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RESEARCH ARTICLES

Absolute Configuration of *cis*- and *trans*-2-(*o*-Bromophenyl)cyclohexanols and (+)-*cis*-2-(*o*-Bromophenyl)cyclohexylamine

TODD G. COCHRAN*, DARRYL V. WAREHAM, and ALAIN C. HUITRIC

Abstract □ The absolute configurations of (−)-*trans*-2-(*o*-bromophenyl)cyclohexanol (V), (+)-*cis*-2-(*o*-bromophenyl)cyclohexanol (VII), and (+)-*cis*-2-(*o*-bromophenyl)cyclohexylamine (X) have been chemically related to that of (2S)-(−)-2-(*o*-bromophenyl)-cyclohexanone (VI), whose absolute configuration can be reliably assigned from its optical rotatory dispersion and circular dichroism spectra.

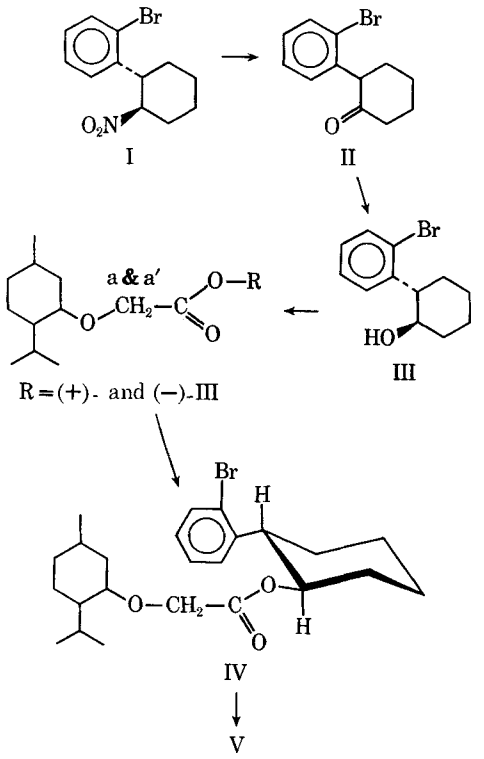
Keyphrases □ *cis*- and *trans*-2-(*o*-Bromophenyl)cyclohexanols and (+)-*cis*-2-(*o*-bromophenyl)cyclohexylamine—synthesis, absolute configuration □ Absolute configuration—cyclohexanol and cyclohexylamine derivatives □ IR spectrophotometry—identity □ NMR spectroscopy—identity □ Optical rotatory dispersion—structure □ Circular dichroism—structure

Concurrent with the study of the optical rotatory dispersion (ORD) and circular dichroism (CD) of the aromatic chromophore, it became necessary to synthesize, resolve, and assign the absolute configuration to a number of substituted 2-arylcyclohexanols and cyclohexylamines. Galpin and Huitric discussed the resolution (1) and absolute configurations (2) of (1S,2R)-(+)-*trans*-2-*o*-tolylcyclohexanol and (1R,2R)-(−)-*cis*-2-*o*-tolylcyclohexanol. The assignment of absolute configuration was based on the sign of the Cotton effect of the (2R)-(+)-2-*o*-tolylcylcohexanone obtained upon oxidation of the *cis*- and *trans*-alcohols, and it has recently been confirmed by single-crystal X-ray diffraction analysis of the 3-nitro-4-bromobenzoate of the (+)-*trans*-alcohol (3). In this paper, the authors report on the synthesis and optical resolution of (−)-*trans*-2-(*o*-bromophenyl)cyclohexanol (V) and its conversion to (−)-2-(*o*-bromophenyl)cyclohexanone (VI), (+)-*cis*-2-(*o*-bromophenyl)cyclohexanol (VII), and (+)-*cis*-2-(*o*-bromophenyl)cyclohexylamine (X). The absolute configuration of this series of compounds can be related to that of the ketone VI, whose absolute configuration is assigned from its ORD and CD spectra.

