Electronic Properties. Various electronic properties of CF_3-C≡SF_3 are summarized in Table III. The molecule has a calculated ionization potential of 12.87 eV for a degenerate orbital. The degenerate HOMOs are composed of predominantly the π part of the C≡S bond. The orbitals are strongly polarized toward carbon with 1.18 e on C and 0.55 e on S. The charge distributions are as expected. The fluorines are negatively charged, whereas the carbon in the CF_3 group and the sulfur are positively charged. The fluorines bonded to carbon have a significantly lower negative charge than those bonded to sulfur. The central carbon is quite negative, and both the C—C and C≡S bonds are thus quite polar. As previously proposed,[1] the molecule has some ylidic character (**1a**). The calculated dipole moment is 1.21 D, which is half that of the previously calculated value.[2] The electronic properties discussed above show essentially no variation upon bending the CCS bond angle by 8.4°. For example, the degeneracy of the HOMOs is broken by only 0.01 eV in the C_s structure.

The charges on the fluorines in the CF_3 group are typical of those found in fluorocarbons, which usually fall in the range of 0.15–0.18 e with our basis set.[3,24] For example, $q(F) = -0.15$ e in CF_4. The charge distribution also argues against the presence of negative hyperconjugation in $CF_3C{\equiv}SF_3$.

Acknowledgment. We thank Dr. A. Komornicki of Polyatomics Research for the use of GRADSCF and S. Graffunder of CRAY Research for assistance in using the CRAY XMP/48 at CRAY Research. We thank J. C. Calabrese for helpful comments on the crystal structure analysis. We are especially grateful to Prof. C. J. Marsden of the University of Melbourne for constructive criticism of our work.

Note Added in Proof. In order to approximately account for correlation corrections, MP2 calculations (GRADSCF on a CRAY-1A) with the [6s4p1d/4s2p1d/4s2p] basis set including all valence electrons were performed at the optimum geometries for θ(CCS) = 180° and 171.6°. The geometric parameters from θ = 171.6° were used to generate structures with θ = 161.6° and 151.6°, and MP2 calculations also were done at these two geometries. (Each point required 8200 s of CPU time.) The lowest energy is found for θ = 171.6°, and the energy for θ = 180° is 0.10 kcal/mol higher in energy. Compared to the energy for θ = 171.6°, the energy for θ = 161.6° is 0.53 kcal/mol higher and for θ = 151.6° it is 1.70 kcal/mol higher. The minumum thus lies between θ = 170° and 180° at the MP2 level. Without complete geometry optimization with a correlated wave function, we cannot distinguish whether the molecule is linear or slightly bent considering the very small energy difference of only 100 cal/mol. Clearly the molecule is not bent significantly, and the MP2 results are consistent with our discussion and the experimental X-ray crystal structure.

Chiroptical Properties of Planar Acyclic 1,3-Dienes and α,β-Unsaturated Aldehydes: The Planar Diene Rule[1]

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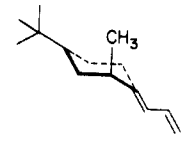
Contribution from the Department of Chemistry, Florida State University, Tallahassee, Florida 32306-3006. *Received November 18, 1985*

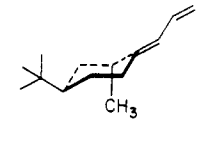
Abstract: The "planar diene rule" has been modified. The CD spectral results obtained with, inter alia, (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetaldehyde, (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylidenylpropene, (*S*)-(+)-(4-hydroxy-2,2,6,6-tetramethylcyclohexylidenyl)propene, and (*S*)-(+)-4-(*tert*-butyldimethylsiloxy)-2,2,6,6-tetramethylcyclohexylideneacetaldehyde are consistent with the hypothesis that a C–C bond is more dominant than a C–H bond and that a CH_3 group is more dominant than a ring CH_2. The absolute configuration, geometry, and conformations of a series of hindered 2,2,6,6-tetramethylcyclohexylidene derivatives of acetic acid, acetone, and acetaldehyde are discussed. X-ray structure of 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid is presented.

Examination of the long-wavelength π–π^* Cotton effects of a large number of chiral acyclic planar 1,3-dienes and α,β-unsaturated aldehydes of known absolute configuration led to the formation of a "planar diene rule"[2] (Figure 1). This rule states that "after the 1,3-diene or α,β-unsaturated aldehyde chromophore and all the atoms attached to it are placed in a single plane, *oriented as shown in the diagram* (Figure 1), atoms or groups of atoms falling above the plane will make a positive contribution and those falling below the plane will make a negative contribution to the Cotton effect for the long-wavelength π–π^* transition".

As applied to (*R*)-(+)-**1** (Figure 1), the chromophore is placed in the plane *as shown*, and one notes that the plane not only contains the four carbon atoms of the diene but also carbon atoms 2 and 6 of the cyclohexane ring and their attached equatorial hydrogen atoms.[2] Those atoms or groups of atoms lying in the plane will make very little, if any, contribution to the long-wavelength π–π^* Cotton effect. The other atoms or groups of atoms closest to the chromophore[3] will determine the sign of the Cotton effect. Those found above the chromophore plane will make a positive contribution and those below a negative one, so that in (*R*)-(+)-**1** one notes that the allylic axial methylenes (ring CH_2) C_3 and C_5 as well as C_4 fall in the (+) space, whereas the allylic hydrogens H_A and H_B fall in the (–) space. This observation is consistent with the hypothesis[2,3] that a C–C bond is more dominant than a C–H bond in their respective contributions to the chiroptical properties of a molecule. It was also concluded, based on the Cotton effect observed for (*E*,2*S*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidenyl)propene (**2**) and (*Z*,2*S*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidenyl)propene (**3**) that an axial ring CH_2 group is more dominant than an axial methyl group.[2] However, this can be misleading since in these molecules one is really comparing *one* axial methyl with *two* ring CH_2 groups. The intent of this article is to clarify this point.



(*E*, 2*S*, 4*R*)-(+)-**2**



(*Z*, 2*S*, 4*R*)-(+)-**3**

(1) This work was supported by a grant from the National Science Foundation.

(2) Duraisamy, M.; Walborsky, H. M. *J. Am. Chem. Soc.* **1983**, *105*, 3264.

(3) Snatzke, G. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 363.

0002-7863/86/1508-2691$01.50/0

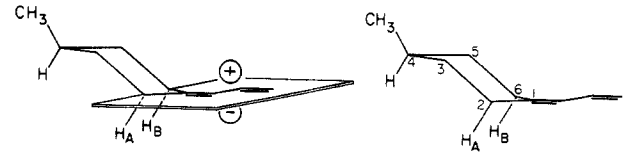
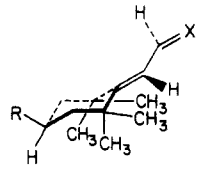


Figure 1. Planar diene rule as applied to (*R*)-(+)-**1**.

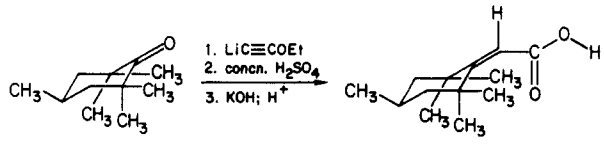
Syntheses

Originally the syntheses of the axially substituted 6-methyl derivative of **2** were attempted but met with failure due to the ease of epimerization of one or at times both of the axial methyl groups. The systems that were finally selected for study were the 1,3-dienes **5**, **7**, and **8** and the α,β-unsaturated aldehydes **4**, **6**, and **8a**.



	R	X
(*S*)-(+)-**4**	CH_3	O
(*S*)-(+)-**5**	CH_3	CH_2
(*S*)-(+)-**6**	$OSi(CH_3)_2$-*t*-Bu	O
(*S*)-(+)-**7**	$OSi(CH_3)_2$-*t*-Bu	CH_2
(*S*)-(+)-**8**	OH	CH_2
(*S*)-(+)-**8a**	OH	O

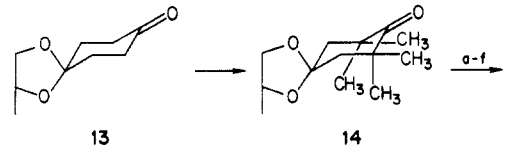
The starting material for the syntheses of **4** and **5** was 2,2,4,6,6-pentamethylcyclohexylideneacetic acid (**10**) which has previously been prepared in yields of 15%[4] and 35%.[5] The condensation of 2,2,4,6,6-pentamethylcyclohexanone (**9**) with the lithium salt of ethoxyacetylene gave the acetylenic alcohol which upon treatment with concentrated sulfuric acid in THF yielded the rearranged ethyl ester of **10**. Saponification gave the desired acid **10** in 65% overall yield.



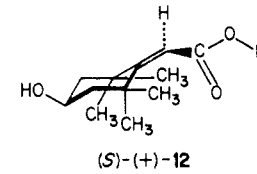
9 **10**

The (±)-**10** was resolved with both (+)- and (−)-α-phenylethylamine to give (*S*)-(+)-**10** and (*R*)-(−)-**10** respectively. The optical purity[6] of the resolved acids was determined by converting them into their corresponding diastereomeric amides using the acid chloride of **10** and optically pure (−)-α-phenylethylamine (see Experimental Section).

Synthesis of (±)-4-hydroxy-2,2,6,6-tertramethylcyclohexylideneacetic acid (**12**) was accomplished starting with ketone **13** prepared by the procedure of Marshall and Flynn[7] and converted to the 2,2,6,6-tetramethyl derivative.[4] The sequence of reactions leading to the acid (±)-**12** was identical with that for the conversion of **9** to (±)-**10** which in this sequence produced 4-oxo-2,2,6,6-tetramethylcyclohexylideneacetic acid (70% yield) which upon reduction with $NaBH_4$ yielded the desired acid (±)-**12**. The acid was resolved into its respective enantiomers by the use of (+)- and (−)-α-phenylethylamine. The absolute configuration of the acid was determined by observing the exciton coupling[8,9]



13 **14**



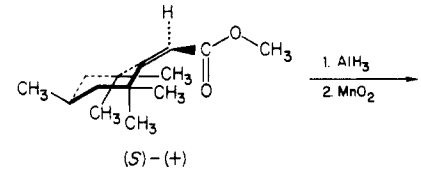
(*S*)-(+)-**12**

(a) LiC≡C—OEt; (b) concn. H_2SO_4; (c) H_3O^+; (d) aqueous KOH; H^+ (e) $NaBH_4$; (f) (+)- and (−)-α-phenylethylamine

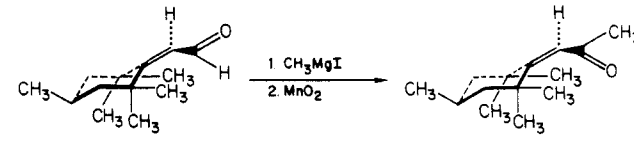
of the benzoate derivative of the methyl ester of (+)-**12** which established it as having an *S* configuration. Optical purity of the resolved acid was established by NMR analysis of the diastereomeric amide (see Experimental Section).

