Substituent Control of Cyclopropylcarbinyl Radical Ring Opening Reactions

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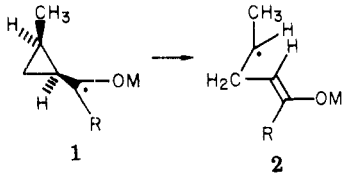
Stereoelectronic and electronic effects of methyl substitution on the regiochemistry of ring opening in the conversion of cyclopropylcarbinyl to but-1-en-3-yl radicals has been reinvestigated. *cis,trans-* and *trans,-trans*-2,3-dimethylcyclopropyl-*3-d*-1-carbinyl alcohols and tri-*n*-butylstannyl ethers have been prepared and converted to their corresponding cyclopropylcarbinyl radicals. ESR detection of the homoallylic radicals produced from these materials through hydrogen atom abstraction by photogenerated *tert*-butoxy radicals allows determination of ring-opening selectivities on the basis of differing α and β splitting constants for H vs. D. The *cis,trans*-dimethyl-substituted radicals undergo conversion to homoallylic radicals by nearly exclusive ring opening of the cyclopropane σ bond bearing the *cis*-methyl substituent. This preference is also measured by the use of product-analysis techniques. The tri-*n*-butylstannyloxy-substituted 2,3-dimethyl-substituted cyclopropyl-*3-d*-carbinyl radicals are generated by reactions of the corresponding aldehydes with tri-*n*-butyltin hydride initiated by AIBN. The homoallylic radicals generated by rearrangement are rapidly trapped by the tin hydride reagent, giving stannyl enol ether. Mass spectrometric analysis of 3-methylvaleraldehyde arising after methanolysis of the reaction mixture is used to determine, in an indirect fashion, ring-opening selectivities which demonstrate a 3.5:1 preference for opening of the *cis*-methyl-substituted bond in rearrangement of the *cis,trans*-dimethylcyclopropylcarbinyl radical. The results above along with those obtained on related systems from other laboratories are discussed in terms of stereoelectronic effects and frontier molecular orbital controls.

Recent studies in our laboratory[2] have been concerned with effects of substituents on product quantum yields from excited-state reactions of bicyclo[3.1.0]hexan-3-ones. These investigations have stimulated thoughts about factors controlling the direction of ring opening in conversions of unsymmetrically alkyl-substituted cyclopropylcarbinyl radicals to their corresponding homoallylic counterparts. In particular we were intrigued by the recent results of Davies and Pereyre[3a] which suggest that methyl substitution in these systems has unusual effects upon ring-opening regiochemistries. These interesting substituent effects are exemplified by the contrastingly different behavior of the *cis*-2-methylcyclopropyl-1-carbinyl radicals **1**, which generate secondary butenyl radicals **2**, and the



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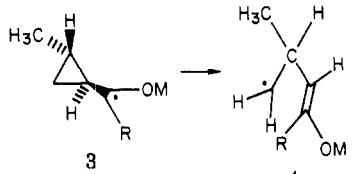

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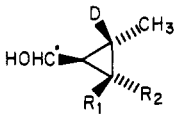
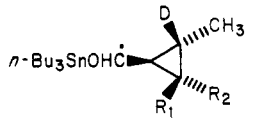
trans-methyl-substituted radicals **3**, which form the primary butenyl radicals **4**. Accordingly, ring cleavages of radicals of this type (M = H or tri-*n*-butylstannyl), generated by hydrogen-atom abstractions of alcohols or stannyl ethers or by the addition of tin radicals to aldehydes or ketones, appear to depend on the stereochemistry of the methyl substituents. Davies and Pereyre[3a] have suggested that the preference for opening of the most substituted cyclopropane bond in the *cis*-methyl systems **1** is due to the attainment of more favorable transition-state conformations which minimize nonbonding interactions between methyl and the OM and R substituents at the carbinyl center. Similar observations and explanations have been presented to rationalize specificities in ring fission of steroid radicals related to the simple systems.[3b-h] Although the regiochemistry of ring opening of **1** is readily understood in terms of stereoelectronic controls, the pure electronic effects of methyl groups in these cases is not clear. This is dramatized by the specificities seen in reactions of the *trans*-methyl radicals **2** where the homoallylic radical yields are not reflective of radical stabilities and apparent C–C bond strengths.

In order to gain additional information about factors controlling substituent effects on the regiochemistry of cyclopropylcarbinyl to homoallylic radical reactions, we have prepared the electronically symmetric cis,trans and trans,trans isomers of 2-deuterio-2,3-dimethylcyclopropyl-1-hydroxycarbinyl (**5ct** and **5tt**) and -1-((tri-*n*-butylstannyl)oxy)carbinyl (**6ct** and **6tt**) radicals for study using ESR and product analysis.



5tt, R_1 = H; R_2 = CH_3
5ct, R_1 = CH_3; R_2 = H



6tt, R_1 = H; R_2 = CH_3
6ct, R_1 = CH_3; R_2 = H

Results

Synthesis of 2-Deuterio-2,3-dimethylcyclopropyl-1-hydroxycarbinyl and -1-((tri-*n*-butylstannyl)oxy)-carbinyl Radicals. These radicals were prepared from the corresponding alcohols **10**, aldehydes **11**, and stannyl ethers **12**, which in turn were made by the sequences outlined in Scheme I Specifically, lithium aluminum deuteride reduction of 4-methoxybut-3-en-2-one followed by careful aqueous acid hydrolysis of the intermediate

(1) (a) Department of Chemistry, University of Maryland, College Park, MD 20742; (b) Camille and Henry Dreyfus Foundation Teacher-Scholar Grantee, 1975–1980.

(2) P. S. Mariano, E. Bay, D. G. Watson, T. Rose, and C. Bracken, *J. Org. Chem.*, preceding paper in this issue.

(3) (a) A. G. Davies, B. Muggleton, J.-Y. Godet, M. Pereyre, and J.-C. Pommier, *J. Chem. Soc., Perkin Trans. 2*, 1719 (1976); (b) A. L. J. Beckwith and G. Phillipou, *Aust. J. Chem.*, **29**, 123 (1976); (c) P. K. Freeman, F. A. Raymond, J. C. Sutton, and W. R. Kindley, *J. Org. Chem.*, **33**, 1448 (1968); R. S. Boikess, M. Mackay, and D. Blithe *Tetrahedron Lett.*, 401 (1971); (d) P. V. Freeman, M. F. Grostic, and F. A. Raymond, *J. Org. Chem.*, **36**, 905 (1971); (e) E. Muller, *Tetrahedron Lett.*, 1835 (1974); (f) R. Sustmann and F. Lubbe, *ibid.*, 2831 (1974).

