

Optically Active Spiro[4.4]nonane Derivatives: Syntheses and Circular Dichroism of $\beta\gamma$ -Unsaturated Ketones

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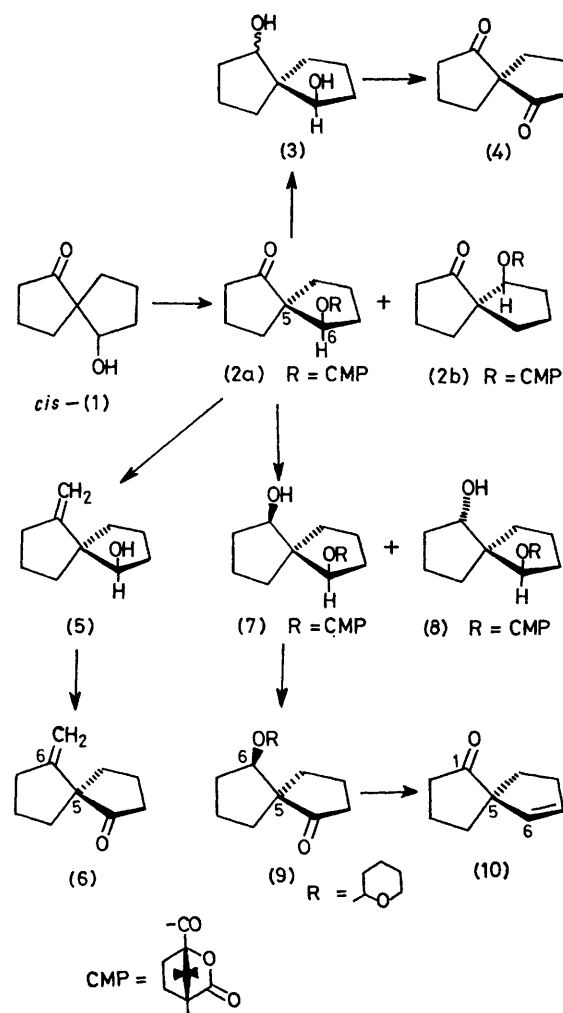
Summary (+)-6-Methylenespiro[4.4]nonan-1-one (**6**) and (–)-spiro[4.4]non-6-en-1-one (**10**) were prepared by synthetic methods establishing the absolute configuration of each, and anti-octant behaviour was observed in the c.d. spectra of (**10**).

CHIROPTICAL properties arising from the interaction between two chromophores in compounds with the spiro[4.4]nonane skeleton have become of interest.¹ As a part of a programme to investigate the interaction between dissymmetrically arranged simple chromophores, we report here the syntheses, absolute configuration, and c.d. spectra of two $\beta\gamma$ -unsaturated ketones (**6**)² and (**10**), which differ from each other in the mutual arrangement of a carbonyl group and an olefinic double bond.

While spiro[4.4]nonane-1,6-dione (**4**) was resolved by Gerlach³ via *trans,trans*-spiro[4.4]nonane-1,6-diol bis-camphanate, we have resolved the more readily available *cis*-ketol (**1**)⁴ by converting it into a diastereomeric mixture of camphanates, which was separated through column chromatography followed by fractional recrystallization, giving (**2a**) $\{[\alpha]_D^{20} -68.8^\circ$ (EtOH), m.p. 115.2–115.5 °C} and (**2b**) $\{[\alpha]_D^{20} +40.2^\circ$ (EtOH), m.p. 110.5–111.3 °C}.† (–)-(2a) was reduced with LiAlH₄ to give the diol mixture (**3**) $\{[\alpha]_D^{20} -80.5^\circ$ (AcOEt) $\}$, which was converted into the known (+)-(5*R*)-dione (**4**) {93% yield from (**2a**), $[\alpha]_D^{20} +135^\circ$ (cyclohexane); lit.,³ (5*S*)-dione, $[\alpha]_D^{20} -135^\circ$ (cyclohexane)}. Thus, the absolute configuration of (–)-(2a) was proved to be (5*R*,6*R*).

Treatment of (–)-(2a) with the Wittig reagent (Ph₃P-MeBr and Bu^tOK in benzene), followed by alkaline hydrolysis, produced the unsaturated alcohol (–)-(5) as an oil $\{[\alpha]_D^{20} -51.8^\circ$ (CH₂Cl₂) $\}$, which was oxidized with CrO₃-pyridine complex to yield (+)-(5*R*)-6-methylenespiro[4.4]nonan-1-one (**6**) as an oil $\{[\alpha]_D^{20} +139.8^\circ$ (MeOH), b.p. 71–75 °C (bath temp.) at 35 mmHg, 2.1% yield from (**2a**) $\}$.

Hydrogenation of (–)-(2a) over Adams catalyst gave a diastereomeric mixture of diol monocamphanates, which was separated by fractional recrystallization into (–)-(7) $\{[\alpha]_D^{20} -24.3^\circ$ (EtOH), m.p. 129.1–130.0 °C} and (–)-(8)



SCHEME

† All new compounds gave satisfactory elemental analyses, and i.r. and n.m.r. spectra.

{ $[\alpha]_D^{20} - 139.9^\circ$ (EtOH), m.p. $185.7-186.1^\circ\text{C}$ } in the ratio 4:1. (–)-(7), after conversion into its tetrahydropyranyl ether, was reduced with LiAlH_4 and oxidized to give the ketol ether (9) in 35% yield from (7). The i.r. spectrum of (9) was identical with that of the racemic ether obtained from the *cis*-ketol (1), establishing the configuration of the ether group in (9) as *cis* to the carbonyl group. The tosylhydrazone of (5*R*,6*R*)-(9) was converted with butyl-lithium into the *endo*-olefin, which, after removal of the protecting group using hydrochloric acid, was oxidized with CrO_3 -pyridine complex to afford (–)-(5*R*)-spiro[4.4]non-6-en-1-one (10) as an unstable oil {[$\alpha]_D^{20} - 317^\circ$ (iso-octane), b.p. 70°C (bath temp.) at 60 mmHg, 3% yield from (9)}.

