 (1956).

(7) Since the products contain more of the less stable *cis* isomer than the thermodynamically predicted distribution, it is important to demonstrate that the more stable acid and bromide are not isomerized during the reaction.

(8) F. R. Jensen and L. H. Gale, *J. Am. Chem. Soc.*, **82**, 145 (1960).

Table II. Product Distribution from Radical Cleavages of *cis*- and *trans*-4-Alkylcyclohexylmercuric Halides

Isomer	Alkylmercuric	Conditions	Yield, %	Product distribution, % *cis*	Product distribution, % *trans*
trans-4-*t*-Butyl	Bromide	Br_2, CCl_4, 0°	55	50.6	49.4
cis-4-*t*-Butyl	Bromide	Br_2, CCl_4, 0°	50	51.5	48.5
trans-4-Methyl	Bromide	Br_2, CCl_4, 0°	62	47.6	52.4
trans-4-Methyl	Bromide	Br_2, CS_2, 0°	. . .	47.2	52.8
cis-4-Methyl	Bromide	Br_2, CCl_4, 0°	67	47.4	52.6
trans-4-*t*-Butyl	Chloride	SO_2Cl_2, CS_2, 46°	28	70.2	29.8
cis-4-*t*-Butyl	Chloride	SO_2Cl_2, CS_2, 46°	38	69.2	30.8

yield (3%) of 4-*t*-butylcyclohexyl chloride. Higher yields were obtained when sulfuryl chloride was used as the chlorination agent in carbon disulfide. Both *cis*- and *trans*-4-*t*-butylcyclohexylmercuric chlorides gave identical mixtures of *cis*- and *trans*-4-*t*-butylcyclohexyl chlorides containing 69.7 ± 0.5% *cis*-chloride as determined by nmr analysis (Table II).

Discussion

Hunsdiecker Reaction. The Hunsdiecker reaction is generally represented as a free-radical chain decomposition of the intermediate acyl hypobromite (Br_2 may also participate in the chain process).[9]

Acyl hypobromite formation and decomposition

$$RCO_2Ag + Br_2 \longrightarrow RCO_2Br + AgBr \qquad (1)$$

$$RCO_2Br \longrightarrow RCO_2\cdot + Br\cdot \qquad (2)$$

Chain decomposition

$$RCO_2\cdot \longrightarrow R\cdot + CO_2 \qquad (3)$$

$$R\cdot + RCO_2Br \longrightarrow RBr + RCO_2\cdot \qquad (4)$$

Therefore, the product-forming step is probably the abstraction of bromine from the acyl hypobromite by the 4-alkylcyclohexyl radical. The present results indicate that this atom transfer reaction with both 4-methyl- and 4-*t*-butylcyclohexyl radicals gives nearly statistical product distributions. The small net retention of configuration may arise from thermal decomposition of the acyl hypobromite, reaction 1, followed by rapid cage

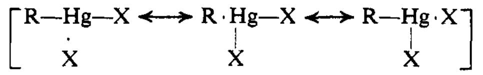
$$RCO_2Br \longrightarrow [RCO_2\cdot Br\cdot] \longrightarrow [R\cdot \quad CO_2 \quad Br\cdot] \longrightarrow RBr + CO_2 \qquad (5)$$

recombination of alkyl radical and bromine atom. A solvent cage mechanism has been invoked[10] to account for the retention of configuration observed in the thermal decomposition of optically active α-methylbutyryl peroxide.[11]

These results contrast with those of Eliel and Acharya,[1] who reported that the Hunsdiecker reaction with *cis*- and *trans*-4-*t*-butylcyclohexanecarboxylic acids yields identical mixtures of *cis*- and *trans*-4-*t*-butylcyclohexyl bromides containing 65 ± 3% of the *trans* isomer. The present reactions were carried out at 0° for a period of 1–1.5 hr (52–67% yield), but the major amount of carbon dioxide evolution was over in several min, while those of Eliel and Acharya were carried out in refluxing carbon tetrachloride for 1–5 hr (31% yield). It is likely then that the difference in results is due to selective decomposition of the more unstable *cis*-4-*t*-butylcyclohexyl bromide at the higher temperature; indeed, both the previous studies of Eliel and Acharya[1] and Green, Chu, and Walia[2,3] and the present study have presented data supporting this conclusion.