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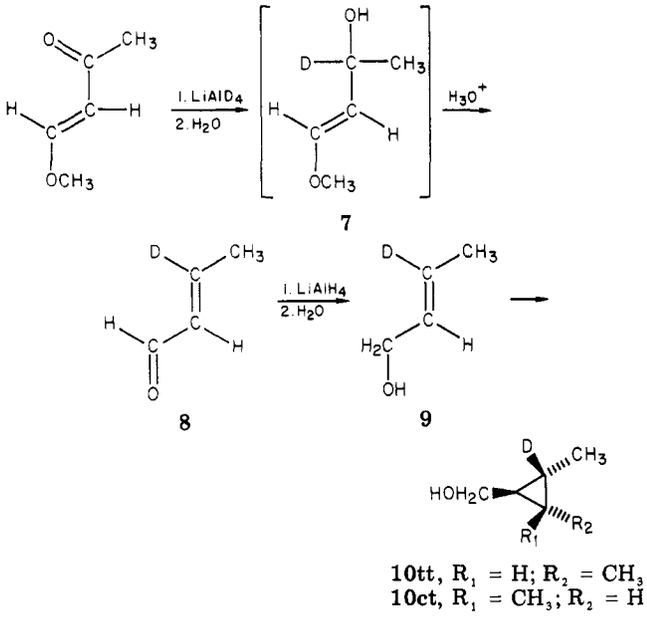
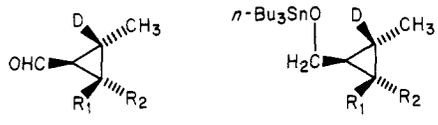
Scheme I



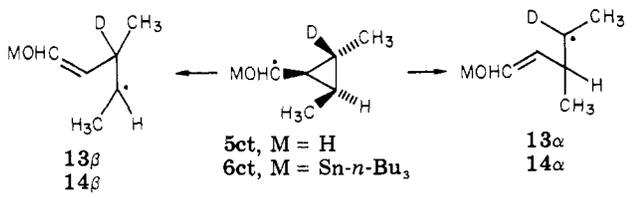
allylic alcohol **7** gave the unstable *trans*-3-deuteriobutenal **8**. This aldehyde was reduced immediately with $LiAlH_4$ furnishing deuteriocrotyl alcohol **9**. Simmons–Smith methylcyclopropanation[4] of **9** led to formation of a separable mixture of cyclopropylcarbinols **10tt** and **10ct** in a 2:1 ratio. Active MnO_2 oxidation of the individual carbinols gave the epimeric aldehydes **11**. Alternatively, the



cyclopropanecarboxaldehydes could be generated as an epimeric mixture by oxidation of the alcohols **10**. Separation is then accomplished by GLC. Lastly, the cyclopropylcarbinyl tri-*n*-butylstannyl ethers **12** were independently prepared by transetherification with tri-*n*-butylstannyl methyl ether and **10ct** or **10tt**.

Free-Radical Generation. The cyclopropylcarbinyl radicals **5** and **6** were generated at −120 °C in liquid cyclopropane from the corresponding alcohols or tributyltin ethers, **10** and **12**, by reaction with photolytically generated *tert*-butyloxy radicals. Rearrangement to the homoallylic radicals occurs more rapidly under these conditions than does ESR detection of the initially formed cyclopropylcarbinyl radicals. The ESR spectra obtained (Figure 1) were first order and allowed unequivocal assignments of structure to the homoallylic radicals produced.

Ring opening of **5ct** and **6ct** can take place in one of two fashions leading to the α- or β-deuterated butenyl radicals **13**α or **13**β, respectively. It is possible to calculate the ESR



spectrum expected for each of the butenyl radicals from

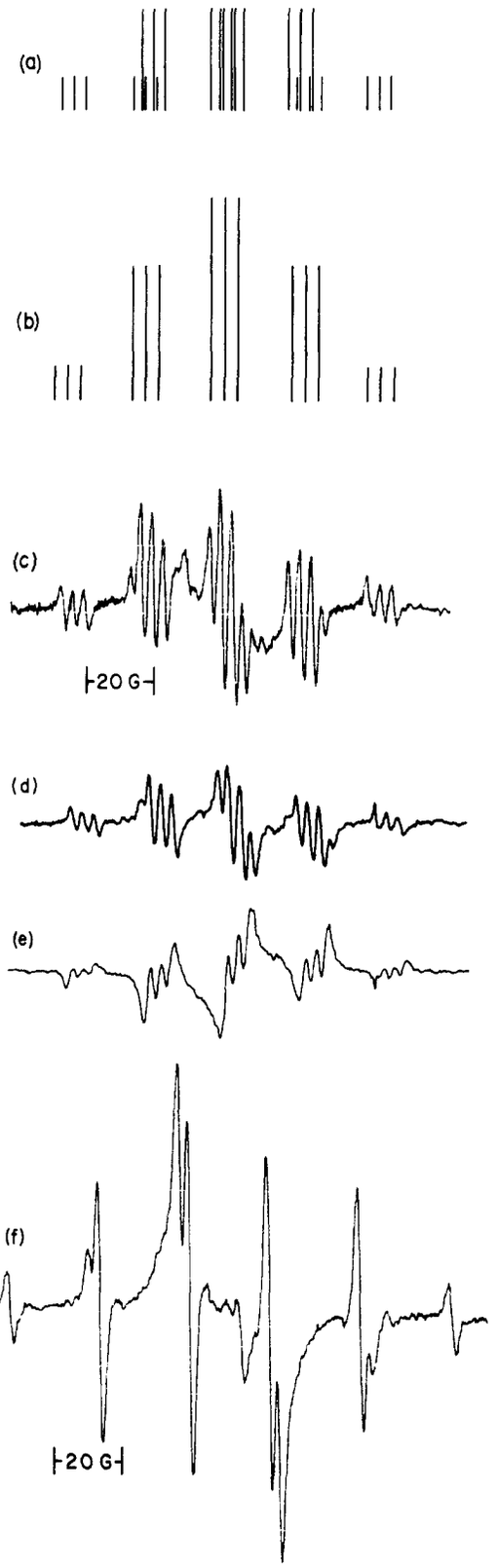
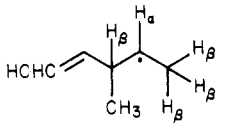


