

trans-1 and -2 and for presumably unassisted *tert*-butylcyclohexane¹⁶ as a function of ionizing voltage. With heavy precedent,¹⁰ this assistance mechanism should increase the competitive rate for loss of C₄H₉ in *trans*-1 and -2 but not in *tert*-butylcyclohexane as the ionizing energy is lowered. This is precisely what is found (Figure 2).

(3) The unusual observation of homolytic substitution at carbon may be reasonably ascribed to the nature of the substituting group. Consider the following competition. When neutral bromine radical approaches a hydrocarbon chain, S_H2 reaction at hydrogen or carbon leads, respectively, to an alkyl radical and hydrogen bromide or alkyl bromide. The 18-kcal mol⁻¹ difference in bond strength¹⁷ favoring hydrogen bromide, if reflected in the competitive transition states, will powerfully direct substitution at hydrogen as is always observed.³ On the other hand S_H2 reaction by alkylated bromine radical (RBr^{•+}) on hydrogen will produce alkyl radical and the hydridoalkylhalonium ion, while attack at carbon produces alkyl radical and dialkylhalonium ion. Kinetic evidence¹⁸ and analogy to carbenium ion stabilities suggest that the dialkylhalonium ion is considerably more stable than the hydridoalkylhalonium ion, thus favoring S_H2 reaction at carbon. Although, in the intramolecular cases herein, the dialkylhalonium ion product of the S_H1 reaction at carbon has the recognized special stability of the five-membered ring,⁷ this is not prerequisite to homolytic displacement at carbon as demonstrated by recent ion cyclotron resonance results showing that RBr^{•+} will displace bromine radical from RBr to form acyclic dialkylbromonium ions.^{19,20}

The observation in electron impact mass spectrometers of homolytic displacement at carbon⁵ may now be added to the Barton²¹ and Hofmann-Loeffler-Freitag²² reactions as demonstration that mass spectrometry should be a subject of increasing awareness to the field of free-radical chemistry.¹¹

References and Notes

- R. A. Ogg, Jr., and M. Polanyi, *Trans. Faraday Soc.*, **31**, 482 (1935).
- W. A. Pryor, "Free Radicals", McGraw-Hill, New York, 1966 p 151 ff.
- K. U. Ingold and B. P. Roberts, "Free Radical Substitution Reactions", Wiley-Interscience, New York, Chapter V, p 72 ff.
- J. H. Incremona and C. J. Upton, *J. Am. Chem. Soc.*, **94**, 301 (1972); G. Maynes and D. E. Applequist, *ibid.*, **95**, 856 (1973); C. J. Upton and J. H. Incremona, *J. Org. Chem.*, **41**, 523 (1976); D. E. Applequist and L. F. McKenzie, *ibid.*, **41**, 2262 (1976). See also B. B. Jarvis, *ibid.*, **35**, 924 (1970); J. M. Hoffmann, K. J. Graham, and C. F. Rowell, *ibid.*, **40**, 3005 (1975); and earlier references therein. Related studies with other leaving groups and leading references may be found in B. D. Gupta, T. Funabiki, and M. D. Johnson, *J. Am. Chem. Soc.*, **98**, 6697 (1976); M. D. Johnson, T. Funabiki, and B. D. Gupta, *J. Chem. Soc., Chem. Commun.*, 653 (1977); N. A. Porter and J. R. Nixon, *J. Am. Chem. Soc.*, **100**, 7116 (1978). For an early review see K. Heusler and J. Kalvoda, *Angew. Chem., Int. Ed. Engl.*, **3**, 525 (1964).
- F. W. McLafferty, *Anal. Chem.*, **34**, 2 (1962).
- C. C. Van de Sande and F. W. McLafferty, *J. Am. Chem. Soc.*, **97**, 2298 (1975).
- A review on halonium ions in solution has appeared: George A. Olah, "Halonium Ions", Wiley-Interscience, New York, 1975. The unique mechanism of formation of five-membered-ring halonium ions in mass spectrometers^{5,6} supports proposals that this ring size is favored in solution for thermodynamic rather than kinetic reasons. See P. E. Peterson, B. R. Bonazza, and P. M. Henrichs, *J. Am. Chem. Soc.*, **95**, 2222 (1973); R. D. Wieting, R. H. Staley, and J. L. Beauchamp, *ibid.*, **96**, 7552 (1974). A recent paper with leading references is S. D. Beatty, S. D. Worley, and S. P. McManus, *ibid.*, **100**, 4254 (1978).
- Measured on a Du Pont 21-490 mass spectrometer at 120 °C source temperature from *m/e* 39 to the molecular ion. The percent total ionization Σ₃₉ (eV) is 27% (70 eV), 65% (8 eV). The electron voltages (eV) are uncalibrated. At 8 eV the only processes exhibiting ion intensity are *m/e* 91 and the rearrangement loss of HCl, *m/e* 84.
- F. W. McLafferty, D. J. McAdoo, and J. S. Smith, *J. Am. Chem. Soc.*, **91**, 5400 (1969).
- These ideas and supporting evidence are well presented in D. H. Williams and I. Howe, "Principles of Organic Mass Spectrometry", McGraw-Hill, London, 1972, Chapter 4; F. W. McLafferty, "Interpretation of Mass Spectra", 2nd ed., Benjamin, Reading, Mass., 1973, Chapter 8. See also R. H. Shapiro and T. F. Jenkins, *Org. Mass Spectrom.*, **2**, 771 (1969); H. E. Schoemaker, N. M. M. Nibbering, and R. G. Cooks, *J. Am. Chem. Soc.*, **97**, 4415 (1975), and references therein for especially effective use of these ideas. A recent paper with leading references is H. Schwarz and M. T. Reetz, *Angew. Chem., Int. Ed. Engl.*, **15**, 705 (1976).

