Registry No.—**1**, 272-23-1; **1** methiodide, 18366-61-5; **1a**, 13362-81-7; **1b**, 1759-30-4; **1b** picrate, 3395-13-9; **1c**, 18354-51-3; **1d**, 18354-52-4; **1e**, 18354-53-5; **1e** picrate, 18366-62-6; **1f**, 18354-54-6; **1f** picrate, 18366-63-7; **1g**, 18354-55-7; **1g** picrate, 18366-64-8; **1h**, 18425-96-2; **1h** picrate 18366-65-9; **1i**, 18354-56-8; **1j**, 18354-57-9; **1k**, 18354-58-0; **1l**, 18354-59-1; **1m**, 18366-53-5; **1n**, 18366-54-6; **1o**, 18366-55-7; **2**, 272-67-3; **2a**, 1759-29-1; **2b**, 13362-83-9; **2c**, 18366-58-0; **2d**, 18366-59-1; **2e**, 18366-60-4; **2e** picrate, 18425-97-3.

Determination of the Absolute Configuration of a Spiro Quaternary Ammonium Salt *via* Stevens Rearrangement[1,2]

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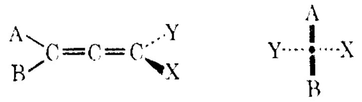
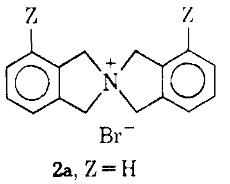
The levorotatory isomer of 4,4′-dimethoxy-1,1′,3,3′-tetrahydrospiro[isoindole-2,2′-isoindolium] bromide (**2b**) underwent Stevens rearrangement to give (−)-4,8-dimethoxy-5,7,12,12a-tetrahydroisoindolo[2,1-*b*]isoquinoline (**5a**). The absolute configuration of the latter substance was shown to be *S* by ozonolytic degradation to a derivative (**6**) of (*S*)-aspartic acid. The distribution of methoxy groups in **5a** was determined by nmr spectroscopy. These results permit an assignment of the *R* configuration to the levorotatory spiro salt, in accord with Lowe's rule, the helix conductor model and the Eyring-Jones model of optical activity. It is pointed out that a seeming failure of these rules and models in another substance might be due to swamping by other long-range effects.

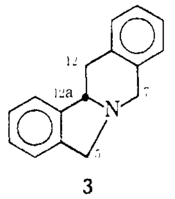
Lowe[3] has pointed out that allenes having the absolute configuration **1** are dextrorotatory at the sodium D line when A is more polarizable than B and X is more polarizable than Y. This rule, like the "conformational dissymmetry rule,"[4] can be arrived at by use of a helical conductor model of optical activity.[2a] Lowe[3] suggested further that this rule may be applicable to other axially dissymmetric series of compounds, as the spirans, but doubt on this latter point has been raised by the recent work of Krow and Hill.[5] We wish to report our assignment of the *R* configuration to the levorotatory isomer of the spiro quaternary salt **2b**, consistent with Lowe's rule[3] and with the Jones–Eyring model of optical activity[6] and to suggest a reason for the *seeming* failure of Lowe's rule for the compound of Krow and Hill.



1



2a, Z = H
b, Z = OCH$_3$
c, Z = NO$_2$



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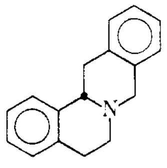

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Racemic **2b** was prepared from 3-methoxyphthalic anhydride[7] *via* reduction with lithium aluminum hydride,[8] treatment of the diol with phosphorus tribromide and reaction of the crude dibromide with ammonia. Its nmr spectrum was comparable with that of a sample of the unsubstituted spiro salt **2a** prepared by reaction of *o*-xylylene dibromide with ammonia.[9] The quaternary hydroxide, formed by reaction with silver oxide, gave a salt with *d*-camphor-ω-sulfonic acid that could be resolved by crystallization from acetone–methanol mixtures. The less soluble diastereomer gave the levorotatory spiro bromide, $[M]_D$ −41°, on treatment with hydrogen bromide in methanol. The rotation varied only slightly with concentration but could be more than doubled by the addition of several equivalents of lithium bromide, indicating that the counterion also plays a role in determining the rotatory properties of this substance. The ORD curve of a dilute solution in methanol showed a relatively small negative Cotton effect, amplitude[10] $[a = -14\ (270\text{–}250\ \text{m}\lambda)]$ on a strong negative background, $[M]_{235}$ −10,600.