Figure 1. Calculated and experimentally obtained ESR spectra of homoallylic radicals. Included are calculated stick spectra for (a) **13**β and (b) **13**α and recorded spectra for (c) **13**β, (d) **14**β, (e) mixture of **13**β and **13**α, and (f) **15**.

knowledge of H_α and H_β hyperfine coupling constants obtained from the spectrum (Figure 1f) of the all-hydrogen radical **15** (a_{H_α} = 20.5 G and a_{H_β} = 23.6 G) and the *g* factor for hydrogen vs. deuterium.[5] The hyperfine-splitting

(4) J. Furukawa, N. Kawabata, and J. Nishimura, *Tetrahedron Lett.*, 3495 (1968).

(5) D. J. Pasto and C. R. Johnson, "Organic Structure Determination", Prentice-Hall, Engelwood Cliffs, NJ, 1969, p 222.



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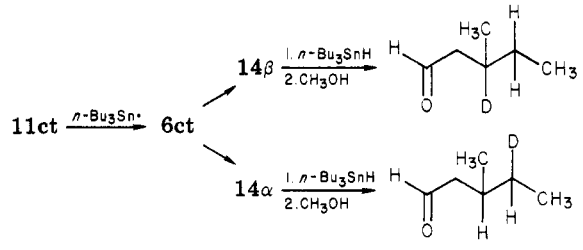
constants obtained in this fashion (a_{D_α} = 3.1 G and a_{D_β} = 3.6 G) are employed in constructing the stick spectra for radicals 13β and 13α displayed in Figure 1a,b, respectively. Comparison of these spectra with those recorded for the homoallylic radicals arising from **5ct** and **6ct** (Figure 1c,d, respectively) clearly indicates that radicals 13β are formed to the near exclusion of 13α. Thus, conversion of these dimethylcyclopropylcarbinyl radicals proceeds with preferential ring opening of the cyclopropane bond adjacent to the *cis*-methyl substituent.

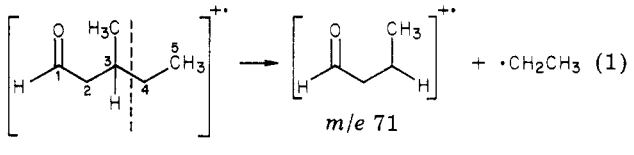
In order to ensure that this selectivity for cleavage of the cyclopropane bonds is not due to an unlikely deuterium isotope effect, the spectrum of the homoallylic radical derived from the trans,trans-substituted carbinol **10tt** was recorded (Figure 1e). As expected, this spectrum is less well-defined since it contains a larger number of lines due to the presence of a mixture of radicals 13β and 13α. Moreover, the ca. 2-G greater width of the spectrum further suggests the presence of radical 13α in the product mixture.

The direction of cyclopropane ring opening in these radical reactions was also explored by the use of product-analysis techniques. Accordingly, abstraction of a carbinyl hydrogen atom of **10ct** by a *tert*-butyloxy radical would produce the radical **5ct**. It was hoped that ring opening, producing homoallylic radicals 13β and 13α, would be followed by rapid intramolecular hydrogen-atom abstraction forming the enoxyl radicals 16β and 16α, respectively.[6] If this latter process were to occur more rapidly than return of homoallylic to cyclopropylcarbinyl radicals, the ratio of 3- to 4-deuterio-3-methylvaleraldehyde ultimately produced would reflect the kinetic distribution of homoallylic radicals generated competitively from **5ct**. However, mass spectrometric analysis of 3-methylvaleraldehyde produced from pyrrolysis of di-*tert*-butyl peroxide in the presence of either **10ct** or **10tt** indicated that the ratio of 3- and 4-deuterium-labeled aldehydes produced was independent of starting alcohol stereochemistry. The symmetrically substituted cyclopropylcarbinyl radical generated from **10tt** should show no preference for D- or H-substituted cyclopropane bond cleavage (beyond that expected due to a small deuterium isotope effect); thus, scrambling of the label in the conversion of **5ct** to valeraldehyde strongly implicates slow intramolecular hydrogen-atom transfer (13 → 16) compared to equilibration (13β ⇄ 5 ⇄ 13α). Thus, contrary to earlier indications arising from the work of Davies and Muggelton,[6] product analysis of cyclopropylcarbinol reaction mixtures is not useful in our case in determining ring-opening regioselectivities.

An alternate approach suggested by the Davies and Pereyre's[3a] work was taken. The cyclopropyl(stannyloxy)carbinyl radical **16ct** can be generated at 80 °C by reaction of the corresponding carboxaldehyde **11ct** with tri-*n*-butyltin hydride and AIBN. Under these conditions the stannyl radical produced should add to the aldehyde carbinyl oxygen, giving **6ct** followed by ring opening to 14β and/or 14α. The homoallylic radicals produced in this way should be rapidly trapped by hydrogen-atom transfer from excess tin hydride in the reaction mixture. Methanolysis of the formed stannyl enol ethers would give 3-methylvaleraldehyde having the deuterium label in either the 3 (from 14β) or 4 position (from 14α).



