the pH of the soln was brought to 6.2 with cold, concd, aqueous NaOH, while the temp of the reaction mixt was maintained below −20°. The temp was allowed to rise to +5° and the crystalline product was isolated by filtration and recrystn from hot H_2O. The product was washed with a small amount of cold H_2O and EtOH and then dried to yield 1.92 g (Table I).

7-(β-D-Ribofuranosyl)imidazo[4,5-*d*]-*v*-triazin-4-one (2a) from 2b. To MeOH satd at 0° with NH_3 (150 ml) was added **2b** (5 g, 1.86 mmoles) and the mixt was stirred at room temp for 7 hr. The solvent was removed *in vacuo* to afford a yellow crystalline solid which was dried (P_2O_5 overnight). This residue was triturated with CH_3CN (50 ml), collected, washed with CH_3CN (30 ml), and then dried to yield 3.3 g. This was dissolved in H_2O (50 ml), and the soln was acidified with Dowex 50 (H^+, 100–200 mesh, 5 g) to pH 4. The resin was removed, and the filtrate was evapd to dryness to give a light yellow powder (2.6 g). This was recrystd from H_2O (18 ml) and EtOH (72 ml) to give 1.9 g of **2a**, which was identical with the product prepared by ring closure of 5-amino-4-carboxamido-1-(β-D-ribofuranosyl)imidazole.

Acknowledgments. The authors wish to thank Miss K. Dimmitt for the pK_a determinations and Dr. R. Sidwell, Dr. G. Khare and Mr. J. Huffman for performing the antiviral and cell toxicity screening.

References

(1) L. L. Bennett and J. A. Montgomery, "Methods in Cancer Research," Vol. 3, H. Busch, Ed., Academic Press, New York, N. Y., 1967, p 549.
(2) J. A. Montgomery, H. J. Thomas, and S. J. Clayton, *J. Heterocycl. Chem.*, 7, 215 (1970).
(3) J. A. Montgomery and H. J. Thomas, *Chem. Commun.*, 265 (1970).
(4) (a) J. A. Montgomery and H. J. Thomas, *J. Org. Chem.*, **36**, 1962 (1971); (b) W. Hutzenlaub, R. L. Tolman, and R. K. Robins, *J. Med. Chem.*, submitted for publication, C. W. Smith, R. W. Sidwell, R. K. Robins, and R. L. Tolman, *ibid.*, submitted for publication.
(5) (a) J. A. Montgomery and H. J. Thomas, *Chem. Commun.*, 458 (1969); (b) M. A. Stevens, H. W. Smith, and G. B. Brown, *J. Amer. Chem. Soc.*, **82**, 3189 (1960).
(6) J. F. Gerster and R. K. Robins, *ibid.*, 87, 3752 (1965).
(7) J. A. Montgomery and K. Hewson, *ibid.*, 79, 2259 (1957).
(8) J. A. Montgomery and K. Hewson, *J. Org. Chem.*, **33**, 432 (1968).
(9) M. R. Grimmett, *Advan. Heterocycl. Chem.*, **12**, 171 (1970).
(10) R. P. Panzica, R. J. Rousseau, R. K. Robins, and L. B. Townsend, *J. Amer. Chem. Soc.*, in press.
(11) R. W. Sidwell and J. H. Huffman, *Appl. Microbiol.*, **22**, 797 (1971).
(12) "Handbook of Biochemistry Selected Data for Molecular Biology," H. A. Sober, Ed., Chemical Rubber Co., Cleveland, Ohio, 1968, p J-98.
(13) K. Suzuki and I. Kumashiro, U. S. Patent 3,450,693 (1969); *Chem. Abstr.*, 71, 81698 (1969).
(14) T. Saito, M. Yoshikawa, T. Meguro, K. Kusashio, T. Kato, I. Kumashiro, and T. Takenishi, Japanese Patent 6908 (1967); *Chem. Abstr.*, 68, 40025 (1968).