It was necessary to protect the hydroxyl group for the preparation of the α,β-unsaturated aldehyde and methyl ketone derivatives of (*S*)-(+)-**12**. This was conveniently done by making the *tert*-butyldimethylsilyl derivative from the methyl ester of (*S*)-(+)-**12**. Reduction with aluminum hydride followed by MnO_2 oxidation gave the silyl-protected aldehyde (*S*)-(+)-**6**. Methylmagnesium iodide addition to (*S*)-(+)-**6** followed by MnO_2 oxidation provided (*S*)-(+)-4-(*tert*-butyldimethylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenylacetone.

The (*S*)-(+)-**10** acid was converted to its methyl ester and reduced with aluminum hydride to the corresponding carbinol which was oxidized by MnO_2 to yield the (*S*)-(+)-**4** aldehyde. Addition of methylmagnesium iodide to the aldehyde and oxidation with MnO_2 yielded the methyl ketone **11**.



(*S*)-(+)



(*S*)-(+)-**4** (*S*)-(+)-**11**

The chiral 1,3-dienes were prepared from their precursor aldehydes by treatment with methylenetriphenylphosphorane. The ultraviolet and CD spectral data are given in Table I.

Relative and Absolute Configurations

The absolute configuration of (+)-**10** has previously been assigned the *S* configuration on the basis of a comparison of the Cotton effects with known (*S*)-(+)-4-methylcyclohexylideneacetic acid whose absolute configuration had been established by Gerlach.[10] As can be seen from Table II, methyl (*S*)-(+)-4-hydroxycyclohexylideneacetate, (*S*)-(+)-4-hydroxyl-2,2,6,6-tetramethylcyclohexylideneacetic acid, and its methyl ester have also been related by the sign of their Cotton effects to (*S*)-(+)-4-methylcyclohexylideneacetic acid. The absolute configuration of the benzoate derivatives of methyl (+)-4-hydroxycyclohexylideneacetate and methyl (+)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetate were established as *S* by use of the CD exciton chirality method.[8,9] Thus, an independent test confirmed the original assignments of the absolute configurations. Table II lists the absolute configurations and Cotton effects for

(4) Walborsky, H. M.; Turner, L. M. *J. Am. Chem. Soc.* **1972**, *94*, 2273.
(5) Arnett, J. F.; Walborsky, H. M. *J. Org. Chem.* **1972**, *37*, 3678.
(6) Raban, M.; Mislow, K. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Eds.; Interscience: New York, 1967; Vol. 2, p 199.
(7) Marshall, J. A.; Flynn, G. A. *Synth. Commun.* **1979**, *9*, 123.
(8) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy Exciton Coupling in Organic Chemistry*; University Science Books: Mill Valley, NY, 1983.
(9) The exciton results are reported in a paper that has been submitted for publication.
(10) Gerlach, H. *Helv. Chim. Acta* **1966**, *49*, 1291. (*R*)-(−)-**10** was actually compared to (*R*)-(−)-4-methylcyclohexylideneacetic acid. For the sake of clarity of presentation, the comparison in this paper is (*S*)-(+)-**10** with (*S*)-(+)-4-methylcyclohexylideneacetic acid.

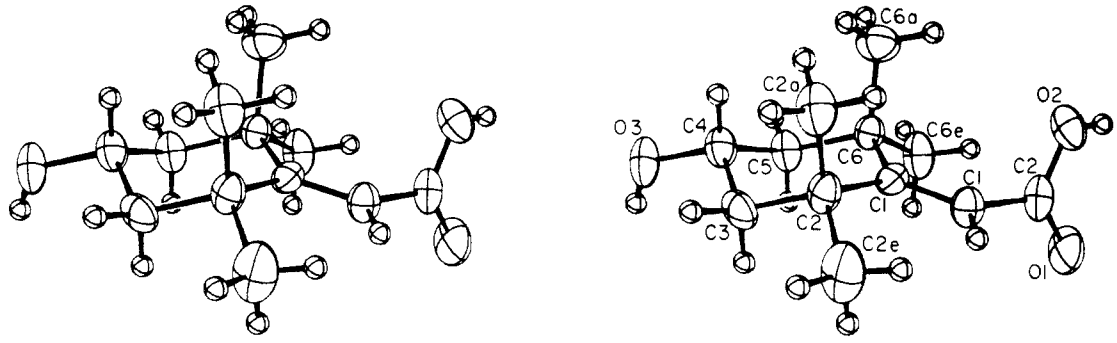
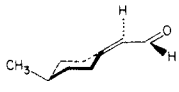
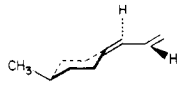
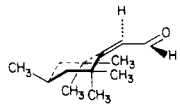
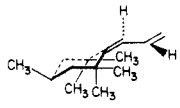
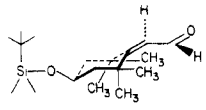
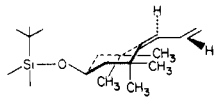
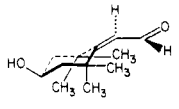
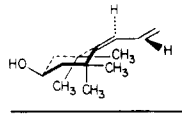


Figure 2. Stereoscopic view of 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid.

Table I. $\pi-\pi^*$ UV and CD Data of Chiral α,β-Unsaturated Aldehydes and 1,3-Dienes

		UV, λ_{max} (nm)[b]	CD,[a,b] $\Delta\epsilon$
	(*S*)-(+)	230 (ϵ 19 500)[d]	−2.08[d]
	(*S*)-(−)	237 (ϵ 24 300)[d]	−2.73[d]
	(*S*)-(+)-**4**	242 (ϵ 11 600)	+12.45
	(*S*)-(+)-**5**	244 (ϵ (20 200)	+10.51
	(*S*)-(+)-**6**	241 (ϵ 13 300)	+11.94
	(*S*)-(+)-**7**	242 (ϵ 22 200) 236 (ϵ 21 000)	+11.94
	(*S*)-(+)-**8a**	242 (ϵ 13 700)	+16.38
	(*S*)-(+)-**8**	241 (ϵ 20 600)[c]	+13.59[c]

[a] Corrected to 100% ee. [b] Solvent, cyclohexane. [c] Solvent, acetonitrile. [d] Data taken from ref 2.

a series of α,β-unsaturated esters and acids.

Geometry Conformation

A question arises, in the case of the 2,2,6,6-tetramethylcyclohexylidene systems, as to the effect of steric interactions on the structure of the molecule. Does the cyclohexane ring become distorted to relieve the $A^{1,3}$ strain[11] or is the strain relieved by having the 1,3-diene or α,β-unsaturated carbonyl skewed out of planarity? The X-ray structure, Figure 2, of 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid clearly shows that the cyclohexane ring maintains its geometric integrity. The six-membered ring has the normal chair conformation, with relatively little distortion as indicated by the torsional angles. These values are near 60° for the "lower" portion of the ring; a modest flattening near the exocyclic function leads to a reduction of the torsion angles to about 40° for the ring bonds involving C-1. This places

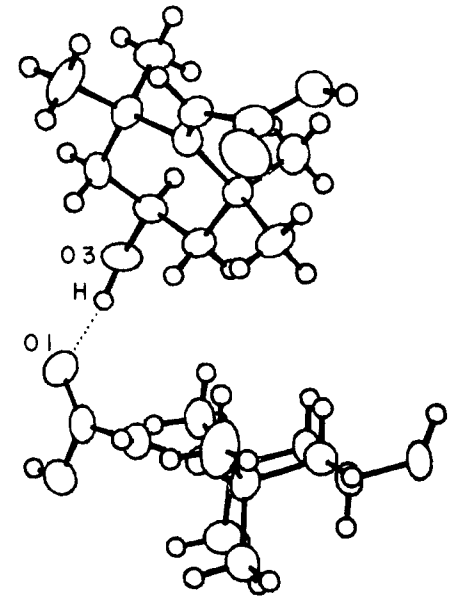
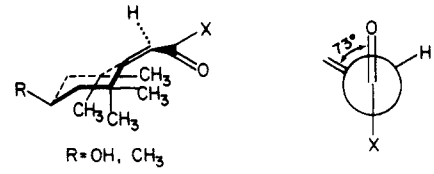


Figure 3. ORTEP plot illustrating intermolecular hydrogen bonding of 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid.

the equatorial methyl groups in the 2- and 6-position slightly above the plane in Figure 1 as is also the case for equatorial hydrogens in the 2-positions.[2]

Steric interactions between the equatorial methyl groups and the carboxylic acid function preclude planarity of the olefin–carbonyl conjugated system and is responsible for the observed 73° dihedral angle between the four-atom planes containing the olefin and carbonyl functions. This situation should also obtain



R = OH, CH_3

X = OH, OCH_3, CH_3

for the 4-methyl analogue **10** as well. The methyl ester derivatives would not be expected to alter the geometry in a significant way nor should there be any significant change in the conversion of the carboxyl group to a methyl ketone (X = CH_3).

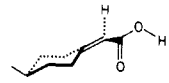
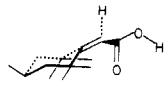
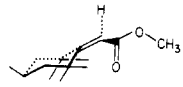
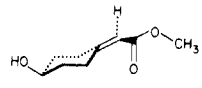
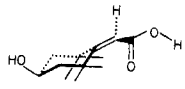
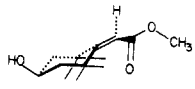
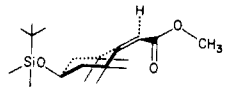
The predominant hydrogen bonding interactions in 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid are intermolecular between the 4-hydroxyl group and the carbonyl oxygen atom of an adjacent molecule as shown in Figure 3. The intermolecular O-1 to O-3 distance, 2.788 Å, is typical for oxygen atoms involved in moderate hydrogen bonding interactions.[12]

Consistent with the X-ray structure (solid) are the data obtained from ^{1}H NMR (solution). Table III clearly shows that one can

(11) For an excellent review, see: Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

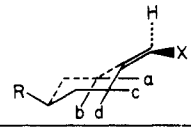
(12) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*; Wiley: New York, 1980; p 221.