High-resolution mass spectrometric analysis of 3-methylvaleraldehyde demonstrated the presence of a strong peak at *m/e* 71.04953 corresponding to a radical cation fragment of molecular formula C_4H_7O (calcd *m/e* 71.04969). This would arise by cleavage of the C-3–C-4 bond as shown in eq 1. Thus, mass spectrometric analysis



(1)

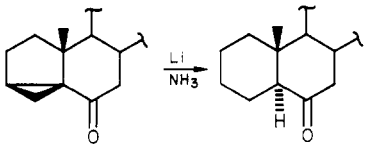
was utilized in determining the 3-*d* to 4-*d* 3-methylvaleraldehyde ratios on the basis of the relative corrected intensities of the *m/e* 71 and 72 peaks. The 3-*d* to 4-*d* ratio in aldehyde obtained from the symmetric cyclopropanecarboxaldehyde **11tt** (via radical **16tt**) was 0.9, reflecting a small secondary deuterium isotope effect of 1.1 for cyclopropane bond cleavage. In contrast, rearrangement of the cyclopropylcarbinyl radical **6ct** derived from aldehyde **11ct** gave after trapping and methanolysis 3-methylvaleraldehyde with a 3-*d* to 4-*d* ratio of 3.5. Thus, product analysis of cyclopropylcarbinyl radical ring-opening reactions, in systems where the electronic effects of substituents are neutralized, demonstrates a strong preference (78%) for cleavage of the *cis*-methyl-substituted cyclopropane bond (**6ct** → 14β). This result, which qualitatively matches that obtained by use of ESR detection of the homoallylic radicals, sets only a lower limit for the ratio of rate constants for *cis*-methyl to *trans*-methyl σ-bond cleavage since radical equilibration could still be competitive with trapping.

(6) A. G. Davies and B. Muggleton, *J. Chem. Soc., Perkin Trans. 2*, 502 (1976); P. Blum, A. G. Davies, and R. A. Henderson, *J. Chem. Soc., Chem. Commun.*, 569 (1978).

(7) (a) J.-Y. Godet and M. Pereyre, *J. Organomet. Chem.*, **40**, C23 (1972); (b) M. Pereyre and J.-Y. Godet, *Tetrahedron Lett.*, 3653 (1970).

Discussion

The literature contains numerous examples of cyclopropylcarbinyl radical ring-opening reactions which are subject to interesting regiochemical controls offered by substituents and structural features. Among the most intriguing of these are the dissolving metal reductions of cyclopropyl ketones studied by Dauben and co-workers.[8] Reductive ring openings of the ridigly structured steroidal ketones 17 and 18, for example, occur via the intermediacy



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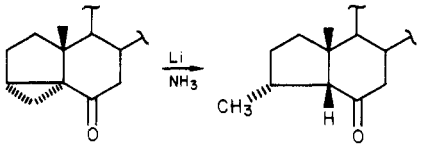

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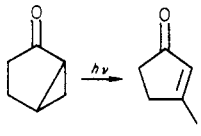
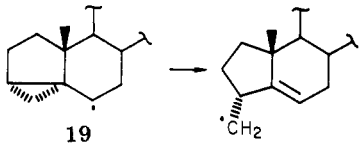
of corresponding radical anions through cleavage of the cyclopropane bond having better overlap with the adjacent carbinyl p orbital. In these cases, stereoelectronic control appears to dominate over other factors in determining reaction regiochemistry. Conformational influences of this type appear to control the direction of photochemical ring-opening processes of constrained cyclopropyl ketones,[9] exemplified by the conversion of bicyclo[3.1.0]hexan-2-one to 3-methylcyclopent-2-en-1-one (eq 2).[9c]



(2)

This same feature is also important in directing the course of cyclopropylcarbinyl to homoallyl radical rearrangements for systems in highly confined geometric environments. In those cases explored, the cyclopropane bond with better overlap of the carbinyl p orbital is preferentially ruptured. Transformations of the steroidal (**19**[3b]) and bicyclic stannyloxy (**20**[3a]) radicals demonstrate



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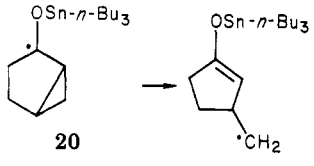

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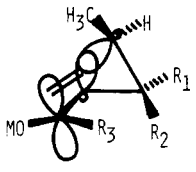
this point and suggest that stereoelectronic controls of this type are exceptionally important.

The course of radical-anion, excited-state, and neutral-radical reactions of this type in unconstrained systems appears to be influenced by substituents oriented cis to the carbinyl center. Our present results and those obtained earlier by Davies[3a] strongly suggest that the selectivity noted in conversion of the cyclopropylcarbinyl radicals **1**, **5ct**, and **6ct** to homoallyl radicals **2**, **13β**, and **14β** is due to minimization of nonbonded interactions between cis-related groups at the carbinyl center and cyclopropane ring in transition states **21**‡ vs. **22**‡ for these processes. The



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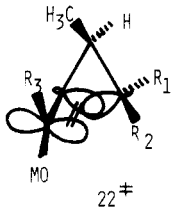

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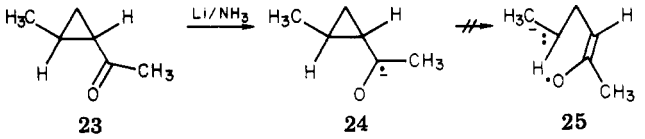
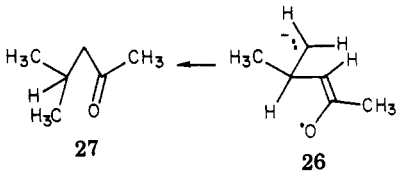
examples found in rearrangements **5ct** → **13β** and **6ct** → **14β** are important in providing evidence for this rationale since all other electronic influences of substituents on σ-bond-cleavage selectivities are nullified.

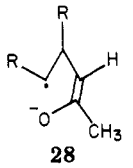
The precise nature of electronic effects offered by alkyl substitution on the selectivies for ring opening in these processes has yet to be fully elaborated. Indeed, several seemingly puzzling observations have escaped a complete and unifying rationale. First, ring-cleavage reactions in metal–ammonia reductions of *trans*-alkyl-substituted cyclopropyl ketones proceed with breakage of the less substituted bond, e.g., **23** → **27**. The currently accepted



23 24 25



27 26



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rationale for this selectivity is based upon the assumption that ring opening of the initially formed radical anion **24** generates the primary carbanion **26** rather than the less stable secondary anion **25**.[8] More reasonable pathways leading to formation of carbon radical enolate anions such as **28** have not been fully considered since it was felt that incorrect regiochemical predictions, based upon radical-stabilizing abilities of alkyl substituents, would result. Another intriguing observation is seen in the transformation of the *trans*-methylcyclopropylcarbinyl radicals **3** to their primary (**4**) rather than secondary homoallylic counterparts.[3] Moreover, control of ring opening by the *trans*-methyl group is the same even when electron-donating polar substituents are not present at the carbinyl center.[3a,10] Clearly, alkyl-substituent effects on radical

(8) (a) W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, **35**, 374 (1970); (b) W. G. Dauben and E. J. Deviny, *ibid.*, **31**, 3794 (1966); (c) A. J. Bellamy, E. A. Campbell, and I. R. Hall, *J. Chem. Soc., Perkin Trans. 2*, 1347 (1974).

