parameter relationships were computed using an IBM 7094 computer (*cf.* ref 6).

**Compounds Studied.**—The 1-phenyl-3-(5-aryl-2-furyl)propenones (I) and 1-phenyl-3-(5-aryl-2-thienyl)propenones (II) were prepared by condensation of acetophenone with 5-aryl-2-furfuraldehydes and 5-aryl-2-thiophenecarboxaldehydes, respectively, following the procedure described earlier.[22,23] All compounds were recrystallized from appropriate solvents[22,23] until constant melting point was obtained. The 1-phenyl-3-arylpropenones (III) were obtained by condensation of acetophenone with substituted benzaldehydes according to previous reports.[24,25] The chalcones were recrystallized from ethanol and the purity was checked by tlc on $Al_2O_3$ or $SiO_2$ (Silufol). The melting points of all compounds agreed well with those described.[22-25]

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**Registry No.**—**1**, 38899-16-0; **2**, 38899-17-1; **3**, 38899-18-2; **4**, 38899-19-3; **5**, 38899-20-6; **6**, 38898-73-6; **7**, 38898-74-7; **8**, 38898-75-8; **9**, 38898-76-9; **10**, 38898-77-0; **11**, 38898-78-1; **12**, 38898-79-2; **13**, 38898-80-5; **14**, 38898-81-6; **15**, 38898-82-7; **16**, 38898-83-8; **17**, 38898-84-9; **18**, 22965-98-6; **19**, 22252-15-9; **20**, 22252-14-8; **21**, 614-47-1; **22**, 22966-07-0; **23**, 22252-16-0; **24**, 22966-13-8; **25**, 22966-17-2; **26**, 24721-24-2; **27**, 2960-55-6; furan, 110-00-9; thiophene, 110-02-1.

**Acknowledgments.**—We wish to thank Associate Professor Š. Toma for samples **18–27**.

# Synthesis and Spectral Properties of N-Sulfated and/or O-Sulfated Amino Alcohols

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*Received November 7, 1972*

N-Sulfated and/or O-sulfated amino alcohols and 2-deoxy-2-sulfoamino-D-glucose were synthesized and their nmr and ir spectra were measured for the analysis and structural elucidation of sulfated polysaccharides. N-Sulfation of alkylamines and amino alcohols results in a downfield shift of the signal of the proton attached to the carbon atom bearing the amino group by 0.21–0.48 ppm, while O-sulfation results in a downfield shift of the proton attached to the carbon atom bearing *O*-sulfate by 0.36–0.65 ppm. Some discussions are made on the effect of N-sulfation of 2-deoxy-2-amino-D-glucose on H-1 and H-2. Comparison of ir spectra of these sulfate esters revealed two characteristic absorptions (1420–1450 and 1200–1220 $cm^{-1}$) in *N*-sulfates.

In recent years, some reports have appeared on the structural elucidation of natural mucopolysaccharides[1-3] and synthetic sulfated polysaccharides[4] by using nmr spectra. In general, nmr spectra of these compounds are fairly complicated even by using a high-resolution nmr spectrograph, but the chemical shift of the proton attached to the carbon atom bearing the *O*-sulfate and *N*-sulfate group, and that on the adjacent carbon atom, give important clues for spectral analyses of these compounds. As a model compound for sulfated sugars, we synthesized N-sulfated and/or O-sulfated cyclic and acyclic amino alcohols, and their nmr spectra were measured to examine the effect of N- or O-sulfation on the chemical shift of the proton attached to the carbon atom bearing the sulfate group and that on the adjacent carbon.

Although ir spectra of *O*-sulfates have been reported,[5] those due to *N*-sulfate have hardly been documented.[6,7] Therefore, ir spectra of the synthesized compounds were also measured to examine the absorptions characteristic of the *N*-sulfate group.

## Results and Discussion

Cyclic and acyclic alkylamine and amino alcohol sulfates were synthesized systematically. Analytical data for amino alcohol sulfates are given in Table I.