The synthesis and optical resolution of *trans*-2-(*o*-bromophenyl)cyclohexanol (V) are depicted in Scheme I. Racemic 2-(*o*-bromophenyl)cyclohexanone (II) was obtained from the permanganate oxidation (4, 5) of the potassium aci-nitro salt of *trans*-2-(*o*-bromophenyl)-nitrocyclohexane (I), which was previously prepared as an intermediate in the synthesis of the *cis*- and *trans*-2-(*o*-bromophenyl)cyclohexylamines (6). Reduction of II with lithium aluminum hydride gave *trans*-2-(*o*-bromophenyl)cyclohexanol (III) as the predominant isomer. The racemic mixture of alcohols III was resolved by fractional crystallization of its diastereomeric (−)-menthoxyacetate esters, in the manner described by Galpin and Huitric for the resolution of *trans*-2-*o*-tolylcyclohexanol (1). The resolution was conveniently followed by NMR spectroscopy, utilizing the magnetic nonequivalence of the geminal methylene protons (hydrogens a and a′) on the acetate portion of the esters.[1] This nonequivalence is sufficiently different in the two diastereomeric esters to allow the progression of the separation of the two diastereomers to be readily followed by NMR.

Figure 1 shows the pertinent portions of the NMR spectra of a 50:50 mixture of the diastereomers (A) and

[1] For a general discussion of the use of NMR spectroscopy as a monitor for optical purity, see Raban and Mislow (7). For the specific application to (−)-menthoxyacetates, see Galpin and Huitric (1).



Scheme I

the pure menthoxyacetate IV (B). The signals of the methylene hydrogens (a and a′) appear as highly skewed doublets with geminal coupling of 15.5 Hz.; but the nonequivalence is not the same in the two diastereomers, thus making them readily distinguishable. The NMR spectrum of the pure (−)-*trans*-2-(*o*-bromophenyl)-cyclohexyl (−)-menthoxyacetate (IV) shows no indication of the presence of the other diastereomer, indicating that this ester is of at least 90% optical purity (95% diastereomeric purity).[2] Basic hydrolysis of IV afforded the (−)-*trans*-alcohol V.

The chemical conversion of V to the other compounds in this series is depicted in Scheme II. All conversions involve chemical modification at C-1; thus the absolute configuration of the benzylic carbon, C-2, is conserved. Chromic acid oxidation of V in a two-phase ether–aqueous system afforded (−)-2-(*o*-bromophenyl)cyclohexanone (VI). Reduction of VI with triisobutylaluminum (8) yielded (+)-*cis*-2-(*o*-bromophenyl)cyclohexanol (VII) as the predominant isomer. The *cis*-isomer VII was obtained in pure form by column chromatography on neutral alumina, followed by crystallization from hexane. The relative stereochemistry of the C-1 hydroxyl group of the *cis*- and *trans*-alcohols V and VII can be readily determined from the NMR spectra, which are consistent with the conformations shown in Scheme II.[3] The *trans*-alcohol V was converted to its tosylate (VIII) by the usual procedure and then to its C-1 epimeric azide by the stereospecific displacement of the tosylate with sodium azide in dry *N*-methylpyrroli-