Transformations in the Morphine Series. 5.[1] Reaction of Codeinone with Dimethyloxosulfonium Methylide. Structure and Analgetic Activity of the Product and Its Reduced Form

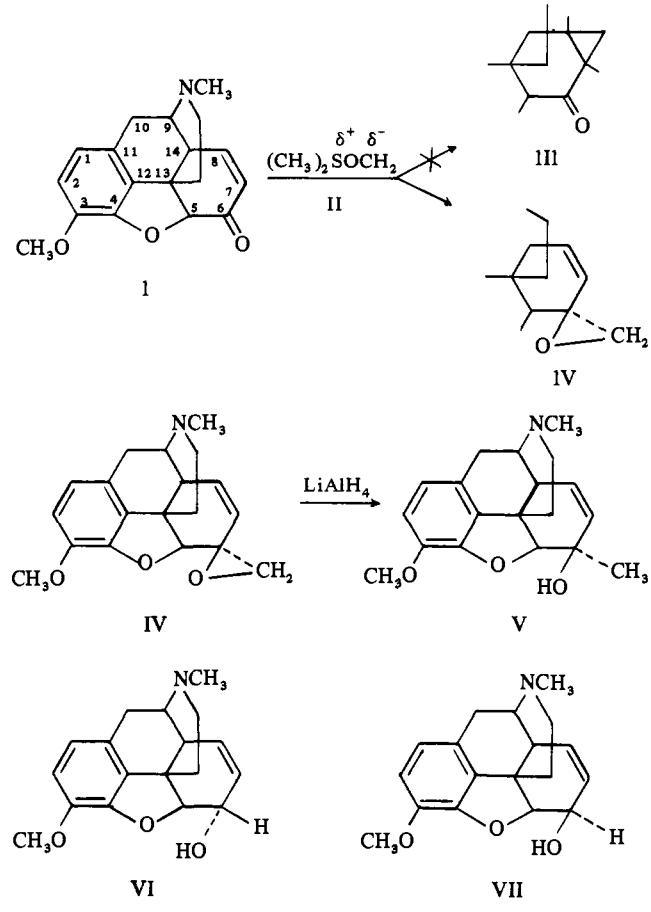
Lewis J. Sargent* and Arthur E. Jacobson

Laboratory of Chemistry, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland 20014. *Received February 25, 1972*

A novel oxirane derivative of codeinone was produced when the latter was interacted with dimethyloxosulfonium methylide. LAH reduction of the oxirane led to the previously unknown 6-methylisocodeine. Analgetic data for the new derivatives were determined (in mice) and compared with those of codeine, isocodeine, and 6-methylcodeine.

In exploring the preparation and utility in organic synthesis of dimethyloxosulfonium methylide, Corey and Chaykovsky[2] were able to demonstrate, in a comprehensive manner, that this ylide interacts with the carbonyl function of aromatic and nonconjugated aldehydes and ketones to form oxiranes, and with α,β-unsaturated ketones to produce cyclopropyl ketones. Both reactions were found to proceed with a high degree of stereospecificity.

In continuing our studies on transformations in the morphine series, it occurred to us that it would be of interest to study the reaction of the above oxosulfonium ylide with the α,β-unsaturated ketone system present in codeinone. Based on Corey's observations, this would be expected to yield a novel *exo*-7,8-cyclopropyl derivative with possible useful pharmacological properties.



Accordingly, when codeinone (I), prepared in good yield through silver carbonate oxidation of codeine,[3] was interacted with dimethyloxosulfonium methylide (II) (prepared *in situ* from dimethyloxosulfonium chloride[2]), the syrupy product proved to be a mixture (on silica gel tlc), consisting of a small quantity of a new substance showing the expected mass peak of 311 resulting from methylene transfer to codeinone (mass peak 297), some codeine (mass peak 299), and a quantity of noncrystallizable oil. Separation of the desired product was achieved *via* silica gel column chromatography followed by crystallization from ether. Having a homogeneous sample of the new substance in hand, we were greatly surprised to find its ir spectrum completely devoid of carbonyl absorption. Had the methylene transfer from the ylide occurred as postulated by Corey, *viz.*, addition across the double bond of the α,β-unsaturated system