Since it is difficult to avoid contamination of *O*-monosulfate in acyclic *N,O*-disulfates by the method of Reitz and others,[8] we modified the method of Wolfrom and Juliano[9] to synthesize *N,N,O*-trisulfates, and their mild acid hydrolysis afforded *N,O*-disulfates in a comparatively good yield. On the other hand, cyclic *N,O*-disulfates are invariably accompanied with *O*-monosulfates, and trisulfate is not formed even on modification of the reaction conditions. Trans and cis cyclic *N,O*-disulfates were isolated by repeated recrystallization in 19.5 and 22.1% yield, respectively.

The starting 2-aminocyclohexanol was obtained by low-pressure hydrogenation of 2-acetaminophenol over rhodium catalyst, which was used in hydrogenation of alkoxyaniline,[10] separation of trans and cis compounds from the resultant product by chromatography over silica gel, and acid hydrolysis. These trans and cis compounds were identified by nmr spectra. This is simpler and gives a better yield than by the known definitive synthesis of trans[11] and cis[12] compounds.

Dodgson[6] obtained the potassium salt of 2-deoxy-2-sulfoamino-D-glucose by sulfation of 2-deoxy-2-amino-D-glucose with pyridine–sulfur trioxide. We used the same reagents and obtained 2-deoxy-2-sulfoamino-D-glucose as its sodium salt as needle crystals by recrystallization from methanol–water.

Nmr spectra of acyclic alkylamine and amino alcohol sulfates are summarized in Table II. As will

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TABLE I

CONSTANTS OF AMINO ALCOHOL SULFATES

| Registry no. | Compd | Yield,[a] % | Mp, °C Obsd | Mp, °C Lit. | N Calcd | N Found | S Calcd | S Found |
|---|---|---|---|---|---|---|---|---|
| 38911-08-9 | $HOCH_2CH_2NHSO_3Na$ | 22.3 | 136–137 | | 8.59 | 8.21 | 19.60 | 19.38 |
| | $^-O_3SOCH_2CH_2NH_3^+$ | 44.7 | 274–277 | 277–279[b] | | | | |
| | $NaO_3SOCH_2CH_2NHSO_3Na$ | 54.4 | 212–215 | 220–221[c] | | | | |
| 38974-12-8 | $NaO_3SOCH_2CH_2N(SO_3Na)_2$ | 72.3 | 212–215 | | 3.81 | 3.81 | 26.19 | 25.87 |
| | $HOCH_2CH_2CH_2NHSO_3Na$ | 18.2 | 141–142 | *d* | | | | |
| | $^-O_3SOCH_2CH_2CH_2NH_3^+$ | 76.6 | 234–236 | 226–227.5[b] | | | | |
| 38911-09-0 | $NaO_3SOCH_2CH_2CH_2NHSO_3Na$ | 27.1 | 234–236 | | 5.02 | 4.92 | 22.97 | 23.23 |
| 38911-10-3 | $NaO_3SOCH_2CH_2CH_2N(SO_3Na)_2$ | 51.1 | 198–201 | | 3.67 | 3.71 | 25.23 | 25.76 |

$[(CH_2)_4CHOR_1CHNHR_2]$

| $R_1$ | $R_2$ | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 38899-01-3 | H | $SO_3Na$ | trans | 41.5 | 232 dec | | 6.45 | 6.56 | 14.75 | 14.57 |
| | $SO_3^-$ | $H_2^+$ | trans | 27.2 | 300 dec | 300 dec[b] | | | | |
| 38899-02-4 | $SO_3Na$ | $SO_3Na$ | trans | 19.5 | 211 dec | | 4.39 | 4.26 | 20.09 | 19.63 |
| 38899-03-5 | H | $SO_3Na$ | cis | 39.9 | 251 dec | | 6.45 | 6.35 | 14.75 | 14.71 |
| | $SO_3^-$ | $H_2^+$ | cis | 25.6 | 295 dec | 289–290[e] dec | | | | |
| 38899-04-6 | $SO_3Na$ | $SO_3Na$ | cis | 22.1 | 186–187 | | 4.39 | 4.17 | 20.09 | 19.84 |
| 38899-05-7 | 2-Deoxy-2-sulfoamino-D-glucose (Na)[f] | | | 34.1 | 235 dec | | 4.98 | 4.60 | 11.40 | 11.30 |