Halogen Cleavage of Alkylmercuric Halides. The available data support a free-radical chain reaction for the halogen cleavage of alkylmercuric halides in nonpolar solvents and an inert atmosphere.[5,12] A generalized free-radical chain mechanism which is consistent with the available data is

$$X\cdot + RHgX \longrightarrow$$



$$\left[\underset{X}{R\cdot}\!-\!Hg\!-\!X \longleftrightarrow R\cdot \underset{X}{Hg}\!-\!X \longleftrightarrow R\!-\!\underset{X}{Hg}\cdot X \right] \qquad (6)$$

I

$$I \longrightarrow R\cdot + HgX_2 \qquad (7)$$

$$R\cdot + X_2 \longrightarrow RX + X\cdot \qquad (8)$$

Thus, the isomer distribution from the bromine cleavage of either *cis*- or *trans*-4-*t*-butylcyclohexylmercuric bromides is expected to represent the stereochemical outcome of the reaction of the 4-*t*-butylcyclohexyl radical with bromine. The present results demonstrate that bromine cleavage of either *cis*- or *trans*-4-*t*-butylcyclohexylmercuric bromides yields an identical and nearly statistical product distribution. These results agree with those from the earlier bromine cleavage of *cis*- and *trans*-4-methylcyclohexylmercuric bromides[5] and demonstrate that the reaction of 4-substituted cyclohexyl radical with bromine as the halogen donor is nonselective.[13]

Russell and Brown[14] have demonstrated that sulfuryl chloride is a free-radical type chlorination agent and that in the chlorination of hydrocarbons the abstracting species is either $\cdot SO_2Cl$ or $Cl\cdot$ depending on the reaction conditions. It is likely that the cleavage of alkylmercuric chlorides by sulfuryl chloride in refluxing carbon disulfide proceeds by the reaction sequence shown above, eq 6, 7, and 8, where $X\cdot$ is $Cl\cdot$ and X_2 is SO_2Cl_2. The product-forming step is then the reaction of alkyl radical with sulfuryl chloride. Our results demonstrate that the abstraction of chlorine atom from sulfuryl chloride by 4-*t*-butylcyclohexyl radical gives preferential formation of the *cis*-chloride. These results are similar to the findings of Greene, Chu, and Walia[2,3] with alkyl hypochlorite and carbon tetrachloride as chlorine atom donors.

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(9) J. Kleinberg, *Chem. Rev.*, **40**, 381 (1947); R. G. Johnson and R. K. Ingham, *ibid.*, **56**, 219 (1956); C. V. Wilson, *Org. Reactions*, **9**, 332 (1957).

(10) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p 502.

(11) M. S. Karasch, J. Kuderna, and W. Nudenberg, *J. Org. Chem.*, **19**, 1283 (1955).

(12) J. Keller, Ph.D. Dissertation, University of California at Los Angeles, 1948, as quoted in S. Winstein and T. G. Traylor, *J. Am. Chem. Soc.*, **78**, 2597 (1956).

(13) The possibility of isomerization of the starting materials with these reaction conditions has been ruled out. Unpublished results with J. J. Miller.

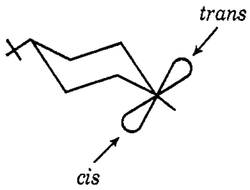
(14) G. A. Russell and H. C. Brown, *J. Am. Chem. Soc.*, **77**, 4031 (1955).

Table III. Stereochemistry of Abstraction Reactions of 4-Substituted Cyclohexyl Radicals

Substituent	Source	Halogen transfer agent	Temp, °C	RX *cis*:*trans*	Ref
Methyl or *t*-butyl	Acyl hypobromite	RCO_2–Br[a]	0	1:1	This work
Methyl or *t*-butyl	Alkylmercuric bromide	Br–Br	0	1:1	This work
t-Butyl	Alkylmercuric chloride	SO_2Cl–Cl	46	2.3:1	This work
t-Butyl	Acyl peroxide	Br–Br	0	~1:1	2, 3
t-Butyl	Acyl peroxide	$CHBr_2CHBr$–Br	50	~1:1	4
t-Butyl	Acyl peroxide	CCl_3–Br	80	2.2:1	2, 3
t-Butyl	Alkyl hypochlorite	RO–Cl	0–80	2:1	2, 3
t-Butyl	Acyl peroxide	CCl_3–Cl	80	2.7:1	2, 3
Chloro	$h\nu$, Cl_2	Cl–Cl	−30, 40	1:1.1	*b*
Bromo	$h\nu$, Cl_2	Cl–Cl	−30, 40	1:1.1–1.85	*b*
Bromo	$h\nu$, RO–Cl	RO–Cl	−30	1.3:1	*b*

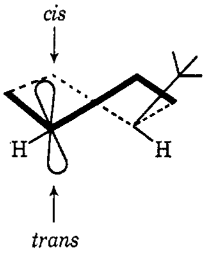
[a] Br_2 intervention is also possible. [b] G. A. Russell, A. Ito, and R. Konaka, *J. Am. Chem. Soc.*, **85**, 2988 (1963).