Table II. Cotton Effects and Absolute Configurations of α,β-Unsaturated Acids and Esters

compound		CD[a] $\pi-\pi^*$	CD[a] $n-\pi^*$	solvent
	(*S*)-(+)	$\Delta\epsilon_{226}$ + 3.08[b]	$\Delta\epsilon_{280}$ - 0.01[b]	C_2H_5OH
	(*S*)-(+)	$\Delta\epsilon_{214}$ +12.30	$\Delta\epsilon_{251}$ -2.48	cyclohexane
	(*S*)-(+)	$\Delta\epsilon_{208}$ +13.48	$\Delta\epsilon_{247}$ -3.69	cyclohexane
	(*S*)-(+)	$\Delta\epsilon_{218}$ +2.90	$\Delta\epsilon_{247}$ -0.31	cyclohexane
	(*S*)-(+)	$\Delta\epsilon_{208}$ +22.60	$\Delta\epsilon_{246}$ -7.11	CH_3CN
	(*S*)-(+)	$\Delta\epsilon_{210}$ +17.83	$\Delta\epsilon_{247}$ -4.82	cyclohexane
	(*S*)-(+)	$\Delta\epsilon_{208}$ +16.98	$\Delta\epsilon_{247}$ -4.53	cyclohexane

[a] Corrected to 100% ee. [b] The Cotton effects were actually determined for the (*R*)-(-) enantiomer.

Table III. ^1H NMR of Equatorial and Axial Methyl Groups[a]



R	X	*a*	*b*	*c*	*d*
OH	$COOCH_3$	1.36	1.20	1.26	1.22
CH_3	$COCH_3$	1.35	1.13	1.17	1.16
CH_3	CHO	1.47	1.20	1.49	1.22
CH_3	$CH=CH_2$	1.27	1.13	1.33	1.17

[a] Given in ppm with Me_4Si as standard (see Experimental Section).

identify each of the four methyl groups located in the 2- and 6-position of the ring. This confirms that the six-membered ring is rigid and that there is no chair–chair interconversion, at least on the NMR time scale. Moreover, the data also show that the ring is not flattened at the exocyclic double bond, at least to the extent that the double bond bisects the methyl groups attached to carbon atoms 2 and 6 of the ring. The six-membered ring can be viewed as a possessing a rigid chair conformation.

Examination of the data in Table IV provides information which bears on the s-cis, s-trans conformations of a number of α,β-unsaturated esters, ketones, and aldehydes. The s-trans or s-cis conformation can be discerned from the *r* ratio of carbonyl band area to C=C band area. Absolute values for *r* to ascertain whether a molecule is in an s-cis or s-trans conformation cannot be given, but a trend to one or the other conformer can be established. For example, in related molecules **1–3**, Table IV, one can see that **3** has a higher *r* value than **1** and **2**, thus indicating that the aldehyde has a greater tendency to be *transoidal*[13] and planar. Consistent with this interpretation is the observation that $\Delta\nu$ is lower[13] than 60 cm^{-1} and that the molar absorptivity (ϵ) is high (19 500) at λ_{max} = 230 nm. The same trend is observed for compounds **4–10**. Notice that the aldehydes, compounds **6**, **9**, and **10**, are the only α,β-unsaturated carbonyls that possess an s-trans planar configuration. These observations are not unexpected in view of the $A^{1,3}$ strain that is involved with the esters, **5** and **8**, and the ketones, **4** and **7** (see comments column, Table IV). $A^{1,3}$ strain is minimized in the case of α,β-unsaturated aldehydes or in the 1,3-dienes since in the planar transoidal conformation only a proton protrudes toward the methyl groups in the 2- or 6-positions of the cyclohexane ring.

(13) Bienvenue, A. *J. Am. Chem. Soc.* **1973**, *95*, 7345. Faulk, D. D.; Fry, A. *J. Org. Chem.* **1970**, *35*, 364. Groves, J. K.; Jones, N. *Tetrahedron* **1969**, *25*, 223. Cottee, F. H.; Straugham, B. P.; Timmons, C. J.; Forbes, W. F.; Shilton, R. *J. Chem. Soc. B* **1967**, 1146. Noack, K.; Jones, R. N. *Can. J. Chem.* **1961**, *39*, 2225.

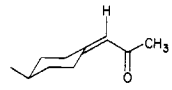
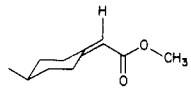
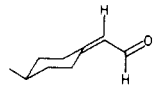
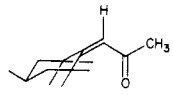
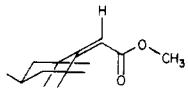
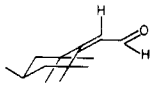
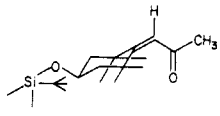
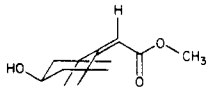
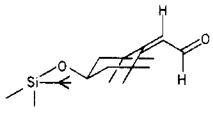
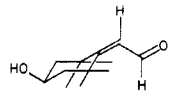
Planar Diene Rule

Having established the absolute configuration, geometry, and conformation of the α,β-unsaturated aldehydes **4**, **6**, and **8a** and the 1,3-dienes **5**, **7**, and **8**, we are now in a position to comment on their relationship to the planar diene rule. The Cotton effects for those molecules are given in Table I. Placing molecules **4–8** in the plane, Figure 1, as prescribed for the rule would place the axial methyl groups above the plane in the (+) space and the ring CH_2 groups in the (-) space. If, as hypothesized, the ring CH_2 is more dominant than an axial CH_3 group, then the planar diene rule would predict a (-) Cotton effect. This is clearly not the case. The basis for the earlier sequence ring CH_2 > CH_3 > H was flawed since it was based on the result from molecules such as (*E*,2*S*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidenyl)propene and (*E*,2*S*,4*R*)-(+)-2-methyl-4-*tert*-butylcyclohexylideneacetaldehyde, as well as the corresponding *Z* isomers. In these cases, one was really comparing an axial CH_3 group with two ring CH_2 groups. In the case of molecules **4–8**, we are now comparing the effect of *two* axial methyl groups with *two* ring CH_2 groups. On this basis, it is clear that an axial methyl group is more dominant than a ring CH_2 group, and therefore the sequence should read CH_3 > ring CH_2 > H.

Experimental Section

Melting points were determined with a Mel-Temp apparatus. All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with Perkin-Elmer Model 257 grating spectrophotometer using a polystyrene 1601-cm^{-1} bond for calibration. Nuclear magnetic resonance (NMR) spectra were recorded on a Brucker 200-MHz or 270-MHz spectrometer. The solvent used was $CDCl_3$ unless noted otherwise, with Me_4Si and $CHCl_3$ (7.26 ppm) as internal standards. The chemical shifts are given in δ (ppm) downfield from Me_4Si and the coupling constants are in hertz. The microanalyses were performed by

Table IV. IR and UV Data of α,β-Unsaturated Esters, Ketones, and Aldehydes

	compound	$\nu_{C=O}$, cm^{-1}	I,[a] cm	$\nu_{C=C}$	I,[a] cm	$\Delta\nu$, cm^{-1}	r[b]	UV, λ, nm, (ε)	comments
1		1692	12.4	1625	12	67	0.82	236 (13 600)	planar s-cis
2		1722	13.1	1655	10.3	67	1.5	218 (16 500)	planar s-cis, s-trans
3		1684	13.7	1640	3.6	44	2.6	230 (19 500)[2]	planar s-trans
4		1691	12.9	1609	5.7	82	1.7	240 (5800)	nonplanar s-cis
5		1722	13.9	1620	5.6	102	2.6	226 (6100)	nonplanar s-cis
6		1662	13.7	1588	2.3	74	6.5	242 (11 600)	~planar s-trans
7		1690	12.8	1604	5.1	86	1.2	240 (6600)	nonplanar s-cis
8		1725	13.7	1622	2.6	103	2.4	218 (6900)	nonplanar s-cis
9		1662	13.2	1591	2.6	71	6.6	240 (11 300)	~planar s-trans
10		1670	13.8	1600	3.8	70	4.7	242 (13 700)	~planar s-trans

[a] Intensity, concentration 0.5 M in CCl_4 for esters and ketones and 0.03 M in CCl_4 for aldehydes. [b] Ratio of C=O band area to C=C band area.

Beller Laboratories, Göttingen, Germany.

Optical rotations were measured at either the 546.1-nm mercury line or the 589.3-nm sodium line on a Bendix-Ericson Model 987 ETL/NPL polarimeter equipped with a Bendix Model DR-1 digital display. The accuracy was ±0.002°, and the cell length was 0.4 dm.

Ultraviolet (UV) spectra were recorded with a Cary 219 spectrophotometer. Circular dichroism (CD) spectra were recorded with JASCO Model J-500C spectrophotometer. The cell path lengths used in UV and CD measurements were 1 and 0.1 cm, respectively. All spectral grade solvents were purified and distilled before use.

For column chromatography, silica gel (70–230 mesh) (Merck) was used unless noted otherwise. Radial chromatography thin-layer separations were performed with Merck silica gel 60 PF_{254} by using Harrison Research Chromatotran Model 7924T.

2,2,4,6,6-Pentamethylcyclohexylideneacetic Acid (10). A dry 2-L three-necked flask equipped with a mechanical stirrer, pressure equivalizing dropping funnel, and rubber septum was maintained under nitrogen atmosphere and charged with 34.37 g (0.491 mol) of ethyl ethynyl ether and 1 L of dry ether. This solution was cooled to −78 °C, and 279 mL (0.446 mol) of a 1.6 M solution of *n*-BuLi was added dropwise to give a thick slurry of lithium salt. A solution of 75 g (0.446 mol) of 2,2,4,6,6-pentamethylcyclohexanone[4] (**9**) dissolved in 200 mL of dry ether was added over a 1-h period. The reaction mixture was stirred at −78 °C for 1 h and allowed to warm to room temperature for an additional 1 h and quiched upon addition of water. The aqueous layer was extracted with three 200-mL portions of ether and the combined organic layer washed with water (2 × 200 mL) and dried over anhydrous Na_2SO_4. Removal of solvent gave 110 g of red oil of acetylene alcohol: IR (film) 3600 (sharp, free OH), 3490 (br, bonded OH), 3000–2840 (m), 2280, 1470, 1400–1370, 1300, 1235, 1200, 1120–930, and 880–815 cm^{-1}. The crude acetylene alcohol in 500 mL of dry THF was cooled to 0 °C, and 11 mL of concentrated sulfuric acid was added. This mixture was allowed to come to room temperature and stirred for 10 h to give the rearranged ester (TLC). The reaction mixture was diluted with water and extracted using ether (3 × 500 mL) to give 100 g of crude rearranged ester.

