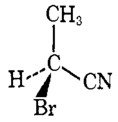
Theoretical and Experimental Studies of Optically Active Bridgehead-Substituted Adamantanes and Related Compounds

Jon Applequist, Prince Rivers, and Douglas E. Applequist

Contribution from the Department of Biochemistry and Biophysics,
Iowa State University, Ames, Iowa 50010, and the Department of Chemistry
and Chemical Engineering, University of Illinois, Urbana, Illinois 61801.
Received March 21, 1969

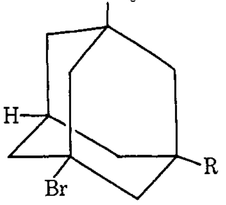
Abstract: An experimental and theoretical study of the optical activity of α-bromopropionitrile (**1**) and an analogous bridgehead-substituted adamantane derivative, 3-methyl-5-bromo-1-cyanoadamantane (**2c**), has been carried out. The synthesis and resolution of **2c** *via* the corresponding carboxylic acid (**2a**) and amide (**2b**) are described. Specific rotations of less than 1° are found for each of **2a–c**, confirming expectations of a large reduction in rotation when molecular asymmetry is due to substituents at the adamantane bridgeheads. A theoretical interest in **1** and **2c** exists because the symmetry of the substituents is such that first-order (pairwise) contributions to the rotation are expected to vanish. An "atom polarizability" model, treated earlier by Boys, is considered as a basis for calculating higher order contributions in these molecules. The basic assumption is that the atoms are isotropically polarizable point particles located at their nuclei. A simple generalization of polarizability theory is presented, in which perturbation contributions of any order may be easily calculated. The calculations are carried out for the third- and fourth-order contributions to rotation in **1** and **2c** for the atom polarizability model, noting that the first and second orders vanish. The main conclusions are: (i) the calculated and observed rotatory dispersion constants are roughly comparable in magnitude, suggesting that the assumed mechanism of optical activity is significant; (ii) the fourth-order contributions are larger than those of third order, implying that a number of still higher terms are also important, and raising serious doubts about the usefulness of the perturbation expansion; (iii) it is not possible to correlate sign of rotation with absolute configuration on the basis of the third- and fourth-order calculations.

An interesting case among optically active compounds is that exemplified by α-bromopropionitrile (**1**).[1-3] Each group attached to the asymmetric carbon atom is symmetric about its bond axis, and as a result each pair of groups has a plane of symmetry. While the optical activity of many compounds is believed to arise from pairwise interactions (or first-order perturbations) between chromophoric groups, it is evident from the symmetry of such pairs that this cannot be the case for **1**. It has been concluded[1-3] that the rotation in this case ($[\alpha]^{25}\text{D}$ $-19.3 \pm 3.8°$, neat)[1] must come from three-way and higher interactions (or second-order and higher perturbations).



1(L configuration)

The purpose of this work is to investigate the analogous case of compounds in which the four groups are placed at the bridgehead positions of adamantane as in **2a–c**. The groups are then arranged tetrahedrally just as if they were attached to a central carbon atom, except that the distances between groups are increased by a factor of about 2–3 (depending on how one defines the location of the group). Two objectives were considered. (i) The effect of this change in distance on the magnitude of the rotation should provide a test of the above ideas about the origin of optical activity in these molecules. (ii) It was hoped that the adamantane derivatives would prove unusually suitable for a theoretical calculation of optical activity, since the geometry is relatively fixed and the distances between groups are relatively large, thus avoiding certain theoretical difficulties present in more compact or more flexible molecules. In this report we describe the synthesis and properties of the optically active compounds **2a–c** and some attempts to realize these theoretical objectives.



2a, R = CO_2H
b, R = $CONH_2$
c, R = CN

Regarding objective i, one might anticipate certain orders of magnitude of the distance effect. If first-order interactions were significant, their contribution to the rotation would be expected to vary as $1/r^2$, where r is the distance between the two interacting groups, according to the polarizability theory of Kirkwood.[4] Thus the rotation of the adamantane derivative would be smaller by a factor of *ca.* 4–9 than that of the corresponding "methane" derivative if such interactions were predominant. For second- and third-order interactions between polarizable groups, it can be shown that the contribution to the rotation varies as $1/r^5$ and $1/r^8$, respectively, where r now represents a factor by which all of the intergroup distances are multiplied. The re-

---

[1] K. L. Berry and J. M. Sturtevant, *J. Am. Chem. Soc.*, **63**, 2679 (1941).

[2] W. J. Kauzmann, J. E. Walter, and H. Eyring, *Chem. Rev.*, **26**, 339 (1940).

[3] W. Kauzmann, F. B. Clough, and I. Tobias, *Tetrahedron*, **13**, 57 (1961).

[4] J. G. Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937).