4-Substituted Cyclohexyl Radicals. The available data on the stereochemistry of abstraction reactions by 4-substituted cyclohexyl radicals are summarized in Table III. A statistical product distribution is readily understandable if it is assumed that a 4-substituted cyclohexyl radical has a chair conformation and that the radical site is planar.[15] Reaction of I with a very reactive halogen donor with small bulk could reasonably give approximately equal yields of *cis*- and *trans*-halides. A product distribution containing more of the *trans* isomer can also be explained on the basis of structure I by invoking either product development control or steric hindrance to attack from the *cis* side with a bulky halogen donor. The rationale for a product distribution containing more of the *cis* isomer is much less clear and has been the subject of some speculation. An early view[2,3] that the preference for *cis* isomer (from abstraction of chlorine from ROCl) results from abstraction by a tetrahedral radical is generally inconsistent with the esr data for alkyl radicals;[15] however, support for this suggestion has been advanced.[16] Alternatively, Symons has suggested that there is an electron-rich region involving the two axial hydrogens on the 2 and 6 carbons of the planar cyclohexyl radical,[17] and thus the electron-rich chlorine atom from the alkyl hypochlorite should attack on the side opposite to these axial hydrogens, yielding *cis*-halide. In disagreeing with this hypothesis, Greene, Chu, and Walia consider that the chlorine atom would be more negative at the transition state for the abstraction reaction than at the ground state and would prefer to attack an electron-rich site which in this case would give *trans*-halide.



I

Greene, Walia, and Chu have another suggestion to explain the preference for *cis*-halide, namely that the geometry of the 4-*t*-butylcyclohexyl radical "at the transition state for the atom transfer step which produces *cis*-chloride may be appreciably removed from a chair conformation." [2,3] They proposed two different twist-boat conformations for the 4-*t*-butylcyclohexyl radical, one of which (II) would exhibit a definite preference for attack from a direction yielding *cis*-halide.



II

While definitive information on the ground-state conformation of the 4-*t*-butylcyclohexyl radical is not available, several lines of reasoning support the chair conformation I rather than a twist-boat conformation II. Ogawa and Fessenden[18] concluded from an esr study that the cyclohexyl radical exists in two conformations which interconvert with an activation energy of 4.9 ± 0.5 kcal/mol. The geometry about the radical site, deduced from the magnitudes of the hyperfine coupling constants, is consistent with either a chair, boat, or twist-boat conformation for the cyclohexyl radical. However, Ogawa and Fessenden argue that the magnitude of the energy of activation for interconversion of the two conformations supports interconverting chair conformations for cyclohexyl radical. The hyperfine coupling constants for 4-*t*-butylcyclohexyl radical are nearly the same as those for the cyclohexyl radical, suggesting that the 4-*t*-butyl group does not alter the conformation of the cyclohexyl ring.[19]

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[15] Available evidence supports a planar structure for carbon radicals: H. M. McConnell and R. W. Fessenden, *J. Chem. Phys.*, **31**, 1866 (1959); M. Karplus and G. K. Fraenkel, *ibid.*, **35**, 1312 (1961); R. W. Fessenden and R. H. Schuler, *ibid.*, **39**, 2147 (1963); R. W. Fessenden, *J. Phys. Chem.*, **71**, 74 (1967).

[16] F. G. Bordwell, P. S. Landis, and G. S. Whitney, *J. Org. Chem.*, **30**, 3764 (1965).

[17] This hypothesis is based on the esr spectrum of cyclohexyl radical which exhibits a very large hyperfine coupling constant for the two axial hydrogens. The large hyperfine coupling constant is assumed to arise from hyperconjugation: M. C. R. Symons, *Nature*, **198**, 1196 (1963).

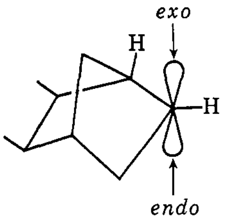
[18] S. Ogawa and R. W. Fessenden, *J. Chem. Phys.*, **41**, 994 (1964).

[19] Unpublished results, L. H. Gale with J. E. Bennett.

In addition, methylenecyclohexane[20,21] and the methyl ether of cyclohexanone oxime,[21] which are approximate models of the cyclohexyl radical, exist predominantly in chair forms. By analogy, it is reasonable to expect the preferred forms of cyclohexyl radicals to be chair forms. Even if chair conformations are the preferred forms, twist-boat conformations as proposed by Greene, *et al.*, may be present in small equilibrium concentrations. However, there is no reason to expect special reactivity from twist-boat forms, and therefore the proposal of reaction in twist-boat conformations does not appear to be consistent with the expected conformation geometry and reactivity of radicals.