TABLE

U.v. and c.d. spectra of (5*R*)-6-methylenespiro[4.4]nonan-1-one (6) and (5*R*)-spiro[4.4]non-6-en-1-one (10) in iso-octane ($n \rightarrow \pi^*$ region).

Compound	U.v.		C.d.	
	λ/nm	ϵ	λ/nm	$\Delta\epsilon$
(5 <i>R</i>)-(6)	322sh	29.2	319sh	+0.90
	310	56.9	309	+1.50
	301	66.1	301	+1.47
	294sh	59.2	293sh	+1.16
	286sh	45.9	285sh	+0.79
(5 <i>R</i>)-(10)	326sh	42.4	327sh	–1.78
	314sh	78.8	315	–3.07
	306	86.8	306	–3.14
	298sh	76.4	298sh	–2.52

Though the molecules of (5*R*)-(6) and (5*R*)-(10) are slightly flexible, it can easily be seen from molecular models that the olefinic double bond of each compound is always placed in the upper left (or lower right) rear octant with respect to the carbonyl group. Hence, the observed sign

‡ According to this mechanism, the c.d. of the 16,17-fused cyclobutene adduct of 3-acetoxypregna-5,16-dien-20-one can be reasonably explained on the basis of the conformation depicted in Figure B, rather than the unstable conformation (Figure A) assumed by Crabbé (see P. Crabbé, 'ORD and CD in Chemistry and Biochemistry,' Academic Press, New York, 1972, p. 49).

§ In case of (6), the computed rotational strength varied from a large positive value to small negative one ($+10^{-65}$ to -10^{-66} S.I.) [$R(\text{S.I.}) = 1.11 \times 10^{-25} R(\text{c.g.s.})$] depending upon the change of conformation. A consideration of the population of conformers could explain the observed positive sign of (6).

¹ A. Meyer, H. Neudeck, and K. Schlögl, *Tetrahedron Letters*, 1976, 2233 and references cited therein; G. Haas, P. B. Hulbert, W. Klyne, V. Prelog, and G. Slatzke, *Helv. Chim. Acta*, 1971, 54, 491; G. Krow, in 'Topics in Stereochemistry,' ed. E. L. Eliel and N. L. Allinger, Interscience, New York, 1970, vol. V, p. 31.

² (5*S*)-(6) has been prepared from the (5*S*)-enantiomer of the diketone (4) by a partial Wittig reaction, yet quantitative optical data have not been reported: D. A. Lightner and G. D. Christiansen, *Tetrahedron Letters*, 1972, 883; D. A. Lightner, G. D. Christiansen, and J. L. Melquist, *ibid.*, p. 2045.

³ H. Gerlach, *Helv. Chim. Acta*, 1968, 51, 1587.

⁴ D. J. Cram and H. Steinberg, *J. Amer. Chem. Soc.*, 1954, 76, 2753; E. Hardegger, E. Maeder, H. M. Semarne, and D. J. Cram, *ibid.*, 1959, 81, 2729.

⁵ A. Moscovitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, 84, 1945; K. Mislow and J. G. Berger, *ibid.*, p. 1956; E. Bunnenberg, C. Djerassi, K. Mislow, and A. Moscovitz, *ibid.*, p. 2823 and 5003; A. Moscovitz, A. E. Hansen, L. S. Forster, and K. Rosenheck, *Biopolymers Symposia*, 1964, 1, 75.

⁶ W. Klyne and D. N. Kirk, *Tetrahedron Letters*, 1973, 1483.

⁷ J. A. Schellman, *Accounts Chem. Res.*, 1968, 1, 144.

⁸ E. G. Höhn and O. E. Weigang, Jr., *J. Chem. Phys.*, 1968, 48, 1127.

of the c.d. of (6) in the $n \rightarrow \pi^*$ region was consistent with the prediction from the generalized octant rule⁵ for $\beta\gamma$ -unsaturated ketones. However, (10) showed dissignate⁶ behaviour with a large $\Delta\epsilon$ value compared to (6), irrespective of its enhanced absorption in the u.v. spectrum (see Table).

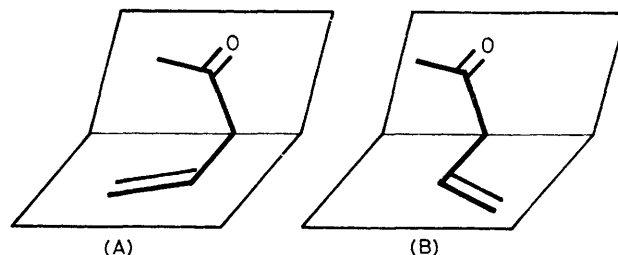


FIGURE. Mutual disposition of the carbonyl group and double bond.

The generalized octant rule was proposed, however, for the case in which the carbonyl group and olefinic double bond are arranged as in Figure A, and seems not to be applicable to the case of (10) (Figure B). This fact shows that the sign of the c.d. in the $n \rightarrow \pi^*$ region is inevitably dependent upon the direction of the double bond as well as its position in the carbonyl octant. We therefore employed the method of Schellman⁷ and Weigang⁸ based on μ - m coupling,[‡] whereby the observed sign of the c.d. of (10) was found to be explainable in every conformation examined.[§]

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