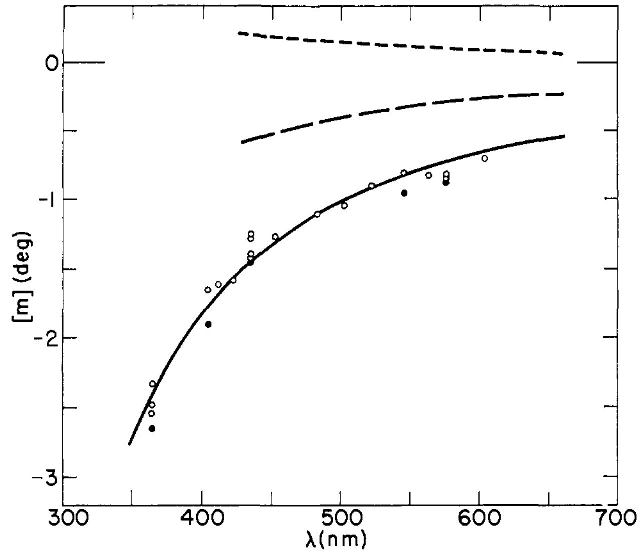


Figure 1. Optical rotatory dispersion of 3-methyl-5-bromo-1-cyanoadamantane in *cis*-decalin: ○, 24°; ●, 46°. (———) Least-squares fit of 24° data to eq 15. (– – – –) Third-order calculation, all atoms. (— — —) Fourth-order calculation, substituent atoms only. Signs of calculated curves are reversed from those in text.

duction in rotation for the adamantane derivatives would then be about two to four orders of magnitude if these higher order interactions predominate. It will be seen that the observed rotations are roughly consistent with the notion that higher order interactions predominate in these compounds. However, in our theoretical analysis we do not try to consider interactions of a substituent group as a whole with its neighbors and therefore do not explore fully the observed distance effect.

Regarding objective ii, it must be recognized that at least three separate mechanisms may contribute to the optical rotation of a given compound.[4,5] Here we will consider only the so-called "polarizability" mechanism, which involves induced electric dipolar interactions between groups. Our aim will be to gain some idea as to the relative importance of this particular mechanism. The polarizability theory of Kirkwood[4] is inadequate for our cases, since he has treated only the first-order contribution. We have therefore adopted for the present the earlier approach of Boys,[6] in which the atoms are regarded as the interacting units and are treated as isotropic particles. This will be referred to as the "atom polarizability mechanism." Boys indicated a method of calculating higher-order interactions for this mechanism, and gave a formula for the rotation due to third-order (four-way) interactions, which are the lowest order that contribute when the interacting units are isotropic. In this paper we reduce the theory to a relatively simple form, and use the results, in addition to Boys' formula, to calculate the third- and fourth-order contributions to the rotation.

An advantage of the atom polarizability theory is that the only physical quantities required for the calculation are the polarizabilities and coordinates of all of the atoms, and these are known fairly accurately. No other mechanism of optical activity is based on such readily accessible information. The theory is limited to the wavelength range above any electronic absorption bands, where the classical treatment of polarization is valid and where atom polarizabilities have been determined. For our purposes this is adequate, since the rotatory dispersion measurements are limited to the same range.

Experimental Results

3-Methyl-5-bromoadamantane-1-carboxylic acid (**2a**) was synthesized in three steps from 1-methyladamantane, as described in the Experimental Methods section. After a substantial number of unsuccessful efforts to resolve **2a**, it was found that the quinine salt was fractionated in 10% aqueous acetone at 50–55°. Five recrystallizations from this medium raised the melting point of the quinine salt from 173–175° to 189–190°, the melting point of the recovered free acid from 132–134° to 138–139°, and the specific rotation of the acid $[\alpha]^{25}\mathrm{D}$ from 0 to $-0.36 \pm 0.03°$ (all taken at 6 g/dl in chloroform). Five additional recrystallizations changed none of these quantities. The rapid changes in the melting points and rotations, followed by abrupt and complete resistance to further change, provide strong evidence, but not proof, that resolution was complete. Attempts were made to purify the more soluble salt from the mother liquors, but the maximum specific rotation of the acid recovered therefrom was +0.22°. The acid **2a** was converted by way of its amide **2b** to the nitrile **2c**.

The most precise optical rotatory measurements were made on **2c** in *cis*-decalin ($n^{20}\mathrm{D}$ 1.4807), given in terms of intrinsic molar rotations [*m*] (eq 1) in Figure 1 and Table III. The solvent was chosen for its nonpolar character in order to minimize effects of solvent–solute interactions on the rotation. Measurements of [*m*] at 46° were the same as those at 24° within experimental error, suggesting that such effects are indeed negligible. Some further values of [*m*] for the various compounds in chloroform ($n^{20}\mathrm{D}$ 1.4476) are given in Table I.

Table I. Rotations of Adamantane Derivatives in Chloroform at 25°

Compound	Concn, g/dl	[*m*], deg 546 nm	589 nm
2a (acid)	3.8	−0.85 ± 0.11	−0.61 ± 0.1
2b (amide)	4.1	−0.61 ± 0.09	−0.76 ± 0.15
2c (nitrile)	3.3	−0.81 ± 0.27	−0.41 ± 0.15

Theory

The specific rotation [α] in (deg/dm)(cm³/g) is related to a quantity we define as the *intrinsic molar rotation* [*m*] by[7]

$$[\alpha] = \left(\frac{n^2 + 2}{3}\right)\left(\frac{n^2 + 5}{6}\right)\frac{100}{M}[m] \qquad (1)$$

---

(5) J. A. Schellman, *Accounts Chem. Res.*, **1**, 144 (1968).

(6) S. F. Boys, *Proc. Roy. Soc., Ser. A*, **144**, 655 (1934).

(7) Equations 1 and 2 are identical with generally accepted formulas[2] except for the factor $(n^2 + 5)/6$ in eq 1. This factor was obtained by Boys,[6] but was omitted by Born,[8] Condon,[9] and Kauzmann, *et al.*,[2] all of whom gave solutions to Maxwell's equations for essentially the same macroscopic problem. An examination of the various derivations shows that the discrepancy arises from the manner in which the Lorentz field is introduced, and that Boys carried this out in a way which avoids approximations made by the other writers. We conclude that Boys' result correctly represents the Lorentz field effect, contrary to widespread belief. A summary of the pertinent derivations will be supplied to interested readers on request.