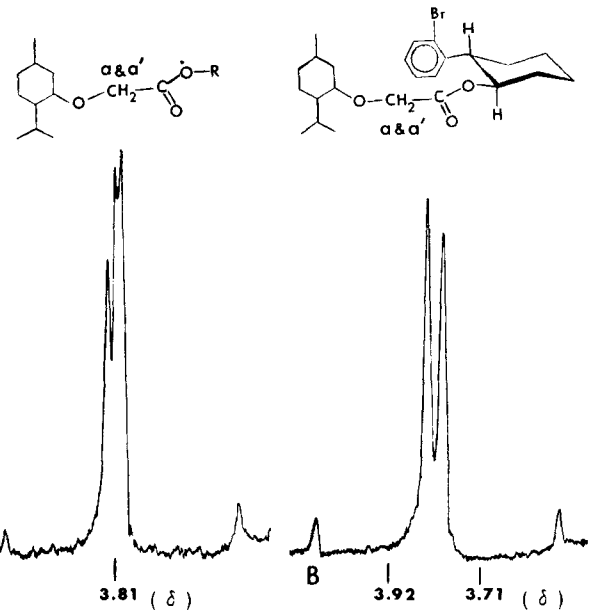
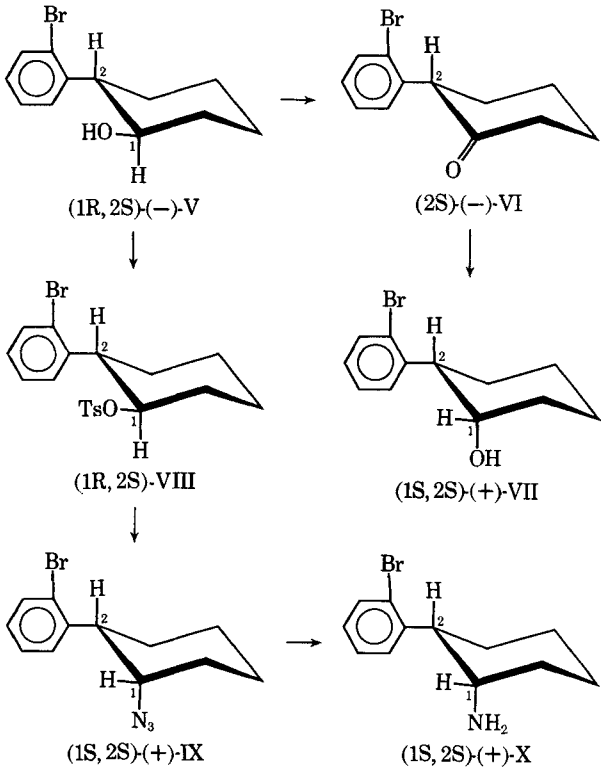


Figure 1—*Portions of the 60-MHz. NMR spectra (250 Hz. sweep width) of the* trans-*2-(o-bromophenyl)cyclohexyl (−)-menthoxyacetates measured in chloroform-*d *at 37°. Key: A, 50:50 mixture of diastereomers [R = (+)- and (−)-III]; and B, pure IV.*

done (10). The (+)-*cis*-azide (IX) was obtained as the exclusive displacement product from this reaction.[4]

The *cis*-configuration of this azide and the *trans*-configuration of the tosylate VIII are confirmed from their NMR spectra, parts of which are shown in Fig. 2. Spectrum A shows the signal of H-1 at δ 4.68 and of



Scheme II

[2] This NMR method has an estimated sensitivity of at least 95% in determining diastereomeric purity. This is discussed further by Raban and Mislow (7).

[3] Determination of the conformation and relative configuration of *cis*- and *trans*-2-arylcyclohexanols by NMR was discussed by Huitric *et al.* (9).

[4] Djerassi *et al.* (11) demonstrated that the similar displacement of steroidal mesylates with sodium azide in dimethyl sulfoxide proceeds with a high degree of stereospecificity.

H-2 at δ 3.33 for the tosylate VIII. The width of about 25 Hz. and the apparent six-peak multiplet for each signal are consistent with both H-1 and H-2 having axial orientations and being adjacent to two axial and one equatorial hydrogens. The signal of H-1 gives apparent coupling of $J_{aa} \simeq 10.5$ and $J_{ae} \simeq 4.0$ Hz. Spectrum B shows the signal of H-1 at δ 4.10 and H-2 at δ 3.24 for the azide IX. The narrow signal of H-1 (half-weight width of about 7 Hz.) is consistent with H-1 having an equatorial orientation.The six-peak multiplet of H-2 indicates that this hydrogen has an axial orientation and is adjacent to one axial and two equatorial hydrogens. The apparent coupling constants are $J_{aa} \simeq 11.5$ and $J_{ae} \simeq 3$ Hz. Thus, the NMR spectra also establish that in chloroform both VIII and IX have a very high time-average population of the chair conformation with the *o*-bromophenyl group in an equatorial orientation.

Lithium aluminum hydride reduction of the azide IX afforded (+)-*cis*-2-(*o*-bromophenyl)cyclohexylamine (X) in good yield. Formylation of this amine in a toluene–formic acid mixture produced (+)-*cis*-2-(*o*-bromophenyl)cyclohexyl formamide (XI), which was physically and spectrally identical to the formamide of the (+)-*cis*-2-(*o*-bromophenyl)cyclohexylamine previously resolved through its (−)-menthoxyacetamide (6).