The crude ester was taken in a 1-L round-bottomed flask, and a 20% solution of potassium hydroxide (35 g in 175 mL of water) was added. The reaction mixture was made homogeneous by the addition of excess ethyl alcohol (500 mL) and refluxed for 3 h. Most of the alcohol was removed under reduced pressure, and the neutral fraction (20 g) was extracted into ether (3 × 100 mL). The solution was made acidic by adding ice-cold concentrated hydrochloric acid, and the precipitated carboxylic acid was extracted into hexane. The organic layer was further washed with diluted HCl and water and dried (Na_2SO_4). Removal of solvent gave pure (2,2,4,6,6-pentamethylcyclohexylideneacetic acid (**10**), 61 g, 65% overall yield from 2,2,4,6,6-pentamethylcyclohexanone: mp 91–93 °C [lit.[4,5] mp 91–93 °C]. IR and ^1H NMR spectra were identical with those reported in the literature.[4,5]

(*S*)-(+)-2,2,4,6,6-Pentamethylcyclohexylideneacetic Acid (10). The racemic 2,2,4,6,6-pentamethylcyclohexylideneacetic acid was resolved with (+)-α-phenylethylamine. To a solution of 60 g of the carboxylic acid (0.285 mol) in 500 mL of ethyl acetate was added 34.57 g (0.285 mol) of the amine and heated on a steam bath. On cooling to 0 °C, white needles were separated. The salt was collected and recrystallized further 10 times in the same solvent at 0 °C to give 8.50 g of the resolved salt. The salt was decomposed with cold 2 N NaOH, and the liberated amine was extracted with ether. The aqueous solution was poured into ice-cold HCl with stirring. The carboxylic acid was extracted into hexane (3 × 100 mL) and the combined hexane solution washed once with dilute HCl and twice with water and dried (Na_2SO_4). Removal of solvent gave 5.30 g of (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetic acid (**10**), which

solidified on standing: mp 72–74 °C, $[\alpha]^{31}_{Hg}$ +34.42 ± 0.03° (*c* 1.20, C_2H_5OH), $[\alpha]^{31}_{Hg}$ +51.46 ± 0.07° (*c* 1.10, $CHCl_3$), 46.50% ee; UV (*c* 1.14 × 10^{-4}, cyclohexane) λ_{226} ε 6000 and λ_{211} ε 5000 (sh); CD (*c* 1.14 × 10^{-3}, cyclohexane) $\Delta\epsilon_{251}$ −1.15 and $\Delta\epsilon_{214}$ +5.72.

(*R*)-(−)-2,2,4,6,6-Pentamethylcyclohexylideneacetic Acid (10). The partially enriched with (−)-acid (48 g, 0.228 mol) recovered from (+)-α-phenylethylamine resolution was taken in 300 mL of ethyl acetate, and 27.64 g (0.228 mol) of (−)-α-phenylethylamine was added. The solution was heated on a steam bath and cooled to 0 °C to give fine crystals of (−)-amine salt. The crystals were collected and further recrystallized from ethyl acetate for 20 times at 0 °C to give 6.32 g of resolved salt. Decomposition and workup as earlier gave 4 g of (*R*)-(−)-acid **10** as a semisolid: mp 63–64 °C [lit.[4] mp 66–68 °C]; $[\alpha]^{25}_{Hg}$ −49.67 ± 0.09° (*c* 1.18, C_2H_5OH), $[\alpha]^{25}_{Hg}$ −73.25 ± 0.06° (*c* 1.09, $CHCl_3$), 66.67% ee [lit.[4] $[\alpha]^{24}_{Hg}$ −53.20° (*c* 1, $CHCl_3$)]; UV (*c* 1.59 × 10^{-4}, cyclohexane) λ_{227} ε 6600; CD (*c* 1.59 × 10^{-3}, cyclohexane) $\Delta\epsilon_{250}$ +1.87 and $\Delta\epsilon_{213}$ −8.67.

Optical Purity of (*R*)-(−)-2,2,4,6,6-Pentamethylcyclohexylideneacetic Acid (10). To a cooled (0 °C) solution of DMF (0.77 mL, 10 mmol) in 10 mL of CH_2Cl_2 was added 0.26 mL (3 mmol) of oxalyl chloride. The resulting slurry was stirred at 0 °C for 1 h, and the volatile fractions were removed under reduced pressure to give white powder of *N,N*-dimethylchloromethyleneiminium chloride.[14] Anhydrous ether (20 mL) was added and cooled to −28 °C. (*R*)-(−)-2,2,4,6,6-Pentamethylcyclohexylideneacetic acid (0.105 g, 0.5 mmol, $[\alpha]^{25}_{Hg}$ −49.67 ± 0.09°) in 5 mL of ether was added and stirred for 2 h.[15] Optically pure (−)-α-phenylethylamine (0.45 mL) was added to give immediate white precipitate. The reaction mixture after 10 min at −28 °C was allowed to warm up to 0 °C in 30 min. Water was added, and the diastereomeric amides formed were extracted into ether. The ether layer was washed successively with diluted HCl, water, aqueous NaOH, and water and dried over Na_2SO_4. Removal of solvent gave a mixture of (1′*S*,*R*)-*N*-1′-(phenylethyl)-2,2,4,6,6-pentamethylcyclohexylidenylacetamide and (1*S*,*S*)-*N*-1′-(phenylethyl)-2,2,4,6,6-pentamethylcyclohexylidenylacetamide as a crystalline solid (0.14 g, 89% yield) in the ratio of 5:1 (83.33:16.66), respectively (from the integration of two olefinc proton singlets at 5.82 and 5.76 ppm, and the optical purity of (*R*)-(−)-2,2,4,6,6-pentamethylcyclohexylideneacetic acid (**10**) ($[\alpha]^{25}_{Hg}$ −49.67 ± 0.09°) was estimated to be 66.67% ee) mp 135–137 °C; IR ($CHCl_3$) 3420, 2950, 2910, 2875, 2825, 1650, 1620, 1495, 1460, 1400–1370, 1340–1285, 1260–1190, 1150–1080, and 1040–1000 cm^{-1}; ^1H NMR (C_6D_6) 0.80, 0.82 (2d, *J* = 6.60, 3 H), 0.99, 1.03, 1.10, 1.30, 1.43, 1.45, 1.50 (7s, 12 H, ring methyls), 1.22 (d, *J* = 7, 3 H), 0.90–1.60 (m, 4 H, ring methylenes), 1.72 (br m, 1 H), 5.20–5.40 (br m, 2 H), 5.76, 5.82 (2s, in the ratio of 1:5, 1 H, olefinic H), and 7.00–7.30 (m, 5 H); ^{13}C NMR 21.34, 21.40 (2 CH_3), 22.63 (CH_3), 23.97 (CH), 30.06, 30.18 ($2CH_3$), 31.66, 31.48 ($2CH_3$), 32.34 (CH_3), 32.94 (CH_3), 37.58, 37.61 (2C), 38.00 (C), 48.57, 48.70 (2CH), 49.40 (CH_2), 51.76, 51.84 ($2CH_2$), 118.62 (CH), 126.36 (2CH), 127.21 (CH), 128.52 (2CH), 143.11, 143.23 (2C), 160.44, 160.56 (2C), and 169.76 (C=O).

Anal. Calcd for $C_{21}H_{31}NO$: C, 80.51; H, 9.90; N, 4.47. Found: C, 80.57; H, 9.94; N, 4.50.

(1′*S*,*R*)-*N*-1′-(Phenylethyl)-2,2,4,6,6-pentamethylcyclohexylidenylacetamide. The disastereomeric amide mixture (5:1) from the above reaction on crystallization from CH_2Cl_2 gave pure single isomer corresponding to the major fraction. Recrystallization from CH_2Cl_2 (2 more times) was obtained (1′*S*,*R*)-*N*-1′-(phenylethyl)-2,2,4,6,6-pentamethylcyclohexylidenylacetamide: mp 152–154 °C; $[\alpha]^{25}_{Hg}$ −113.92 ± 0.20° (*c* 1.16, $CHCl_3$); ^1H NMR (C_6D_6) 0.82 (d, *J* = 6.60, 3 H), 1.03 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.22 (d, *J* = 7, 3 H; $C_6H_5CH(CH_3)NH$), 1.30 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 0.90–1.60 (m, 4 H), 1.72 (br m, 1 H), 5.20–5.40 (m, 2 H, $C_6H_5CH(CH_3)NH$), 5.82 (s, 1 H, olefinic H), and 7.00–7.30 (m, 5 H); ^{13}C NMR 21.37 (CH_3, $C_6H_5CH(CH_3)NH$), 22.62 ($CHCH_3$), 23.99 ($CH(CH_3)$), 30.22 (CH_3), 31.69 (CH_3), 32.34 (CH_3), 32.94 (CH_3), 37.60 (C), 38.03 (C), 48.73 (CH), 49.39 (CH_2), 51.75 (CH_2), 118.78 (CH), 126.37 (2CH), 127.28 (CH), 128.55 (2CH), 143.04 (C), 160.57 (C), and 169.79 (C=O); UV (*c* 0.69 × 10^{-4}, CH_3CN) λ_{206} ε 19 300; CD (*c* 0.69 × 10^{-3}, 0.69 × 10^{-2}, CH_3CN) $\Delta\epsilon_{266}$ +0.69, $\Delta\epsilon_{260}$ +1.06, $\Delta\epsilon_{254}$ +1.25, $\Delta\epsilon_{247}$ +1.04, and $\Delta\epsilon_{215}$ −18.36.

Methyl (*S*)-(+)-2,2,4,6,6-Pentamethylcyclohexylideneacetate. A solution of (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetic acid (**10**) (5 g, $[\alpha]^{31}_{Hg}$ +34.42 ± 0.03°, 46.50% ee) in 10 mL of ether was cooled to 0 °C. A freshly distilled CH_2N_2 was added until yellow color persists. The solvent was evaporated, and the product was filtered through 10 g of silica gel using CH_2Cl_2. Removal of solvent gave pure methyl (*S*-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetate in quantitative yield (5.30 g) as a colorless liquid: $[\alpha]^{31}_{Hg}$ +38.35 ± 0.02° (*c* 1.01, C_2H_5OH); IR (0.05 M solution in CCl_4) 2945, 2900, 2820, 1725, 1625, 1470, 1440, 1400–1370, 1270–1110, and 1080–1020 cm^{-1}; ^1H NMR 0.87 (d, *J* = 6.60, 3 H), 1.13 (s, 3 H), 1.16 (s, 6 H), 1.32 (s, 3 H), 0.90–1.70 (m, 4 H), 1.86 (m, 1 H), 3.69 (s, 3 H), and 5.80 (s, 1 H); UV (*c* 1.39 × 10^{-4}, cyclohexane) λ_{226} ε 6100 and λ_{210} ε 5600; CD (*c* 1.39 × 10^{-3}, cyclohexane) $\Delta\epsilon_{247}$ −1.71 and $\Delta\epsilon_{208}$ +6.27.