in codeinone, the resulting *exo*-7,8-cyclopropyl dihydrocodeinone (III) would be expected to show characteristic ir carbonyl absorption. Since the mass peak (311) of the new substance is good evidence that addition of methylene had taken place, the possibility of oxirane IV formation at the 6-carbonyl function now presented itself. That this latter reaction had indeed occurred was demonstrated by an nmr study† of IV and its LAH reduction product. The oxirane ring was easily cleaved by LAH to yield a *new* compound, 6-methylisocodeine (V), isomeric with the 6-methylcodeine (of unknown conformation about C-6) previously obtained by Findlay and Small through reaction of codeinone with methyl lithium.[5] Steric factors inherent in the codeinone configuration may possibly have favored reaction of the ylide at the more accessible 6-carbonyl function rather than across the 7,8 double bond. The assignment of stereochemistry of the new isomer was based on a comparison of its nmr and ir spectra with those of codeine (VI) and isocodeine (VII) whose hydroxyl group configurations about C-6 are known.[6]

Corey has demonstrated that methylene transfer from the ylide (II) to various cyclohexanones occurs selectively so that the newly generated oxirane carbon-carbon linkage is equatorial. In the case of codeinone, an examination of Dreiding models shows that, for steric reasons, the equatorial oxirane carbon--carbon linkage would be most favored. Thus, on reductive opening of the oxirane the hydroxyl group of the resulting tertiary carbinol would have the *isocodeine* (VII) configuration. It follows that the hydroxyl group in Findlay's 6-methylcodeine must have the codeine (VI) configuration. Both of these points were confirmed by nmr analysis as follows. It was noted in the nmr spectrum of isocodeine that the H_{14} proton was deshielded by the hydroxyl group at C-6 ($\delta_{H_{14}}$ 3.08) due to the 1,4-diaxial relationship between these atoms. The deshielding effect of this oxygen atom was not observed in the nmr spectrum of codeine ($\delta_{H_{14}}$ 2.66), where the C-6 hydroxyl group is known to be equatorially oriented. Similarly, the H_{14} proton was deshielded in the oxirane IV ($\delta_{H_{14}}$ 3.08) and in 6-methylisocodeine (V) ($\delta_{H_{14}}$ 3.18) but remains unaffected in 6-methylcodeine ($\delta_{H_{14}}$ 2.76). The respective relationships of compounds IV and V with isocodeine and 6-methylcodeine with codeine are thus established.†

Pharmacology. Table I shows the respective analgetic activities of the oxirane IV and 6-methylisocodeine (V) compared with those of codeine, isocodeine, and 6-methylcodeine as determined in mice (sc, hot plate).[7] It is interesting to note that the same pattern of enhanced analgetic activity results in going from isocodeine to 6-methylisocodeine as with the codeine-6-methylcodeine pair.

Table I

Compound	ED_{50}, mg/kg
Oxirane (IV)	6.7
6-Methylisocodeine (V)	5.3
Isocodeine	12.0
6-Methylcodeine	3.8
Codeine	7.5

Experimental Section‡

Oxidation of Codeine to Codeinone (I). Utilizing the technique developed by Rapoport, *et al.*,[3] the oxidation of 36 g of codeine in 750 ml of dry C_6H_6 with 168 g of commercial Ag_2CO_3 (Baker) eventually yielded 17 g of pure codeinone, mp 184–185° (corr).

Reaction of Dimethyloxosulfonium Methylide with Codeinone. Following the general procedure outlined by Corey and Chaykovsky[2] a solution of the ylide was prepared under dry N_2 from 3 g (0.072 mole) of NaH (57% mineral oil dispersion), 9.2 g (0.072 mole) of trimethyloxosulfonium chloride, and 120 ml of dry THF. When the H_2 evolution had apparently ceased (4 hr), the system was warmed to 55°, and a solution of 16.4 g (0.055 mole) of codeinone in 425 ml of dry THF was slowly added with stirring during 1.75 hr. Heating and stirring were maintained for another hour, and the reaction mixture was kept at 25° overnight. After filtration, concentration afforded an oil which was heated to 100° (0.5 mm) to remove as much of by-product DMSO as possible. The residual honey-like syrup weighed 18 g.