Although these reactions can be expected to proceed with a high degree of stereospecificity, a small amount of racemization cannot be ruled out. Therefore, the optical purity of the compounds subsequent to ester IV cannot be stated with certainty.[5] However, since the specific rotation of the formamide XI agrees within 1% of that of the identical formamide obtained from the *cis*-amine resolved as its (−)-menthoxyacetamide (6), the optical purity of the entire series would appear to be quite high.

The absolute configuration of the ketone VI and of the benzylic carbon, C-2, of the compounds that have been related to it can be reliably obtained from the sign of the Cotton effect of the $n \rightarrow \pi^*$ transition of the carbonyl chromophore, as determined from ORD and CD spectra. The NMR spectrum of VI is consistent with a conformation in which the cyclohexane ring is in a chair form with the aryl group in an equatorial orientation, as seen for other 2-arylcyclohexanones (13). This equatorial orientation of the aromatic ring prevents the direct application of the octant rule (14) for assignment of absolute configuration. However, Galpin and Huitric (2) were able to assign the absolute configuration of (+)-2-*o*-tolylcyclohexanone as (2R) by comparison with the ORD curve of 3-β-phenyl-2-cholestanone, and their assignment has recently been proven correct by X-ray crystallographic studies (3). The ORD and CD spectra of (−)-2-(*o*-bromophenyl)cyclohexanone VI, shown in Fig. 3, are almost exact mirror images, both qualitatively and quantitatively, of those reported for (2R)-(+)-2-*o*-tolylcyclohexanone (2); thus the (−)-ketone VI can be reliably assigned a (2S) configuration. This establishes a (2S) configuration for the benzylic carbon of the compounds that were related chemically with VI.

[5] Brown and Garg (12) showed that the two-phase oxidation procedure used for obtaining VI from V proceeds without racemization of asymmetric centers adjacent to a carbonyl.

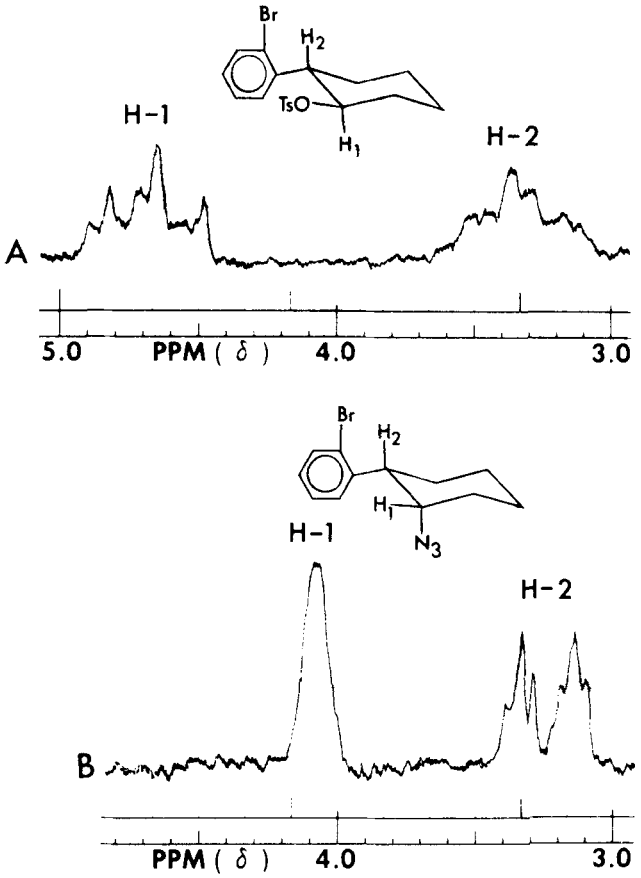


Figure 2—*Portions of the 60-MHz. NMR spectra of VIII (A) and IX (B) measured in chloroform-*d *at 37°.*

The ORD and CD spectra of the *cis*-alcohol VII and *cis*-amine X show Cotton effects of the same sign for the ^1L_a and ^1L_b transitions of the aromatic chromophore. This similarity is also true between the *trans*-alcohol V and (+)-*trans*-2-(*o*-bromophenyl)cyclohexylamine of the same chirality, whose resolution (6) and absolute configuration (15) were reported. This indicates a similarity in the nature of the dissymmetric perturbation of the aromatic chromophore by the amino and hydroxyl substituents. The ORD and CD spectra of the *cis*- and *trans*-amines and alcohols will be discussed in detail in a subsequent publication.