[a] From the starting amino alcohol or 2-deoxy-2-amino-D-glucose. [b] C. S. Dewey and R. A. Bafford, *J. Org. Chem.*, **30**, 491 (1965). [c] Trihydrate, ref 9. [d] Reference 14. [e] T. Taguchi, M. Kojima, and T. Muro, *J. Amer. Chem. Soc.*, **81**, 4322 (1959). [f] Potassium salt monohydrate, mp 171° dec: A. G. Lloyd, F. S. Wusteman, N. Tudball, and K. S. Dodgson, *Biochem. J.*, **92**, 68 (1964).

TABLE II

CHEMICAL SHIFTS (δ SCALE) FOR ACYCLIC ALKYLAMINE AND AMINO ALCOHOL SULFATES

| Registry no. | Compd | CHNDR | CHCH₂NDR | CHCH₂CH₂NDR |
|---|---|---|---|---|
| 38911-11-4 | $CH_3CH_2NDSO_3Na$ | 2.97 | 1.11 | |
| 38911-12-5 | $HOCH_2CH_2ND_2$ | 2.87 | 3.67 | |
| 38911-13-6 | $HOCH_2CH_2ND_3^+Cl^-$ | 3.12 | 3.80 | |
| 38974-13-9 | $HOCH_2CH_2NDSO_3Na$ | 3.09 | 3.69 | |
| 14849-14-0 | $^-O_3SOCH_2CH_2ND_3^+$ | 3.30 | 4.27 | |
| 38960-84-8 | $NaO_3SOCH_2CH_2ND_2$ | 2.86 | 4.03 | |
| 38911-15-8 | $NaO_3SOCH_2CH_2NDSO_3Na$ | 3.24 | 4.15 | |
| 38911-16-9 | $CH_3CH_2CH_2NDSO_3Na$ | 2.89 | 1.52 | 0.89 |
| 38911-17-0 | $HOCH_2CH_2CH_2ND_2$ | 2.70 | 1.68 | 3.66 |
| 38911-18-1 | $HOCH_2CH_2CH_2ND_3^+Cl^-$ | 3.15 | 1.89 | 3.74 |
| 38911-19-2 | $HOCH_2CH_2CH_2NDSO_3Na$ | 3.06 | 1.80 | 3.70 |
| 38911-20-5 | $^-O_3SOCH_2CH_2CH_2ND_3^+$ | 3.18 | 2.08 | 4.19 |
| 38911-07-8 | $NaO_3SOCH_2CH_2CH_2ND_2$ | 2.72 | 1.80 | 4.13 |
| 38960-85-9 | $NaO_3SOCH_2CH_2CH_2NDSO_3Na$ | 3.09 | 1.93 | 4.15 |

be seen in this table, N-sulfation produces a chemical shift of the proton attached to the carbon atom bearing the amino group downfield by 0.21–0.36 ppm compared to that of the corresponding proton in nonsulfated free amines. The same shift is also seen in conjugated amines. The chemical shift of the proton attached to the carbon atom bearing *O*-sulfate moves to a lower magnetic field by 0.36–0.47 ppm by O-sulfation, and this proton, in both cyclic and acyclic amino alcohols, resonates at *ca.* 1 ppm lower field than that attached to the carbon atom bearing *N*-sulfate. This approximately corresponds to the difference between the corresponding nonsulfated compounds and is considered to be the difference in the electronegativity of N and O. See Table III.

The coupling constants of CHNDR and CHOR in *trans*-2-aminocyclohexanol and its sulfate ester are $J_{aa}$ = 9 and $J_{ae}$ = 4.5 cps, and one of its conformers, in which both amino and hydroxyl groups are diequatorial, is considered to be fixed. The chemical shift of the proton attached to the carbon atom bearing the amino group is at a lower field by 0.23 ppm by N-sulfation compared to that of the corresponding proton in nonsulfated free amines, and the downfield shift is 0.33 ppm in conjugated amines. A similar effect of O-sulfation on the corresponding proton is a downfield shift of 0.65 ppm, indicating that the effect of O-sulfation is greater.