(8) M. Born, "Optik," Verlag von Julius Springer, Berlin, 1933, pp 403–413.

(9) E. U. Condon, *Rev. Mod. Phys.*, **9**, 432 (1937).

where n is the refractive index of the medium and M is the molecular weight of the optically active substance. $[m]$ is given theoretically by

$$[m] = 288\pi^2 N_0 \beta/\lambda^2 \tag{2}$$

where N_0 is Avogadro's number, λ is the wavelength of the polarized light *in vacuo*, and β is the *molecular rotatory parameter*, whose value is to be calculated here for a particular model. The usual units of $[m]$ are (deg/mm)·(cm^3/mol), but will be abbreviated here simply as "deg."

We consider a model in which the atoms of a molecule are regarded as classical, *isotropically* polarizable point particles, located at the positions of the nuclei. This picture becomes increasingly suitable as the distance between atoms increases; the adamantane case is particularly attractive for this reason, since many of the important interactions involve large distances.

Optical rotation arises in the model as a result of the mutual polarization of the various atoms under the influence of the field of incident light. If the electric field of the light at atom j is $\mathbf{E}_j$, then the induced dipolar fields of the atoms give rise to a component $\boldsymbol{\mu}_i$ of the electric dipole moment of atom i given by

$$\boldsymbol{\mu}_i = \mathbf{B}\mathbf{E}_j \tag{3}$$

where $\mathbf{B}$ is a tensor which depends on the manner in which the dipolar field of atom j is relayed to atom i. When the molecules are randomly oriented, it can be shown either by an averaging procedure similar to that of Boys[6] or, more directly, by translating the general theory of Born[8] into the present model, that the interaction given by eq 3 leads to a contribution to β given by

$$\beta' = \frac{1}{6}\mathbf{r}_{ij}\cdot\mathbf{b} \tag{4}$$

where $\mathbf{r}_{ij}$ is the vector from atom i to atom j, given by

$$\mathbf{r}_{ij} = x_{ij}\mathbf{e}_1 + y_{ij}\mathbf{e}_2 + z_{ij}\mathbf{e}_3 \tag{5}$$

and

$$\mathbf{b} = (B_{32} - B_{23})\mathbf{e}_1 + (B_{13} - B_{31})\mathbf{e}_2 + (B_{21} - B_{12})\mathbf{e}_3 \tag{6}$$

where B_{kl} is the element of the kth row and lth column of the matrix representation of $\mathbf{B}$, and $\mathbf{e}_1$, $\mathbf{e}_2$, and $\mathbf{e}_3$ are mutually perpendicular unit vectors of a right-handed coordinate system fixed with respect to the molecule. The total β is the sum of all possible contributions of the type in eq 4. The perturbation approach generally used in optical activity theory[4,6] gives β as an infinite series

$$\beta = \beta_1 + \beta_2 + \cdots \tag{7}$$

where β_n is the nth order perturbation term, which in the present model is the total of all contributions resulting from the n-fold relaying of induced moments from one atom to another *via* their dipolar fields. It is usually assumed that the series is rapidly converging, so that the lowest order term dominates the sum. Since only asymmetric groups of atoms can contribute to β, it is evident that β_1 and β_2 must vanish for isotropic atoms, since these involve interactions between at most two and three atoms, respectively.[6] The smallest asymmetric group contains four atoms, and such groups contribute only to β_3 and higher terms. The first two of these are considered in the present paper, so we write out their formulas. Summing each index over all atoms in the molecule, excluding those noted, we write

$$\beta_3 = \frac{1}{6}\sum_i \sum_{j\neq i} \sum_{k\neq j} \sum_{l\neq k} \quad \cdot\mathbf{b}_{ijkl} \tag{8}$$

where $\mathbf{b}_{ijkl}$ is defined in accordance with eq 6 in terms of the tensor

$$\mathbf{B}_{ijkl} = \boldsymbol{\alpha}_i\mathbf{D}_{ij}\boldsymbol{\alpha}_j\mathbf{D}_{jk}\boldsymbol{\alpha}_k\mathbf{D}_{kl}\boldsymbol{\alpha}_l \tag{9}$$

where $\boldsymbol{\alpha}_i$ is the polarizability tensor of atom i, and is treated as a scalar for isotropic atoms; $\mathbf{D}_{ij}$ is the dipole field tensor, whose matrix form is [10]

$$\mathbf{D} = \frac{3}{r^5}\begin{bmatrix} x^2 - r^2/3 & xy & xz \\ xy & y^2 - r^2/3 & yz \\ xz & yz & z^2 - r^2/3 \end{bmatrix} \tag{10}$$

where the subscript ij is implied on $\mathbf{D}$, r, x, y, and z. $\mathbf{B}_{ijkl}$ represents, *via* eq 3, the dipole moment induced in atom i by the dipolar field transmitted from atom l by successive relays through atoms k and j.

Similarly

$$\beta_4 = \frac{1}{6}\sum_i \sum_{j\neq i} \sum_{k\neq j} \sum_{l\neq k} \sum_{m\neq l}\mathbf{r}_{im}\cdot\mathbf{b}_{ijklm} \tag{11}$$

where $\mathbf{b}_{ijklm}$ is defined in terms of the tensor

$$\mathbf{B}_{ijklm} = \boldsymbol{\alpha}_i\mathbf{D}_{ij}\boldsymbol{\alpha}_j\mathbf{D}_{jk}\boldsymbol{\alpha}_k\mathbf{D}_{kl}\boldsymbol{\alpha}_l\mathbf{D}_{lm}\boldsymbol{\alpha}_m \tag{12}$$

The extension to other orders of perturbation is obvious. In the form given here, the equations are both simpler and more general than previous results of polarizability theory. The first-order treatment of Kirkwood[4] and the third-order treatment of Boys[6] are special cases of the above. In particular, Boys' equation for the rotation of a group of four isotropic units can be derived from eq 8. Because of its simpler form, eq 8 is the more easily adapted to a computer program, though it was found that a program based on Boys' equation was the faster in execution.