- M. M. Green, T. J. Mangner, S. P. Turner, and F. J. Brown, *J. Am. Chem. Soc.*, **98**, 7082 (1976).
- See ref 6-8 of ref 11 above and the following: D. W. Turner, C. Baker, A. D. Baker, and C. R. Brundle, "Molecular Photoelectron Spectroscopy", Wiley-Interscience, London, 1970, Chapter 8; Y. Gounelle, C. Menard, J. M. Pechine, D. Solgadi, F. Menes, and R. Botter, *J. Electron Spectrosc. Relat. Phenom.*, **7**, 247 (1975); J. A. Hashmall and E. Heilbronner, *Angew. Chem., Int. Ed. Engl.*, **9**, 305 (1970).
- All materials gave mass and NMR (¹³C and ¹H) spectra consistent with their structure. The *cis* and *trans* isomers of 1 were prepared from 4-*tert*-butylcyclohexanecarboxylic acid (we are grateful to Professor Harold Hart for this material) following the method of F. W. Baker, H. D. Holtz, and L. M. Stock, *J. Org. Chem.*, **28**, 514 (1963). The *cis* and *trans* isomers of 1 and 2 were also prepared from the alcohols following the method of E. L. Eliel and R. G. Haber, *J. Org. Chem.*, **24**, 143 (1959). GLC on QF-1 columns served to separate the stereoisomers in all cases.
- Alkylcyclohexanes are known on electron impact to lose the alkyl group as alkyl radical and, with the transfer of hydrogen atom, as the alkane. See K. Biemann, "Organic Chemical Applications", McGraw-Hill, New York, 1962, p 78 ff.
- The present results do not exclude additional front-side displacement since loss of *tert*-butyl is observed in the *cis* isomers. The less favored *cis* loss may, though, arise by simple cleavage as in *tert*-butylcyclohexane¹⁴ or by isomerization mechanisms. Work is in progress on these points.
- tert*-Butylcyclohexane was prepared from the ketone following the method of Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).
- "Handbook of Chemistry and Physics", 49th ed., Chemical Rubber Co., 1968-1969, p F-158 ff and references therein.
- See G. A. Olah in ref 7 herein, Chapter 2, pp 6, 7.
- R. H. Staley, R. D. Wieting, and J. L. Beauchamp, *J. Am. Chem. Soc.*, **99**, 5964 (1977).
- Ingold and Roberts, in ref 3 herein, p. 73, have, consistent with the overall view taken here, proposed that a more favorable free energy change for substitution at carbon over hydrogen would be the key to observation of the S_H2 or S_H1 reaction at carbon. The mass spectrometer accomplishes this by the change to the charged radical, an uncommon, but not inaccessible, intermediate in solution. See S. D. Ross, M. Finkelstein, and E. J. Rudd, "Anodic Oxidation", Academic Press, New York, 1975.
- M. M. Green, J. G. McGrew II, and J. M. Moldowan, *J. Am. Chem. Soc.*, **93**, 6700 (1971).
- M. M. Green, M. W. Armstrong, T. L. Thompson, K. J. Sprague, A. J. Haas, J. J. Artus, and J. M. Moldowan, *J. Am. Chem. Soc.*, **98**, 849 (1976).
- Senior undergraduate fellow from Kalamazoo College. We are grateful to the National Institute of General Medical Science and the Petroleum Research Fund, administered by the American Chemical Society, for support of this research and to Professor David Forsyth for helpful discussions.