Isolation of the Oxirane IV. A solution of 9 g of the above syrup in 30 ml of $CHCl_3$–MeOH (60:40 mixture) was placed on a 5.5 cm × 60 cm column prepared from a slurry of 500 g of silica gel (70–325 mesh, E. Merck-Darmstadt) in the same solvent mixture, and 10-ml fractions were automatically collected. Silica gel tlc slides were used to follow the course of elution; products were detected by utilizing a 3% $Ce(SO_4)_2$ in 3 *N* H_2SO_4 spray with subsequent heating. After combining the appropriate column chromatography fractions (60–90), solvent removal yielded 1.8 g of oily crystals from which 0.8 g of DMSO was removed (pipette). Trituration of the residual material with a minimum of cold MeOH yielded 0.53 g (*ca.* 6%) of oxirane, mp 195–198°. The analytical sample, crystallized from Et_2O, had mp 201–203° (corr). *Anal.* ($C_{19}H_{21}NO_3$) C, H, N; *m/e* 311.

Fractions 95–200 were combined and eventually yielded a magma of oily crystals from which 2.5 g of crude codeine§ (ir, tlc, *m/e* 299) was obtained on trituration with Et_2O. The remaining tacky syrup could not be crystallized and showed an indefinite tlc pattern as well as ir spectrum. Much colored material was retained by the column.

Reduction of the Oxirane to 6-Methylisocodeine (V). A solution of 1 ml (*ca.* 1.2 equiv) of 1.15 *M* ethereal LAH in 8 ml of dry Et_2O was added dropwise to a stirred solution of 0.3 g (*ca.* 1 mmole) of oxirane IV in 75 ml of dry ether, and the system heated under reflux for 1 hr. Excess hydride was destroyed with a few drops of H_2O (cooling), and the layers were separated. The ethereal solution was extracted with three 25-ml portions of 1 *N* HCl, and the ice-cold acid solution basified with a slight excess of cold 2 *N* NaOH. After five extractions with Et_2O, the combined extracts were washed with H_2O, dried (Na_2SO_4), and concentrated (*in vacuo*) to a colorless, crystalline solid (150 mg). Recrystallization from *i*-PrOH yielded V as 4-sided plates, mp 223–225° (corr); the substance sublimes without decomposition at 150–160° (0.5 mm). *Anal.* ($C_{19}H_{23}NO_3$) C, H, N; *m/e* 313. The ir (in $CHCl_3$) showed a strong hydroxyl band at 3600 cm^{-1}.

Acidification (HCl) of the above NaOH solution followed by rebasification with concd NH_4OH and extraction with ether eventually yielded 80 mg of a colorless, crystalline solid which crystallized in slender prisms (*i*-PrOH), mp 245–248°. This material gave a positive diazosulfanilic test, indicative of 4,5-oxide cleavage.

Acknowledgment. We are indebted to Dr. Herman J. C. Yeh for the nmr spectra obtained with a Varian 100-MHz instrument. A few preliminary nmr spectra were obtained by Dr. Li-Ming Twanmoh of the National Cancer Institute.

References

(1) M. Mokotoff, *J. Org. Chem.*, **33**, 3556 (1968) (paper 4).
(2) E. J. Corey and Michael Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).
(3) H. Rapoport and H. N. Reist, *ibid.*, **77**, 490 (1955).
(4) A. E. Jacobson, H. J. C. Yeh, and L. J. Sargent, *Org. Magn. Resonance*, in press.
(5) S. P. Findlay and L. F. Small, *J. Amer. Chem. Soc.*, **72**, 3249 (1950).

†For a detailed analysis of the nmr spectra of these compounds, involving decoupling experiments by double resonance and a Nuclear Overhauser Effect (NOE) to examine the "ring current" of the oxirane, *cf.* Jacobson, *et al.*[4]

‡Elemental analyses as well as mass spectra were carried out by the Analytical Services Section of this Laboratory. Satisfactory C, H, and N values (±0.4%) were obtained for compounds IV and V.

§The presence of codeine in the product mixture is probably due to the reduction of a portion of starting codeinone by unreacted NaH.