(9) (a) W. G. Dauben, L. Schutte, and R. E. Wolf, *J. Org. Chem.*, **34**, 1849 (1969); W. G. Dauben, L. Schutte, R. E. Wolf, and E. J. Deviny, *ibid.*, **34**, 2512 (1969); (b) L. D. Hess and J. N. Pitts, *J. Am. Chem. Soc.*, **89**, 1973 (1967); (c) H. E. Zimmerman, K. G. Hancock, and G. C. Licke, *ibid.*, **90**, 4892 (1968).

(10) The ring-opening selectivity displayed in rearrangement reactions of cyclopropylcarbinyl radicals does not appear to be completely rationalized by arguments based upon polar factors operating in an analogous way to those controlling radical anion reactions.[3a]

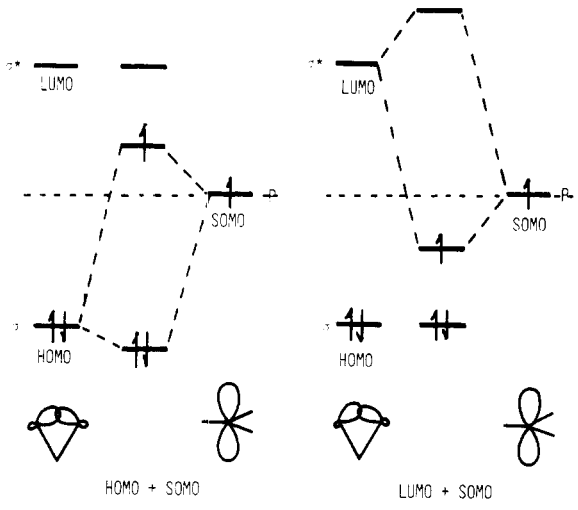


Figure 2. SOMO interactions with cyclopropane LUMO and HOMO orbitals in cyclopropylcarbinyl to homoallyl radical rearrangements.

stability and, thus, on σ-bond-dissociation energies are not the controlling features determining the direction of ring opening of unsymmetrically substituted cyclopropylcarbinyl radicals when stereoelectronic influences are missing.

To our knowledge, no satisfactory rationale has yet been provided to explain these intriguing observations. In light of this, it appeared worthwhile to look at these processes from the viewpoint of frontier molecular orbital theory. Substituent effects on ring-opening regiochemistry should be mainfested in the relative energy contents of transition states resulting from interaction of alkyl-substituted vs. unsubstituted cyclopropane σ bonds with the carbinyl radical center. The position of the transition states along the reaction coordinate along with Coulombic, electrostatic, entropic, and orbital perturbation[11] factors all contribute to the overall energetic requirements for competing bond-cleavage processes. In the absence of steric effects and when the processes being compared have similar early transition states, the attractive forces between the reaction centers resulting from frontier-orbital interactions can be sufficiently large so as to serve as the source of regiocontrol.[12] Importantly, the observed alkyl-substituent controls on cyclopropylcarbinyl to homoallyl radical reactions and analogous processes of anion radicals can be nicely explained by using simple FMO theory. As can be seen by inspection of Figure 2, a greater degree of perturbation stabilization is derived from the interaction of carbinyl radical SOMO and cyclopropane LUMO orbitals than of the SOMO–HOMO pairs. The magnitude of this stabilization will be influenced by substituents attached to the cleaving cyclopropane σ bond and carbinyl center due to their effect upon the energy difference between SOMO and LUMO orbitals.[13] Thus, cyclopropane σ bonds substituted with electron-donating groups such as methyl will be less rapidly cleaved in this process than those which are unsubstituted in systems bearing either electron-donating (OH or $OSnBu_3$) or no substituents at the carbinyl center (see Figure 3). In these cases, alkyl substitution increases the LUMO energy, and, thus, the SOMO–LUMO energy gap. Indeed, this concept rationalizes completely the results observed for ring opening of cyclopropylcarbinyl radicals when stereoelectronic influences are absent. Furthermore, dissolving-metal reductions of cyclopropyl ketones should be subject to the same SOMO–LUMO controls since the SOMO orbital at the radical center should be of high energy due to the oxyanion substituent.[13]

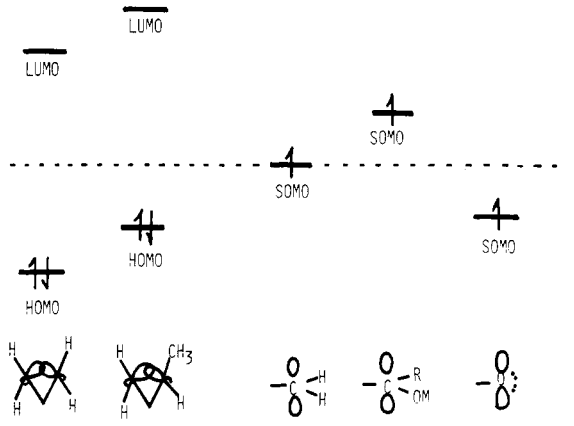
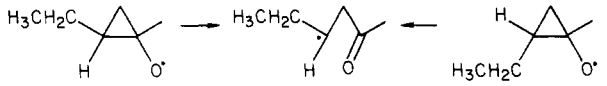


Figure 3. Dependence of SOMO, LUMO, and HOMO energies on substituents.

Another interesting test of this FMO application is found in the ring-opening reactions of the stereoisomeric alkylcyclopropyloxy radicals **29** and **31**.[14] Rearrangements



29 **30** **31**

of these systems have been reported to generate the secondary radicals **30** independent of alkyl-substituent stereochemistry. In this case, the FMO interaction of importance is SOMO–HOMO due to the low energy of the p orbital centered on the electronegative oxygen. Accordingly, alkyl substituents which raise the HOMO energy should enhance this interaction and, thus, the rate of bond cleavage.[15]

In summary, substituent effects on the selectivity of ring opening in cyclopropylcarbinyl radical rearrangements and in reductive cleavages of cyclopropyl ketones can be conveniently understood in the framework provided by FMO theory or in terms of stereoelectronic controls. Furthermore, these same factors must also be at work in controlling the regiochemistry of cyclopropane bond rupturing processes in the excited-state chemistry of cyclopropyl ketones and in pathways which proceed through the intermediacy of cyclopropyldicarbinyl[16] and related[2,17] diradicals.