The various halogen transfer agents in Table III can be divided into two general groups based on the *cis–trans* product distribution: (A) halogen transfer reagents which yield approximately statistical product distribution, and (B) reagents which yield more *cis* isomer. Acyl hypobromites, bromine, chlorine, and tetrabromoethane fall into group A, while bromotrichloromethane, carbon tetrachloride, sulfuryl chloride, and *t*-alkyl hypochlorites fall into group B.

It is significant that three out of the four halogen donors in group A give an *exo*:*endo* product distribution with either norbornyl or dihydroaldrinyl radical of *ca.* 70:30 while four out of the four in group B give >95% *exo*-halide.[22–24] One of the halogen donors, tetrabromoethane, has not been investigated with norbornyl or dihydroaldrinyl radical. The absence of *endo* product from halogen donors in group B has been correlated with their larger bulk and resultant increased steric interactions in attacking the (assumed) "bridged radicals" from the *endo* side.[22,23]



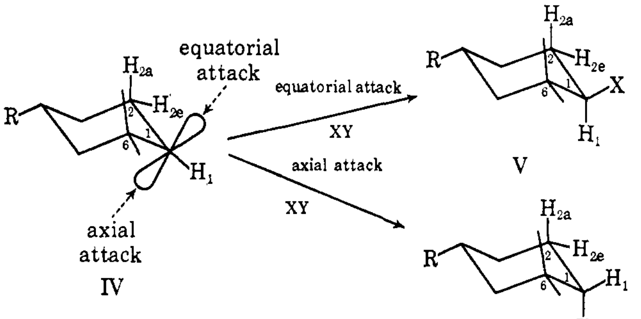
III

Steric effects, however, clearly do not explain the product distributions from cyclohexyl radical reactions. If one assumes a chair conformation for 4-substituted cyclohexyl radical (I), then the bulky halogen donors should give more *trans*-halide since steric interactions are expected to be greater in attack from the *cis* direction. In actual fact the bulkier halogen donors almost universally give *more cis halide.* The exception is tetrabromoethane which yields approximately statistical product distribution.[4] (However, these latter results are suspect because of the low yield and the known instability of *cis*-4-*t*-butylcyclohexyl bromide at elevated temperatures.)

It is desirable to have a single explanation for the orientation of radical substitution. In considering the various halogen transfer reagents, it is apparent that reactions with reagents in group A, except with tetrabromoethane, are more exothermic than reactions with those in group B (due to lower bond dissociation energies for reagents in group A *vs.* the same type of halogen donor in group B). Therefore, the compounds in group A are expected to have less bonding in the transition state and to be less selective in their reactions. What must be accounted for then with the cyclohexyl radical is preferred formation of the thermodynamically and sterically *less* favored products in reactions which require *more* bond formation in the transition state. The 2-norbornyl radical does yield the thermodynamically and sterically more favorable products in reactions which have appreciable bond formation in the transition state. A unifying explanation of these reaction preferences arises from a consideration of torsional effects.[25]

Torsional effects can be visualized as bond–bond interactions, independent of the size of substituents, which attain a maximum at a dihedral angle of 0°. The role of torsional effects in atom transfer reactions with 4-alkyl-substituted cyclohexyl radical is illustrated by structures IV, V, and VI and by the corresponding Newman projections of the C_1–C_2 bonds, IV′, V′, and VI′.

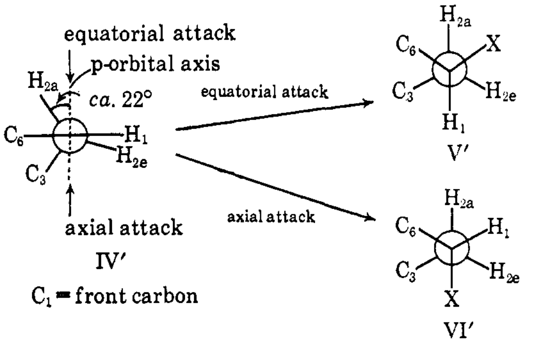
The conformation of the substituted cyclohexyl radical is likely a chair IV with the dihedral angle between C–H_{2a} and the axis of the p orbital about 22° based on esr data. Reaction of IV from the equatorial direction will result in development of torsional interactions because the hydrogen on C_1 must eclipse the equatorial hydrogens on C_2 and C_6 at some stage in the reaction. For axial attack, no such interactions occur during the course of the reaction. Therefore in reactions with halogen transfer reagents in group B which demand substantial amounts of bond making in the transition state, the preferred reaction path will be axial attack. With less selective reagents of group A (reagents with



IV

V

VI



IV′

C_1 = front carbon

V′

VI′

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[20] T. J. Gerig, *J. Am. Chem. Soc.*, **90**, 1065 (1968).

