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SENSITIVITY OF CIRCULAR DICHROISM OF β-DIKETONES TO MINUTE CHANGES IN THE ORIENTATION OF CHROMOPHORES

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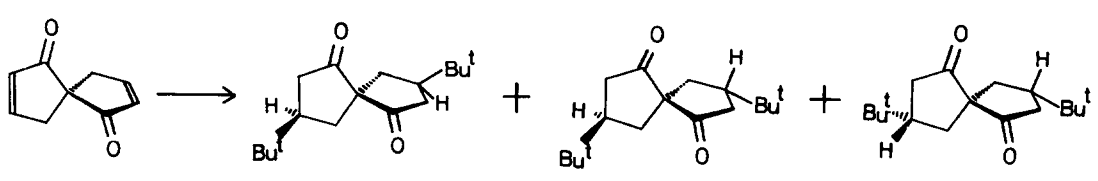
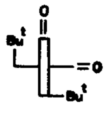
Summary: Three optically active diastereomers of 3,8-di-*t*-butylspiro[4.4]nonane-1,6-dione have been prepared. Their c.d. spectra showed very different features to each other in spite of the same configuration at their spiro centers, showing the sensitivity of c.d. to minute changes in the orientation of chromophores.

The optical activity of compounds with C_2 symmetry has been discussed mainly on the basis of their chirality (the sense of screw) without giving much attention to the minute changes in the mutual array of chromophores.$^{1,2)}$ For obtaining close insight into the chiroptical properties of C_2 compounds with simple chromophores, we have synthesized three diastereomers of β-diketones, **1a**, **1b**, and **1c**, which are assumed to differ only slightly from each other in the orientation of two carbonyls.

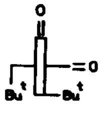
These optically active diketones were prepared from optically pure (*R*)-(+)-spiro[4.4]nona-2,7-diene-1,6-dione (**2**)$^{3)}$ by the 1,4-addition of *t*-butylmagnesium chloride in ether. The reaction product was chromatographed on silica gel to give three diastereomeric (5*R*)-3,8-di-*t*-butylspiro[4.4]nonane-1,6-dione, **1a** ($[\alpha]_{589}$ -51.7°, MeOH), **1b** ($[\alpha]_{589}$ +43.0°, MeOH), and **1c** ($[\alpha]_{589}$ +184°, MeOH). The isolated yields of **1a**, **1b**, and **1c** were 21, 55, and 1.4%, respectively, when



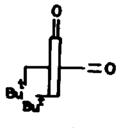
2 **1a** **1b** **1c**



trans,trans



cis,trans

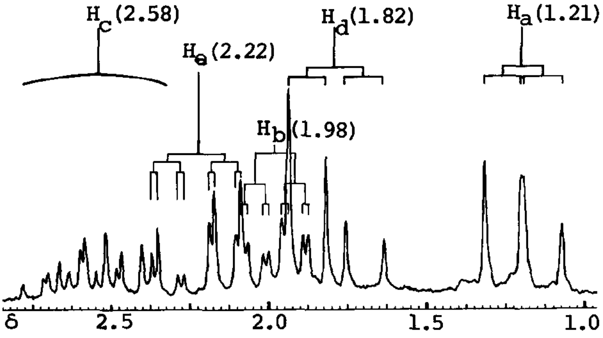


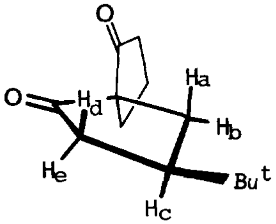
cis,cis

the reaction temperature was -60°C, and 2.7, 14, and 12% in the refluxing condition. Their relative configurations were determined by the analysis of NMR spectra in benzene-d_6. The dione **1b**, which showed two peaks of unequivalent *t*-butyls (δ 0.700 and 0.715), was readily identified as *cis,trans*-(*3R,5R,8S*)-isomer with no symmetry axis, while other two isomers (*t*-butyl; δ 0.697 and 0.698) were assigned *cis,cis*-(*3S,5R,8S*) or *trans,trans*-(*3R,5R,8R*) configurations with C_2 symmetry. Further, five types of protons in two equivalent cyclopentanone rings of **1a** were assigned as depicted in Figure 1 based on the splitting pattern and coupling constants,[4)] whereby the five-membered rings were proved to be puckered in such a way that the *t*-butyl groups assume quasi-equatorial orientations. The unusually high field resonance of H_a (δ 1.21) compared to H_b (δ 1.98) could be attributed to the magnetic anisotropy of the carbonyl group in the other cyclopentanone ring (and the solvent effect of benzene). Since this situation should be possible only for *trans,trans*-isomer in which H_a proton in one ring is brought close to the carbonyl in the other ring, **1a** was established to have *trans,trans*-configuration, and, eventually, *cis,cis*-configuration was assigned to **1c**, which shows unresolvable multiplets at δ 1.5 and δ 2.0 in NMR spectra.[5)]

The u.v. and c.d. spectra of (-)-**1a**, (+)-**1b**, and (+)-**1c** are shown in Figure 2. The observed Cotton effects for these three (*5R*)-diones in the n → π* region demonstrate marked differences from each other in spite of their close resemblance in structure and the same absolute configuration at their spiro centers.

