of *m*- and *p*-isomers (du Pont Electrochemicals Department RH-870) was on hand. A mixture of 315 g. of this acid, 520 ml. of ethanol, and 2.5 l. of benzene was brought to boiling and stirred for 1 hr. The mixture was chilled and filtered. There was recovered 117 g. of almost pure *p*-isomer, m.p. 255°, m.m.p. 255° on a heated bar (lit.[5] m.p. 244°). The filtrate was concentrated to a small volume. Ethanol, 1.2 l., was added and the mixture was saturated with hydrogen chloride gas. After 20 hr. it was distilled to give 217 g. of diethyl phenylenediacetates, b.p. 127–130° (1.1 mm.). Hydrogenation was performed over 3 g. of ruthenium dioxide in 250 ml. of ethanol at 135° and 1565 p.s.i. Hydrogen, 1.4 moles (54%), was absorbed. Rehydrogenation resulted in no further uptake. The product, 174.5 g., boiled at 115–133° (0.15 mm.). The infrared spectrum showed the presence of ester groups and absence of aromatic or unsaturated links. The diester, 70.0 g., was boiled under reflux for 5 hr. with 70 g. of sodium hydroxide, 200 ml. of ethanol, and 300 ml. of water. The ethanol was distilled, and the residue was cooled and acidified with 12 *N* hydrochloric acid. After 3 days, the precipitate was filtered, rinsed with water, and air dried to give 51.0 g. of mixed cyclohexane-1,3- and 1,4-diacetic acids, m.p. 130–132°.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.1. Found: C, 59.7; H, 8.1.

Bicyclo[3.3.1]nonan-3-one (2a).—The mixture of cyclohexanediacetic acids, 26.0 g. (0.13 mole), was mixed with 50 ml. of acetic anhydride, and acetic acid was distilled over a 1-hr. period. The remainder was distilled through a Claisen head at 150 mm. using a pale blue flame. The distillate was taken up in 100 ml. of ether and washed with 100 ml. of water and with 150 ml. of 15% sodium carbonate solution. The aqueous layers were back extracted with 50 ml. of hexane. The organic layers were dried and the solvents were evaporated. Short-path distillation of the residue at 15 mm., followed by crystallization of the residue at −80° from hexane, gave 4.6 g. of an off-white solid. Sublimation at 140° (18 mm.) gave 4.06 g. (22.6%) of pure ketone, m.p. 180–182°. The use of barium oxide in place of acetic anhydride in the distillation gave a lower yield of the same ketone.

Anal. Calcd. for $C_9H_{14}O$: O, 11.6. Found: O, 11.7.

The carbonyl group absorption in the infrared spectrum[6] of this ketone was split into two bands at 1706 and 1717 cm.$^{-1}$. The 2,4-dinitrophenylhydrazone[7] melted at 208–209° after one recrystallization from ethanol–ethyl acetate.

Similarly, esterification of pure *p*-phenylenediacetic acid gave diethyl ester, m.p. 59–59.5° (lit.[5] m.p. 59–59.5°); hydrogenation gave the diethyl ester of cyclohexane-1,4-diacetic acid; and hydrolysis provided cyclohexane-1,4-diacetic acid, m.p. 164–165°, which was analyzed.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.1. Found: C, 59.8; H, 8.2.

Distillation of the 1,4-diacid from barium oxide gave no ketonic product, proving that the ketone described above was derived from cyclohexane-1,3-diacetic acid.

Bicyclo[3.3.1]nonan-3-one Oxime (2b).—The crude oxime, b.p. 113–115° (1.0 mm.), 12.25 g., was obtained as described[2] from 12.79 g. (0.0925 mole) of ketone as a white solid in the receiver, m.p. 108–114°. Recrystallization from 30 ml. of hexane gave 10.10 g. (71.3%) of oxime, m.p. 108–109°.

Anal. Calcd. for $C_9H_{15}ON$: N, 9.14. Found: N (Dumas), 9.36.

3-Azabicyclo[4.3.1]decan-4-one (3).—The oxime **2b**, 9.92 g. (0.065 mole), led by Beckmann rearrangement[8] to a lactam which sublimed at 100–160° (0.45 mm.), 6.2 g. This was taken up in 25 ml. of hexane and crystallized at −80° to give 3.30 g. of white solid. Crop 2, 1.26 g., and crop 3, 0.98 g., were obtained by evaporation of the solvent and crystallization again at −80°. The combined yield was 55.9%.