EXPERIMENTAL[6]

2-(o-Bromophenyl)cyclohexanone (II)—To a stirred solution of 10.5 g. (0.037 mole) of *trans*-2-(*o*-bromophenyl)nitrocyclohexane (I) (6) in 735 ml. of dioxane was slowly added 735 ml. (0.145 mole) of 0.2 *M* aqueous potassium hydroxide. The resulting clear solution was stirred at room temperature for 40 min., cooled in an ice–salt bath to 0°, and then brought to a pH of approximately 7.5 by the rapid addition of 295 ml. (0.59 mole) of 2.0 *M* aqueous magnesium sulfate. A solution of 4.2 g. (0.026 mole) of potassium permanganate in 100 ml. of water was added with stirring over a period of 30

[6] Melting points were determined on a Kofler micro hotstage and are corrected. Specific rotations were measured at ambient room temperature with a Rudolph polarimeter using a sodium lamp and a 2-dcm. tube. IR spectra were obtained on a Beckman IR5-A spectrophotometer. All NMR spectra were measured in the solvent specified on a Varian A-60 spectrometer using tetramethylsilane (TMS) as an internal reference. The ORD and CD spectra were obtained on a Cary 60 spectropolarimeter equipped with a model 6001 CD accessory. All VPC analyses were done on an F&M 5750 gas chromatograph equipped with hydrogen-flame detectors. Elemental analyses were performed by Huffman Laboratories, Wheatridge, Colo.

min. at 0–5°. This wine-colored mixture was stirred for an additional 20 min. and then extracted with 2 l. of ether in four portions. The combined ether solutions were washed with water, 10% hydrochloric acid, and water until neutral and then dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded a pale-yellow oil, which was taken up in a small amount of ether and crystallized from hexane–ether (10:1). Decolorization with charcoal and recrystallization afforded 8 g. (87%) of colorless crystals, m.p. 58.2–59°, IR (mineral oil) 5.85 μ (C=O); NMR ($CDCl_3$) δ 4.08 (broad mult., half-width 19 Hz., 1 H, axial H on C-2).

Anal.—Calcd. for $C_{12}H_{13}BrO$: C, 56.94; H, 5.18. Found: C, 56.83; H, 5.28.

***trans*-2-(*o*-Bromophenyl)cyclohexanol (III)**—A solution of 7.8 g. (0.031 mole) of II in 150 ml. of anhydrous ether was added over a period of 1 hr. to a stirred slurry of 1.18 g. (0.031 mole) of powdered lithium aluminum hydride in 250 ml. of anhydrous ether. The mixture was stirred for an additional 1 hr.; then the excess lithium aluminum hydride was destroyed by the dropwise addition of an aqueous 40% Rochelle salts solution. This mixture was diluted with water and acidified with 10% hydrochloric acid. The ether layer was separated, and the aqueous phase was extracted twice with ether. The combined ethereal solutions were washed with water, 10% sodium carbonate, and water until neutral and then dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded 7.64 g. (97%) of a colorless oil, which solidified upon standing. Analysis of this solid by VPC on an Apiezon column at 200° showed this material to be composed of 88% of the *trans*-alcohol III, 6% of its *cis*-isomer, and 6% of the debrominated 2-phenylcyclohexanols in the same *trans*/*cis* ratio. Repeated fractional crystallization of this mixture from hexane at room temperature yielded the pure *trans*-alcohol III, m.p. 73-73.5°; IR (mineral oil) 3.0 μ (O—H).

Anal.—Calcd. for $C_{12}H_{15}BrO$: C, 56.49; H, 5.93. Found: C, 56.62; H, 6.01.

