

Contrasting Circular Dichroism $n \rightarrow \pi^*$ Cotton Effects of (1*R*,5*S*,6*S*)-6(*endo*)-Methylbicyclo[3.2.1]octan-8-one and (1*S*,2*S*,4*R*)-2(*endo*)-Methylbicyclo[2.2.1]heptan-7-one¹

Stephen L. Rodgers, Nagabushanam Kalyanam, and David A. Lightner*

Department of Chemistry, University of Nevada, Reno, NV 89557, U.S.A.

The title compounds, with their lone dissymmetric perturber methyl groups in very similar locations relative to the C=O group, exhibit $n \rightarrow \pi^*$ Cotton effects of considerably different magnitudes in their circular dichroism spectra run in *n*-pentane: $\Delta\epsilon_{302} = -2.4$ for the former, $\Delta\epsilon_{295} = -0.6$ for the latter.

Circular dichroism (c.d.) data from conformationally restricted cyclic ketones with only one dissymmetric perturber has proved to be of considerable value in assessing the quantitative contribution² of the perturbers to the $n \rightarrow \pi^*$ Cotton effect (C.E.)³ C.d. studies of such ketones have also led to the first unequivocal examples of 'anti-octant' or dissignate⁴ effects, *e.g.* 4(ax.)-substituted-adamantan-2-ones^{1,5} and 2(*exo*)-methylbicyclo[2.2.1]heptan-7-one.⁶ In connection with our explorations of the third nodal surface in the octant rule,⁷ we prepared both the 2(*endo*)- and 2(*exo*)-methylbicyclo[2.2.1]heptan-7-ones⁶ then proceeded to prepare the similar 2(*endo*)-

and 2(*exo*)-methylbicyclo[3.2.1]octan-8-ones.† To our surprise, (1*R*,5*S*,6*S*)-6(*endo*)-methylbicyclo[3.2.1]octan-8-one (**1**) exhibited a considerably enhanced $n \rightarrow \pi^*$ C.E. ($\Delta\epsilon_{302} = -2.4$) as compared with that ($\Delta\epsilon_{295} = -0.6$) from (1*S*,2*S*,4*R*)-2(*endo*)-methylbicyclo[2.2.1]heptan-7-one (**2**).

The ketone (**1**) was prepared from 8,8-ethylenedioxybicyclo[3.2.1]oct-6-ene⁸ by the route followed in preparing (**2**) from 7,7-dimethoxybicyclo[2.2.1]hept-2-ene.⁶ The absolute

† Satisfactory analyses and spectral data were obtained for all new compounds.

configuration of (1) was determined by conversion of an optically active precursor, (–)-8,8-ethylenedioxybicyclo[3.2.1]octan-6(*exo*)-ol,⁹ into bicyclo[3.2.1]octan-6-one which exhibited a (+) C.E., and thus has the (1*S*,5*R*) configuration. Its enantiomeric excess (e.e.) was determined by an ¹⁹F n.m.r. study of the Mosher ester of the (–)-alcohol (above).¹¹

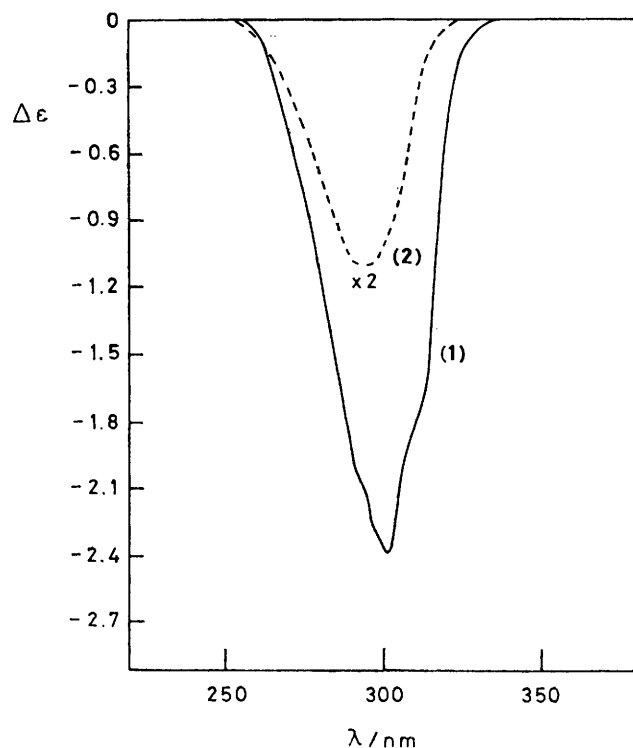
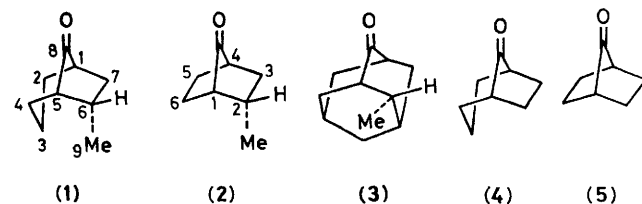


