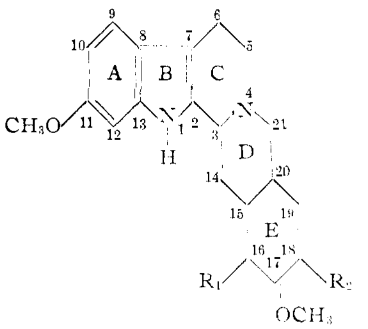
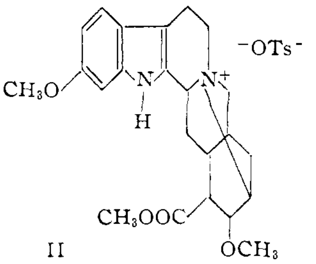
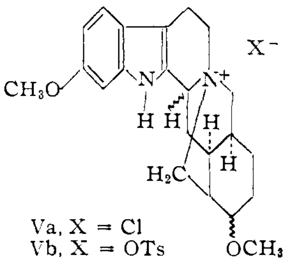


I, $R_1 = -CO_2CH_3$, $R_2 = -O_2CC_6H_2(OCH_3)_3$
III, $R_1 = -CO_2CH_3$, $R_2 = -OSO_2C_7H_7$
IV, $R_1 = -CH_2OH$, $R_2 = -H$



II



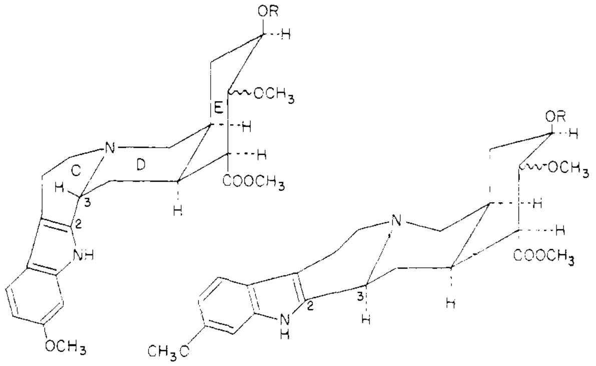
Va, X = Cl
Vb, X = OTs

The formation of the quaternary tosylate II from methyl reserpate 18-tosylate (III) on refluxing in collidine furnished conclusive proof that rings D and E in I are *cis*-linked. On the assumption that the displacement of the 18-tosyloxy group involves a concerted mechanism leading to inversion at C_{18}, we advanced the postulate that the 18-hydroxyl function and hence also the 16-carbomethoxy group[2] in I and III were *cis*-oriented in respect to *the hydrogen atoms at the ring junction* carbon atoms C_{15} and C_{20}. Application of Hudson's rotation rule to reserpine lactone[2a] then led to the assignment of the β-configuration to the functional group at C_{18} and hence also to the other substituents mentioned above.

In order to test the validity of the above assumption, we have recently essayed the preparation of the O-tosylate of the primary alcohol reserpinol (IV),[2b] since it was clear that the formation in this case of a quaternary salt would be incompatible with the postulated *cis*-relationship of the 16- and 18-substituents and the ring junction hydrogens. Indeed, elimination of the tosyloxy group occurred already on treatment of IV with *p*-toluenesulfonyl chloride in pyridine at room temperature. The crystalline product which deposited in 50% yield from the reaction mixture (m.p. 352–353°, $[\alpha]^{23}\text{D}$ +73.6° (*c*, 0.713 in water) after recrystallization from methanol) proved to be a quaternary chloride $C_{22}H_{29}N_2O_2Cl$ (calcd. C, 67.94; H, 7.52; N, 7.20; Cl, 9.12; found: C, 67.92; H, 7.53; N, 7.17; Cl, 8.90) by the following criteria: a free base could not be extracted from alkaline solution by organic solvents; it could not be titrated with perchloric acid in acetic acid solution, nor with base in aqueous solution as could be reserpinol hydrochloride (*pK'*a 7.70); its infrared spectrum lacked a band in the 3.8 to 4.0 μ region characteristic for $\gt NH^+$.

From the pyridine mother liquor there was obtained after dilution with water and alkalinization a small amount of a chloroform-extractable substance which melted at 310–312° after recrystallization from methanol. The analysis (calcd. for $C_{29}H_{36}N_2O_5S$: C, 66.38; H, 6.92; N, 5.34; S, 6.11; found: C, 65.91; H, 6.51; N, 5.35; S, 5.59) and the infrared data (bands at 8.56, 8.95, 9.71 and 9.94 μ characteristic for the tosylate ion, no absorption in 3.8–4.0 region) suggest the quaternary tosylate corresponding to the above chloride.