The unsubstituted spiro quaternary salt **2a** has been shown by Wittig[11] to undergo a Stevens rearrangement[12] with strong bases to form **3** (necessarily racemic). Optically active bases of the series **3** contain an asymmetric center that might, in analogy with the work of Corrodi and Hardegger[13] with alkaloids containing the tetrahydroprotoberberine nucleus, **4**, be related to that of a derivative (**6**)[14] of aspartic acid (**7**), the configuration of which is known.[15] It is to be expected, on the basis of earlier work,[12,16,17] that the bond-break-

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[1] IX. A Useful Model of Optical Acitivity.

[2] (a) VIII: J. H. Brewster, "Topics in Stereochemistry," Vol. 2, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, New York, N. Y., 1967, p 1. (b) VII: J. H. Brewster and J. G. Buta, *J. Amer. Chem. Soc.*, **88**, 2233 (1966).

[3] G. Lowe, *Chem. Commun.*, 411 (1965).

[4] J. H. Brewster, *J. Amer. Chem. Soc.*, **81**, 5475 (1959).

[5] G. Krow and R. K. Hill, *Chem. Commun.*, 430 (1968).

[6] L. L. Jones and H. Eyring, *Tetrahedron*, **13**, 235 (1961); *J. Chem. Educ.*, **38**, 601 (1961).

[7] J. E. Leffler and B. M. Graybill, *J. Phys. Chem.*, **63**, 1457 (1959).

[8] E. L. Schumann, M. G. Van Campen, Jr., and C. H. Tilford, *J. Org. Chem.*, **23**, 763 (1958).

[9] M. Scholz, *Ber.*, **24**, 2402 (1891).

[10] C. Djerassi and W. Klyne, *J. Chem. Soc.*, 4929 (1962).

[11] G. Wittig, H. Tenhaeff, W. Schock, and G. Koenig, *Ann.*, **572**, 1 (1951).

[12] T. S. Stevens, *Progr. Org. Chem.*, Vol. 7, J. W. Cook and W. Carruthers, Ed., Plenum Press, New York, N. Y., 1968, p 48.

[13] H. Corrodi and E. Hardegger, *Helv. Chim. Acta*, **39**, 889 (1956).

[14] S. Korman and H. T. Clarke, *J. Biol. Chem.*, **221**, 113 (1956).

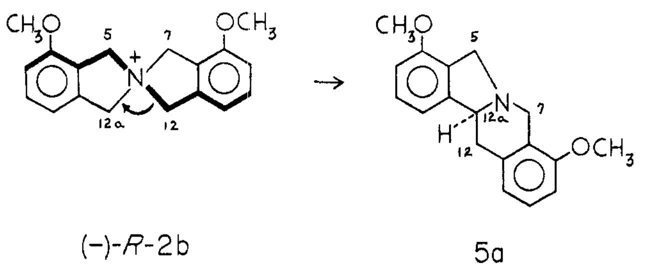
[15] J. P. Greenstein, *Advan. Protein Chem.*, **9**, 184 (1954).

[16] J. H. Brewster and M. W. Kline, *J. Amer. Chem. Soc.*, **74**, 5179 (1952).

[17] R. K. Hill and T. H. Chan, *ibid.*, **88**, 866 (1966).

ing and bond-making phases of the Stevens rearrangement will occur on the same side of the intact ring. Rearrangement of optically active **2b**, then, should occur with retention of dissymmetry and there should be a simple relation between the configuration of the spiro salt and the rearranged amine (*cf. e.g.*, Chart I).

CHART I



It is readily seen, however, that establishment of this configurational relationship requires a determination of the pattern of distribution of methoxy groups. Four amines with an *S* configuration at position 12a are possible; two (**5a** and **5b**) could arise from the *R* spiro salt and two (**5c** and **5d**) from the *S* isomer (Chart II). Mechanistic considerations are not of much help here since the effects of *o*- or *m*-methoxy groups on migration rates in Stevens rearrangements of N-benzylphenacylammonium salts are not very different[12] and may not be relevant in this more rigid system.