Computations based on eq 8 and 11 may be speeded by noting the following facts for the isotropic atom case. (i) The term in the sum for a given set of indices (i,j,k,l) is the same as for the reverse set (l,k,j,i), because both $\mathbf{r}_{il}$ and $\mathbf{b}_{ijkl}$ change sign with this reversal. The same holds for any number of indices. Therefore, it suffices to calculate only half of the terms, multiplying each by two, and selecting them so that the first index is less than the last. (ii) Only terms in which there are at least four different indices need be included, because interactions within smaller sets of atoms do not contribute to the rotation.

Calculations

Intrinsic molar rotations of 3-methyl-5-bromo-1-cyanoadamantane (**2c**) and L-α-bromopropionitrile (**1**) have been calculated on an IBM 360/65 computer. Atomic coordinates were calculated from the following bond lengths given by Pauling[11] (ångström units): C–C, 1.540; C–H, 1.095; C–Br, 1.912; C–N (nitrile), 1.153. For C–C (nitrile) the value 1.460 found for

---

(10) C. J. F. Böttcher, "Theory of Electric Polarization," Elsevier Publishing Co., Amsterdam, 1952, p 449.

(11) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, Chapter 7.

Table II. Atomic Refractivity Dispersion Parameters

Atom	A, cm^3	λ_a, nm
H	1.0149	67.3
C (aliphatic)	2.5138	100.2
C (nitrile)	2.2860	89.7
N (nitrile)	3.0512	85.1
Br	8.4409	109.2

Table III. Theoretical and Experimental Optical Rotatory Parameters

	$[m]_D$, deg	$K \times 10^{-6}$, deg nm^2	λ_c, nm
3-Methyl-5-bromo-1-cyanoadamantane (**2c**)			
Third-order theory (all atoms)	−0.0812	−0.0257	176
Third-order theory (substituent atoms only)	−0.0953	−0.0302	174
Fourth-order theory (substituent atoms only)	+0.279	+0.0867	191
Exptl (24°, *c* 4.4, *cis*-decalin)[a]	−0.684 ± 0.008	−0.205 ± 0.002	218 ± 4
L-α-Bromopropionitrile (**1**)			
Third-order theory (all atoms)	+4.24	+1.31	196
Fourth-order theory (all atoms)	+100.4	+30.8	201
Exptl (25°, neat)[b]	−15.9 ± 3.1	−4.38 ± 0.85	262

[a] This work. Uncertainties are standard deviations found from a weighted least-squares fit of 20 points to the relation $1/[m] = (\lambda^2/K) - (\lambda^2_c/K)$. [b] Data of Berry and Sturtevant.[1] Uncertainties are limits of error fixed by known limits on the degree of optical purity.

acetonitrile[12] was used. The CCN angle was assumed to be 180°, and all other bond angles were assigned the tetrahedral value arccos ($^1/_3$). Methyl groups were placed in exactly staggered conformations. The absolute configurations were those indicated in structures **1** and **2**. In the case of **1** this can be identified with the levorotatory form,[13] but no such identification has yet been made for **2**.

The atom polarizabilities α were obtained from the atomic refractivities R by means of the relation

$$\alpha = 3R/4\pi N_0 \tag{13}$$

Values of R were taken from the empirical data of Vogel,[16] supplemented by Eisenlohr's values[16] for nitrile N. The data at 434, 589, and 656 nm were fitted to the relation

$$R = A\lambda^2/(\lambda^2 - \lambda_a^2) \tag{14}$$

where A and λ_a are constants, whose values are given in Table II. Equation 14 fits the empirical data to within 0.1%. Additional data of Vogel at 486 nm were found to deviate consistently from the same relation by about 1%, and were rejected to avoid what is apparently a small systematic error at this wavelength.

Rotations were calculated at four wavelengths in the range 434–656 nm, and in every case these were found to fit precisely the one-term Drude dispersion formula

$$[m] = K/(\lambda^2 - \lambda_c^2) \tag{15}$$

where K and λ_c are constants. The results are given in Table III, along with the experimental data.

To indicate the extent of the calculations, compound **1**, containing nine atoms, required 1512 third-order terms (eq 8) and 15,120 fourth-order terms (eq 11). Compound **2c**, containing 30 atoms, would have required 328,860 third-order terms, but it was found that this number could be reduced without approximation to 15,624 by using symmetry arguments to eliminate all terms involving less than three substituent atoms (atoms in groups attached to the bridgehead carbons). The fourth-order calculation involving all 30 atoms of **2c** was not undertaken, because this would have required at least 10^5 terms, and the results for the third-order calculation suggested that it would suffice to consider *only* interactions among the eight substituent atoms, requiring 840 third-order and 7560 fourth-order terms. All steps in the calculations were carried out to 16 significant figures to minimize cumulative rounding-off errors occurring in the long summations. The accuracy of the arithmetic was checked by repeating each type of calculation with a variety of formulas derivable from eq 8 and 11.