Figure 1. C.d. spectra of (1*R*,5*S*,6*S*)-6(*endo*)-methylbicyclo[3.2.1]octan-8-one (1) and (1*S*,2*S*,4*R*)-2(*endo*)-methylbicyclo[2.2.1]heptan-2-one (2) run at room temperature in n-pentane solvent on a JASCO J-40A instrument equipped with a photoelastic modulator. The spectra are corrected to 100% enantiomeric excess.

The c.d. spectra of (1) and (2) in n-pentane gave monosignate curves (Figure 1) and surprisingly different intensities. There is essentially no temperature dependence of the c.d. spectrum of (1) in isopentane from +27 to -110 °C. Our expectation was that (1) and (2) should exhibit similar $\Delta\epsilon^{\max}$ values, *ca.* -0.6, the value previously shown for (2)⁸ and one quite comparable to that ($\Delta\epsilon_{305} = -0.54$)¹ for (–)-(1*R*,3*S*,4*S*)-4(eq.)-methyladamantan-2-one (3) which has its lone dissymmetric methyl perturber in a comparable spatial position relative to the C=O group. The larger $\Delta\epsilon$ value (-2.4) for (1) was unexpected, especially since (i) molecular models suggested that the methyl groups of both (1) and (2) are in similar geometric positions relative to the C=O group, and (ii) we felt that the carbocyclic rings would not be exceptionally twisted, and that any distortion would be similar for the two molecules. The large discrepancy between the $\Delta\epsilon$ values for (1) and (2) argued for distortion of the skeleton of (1).

In order to deduce an approximate structure for (1), we obtained its energy-minimised geometry by means of Allinger's MM2 molecular mechanics computation method.¹² The relevant results are given in Table 1 along with those for (2)

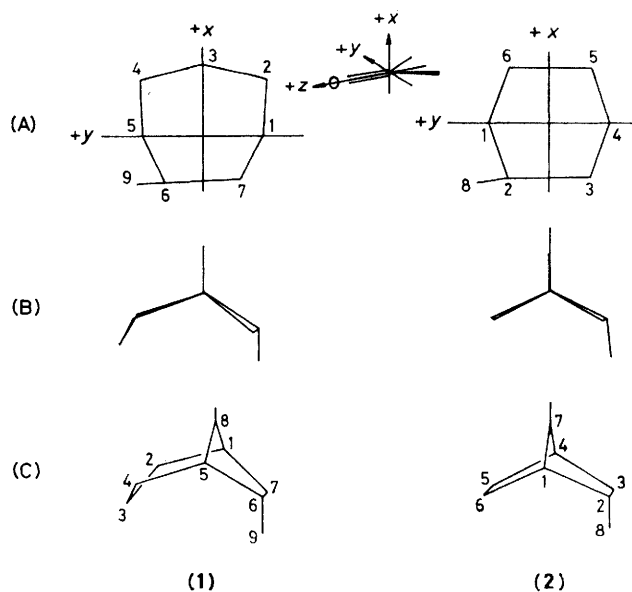


Figure 2. (A) Octant diagrams (ref. 13) for the bicyclic ketones (1) and (2). (B) View of the ketones (1) and (2) as seen from +y to -y and showing twist of rings as calculated by MM2 (ref. 12). (C) Carbon-carbon and carbon-oxygen bonds of the ketones (1) and (2) as seen from normal perspective. All diagrams were displayed from the MM2 energy-minimised atomic co-ordinates.

Table 1. Comparison of selected torsion angles (ω) determined for the bicyclic ketones (1), (4) and (2), (5) by MM2 molecular mechanics calculations.^a