The dimethoxy spiro compound **2b** proved to be much more resistant to Stevens' rearrangement than was the parent compound **2a**, which gave up to 41% of ±**3** under a variety of conditions. In a number of instances more than 70% of starting material (**2b**) was recovered. Best results were obtained when the quaternary hydroxide was treated with sodium hydride in diglyme; isolation of the water insoluble, acid soluble fraction and crystallization from methanol gave 7–11% of a substance with nmr spectra, as base and as methiodide, clearly analogous to those of the unsubstituted compound **3**. The levorotatory spiro salt gave a levorotatory base $[M]_D$ −511° ($CHCl_3$), −672° (CH_3OH), showing a plain negative ORD curve as free base in methanol and, as hydrochloride, a small negative Cotton effect, $a = 7$ (279–270 mμ), on a strong negative background.

The absolute configuration of the asymmetric center of the rearrangement product was shown to be *S* by ozonolysis[13] to the aspartic acid derivative **6**. The mercuric salt of **6** was dextrorotatory in 0.05 *N* NaCl and levorotatory in 0.5 *N* HCl, as was a sample prepared[14] from L-aspartic acid (**7**). It is of interest that the analogous tetrahydroprotoberberine nucleus, **4**, is also levorotatory (D line) in the *S* configuration.[13] No conclusions about optical purity can be drawn from this work because sizeable losses were incurred in the purification of intermediates by crystallization and optical fractionation may have occurred.

The data given above indicate that the product of the Stevens rearrangement is one of the four positional isomers **5a–d** and has the absolute configuration shown in the drawings. Nmr evidence indicates that this substance has the structure **5a** and, thus, that the spiro compound had the *R* configuration. As seen in Table I the protons of the benzylammonium methylene

CHART II

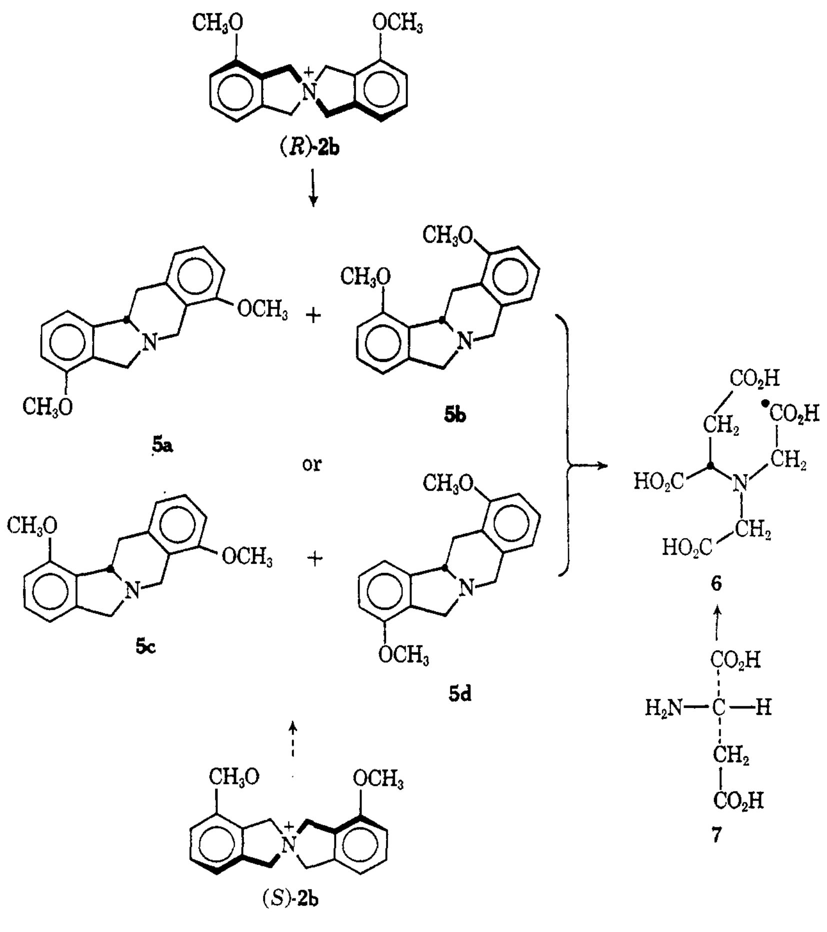


TABLE I

NMR CHEMICAL SHIFTS FOR QUATERNARY SALTS IN TRIFLUOROACETIC ACID

Salt	Cps from TMS at 60 Mc	
	Ar**CH**$_2$N $<$ $^+$	**CH**$_3$N $<$ $^+$
Dimethylisoindolinium iodide	297	210
Dimethyltetrahydroisoquinolinium iodide	279	202
2a	305	
2b	303, 300	
3·CH$_3$I	287, 303	212 (180)
5a·CH$_3$I	282, 298	211 (180)