The results were fairly sensitive to the polarizabilities and coordinates used. For example, the atomic refractivities tabulated by Eisenlohr[16] differ from the later values of Vogel (adopted here) by 1–7%. When used in the third-order calculation for compound **2c** Eisenlohr's values gave a rotation which is about half of that based on Vogel's data. The effect of decreasing each bond length by 0.01 Å on the third-order rotation of **2c** was also tested. The largest changes in rotation occurred for the C–C bond (21% increase) and the C–Br bond (16% decrease).

The possible distortion of molecular structure in compound **2c** due to interactions between polar groups has also been considered. For example, repulsions between the electronegative atoms Br and N should result in some mutual displacement from their assumed positions. The most dramatic effect was found for displacement of N, where a lateral movement of 0.003 Å in a direction away from Br resulted in a third-order $[m]_D$ of +0.695° and a fourth-order value (substituent atoms only) of +1.259°; the total thus exceeds the experimental value in magnitude. A displacement of this sort seems physically reasonable, and probably plays an important role in the rotation.[2,17]

A striking effect was also found by rotating the methyl group away from the assumed staggered conformation. In compound **2c** the third-order $[m]_D$ (all atoms included) passes through nearly equal and opposite maxima of ±383° at conformations ±30° from the

---

(12) R. Trambarulo and W. Gordy, *Phys. Rev.*, **79**, 224 (1950).

(13) This assignment is based on the synthetic sequence of Berry and Sturtevant,[1] starting with L-α-bromopropionic acid, whose "probable" identification with the levorotatory form by Freudenberg and Markert[14] was later confirmed by studies of the kinetics of its conversion to ethyl lactate.[15]

(14) K. Freudenberg and L. Markert, *Ber.*, **60**, 2447 (1927).

(15) W. A. Cowdrey, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1208 (1937).

(16) Collected by J. R. Partington, "An Advanced Treatise on Physical Chemistry," Vol. 4, Longmans Green and Co., London, 1953, p 42 ff.

(17) C. O. Beckmann and K. Cohen, *J. Chem. Phys.*, 4, 784 (1936).

staggered position, and takes the value +0.239° at the eclipsed position. A statistical–mechanical average rotation was calculated from values obtained at 10° conformation intervals, assuming a 3 kcal, threefold, sinusoidal rotational barrier with maxima at the eclipsed positions. At 25° the average third-order $[m]_D$ was found to be −0.0447°. As expected, this is comparable to the value −0.0812° for the staggered conformation alone. The effect of internal rotation could be much more significant if the rotational barrier were not symmetric about the staggered position. However, it would seem that effects leading to such an asymmetry, if any, are very small. The other difficulties discussed below appear more serious at present.

Discussion

The most interesting facts that emerge from the calculations are the following. (i) The calculated and observed rotatory dispersion constants are roughly comparable in magnitude, suggesting that the atom polarizability mechanism is of major importance in these compounds. (ii) The fourth-order terms are in each case larger than those of third order, implying that the complete contribution from this mechanism requires a number of terms of still higher order. (iii) The sign of the calculated contributions for compound **1** is in disagreement with experiment, based on the known configuration of this compound. Since it appears likely that higher order terms, possibly of opposite sign, are of major significance, this discrepancy does not necessarily raise doubts about the atom polarizability mechanism, though the presence of other mechanisms could equally well account for the discrepancy. In this connection, the comparison between theory and experiment for compound **2c** does not permit any conclusion regarding the absolute configuration of this compound. The calculations do not even demonstrate that compounds **1** and **2c** having the same configuration of substituent groups have the same sign of rotation, since the role of the higher order terms remains in doubt.

The failure of the perturbation series to converge rapidly contradicts the usual assumption that the lowest term is dominant,[3,4,6] and raises serious doubts about the usefulness of the series. The apparent reason for this failure is that the number of terms in equations such as (8) and (11) increases rapidly with increasing order, while the magnitudes of individual terms fall off rather slowly, the additional factor with each successive order being about α/r^3, where α is an atom polarizability (comparable to an atomic radius cubed) and r is an interatomic distance. These features are shared to a large extent by other perturbation treatments of optical activity, and it would therefore appear that no such treatment is on secure ground without an investigation of the higher order contributions.

One interesting aspect of the adamantane derivatives is that the large distances involved in many of the interactions should cause the perturbation series to converge more rapidly than in smaller molecules such as **1**, since the higher terms fall off more rapidly with distance. The first two terms (Table III) support this, though they do not suggest rapid convergence even in the adamantane case. It would be feasible, but expensive and perhaps unpromising, to proceed with the calculation of the next few terms in the expansion. We have abandoned this approach for the present because the results to date suggest that other alternatives should be explored, including the possibility of an exact calculation of β in closed form.

Unfortunately we are as yet unable to determine whether the atom polarizability model accurately accounts for optical activity in any compound. It is a matter of considerable interest to answer this question, since the theory could be applied to any molecule whose geometry is known. Boys' justification for the model was that molecular polarizabilities, and a number of cases of molecular anisotropies,[18] could be accounted for by the same model, in which atoms are regarded as isotropic. Other writers[19,20] have considered a "bond polarizability" model to be more generally applicable to the theory of molecular polarizability; in this case each bond is regarded as an anisotropic polarizable unit. The optical rotation could be calculated to any order for this model by the theory given here, though the large discrepancies in anisotropies assigned to various bonds[21] make this possibility unattractive. A rigorous theoretical justification for either of these models is not likely to be easy. The translation of Born's general theory[8] into a polarizability theory of optical activity is made by assuming that the interacting units do not exchange electrons, and this is not generally true for either atoms or bonds. However, this does not rule out the possibility that the models could serve as reasonable approximations, as their ability to account for certain molecular anisotropies suggests.

