

Figure 1. Cryptands used for activating enolates.

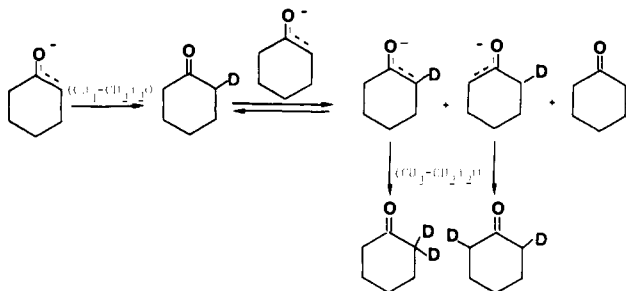


Figure 2.

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.

Acknowledgment. This work was supported by D.G.R.S.T. (PSCOM No. 77 7 0310).

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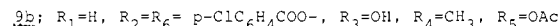
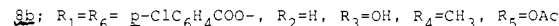
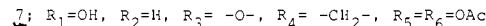
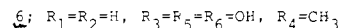
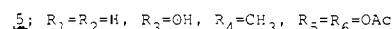
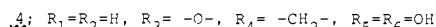
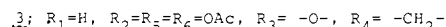
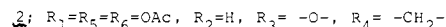
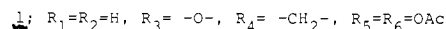
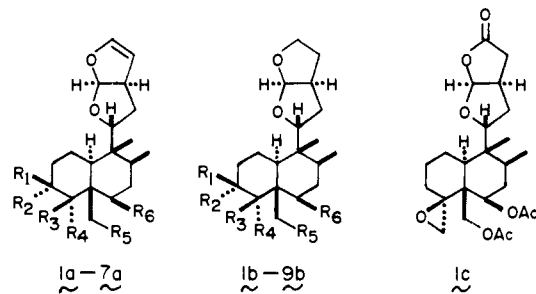
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Absolute Stereochemistries of 3-Epicaryoptin, Caryoptin, and Clerodin as Determined by Chiroptical Methods

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, 5α -cholestane- $3\beta,4\alpha,6\alpha$ -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-

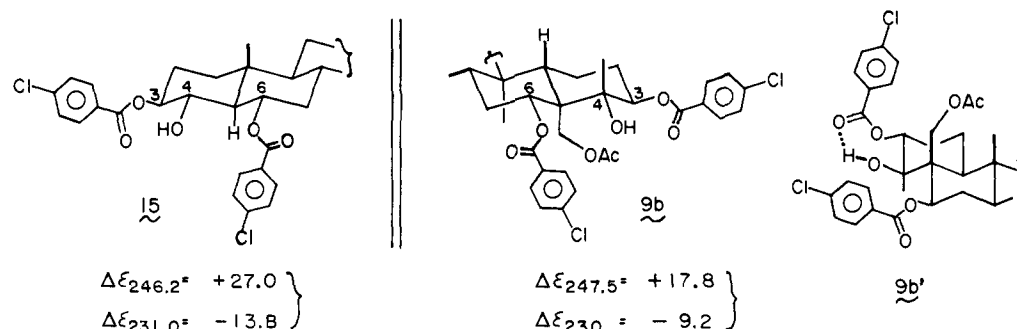
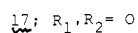
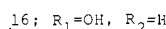
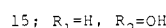
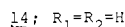
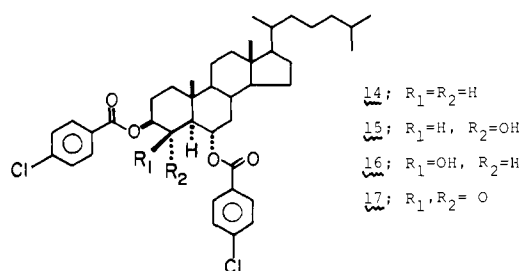
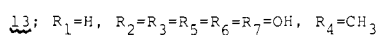
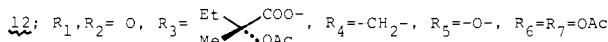
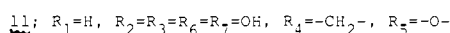
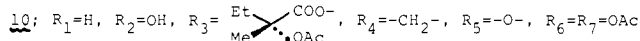
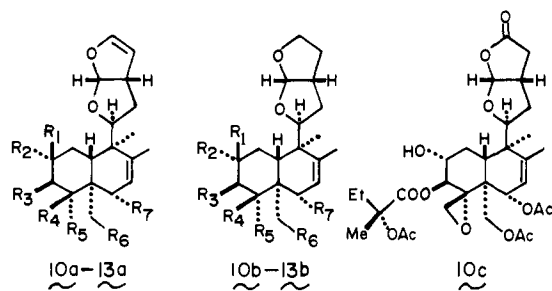