(+) and (−)-*trans*-2-(*o*-Bromophenyl)cyclohexyl (−)-Menthoxyacetates—To a solution of 6.7 g. (0.026 mole) of III and 23 ml. (0.29 mole) of dry pyridine in 100 ml. of anhydrous ether was slowly added a solution of 6.7 g. (0.028 mole) of (−)-menthoxyacetyl chloride[7] (14) in 30 ml. of anhydrous ether. This mixture was allowed to stand at room temperature for 2 days and was then diluted with 100 ml. of ether. This ethereal solution was washed with cold 10% hydrochloric acid, water, cold 10% sodium carbonate, and water until neutral and then dried over anhydrous sodium sulfate. Filtration and removal of solvent yielded 11.8 g. (99%) of viscous oil.

(−)-*trans*-2-(*o*-Bromophenyl)cyclohexyl (−)-Menthoxyacetate (IV)—This compound was obtained by fractional crystallization of the mixture of diastereomeric menthoxyacetates from hexane at room temperature. The crude ester mixture was dissolved in 100 ml. of hot hexane and allowed to cool to room temperature. Compound IV crystallizes first in rocklike crystals. The most soluble diastereomer crystallizes in needle-shaped crystals. The rocklike crystals were recrystallized from hexane to a constant melting point, affording 7.8 g. from 28 g. of ester of colorless crystals, m.p. 111.7–112.7°; $[\alpha]_D = -43°$ (c 6, chloroform); IR (mineral oil) 5.70 μ (C=O). The NMR spectrum indicated the presence of only one diastereomer.

(−)-*trans*-2-(*o*-Bromophenyl)cyclohexanol (V)—To a solution of 2 g. of IV in 30 ml. of 95% ethanol was added 15 ml. of aqueous 25% sodium hydroxide, and the resulting mixture was refluxed for 3 hr. The solution was cooled, diluted with 100 ml. of cold water, and extracted with three 50-ml. portions of ether. The ethereal extracts were washed with water until neutral and then dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded a pale-yellow oil, which was vacuum distilled to give an essentially quantitative yield of colorless oil, b.p. 104–106° at 0.1 mm.; $[\alpha]_D = -68°$ (c 5, methanol); IR (neat) 2.95 μ (O—H). The NMR spectrum was identical to that of its racemic modification III.

(−)-2-(*o*-Bromophenyl)cyclohexanone (VI)—To a stirred solution of 510 mg. (2.0 mmoles) of V in 15 ml. of ether was added a solution of 1.0 g. (3.3 mmoles) of sodium dichromate dihydrate and 0.8 ml. of 96% sulfuric acid in 15 ml. of water; the resulting mixture was stirred for 5 hr. and then diluted with 15 ml. of ether. The two phases were separated, and the aqueous layer was extracted with two 15-ml. portions of ether. The combined ethereal solutions were washed with water, 10% sodium carbonate, and water until neutral and then dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded an oil which was shown by VPC analysis on an XE-60 column at 200° to contain less than 5% of the starting alcohol V. This material was crystallized from hexane to give 400 mg. (80%) of colorless crystals, m.p. 82.5–83.5°; $[\alpha]_D = -16°$ (c 3, methanol); IR (mineral oil) 5.86 μ (C=O). The NMR spectrum was identical to that of its racemic modification II. ORD in methanol (c 0.102 $[M]_{400}$ −248°, $[M]_{307}$ −2830° (trough), $[M]_{274}$ +4120° (peak), $[M]_{272}$ +3600° (trough), $[M]_{268}$ +4170° (peak), $[M]_{258}$ +3380° (trough), $[M]_{240}$ +4750°; CD in methanol (c 0.102) $[\theta]_{325}$ 0.0°, $[\theta]_{286}$ −5060°, $[\theta]_{246}$ 0.0°, $[\theta]_{240}$ +500°.