In the case of *cis*-2-aminocyclohexanol, there must be a rapid inversion between two chair conformers, since the CHNDR and CHOR of *cis*-2-aminocyclohexanol are broad and there is only a relatively sharp single peak of methylene.

The effect of N-sulfation of 2-deoxy-2-amino-D-glucose is a downfield shift of the C-2 proton by 0.57 ppm for the α anomer and by 0.47 ppm for the β anomer compared to the chemical shift of the corresponding proton in nonsulfated free amine (α anomer, δ 2.63; β anomer, δ 2.51). The downfield shifts for anomeric protons are 0.23 ppm for the equatorial proton and 0.14 ppm for the axial proton. Of more significance is the fact that almost the same downfield shift is also seen in conjugated amine.

Dodgson and others[5] studied the ir spectra of *O*-sulfate esters of alcohols, amino alcohols, and hydroxylated amino acids and reported that absorptions due to S–O vibration appear at 1150–1230 and 1350–1450

TABLE III

CHEMICAL SHIFTS (δ SCALE) FOR *cis*- AND *trans*-2-AMINOCYCLOHEXANOL SULFATES AND α- AND β-2-DEOXY-2-SULFOAMINO-D-GLUCOSE

| Compd $\lceil(CH_2)_4\rceil$ $\lfloor CHOR_1\text{-}CHNDR_2$ | | | Trans | | | Cis | | Δ (cis–trans) | |
|---|---|---|---|---|---|---|---|---|---|
| | | Registry no. | $CHOR_1$ | $CHNDR_2$ | Registry no. | $CHOR_1$ | $CHNDR_2$ | $CHOR_1$ | $CHNDR_2$ |
| $R_1$ | $R_2$ | | | | | | | | |
| H | D | 38899-06-8 | 3.33 | 2.67 | 38899-07-9 | 3.82 (17[a]) | 2.80 (23[a]) | 0.49 | 0.13 |
| H | $D_2{}^+Cl^-$ | 38899-08-0 | 3.56 | 3.00 | 38899-09-1 | 4.10 (16) | 3.37 (23) | 0.54 | 0.37 |
| H | $SO_3Na$ | | 3.34 | 2.90 | | 4.03 (17) | 3.26 (25) | 0.69 | 0.36 |
| $SO_3^-$ | $D_2{}^+$ | 38898-64-5 | 4.28 | 3.23 | 38898-65-6 | 4.66[b] | 3.46 (24) | 0.38 | 0.23 |
| $SO_3Na$ | D | 38898-66-7 | 3.98 | 2.68 | 38898-67-8 | 4.47 (18) | 2.89 (22) | 0.49 | 0.26 |
| $SO_3Na$ | $SO_3Na$ | | 4.13 | 3.18 | | 4.70[b] | 3.31 (25) | 0.57 | 0.13 |

| | α (38904-97-1) | | β (38904-98-2) | |
|---|---|---|---|---|
| | H-1 ($J_{12}$) | H-2 ($J_{23}$) | H-1 ($J_{12}$) | H-2 ($J_{23}$) |
| 2-Deoxy-2-sulfoamino-D-glucose | 5.42 (3.5) | 3.20 (10.0) | 4.70 (8.0) | 2.98 (10.0) |

[a] Peak width (cps). [b] Overlapping with the peak of water.

$cm^{-1}$ and that due to C–O–S vibration at 770–810 $cm^{-1}$ in covalent sulfates, while only the absorption due to S–O vibration appears at 1210–1250 $cm^{-1}$ in acid sulfates. Ir spectra of heparin and 2-deoxy-2-sulfoamino-D-glucose have been reported,[6,7] but those of simple *N*-sulfate esters are very few.[6] We therefore measured the ir spectra of N-sulfated and/or O-sulfated amino alcohols used in the present work, and found that they exhibited absorptions due to S–O vibration within the prescribed limits 1170–1250 and 1420–1450 $cm^{-1}$.