Anal. Calcd. for $C_9H_{15}ON$: N, 9.14. Found: N, 8.84, (crop 1), 8.77 (crop 2), 8.73 (crop 3).

These fractions did not melt sharply but rather became semisolid at 80–120°. They were evidently polymerizing during the determination.

Nopinone Oxime (6b).—"Sulfate" β-pinene, from Hercules Powder Co., was established as 91% pure by vapor phase chromatography. It was ozonized as described by Meinwald and Gassman[1] to give nopinone, b.p. 92° (16 mm.), 99+% pure by v.p.c. The oxime was prepared as described.[2] Distillation of the oxime prepared from 38.2 g. of nopinone gave 40.1 g., b.p. 107° (1.5 mm.). It crystallized slowly and completely. Recrystallization from 20 ml. of heptane gave 33.2 g. oxime, m.p. 61.5–65.0°.

Anal. Calcd. for $C_9H_{15}ON$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.50, 70.46; H, 9.99, 10.06; N, 8.86, 8.97.

7,7-Dimethyl-2-azabicyclo[4.1.1]octan-3-one (7).—The Beckmann rearrangement of 23.1 g. of oxime was carried out using sodium hydroxide and benzenesulfonyl chloride.[8] The chloroform extract was concentrated and diluted with 800 ml. of ether. Flocculent material was filtered. The filtrate was concentrated and distilled at 0.3 mm. up to 130°. The distillate solidified in the receiver and considerable undistillable residue remained. After three sublimations and crystallization from 15 ml. of heptane, the lactam weighed 9.85 g. (42.6%) and melted at 111.0–113.0°.

Anal. Calcd. for $C_9H_{15}ON$: C, 70.6; H, 9.9; N, 9.14. Found: C, 70.5, 70.3; H, 9.9, 9.9; N, 8.91, 8.91.

The infrared spectrum was consistent with that of a lactam, although no 6.50-μ band was observed.

Polymerizations.—Lactam **3**, 1.50 g., was polymerized by heating with 1 drop of water and 1 drop of 85% phosphoric acid[2,4] in a sealed glass tube under nitrogen for 8.5 hr. at 223°. The polyamide 4 of *cis*-3-aminomethylcyclohexylacetic acid weighed 1.32 g. (88.0%) after washing with water and acetone. It melted at 297° and had an inherent viscosity in *m*-cresol of 0.21.

Lactam **7** was polymerized similarly by 5% of 85% phosphoric acid at 200° for 17 hr., and a 75% yield of product was obtained after methanol extraction. The polyamide **8** of *cis*-3-amino-2,2-dimethylcyclobutanepropionic acid melted at 358° and possessed an inherent viscosity of 0.62 in *m*-cresol. The use of less phosphoric acid for longer times led to lower molecular weight polymer, while the use of sodium hydride–acetic anhydride gave only dark oils.

Acknowledgment.—We are indebted to the following individuals and their associates: Mr. I. D. Plank and Mr. W. Childress and their associates for the microanalyses, Mr. H. E. Cupery for the hydrogenations, Mrs. Janet W. Willoughby and Mr. George Elechko for excellent technical assistance, and Dr. P. W. Morgan and Dr. R. G. Beaman for unfailing encouragement.

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Products from the Acetolysis of (−)-(S)-Bicyclo[2.2.2.]octyl-2 *p*-Bromobenzenesulfonate. A Reinvestigation[1]

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Received May 23, 1963

In a previous publication[2] it was reported that acetolysis of (−)-bicyclo[2.2.2]octyl-2 *p*-bromobenzenesulfonate resulted in a mixture of (+)-acetates which upon reduction with lithium aluminum hydride yielded a mixture of alcohols consisting of 65 ± 3% bicyclo-[2.2.2]octanol-2 and 35 ± 3% of axial bicyclo[3.2.1]-octanol-2. The mixture was separated using preparative vapor phase chromatography, but only 4–6-mg. quantities of each component were isolated in a pure state, since the peaks overlapped considerably because