TABLE II

NMR CHEMICAL SHIFTS FOR AROMATIC METHYL GROUPS, Ar**CH**$_3$, IN TRIFLUOROACETIC ACID

Compound	Cps from TMS at 60 Mc
Toluene	136
2-Methylanisole	133
3-Methylanisole	137
2,3-Dimethylanisole	134, 130

groups (Ar**CH**$_2$N$^+$) give sharp singlets at different positions in tetrahydroisoquinolinium and isoindolinium salts (δ 4.65 and 4.95, respectively). Thus positions 7 and 5 should be distinguishable in the methiodide of any of the four positional isomers. The presence of an *o*-methoxy group has an appreciable shielding effect in the spiro salt **2b** (Table I) and in the methylanisoles (Table II). The separation of the two peaks should, then, be the same as in the methiodide of **3** (15–16 cps at 60 mc in trifluoroacetic acid) if the product has either structure **5a** or **5b** (both derived from (*R*)-**2b**). The separation should be larger (19–21 cps) if the structure is **5c** and smaller (11–13 cps) if it is **5d** (both derived from (*S*)-**2b**). The observed separation (16 cps) and the observed upfield shift (5 cps) of the peaks in the methiodide indicate that the amine is isomer **5a** (compare **2a** and **2b** in Table I). The remaining benzylic protons appear, in the methiodide of **3**, to form an ABX system (δ_A 3.43, δ_B 3.80, δ_X 5.38; J_{AB} = 16 Hz; $J_{AX} = J_{BX}$ = 6 Hz). In the dimethoxy derivative the pattern appears to be similar, though the AB portion is obscured; the signal for the methine proton at 12a is shifted upfield by about 2 cps, consistent with the presence of a *m*-methoxy group (compare **2a** and **2b** in Table I).

Amines of series **3** and **5** would be expected to give two methiodides, one with a *cis* and one with a *trans* ring fusion. The quaternary methyl protons would be expected to give distinctly different signals, since the *cis* compound is more flexible and its methyl group can receive some shielding from the tetrahydroisoquinoline aromatic nucleus. Thus the methyl signal for the more flexible dimethyltetrahydroisoquinolinium salts is a singlet at δ 3.37 while that for the isoindolinium salts is a singlet at δ 3.50. In all the methiodides of series **3** and **5** sharp singlets were observed at about δ 3.52 and 3.00, in varying ratios but integrating *together* to three protons. The comparisons above were made with samples in which the peak at δ 3.52 predominated. It seems likely that this corresponds to the rigid *trans* isomer, for here the methyl group would have an environment most like that found in the isoindolinium salt. In this isomer the benzylammonium methylene (5 and 7) groups should not show significant geminal splitting because each proton of a given pair has almost exactly the same environment as its twin (see Figure 1). The protons of benzylmethylene group 12, however, would be held rigidly in quite different environments and the observed ABX splitting would thus be expected.

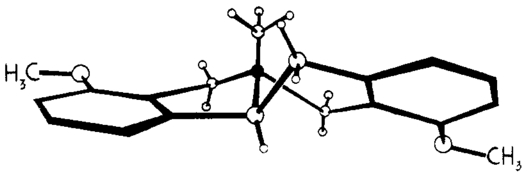


Figure 1.—**trans**-Methiodide of (*S*)-**5a**. The quaternary nitrogen is shown in black; the iodide ion is not shown.