Figure 1. The 3-epicaryoptin derivative **9b** previously proposed is antipodal to steroidal dibenzoate **15** in principal chiral centers. However, the comparison of the CD exciton Cotton effects of these compounds indicates that the 3-epicaryoptin derivative should be expressed in the enantiomeric form of **9b**, the twisted benzoate conformation **9b'** proposed by Munakata being unreasonable.



oxane in EtOH). Moreover, compounds **16** and **17** also exhibit positive first and negative second Cotton effects of $\Delta\epsilon_{248.5} = +26.2/\Delta\epsilon_{231.0} = -15.5$ (2% dioxane in EtOH), and $\Delta\epsilon_{247.0} = +17.4/\Delta\epsilon_{230.0} = -7.6$ (3% dioxane in EtOH), respectively. Since the reported CD Cotton effects of 3-epicaryoptin derivative **9b** are of positive exciton chirality, $\Delta\epsilon_{247.5} = +17.8/\Delta\epsilon_{230} = -9.2$ (20% dioxane in EtOH),⁴ comparison of the data of **9b** and **15** leads to the conclusion that the absolute configuration of 3-epicaryoptin should be revised and expressed in the enantiomeric form of **3a**, although the absolute configuration of clerodrin has been proposed as **1a** by the X-ray studies.⁵ The same is true for the case of caryoptin; since the reported CD Cotton effects of **8b** are $\Delta\epsilon_{247.5} = -28.8/\Delta\epsilon_{230} = +7.5$ (20% dioxane in EtOH),⁴ the absolute configuration of caryoptin should be the mirror image of **2a**.

The above conclusion is confirmed by the following molecular rotation data.¹² Catalytic hydrogenation of the furo-furan ring of **1a–7a** gives dihydro compounds **1b–7b**. The molecular rotation difference between dihydro and unsaturated compounds, $\Delta[\phi]_D = [\phi]_D^b$ (dihydro) $- [\phi]_D^a$ (unsaturated), is always positive and almost constant ($\sim +130^\circ$) throughout the series of clerodrin, caryoptin, and 3-epicaryoptin (Table I).

Table I. Molecular Rotation Difference between Dihydro or Lactone and Unsaturated Compounds of Clerodane Diterpenes^{a–c}

	$[\phi]_D^a$, deg	$[\phi]_D^b$, deg	$[\phi]_D^{c,d}$, deg	$\Delta[\phi]_D$, deg
clerodrin derivatives				
1a \rightarrow 1b	-204.2	-87.3		+116.9
1a \rightarrow 1c	-204.2		-103.6	+100.6
4a \rightarrow 4b	-157.7	-17.6		+140.1
5a \rightarrow 5b	-139.7	-26.3		+113.4
6a \rightarrow 6b	-197.4	-53.2		+144.2
caryoptin derivatives				
2a \rightarrow 2b	-448.2	-311.6		+136.6
7a \rightarrow 7b	-373.9	-330.3		+43.6
3-epicaryoptin				
3a \rightarrow 3b	-344.8	-207.7		+137.1
clerodrin A derivatives				
10a \rightarrow 10b	+44.9	+185.0		+140.1
10a \rightarrow 10c	+44.9		+205.5	+160.6
11a \rightarrow 11b	+75.3	+233.3		+158.0
12a \rightarrow 12b	+192.9	+425.3		+232.4
13a \rightarrow 13b	+151.8	+283.2		+131.4

^a $\Delta[\phi]_D = [\phi]_D^b - [\phi]_D^a$, or $[\phi]_D^c - [\phi]_D^a$. ^b The molecular rotation data were calculated from the specific rotation values reported in ref 6, 7, and 13. ^c Solvent: pyridine for **4a**, **6a**, **11a**, **11b**, **13a**, and **13b**, and $CHCl_3$ for others. ^d Lactone.