The u.v. and c.d. of the parent compound, spiro[4.4]nonane-1,6-dione (**3**), have been extensively studied experimentally and theoretically.[6-11)] (*S*)-**3** has been expected to show negative c.d. in the longer wavelength side of n → π* region on the basis of symmetry and chirality consideration in connection with MO cal-





Coupling Constants (Hz)

$\lvert J_{ab}\rvert$	= 12.5	$\lvert J_{de}\rvert$	= 17.9
$\lvert J_{ac}\rvert$	= 11.7	$\lvert J_{cd}\rvert$	= 12.4
$\lvert J_{bc}\rvert$	= 6.6	$\lvert J_{ce}\rvert$	= 7.9

Figure 1. 100 MHz NMR spectra of ring protons of **1a** in benzene-d_6. (δ-value in parentheses)

culation, and little attention has been given to the effect of changes in its skeletal conformation. Actually, the more pronounced temperature dependence of the c.d. of **3** in EPA solvent than in nonpolar solvent was attributed to asymmetric solvation.$^{10)}$ However, the marked differences and trends of variation in c.d. spectra in isooctane solvent between **1a**, **1b**, and **1c**, which closely resemble to each other in molecular skeleton, suggest that even a slight skeletal change can exert much influence on the chiroptical behavior of **3**.

Now the contributing factors to the c.d. of **1a**, **1b**, and **1c** in the n→π* region may be supposed to be the perturbation by the *t*-butyl group and puckered five-membered ring skeleton as well as the interaction between two carbonyl groups. The contribution from the puckered cyclopentanone ring skeleton is positive for the individual (*R*)-3-*t*-butylcyclopentanone unit irrespective of the puckering form of five membered ring so far as the *t*-butyl group adopts quasi-equatorial orientation as is shown by NMR spectra. (For example, see the octant projection of one of the possible conformers$^{12)}$ shown in Figure 3.) In addition, because of the close position of *t*-butyl group to the nodal plane, its perturbation

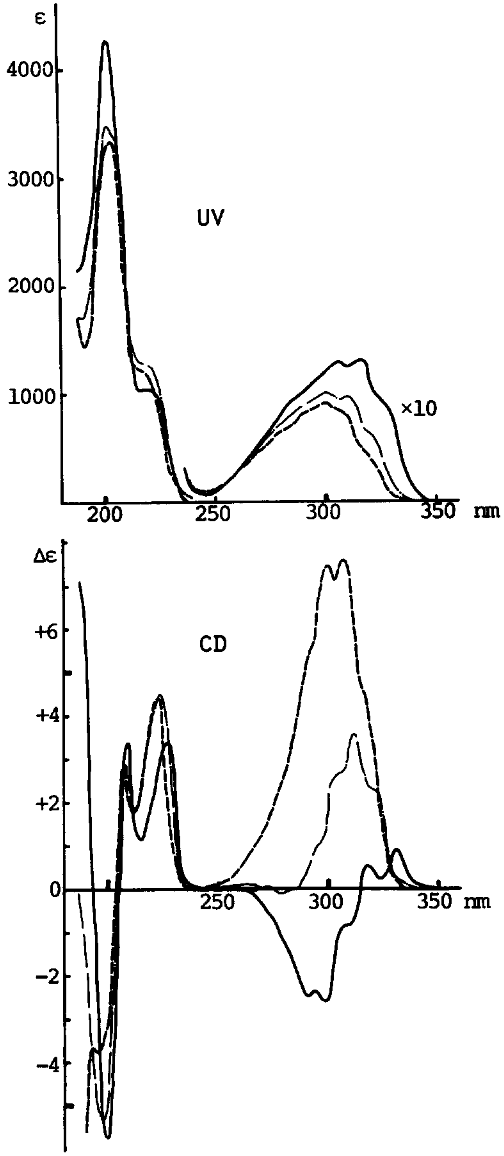


Figure 2. U.v. and c.d. spectra of (*3R*,*5R*,*8R*)-(−)-**1a** (———), (*3R*,*5R*,*8S*)-(+)-**1b** (-•-•-), and (*3S*,*5R*,*8S*)-(+)-**1c** (-----) in isooctane.

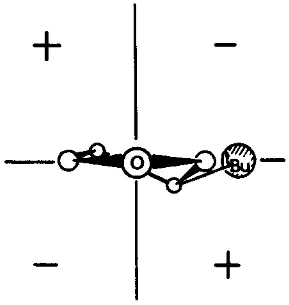


Figure 3. Octant projection of puckered (*R*)-3-*t*-butylcyclopentanone.$^{12)}$

effect on the $n \rightarrow \pi^*$ transition is supposed to be small as has already been reported by Kirk.[13] Therefore, the expected contribution to the sign of c.d. from the perturbation by carbon frame-work is positive for (*3R,5R,8R*)-*trans,trans*-**1a** (composed of two (*R*)-3-*t*-butylcyclopentanone), and negative for (*3S,5R,8S*)-*cis,cis*-**1c** (composed of two (*S*)-3-*t*-butylcyclopentanone), while that for (*3R,5R,8S*)-*cis,trans*-**1b** is zero, since the contributions from two rings are conpensated each other.

The trends of the observed c.d. spectra are, however, entirely in disagreement with these expectations. Hence the large differences in c.d. behavior between **1a**, **1b** and **1c** should be attributed to the dominant effect of the arrangement of two carbonyl groups, though the changes in their mutual disposition are not so large. Thus, aside from the apparent coincidence of c.d. signs in the longest wavelength side of $n \rightarrow \pi^*$ region with expectations from the chirality and MO consideration,[9,10] the observed sensitivity of c.d. spectra to the chromophoric array is very remarkable and noticeable, showing the need of much precautions for predicting the c.d. sign based only on the chirality or the configuration of asymmetric center without close examination of the conformation and orientation of chromophores.

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