The nmr spectra of the tertiary amines point to this same conclusion. Here the benzylamine methylene groups (5 and 7) give rise to a double quartet,[18] indicating that the anisotropy of the nitrogen atom makes the protons of each benzyl group nonequivalent.[19] In the parent amine **3**, one pair appears to show δ 3.73, 4.30 (J = 11 Hz), while the other shows δ 3.89, 4.17 (J = 15 Hz). The dimethoxy compound gives evidence for two pairs with similar coupling constants but larger chemical shift separations: δ 3.63, 4.43 (J = 11 Hz), 3.75, 4.32 (J = 16 Hz). These changes indicate that the methoxy groups influence both methylene groups in the same way and to about the same extent. The effect seems simply to be an amplification of the effect of the nitrogen atom. The signal for the other methylene group is seen as the AB part of an ABX pattern (δ 2.84, 3.32 (J_{AB} = 15 Hz, $J_{AX} + J_{BX}$ = 8 Hz) in **3** and [δ 2.82, 3.27 (J_{AB} = 16.5 Hz, $J_{AX} + J_{BX}$ = 8 Hz)] in the dimethoxy compound. Here the effect of the methoxy groups is almost negligible. It seems reasonable to assume that the methoxy effect depends on proximity; if so, then methoxy groups must be near both 5 and 7 as in structure **5a**.

All of the nmr data thus support structure **5a** for the Stevens rearrangement product, on which grounds we assign the *R* configuration to the levorotatory isomer of the spiro salt **2b**. We recognize the desirability of obtaining additional evidence for structure **5a** by unambiguous synthesis and for the configuration of **2b** by the X-ray method and hope to undertake work on both matters.

Experimental Section[20]

2,3-Bis(hydroxymethyl)anisole was prepared by methylation of 2,3-dimethylphenol,[6] oxidation with basic potassium permanganate to give the anhydride[6,7] and reduction with lithium aluminum hydride,[7] mp 92–93° (lit.[7] mp 95–96°).

4,4'-Dimethoxy-1,1',3,3'-tetrahydrospiro[isoindole-2,2'-isoindolium] Bromide (2b).—A solution of 60 g of 2,3-bis(hydroxymethyl)anisole in 1 l. of anhydrous ether was cooled in ice while

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[18] See S. Naruto, S. Arakawa, and H. Kaneko, *Tetrahedron Lett.*, 1705 (1968), for a similar case.

[19] H. P. Hamlow, S. Okuda, and N. Nakagawa, *ibid.*, 2553 (1964); F. Bohlmann, *ibid.*, 176 (1965).

[20] All melting points were determined on a Fisher-Johns melting point block and are uncorrected. Elemental analyses were performed at Purdue by Dr. C. S. Yeh and her staff. Optical rotations were determined on a Zeiss polarimeter, using a 2-dm cell and ORD curves were obtained on a Bendix Polarmatic, Model 62, using a 250-W xenon arc lamp. Nmr spectra were recorded on Varian A-60 and A-60-A instruments using tetramethylsilane as internal standard.

81 g of phosphorus tribromide was added dropwise, with stirring. The mixture was allowed to warm to room temperature, with stirring, and let stand overnight. It was then cooled again in ice and 230 ml of concentrated aqueous ammonia (a fivefold excess) was added to the stirred mixture, dropwise and with caution during the initial vigorous stages of the reaction. Stirring was continued for 36 hr and the mixture was then allowed to stand several days. The solid was collected and stirred with warm ethanol; undissolved inorganic salts were removed by filtration and the solution was cooled to give 30 g (46%) of **2b**, mp 157–159°. The microanalytical sample, purified by recrystallization from deionized water, had mp 159–160°: nmr ($CDCl_3$–DMSO-d_6 3:1) δ 3.95 (s, 6, Ar**OCH_3**), 5.27, 5.47 (s, 4, s, 4, Ar**CH_2**$N-^+$), 5.58 (s, 2, H_2O), 7.05–7.73 (m, 6, Ar**H**).

Anal. Calcd for $C_{18}H_{20}ON_2Br \cdot H_2O$: C, 56.84; H, 5.79; Br, 21.05; H, 3.68. Found: C, 56.90; H, 5.99; Br, 20.37; N, 3.96.