Thus, the molecular rotation difference $\Delta[\phi]_D$ is mainly due to the chiroptical change of the furo-furan ring, the contribution of the *trans*-decalin moiety being negligible. In the case of clerodrin A series **10a–13a**, $\Delta[\phi]_D$ is also always positive and almost constant ($\sim +150^\circ$, Table I). Similar values of $\Delta[\phi]_D$ are observed in the case of lactone formation (**1a** \rightarrow **1c** and **10a** \rightarrow **10c** in Table I). Since the relative stereochemistries of the furo-furan ring and other principal chiral centers of **1a**, **2a**, **3a**, and **10a** are identical with one another, the rotation data strongly indicate that all of these compounds have the same absolute configuration. Moreover, since the absolute configuration of **10a** had been doubly established by the X-ray Bijvoet and chemical correlation methods,^{7,8} the absolute stereochemistries of clerodrin, caryoptin, and 3-epicaryoptin should be represented in the enantiomeric forms of **1a**, **2a**, and **3a**, respectively.¹⁴

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References and Notes

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- S. F. Mason, R. H. Seal, and D. R. Roberts, *Tetrahedron*, **30**, 1671 (1974);

- H. Akimoto and S. Yamada, *Tetrahedron*, **27**, 5999 (1971), and references cited therein.
- (3) In this paper, the absolute stereochemistries of clerodin, caryoptin, and 3-epicaryoptin are illustrated as proposed by Paul et al.⁵ and by Munakata and his co-workers,⁴ respectively.
 - (4) S. Hosozawa, N. Kato, and K. Munakata, *Tetrahedron Lett.*, 3753 (1974).
 - (5) I. C. Paul, G. A. Sim, T. A. Hamor, and J. M. Robertson, *J. Chem. Soc.*, 4133 (1962); the reported final *R* value is 15.8%, and six Bijvoet pairs were compared. In one pair, however, the calculated and observed values disagree with each other.
 - (6) D. H. R. Barton, H. T. Cheung, A. D. Cross, L. M. Jackman, and M. Martin-Smith, *J. Chem. Soc.*, 5061 (1961).
 - (7) N. Kato, M. Shibayama, and K. Munakata, *J. Chem. Soc., Perkin Trans. 1*, 712 (1973); N. Kato, S. Shibayama, K. Munakata, and C. Katayama, *Chem. Commun.*, 1632 (1971).
 - (8) N. Kato, K. Munakata, and C. Katayama, *J. Chem. Soc., Perkin Trans. 2*, 69 (1973); the final *R* value is 9.88% and all of the observed 31 Bijvoet pairs show correct intensity differences. The absolute configuration of **10a** has been also established by the chemical correlation of (*R*)-(-)-2-hydroxy-2-methylbutyric acid.⁷
 - (9) (-)-Clerodin has been isolated from *Clerodendron infortunatum* (Verbenaceae) and *Caryopteris divaricata* Maxim; (-)-caryoptin from *Caryopteris divaricata* Maxim; (-)-3-epicaryoptin from *Clerodendron calamitoides* L.; (+)-clerodendrin A from *Clerodendron tricotomum* Thunb.
 - (10) Dibenzoate **15** was synthesized from cholest-5-ene-3 β ,4 α -diol¹¹ by hydroboration and partial benzylation. The 100-MHz NMR spectrum of **15** exhibits peaks at δ 5.52 (1 H, td, *J* = 11.0, 4.3 Hz), 5.01 (1 H, td, *J* = 9.7, 5.3 Hz), and 4.18 ppm (1 H, t, *J* = 9.7 Hz), establishing the assigned relative configuration. The stereochemistries of compounds **14**, **16**, and **17** are also established by the NMR coupling constants. Experimental details for the preparation of these compounds will appear elsewhere.
 - (11) L. F. Fieser and R. Stevenson, *J. Am. Chem. Soc.*, **76**, 1728 (1954).
 - (12) The molecular rotation data were calculated from the specific rotation values reported in ref 6, 7, and 13.
 - (13) S. Hosozawa, N. Kato, and K. Munakata, *Phytochemistry*, **12**, 1833 (1973); S. Hosozawa, N. Kato, and K. Munakata, *ibid.*, **13**, 308, 1019 (1974).
 - (14) After this communication was accepted for publication, we received (Sept 20) private information from Professor D. Rogers, Imperial College, London, that he and his co-workers independently came to the same conclusion as we did, by X-ray studies of 3-epicaryoptin, and that Professor G. A. Sim, one of the authors of the original paper on the X-ray of clerodin, revised the original assignment of clerodin. We thank Professor Rogers for this information prior to publication; D. Rogers, G. G. Unal, D. J. Williams, S. V. Ley, G. A. Sim, B. S. Joshi, and K. R. Ravindranath, *J. Chem. Soc., Chem. Commun.*, submitted for publication.

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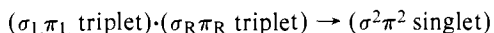
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Dimerization of Carbene to Ethylene

Sir:

As yet, the dimerization of two carbenes to ethylene has not been reported as an experimental fact,¹ and a considerable number of organic chemists appear to believe that this is due to an energy barrier separating reactants and products. The theoretical calculations reported here show this not to be the case.