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Alkali Metal Enolates and Cryptands. A Novel Type of Strong Base

Sir:

In the course of our investigations, we have found that alkali metal enolates in the presence of cryptands (Figure 1) exhibited exceptionally strong basicity at room temperature.

Proton abstraction takes place within a few minutes not only from organic acids usually ionized by standard bases, but also from very weak acids such as triphenylmethane and diphenylmethane. Diethyl ether is attacked by the activated enolate and cyclohexyl chloride is quantitatively transformed into cyclohexene.

Lithium, sodium, and potassium enolates of cyclohexanone¹ were respectively prepared in diethyl ether and in THF by the usual procedures.² All reactions were carried out under nitrogen with 0.5 M solutions of each enolate. One equivalent of cryptand was added to the enolate solution.³ The solution must be free of ketone and free of the basic reagent used in its preparation; this important feature must be carefully controlled since the presence in the medium of another base could perturb the results.

When triphenylmethane (pK_a = 31.5) was added to any of the enolate-cryptand solutions, the red color of the carbanion appeared instantaneously (in the absence of cryptand, no reaction occurs). The same observations were made using diphenylmethane (pK_a = 33) instead of triphenylmethane. Toluene (pK_a ≈ 37) is not ionized by the same procedure.

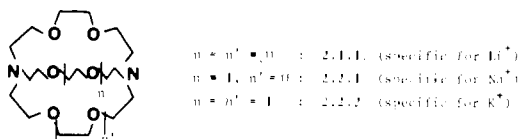


Figure 1. Cryptands used for activating enolates.

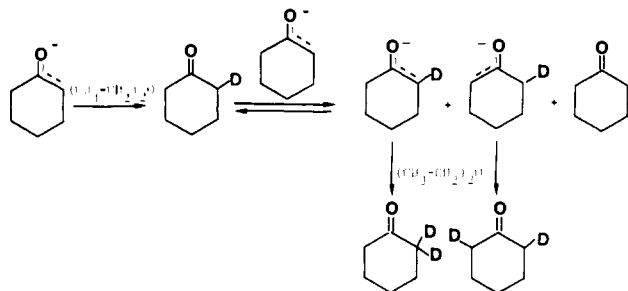


Figure 2.

When this experiment was carried out using trideuteriomethylbenzene, some cyclohexanone was regenerated which had not incorporated deuterium as could be shown by mass spectrometry. The regeneration of the cyclohexanone will be justified subsequently.

Since we observed the regeneration of $\sim 25\%$ of the starting ketone when adding the cryptand to the enolate solutions, we performed the following experiment. In perdeuterated diethyl ether, the regenerated ketone was shown by mass spectrometry to be deuterated (monodeuterated cyclohexanone, 22% of the regenerated ketone; dideuterated cyclohexanone, 3% of the regenerated ketone; 75% of the regenerated ketone contained no deuterium). When the enolate-cryptand solution was hydrolyzed, additional ketone was recovered which had also incorporated $\sim 20\%$ deuterium. These results show that a rapid exchange took place before hydrolysis between the ketone regenerated by the cryptand and the remaining activated enolate (Figure 2). These observations demonstrate the ability of the enolates to attack diethyl ether when they are activated by cryptands. Undoubtedly, THF must be attacked in the same way. The cryptand itself was attacked as it was shown by regeneration of ketone when cryptand was added to the enolate solution in benzene.

In another experiment, we found that cyclohexyl chloride, which did not undergo any reaction after 2 h when added to enolate solutions free of cryptands, was instantaneously and quantitatively transformed into cyclohexene when added to any of the enolate-cryptand solutions. No alkylation of the enolate occurs and all of the cyclohexanone is recovered.

The few results depicted above demonstrate unambiguously the strong basic ability of enolate cryptand solutions. More detailed results will appear in a full paper. We are presently exploring the use of these new bases for a variety of reactions.