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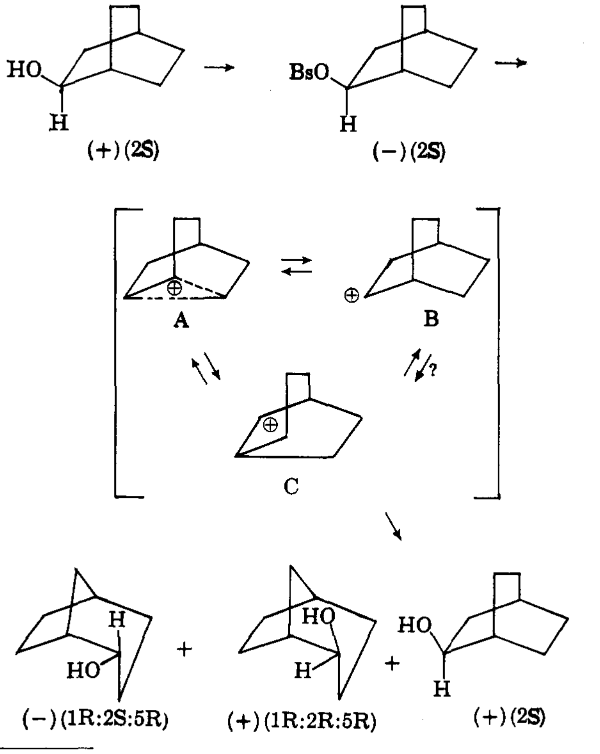
[1] This work was supported by research grant Cy-4065, National Institutes of Health, Public Health Service.

[2] H. M. Walborsky, M. E. Baum, and A. A. Youssef, *J. Am. Chem. Soc.*, **83**, 988 (1961).

of very similar retention times. Since only small amounts of material were available, the optical rotations of the alcohols were in doubt.

The preceding product analysis was repeated in order to obtain more accurate data. A sample of (+)-(*S*)-bicyclo[2.2.2]octanol-2, $[\alpha]^{25}\text{D}$ +5.7° (14.3% optical purity[3]) was converted to the *p*-bromobenzenesulfonate ester, m.p. 79.5–81.0°. In the previous work the brosylate was recrystallized, until m.p. 88–88.5° and a partial resolution may have been effected. In this work the brosylate, m.p. 79.5–81.0°, was subjected to acetolysis after it was shown not to be contaminated by unchanged alcohol. The acetolysis product, $[\alpha]^{28}\text{D}$ +0.82 ± 0.03°, was reduced with lithium aluminum hydride to yield a mixture of alcohols, $[\alpha]^{25}\text{D}$ +2.3 ± 0.2°. The alcohol mixture was analyzed by v.p.c. using a 150-ft. triscyanoethoxypropane Golay column. The mixture was shown to consist of 54.1% bicyclo[2.2.2]octanol-2, 43.0% axial bicyclo[3.2.1]octanol-2, 1.7% equatorial bicyclo[3.2.1]octanol-2, and 1.2% of an unknown component.

Preparative v.p.c. yielded a sample of bicyclo[2.2.2]octanol-2, $[\alpha]^{25}\text{D}$ +2.52°, which corresponds to 44% retention of activity. However, this sample was shown to contain 3% of equatorial bicyclo[3.2.1]octanol-2 which should, if it retained optical activity, be levorotatory.[4] Using a minimum value,[5] $[\alpha]\text{D}$ 17.2°, for the rotation of equatorial alcohol and assuming complete retention of activity in going from bicyclo[2.2.2]octanol of 14.3% optical purity, the equatorial alcohol should have a rotation of −3.1°. Since it is present to the extent of 3% in the bicyclo[2.2.2]octanol-2, it would have the effect of raising the rotation of solvolysis alcohol by 0.19°. Therefore the maximum amount of retention of activity and configuration would be 47%. In contrast to our earlier work[2] the axial bicyclo[3.2.1] alcohol isolated was shown to be dextrorotatory, $[\alpha]^{24}\text{D}$ 1.85°, and should be assigned the (1R:2R:5R) configuration[2] which is in agreement with the findings of Berson[3] on the relative configurations of (+)-axial and (−)-equatorial bicyclo[3.2.1]octanol-2.