(6) K. W. Bentley and H. M. E. Cardwell, *J. Chem. Soc.*, 3252 (1955); H. Mackay and D. Crowfoot Hodgkin, *ibid.*, 3261 (1955); H. Rapoport and G. B. Payne, *J. Org. Chem.*, **15**, 1093 (1950); H. Rapoport and G. B. Payne, *J. Amer. Chem. Soc.*, **74**, 2630 (1952); H. Rapoport and J. B. Lavigne, *ibid.*, **75**, 5329 (1953).
(7) N. B. Eddy and D. Leimbach, *J. Pharmacol. Exp. Ther.*, **107**, 385 (1953); A. E. Jacobson and E. L. May, *J. Med. Chem.*, **8**, 563 (1965).

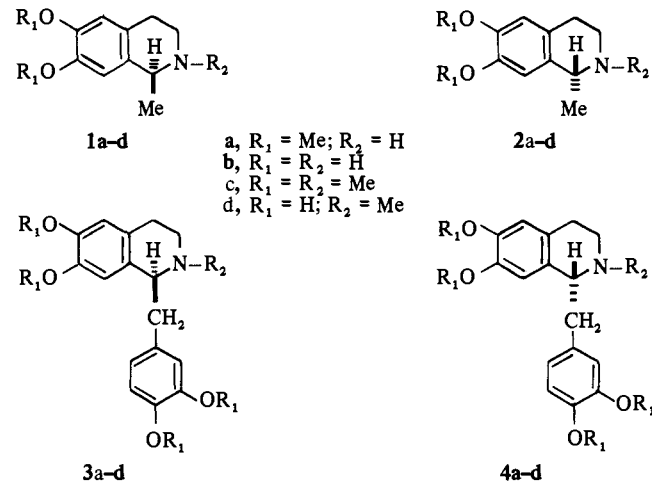
Alkaloids in Mammalian Tissues. 2.[1] Synthesis of (+)- and (−)-1-Substituted-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinolines

S. Teitel,* J. O'Brien, and A. Brossi

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110. *Received January 27, 1972*

It has been suggested that dopamine and acetaldehyde or 3,4-dihydroxyphenylacetaldehyde condense in mammalian tissues to afford 1-substituted tetrahydroisoquinoline "alkaloids" which could induce a variety of pharmacological responses.[2-8] However, such *in vivo* reactions might be catalyzed by enzymes to form a single optical isomer which can expected to differ from its antipode in biological activity.[9,10] Thus, to evaluate this concept of "alkaloid" formation in man, especially in relation to the behavioral changes induced by alcoholism and to other disorders, both optical isomers are necessary.

Based on this consideration, the enantiomeric salsolinols **1b** and **2b** and tetrahydropapaverolines **3b** and **4b** were synthesized by O-demethylation of the corresponding known isomeric salsolidines[11,12] **1b** and **2b** and norlaudanosines[13] **3b** and **4b** and further characterized as their *N*-methyl derivatives. The assignment of their absolute configuration was substantiated by conversion of **1b** and **3b** into (*S*)-carnegine (**1c**) and (*S*)-laudanosine (**3c**), respectively.



Experimental Section†

(−)-(1*S*)-6,7-Dihydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline Hydrobromide [(*S*)-(−)-Salsolinol Hydrobromide] (1b·HBr). A solution of 20 g (0.1 mole) of (*S*)-(−)-salsolidine[12] (**1a**), mp 47–48° [α]D −59.1° (*c* 4, EtOH) [lit.[11] mp 47.5–48.5°, [α]^{16}D −59.7° (*c* 20, EtOH)], in 200 ml of 48% HBr was refluxed for 10 hr, cooled, and evaporated under reduced pressure. The residue was crystallized from a mixture of EtOH–Et_2O to give 17.7 g (68%) of **1b·HBr**: mp 174–175°; [α]D −30.9° (MeOH); nmr δ 1.51 (d, 3, *J* = 7 Hz, CH_3), 2.70–3.40 (m, 4, CH_2CH_2), 4.35 (b, 1, CH), 6.54, 6.60 (2s, 2, aromatics), 8.50–9.50 (b, 4, 2 OH and N^+H_2); uv_{max} 225 nm (ε 6450) (infl), 288 (3890); ORD (*c* 0.27, MeOH) $[\phi]_{700}$ −63°, $[\phi]_{589}$ −65°, $[\phi]_{298}$ 0° (pk), $[\phi]_{270}$ −1570° (tr), $[\phi]_{262}$ −1450° (pk), $[\phi]_{242}$ −3370° (tr), and $[\phi]_{228}$ −1930° (pk); CD (*c* 0.001 *M*, MeOH) $[\theta]_{310}$ 0, $[\theta]_{285}$ +1160, $[\theta]_{241}$ −960, and $[\theta]_{215}$ +3770. *Anal.* ($C_{10}H_{13}NO_2$·HBr) C, H, N.