The requirement that electron exchange between interacting units be avoided led Kirkwood[4] to propose that various polyatomic groups be taken as interacting units. Since these are in general anisotropic, the first-order contribution is significant. Thus a pair of groups is the smallest system contributing to the rotation in Kirkwood's theory, while a set of four atoms is the smallest in Boys' theory. We note here a degree of equivalence between the two approaches: an anisotropic group contains at least two atoms, so that four atoms constitute the smallest significant system in both cases. To some extent, therefore, the same contributions to the rotation are included in the first-order theory of Kirkwood and the third-order theory of Boys. The use of known group anisotropies in Kirkwood's approach has the possible virtue of including the equivalent of certain higher order atom polarizability terms as well. On the other hand, the atom polarizability model has the virtue of not requiring knowledge of group anisotropies, which are often difficult to determine. In addition, we have noted above the shortcoming in Kirkwood's approach which requires that the molecules involved in this study be subdivided into groups whose first-order contributions vanish for reasons of symmetry. The same symmetry arguments do not apply to all four-atom sets in the molecules, and hence the Boys term does not vanish.

Finally, we return to the question raised in the introductory section regarding the "distance effect" in the adamantane derivatives. By comparing the experimental magnitudes of $[m]_D$ for compounds **1** and **2c**

---

[18] H. A. Stuart, "Molekülstruktur," Verlag von Julius Springer, Berlin, 1934, p 183 ff.

[19] K. G. Denbigh, *Trans. Faraday Soc.*, **36**, 936 (1940).

[20] C. G. LeFèvre and R. J. W. LeFèvre, *Rev. Pure Appl. Chem.*, **5**, 261 (1955).

[21] R. L. Rowell and R. S. Stein, *J. Chem. Phys.*, **47**, 2985 (1967).

(Table III), we see that the distance effect is a 23-fold decrease in this case. Similarly, a comparison of the data for compound **2a** with the rotation of L-α-bromopropionic acid ($[m]^{25}$D = $-26.3°$, neat)[22] gives a distance effect of about 43-fold in this case. As expected, these effects are larger than predicted for first-order contributions. Assuming that the intergroup distances increase by a factor of 2 in these molecules, then the second-order contributions would fall off by a factor of $2^5 = 32$, which is comparable to the observed effects. Thus it may be that a second-order "group polarizability" calculation could account for the observed rotations. However, in view of the difficulties found here with the convergence of the perturbation series, such a conclusion would be unjustified in the absence of a calculation which considers higher orders as well.

Experimental Methods[23]

1-Methyladamantane was prepared in 10–60% yields by the method of Schleyer and Nicholas.[24] The crude melting point was 95–97°, and that of sublimed material was 103–104° (lit.[24] 104.6–105.1°). Gas chromatographic analysis indicated the crude product to be greater than 97% pure.

1-Methyl-3-bromoadamantane was prepared following the general procedure of Landa, Kriebel, and Knobloch.[25] A solution of 25 g (0.11 mol) of 1-methyladamantane and 150 ml of bromine was refluxed for 4 hr at 100°, then allowed to cool to room temperature and stand overnight. The solution was poured over ice and 300 ml of chloroform added. Sodium bisulfite was added in small portions until the red color of bromine no longer persisted. The chloroform layer was separated, washed twice with water, and dried over calcium chloride. Chloroform was removed under reduced pressure and the residual oil distilled under vacuum. The fraction boiling at 80–85° (2.5 mm) was collected. Distillation through a 6-in. Vigreux column gave 33 g (90%), bp 98–99° (4.5 mm).

Anal. Calcd for $C_{11}H_{17}Br$: C, 57.62; H, 7.47; Br, 34.89. Found: C, 57.76; H, 7.24; Br, 34.52.

3-Methyladamantane-1-carboxylic Acid. A mixture of 10 g (0.044 mol) of 1-methyl-3-bromoadamantane and 150 ml of concentrated sulfuric acid was cooled in an ice–salt bath to 0° and 50 ml of 98% formic acid added dropwise. The mixture turned red, then orange, and was stirred vigorously overnight. The resulting solution was poured over ice and allowed to stand for 2 hr, during which the acid precipitated. The mixture was extracted with two portions of ether and the combined ether extracts were washed with water. The ether solution was extracted three times with 25-ml portions of a 20% sodium hydroxide solution. The combined basic extracts were acidified with dilute sulfuric acid and gave 6.5 g (78%) of the acid, mp 100–101°.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.13; H, 9.34. Found: C, 74.31; H, 9.16.

3-Methyl-5-bromoadamantane-1-carboxylic acid was prepared following the general bromination procedure of Stetter and Mayer.[26] The entire reaction setup was placed in a glove-bag under an argon atmosphere with an 800-ml beaker of phosphorus pentoxide. The apparatus, which consisted of a 300-ml flask fitted with a drying tube (calcium chloride and phosphorus pentoxide) and a stirrer, was placed in the glove-bag along with 100 ml of bromine (distilled from phosphorus pentoxide), 60 g of aluminum bromide, and 30 g (0.15 mol) of 3-methyladamantane-1-carboxylic acid. While argon flushed the system, it was dried out for at least 4 hr. The bag was tied up around the bottom of the flask so that the reaction mixture could be chilled. The bromine and aluminum bromide were placed in the flask and the mixture cooled for 1 hr. While the mixture was stirred and chilled, 3-methyladamantane-1-carboxylic acid was added portionwise over a period of 4 hr. The mixture was allowed to stand for 48 hr in an ice–water bath, allowed to warm up to room temperature, and stirred for 6 hr. The reaction mixture was slowly poured over ice and 500 ml of chloroform added. Sodium bisulfite was added with constant agitation until the red bromine color disappeared. The chloroform layer was separated and the aqueous layer washed twice with 100 ml of chloroform. The chloroform solution was washed twice with water, followed by three extractions employing 200 ml of 10% sodium hydroxide. After the addition of 200 g of ice, the sodium hydroxide solution was acidified with cold, dilute sulfuric acid. The mixture was allowed to stand for 2 hr. The crude acid was separated by filtration and dissolved in 300 ml of 30% aqueous methanol and chilled. The acid precipitated as a colorless powder, mp 132–134°, and was recrystallized from cyclohexane to give 35 g (80%) of pure material, mp 134–135°.