[21] F. R. Jensen and B. H. Beck, *ibid.*, **90**, 1066 (1968).

[22] E. C. Kooyman and G. C. Vegter, *Tetrahedron*, **4**, 382 (1958).

[23] S. J. Cristol, L. K. Gaston, and T. Tiedman, *J. Org. Chem.*, **29**, 1279 (1964).

[24] F. D. Greene, M. L. Savitz, F. D. Osterholtz, H. H. Lau, W. N. Smith, and P. M. Zanet, *ibid.*, **28**, 55 (1963).

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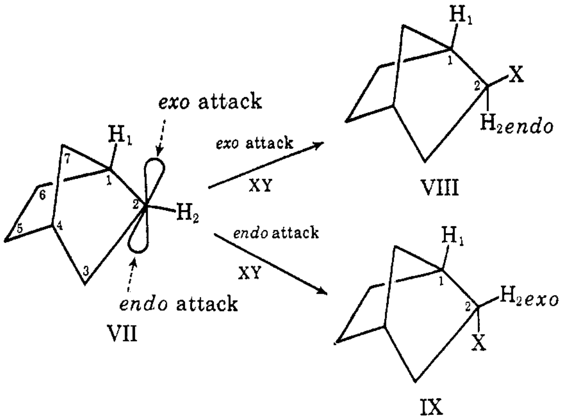
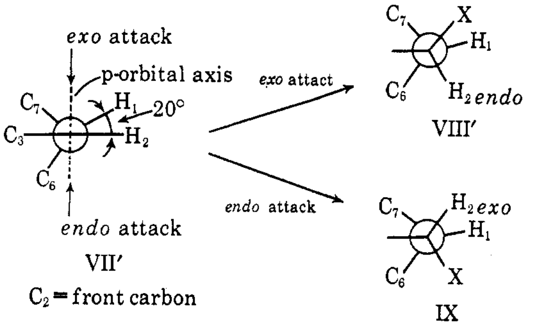
lower dissociation energies) bond formation is not far advanced during the transition state, and therefore, a statistical product distribution will result.[26]

Schleyer has noted that torsional effects on the reactions of 2-norbornyl radicals will favor *exo* attack.[25] The observed results are about 70% *exo* from halogen transfer reactions with reagents of group A and 95% *exo* from reactions of group B. The role of torsional effects with norbornyl radical is the same as with cyclohexyl radical; however, in contrast to the cyclohexyl system, with 2-norbornyl compounds bond opposition develops in formation of the less stable and sterically unfavored *endo* product (structures VII, VIII, IX and VII′, VIII′, IX′). Because the reagents in group B require more bond making and structure development in the transition state, they favor a high proportion of *exo* products. Conversely, the less selective reagents of group A favor more statistical distribution of products.





Experimental Section[27]

Reagents. Anhydrous bromine was prepared by shaking analytical reagent grade with concentrated sulfuric acid and then distilling the bromine layer. Carbon tetrachloride was distilled from calcium hydride and stored over calcium hydride.

Preparation of *cis*-4-*t*-Butylcyclohexanecarboxylic Acid. In a typical preparation, 30.0 g (0.168 mol) of recrystallized *p*-*t*-butylbenzoic acid, 300 ml of glacial acetic acid, and 1 g of 5% rhodium on alumina were placed in a 500-ml Parr bomb and hydrogenated overnight. Following filtration, the clear liquid was added to a fourfold excess of water and the solid filtered and dried. The solid was dissolved in a hot solution of 250 ml of absolute methanol containing 20 g (0.263 mol) of thiourea (Pfansteihl Chemical Co., recrystallized once from absolute methanol, mp 177–179°).[28] Needle-like crystals (mp 194–198°) formed in the solution upon cooling. Following removal of these crystals, the methanolic solution was reduced in volume and 100 ml of concentrated HCl added. The solid was filtered, dried, and recrystallized once from toluene yielding 18.5 g of pure *cis*-4-*t*-butylcyclohexanecarboxylic acid (60%), mp 117–118° (lit.[29] 117.5–118°).[29]