Anal. Calcd for $C_{14}H_{24}O_2$: C, 75.00; H, 10.71. Found: C, 75.16; H, 10.61.

(*S*)-(+)-(2,2,4,6,6-Pentamethylcyclohexylidenyl)ethanol. To a slurry of AlH_3 (freshly prepared from 2.29 g, 60 mmol of $LiAlH_4$ and 2.68 g, 20 mmol of anhydrous $AlCl_3$ in 125 mL of ether at 0 °C for 1 h) was added a solution of methyl (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetate (4.50 g, 20 mmol, $[\alpha]^{31}_{Hg}$ +38.35 ± 0.02°, 46.50% ee) in 25 mL of ether, for 30 min dropwise at 0 °C. After stirring for 30 min at the same temperature, the reaction mixture was hydrolyzed with a careful addition of water. The resulting white precipitate was dissolved by adding cold aqueous HCl. The product was extracted into ether (3 × 100 mL) and the combined organic layers were washed with water, $NaHCO_3$, and water and dried over Na_2SO_4. Removal of solvent gave 4 g of crude product which was purified by passing through a silica gel (80 g) column using hexane–ether solvent mixtures. The fractions containing the pure product was collected and removal of solvent afforded 3.80 g (96%) of (*S*)-(+)-(2,2,4,6,6-pentamethylcyclohexylidenyl)ethanol as a colorless liquid: $[\alpha]^{32}_{Hg}$ +23.26 ± 0.04° (*c* 1.10, C_2H_5OH); IR (film) 3300 (br, OH), 2950–2820, 1630 (w), 1470, 1400–1370, 1260–1190, 1050, and 1000 cm^{-1}; ^1H NMR 0.88 (d, *J* = 6.60, 3 H), 1.13 (s, 3 H, CH_3), 1.15 (s, 6 H, $2CH_3$), 1.18 (s, 3 H, CH_3), 0.80–1.50 (m, 4 H), 1.65 (s, 1 H, OH), 1.82 (m, 1 H), 4.39 (d, *J* = 5, 2 H), and 5.48 (t, *J* = 5, 1 H); UV (*c* 1.43 × 10^{-4}, cyclohexane) λ_{200} ε 9500; CD (*c* 1.43 × 10^{-3}, cyclohexane) $\Delta\epsilon_{205}$ +6.02.

Anal. Calcd for $C_{13}H_{24}O$: C, 79.59; H, 12.24. Found: C, 79.61; H, 12.29.

(*S*)-(+)-2,2,4,6,6-Pentamethylcyclohexylideneacetaldehyde (4). To a solution of (*S*)-(+)-(2,2,4,6,6-pentamethylcyclohexylidenyl)ethanol ($[\alpha]^{32}_{Hg}$ +23.26 ± 0.04°, 46.50% optically pure, 1 g) in 46 mL of pentane was added 10 g of active MnO_2 and the mixture stirred at room temperature for 1 h. The product was filtered free of MnO_2 and concentrated. Purification by passing through silica gel (25 g) column using hexane–ether solvent mixtures gave pure (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetaldehyde (**4**) (0.90 g, 91%) as a liquid: $[\alpha]^{32}_{Hg}$ +71.22 ± 0.15° (*c* 1.07, C_2H_5OH); IR (0.05 M solution in CCl_4) 2960, 2920, 2870, 2850, 2750 (w), 2730 (w), 1735 (w), 1665, 1595, 1470, 1390, 1375, 1230, 1200, 1168, 1140, 955, and 875 cm^{-1}; ^1H NMR 0.95 (d, *J* = 6.50, 3 H), 1.20 (s, 3 H), 1.22 (s, 3 H), 1.47 (s, 3 H), 1.49 (s, 3 H), 1.08–1.75 (m, 4 H), 1.88 (m, 1 H), 6.05 (d, *J* = 7, 1 H), and 10.44 (d, *J* = 7, 1 H); ^{13}C NMR 22.76 (CH_3CH–), 23.82 (CH_3CH), (CH_3), 33.05 (CH_3), 33.37 (CH_3), 36.03 (CH_3), 38.32 (C), 39.36 (C), 47.88 (CH_2), 51.24 (CH_2), 126.81 (CH), 178.29 (C), and 192.90 (HC=O); UV (*c* 1.14 × 10^{-4}, 1.14 × 10^{-2}, cyclohexane) λ_{390} ε 7, λ_{370} ε 24, λ_{354} ε 44, λ_{341} (ε 50, λ_{328} ε 50, λ_{296} ε 100, λ_{242} ε 11 600, and λ_{213} ε 3100; CD (*c* 1.14 × 10^{-3}, 1.14 × 10^{-2}, cyclohexane) $\Delta\epsilon_{393}$ −0.07, $\Delta\epsilon_{374}$ −0.29, $\Delta\epsilon_{358}$ −0.437, $\Delta\epsilon_{343}$ −0.39, $\Delta\epsilon_{330}$ −0.24, $\Delta\epsilon_{308}$ −0.10, $\Delta\epsilon_{244}$ +5.79, $\Delta\epsilon_{204}$ −1.95.

Anal. Calcd for $C_{13}H_{22}O$: C, 80.41; H, 11.34. Found: C, 80.40; H, 11.25.

(*S*)-(+)-(2,2,4,6,6-Pentamethylcyclohexylidenyl)propene (5). To a stirred suspension of 1.96 g (5.50 mmol) of anhydrous methyltriphenylphosphonium bromide in 30 mL of dry ether at −25 °C under nitrogen atmosphere was added 3.12 mL (5 mmol) of 1.6 M solution of *n*-BuLi. The resulting yellow solution was stirred for 10 min, and 0.97 g (5 mmol) of (*S*)-(+)-2,2,4,6,6-pentamethylcyclohexylideneacetaldehyde (**4**) ($[\alpha]^{32}_{Hg}$ +71.22 ± 0.15°, 46.50% ee) in 5 mL of ether was added. After 30 min at −25 °C, the reaction mixture was stirred at room temperature for 30 min and hydrolyzed by adding wet ether. The ether solution was filtered free of solid and concentrated. The crude product was passed through 20 g of silica gel column using hexane as eluent to give 0.46 g (48%) of (*S*)-(+)-(2,2,4,6,6-pentamethylcyclohexylidenyl)-propene (**5**) as a colorless liquid: $[\alpha]^{32}_{Hg}$ +87.68 ± 0.31° (*c* 1.17, C_2H_5OH); IR (film) 3080 (sharp), 2980–2840 (m), 1800 (w), 1625, 1580 (w), 1470, 1400–1370, 1270–1190, 1010, and 920, ($CHCl_3$) 3070 (w), 2945, 2900, 2860, 1800 (w), 1708 (w), 1622 (sharp), 1470, 1390, 1370, 1010, and 920 cm^{-1}; ^1H NMR, 0.90 (d, *J* = 6.60, 3 H), 1.13 (s, 3 H), 1.17 (s, 3 H), 1.27 (s, 3 H), 1.33 (s, 3 H), 1.00–1.60 (m, 4 H), 1.81 (m, 1 H), 4.95–5.10 (m, 2 H CH=CH=CH_2), 6.07 (br d, *J* = 11, 1 H, C*H*=CH=CH_2), and 6.95 (m, *J* = 10, 11, 17, 1 H, CH=C*H*=CH_2); ^{13}C NMR 23.10 (CH_3CH), 24.11 (CH_3CH), 30.74 (CH_3), 33.15 (CH_3), 33.77 (CH_3), 33.84 (CH_3), 36.76 (C), 38.03 (C), 49.07 (CH_2), 52.23 (CH_2), 115.44 (CH_2), 124.69 (CH, 135.61 (CH), and 155 (C); UV (*c* 1.28 × 10^{-5}, cyclohexane) λ_{244} ε 20 200; CD (*c* 1.28 × 10^{-4}, cyclohexane) $\Delta\epsilon_{243}$ +4.89 and $\Delta\epsilon_{200}$ −1.01.

(14) Fugisawa, T.; Mori, T.; Tsuge, S.; Sato, T. *Tetrahedron Lett.* **1983**, 1543.

(15) The reaction was carried out at −28 °C in order to avoid racemization which occurs at ambient temperatures.

Anal. Calcd for $C_{14}H_{24}$: C, 87.50; H, 12.50. Found: C, 87.10; H, 12.65.

2′,2′,6′,6′-Tetramethylspiro[cyclohexan-1-one-4,4′-[1,3]-5-methyldioxolane] (14). The title compound was prepared by using a reported procedure for 2,2,4,6,6-pentamethylcyclohexanone (**9**). A dry 3-L, three-necked flask was loaded with 129 g (3.23 mol) of 60% sodium hydride dispersion in mineral oil. The oil was removed by washing 3 times with hexane. Dry dimethoxyethane (1 L) was added, and the suspension was mechanically stirred under nitrogen atmosphere. The contents of the flask were cooled to 0 °C, and a solution of 110 g (0.647 mol) of spiro[cyclohexan-1-one-4,4′-[1,3]-5-methyldioxolane] (**13**)[7] in 200 mL of dimethoxyethane was added dropwise. After the evolution of H_2 ceased, a solution of 459 g (3.23 mol) of methyl iodide dissolved in 1 L of DME was added over a 12-h period. The reaction was allowed to come to room temperature and stirred overnight. Water was added slowly until H_2 gas evolution ceased. The reaction mixture was poured into ice and extracted with three 1.2-L portions of hexane. The combined hexane extracts were dried (Na_2SO_4) followed by solvent removal under reduced pressure, giving a clear yellow oil. Vacuum distillation afforded 117 g (80%) of 2′,2′,6′,6′-tetramethylspiro[cyclohexan-1-one-4,4′-[1,3]-5-methyldioxolane] (**14**) as a colorless liquid: bp 84–86 °C (1 mm); IR (film) 2970, 2930, 2860, 1705, 1480–1430, 1390–1340, 1250–1170, 1115, and 1070–820 cm^{-1}; ^1H NMR 1.14 (s, 3 H), 1.15 (s, 6 H), 1.16 (s, 3 H), 1.28 (d, J = 6.50, 3 H), 2.02 (sextet, or m, J = 3, 13, 4 H), 3.43 (t, J = 7.50, 1 H), 4.05 (t, J = 6, 1 H), and 4.21 (m, 1 H); ^{13}C NMR 18.56 ($CHCH_3$), 27.56 ($2CH_3$), 27.67 (CH_3), 27.76 (CH_3), 43.07 (C), 43.18 (C), 46.58 (CH_2), 47.76 (CH_2), 70.09 (CH_2), 71.43 (CH), 107.36 (C), and 218.11 (C=O).

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.02; H, 9.73. Found: C, 69.07; H, 9.85.