If solely an unsymmetrical nonclassical ion A were produced in the acetolysis of the brosylate, one would predict that the resulting products would not be racemized. On the other hand if the symmetrical classical ion B were initially formed, the expected stereochemical findings would be that of mainly racemization with some inversion of configuration.

The stereochemical findings in the acetolysis can be rationalized by postulating the initial formation of an optically active nonclassical ion A which may be converted to an optically active classical ion C. Reaction of A and C with solvent leads to the formation of optically active products. However, A and C may also be converted to the optically inactive classical ion B and this would then account for the observed racemization. It should be pointed out that if extensive 6–2 hydride shift occurred[6] then the observed racemization could be accounted for without resorting to the formation of the classical ions B and C.

An alternate explanation has been advanced by H. C. Brown[7] who argues that if the interconversion of classical ions B and C is extremely rapid ("windshield wiper effect") then attack by solvent would be favored from the side of the molecule that the brosylate anion departed from and this too, would result in retention of configuration.

Experimental

(−)-(*S*)-Bicyclo[2.2.2]octyl-2 *p*-Bromobenzenesulfonate.—To 6.3 g. of (+)-(*S*)-bicyclo[2.2.2]octanol-2,[8] $[\alpha]^{25}\text{D}$ +5.7° (chloroform, *c* 4.4), dissolved in 50 ml. of freshly dried and distilled pyridine was added at 0° 19.0 g. of *p*-bromobenzenesulfonyl chloride. The mixture was refrigerated at 0–5° for 60 hr. and then poured on ice and the precipitated material taken up in ether. The ether solution was filtered and dried and the ether removed *in vacuo* to yield 17.3 g. of brosylate, m.p. 79.5–81.0°, $[\alpha]^{29}\text{D}$ −0.2 ± 0.3° (AcOH, *c* 10.41). The infrared spectrum showed the absence of starting alcohol.

Acetolysis of (−)-(*S*)-Bicyclo[2.2.2]octyl *p*-Bromobenzenesulfonate.—The acetolysis was run as previously described[2] to yield 5.8 g. (70%) of the acetate mixture, b.p. 64.5° (3 mm.), $n^{23}\text{D}$ 1.4702, and $[\alpha]^{28}\text{D}$ +0.82 ± 0.02 (neat, 1 dm.).

The mixture of acetates (5.8 g.) was reduced with lithium aluminum hydride to yield 4.0 g. (92%) of the alcohol mixture, m.p. 200–206°, $[\alpha]^{28}\text{D}$ +2.3° ± 0.2° ($CHCl_3$, *c* 10.9). A chloroform solution of the alcohol mixture was analyzed by v.p.c. using a 150-ft. triscyanoethoxypropane Golay column. At a helium flow rate of 30 ml./min. and a column temperature of 57° the retention times of the alcohols, relative to chloroform, were found to be 17.3 min. for axial bicyclo[3.2.1]octanol-2 (43.0%), 19.4 min. for bicyclo[2.2.2]octanol-2 (54.1%), and 20.5 min. for equatorial bicyclo[3.2.1]octanol-2 (1.7%). A small amount of unknown impurity appeared at 12 min. (1.2%). The values in parentheses represent the per cent composition as determined by measuring the areas under the peaks.

Repetitive v.p.c. using a 15 ft. × $^3/_8$ in. 20% DEGS on 60/80 Chromosorb-W column[9] and a column temperature of 150°

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(3) J. A. Berson and D. Willner, *J. Am. Chem. Soc.*, **84**, 675 (1962); J. A. Berson and P. Reynolds-Warnhoff, *ibid.*, **84**, 683 (1962).

(4) The levorotation is based on the observation[3] that (−)-equatorial and (+)-axial bicyclo[3.2.1]octanol-2 are epimers.

(5) This value was reported to us by Professor J. Berson.

(6) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **76**, 4501 (1954).

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(9) We wish to acknowledge the assistance of Dr. E. Taft in carrying out this separation.

yielded 44 mg. of bicyclo[2.2.2]octanol-2, $[\alpha]^{25}_{\mathrm{D}} + 2.52°$ ($CHCl_3$, *c* 4.4), which was shown by analytical v.p.c. to contain 3% of equatorial bicyclo[3.2.1]octanol-2 and 56 mg. of pure axial bicyclo[3.2.1]octanol-2, $[\alpha]^{25}_{\mathrm{D}} +1.85°$ ($CHCl_3$, *c* 5.6).