(+)-(1*R*)-6,7-Dihydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline Hydrobromide [(*R*)-(+)-Salsolinol Hydrobromide] (2b·HBr). In a manner similar to the procedure for **1b·HBr**, 10 g (0.05 mole) of (*R*)-(+)-salsolidine[12] (**2a**), mp 47–48°, [α]D +59.0° (*c* 2, EtOH) [lit.[11] mp 47.5–48.5°, [α]^{16}D +59.9° (*c* 25, EtOH)], was O-demethylated to give 9 g (69%) of **2b·HBr**: mp 174–175°; [α]D +30.0° (MeOH); identical in nmr and uv with **1b·HBr**; ORD and CD mirror images of **1b·HBr**. *Anal.* ($C_{10}H_{13}NO_2$·HBr) C, H, N.

(1*S*)-6,7-Dihydroxy-1,2-dimethyl-1,2,3,4-tetrahydroisoquinoline Hydrobromide [(*S*)-*N*-Methylsalsolinol Hydrobromide] (1d·HBr). To a solution of 7.3 g (0.033 mole) of (*S*)-(−)-carnegine[12] (**1c**), oil, [α]D −24.3° (*c* 2, EtOH) [lit.[11] oil, [α]^{18}D −24.4° (*c* 9, EtOH)], in 50 ml of CH_2Cl_2 at −70° was added over 15 min 30 ml of 5% BBr_3 in CH_2Cl_2. After stirring at 25° for 17 hr, the reaction mixture was cooled to 4°, and 100 ml of MeOH was added over 15 min and then evaporated. The residue was crystallized from a mixture of EtOH–Et_2O to give 8 g (89%) of **1d·HBr**: mp 180–182°; [α]D 0°; $[\alpha]_{365}$ +37°; nmr δ 1.55 (d, 3, *J* = 6.5 Hz, CH_3CH), 2.82 (s, 3, CH_3N), 2.70–3.70 (m, 4, CH_2CH_2), 4.43 (q, 1, *J* = 6.5 Hz, CH), 6.58 (s, 2, aromatic), 8.88, 9.02 (2s, 2, 2 OH), 10.10 (b, 1, N^+H); uv_{max} 225 nm (ε 6750) (infl), 288 (4000); ORD (*c* 0.274, MeOH) $[\phi]_{700}$ −7°, $[\phi]_{589}$ −3°, $[\phi]_{299}$ +2250° (pk), $[\phi]_{279}$ −1250° (tr), $[\phi]_{238}$ +1000° (pk), and $[\phi]_{225}$ −3500° (tr); CD (*c* 0.01 *M*, MeOH) $[\theta]_{306}$ 0, $[\theta]_{280}$ +2500, $[\theta]_{250}$ 0, $[\theta]_{234}$ 4100, $[\theta]_{220}$ +2000, and $[\theta]_{210}$ +11000. *Anal.* ($C_{11}H_{15}NO_2$·HBr) C, H, N.

(1*R*)-6,7-Dihydroxy-1,2-dimethyl-1,2,3,4-tetrahydroisoquinoline Hydrobromide [(*R*)-*N*-Methylsalsolinol Hydrobromide] (2d·HBr). By the procedure given for the preparation of **1d·HBr**, 5.8 g (0.026 mole) of (*R*)-(+)-carnegine[12] (**2c**), oil, [α]D +24.6° (*c* 2, EtOH) [lit.[11] oil, [α]^{19}D +24.6° (*c* 3, EtOH)], afforded 7.1 g (85%) of **2d·HBr**: mp 180–182°; [α]D 0°; $[\alpha]_{365}$ −36.1°; identical in nmr and uv with **1d·HBr**; ORD and CD mirror images of **1d·HBr**. *Anal.* ($C_{11}H_{15}NO_2$·HBr).