Entry	Torsion angle, ω /°		Torsion angle, ω /°	
	(1)	(4)	(2)	(5)
(i)	$\omega(1-7-6-5)$	-9.61	$\omega(1-2-3-4)$	-2.708
(ii)	$\omega(4-5-6-9$ or $H^{8n})^b$	49.07	$\omega(6-1-2-8$ or $H^{2n})$	58.12
(iii)	$\omega(2-1-7-H^{7n})$	-29.07	$\omega(5-4-3-H^{3n})$	-49.76
(iv)	$\omega(H^8-5-8-O)$	12.72	$\omega(H^1-1-7-O)$	-0.069
(v)	$\omega(H^1-1-8-O)$	-15.83	$\omega(H^4-4-7-O)$	0.062
(vi)	$\omega(4-5-8-O)$	-108.59	$\omega(6-1-7-O)$	-122.81
(vii)	$\omega(2-1-8-O)$	-105.89	$\omega(5-4-7-O)$	124.05
(viii)	$\omega(6-5-8-O)$	130.71	$\omega(2-1-7-O)$	122.69
(ix)	$\omega(7-1-8-O)$	-136.20	$\omega(3-4-7-O)$	-124.10
(x)	$\omega(8-5-6-9$ or $H^{6n})$	169.99	$\omega(7-1-2-8$ or $H^{2n})$	161.74
(xi)	$\omega(8-1-7-H^{7n})$	-142.44	$\omega(7-4-3-H^{3n})$	-154.17
				0.000
		0.023		51.35
		36.33		-51.34
		-36.35		0.127
		13.89		-0.142
		-13.89		-123.90
		-108.37		123.89
		108.37		124.16
		133.71		-124.16
		-133.70		155.75
		150.22		-155.75
		-150.26		

^a Ref. 12. Limited certainty in the values begins with the fourth significant figure. ^b n = *endo*.

and the parent, symmetric (de-methyl) ketones of (1) and (2). It is clear from the MM2 calculation that when bicyclo[3.2.1]octan-8-one (4) is substituted by an *endo*-Me group at C-6, the resulting ketone (1) is distorted relative to the parent (Figure 2). More distortion obtains here than the change in the parallel series from bicyclo[2.2.1]heptan-7-one to (2), as can be seen particularly in entries i, ii, viii, and x of Table 1 and in Figure 2. To determine whether ring contributions might affect the observed C.E.s significantly, we used the procedure of Kirk² to calculate $C_{\alpha}-H$ and $C_{\alpha}-C_{\beta}$ contributions. For (1), these totalled $\delta\Delta\epsilon = +0.13$; for (2), they totalled $\delta\Delta\epsilon = \pm 0.00$, insignificant compared with the observed $\Delta\epsilon$ values, -2.4 and -0.60 , respectively. One final ring contribution in (1) needed to be ascertained, that from C-3. According to MM2, C-3 is barely (-0.04 Å) displaced from the xz plane. In view of its near coincidence with an extended $C=O$ symmetry plane (Figure 2) and the xz plane of the octant rule,¹³ we do not count it as a significant factor. We are left, finally with the contribution of the dissymmetric Me perturber. In the MM2 calculations, the energy-minimised Cartesian coordinates of the methyl carbon atoms of (1) and (2) [with the origin (0,0,0) at the $C=O$ carbon atom, Figure 2] are given as ($x = 1.227, y = -1.525, z = -3.203$ Å) for C-9 of (1) and ($x = 1.422, y = -1.423, z = -3.161$ Å) for C-8 of (2). Thus, C-9 of (1) is 0.2 Å closer to the yz octant symmetry plane (Figure 2) and 0.1 Å farther away from the xz octant symmetry plane than the corresponding C-8 of (2). One would not at first think that these small differences could be the cause of the observed large $\Delta\epsilon$ differences. However, as has been pointed out previously,⁷ theory predicts that large changes in rotatory strength can result from small changes in the position of the methyl perturber. Alternatively, $\Delta\epsilon$ values can be nearly identical, *e.g.* $\Delta\epsilon$ ca. 0.6 for (2) and (3), when the lone dissymmetric perturbers are located at different sites, *cf.* xyz coordinates of C-8 of (2) and the co-ordinates ($x = 1.505, y = -2.569, z = -2.470$ Å), as calculated by MM2, of the methyl carbon atom of (3).

We conclude that the methyl groups of (1) and (2) are the major contributors to the observed C.E.s. Ring atom and $C_{\alpha}-H$ contributions from distorted (MM2) carbocyclic rings of (1) or (2) are probably less important here¹³ than in (+)-*trans*-3-methyl-4-*t*-butylcyclohexanone, which exhibits $\Delta\epsilon_{300}^{\max}$

$= +3.6$.¹⁴ Consequently, we view the importance of any ring distortion in (1) or (2) to be its effect on positioning the methyl groups in different locations relative to the $C=O$ group. Although in (1), (2), and (3) the methyl groups lie along a primary zig-zag and give octant-consignate⁴ contributions, the difference in magnitudes of the contributors could not necessarily be expected from earlier experimental work.^{1-3,5,8,15} Further investigations of this effect are being carried out using the CNDO/S method previously described.⁷

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