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References and Notes

- (1) Similar results have been performed from propanone and acetophenone.
- (2) H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, New York, 1972.
- (3) Lithium enolate cryptand [2.1.1]; sodium enolate cryptand [2.2.1]; potassium enolate cryptand [2.2.2] (the cryptand complexes selectively the alkaline cation and the enolate is entirely solubilized).

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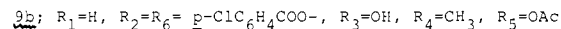
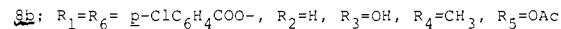
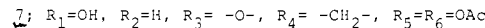
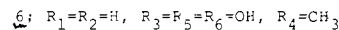
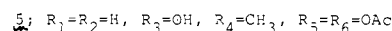
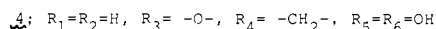
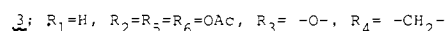
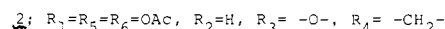
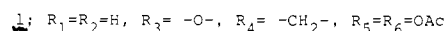
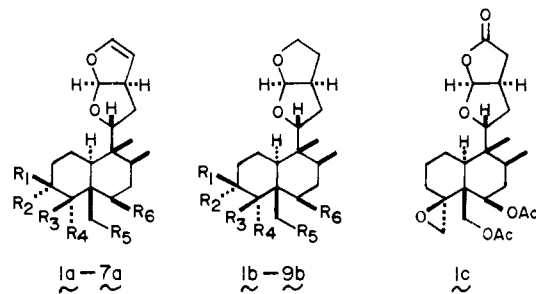
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Absolute Stereochemistries of 3-Epicaryoptin, Caryoptin, and Clerodin as Determined by Chiroptical Methods

Sir:

It is well known that the absolute stereochemistries as determined by the X-ray Bijvoet and CD exciton chirality methods are consistent with each other.¹⁻³ In the cases of insect antifeeding diterpenes, 3-epicaryoptin (**3a**) and caryoptin (**2a**), however, Munakata and his co-workers have claimed⁴ that the absolute configuration by the CD exciton method disagrees with that derived from the X-ray results⁵ of clerodin (**1a**),⁶ proposing the benzoate conformation twisted by the seven-membered intramolecular hydrogen bonding as shown in **9b'** of Figure 1, in order to account for the discrepancy. On the



other hand, they have determined the absolute configuration of clerodendrin A (**10a**)⁷ of same clerodane skeleton by the X-ray method.⁸ If these results are correct, it is worth noting that, as they have pointed out, compounds **1a**, **2a**, and **3a** are antipodal to **10a** in all corresponding chiral centers, in spite of isolation from the plants of same genus.⁹ Therefore, it is significant to check the possibility of the benzoate conformation being twisted by a hydrogen bonding, and to determine the absolute configuration of **1a**, **2a**, and **3a**, for biosynthetic correlations.

In this paper, we report some chiroptical data leading to the conclusion that clerodin, caryoptin, and 3-epicaryoptin should be expressed in the enantiomeric forms of formulas **1a**, **2a**, and **3a**, respectively. As shown in Figure 1, 5 α -cholestane-3 β ,4 α ,6 α -triol 3,6-bis(*p*-chlorobenzoate) (**15**)¹⁰ is a suitable model compound for examining whether the benzoate group of 3-epicaryoptin derivative **9b** is really twisted in its conformation by the intramolecular hydrogen bonding or not, because dibenzoates **9b** and **15** are antipodal to each other in principal chiral centers, i.e., 3, 4, and 6 positions. The CD spectrum of **15** exhibits typical exciton split Cotton effects, $\Delta\epsilon_{246.2} = +27.0/\Delta\epsilon_{231.0} = -13.8$ (EtOH), corresponding to the normal positive exciton chirality between the two benzoate groups. Thus, it is clear that the benzoate conformation in question is not twisted by the adjacent hydroxyl group. This fact is supported by the following CD data. Dibenzoate **14**, having no hydroxyl group, shows CD Cotton effects of same sign and of similar amplitude, $\Delta\epsilon_{247.5} = +28.8/\Delta\epsilon_{230.0} = -13.9$ (5% di-