the corresponding aldehyde in low yield.

Experimental Section

Materials. The 3,3-dialkyl-2-oxo acids and esters were prepared as described previously.[3] Trimethylpyruvic acid was obtained by the permanganate oxidation of pinacolone after the method of Anders.[10]

Decarboxylation and Oxidative Decarboxylation of 1. When 12.6 g (0.096 mol) of trimethylpyruvic acid (1) was heated with 0.5 g (0.004 mol) of $CuCO_3 \cdot Cu(OH)_2$ at 130–140 °C for 10 min, 12 g (95%) of unreacted 1 resulted.

A mixture of 8 g (0.06 mol) of 1, 3.5 g (0.55 mol) of Cu powder, and 50 mL of quinoline then was heated at 175 °C for 1 h, and considerable gas evolution was noted. Distillation of the reaction mixture afforded 4.0 g (77%) of product: bp 66–73 °C; IR (neat) 2710 and 1725 cm^{-1}; ^1H NMR (CCl_4) δ 1.09 (s, 9, $(CH_3)_3$), 9.53 (s, 1, CHO); 2,4-dinitrophenylhydrazone mp 209–210 °C (EtOH), lit.[11] for pivalaldehyde 2,4-dinitrophenylhydrazone, mp 210 °C.

Oxygen was passed through a similar reaction mixture at 125 °C for 1 h. It was allowed to cool, poured into dilute HCl, and worked up to give 2.9 g (38%) of pivalic acid (3): bp 163–165 °C, mp 35–36 °C (lit.[12] bp 163–164 °C, mp 35.5 °C).

Cobaltous acetate tetrahydrate (0.3 g, 0.0012 mole) was added to 7.6 g (0.058 mol) of 1, 2.0 g (0.03 mol) of Cu powder, and 50 mL of quinoline, and O_2 was passed thru the mixture at 100 °C for 1.25 h. It was worked up as in the previous experiment, and 2.5 g (42%) of 3 resulted. A similar experiment was conducted at 110–120 °C, and the evolved CO_2 was collected by passage thru Ascarite. Approximately 96% of the theoretical amount of CO_2 was evolved, and 3.75 g (60%) of 3 was isolated.

Oxidative Decarboxylation of 2. A mixture of 10 g (0.034 mol) of 3,3-dipentyl-2-oxooctanoic acid (2), 2.5 g (0.04 mol) of Cu powder, 0.4 g (0.0016 mol) of $Co(OAc)_2 \cdot 4H_2O$, and 75 mL of quinoline was heated at 150 °C for 2.5 h, while O_2 was passed thru the system. After treatment with dilute HCl, extraction with Et_2O, and distillation, two main fractions (4.6 g) were collected. The most abundant (60%), bp 104–105 °C (0.5 mm), had an ^1H NMR spectrum and retention time on a SE-30 GC column identical with those of 6-pentyl-5-undecene (5), prepared by the dehydration of tripentylcarbinol.[13] The higher boiling component (30%), bp 145–149 °C (0.5 mm), had infrared and NMR spectra identical with those of a known sample of 2,2-dipentylheptanoic acid (4).[1d]

When 2 was heated with Cu powder and O_2 in quinoline solution at 100 °C for 24 h, a mixture resulted that contained 5 and unknown components as shown by GC analysis. However, under comparable conditions except $Co(OAc)_2 \cdot 4H_2O$ was used instead of Cu powder, the reaction product consisted of 73% of 8, 10% of 5, and 17% of 2, as determined by GC. The tripentylcarbinol (8) was isolated by preparative GC, n^{25}_D 1.4472 (lit.[13] n^{20}_D 1.4470), and identified by comparison of NMR and IR spectra with a known sample.

Attempts To Decarbonylate 9. Samples (4 g) of the keto ester 9 were heated at variable temperatures (150–270 °C) with Fe powder and finely ground soft glass, Pd–$BaSO_4$, $[(C_6H_5)_3P]_3RhCl$, H_2CrO_4, and alkaline $KMnO_4$. Only in the latter case did a straightforward reaction result, and 70% of 3,3-dipentyl-2-oxooctanoic acid (2) was obtained.