Experimental Section

General Procedures. 4-Methoxy-3-buten-2-one (Aldrich), azobis(isobutyronitrile) (Aldrich), 1,1-dibromoethane (Eastman), diethylzinc (Alfa), and lithium aluminum deuteride (Alfa) were

(11) C. A. Coulson and H. C. Longuet-Higgins, *Proc. R. Soc. London, Ser. A*, **192**, 16 (1947).
(12) G. Klopman, *J. Am. Chem. Soc.*, **90**, 223 (1968); L. Salem, *ibid.*, **90**, 543, 553 (1968).
(13) Alternatively, one can consider interactions of the cyclopropane LUMO with the occupied π^* MO of the radical anion.
(14) P. M. Blum, Ph.D. Dissertation, University of London, 1977.
(15) (a) Ring opening of *trans*-2-methylcyclobutylcarbinyl radical occurs with an 8:1 selectivity favoring cleavage of the substituted bond.[15b] Perhaps radical-stabilizing effects are more important than FMO interactions in this case due to later transition states caused by decreased exothermicities for these processes compared to those in the cyclopropane systems. (b) A. L. J. Beckwith, Abstracts Colloque Internationale, CNRS, Radicaux Libres Organiques, Aix-en-provence, France, 1977, p 7.
(16) Godet and Pereyre[7a] have found a ρ value for ring opening of 2-para-substituted phenylcyclopropylcarbinyl radicals of ca. +0.5, consistent with the FMO concepts presented above.
(17) P. S. Mariano and J. K. Ko, *J. Am. Chem. Soc.*, **95**, 8670 (1973).

commercially available. NMR spectra were recorded on Varian HA-100 or T-60 (proton) and JEOL PS-100 (carbon) spectrometers with $(CH_3)_4Si$ as internal standard. Infrared spectra were taken on a Beckman IR-8 spectrometer. ESR spectra were recorded on a Varian E-6S spectrometer. Gas chromatographic analyses were made with a Varian-940 instrument and separations were performed with a Varian-2720 instrument. Mass spectrometric measurements were made with a CEC-21-110 double-focusing mass spectrometer.

***trans*-2-Buten-3-*d*-1-ol (9).** A solution of 35.8 g (0.36 mol) of 4-methoxy-3-buten-2-one in 40 mL of ether was added dropwise to a slurry of 5 g (0.12 mol) of lithium aluminum deuteride and 100 mL of ether. This slurry was refluxed for 45 min after addition was complete. The reaction mixture was cooled and treated by successive dropwise addition of 5 mL of water, 5 mL of 15% aqueous sodium hydroxide, and 15 mL of water. The white precipitate produced was removed by suction filtration. The filtrate was stirred with 20 mL of 10% sulfuric acid at 0 °C for 2 min. The ether layer was then separated from the aqueous acid and the acid layer extracted with ether. The combined ethereal layers were neutralized with sodium bicarbonate and dried (sodium sulfate). This ethereal solution was then added dropwise to a slurry of 20.25 g (0.53 mol) of lithium aluminum hydride and 18 mL of ether. The slurry was stirred for 30 min after addition was complete and then treated by successive dropwise addition of 20 mL of water, 20 mL of 15% sodium hydroxide, and 60 mL of water. The precipitate was removed by suction filtration. The filtrate was dried (sodium sulfate) and concentrated by distillation through a Vigreux column. The residue was purified by atmospheric distillation through a 30-cm unpacked vacuum-jacketed column with a 50:1 reflux ratio. Since all impurities were lower boiling than the desired product, this distillation was run until the head temperature reached 100 °C; at this point the residue was cooled and collected. This procedure yielded 7.0 g (27%) of ca. 95% pure deuterated alcohol **9**. Mass spectrometry revealed >93% deuterium incorporation: ^{1}H NMR (CCl_4) δ 1.70 (s, 3 H), 3.74 (s, H), 3.90 (d, 2 H, J = 6 Hz), 5.58 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.55 (q, CH_3), 63.10 (t, C-1), 126.15, 127.07, 128.00 (t, C-3), 130.30 (d, C-2); mass spectrum, m/e (relative intensities) 73 (38), 58 (100), 42 (19), 40 (19), 30 (21); high-resolution mass spectrum, m/e 73.063970 (C_4H_4OD requires 73.063787).

***trans*-2,*trans*-3- and *trans*-2,*cis*-3-Dimethylcyclopropyl-2-*d*-methanols (10tt and 10ct).** To a flask containing 100 mL of dry diisopropyl ether was added 11.7 g (0.16 mol) of *trans*-2-buten-3-*d*-1-ol (**9**) and 29 g (0.23 mol) of diethylzinc. Ethylidene iodide[18] (90 g, 0.32 mol) was added through a dropping funnel over a 30-min period while stirring at room temperature. The exothermic reaction took place immediately. After addition was complete, the reaction mixture was allowed to stand at room temperature overnight, carefully poured into 250 mL of ice-cold 5% hydrochloric acid, and extracted with ether. The ethereal layers were combined and successively washed with water and saturated sodium bicarbonate. After drying (sodium sulfate), concentration was effected by distillation through a Vigreux column. The residue was then carefully distilled (71–83 °C, 60 torr) through a vacuum-jacketed column at reduced pressure, giving 12 g (74%) of a mixture of *trans*-2,*trans*-3-dimethylcyclopropyl-2-*d*-methanol (**10tt**) and *trans*-2,*cis*-3-dimethylcyclopropyl-2-*d*-methanol (**10ct**) in a ratio of about 2:1. The isomers were separated by preparative GLC (25 ft × $^3/_8$ in., 15% dinonyl phthalate, 60–70 mesh ABS Anakrom, 120 °C, inlet pressure of 18 psig). **10tt**: ^{1}H NMR ($CDCl_3$) δ 0.19–0.83 (m, 2 H), 1.05 (d, 3 H, J = 5.5 Hz), 1.03 (s, 3 H), 3.02 (s, 1 H), 3.43 (d, 2 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 66.51 (t, CH_2), 29.20 (d, C-1), 15.51, 14.57, 13.63 (t, C-2), 14.87 (d, C-3), 12.04 (q, CH_3); mass spectrum, m/e (relative intensities) 101 (3), 83 (26), 70 (38), 68 (52), 57 (100), 42 (59); high-resolution mass spectrum, m/e 101.094730 ($C_6H_{11}OD$ requires 101.095087). **10ct**: ^{1}H NMR ($CDCl_3$) δ 0.42–1.01 (m, 2 H), 1.17 (s, 3 H), 1.20 (d, 3 H, J = 7 Hz), 1.93 (s, 1 H), 3.70 (dq, 2 H, J = 8 and 13 Hz); ^{13}C NMR ($CDCl_3$) δ 62.36 (t, CH_2), 26.35 (d, C-1), 19.14, 18.47, 17.53 (t, C-2), 18.39 (d, C-3), 18.12 (q, CH_3), 12.77 (q, CH_3); mass spectrum, m/e (relative intensities) 101 (1), 83 (14), 70 (32), 68 (46), 57 (100), 42 (65); high-resolution mass spectrum m/e 101.094930 ($C_6H_{11}OD$ requires 101.095087).