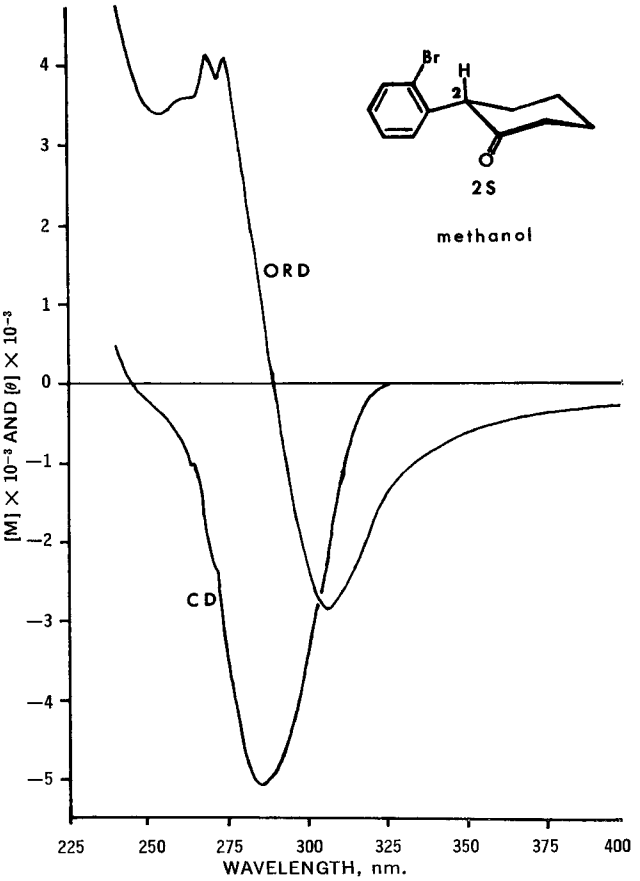


Figure 3—*ORD and CD curves of* (−)-*2*-(o-*bromophenyl*)*cyclohexanone VI.*

(+)-*cis*-2-(*o*-Bromophenyl)cyclohexanol (VII)—A solution of 0.48 g. (1.9 mmoles) of VI in 15 ml. of dry benzene was added over 15 min. to a stirred solution of 1.2 g. (6.1 mmoles) of triisobutylaluminum[8] in 25 ml. of dry benzene under nitrogen, and the resulting solution was stirred for an additional 45 min. This mixture was decomposed by the careful addition of 10 ml. of cold water while stirring and cooling in an ice bath, acidified with 10% hydrochloric acid, and extracted with 75 ml. of ether in three portions. The ethereal solution was washed with water until neutral and dried over anhydrous sodium sulfate. Filtration and removal of solvent yielded 0.47 g. of an oil, which was shown by VPC analysis on an Apiezon column at 200° to be a mixture of the *cis*- and *trans*-alcohols in a ratio of 4:1. Column chromatography of this mixture on alumina (Merck, neutral), using hexane and hexane–benzene mixtures as eluents, yielded the pure *cis*-alcohol VII, which was crystallized from hexane to give 250 mg. of colorless crystals, m.p. 63–63.5°; $[\alpha]_D = +123°$ (c 5, methanol); IR (mineral oil) 2.90 and 2.98 μ (free and bonded O—H).

Anal.—Calcd. for $C_{12}H_{15}BrO$: C, 56.49; H, 5.93. Found: C, 56.50; H, 6.03.

Tosylate of (−)-*trans*-2-(*o*-Bromophenyl)cyclohexanol (VIII)—To an ice-cold solution of 1.72 g. (6.75 mmoles) of V in 25 ml. of dry pyri-

[7] For an improved synthetic method for the preparation of this reagent, see Cochran and Huitric (6).

[8] K & K Laboratories.

dine was added 1.72 g. (9.0 mmole) of *p*-toluenesulfonyl chloride; the resulting solution was allowed to stand at refrigerator temperature for 2 days and was then diluted with 100 ml. of ice water and extracted with three 50-ml. portions of ether. The ethereal solution was washed with ice cold water, 10% hydrochloric acid, 10% sodium carbonate, and water until neutral and then dried over anhydrous sodium sulfate. The solution was filtered and concentrated to a volume of 5 ml., diluted with 10 ml. of hexane, and cooled in an ice bath to give 1.65 g. (60%) colorless fluffy crystals, m.p. 85–86°; IR (mineral oil) 8.55 μ (—SO_3—); NMR ($CDCl_3$) δ 2.32 (s, 3H, arom. —CH_3).