The characteristic absorptions of the *N*-sulfate group can be divided into the following two kinds.

(1) $\nu_{as}(SO_2)$ 1420–1450 $cm^{-1}$. The starting amine and *O*-sulfates do not show any absorption in this region or exhibit a sharp absorption of weak intensity in the region of 1390–1410 $cm^{-1}$, while the *N*-sulfate shows absorption of relatively broad width and median intensity at 1420–1450 $cm^{-1}$.

(2) $\nu_s(SO_2)$ 1200–1220 $cm^{-1}$. Both *N*-sulfates and *O*-sulfates have several absorptions of strong intensity or one broad absorption, and absorption of the *N*-sulfates is in a lower wavenumber side by 10–48 $cm^{-1}$ than that of the corresponding *O*-sulfates.

Absorption due to C–N–S vibration appears in the same region in the starting amine and there is no characteristic absorption for *N*- and/or *O*-sulfates.

Nmr and ir spectral data of sulfated esters measured in the present work should give important information for nmr and ir analyses of natural N-sulfated and/or O-sulfated polysaccharides.

## Experimental Section

Nmr spectra were measured at 35° with a Varian T-60 nmr spectrometer operated at 60 MHz (for alkylamine and amino alcohol sulfates) or measured at 32° with a Varian HA-100 nmr spectrometer operated at 100 MHz (for 2-deoxy-2-sulfoamino-D-glucose) in $D_2O$ containing sodium 4,4-dimethyl-4-silapentane-1-sulfonate as an internal standard. Ir spectra were measured in KBr pellets with a Shimadzu IR-27G spectrophotometer.

The sodium salts of ethylsulfamic acid and propylsulfamic acid were prepared according to the usual procedure.[13] Selective N-sulfation of amino alcohol was carried out by the method of Warner and Coleman,[14] and selective O-sulfation by the method of Reeves and Guthrie.[15]

**Disodium 2-Sulfatoethylsulfamate.**—To the solid complex prepared from $SO_3$ (11 ml) and dry pyridine (44 ml), distilled 2-aminoethanol (5 ml) was added dropwise, with sitrring, over a period of 4 hr. The reaction mixture was heated at 60° for 1 hr and kept at room temperature overnight. The pyridine supernatant was decanted and the solid residue was neutralized, under vigorous stirring and cooling, with 1 *N* methanolic MeONa. The precipitate formed was collected by filtration, dissolved in water, and added with 10% barium acetate solution. After $BaSO_4$ was filtered off, the filtrate was passed through a column of Dowex 50W X8 ($Na^+$ form, 20–50 mesh). The eluate was evaporated to dryness, the residue was crystallized from methanol–water, and recrystallization was repeated with the same solvent, yield 22.0 g (72.3%) of trisodium 2-sulfatoethylimidodisulfonate.

Trisodium 2-sulfatoethylimidodisulfonate (5 g) dissolved in water (50 ml) was adjusted to pH 1.2 with Dowex 50W X8 ($H^+$ form, 20–50 mesh), stirred at room temperature for 1 hr, and filtered. After the filtrate was neutralized with 2 *N* NaOH solution and added to 10% barium acetate solution, $BaSO_4$ was filtered off and the filtrate was passed through a column of Dowex 50W X8 ($Na^+$ form, 20–50 mesh). The eluate was evaporated to dryness, and the residue was crystallized from methanol–water, yield 2.72 g (75.2%) of disodium 2-sulfatoethylsulfamate.

**Disodium 3-Sulfatopropylsulfamate.**—Mild acid hydrolysis of trisodium 3-sulfatopropylimidodisulfonate (4.83 g) at pH 1.2 for 2 hr, prepared by a method virtually identical with that described for trisodium 2-sulfatoethylimidodisulfonate, gave disodium 3-sulfatopropylsulfamate, yield 1.91 g (53.0%).