Preparation of *trans*-4-*t*-Butylcyclohexanecarboxylic Acid. In a typical preparation 30.0 g (0.163 mole) of crude acid from the catalytic hydrogenation of *p*-*t*-butylbenzoic acid was converted to the ethyl ester and isomerized by stirring with 22.4 g (0.20 mol) of potassium *t*-butoxide dissolved in 100 ml of purified dimethyl sulfoxide at room temperature for 10 hr. The initial isomer distribution was 77% *cis*-4-*t*-butylcyclohexanecarboxylic acid based on glpc analysis. (The crude acid was treated with diazomethane and the resulting esters were analyzed on an 8-ft Carbowax column at 177° with a helium flow rate of 78 cc/min.)[30] The recovered ethyl ester from potassium *t*-butoxide treatment analyzed by glpc to be 85% ethyl *trans*-4-*t*-butylcyclohexanecarboxylate. The ethyl ester was hydrolyzed and the crude acid recrystallized (*n*-heptane) yielding 21.1 g of pure *trans*-4-*t*-butylcyclohexanecarboxylic acid (70%), mp 174–175° (lit.[29] 174–175°).

Preparation of *cis*-4-Methylcyclohexanecarboxylic Acid. Predominantly *cis* acid was prepared by the low-pressure hydrogenation of recrystallized *p*-toluic acid in the presence of either platinum oxide[31] or 5% rhodium on alumina catalyst and has bp 129–130° (12.5 mm). The crude *cis* acid was purified either by recrystallization or chromatography on silica gel yielding pure *cis*-4-methylcyclohexanecarboxylic acid, mp 31.2–31.4° (lit.[31] bp 135° (20 mm) and mp 13°).

Preparation of *trans*-4-Methylcyclohexanecarboxylic Acid. Predominantly *trans* acid was prepared by the high-pressure hydrogenation of recrystallized *p*-toluic acid in the presence of Raney nickel.[32] The crude *trans* acid was purified by recrystallization yielding pure *trans*-4-methylcyclohexanecarboxylic acid, mp 110.7–111.9°.

Preparation of *cis*- and *trans*-4-Methylcyclohexyl Bromides. The preparation of pure *cis*- and pure *trans*-4-methylcyclohexyl bromides from the stereospecific bromine cleavage of *cis*- and *trans*-4-methylcyclohexylmercuric bromides, respectively, has been described previously.[5]

Preparation of *cis*- and *trans*-4-Butylcyclohexyl Bromides. Pure *cis*- and pure *trans*-4-*t*-butylcyclohexyl bromides were prepared from the stereospecific bromine cleavage of *cis*- and *trans*-4-*t*-butylcyclohexylmercuric bromides, respectively.[5] The pure *cis*-4-*t*-butylcyclohexyl bromide has bp 64–65° (1 mm) and mp 23–25°, and exhibited a nmr spectrum (neat) with -CHBr absorption (broad singlet) at τ 5.41 (relative to TMS) (lit.[33] bp 71° (2 mm) and mp 23–25°). The pure *trans*-4-*t*-butylcyclohexyl bromide has bp 64–65° (1 mm) and mp 0–3°, and exhibits a nmr spectrum (neat) with -CHBr absorption (multiplet) at τ 6.12 (relative to TMS).

Hunsdiecker Reaction with *cis*- and *trans*-4-Alkylcyclohexanecarboxylic Acids. Two methods of reaction were used: normal addition wherein a solution of bromine in carbon tetrachloride was added to a stirred suspension of the silver salt in the same solvent, and inverse addition wherein the dry, powdered silver salt was added to a solution of bromine in carbon tetrachloride. A typical

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[26] It is to be expected that there is not an abrupt transition between halogen donors in group A and group B. An exact correlation is not obtained by simply summing the reported bond dissociation energies of the starting halogen derivatives and products (C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp 48–50; T. L. Cottrell, "The Strengths of Chemical Bonds," 2nd ed, Butterworths Scientific Publications, London, 1958, pp 276–289). Unfortunately, the reported bond energies are not always entirely reliable. The dominant factor in the concept presented here is the degree of development of structure in the transition, and an exact 1:1 relationship between the differences in bond dissociation energies and the degree of development of the transition, except for atom transfer reagents involving the same halogen, is not to be expected.

A complete comparison of bond dissociation energies with product distributions will be reported soon.

[27] All melting points and boiling points are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory, Department of Chemistry, University of California, Berkeley, Calif. Infrared analyses were made on a Baird Associates, Inc., double-beam infrared recording spectrophotometer. The nuclear magnetic resonance spectra were measured on a Varian A-60 spectrometer. Gas–liquid partition chromatographs were obtained with an Aerograph A-90-P unit. All distillations were performed with a 15-in. Podbielniak-type column with a tantalum wire spiral.

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[30] J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry," 2nd ed, Prentice-Hall, Inc., Englewood Cliffs, N. J., 1962, pp 373–374.