***trans*-2,*trans*-3- and *trans*-2,*cis*-3-Dimethylcyclopropane-2-*d*-carboxaldehydes (11tt and 11ct).** The mixture of 2,3-dimethylcyclopropylmethanol isomers **10tt** and **10ct** (290 mg, 0.0029 mol) was added to 8.5 g (0.098 mol) of active manganese dioxide in 70 mL of *n*-pentane. This slurry was stirred for 3 h at room temperature under an inert atmosphere. The solids were removed by suction filtration through a Celite pad. The pentane was removed by distillation with a Vigreux column. Purification and separation of the isomeric aldehydes were performed by preparative GLC (15 ft × $^5/_{16}$ in., 10% SE-30, 60–70 mesh ABS Anakrom, 100 °C, inlet pressure of 10 psig), yielding 35 mg (12%) of *trans*-2,*cis*-3-dimethylcyclopropane-2-*d*-carboxaldehyde (**11ct**) and 64 mg (22%) of *trans*-2,*trans*-3-dimethylcyclopropane-2-*d*-carboxaldehyde (**11tt**). **11ct**: ^{1}HMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.35 (d, 3 H, J = 1 Hz), 1.39–1.98 (m, 2 H), 9.40 (d, 1 H, J = 5 Hz); mass spectrum, m/e (relative intensities) 99 (6), 84 (90), 70 (58), 56 (81), 42 (100); high-resolution mass spectrum, m/e 99.081162 (C_6H_9OD requires 99.079332). **11tt**: ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.15 (d, 3 H, J = 6 Hz), 1.30–1.65 (m, 2 H), 9.09 (dd, 1 H, J = 2 and 5 Hz); mass spectrum, m/e (relative intensities) 99 (10), 84 (98), 70 (50), 56 (45), 42 (100); high-resolution mass spectrum, m/e 99.081554 (C_6H_9OD requires 99.079332).

Procedure for ESR Studies. To a quartz ESR tube (4-mm diameter) was added 90 μL of one isomer of the deuterated cyclopropylmethanols and 120 μL of di-*tert*-butyl peroxide. This ESR tube was attached to a vacuum line and degassed by three freeze–thaw cycles. Next, 125 mL of cyclopropane gas at 600 torr was frozen into the ESR tube with liquid nitrogen. The ESR tube was then sealed with a hand torch above the still frozen sample, warmed, and placed in the cavity of the ESR spectrometer inside a specially constructed cryoprobe. The cryoprobe was cooled by passing dry nitrogen through a liquid nitrogen heat exchanger. This cold nitrogen stream was then passed over a small heating element placed just before the sample in the ESR cavity. The temperature was monitored by a thermocouple at the base of the ESR tube and controlled by varying the nitrogen flow rate and the electric current in the heating element. Irradiation of the sample in the cavity was performed with a 500-W Illumination Industries short-arc high-pressure mercury lamp focused on the sample by a quartz collimator. A 20-cm water cell with quartz windows filtered the light. Similar studies were also done on the tri-*n*-butylstannyl ethers (**12tt** and **12ct**) of the cyclopropylmethanols **10tt** and **10ct**. Solutions of the tin ethers were prepared by mixing 250 mg (0.00070 mol) of tri-*n*-butyltin methoxide (Alfa) and 90 mg (0.00089 mol) of the cyclopropylmethanol. The methanol formed by reaction as well as unreacted cyclopropylmethanol were removed by room temperature vacuum distillation, leaving behind the nonvolatile cyclopropylstannyl ether. ESR spectra of the cyclopropylstannyl ethers were obtained in the same manner as for those of the cyclopropylmethanols.

Thermolytic Generation of Cyclopropylcarbinyl Radicals. The cyclopropylmethanol **10tt** or **10ct** and di-*tert*-butyl peroxide were mixed in a 3:1 mole ratio in a heavy-walled glass tube, degassed by three freeze–thaw cycles, and sealed. These tubes were heated at 140 °C for 2 h, cooled, and carefully opened. Gas chromatographic separation of the product mixture (10 ft × $^5/_{16}$ in., 5% XE-60, 60–70 mesh ABS Anakrom, 80 °C, inlet pressure of 10 psig) yields 3-methylvaleraldehyde which was subjected to mass spectroscopic analysis (see Results).

Generation of Cyclopropylcarbinyl Radicals by Reduction of Cyclopropyl Aldehydes. A mixture of approximately 30 mg (0.0003 mol) of the cyclopropyl aldehyde **11tt** or **11ct**, 180 mg (0.00062 mol) of tri-*n*-butyltin hydride (Alfa), and 25 mg (0.00015 mol) of azobis(isobutyronitrile) was heated at 80 °C for 2 h. The reaction was then quenched by addition of 300 μL of methanol followed by refluxing for 30 min. Preparative GLC (15 ft × $^5/_{16}$ in., 20% SE-30, 60–70 mesh ABS Anakrom, 120 °C, inlet pressure of 12 psig) yielded 10 mg (29%) of the 3-methylvaleraldehyde which was subjected to mass spectroscopic analysis.