**(±)-*trans*- and (±)-*cis*-2-Aminocyclohexanol.**—Anhydrous 2-acetaminophenol (15.1 g, 0.1 mol) suspended in 120 ml of anhydrous ethanol was hydrogenated in the presence of 5% Rh on $Al_2O_3$ (6.6 g) under 42 psi at 64°. Treatment of the reaction mixture gave a crystalline product which contained two components, as observed by silica gel thin layer chromatography. The rhombic crystals, mp 144–145°, were obtained by fractional crystallization from methanol and prismatic crystals, mp 123–124° by fractional crystallization of the mother liquor from acetone. The residual mixture was chromatographed over silica gel and separated into two components by elution with chloroform–acetone (1:1), yield of rhombic crystals 5.93 g, prismatic crystals 7.65 g (total yield 86.4%).

After each compound was refluxed for 2 hr with 6 *N* HCl, each reaction mixture was evaporated to dryness and the residue was washed with acetone and crystallized from ethanol–benzene. The hydrolysate of the rhombic crystals gave (±)-*cis*-2-aminocyclohexanol hydrochloride, mp 190–191°, and that of prismatic crystals gave (±)-*trans*-2-aminocyclohexanol hydrochloride, mp 175–176°.

Treatment of each aminocyclohexanol hydrochloride by the usual procedure gave (±)-*cis*-2-aminocyclohexanol, mp 70–71°, bp 111° (35 mm), and (±)-*trans*-2-aminocyclohexanol, mp 61–62°, bp 121° (30 mm).

**Sodium *trans*-2-Sulfoaminocyclohexanol.**—To a solution of *trans*-2-aminocyclohexanol (7.0 g) in water (90 ml), pyridine–$SO_3$ (10.1 g) was added in small portions over a period of 2 hr, with sufficient 10% NaOH added gradually to maintain the pH at about 11.2–11.4. At the end of the reaction time, the reaction mixture was concentrated *in vacuo* to 50 ml, and added to ethanol (160 ml). After the resulting precipitate was removed by centrifugation, acetone (630 ml) was added to the supernatant.

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The precipitate was collected and crystallized from 95% ethanol, giving 5.70 g of long, hexagonal crystals (41.5%).

*trans*-**2-Aminocyclohexyl Sulfate.**—To a suspension of *trans*-2-aminocyclohexanol (1.15 g) in dry $CHCl_3$, chlorosulfonic acid (0.67 ml) in $CCl_4$ (2 ml) was added dropwise below 0° during 1 hr. After stirring for 2 hr at room temperature, the reaction mixture was evaporated to dryness and freed from HCl *in vacuo* over KOH pellets. The residue was dissolved in ice water, and the solution was neutralized with solid $BaCO_3$ and then with $Ba(OH)_2$ solution. The precipitate was filtered off, and the filtrate was concentrated to a small volume and passed through a column of Dowex 50W X8 ($H^+$ form, 20–50 mesh) to remove the starting material. The eluate was neutralized with Dowex 1 X2 ($OH^-$ form, 100–200 mesh) and concentrated, and the residue was crystallized from water, giving 0.53 g (27.2%) of prismatic crystals.

**Disodium** *trans*-**2-Sulfoaminocyclohexyl Sulfate.**—(±)-*trans*-2-Aminocyclohexanol (1.52 g) was sulfated by a method virtually identical with that described for disodium 2-sulfatoethylsulfamate, giving 0.82 g (19.5%) of needle crystals.

All the sulfated *cis*-2-aminocyclohexanols were prepared by the method used to prepare the corresponding trans derivatives described above.