Anal. Calcd for $C_{12}H_{17}O_2Br$: C, 52.74; H, 6.22; Br, 29.30. Found: C, 52.86; H, 6.24; Br, 29.26.

Resolution of 3-Methyl-5-bromoadamantane-1-carboxylic Acid. A solution of 32.8 g (0.1 mol) of quinine and 27.3 g (0.1 mol) of 3-methyl-5-bromoadamantane-1-carboxylic acid was prepared in 1 l. of 10% hot aqueous acetone. The solution was treated with charcoal and filtered hot. The solution was placed in a water bath maintained between 50 and 55° overnight and stirred constantly. This gave 20 g (33%) of salt, mp 179–180°. The same procedure was repeated with reduction in solvent volume and temperature to a point which allowed crystallization to occur over a period of 4–6 hr. After four recrystallizations the melting point of the salt reached a maximum of 189–190°.

The following general procedure was employed in the cleavage of all salts described. The salt was treated with concentrated hydrochloric acid followed by the addition of distilled water. The mixture was then extracted twice with chloroform. The chloroform solution was washed twice with water. It was then extracted twice with a concentrated solution of sodium hydroxide. After separation, ice was added to the sodium hydroxide solution followed by cold hydrochloric acid until the mixture was acid. The precipitated acid was taken up in ether and dried with calcium chloride.

3-Methyl-5-bromoadamantane-1-carboxamide. A solution containing 10 g (0.036 mol) of 3-methyl-5-bromoadamantane-1-carboxylic acid in 20 ml of thionyl chloride was refluxed on a steam bath for 1 hr. The excess thionyl chloride was removed under reduced pressure. The residue was chilled and added to a cold, concentrated solution of aqueous ammonia. The mixture was stirred overnight. The residue was taken up in ether, and the ether solution was washed twice with water. The separated ether solution was dried over sodium sulfate. The ether was removed. The solid residue was recrystallized from ethanol and gave 7.2 g (70%), mp 112–114°.

Anal. Calcd for $C_{12}H_{18}NOBr$: C, 52.93; H, 6.61; N, 5.14; Br, 29.41. Found: C, 53.10; H, 6.62; N, 4.89; Br, 28.52.

The identical procedure was followed in the preparation of the optically active 3-methyl-5-bromoadamantane-1-carboxamide from the optically active acid (10 g, 0.036 mol), and gave 7.5 g (74%) of the amide, mp 116–117°.

Anal. Calcd for $C_{12}H_{18}NOBr$: C, 52.93; H, 6.61; N, 5.14. Found: C, 52.81; H, 6.93; N, 5.30.

3-Methyl-5-bromo-1-cyanoadamantane was prepared by the general procedure of Krynitsky and Carhart.[27] A mixture of 3 g (0.011 mol) of 3-methyl-5-bromoadamantane-1-carboxamide, 5 ml of dry benzene, and 3 ml (0.03 mol) of thionyl chloride was placed in a flask fitted with a reflux condenser and a calcium chloride drying tube. The flask was placed in a preheated bath maintained at 75–80°. The mixture was refluxed for 5 hr. The system was allowed to reach room temperature, chilled in an ice bath, and poured into 25 g of ice and water. Cold, 50% sodium hydroxide solution was added until the mixture was alkaline to litmus. The mixture was extracted with ether. The ether solution was washed with water and dried over sodium sulfate. The ether–benzene solvent was removed under reduced pressure and the oily residue was recrystallized, with difficulty, from a methanol–water mixture. A colorless crystalline product (1.6 g, 60%) was obtained, mp 65–66°.

Anal. Calcd for $C_{12}H_{16}NBr$: C, 56.69; H, 6.29; N, 5.51; Br, 31.49. Found: C, 56.45; H, 6.42; N, 5.29; Br, 31.76.

The identical procedure was followed in the preparation of the optically active 3-methyl-5-bromo-1-cyanoadamantane from optically active 3-methyl-5-bromoadamantane-1-carboxamide (3 g, 0.011 mole) and gave 1.3 g (50%) of product, mp 68–69°.

Anal. Calcd for $C_{12}H_{16}NBr$: C, 56.69; H, 6.29; N, 5.51; Br, 31.49. Found: C, 56.93; H, 6.37; N, 5.41; Br, 30.51.

---

[22] L. Ramberg, *Ann. Chem.*, **370**, 234 (1909).

[23] Melting points are uncorrected. Microanalyses were done by Mr. Josef Nemeth and associates.

[24] P. von R. Schleyer and R. D. Nicholas, *Tetrahedron Letters*, 305 (1961).

[25] S. Landa, S. Kriebel, and E. Knobloch, *Chem. Listy*, **48**, 61 (1954).

[26] H. Stetter and J. Mayer, *Chem. Ber.*, **95**, 667 (1962).