Acknowledgment.—We are indebted to Professor J. A. Berson for many valuable and stimulating discussions.

Nuclear Magnetic Resonance Identification of Substitutional Isomers in Chelated Polycyclic Aromatic Systems[1]

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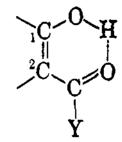
Some time ago we made a study of chemical shifts in chelated phenols which contain the structure I, where Y = -H, —CH_3, and -OCH_3, and from the results obtained[3] it seems likely that magnetic resonance methods may be useful in distinguishing between isomers of phenols with chelating substituents. The arguments which we will employ can easily be extended to other systems. The results exhibit two aspects by means of which the isomers may be distinguished on the basis of their high-resolution proton magnetic resonance spectra.

A. From the -OH Proton Chemical Shift.—In aromatic systems, the shift of a chelated -OH proton relative to the -OH peak in the corresponding parent phenol is quite large. We have found that this chemical shift is a linear function of the bond order of bond C-1=C-2, with the slope depending somewhat upon the substituent Y.[3] Therefore, the -OH proton shift in an unknown structure establishes whether or not the -OH group is *ortho* to substituent Y. If it is, the shift determines also the approximate bond order between the two carbons of the aromatic nucleus to which the -OH and -Y groups are attached. In turn, since approximate bond orders are known, and differ considerably for the various bonds in many aromatic systems, the bond order inferred from the -OH proton shift gives the location of the chelated structure in the molecule.

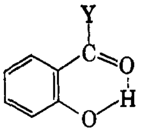
B. From the Chemical Shift of the Protons in Y.—A large part of the chemical shift of a proton, which is situated near an aromatic system, arises from the π-electronic ring currents induced in the aromatic system when the molecule is placed in a magnetic field.[4,5] It is this effect which leads to the other method of assigning the substituent position in polynuclear aromatic systems.


I

Method A is straightforward, direct, and requires little amplification.[3] Method B we will discuss in more detail. To a first approximation, the π-electron currents induced in each six-membered ring can be replaced by an elementary dipole situated at the center of the ring. Each dipole exerts a secondary magnetic field at Y, which is inversely proportional to the third power of the distance between the dipole and Y. This secondary field is in the same direction as the applied magnetic field, provided Y lies in the same plane as the aromatic system. If Y does not lie in this plane, then the effective field is reduced until, eventually, the applied field may be opposed by the secondary field. The maximum opposition to the applied field occurs when Y lies on the perpendicular drawn through the center of the dipole.

It is quite easy to show[4,5] that when Y does lie in the same plane as the aromatic system, then each secondary field causes a chemical shift of about $27.58/r^3$ parts per million if *r*, the distance from the protons or other magnetic nuclei in Y to the π-electronic dipole, is expressed in angstrom units. Hence, if the dimensions of the molecule are known, the approximate relative chemical shifts of Y may be predicted for a series of similar compounds. These predicted shifts will be only approximately correct, because the π-electron systems are perturbed to different extents by interaction with the substituents, and this interaction, in its turn, modifies the diamagnetic circulations induced in the substituents. However, these effects are less important than the geometrical considerations outlined above, and they do not affect the qualitative arguments that are used.

The ring current shifts will be modified by solvent interactions, and so our arguments apply to solutions in which the solvent interactions are either negligible or very similar for the solutes in question.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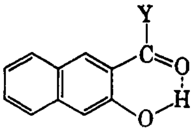
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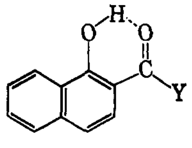
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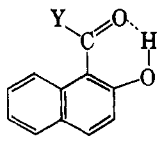
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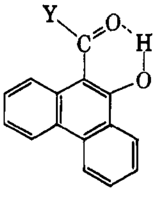
VI

With this qualification, one predicts that the downfield, ring-current shifts in compounds of types II to VI of the Y = H proton absorption peaks should be about 0.175 p.p.m. on going from I to III, somewhat less on going from II to IV, and about 0.55 p.p.m. on going from II and III to V and VI. These predictions

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