It follows from these results that the hydroxymethylene group in IV and, hence, contrary to our previous postulate, the 16-carbomethoxy and 18-hydroxy functions in reserpine are *trans* to the C_{15} and C_{20} hydrogens (*i.e.*, the formation of the quaternary tosylate II from III occurred *with retention* of the configuration at C_{18}). Taking into account our previous deduction regarding the absolute configuration of this carbon atom,[1] the two quaternary salts obtained from reserpinol then have to be formulated as Va and Vb, respectively, with the ring junction hydrogen atoms α-oriented. Considering further that C_3 in reserpine is readily epimerizable,[3] and that its carbomethoxy group can be saponified with alkali without change of configuration[2a] and hence must be equatorial, we suggest that the stereochemistry of reserpine is best expressed by VI (C_2-C_3-axial to ring D) and that of its 3-epimer isoreserpine[3] by VII (C_2-C_3 equatorial to ring D).



VI VII

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[2] (a) L. Dorfman, A. Furlenmeier, C. F. Huebner, R. Lucas, H. B. MacPhillamy, J. M. Mueller, E. Schlittler, R. Schwyzer and A. F. St. Andre, *Helv. Chim. Acta*, **37**, 59 (1954); (b) C. F. Huebner, H. B. MacPhillamy, A. F. St. André and E. Schlittler, THIS JOURNAL, **77**, 472 (1955).

[3] H. B. MacPhillamy, L. Dorfman, C. F. Huebner, E. Schlittler and A. F. St. André, *ibid.*, **77**, 1071 (1955).

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RECEIVED JULY 13, 1955

A COMPOUND WHOSE MOLECULE IS SUPERPOSABLE ON ITS MIRROR IMAGE BUT CONTAINS NO PLANE OR CENTER OF SYMMETRY

Sir:

The presence in any molecule of a plane or center of symmetry is a sufficient condition for optical inactivity,[1] and so far as we are aware, one

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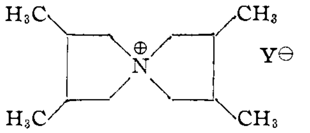
[1] We are here concerned only with optical activity in the fluid state.

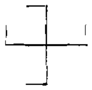
or both of these molecular symmetry elements is possessed by every inactive, non-racemic substance hitherto reported. However, it has long been recognized[2] that any molecule lacking a plane or center, but possessing a *fourfold alternating axis of symmetry,* would still be superposable on its mirror image; and it has been predicted[2] that any compound consisting of such molecules would be experimentally inactive and non-racemic.

We wish now to report the synthesis of what appears to be the first actual substance possessing this rare combination of symmetry elements, namely, the *meso "trans/trans"* diastereomer[3] of 3,4,3′,4′-tetramethylspiro-(1,1′)-bipyrrolidinium *p*-toluenesulfonate[4] (I).

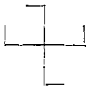


(I)

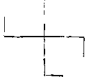
Four diastereomers (three active, one *meso*) would be predicted for this structure. All four have now been prepared. The configurations can be depicted conveniently by the "swastika" projection formulas[5] II–V. Only diastereomer V possesses the desired symmetry characteristics.



Active
cis/cis
II



Active
cis/trans
III



Active
trans/trans
IV

meso
trans/trans
V

meso-2,3-Dimethylbutane-1,4-diol[6a] was converted to its di-*p*-toluenesulfonate, m.p. 108–109.2°, Found: C, 56.06; H, 6.21; S, 14.56. The epimeric DL-diol gave a ditosylate melting at 107–108.3° (mixed m.p. with *meso* epimer depressed), Found: C, 56.43; H, 6.35; S, 14.71. The dextrorotatory diol (m.p. 44–45°, $[\alpha]^{21}\text{D}$ +5.38° (ether)) gave a levorotatory ditosylate, m.p. 90.5–91°, $[\alpha]^{21}\text{D}$ −7.67° (benzene); the levo-diol[7] gave a dextro ditosylate, 90.5–91.3°, $[\alpha]^{20}\text{D}$ +7.75°.

The preparation of *meso* and of DL-3,4-dimethylpyrrolidine has previously[6b] been described. The DL pyrrolidine treated with *dextro*-tartaric acid gave the crude "*dextro-dextro*" tartrate, m.p. 187–189°, $[\alpha]^{22}\text{D}$ +32.2° (water). Using *levo*-tartaric acid, the "*levo-levo*" tartrate was obtained and after twelve recrystallizations showed $[\alpha]^{25}\text{D}$ −36.2°, m.p. 187–189°, Found: N, 5.68. The liquid *dextro* pyrrolidine regenerated from the tartrate yielded a *p*-toluenesulfonate of m.p. 148–150.5°, $[\alpha]^{21}\text{D}$ +17.5° (water); the *levo* tosylate melted at 150–153°, $[\alpha]^{21}\text{D}$ −20.15°.