[27] J. A. Krynitsky and H. W. Carhart, *Org. Syn.*, 32, 65 (1952).

Optical Rotation Measurements. The optical rotatory dispersion of 3-methyl-5-bromo-1-cyanoadamantane was measured in the 365–600-nm range on a Rudolph manual spectropolarimeter Model 200S/340/80AQ6 modified as described elsewhere.[28] The 1-dm polarimeter tube containing the solution was thermostated by means of water circulating around the polarimeter trough. The temperature was measured with an iron–constantan thermocouple inserted in a glass well in the filling port. Rotation readings were repeated five to ten times, giving standard deviations of the mean in the range 0.6–1.3 mdeg, or 1–3% of the mean rotation as limited by the available quantity of the compound. Other optical rotation measurements were made in part on a Bendix Model 143A electronic polarimeter, and in part by Dr. Donald Fraembs of the Bendix Corporation on Bendix Models 1184-00, S/N L40511017 and 1164-00, S/N L40411018.

Acknowledgments. This research was supported in part by grants from the National Institute of General Medical Sciences (GM-13684), the National Science Foundation (GP-4681), and the American Chemical Society Petroleum Research Fund (1690-A,1).

---

[28] J. M. Rifkind and J. Applequist, *J. Am. Chem. Soc.*, **90**, 3650 (1968).

Intermediate Species in the Flash Excitation of a Conjugated Ketone

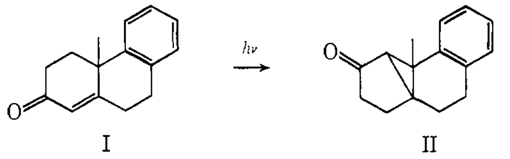
Göran Rämme, Robert L. Strong, and Herbert H. Richtol

Contribution from the Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181.

Received March 26, 1969

Abstract: Excited states and intermediates of the conjugated cyclohexenone 7-keto-13-methyl-5,6,7,9,10,13-hexahydrophenanthrone have been studied flash spectrophotometrically. Two transient species differing in spectral and decay characteristics are observed, the longer lived being the ketyl radical formed by hydrogen-atom abstraction. The shorter lived intermediate is presumed to be a triplet state, but is not the triplet precursor to the isomeric rearrangement or reduction reactions; this latter species was not observed directly, but was detected by triplet–triplet energy transfer to naphthalene. Neither directly observed species was optically active within the limit of detection of the flash spectropolarimeter, although optical activity is retained in the isomeric photoproduct.

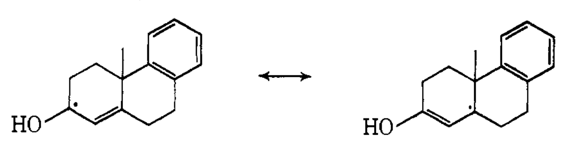
Conjugated cyclohexenones undergo rearrangements photochemically,[1] although at a much lower quantum efficiency than for corresponding cyclohexadienones.[2] A particularly interesting example is 7-keto-13-methyl-5,6,7,9,10,13-hexahydrophenanthrone I which rearranges to the bridged isomeric photoketone II.



(1)

Photoexcitation of either of the enantiomeric forms of I leads to at least 95% retention (but opposite rotation) of the optical activity in II[3] showing that the rearrangement is stereospecific; it cannot take place through complete fission of the 1,10 bond leading to an intermediate having a plane of symmetry, but most involve 4–10 and 1–5 concerted bond formation also.[2] This rearrangement to II proceeds through a triplet state,[2] which must also be optically active and therefore possibly amenable to studies by the flash spectropolarimetric technique.[4] Since I is an α,β-unsaturated ketone, it is an inherently dissymmetric chromophore and therefore should have a much greater rotational strength than corresponding inherently symmetric carbonyl chromophore-containing molecules.[5] (This high rotational strength depends on the angle of skewness of the carbonyl-containing ring, however, which may be significantly altered in the excited state.)

Ketones also undergo photoreduction by way of triplet-state hydrogen abstraction from the solvent molecules, the extent of abstraction being influenced by the nature of the substrate as well as by the rate of isomeric rearrangement. Zimmerman, *et al.*,[2] found that in *t*-butyl alcohol the isomerization (1) was the only irreversible reaction, whereas in isopropyl alcohol a pinacol was formed by dimerization of the radical



(2)

formed by hydrogen abstraction.

The present work was undertaken to determine the nature of the intermediate(s) in the rearrangement and abstraction reactions by direct flash spectrophotometry.

Experimental Section

The flask spectrophotometric apparatus, modified for transient polarimetric measurements, has been described.[4,6] Except for a few runs in which the effect of flash light intensity was determined by varying the flash discharge energy, all of the data reported here

---

[1] K. Schaffner, *Advan. Photochem.*, **4**, 81 (1966).

[2] H. E. Zimmerman, R. G. Lewis, J. J. McCullough, A. Padwa, S. S. Staley, and M. Semmelhack, *J. Am. Chem. Soc.*, **88**, 159, 1965 (1966).

[3] O. L. Chapman, J. B. Sieja, and W. J. Welstead, Jr., *ibid.*, **88** 162 (1966).

[4] P. A. Carapellucci, H. H. Richtol, and R. L. Strong, *ibid.*, **89**, 1742 (1967).

[5] A. Moscowitz, *Proc. Roy. Soc.*, **A297**, 16 (1967).

[6] R. L. Strong and H. H. Richtol in "Fast Reactions and Primary Processes in Chemical Kinetics," S. Claesson, Ed., Almqvist and Wiksell, Stockholm, 1967, p 71.