4-Oxo-2,2,6,6-tetramethylcyclohexylideneacetic Acid. To a dry 3-L, three-necked flask was added 42 g (0.60 mol) of ethyl ethynyl ether and 1.5 L of dry ether. This solution was mechanically stirred and cooled to −78 °C under a nitrogen atmosphere and 411 mL (0.588 mol) of a 1.43 M solution of *n*-BuLi in hexane was added slowly. The resulting salt was stirred for 30 min, and a solution of 133 g (0.588 mol) of 2′,2′,6′,6′-tetramethylspiro[cyclohexan-1-one-4,4′-[1,3]-5-methyldioxolane] (**14**) in 250 mL of dry THF was added over a 1-h period. The reaction mixture was allowed to warm to room temperature and stirred an additional 1 h and quenched upon addition of water. The aqueous layer was separated and extracted with ether (3 × 200 mL), and the combined organic layers were washed with water, dried (Na_2SO_4), and evaporated to give a clear red oil: IR (film) 3700 (sharp), 3460 (br), 2900 (m), 2280, and 1480–810 cm^{-1}.

The above crude acetylene alcohol in 700 mL of dry THF was cooled to 0 °C under nitrogen atmosphere, and 13 mL of concentrated H_2SO_4 was added. This mixture was stirred at 25 °C for 5 h and diluted with 200 mL of 10% H_2SO_4. After the mixture stirred for an additional 30 min, most of the THF was removed under reduced pressure. The reaction mixture was extracted with ether (5 × 100 mL) and concentrated to give crude rearranged ester (single spot on micro TLC). To a solution of rearranged ester in 400 mL of methanol was added 400 mL of 20% aqueous KOH and refluxed on a steam bath for 30 min. The reaction mixture was cooled and diluted with water. The alkaline solution was extracted with ether (3 × 100 mL portions) to remove most of the neutral fractions (20 g) and acidified with cold concentrated HCl. The crude keto acid was extracted into ethyl acetate (5 × 100 mL) and the ethyl acetate layer washed with water, dried (Na_2SO_4), and evaporated to give 112 g (70% overall yield from ketone) of white solid. a small amount was recrystallized from methanol–methylene chloride–hexane to yield 4-oxo-2,2,6,6-tetramethylcyclohexylideneacetic acid: mp 196–198 °C; IR (KBr pellet) 3300–2600 (br), 1710, 1690, and 1480–810 cm^{-1}; ^1H NMR (CD_3OD) 1.26 (s, 6 H), 1.39 (s, 6 H), 2.39 (s, 2 H), 2.48 (s, 2 H), and 6.03 (s, 1 H); ^{13}C NMR (CD_3OD) 29.67 ($2CH_3$), 31.55 ($2CH_3$), 38.49 (C), 39.44 (C), 51.56 (CH_2), 54.66 (CH_2), 118.21 (CH), 164.58 (C), 171.97 (*C*OOH), and 213.27 (C=O); UV (c 5 × 10^{-5}, CH_3CN) λ_{216} ϵ 6500.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.57; H, 8.57. Found: C, 68.69; H, 8.69.

(±)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic Acid (12). A solution of 112 g (0.53 mol) of 4-oxo-2,2,6,6-tetramethylcyclohexylideneacetic acid in 1200 mL of absolute ethyl alcohol was cooled to 0 °C. Sodium borohydride (40 g, 1.06 mol) was added in portions and stirred at 25 °C for 30 min and 50 °C for 1 h and refluxed for 10 min. A small portion was analyzed by micro TLC to make sure of the completion of the reaction. Most of the ethanol was removed under reduced pressure, and the contents of the flask were transferred to a separatory funnel. Dilute cold 10% H_2SO_4 was added, and the acidic aqueous layer was extracted with ethyl acetate (6 times). The combined ethyl acetate solution was washed with water, dried (Na_2SO_4), and evaporated to give white solid. Recrystallization from acetone–hexane yielded 110 g of pure 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (**12**): mp 143–145 °C; IR (KBr pellet) 3400, 3280, 2980, 3300–2500 (br), 1682, 1625, 1465, 1415, 1386, 1345, 1260, 1200, 1160, 1090–940, and 825 cm^{-1}; ^1H NMR 1.18 (s, 3 H), 1.22 (s, 3 H), 1.34 (s, 3 H), 1.36 (s, 3 H), 1.00–2.00 (m, 4 H), 4.20 (m, 1 H), 5.15 (br m, 2 H, O*H*, COO*H*), and 5.86 (s, 1 H); ^{13}C NMR (CD_3OD) 30.01 (CH_3), 31.63 (CH_3), 32.91 (CH_3), 33.26 (CH_3), 38.83 (C), 39.76 (C), 48 (CH_2 under solvent), 51.35 (CH_2), 64.44 (CH), 117.36 (CH), 163.16 (C), and 173.46 (*C*OOH).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 67.90; H, 9.33.

(*S*)-(+)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic Acid (12). The racemic 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (**12**) was resolved with (+)-α-phenylethylamine. To a solution of 104 g of 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (**12**) in 250 mL of ethyl acetate was added (+)-α-phenylethylamine (60 g) and the solution warmed on a steam bath. The clear solution was cooled to 0 °C to precipitate the salt as a thick gum. The solvent was decanted and repeated with ethyl acetate 2 more times. The salt after washing with 100 mL of ether was dissolved in 300 mL of acetone and left overnight at 0 °C. The separated colorless crystals were collected and recrystallized from acetone 7 times at room temperature. The resolved salt was decomposed with aqueous NaOH solution to free the acid from amine. The amine was removed by extracting 3 times with benzene. The alkaline solution was acidified with cold dilute HCl, and the carboxylic acid separated was extracted with ether. The ether solution was washed with diluted HCl and water, dried over Na_2SO_4, and evaporated to yield white solid. Crystallization from acetone gave 20 g of (*S*)-(+)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (**12**): mp 150–154 °C; $[\alpha]^{31}_D$ +30.80 ± 0.20°; CD (c 1.34 × 10^{-4}, CH_3CN) $\Delta\epsilon_{246}$ −2.67 and $\Delta\epsilon_{208}$ +8.48.

(*R*)-(−)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic Acid (12). A solution of 4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (80 g) partially enriched with (−)-acid (from (+)-α-phenylethylamine resolution) and 46 g of (−)-α-phenylethylamine in 600 mL of acetone were heated on a steam bath and cooled to 0 °C. The separated crystals were collected and recrystallized from acetone for 10 more times at +25 °C. The resolved salt on workup as above gave after recrystallization from acetone 15 g of (*R*)-(−)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid: mp 152–154 °C; $[\alpha]^{25}_D$ −30.48 ± 0.09°, 37.14% ee (c 1.16, C_2H_5OH); UV (c 1.24 × 10^{-4}, CH_3CN) λ_{217} ϵ 5000; CD (c 1.24 × 10^{-3}, CH_3CN) $\Delta\epsilon_{247}$ +2.29 and $\Delta\epsilon_{208}$ −8.46.

Optical Purity of (*R*)-(−)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic Acid (12). To a stirred solution of (*R*)-(−)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (**12**) (0.53 g, $[\alpha]^{25}_D$ −30.48 ± 0.09°) and imidazole (0.68 g, 4 equiv) in 5 mL of CH_2Cl_2 was added dimethyl-*tert*-butylsilyl chloride (2.4 equiv) in one lot. The reaction mixture was stirred for 30 min and filtered through 10 g of silica gel using hexane. Removal of solvent gave pure dimethyl-*tert*-butylsilyl (*R*)-(−)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetate in quantitative yield (1.10 g) as a low melting solid: mp 48–52 °C; $[\alpha]^{25}_D$ −18.30 ± 0.40° (c 1.15, C_2H_5OH); IR (CCl_4) 2960, 2925, 2900, 2860, 1705, 1620, 1480, 1470, 1400–1370, 1265, 1205, 1095, and 1000–860 cm^{-1}; ^1H NMR 0.07 (s, 6 H), 0.29 (s, 3 H), 0.30 (s, 3 H), 0.90 (s, 9 H), 0.95 (s, 9 H), 1.17 (s, 3 H), 1.20 (s, 3 H), 1.30 (s, 3 H), 1.36 (s, 3 H), 1.00–1.80 (m, 4 H), 4.03 (m, 1 H), and 5.80 (s, 1 H).

Anal. Calcd for $C_{24}H_{48}O_3Si$: C, 65.45; H, 10.91. Found: C, 65.48; H, 10.81.

Oxalyl chloride (2.20 mL) was added to a solution of DMF (1.50 mL) in 10 mL of CH_2Cl_2 at 0 °C, and the resulting precipitate was stirred for 1 h. The solvent was removed to give a white solid of *N,N*-dimethylchloromethyleneiminium chloride.[14] To this 20 mL of anhydrous ether was added and cooled to −28 °C. Dimethyl-*tert*-butylsilyl(*R*)-(−)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetate (0.85 g, $[\alpha]^{25}_D$ −18.30 ± 0.40°) in 5 mL of ether was added and stirred for 1 h.[15] Optically pure (−)-α-phenylethylamine (0.50 mL) was added and the reaction mixture allowed to come to +25 °C in 1 h. Water was added, and the product was extracted into ether. The ether solution washed with diluted HCl, water, aqueous NaOH, and water and dried over Na_2SO_4. Removal of solvent gave 0.70 g (84%) of a diastereomeric mixture of (1′*S*,*R*)-*N*-1′-(phenylethyl)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenylacetamide and (1′*S*,S)-*N*-1′-(phenylethyl)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenylacetamide in the ratio of 68.57:31.43, respectively (integration of olefinic proton signals at 5.87 and 5.81 ppm in the ^1H NMR spectrum) as a solid: mp 136–152 °C; IR (CCl_4) 3420, 3020, 2950, 2920, 2880, 2850, 1665, 1620, 1480, 1388, 1370, 1260, 1223, 1088, and 880–830 cm^{-1}; ^1H NMR (C_6D_6) 0.20, 0.21 (2s, 6 H), 1.08, 1.09 (2s, 9 H), 1.00–2.00 (m, 19 H, including several methyl signals), 4.16 (m, 1 H), 5.20–5.40 (m, 1 H, CH_3CHNH), 5.65 (br d, 1 H, CHN*H*), 5.81, 5.87

(2s, 1 H), and 7.10–7.30 (m, 5 H) ppm.

Optical purity of (*R*)-(−)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid (**12**) with a rotation of $[\alpha]^{25}_D$ −30.48 ± 0.09° was estimated to be 37.14% ee. Recrystallization of crude diastereomeric amides from petroleum ether gave analytically pure crystalline diastereomeric amides.

Anal. Calcd for $C_{26}H_{43}NO_2Si$: C, 72.72; H, 10.02; N, 3.26. Found: C, 72.54; H, 10.15; N, 3.25.