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experiment using normal addition is described. Into a dried, 250-ml, three-necked, round-bottomed flask fitted with a 50-ml dropping funnel and a Drierite drying tube were placed 10.0 g (0.0345 mol) of the silver salt of *trans*-4-*t*-cyclohexanecarboxylic acid and 100 ml of carbon tetrachloride. The silver salt mixture was cooled in an ice bath and a solution of 5.5 g (0.034 mol) of bromine in 10 ml of carbon tetrachloride was added to the stirred silver salt over a period of 15 min. The reaction proceeded at 0° as evidenced by evolution of carbon dioxide. After stirring the reaction mixture for 1 hr at 0°, the precipitated silver bromide was removed by filtration through filter-aid. The carbon tetrachloride solution was washed successively with 1.25 *M* sodium thiosulfate, water, 10% sodium bicarbonate, and water and dried over anhydrous sodium sulfate. The bulk of the carbon tetrachloride was removed with a rotary evaporator. The crude oil was analyzed by nmr. It was then vacuum distilled yielding 4.5 g of 4-*t*-butylcyclohexyl bromide (60%), bp 64–65° (1 mm). Nmr analysis of the pure material gave the same results, within experimental error, as the crude oil.

Recovery of Carboxylic Acids from Silver Salts. A 2.0-g sample of the silver salt of *cis*-4-*t*-butylcyclohexanecarboxylic acid was reconverted to the starting acid by treatment with concentrated nitric acid. The solid was removed by filtration and washed with water. The recovered acid had mp 116–118°. Similarly, samples of the silver salts of *trans*-4-*t*-butyl- and *trans*-4-methylcyclohexanecarboxylic acids were reconverted to the starting acid, demonstrating that no epimerization of the acids had occurred during formation of the silver salt.

Thermal Stability of *cis*- and *trans*-4-*t*-Butylcyclohexyl Bromides. A distilled mixture of *cis*- and *trans*-4-butylcyclohexyl bromides was allowed to stand at room temperature in light for 14 days. Nmr analysis showed no change in isomer distribution. The same mixture was refluxed in carbon tetrachloride for 2 hr. Nmr analysis demonstrated that 35% decomposition had occurred and the isomer distribution changed. An olefinic hydrogen absorption appeared in the nmr spectrum.

Stability of *trans*-4-Methylcylohexyl Bromide to Hunsdiecker Reaction Conditions. A 7.5-g (0.042 mol) sample of pure *trans*-4-methylcyclohexyl bromide was added to a suspension of 20 g (0.08 mol) of the silver salt of *trans*-4-methylcyclohexylcarboxylic acid in 200 ml of carbon tetrachloride. The Hunsdiecker reaction was carried out in the normal manner yielding 11.8 g of 4-methylcyclohexyl bromide with bp 60.0–60.5° (11 mm). The infrared spectrum of the product indicated the presence of 70% *trans* acid and 30% *cis*-4-methylcyclohexyl bromide. If one assumes that the silver salt yielded a 52:48 mixture of *trans*- and *cis*-4-methylcyclohexyl bromides with a yield of 44% (average yield from silver salts of *cis*- and *trans*-4-methylcyclohexanecarboxylic acids), then the remaining 4-methylcyclohexyl bromide represents a 75% recovery of *trans*-4-methylcyclohexyl bromide. The predicted isomer distribution using the yield and recovery is 75% *trans* and 25% *cis* which is in resonable agreement with the observed product distribution considering the assumptions used and indicates that there has been no significant epimerization of the *trans* isomer to *cis* isomer. The *ca.* 75% recovery of the initially added *trans*-4-methylcyclohexyl bromide demonstrates that only a small proportion of this material has been lost, presumably *via* ester formation which would be especially favored with the high initial concentration of alkyl bromide.

Preparation of *trans*-4-*t*-Butylcyclohexylmercuric Bromide. The pure *trans* isomer was prepared using the procedure described previously for preparation of *trans*-4-methylcyclohexylmercuric bromide.[8] The recrystallized (benzene) pure *trans*-4-*t*-butylcyclohexylmercuric bromide had mp 230–231°.