4,4′-Dinitro-1,1′,3,3′-tetrahydrospiro[isoindole-2,2′-isoindolium] Bromide (2c).—A mixture of 15 g of 2,3-dimethylnitrobenzene in 150 ml of carbon tetrachloride, 36 g of N-bromosuccinimide and 0.3 g of benzoyl peroxide was heated at reflux for 18 hr. The hot solution was transferred to another flask by inverted filtration and the solvent was removed. The dark oil was dissolved in chloroform and boiled with excess ammonia. The resulting solid was filtered, washed with ether and recrystallized (charcoal) from water to give 2.2 g (11%) of product: mp 305° dec; nmr (DMSO-d_6) δ 5.33, 5.55 (s, 4, s, 4, Ar**CH_2**N^+), 7.6–8.3 (m, 6, Ar**H**).

Anal. Calcd for $C_{16}H_{14}BrN_3O_4$: C, 48.98; H, 3.57; Br, 20.41; N, 10.71. Found: C, 49.06; H, 3.81; Br, 20.05; N, 10.58.

Resolution of 4,4′-Dimethoxy-1,1′,3,3′-tetrahydrospiro[isoindole-2,2′-isoindolium] Bromide (2b).—In a typical run 17.0 g of the quaternary salt was dissolved in methanol and 6.5 g of silver oxide was added. The solution was stirred for 15 min, filtered, let stand 6 hr and filtered again; the filter cake was washed with methanol. The solution was neutralized with 10.9 g of *d*-camphor-ω-sulfonic acid. Methanol was removed at the aspirator and ethyl acetate was added to the resulting oil. Crystals separated on refrigeration and a second crop on concentration: yield 14 g; mp 145–180°.

Systematic recrystallization of 42 g of such material, $[\alpha]_{\mathrm{D}}$ +18.7° (methanol), from mixtures of acetone–methanol 2–5:1, decreasing the acetone content as the less soluble isomer accumulated, gave, finally, 8.3 g of less soluble isomer, $[\alpha]_{\mathrm{D}}$ +9.55° (*c* 2.3, methanol), rotation unchanged on further crystallization. This was dissolved in anhydrous methanol and treated with an excess of hydrogen bromide. Anhydrous ether was added to precipitate 5.3 g of the bromide: mp 194–195° $[M]^{25}_{\mathrm{D}}$ −38.2° (*c* 0.425, methanol), −64.1° (*c* 0.425, with LiBr *c* 0.66 in methanol), −76.3° (*c* 0.425, with LiBr *c* 2.18, methanol), −58.0° (*c* 0.46, water); $\lambda_{\max}^{\mathrm{MeOH}}$ 270 mμ; ORD (methanol) $[M]_{585}$ −26° (*c* 0.382); $[M]_{270}$ −2816°, $[M]_{263}$ −2304°, $[M]_{235}$ −10,560° (*c* 7.64×10^{-3}).

The mother liquors from each stage of the resolution were evaporated and the most dextrorotatory of the residues combined to give 9.8 g, $[\alpha]_{\mathrm{D}}$ +22.79° (methanol). A methanol solution of this material was passed through a column of Dowex 1-X8 ion exchange resin, previously washed with sodium hydroxide until the effluent was chloride free and then with methanol. There was recovered 4.7 g of the dextro quaternary hydroxide, $[M]^{25}_{\mathrm{D}}$ +17.4° (*c* 2.15, methanol).

Stevens Rearrangements.—The unsubstituted spiro compound **2a**, mp 297° (lit.[10] mp 295°), gave 41% of **3**, mp 105–106° (lit.[10] mp 109–110°), when phenyllithium was used as the base[10] and 35% when the quaternary hydroxide was treated with sodium hydride in diglyme (below). Dimethoxy compound **2b** gave little or no rearrangement with a variety of methods, large amounts of starting material being recovered. In no instance could rearrangement product be obtained from attempted rearrangement of dinitro compound **2c**.

A solution of 2.8 g of dimethoxy quaternary bromide **2b** in 25 ml of methanol was stirred with 1.0 g of silver oxide. The solid was removed by filtration and washed with methanol. Removal of the solvent from the filtrates gave 2.9 g of a basic oil. This was dissolved in 20 ml of freshly distilled diglyme and the solution was added dropwise to a suspension of 0.7 g of sodium hydride in diglyme under nitrogen. The mixture was stirred at room temperature for 18 hr and then hydrolyzed with 150 ml of water. An oil separated. This was extracted into ether and the ether solution was twice extracted with water to remove diglyme. The ether was extracted with 2 *N* sulfuric acid; the aqueous layer was made basic with concentrated sodium hydroxide. The oil which separated was extracted into ether and the ether solution was dried and evaporated to give an oil which could be crystallized from methanol to give 0.25 g (11%) of amine, mp 153–156°.