Methyl (*S*)-(+)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetate. (*S*)-(+)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic acid **12** (14 g, $[\alpha]^{31}_D$ +30.80 ± 0.20°, 37.52% ee) was dissolved in 10 mL of ethanol and 90 mL of ether and cooled to 0 °C. CH_2N_2 was added until a yellow color persists. The solution was filtered through 30 g of silica gel using ether. Removal of solvent gave 14.92 g of white crystalline solid corresponding to methyl (*S*)-(+)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetate: mp 72–73 °C; $[\alpha]^{25}_D$ +31.31 ± 0.20° (*c* 2, C_2H_5OH); IR (0.05 M solution in CCl_4) 3590 (sharp), 2950 (m), 1730, 1625, 1470, 1440, 1390, 1375, 1200, 1065, 1050, and 930 cm^{-1}; ^1H NMR 1.20 (s, 3 H), 1.22 (s, 3 H), 1.26 (s, 3 H), 1.36 (s, 3 H), 1.37–1.90 (m, 4 H), 3.71 (s, 3 H), 4.09 (m, 1 H), and 5.84 (s, 1 H); UV (*c* 1.07 × 10^{-4}, cyclohexane) λ_{218} ε 6900; CD (*c* 1.07 × 10^{-3}, cyclohexane) $\Delta\epsilon_{247}$ −1.81 and $\Delta\epsilon_{210}$ +6.69.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.02; H, 9.73. Found: C, 68.96; H, 9.84.

Methyl (*S*)-(+)-4-(Dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetate. To a stirred solution of methyl (*S*)-(+)-4-hydroxy-2,2,6,6-tetramethylcyclohexylideneacetate (15 g, $[\alpha]^{25}_D$ +31.31 ± 0.20°, 37.52% ee) and imidazole (9.02 g) (2 equiv) in 60 mL of CH_2Cl_2 was added in portions of 11.94 g (1.20 equiv) of dimethyl-*tert*-butylsilyl chloride at 0 °C. The reaction mixture after stirring for 10 min at 25 °C was filtered through 100 g of silica gel using CH_2Cl_2. Removal of solvent gave 22.60 g of methyl (*S*)-(+)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetate as a colorless liquid: $[\alpha]^{28}_D$ +17.99 ± 0.50° (*c* 2,C_2H_5OH); IR (film) 2950, 2925, 2890, 2850, 1725, 1620, 1470, 1435, 1390, 1372, 1260, 1200, 1090, 1020–930, and 895–790 cm^{-1}; ^1H NMR 0.40 (s, 6 H), 0.88 (s, 9 H), 1.15 (s, 3 H), 1.18 (s, 3 H), 1.22 (s, 3 H), 1.32 (s, 3 H), 1.35–1.80 (m, 4 H), 3.69 (s, 3 H), 4.00 (m, 1 H), and 5.80 (s, 1 H); ^{13}C NMR 4.65 ($2CH_3$), 18.10 (Si—*C*), 25.86 ($3CH_3$), 29.54 (CH_3) 30.69 (CH_3), 32.50 (CH_3), 32.60 (CH_3), 37.72 (C), 38.97 (C), 48.19 (CH_2), 50.53 (CH_2), 51.29 (OCH_3), 64.72 (CH), 115.09 (CH), 164.89 (C), and 169.84 (*C*=O); UV (*c* 7.06 × 10^{-5}, cyclohexane) λ_{218} ε 7600; CD (*c* 7.06 × 10^{-4}, cyclohexane) $\Delta\epsilon_{247}$ −1.70 and $\Delta\epsilon_{208}$ +6.37.

Anal. Calcd for $C_{19}H_{36}O_3Si$: C, 67.05; H, 10.58. Found: C, 67.03; H, 10.66.

(*S*)-(+)-[4-(Dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]ethanol. To a slurry of AlH_3 [freshly prepared from 7.60 g (3 equiv) of $LiAlH_4$ and 8.90 g (1 equiv) of $AlCl_3$ in 250 mL of anhydrous ether at 0 °C for 1 h] was added a solution of methyl (*S*)-(+)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetate (22.60 g, $[\alpha]^{28}_D$ +17.99 ± 0.50°, 37.52% ee) in 50 mL of ether dropwise at 0 °C. After 30 min, cold water was added carefully followed by dilute HCl until all the aluminum salts dissolved (pH 7). The product was extracted with ether (5 × 100 mL), and the combined ether solution was washed with water, dried (Na_2SO_4), and concentrated. Purification by column chromatography over silica gel using hexane–ether solvent mixtures gave pure (*S*)-(+)-[4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]ethanol 20 g as a low melting solid: mp 43–44 °C; $[\alpha]^{31}_D$ +11.87 ± 0.60° (*c* 2,C_2H_5OH); IR (film) 3320 (br), 2900 (m), 1628 (w), 1470, 1390, 1370, 1260, 1230–1170, 1080, 1020, 990, 950, 940, 895, 850, and 790 cm^{-1}, ^1H NMR 0.03 (s, 6 H), 0.88 (s, 9 H), 1.11 (s, 3 H), 1.16 (s, 3 H), 1.165 (s, 3 H), 1.17 (s, 3 H), 1.20–1.80 (m, 5 H), 3.99 (m, 1 H), 4.36 (br d, *J* = 6, 2 H), and 5.45 (t, *J* = 6, 1 H); UV (*c* 1.04 × 10^{-4}, cyclohexane) λ_{200} ε 9600; CD (*c* 1.04 × 10^{-3}, cyclohexane) $\Delta\epsilon_{207}$ +6.50.

Anal. Calcd for $C_{18}H_{36}O_2Si$: C, 69.23; H, 11.53. Found: C, 69.11; H, 11.53.

(*S*)-(+)-4-(Dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetaldehyde (6). (*S*)-(+)-[4-(Dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]ethanol (5 g, $[\alpha]^{31}_D$ +11.87 ± 0.60°, 37.52% ee) in 150 mL of pentane was oxidized with MnO_2 (15 g) for 1 h. The product was filtered free of MnO_2 using ether and concentrated under reduced pressure. The crude product was chromatographed over 150 g of silica gel using hexane–ether solvent mixtures. The fractions corresponding to pure product were combined to give 4 g of (*S*)-(+)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetaldehyde (**6**) as a solid: mp 42–44 °C; $[\alpha]^{30}_D$ +23.61 ± 0.80° (*c* 2, C_2H_5OH); IR (0.05 M solution in CCl_4) 2960, 2930, 2890, 2860, 1668, 1600 (w), 1476, 1460, 1390, 1378, 1265, 1230–1130, 1100, 1080, 960 900, and 800 cm^{-1}; ^1H NMR 0.06 (s, 6 H), 0.89 (s, 9 H), 1.17 (s, 3 H), 1.24 (s, 3 H), 1.44 (s, 3 H), 1.50 (s, 3 H), 1.50–1.90 (m, 4 H), 4.04 (m, 1 H), 6.00 (d, *J* = 7.68, 1 H), and 10.41 (d, *J* = 8.04, 1 H); ^{13}C NMR −4.69 ($2CH_3$), 17.99 (C), 25.78 ($3CH_3$), 32.13 (CH_3), 32.36 (CH_3), 33.60 (CH_3), 35.29 (CH_3), 38.30 (C), 39.42 (C), 46.89 (CH_2), 49.78 (CH_2), 64.39 (CH), 126.36 (CH), 177.40 (C), and 192.70 (HC=O); UV (*c* 8.03 × 10^{-5}, 7.80 × 10^{-3}, cyclohexane) λ_{390} ε 9, λ_{369} ε 28, λ_{353} ε 43, λ_{340} ε 46, λ_{330} ε 41, and λ_{241} ε 13 300; CD (*c* 8.03 × 10^{-4}, 7.80 × 10^{-3}, cyclohexane) $\Delta\epsilon_{395}$ −0.05, $\Delta\epsilon_{375}$ −0.23, $\Delta\epsilon_{358}$ −0.35, $\Delta\epsilon_{343}$ −0.31, $\Delta\epsilon_{330}$ −0.18, $\Delta\epsilon_{319}$ −0.07, $\Delta\epsilon_{244}$ +4.48, and $\Delta\epsilon_{204}$ −2.61.

Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.67; H, 10.96. Found: C, 69.55; H, 11.05.

(*S*)-(+)-[4-(Dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]propene (7). To a stirred suspension of 3.22 g (9 mmol) of methyltriphenylphosphonium bromide in 25 mL of dry ether was added 5.62 mL (9 mmol) of a 1.6 M solution of *n*-BuLi at −28 °C under N_2 atmosphere. After 30 min, 1.40 g (4.51 mmol) of (*S*)-(+)-4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylideneacetaldehyde (**6**) ($[\alpha]^{30}_D$ +23.61 ± 0.80°, 37.52% ee) in 5 mL of ether was added. The reaction mixture was stirred at −28 °C for 30 min and at +25 °C for 1 h, and wet ether was added to hydrolyze the reaction. The product was filtered and concentrated under reduced pressure. The crude product on column chromatography over 25 g of silica gel using hexane as the eluent gave 0.90 g (64%) of pure (*S*)-(+)-[4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]propene (**7**) as a colorless liquid: $[\alpha^{25}_D$ +38.82 ± 0.30° (*c* 1, C_2H_5OH); IR (film) 3070, 2950 (m), 1800 (w), 1625, 1580 (w), 1470, 1415, 1390, 1375, 1265, 1230, 1200, 1170, 1090, 1020, 1010, 994, 955, 920, 895, 850, and 790 cm^{-1}; ^1H NMR 0.07 (s, 6 H), 0.90 (s, 9 H), 1.13 (s, 3 H), 1.21 (s, 3 H), 1.29 (s, 3 H), 1.36 (s, 3 H), 1.37–1.80 (m, 4 H), 4.00 (m, 1 H), 5.00–5.15 (m, 2 H), 6.05 (d, *J* = 11, 1 H), and 6.93 (sextet, *J* = 10, 11, 16, 1 H); UV (*c* 6.56 × 10^{-5}, cyclohexane) λ_{242} ε 22 200, and λ_{236} ε 21 000; CD (*c* 6.56 × 10^{-4}, cyclohexane) $\Delta\epsilon_{240}$ +4.48 and $\Delta\epsilon_{202}$ −0.91.

Anal. Calcd for $C_{19}H_{36}OSi$: C, 74.02; H, 11.68. Found: C, 74.19; H, 11.62.