**Sodium 2-Deoxy-2-sulfoamino-D-glucose.**—2-Deoxy-2-amino-D-glucose (12.9 g) was dissolved in water (180 ml) and the pH of the solution was adjusted to 9.6 by the addition of 10% NaOH. Pyridine–$SO_3$ (11.5 g) was added to the well-stirred solution over a period of 9.5 hr at room temperature. During this addition, the pH of the mixture was maintained between 9.6 and 10 by the addition of 10% NaOH. After stirring overnight at room temperature, the solution was concentrated to *ca.* 40 ml and added to 10% barium acetate solution. Precipitated $BaSO_4$ was filtered off through Radiolite 100 and the filtrate was adjusted to pH 4.6 by the addition of acetic acid and passed slowly through a column of Dowex 50W X8 ($Na^+$ form, 20–50 mesh). The eluate was immediately neutralized with NaOH and concentrated to *ca.* 20 ml. The product was precipitated by the addition of ethanol (400 ml), and the precipitate was collected by centrifugation and washed with ethanol. Solid $Ag_2CO_3$ was added to the solution of the product dissolved in water (50 ml). Precipitated AgCl and excess $Ag_2CO_3$ were centrifuged off and the supernatant was neutralized with Dowex 50W X8 ($H^+$ form, 20–50 mesh). The solution was concentrated to *ca.* 10 ml and the product was precipitated by the addition of ethanol (200 ml). The crude product, a white powder (6.47 g, 34.1%), was twice crystallized from methanol and water after treatment with activated charcoal, giving colorless crystals (3.70 g, 19.5%), $[\alpha]^{25}D$ + 48° (*c* 1, $H_2O$), mp 235° dec.

**Registry No.**—$SO_3$, 7446-11-9; 2-acetaminophenol, 614-80-2; (±)-*cis*-2-aminocyclohexanol hydrochloride, 38898-68-9; (±)-*trans*-2-aminocyclohexanol hydrochloride, 33092-83-0; (±)-*cis*-2-aminocyclohexanol, 38898-70-3; (±)-*trans*-2-aminocyclohexanol, 33092-82-9; 2-aminoethanol, 141-43-5; 3-amino-1-propanol, 156-87-6; 2-deoxy-2-amino-D-glucose, 3416-24-8.

**Acknowledgment.**—The authors express their sincere thanks to the members of the Central Research Laboratories, Sankyo Co., Ltd., for nmr (100 MHz) spectral measurement.

# Radicals and Scavengers. II. Scavengers, Viscosity, and the Cage Effect in a Meisenheimer Rearrangement[1,2]

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*Received November 6, 1972*

Radical scavengers have been used to study the thermal Meisenheimer rearrangement of *N*-benzyl-*N*-methylaniline *N*-oxide (I) in alkaline 80% aqueous ethanol at 70°. Oxygen at ≥1 atm reduces the yield of *N*-benzyloxy-*N*-methylaniline (II) to a minimum of 36%, while the yield under pure $N_2$ is 89%. A thiol and $CCl_4$, at higher concentrations, also reduce the yield of II. The three scavengers lead to benzaldehyde, toluene, and chloroform, not found in their absence. In the viscous solvent cyclohexanol at 70°, the "minimum" yield of II under $O_2$ is 69% of that under $N_2$. Rearrangement in chloroform at 60° gives CIDNP. These results support operation of a 40% cage effect as an important component of the homolytic dissociation–recombination mechanism previously proposed.

Many cases of inefficiency in the production of free radicals have been convincingly interpreted in terms of the "cage effect,"[4] and this phenomenon is now well enough understood to possess predictive value. The organic systems studied have but rarely involved either (a) a stable radical,[2,5,6] or (b) dissociation of only one bond,[2,7-9] the geminate radicals thus being in contact.

The thermal "Meisenheimer" rearrangement of tertiary amine oxides,[10] exemplified by that of *N*-benzyl-*N*-methylaniline *N*-oxide (I) (eq 1), must have both these characteristics if, as proposed by Schöllkopf,[11,12] it proceeds *via* a homolytic dissociation–recombination mechanism (eq 2, 3).

We have recently demonstrated[2] that the rearrangement of I in 80% ethanol–20% water at 70° proceeds with a 37% cage effect. Our evidence was that molecular oxygen at 1 atm, a scavenger of carbon radicals, reduced the yield from 89% (observed under nitrogen) to 33%. Oxygen did not, however, prevent the formation of II altogether; such behavior is diagnostic of a cage effect.

(1) Taken in part from the A.M. theses of R. W. G. (1968), P. A. S. (1969), and E. M. C. (1971), and from the Ph.D. thesis of R. W. W. (1973, in preparation) at Boston University.

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