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(18) R. C. Newman, *Tetrahedron Lett.*, 2541 (1964).

troluem Research Fund, administered by the American Chemical Society, is greatfully acknowledged. E.B. thanks the R. A. Welch Foundation for a Fellowship. We thank Professor Jack Lunsford and Dr. Timothy L. Rose for exceptionally helpful discussions about this work. Our appreciation is expressed to Professor K. Ingold for initial discussions which stimulated our interest on this problem and for providing us with a preprint of a very comprehensive review on free radical chemistry.

Registry No. 5ct, 73156-69-1; **5tt**, 73208-74-9; **6ct**, 73156-70-4; **6tt**, 73208-75-0; **9**, 73156-71-5; **10ct**, 73156-72-6; **10tt**, 73208-76-1; **11ct**, 73156-73-7; **11tt**, 73208-77-2; **12ct**, 73156-74-8; **12tt**, 73208-78-3; **13α**, 73156-75-9; **13β**, 73177-14-7; **14α**, 73156-76-0; **14β**, 73177-15-8; **15**, 73156-77-1; 4-methoxy-3-buten-2-one, 4652-27-1; tributyltin methoxide, 1067-52-3; 3-methylvaleraldehyde-*3-d*, 73156-78-2; 3-methylvaleraldehyde-*4-d*, 73156-79-3.

Mechanism of the Non-Aryne Hydroxydehalogenation of Unactivated Aryl Halides[1,2]

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The hydroxydehalogenation of aryl halides upon reaction with aqueous alkali at temperatures up to 333 °C was examined to determine the nature of an ipso hydroxydehalogenation process reported in 1957 to compete with the aryne mechanism. The reactions of *p*-iodo-, *p*-bromo-, and *p*-chlorotoluene with aqueous solutions of sodium or potassium hydroxide or carbonate, carried out in Pyrex glass tubes with exclusion of traces of transition metals, led in all cases to the same product distribution. *m*-Cresol and *p*-cresol, the two main products, formed with a para/meta ratio of 0.82 ± 0.03, consistent with the occurrence of the aryne mechanism only. Addition of traces of copper salts or conducting the reaction in a Monel bomb, as done by other investigators, caused the occurrence of a non-aryne ipso hydroxydehalogenation. This effect was not produced by nickel, iron, manganese, or cadmium. The ipso hydroxydehalogenation observed in previous studies is identified as a copper-catalyzed process.

Reactions of aryl halides with aqueous alkali metal hydroxides at high temperatures to give phenols were shown by Bottini and Roberts,[3] with attention also to experiments of earlier workers,[4,5] to occur largely via the aryne mechanism. A prominent observation was that *p*-halotoluenes (pXT's) afford mixtures of *p*-cresol (pHOT) and *m*-cresol (mHOT). The mechanism was represented as in Scheme I.

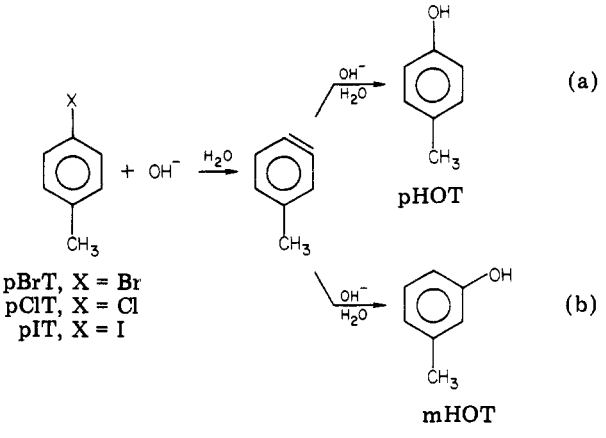
Bottini and Roberts[3] also observed a competing reaction of ipso hydroxydehalogenation that forms only *p*-cresol from a pXT (eq 1). This mode of reaction was more

$$\text{pXT} + \text{OH}^- \xrightarrow{\text{H}_2\text{O}} \text{pHOT} + \text{X}^- \qquad (1)$$

prominent at lower temperatures and with larger halogens. From pIT reacting at 340 °C, they obtained nearly equal amounts of mHOT and pHOT, but the product from the reaction at 250 °C was almost entirely pHOT. They considered but rejected the possibility that the process of pure ipso hydroxydehalogenation was a copper-catalyzed reaction, mainly because reaction of pClT with 4 M NaOH at 340 °C in the presence of pieces of copper wire afforded pHOT and mHOT in the same ratio as in the absence of copper wire.[6]

Bottini and Roberts[3] proposed the ipso hydroxydehalogenation to occur by an S_N2-type mechanism, not further defined. A current textbook considers it to be an example of the S_NAr mechanism.[7]

Scheme I



Possibly closely related was the observation of reaction of pIT with 4 M aqueous NaCl at 340 °C to form pClT.[3]

Our interest in further study of the ipso hydroxydehalogenation stemmed in part from the thought that it might occur by the radical chain $S_{RN}1$ mechanism.[8]

Results

We have conducted a study of the products of reactions of KOH, NaOH, and certain other inorganic bases with *p*-halotoluenes in sealed Pyrex glass tubes. We used glass tubes in order to control the reaction environment, with particular regard to metal ions. Care had to be taken to avoid accidental contamination by traces of transition

(1) Based in part on ref 2.
(2) Zoratti, M. Ph.D. Dissertation, University of California, Santa Cruz, CA, June 1979.
(3) Bottini, A. T.; Roberts, J. D. *J. Am. Chem. Soc.* **1957**, *79*, 1458.
(4) Meharg, V. E.; Allen, I., Jr. *J. Am. Chem. Soc.* **1932**, *54*, 2920.
(5) Shreve, R. N.; Marsel, C. J. *Ind. Eng. Chem.* **1946**, *38*, 254.
(6) Bottini, A. T., research reports to J. D. Roberts, 1956.
(7) Morrison, R. T.; Boyd, R. N. "Study Guide to Organic Chemistry", 3rd ed.; Allyn and Bacon: Boston, MA, 1975; p 379.
(8) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

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