Conversion of (*S*)-(−)-Salsolinol Hydrobromide (1b·HBr) into (*S*)-(−)-Carnegine (1c). To a solution of 1.5 g (5.8 mmoles) of **1b·HBr** in 50 ml of MeOH was added an excess of CH_2N_2 in Et_2O. The mixture was stored at 4° for 4 hr and then at 25° overnight. The resulting solution was evaporated at 40° in a stream of N_2, and the residue suspended in dilute $NaHCO_3$ and extracted with EtOAc. The extract was evaporated to leave 1 g (82%) of **1c** as an oil, identical in [α]D and nmr with authentic **1c**.[11]

(−)-(1*S*)-1-(3,4-Dihydroxybenzyl)-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline Hydrochloride [(*S*)-(−)-Tetrahydropapaveroline Hydrochloride] (3b·HCl). Resolution of (±)-*N*-norlaudanosine[14] (tetrahydropapaverine) with (−)-diacetone-2-keto-L-gulonic acid[15] in *i*-PrOH afforded 67% of (*S*)-(−)-*N*-norlaudanosine (**3a**): mp 98–99°; [α]D −28.1° ($CHCl_3$) [lit. mp 97.5–98.5°,[13] [α]D −21° ($CHCl_3$)[16]].

A solution of 3 g (8.8 mmoles) of **3a** in 30 ml of 55% HI was stirred at 125° for 30 min and evaporated under reduced pressure. The residue was dissolved in 30 ml of H_2O, cooled to 4°, and adjusted under a N_2 atmosphere to pH 8 with NH_4OH. The precipitate was collected under N_2, dissolved in 30 ml of hot 6 *N* HCl, and stored at 4° overnight. The crystals were filtered and dried to give 2 g (70%) of **3b·HCl**: mp 285–286°; [α]D −32.0°. An analytical specimen prepared from 6 *N* HCl exhibited: mp 285–286°; [α]D −32.4°; nmr δ 2.70–3.40 (m, 6, 3 CH_2), 4.37 (m, 1, CH), 6.65–6.80 (m, 5, aromatic), 7.40 (b, 2, 2 OH), 9.15 (b, 2, N^+H_2); uv_{max} 230 nm (ε 11,100) (infl), 286 (6700); ORD (*c* 0.324, MeOH) $[\phi]_{600}$ −92°, $[\phi]_{589}$ −95°, $[\phi]_{301}$ +2650° (pk), $[\phi]_{285}$ −6000° (tr), $[\phi]_{256}$ −2750° (pk), $[\phi]_{233}$ −5000° (tr), and $[\alpha]_{220}$ −2500°; CD (*c* 0.01 *M*, MeOH) $[\theta]_{320}$ 0, $[\theta]_{293}$ +6300, $[\theta]_{280}$ 0, $[\theta]_{276}$ −500, $[\theta]_{264}$ 0, $[\theta]_{235}$ +600, and $[\theta]_{220}$ 0. *Anal.* ($C_{16}H_{17}NO_4$·HCl) C, H, N.

†All melting points (corrected) were taken in open capillary tubes with a Thomas-Hoover melting apparatus. The ultraviolet spectra were measured in EtOH with a Cary recording spectrophotometer Model 14M. Nuclear magnetic resonance spectra were obtained with a Varian Associates Model A-60 spectrophotometer using DMSO-d_6 as solvent and tetramethylsilane as internal reference. Optical rotations were measured with a Perkin-Elmer polarimeter Model 141 at 25° using a 1% solution in H_2O unless noted otherwise. Rotatory dispersion curves were determined at 23° with a Durrum-Jasco spectrophotometer Model 5 using 1-cm, 0.1-cm, or 0.1-mm cells. Circular dichroism curves were measured on the same instrument and are expressed in molecular ellipticity units [θ]. Analyses are indicated only by symbols of the elements, analytical results obtained for these elements were within ±0.35% of the theoretical values. Water of crystallization in compounds **3d·HBr** and **4d·HBr** was determined with the Karl Fischer reagent.