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.87; H, 6.76; N, 4.98. Found: C, 77.09; H, 6.92; N, 4.81.

A portion of the amine was dissolved in benzene and treated with excess methyl iodide to give a salt, mp 215–217° after two crystallizations from absolute methanol.

Anal. Calcd for $C_{19}H_{22}INO_2$: C, 53.90; H, 5.20; N, 3.31; I, 30.02. Found: C, 54.05; H, 5.48; N, 3.26; I, 30.00.

When this procedure was applied to 5.3 g of levorotatory spiro bromide there was obtained, after recrystallization from methanol, 0.27 g of product: mp 135–137°; $[M]^{26}_{\mathrm{D}}$ −511° (*c* 0.54, chloroform), −672° (*c* 0.11, methanol); ORD plain negative in methanol (*c* 5.5×10^{-3}) $[M]_{238}$ −28, 100°; hydrochloride, in methanol (*c* 5.5×10^{-3}); $[M]_{303}$ −12,210°, $[M]_{279}$ −22,230°, $[M]_{270}$ −21,510°, $[M]_{235}$ −50,130°.

Mercuric N,N-bis(carboxymethyl)-(*S*)-aspartate was prepared from L-aspartic acid by alkylation with bromoacetate as described by Korman and Clarke[13]: mp 177–178° dec (lit.[13] mp 180–188°); $[\alpha]^{26}_{\mathrm{D}}$ +10.4° (*c* 0.448, 0.05 *N* NaCl), −8.6° (*c* 0.70, 0.5 *N* HCl).

Anal. Calcd for $C_8H_7NO_8Hg_2 \cdot 0.135HgCl_2$ (based on Cl content): C, 13.09; H, 0.95; N, 1.91; Hg, 63.55; Cl, 3.10. Found: C, 13.00; H, 1.04; N, 1.91; Hg, 63.53; Cl, 3.10.

Ozonolysis of 250 mg of the optically active dimethoxyamine (**5a**) in chloroform and methanol was carried out by the procedure of Corrodi and Hardegger.[12] After destruction of the ozonide with 30% hydrogen peroxide and formic acid the aqueous solution was continously extracted with ethyl acetate for 36 hr. The ethyl acetate solution was extracted with two 25-ml portions of water and the mercuric salt precipitated therefrom by adding mercuric nitrate solution and 1 drop of concentrated hydrochloric acid, following the procedure of Korman and Clarke,[13] $[\alpha]^{28}_{\mathrm{D}}$ +8.3° (*c* 0.12, 0.05 *N* NaCl), −5.6° (*c* 0.72, 0.5 *N* HCl).

Discussion

Spiro salt **2b** has a twofold rotation axis passing through the nitrogen atom (broken line in Figure 2); this is, then, one of the principal axes of polarizability along which electronic displacements, in effect, occur.[21] It seems likely that a second axis coincides with the line that would be formed by intersection of the two planes which each contain one aromatic ring. The third axis is then perpendicular to both at the point of intersection, the nitrogen atom. We establish a right-handed coordinate system, labeling these axes *X*, *Y* and *Z* as shown in Figure 2, in order of increasing polarizability, following the Eyring-Jones model.[6] It is seen at once that all parts of the *R* isomer that do not lie on the *Z* axis lie in octants in which the product of coordinates is positive; in the Eyring–Jones model this means that they will make negative contributions to long wavelength rotatory power, in accord with our present findings.

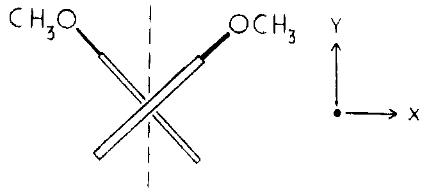

Figure 2.—(*R*)-**2b** in projection along the *Z* axis.

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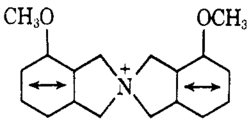
[21] See C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 131.