(S)-(+)-(4-Hydroxy-2,2,6,6-tetramethylcyclohexylidenyl)propene (8). (*S*)-(+)-[4-(Dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]propene (**7**) (0.90 g, $[\alpha]^{25}_D$ +38.82 ± 0.30°, 37.52% ee) in 10 mL of THF was added to 4.38 mL (1.50 equiv) of tetra-*n*-butylammonium fluoride and stirred at room temperature under N_2 atmosphere overnight. The product was filtered through silica gel (5 g) using CH_2Cl_2, and the solvent was removed. The crude product on purification by column chromatography over 20 g of silica gel using hexane–ether solvent mixtures yielded 0.52 g of (*S*)-(+)-(4-hydroxy-2,2,6,6-tetramethylcyclohexylidenyl)propene (**8**) as a liquid: $[\alpha]^{25}_{Hg}$ + 85.80 ± 0.20° (*c* 1.17, C_2H_5OH); IR (CCl_4) 3590 (sharp), 3080, 2950 (m), 1800 (w), 1625, 1470, 1390, 1370, 1225, 1190, 1060, 1045, 1005, 980, and 920 cm^{-1}; ^1H NMR 1.15 (s, 3 H), 1.23 (s, 3 H), 1.30 (s, 3 H), 1.38 (s, 3 H), 1.30–1.95 (m, 5 H), 4.03 (m, 1 H), 5.00–5.16 (m, 2 H), 6.05 (d, *J* = 11, 1 H), and 6.92 (sextet, *J* = 10, 11, 16, 1 H); ^{13}C NMR 30.98 (CH_3), 32.89 (CH_3), 33.29 (CH_3), 33.45 (CH_3), 37.18 (C), 38.55 (C), 48.31 (CH_2), 50.96 (CH_2), 64.49 (CH), 116.21 (CH_2), 124.67 (CH), 135.13 (CH), and 153.73 (C); UV (*c* 1.09 × 10^{-4}, CH_3CN) λ_{241} ε 20 600; CD (*c* 1.09 × 10^{-3}, CH_3CN) $\Delta\epsilon_{242}$ +5.10 and $\Delta\epsilon_{203}$ −0.69.

Anal. Calcd for $C_{13}H_{22}O$: C, 80.41; H, 11.34. Found: C, 80.42; H, 11.41.

(*S*)-(+)-4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetaldehyde (8a). A solution of 0.30 g of (*S*)-(+)-[4-(dimethyl-*tert*-butylsilyloxy)-2,2,6,6-tetramethylcyclohexylidenyl]ethanol ($[\alpha]^{31}_D$ +11.87 ± 0.60°, 37.52% ee) and tetra-*n*-butylammonium fluoride (1.50 mL) in 5 mL of THF was stirred for 6 h. Most of the THF was removed under reduced pressure, and water was added. The separated solid was collected and recrystallized from ether–hexane to give 0.166 g (87%) of (*S*)-(+)-[4-hydroxy-2,2,6,6-tetramethylcyclohexylidenyl]ethanol as a white crystals: mp 140–142 °C: $[\alpha]^{25}_{Hg}$ +29.67 ± 0.56° (*c* 0.33, $CHCl_3$); IR ($CHCl_3$) 3570 (sharp), 3410 (br), 2900 (m), 1625 (w), 1470, 1385, 1370, 1170, 1100, 1030, and 975 cm^{-1}; ^1H NMR 1.15 (s, 3 H), 1.20 (s, 6 H), 1.22 (s, 3 H), 1.24–2.00 (m, 6 H), 4.03 (m, 1 H), 4.39 (d, *J* = 5.69, 2 H), and 5.50 (t, *J* = 5.68, 1 H).

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.72; H, 11.11. Found: C, 72.59; H, 10.93.

The above glycol (0.16 g) in 25 mL of CH_2Cl_2 was oxidized with 1 g of active MnO_2 for 3 h. The product was filtered free of MnO_2 and concentrated. Radial chromatography purification of the crude mixture using 5:1 hexane–ether gave 6 mg of less polar fraction as a solid and was identified as 4-oxo-2,2,6,6-tetramethylcyclohexylideneacetaldehyde: mp 110–112 °C; IR ($CHCl_3$) 2900 (m), 1715, 1660, 1600, 1470, 1405, 1390, 1380, 1308, 1170, 1130, and 1000–860 cm^{-1}; ^1H NMR 1.26 (s, 6 H), 1.49 (s, 6 H), 2.35 (s, 2 H), 2.53 (s, 2 H), 6.07 (d, *J* = 7, 1 H), 10.46 (d, *J* = 7, 1 H); UV (*c* 2.78 × 10^{-4}, 2.78 × 10^{-3}, cyclohexane) λ_{390} ε 7, λ_{372} ε 20, λ_{354} ε 30, λ_{341} ε 35, λ_{327} ε 36, λ_{314} ε 38, λ_{302} ε 43, and λ_{238} ε 9400.

The polar fraction, 146 mg (92%), gave the required (*S*)-(+)-hydroxyaldehyde **8a** as a solid: mp 48–52 °C; $[\alpha]^{25}_{Hg}$ +67.54 ± 0.20° (*c* 0.86, $CHCl_3$); IR (0.03 M solution in CCl_4) 3585 (sharp), 3460 (br), 2900 (m), 1670, 1600, 1476, 1400, 1380, 1220, 1190, 1150, 1070, 1050, and 990–880 cm^{-1}; ^1H NMR 1.20 (s, 3 H), 1.27 (s, 3 H), 1.47 (s, 3 He, 1.53 (s, 3 H), 1.50–2.00 (m, 5 H), 4.12 (m, 1 H), 6.02 (d, J = 7.68, 1 H), and 10.42 (d, J = 8.05, 1 H); UV (*c* 1.23 × 10^{-4}, 1.23 × 10^{-2}, cyclohexane) λ_{390} ε 8, λ_{272} ε 24, λ_{354} ε 43, λ_{341} ε 46, λ_{330} ε 41, λ_{320} ε 33, and λ_{242} ε 3+700; CD (*c* 1.23 × 10^{-3}, 1.23 × 10^{-2}, cyclohexane) $\Delta\epsilon_{392}$ −0.07, $\Delta\epsilon_{373}$ −0.26, $\Delta\epsilon_{357}$ −0.41, $\Delta\epsilon_{342}$ −0.39, $\Delta\epsilon_{330}$ −0.27, $\Delta\epsilon_{320}$ −0.14, $\Delta\epsilon_{242}$ +6.15, and $\Delta\epsilon_{204}$ −2.33.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.46; H, 10.20. Found: C, 73.03; H, 10.20.

X-ray Data for 4-Hydroxy-2,2,6,6-tetramethylcyclohexylideneacetic Acid. Single crystals of $C_{12}H_{20}O_3$ were grown by slow evaporation from acetone solvent. The crystals were orthorhombic, space group $P2_12_12_1$ with a = 7.437 (1) Å, b = 10.122 (2) Å, c = 15.845 (5) Å and d_{calcd} = 1.260 g cm^{-3} for Z = 4 (M_r = 226.32). The intensity data were measured on a CAD4 Enraf Nonius diffractometer (Mo radiation, monochromated, θ–2θ scans). The size of the crystal used for collection was approximately 0.3 × 0.3 × 0.3 mm^3. No absorption correction was necessary (μ = 0.818). A total of 1252 reflections was measured for $\theta \leq 25.0$, of which 944 were considered to be observed [$I \geq 2\sigma(I)$]. The structure was solved by direct methods using MULTAN 78 (Main, Peter MULTAN 78. *A System of Computer Programs for the Solution of Crystal Structures from X-ray Diffraction Data*; Department of Physics, University of York: York, England.) and refined by full-matrix least-squares methods.

In the final refinement, anisotropic thermal parameters were used for non-hydrogen atoms. Most of the hydrogen atoms, with the exception of some of the methyl hydrogen atoms, were measured from a difference Fourier map; the remaining hydrogen atom parameters were calculated assuming idealized geometry. Hydrogen atom contributions were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indexes were R = 5.9 and R_w = 6.5 for the 944 observed reflections. The final difference Fourier map was essentially featureless; the highest residual peaks were in the vicinity of the carboxyl group and had densities of 0.3 e A^{-3}.

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Supplementary Material Available: Crystal data, interatomic distances, selected bond angles, selected torsional angles, table of positional and thermal parameters and their estimated standard deviations, and structure factors (F_{obsd} and F_{calcd}) for $C_{12}H_{20}O_3$ (10 pages). Ordering information is given on any current masthead page.

Enzymic Carboxyl Transfer from *N*-Carboxybiotin. A Molecular Orbital Evaluation of Conformational Effects in Promoting Reactivity

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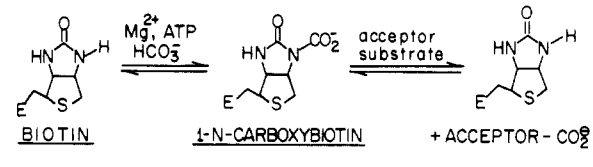
Abstract: On the basis of analysis of conformational energetics and enzymatic reactivity patterns, it is shown that the activation of *N*-carboxybiotin toward carboxyl transfer can be initiated by rotation of the carboxyl group out of the plane of the urea ring of *N*-carboxybiotin. This rotation provides proper polarization and bond weakening as expected from resonance models. It also provides a correct alignment for bond formation between the carbanion derived from the substrate and the carboxyl group of *N*-carboxybiotin. The proposal is supported by molecular orbital calculations on ground-state and transition-state models. These calculations also indicate that puckering of the imidazolidone ring does not lower activation barriers. The activation energy calculated for bond rotation is consistent with measured barriers in related systems. The mechanism accounts for the low nonenzymic activity of *N*-carboxylated ureas, the source of enzymic activation, and the recently reported "triggering" of *N*-carboxybiotin by substrate analogues.

The pioneering work of Lynen[1] established the intermediacy of carboxylated biotin in enzymic carboxyl-transfer reactions. However, the mechanism of transfer has still not been elucidated. The site on biotin that is carboxylated was proposed to be one of the nitrogen atoms or the urea oxygen atom. On the basis of model studies and reactivity analysis, Bruice and Hegarty[2] advocated carboxylation at oxygen. However, later enzymic work by Lane and co-workers[3] has led to the general acceptance of the much less reactive *N*-carboxylated species. Of course, the low reactivity of N-carboxylated ureas toward carboxyl transfer[4,5] makes *N*-carboxybiotin an ideal agent for the safe transfer of a carboxyl group between carboxyl-transfer sites (Scheme I), which is an important function of this enzymic intermediate. However, this lack of reactivity must be dramatically altered in the presence of the enzymic subunit responsible for carboxyl transfer, since, after an acceptor substrate binds, facile transfer of the carboxyl group occurs.[6]

Scheme I



The chemical basis for this change in reactivity is unresolved. Mechanisms that have been proposed rely on enolization of the urea moiety to promote N1–C3 bond cleavage (Scheme IIa–c).[7-10]

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