Preparation of *cis*-4-*t*-Butylcyclohexylmercuric Bromide. Into a 500-ml, round-bottomed flask were added 50 g (0.119 mol) of *trans*-4-*t*-butylcyclohexylmercuric bromide and 100 ml of freshly purified pyridine. The solution was refluxed while small portions of benzoyl peroxide were added at 15-min intervals over a period of 2 hr. A small amount of free mercury formed. The hot pyridine solution was added to a solution of sodium bromide in water and the solid filtered and then dissolved in hot benzene. The solid collected upon cooling of the benzene was the *trans* isomer. The cold benzene solution was extracted with 200 ml of a 1 *M* solution of hydrobromic acid, washed with water, and dried over anhydrous sodium sulfate. The volume of the benzene solution was reduced and a second sample of crude *trans* isomer was collected. The remaining benzene solution was evaporated to dryness and the solid taken up in absolute ethanol. A fibrous solid was collected weighing 10 g (20%), mp 120–140°. The solid was dissolved in carbon tetrachloride and added to an alumina column containing 1000 g of Woelm neutral alumina packed in hexane. The column was developed using a hexane–ether mixture containing increasing amounts of ether to 18%. A solid was eluted from the column and was recrystallized from absolute ethanol. The ethanol yielded 2.0 g (4%) of needles of pure *cis*-4-*t*-butylcyclohexylmercuric bromide, mp 149.2–149.6°.

Anal. Calcd for $C_{10}H_{19}HgBr$: C, 28.61; H, 4.65. Found: C, 28.69; H, 4.72.

Bromine Cleavage of *cis*- and *trans*-4-*t*-Butylcyclohexylmercuric Bromide. Into a 250-ml, three-necked, round-bottomed flask, fitted with a dropping funnel, a nitrogen gas inlet tube, and a drying tube, were placed 100 ml of carbon tetrachloride and 5.0 g (0.012 mol) of *trans*-4-*t*-butylcyclohexylmercuric bromide. A solution of 1.92 g (0.012 mol) of bromine in 10 ml of carbon tetrachloride was added to the cooled (ice bath), stirred reaction mixture over a period of 15 min. The reaction mixture was stirred an additional hour. After removing the mercuric bromide by suction filtration, the solution was treated with 100 ml of a 1 *M* sodium thiosulfate solution, water, cold 10% sulfuric acid, water, 10% sodium bicarbonate, and water and dried over anhydrous sodium sulfate. The carbon tetrachloride was removed using a rotary evaporator and the crude product distilled, yielding 1.44 g of 4-*t*-butylcyclohexyl bromide (55%), bp 64–65° (1 mm). The isomer distribution was determined utilizing nmr spectroscopy. Similarly a sample of *cis*-4-*t*-butylcyclohexylmercuric bromide was cleaved by bromine.

Preparation of *cis*- and *trans*-4-*t*-Butylcyclohexylmercuric Chloride. Into a 1-l. erlenmeyer flask, wrapped with aluminum foil, were placed 40 g (0.095 mol) of *trans*-4-*t*-butylcyclohexylmercuric bromide and 600 ml of absolute ethanol. Silver acetate (15.8 g, 0.095 mol) was added. The flask was sealed and the contents stirred for 8 hr. Silver bromide was removed by filtration and the clear solution treated with 150 ml of concentrated hydrochloric acid. A white solid was collected and recrystallized from benzene, yielding 27.2 g of *trans*-4-*t*-butylcyclohexylmercuric chloride (75%), mp 265°.

Anal. Calcd for $C_{10}H_{19}HgCl$: C, 32.04; H, 5.07. Found: C, 32.25; H, 5.18.

cis-4-*t*-Butylcyclohexylmercuric chloride was prepared by the same procedure starting with *cis*-4-*t*-butylcyclohexylmercuric bromide and has mp 184°.

Cleavage of *cis*- and *trans*-4-*t*-Butylcyclohexylmercuric Chloride by Sufuryl Chloride. Into a 100-ml, round-bottomed flask, fitted with a reflux condenser topped with a drying tube, were added 10 g (0.027 mol) of *trans*-4-*t*-butylcyclohexylmercuric chloride, 35 ml of sulfuryl chloride, and 20 ml of carbon disulfide. After refluxing for 4 hr, the solution was added to 100 ml of carbon tetrachloride and carefully extracted with small amounts of a 1 *M* solution of sodium thiosulfate until all of the sulfuryl chloride was decomposed. The solution was then washed with water and dried over anhydrous sodium sulfate. The carbon tetrachloride was removed on a rotary evaporator and the crude oil distilled at reduced pressure yielding 1.32 g of 4-*t*-butylcyclohexyl chloride (28%), bp 56–57° (1.5 mm). The reported boiling point is 80–85° (12 mm).[1] The relative amounts of *cis*- and *trans*-4-*t*-butylcyclohexyl chloride were determined by nmr analysis employing the absorptions at δ 3.1 and 4.3 as measured of the *cis*- and *trans*-chlorides, respectively. A sample of *cis*-4-*t*-butylcyclohexylmercuric chloride was cleaved by sulfuryl chloride using the same procedure.

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