(+)-*cis*-2-(*o*-Bromophenyl)-1-azidocyclohexane (IX)—A vigorously stirred slurry of 1.5 g. (23 mmole) of dry sodium azide and 0.95 g. (2.3 mmole) of VIII in 50 ml. of dry *N*-methylpyrrolidone under nitrogen was slowly heated in an oil bath (4 hr.) at 90° and maintained at that temperature for 20 hr. The reaction mixture was cooled, diluted with 250 ml. of water, and extracted with three 100-ml. portions of petroleum ether (b.p. 40–50°) followed by three 100-ml. portions of ether. The combined petroleum ether and ether solutions were washed with water and dried over anhydrous sodium sulfate. Filtration and evaporation of solvent using a 40° water bath afforded 0.63 g. (98%) of an oil, which was chromatographed on silica gel, eluting with petroleum ether. A small amount of colorless oil, containing no azide stretching band in the IR, eluted first, followed by pure IX as a clear oil, IR (neat) 4.72 μ (—N_3); $[\alpha]_D = +123°$ (c 4, chloroform).

(+)-*cis*-2-(*o*-Bromophenyl)cyclohexylamine (X)—An ether solution of 0.33 g. of IX, which had not been chromatographed, was stirred with 0.15 g. of powdered lithium aluminum hydride for 2 hr., decomposed by the addition of a few drops of water, and filtered through a sintered-glass funnel. Evaporation of solvent yielded 0.27 g. (90%) of colorless oil, $[\alpha]_D = +95°$ (c 4, methanol); IR (neat) 2.98 and 3.05 μ (N—H).

(+)-*cis*-2-(*o*-Bromophenyl)cyclohexyl Formamide (XI)—A mixture of a solution of 0.25 g. of X in 10 ml. of toluene and 3 ml. of 99% formic acid was heated at gentle reflux for 1 hr. and then at a slightly higher temperature for 18 hr. so that water and formic acid azeotroped into a Dean-Stark tube. The reaction mixture was cooled, diluted with 25 ml. of ether, and washed twice with water, twice with 10% sodium carbonate, and with water until neutral; then it was dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded a yellow oil, which was crystallized from a benzene–hexane mixture to give 150 mg. of off-white crystals, m.p. 159–160°; $[\alpha]_D = +119°$ (c 2, methanol); IR (mineral oil) 3.07 μ (N—H), 5.97 and 6.08 μ (C=O).

The formamide prepared in the same manner from (+)-*cis*-2-(*o*-bromophenyl)cyclohexylamine, which was resolved as its (−)-menthoxyacetamide (6), had the following physical properties: m.p. 158–159°; $[\alpha]_D = +120°$ (c 3, methanol). The IR and NMR spectra of the two formamides were identical.

Anal.—Calcd. for $C_{13}H_{16}BrNO$: C, 55.33; H, 5.72; N, 4.96. Found: C, 55.20; H, 5.72; N. 5.15.

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Azulene Analogs of Pharmacologic Agents I: Amides

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Abstract □ The paper describes the synthesis of 15 azulene analogs of the benzenoid pharmacologic agent procainamide as part of a study of the pharmacodynamic effects of nonbenzenoid aromatic compounds. Three distinct series of compounds were prepared: azulene-1-carboxamides, 1-(3-nitroazulene)-carboxamides, and 1-(3-acetamidoazulene)-carboxamides. The preparation of 3-nitroazuloic acid, a new azulene intermediate, is also described.

Keyphrases □ Procainamide azulene analogs—synthesis □ Azulene analogs, procainamide—synthesis □ Column chromatography—separation □ IR spectrophotometry—structure □ UV spectrophotometry—structure

It is recognized that the presence of aromatic moieties in pharmacodynamic entities of varying specific activity may be prerequisite for optimal activity. These aromatic functions are, for the most part, benzenoid in nature. Several cyclic systems exist which show aromaticity but which are not benzenoid in character (1). Among these, azulene (isomeric to naphthalene), by virtue of its totally hydrocarbon nature, closely resembles benzene and its derivatives but differs in that it has a dipole moment, is a nonalternant hydrocarbon, has a resonance energy