Along the ground-state energy curve the reaction couples two ³B₁ methylenes into a ¹A_g ethylene and corresponds to the rough orbital characterization



where L and R refer to the left and right methylene, respectively, and σ and π to ethylene. While orbital symmetry is conserved, the coupling of two triplets to a singlet for the reactants lies beyond the SCF MO model, and even beyond any pair model. The validity of conventional orbital symmetry rules is therefore not obvious. The theoretical analysis requires a MCSCF wave function and the "minimal bona fide description" involves *all configurations* that can be constructed using the four "reaction orbitals" σ , σ^* , π , π^* , while keeping inner shells and CH bonds as doubly occupied MO's. There are *eight* such configurations, seven singlet coupled and one triplet coupled, if *D*_{2h} symmetry is preserved. The dissociated ground

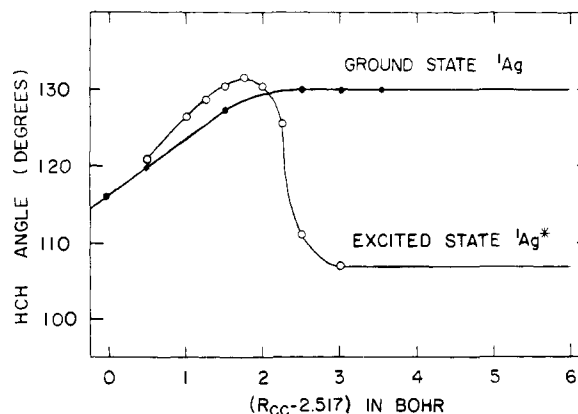


Figure 1. Variations of HCH angle during dissociation of lowest two ¹A_g states of ethylene.

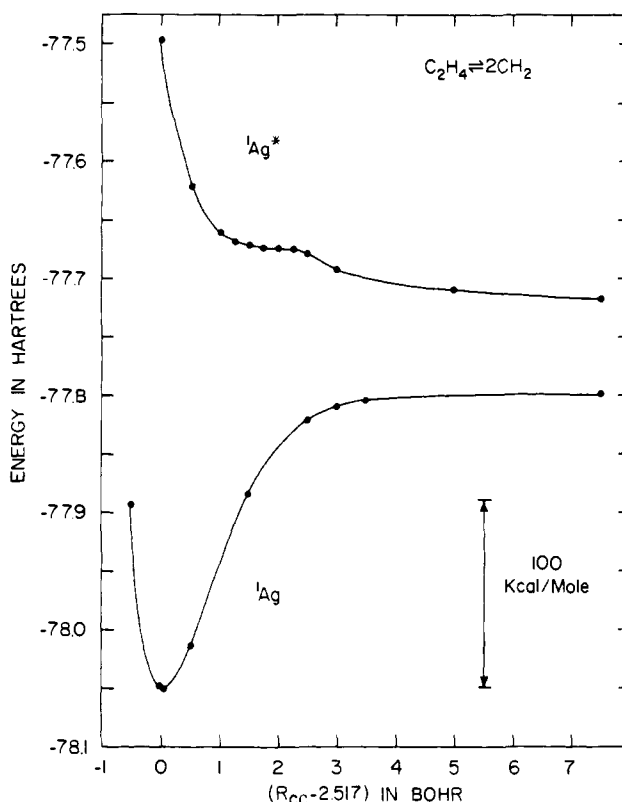


Figure 2. Energy variation of lowest two ¹A_g states of ethylene during dissociation.

state of the system is the superposition of five of these eight configurations.

An ab initio calculation has been carried out based on such an eight-configuration wave function with full optimization of all orbitals, of all configuration mixing coefficients, and of the HCH angle variation along the entire reaction path. This angle variation is displayed in Figure 1. The energy curve resulting for the reaction under conservation of *D*_{2h} symmetry is shown in Figure 2. The reaction energy is found to be 157 kcal/mol (experimental, 167 ± 5 kcal/mol; Hartree-Fock SCF, 121 kcal/mol). The energy curve is remarkably uneventful and the orbital occupation numbers change very gradually (Figure 3). These results imply that *there exists no barrier for this reaction*. In view of the general shapes of the curves shown, we are confident that this conclusion will not change when the calculation is carried out with a more elaborate basis set. (An even-tempered (9s,5p/4s) primitive GTO basis was used, contracted to a (3s,2p/2s) quantitative basis.) We infer that it should be possible to dimerize two methylenes