The n–π* Optical Activity of a Ketone predicted to be Optically Inactive by the Octant and Quadrant Rules: (1*R*,5*R*)-Dimethyladamantan-2-one

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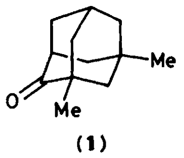
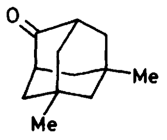
The title compound, which has each of its methyl groups lying in a quadrant or octant rule symmetry plane, exhibits a weak positive n–π* circular dichroism Cotton effect, $\Delta\varepsilon_{292}^{\mathrm{max.}} = +0.009$.

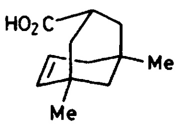
In the twenty-five years since Moffitt *et al.*[1] proposed the octant rule for chiral saturated alkyl ketones, it has enjoyed wide application in interpreting details of absolute configuration and conformation from circular dichroism (c.d.) or optical rotatory dispersion spectral data. The rule divides all space surrounding the carbonyl chromophore into eight regions (octants), and the octant occupied by a particular atom or group (perturber) determines the sign of its contribution to the rotatory strength of the n–π* transition. The octants are derived, in part, from the local symmetry (C_{2v}) of the carbonyl group: reflection of a perturber across either of the symmetry planes leads to a mirror image molecular fragment and hence to a rotatory strength contribution of opposite sign. The quadrants thus defined are further divided into front and back octants by a third surface associated with the non-symmetry-determined nodes of the relevant carbonyl n and π* orbitals.[2] As one observes the ketone, looking down the C=O bond from O to C, groups in the lower right and upper left back octants typically make a positive contribution to the n–π* Cotton effect (C.e.). However, atoms having counterparts symmetrically placed across the carbonyl symmetry planes and atoms lying in symmetry planes are assumed to make no net contribution to the C.e. Thus, according to the octant rule (and quadrant rule), ketones such as (**1**) and (**2**) should give no c.d. C.e. The prediction is understandable for ketone (**2**), which is achiral, however, ketone (**1**) is chiral and should



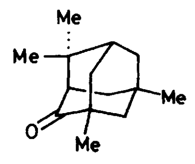
(**1**)



(**2**)



(**3**)



(**4**)

therefore test the limits of the octant rule. We now report on the synthesis and c.d. of (**1**).

Dimethyladamantanone (**1**) was prepared from achiral dimethyladamantanone (**2**)[3] by a route described earlier for the unmethylated parent,[4,5] in which (**2**) is treated successively with NaN_3 in anhydrous $MeSO_3H$ then with alkali to give (±)-1,5-dimethylbicyclo[3.3.1]non-6-ene-3-*endo*-carboxylic acid. The latter was resolved (quinine) to afford the (+)-enantiomer (**3**). Acid (**3**) was converted[6] into ketone (**1**) in three steps: (i) reduction ($LiAlH_4$) to give the hydroxymethyl derivative; (ii) solvolytic cyclization of the latter in hot 98% formic acid to give the diastereoisomeric 1,5-dimethyladamantanol formate esters; and (iii) hydrolytic reduction ($LiAlH_4$) of the formate esters, followed by Jones oxidation to give (**1**).†

The absolute configuration of (**3**), and hence (**1**), was ascertained by converting[5] (**3**) into (**4**),† whose observed c.d. C.e. ($\Delta\varepsilon_{303}^{\text{max.}} = +0.32$, cyclopentane) is determined largely by the equatorial β-Me group of the *gem*-dimethyl grouping. Since the 4,4-dimethyl parent analogue [$\Delta\varepsilon_{303}^{\text{max.}} = +0.61$; 77 ± 3% enantiomeric excess (e.e.)][5] of (**4**), of known absolute configuration and e.e.,[5] has been prepared previously, we believe that the absolute configuration of (**4**) (and its approximate e.e.) can be determined by analogy.

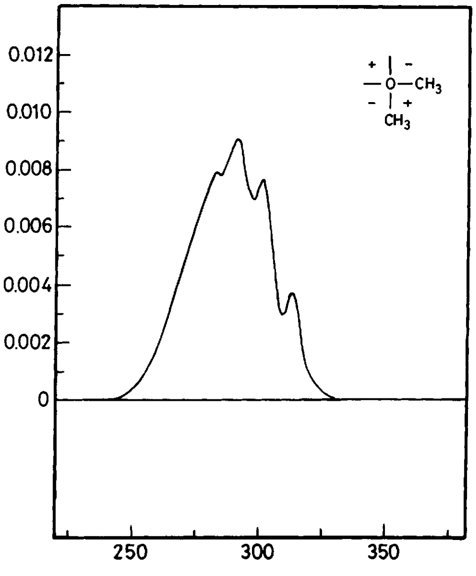


Figure 1. Circular dichroism spectrum of (**1**) (0.05 M) in cyclopentane at 25 °C using a 1 cm path length cuvette and measured on a JASCO J-40 spectropolarimeter equipped with a photoelastic modulator. Data are not corrected for e.e. The c.d. spectrum of racemic ketone‡ serves as the c.d. baseline (Δε = 0) for (**1**), and the spectrum of (**1**) is reproducible within 5%. An octant diagram for (**1**) (inset) shows the Me groups lying on octant symmetry planes.

The c.d. spectrum (Figure 1) of (**1**), predicted by the octant rule to have no n–π* C.e., reveals a single, weak signal showing a (+)-C.e., with the expected vibrational fine structure. The C.e. remains (+) with an essentially invariant rotatory strength at −175 °C in isopentane–methylcyclohexane glass. Molecular mechanics (MM2) calculations[7] reveal (a) no marked preference for ring skeletal distortion from the adamantanone C_{2v} symmetry and (b) staggered Me rotamers. Hence, all atoms of (**1**) lie either on an octant symmetry plane, or they have counterparts similarly placed across the symmetry planes.

Nearly ten years ago, Yeh and Richardson[8] analysed how (**1**) and related adamantanones might be reconciled with the octant rule. They pointed out that the one-electron perturbation model of n–π* optical activity in chiral ketones, which provides the simplest and most direct rationalization for the octant rule, may be insufficient to account for optical activity when carried out only to first order. In first order perturbation only (*additive*) pairwise interactions between the C=O group and dissymetric perturbers are considered, and in this sense the octant rule lacks qualitative completeness. When the one-electron model is carried to higher order perturbation, *multiplicative* terms contribute to the n–π* rotatory strength. Thus ketones such as (**1**), which in first order one-electron perturbation theory are predicted (by the simple octant rule) to have zero optical activity, are in fact predicted to be optically active in second order perturbation, which accounts for three-way interactions among the two Me perturbers and the C=O chromophore. Qualitatively, this means that each Me group of (**1**) destroys a plane of symmetry in the C_{2v} C=O chromophore, hence an octant symmetry plane. Thus, the octant or quadrant symmetry planes are, except for molecules with C_{2v} symmetry, *e.g.* adamantanone, only approximately planes. The deviation from planarity will depend on the location and nature of the perturbation, and while such deviations are not important for more qualitative applications of the octant rule, they can in fact be detected and analysed in molecules like (**1**). We note that the Me perturbers of (**1**) flank the sign-determining octant; more extensive theoretical analyses are in progress.

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† All new compounds reported in this work had satisfactory C,H analyses and spectroscopic properties corresponding to the assigned structures.

‡ Racemic ketone (**1**) is a by-product of the synthesis of (**2**) from 1,3-dimethyladamantane (ref. 3).

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