Reaction of *levo*-3,4-dimethylpyrrolidine with the above *levo*-ditosyldiol in hot dioxane finally gave the desired *meso trans/trans* bipyrrolidinium tosylate (I or V) which after recrystallization from tetrahydrofuran melted at 160–162°, optical rotation zero within experimental error[8]; Found: C, 63.93; H, 8.92; N, 4.09; S, 8.94. The identical product can be obtained by employing the dextrorotatory forms of both reactants.

However, reaction of the *dextro* pyrrolidine with *levo*-ditosyldiol gave a different and active *trans/trans* diastereomer IV, *p*-toluenesulfonate m.p. 150–152.5°, $[\alpha]^{30}\text{D}$ +19.88° (water). Since in this comparable reaction optical activity was not destroyed, it appears improbable that the observed inactivity of V is due merely to racemization.

Using appropriate intermediates, we have also prepared the DL-*cis/trans* diastereomer III, *p*-toluenesulfonate m.p. 181–182°, Found: C, 64.51; H, 8.97; N, 3.57, and its dextrorotatory form, m.p. 177.5–179°, $[\alpha]^{25}\text{D}$ +12.23° (water). Likewise we have made the DL/*cis/cis* diastereomer[9] II, *p*-toluenesulfonate m.p. 185.5–187°, Found: C, 64.27; H, 8.88; N, 3.57.

The limited evidence reported here is consistent with the prediction that a fourfold alternating axis of molecular symmetry would be a sufficient condition for optical inactivity.

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RECEIVED JULY 28, 1955

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[2] For an excellent discussion see G. W. Wheland, "Advanced Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, 1949, pp. 147–151. For earlier mention see Freudenberg, "Stereochemie," F. Deuticke, Leipzig, 1933, p. 601.

[3] The designation "*trans/trans*" signifies that both rings independently have *trans* configurations for the pairs of methyl groups.

[4] Strictly speaking it is the quaternary ammonium cation which has the symmetry elements described.

[5] To interpret the formulas, consider coaxis of the two rings to be perpendicular to paper. The intersecting lines represent the planes of the two rings. The short arms on each line show whether the substituents are *cis* or *trans*.

[6] G. E. McCasland and S. Proskow, (a) THIS JOURNAL, **76**, 3486 (1954); (b) *ibid.*, **76**, 6087 (1954).

[7] *levo*-2,3-Dimethylsuccinic acid was converted to its dextro dimethyl ester (*Ann.*, **538**, 1 (1939)), which on reduction gave the *levo*-diol, m.p. 44.5–45.5°, $]\alpha]^{25}\text{D}$ −5.42°. The *dextro*-diol was similarly prepared.

[8] Polarimetric observations with sodium D light at about 29° were made by three observers using two different solvents and concentrations.

[9] C. R. Noller and C. E. Pannell, THIS JOURNAL, **77**, 1862 (1955), have recently prepared the *cis/cis* diastereomer of the homologous bipiperidinium compound.

[10] On leave at Ohio State University, 1955–1956.

DIRECT ACTION OF COBALT GAMMA RADIATION ON NITRATE ION IN AQUEOUS SOLUTION

Sir:

In the decomposition of water by ionizing radiation, the 100 ev. yields of the intermediate H, OH, H_2 and H_2O_2 may be denoted by G_H, G_{OH}, G_{H_2} and $G_{H_2O_2}$, respectively. In the reduction of Ce^{++++} in 0.8*N* sulfuric acid by ionizing radiation, the 100 ev. yield of Ce^{+++} has been postulated[1] to be equal to $2G_{H_2O_2} + G_H - G_{OH}$ according to a mechanism in which H atom reduces Ce^{++++} and OH radical oxidizes Ce^{+++}.

Cobalt[60] gamma radiation induces[2] a reaction between Ce^{++++} and Tl^+ which increases the 100 ev. yield of Ce^{+++} from 2.52 to 7.85 in 0.8*N* sulfuric acid. The initial 100 ev. yield of Ce^{+++} is independent of the concentration of Tl^+ (10^{-5}

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[1] A. O. Allen, *Radiation Research*, **1**, 87 (1954).

[2] T. J. Sworski, forthcoming publication.