Since the ${}^1L_b$ transition[22] moments for both rings should lie along the *Z* axis,[23] it is to be expected that that transition will not be optically active (see **8**); indeed, we find only a trivial Cotton effect in this region of the spectrum. Aromatic transitions perpendicular to the ${}^1L_b$, but in the plane of the ring, would, on the other hand produce strong Cotton effects at lower wavelengths. The unsymmetrical pairing of transitions shown in **9** would be



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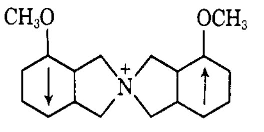

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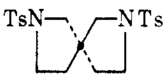
favored over the symmetrical pairing by inductive coupling along the *Z* axis; this coupling of these transitions would be expected[2a, 24] to produce a negative Cotton effect in the *R* isomer. Although we could not penetrate deeply enough into the ultraviolet region to show such a Cotton effect, the last rotation observable ($[M]_{235}$ −10,560°) suggests that it had been approached. It is clear that this system is also consistent with Lowe's[3] empirical rule and, thus, with the simple helical conductor model.[2a]

Exceptions to rules and models are, of course, more significant than examples, not so much because they *disprove* rules but because they indicate how they may be *improved*. Thus Krow and Hill, in the first determination of configuration of a carbon spiro compound,[5] showed that (*S*)-**10** is levorotatory. This constitutes a



(−)-(S)-**10**

clear *formal* exception to Lowe's rule[3] and could, conceivably, turn out to be the first piece of evidence requiring the abandonment of that rule. Before that can happen, however, it is necessary to establish that the phenomena covered by Lowe's rule should, indeed, be expected to *control* the optical rotation of (*S*)-**10**. This point has not been established. The toluenesulfonamide groups are the most polarizable components of the structure and, being certainly bent at the sulfur atom[25−27] and probably bent at the nitrogen atom as well,[27] can be oriented in dissymmetric patterns which might be strongly optically active without relation to Lowe's rule. The pattern in Figure 3, for example, would be expected to be strongly levorotatory by the helix model[2a] and might easily swamp out contributions from forms with other configurations at nitrogen and conformations about N–S and C–S bonds. These complications would vanish were the tosyl groups replaced by nonflexible groups of moderate polarizability, as in the dihydrochloride of the amine or the tetramethyl diquaternary salt, where Lowe's rule should be controlling and where it would lead to an unequivocal prediction that the *S* isomer would be dextrorotatory. We believe that a test of this nature should be made before otherwise widely applicable rules and principles are discarded. Meanwhile, we would point out that when one is using simple rules and models to predict long wavelength rotations it can be dangerous to neglect the possible rotatory effects of highly polarizable groups in highly dissymmetric orientations. If, as in the case of (*S*)-**10**, the magnitude of these effects cannot adequately be estimated, then no firm prediction of sign or magnitude of rotation can be made.

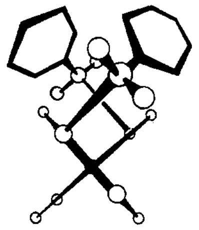


Figure 3.—One conformation of the isomer of (*S*)-**10** having *R* configurations at the nitrogen atoms. Completely analogous conformations would be possible even if the nitrogen atoms were planar. Note the highly developed left-handed helicity around the *Y* axis.

Registry No.—**2b**, 18366-87-5; **2c**, 18426-01-2; **5a**, 18366-88-6; **5a** methiodide, 18366-89-7.

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(22) J. R. Platt, *J. Chem. Phys.*, **17**, 484 (1949).

(23) See P. E. Stevenson, *J. Chem. Educ.*, **41**, 254 (1964), for a brief but clear review of a method for making this prediction.

(24) See, especially, the work of S. F. Mason, cited in ref 2a.

(25) See H. P. Koch and W. E. Moffitt, *Trans. Faraday Soc.*, **47**, 7 (1951), for a theoretical discussion of resonance and structure in sulfones, and J. G. Sime and S. C. Abrahams, *Acta Cryst.*, **13**, 1 (1960), for confirmatory X-ray data on a sulfone.

(26) See A. M. O'Connell and E. M. Maslen, *Acta Cryst.*, **22**, 134 (1967), for an X-ray study of sulfanilamide.

(27) See C. Tamura and G. A. Sim, *J. Chem. Soc.*, 8 (1968), for an X-ray study of a benzenesulfonylhydrazide.