A mixture of 5 g (0.015 mol) of 9 and 50 mL of a hot solution made by mixing 66 g of 85% KOH and 66 g of triethylene glycol was heated at 210 °C for 20 h and then poured into 200 mL of H_2O. The organic layer was taken up in ether and acidified with HCl. After ether extraction and concentration, there was obtained 4 g (89%) of a waxy solid: mp 44–45 °C (from nitromethane); ^1H NMR δ 6.9–7.4 (s, 2, COH, CO_2H), 4.01 (s, 1, CH), 0.5–1.7 (m, 33, CH_3, CH_2); IR 3100–3600 (m), 1700 (s) cm^{-1}; MS, m/e 301, 302; NE 296. Anal. Calcd for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08. Found: C, 72.07; H, 11.89. When the reaction conditions were changed to 160 °C and 17 h, a 94% yield of 3,3-dipentyl-2-hydroxyoctanoic acid (10) resulted. Under similar conditions, 3,3-dihexyl-2-hydroxynonanoic acid was obtained (93%) from ethyl 3,3-dihexyl-2-oxononanoate: bp 190–194 °C (0.5 mm), mp 27–29 °C. Anal. Calcd for $C_{21}H_{42}O_3$: C, 73.63; H, 12.36. Found: C, 73.87; H, 12.42. 3-Butyl-2-hydroxy-3-pentylnonanoic acid was prepared in a like manner from ethyl 3-butyl-2-oxo-3-pentylnonanoate: bp 190–191 °C (0.15 mm); n^{25}_D 1.4610. Anal. Calcd for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08. Found: C, 72.11; H, 12.28.

Registry No. 1, 815-17-8; 2, 26269-42-1; 3, 75-98-9; 4, 52061-77-5; 5, 51677-36-2; 8, 5331-63-5; 9, 25594-04-1; 10, 85613-93-0; 3,3-dihexyl-2-hydroxynonanoic acid, 85613-94-1; ethyl 3,3-dihexyl-2-oxononanoate, 85613-95-2; 3-butyl-2-hydroxy-3-pentylnonanoic acid, 85613-96-3; ethyl 3-butyl-2-oxo-3-pentylnonanoate, 25594-03-0; pivaldehyde, 630-19-3; pivaldehyde 2,4-dinitrophenylhydrazone, 13608-36-1.

(10) Anders, K. *Acta Chem. Scand.* **1953**, *7*, 889.
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Characterization of Tetrahydroisoquinolines Produced by Pictet-Spengler Reactions of Norepinephrine with Formaldehyde and Acetaldehyde

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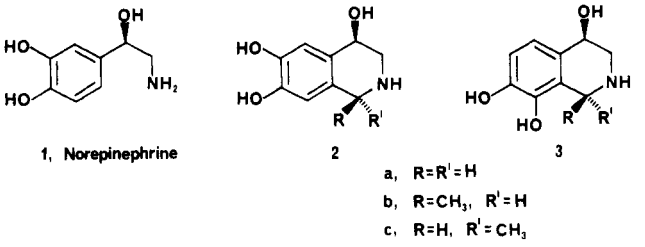
Various symptoms of ethanol intoxication, dependence, and withdrawal may be caused by the reaction of acetaldehyde, the primary metabolite of ethanol, with endogenous catecholamines to produce pharmacologically active tetrahydroisoquinolines.[1] We recently reported that epinephrine (*N*-methyl-1), the major hormone of the adrenal medulla, reacts rapidly with acetaldehyde under physiological conditions to afford a mixture of four isomeric tetrahydroisoquinolinetriols (*N*-methyl-**2b,c** and *N*-methyl-**3b,c**).[2] In the present investigation we have examined the reaction between acetaldehyde and norepinephrine, the transmitter in most sympathetic postganglionic fibers and certain central nervous system tracts.



1, Norepinephrine 2 3

a, R=R'=H
b, R=CH3, R'=H
c, R=H, R'=CH3

Previous investigations demonstrated that acetaldehyde reacts with norepinephrine in vitro and in tissue samples to afford a product thought to be **2b** or **2c**.[1] However due to its labile nature this material had never been isolated or fully characterized, and an attempt to prepare an authentic sample by an independent synthetic route also failed,[3a] presumably for similar reasons.

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(2) Bates, H. A. *J. Org. Chem.* **1981**, *46*, 4931.
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(4) The concentrations of aldehyde and catecholamine in the present study are higher than those employed previously with epinephrine.[2] A comparison of reaction rates must take this into consideration.

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Results and Discussion

Reactions between epinephrine and excess formaldehyde or acetaldehyde were investigated in aqueous solution between pH 0.7 and 7. Initially the reaction of (−)-norepinephrine (1) with aqueous formaldehyde was examined. In neutral or slightly acidic solution, analytical chromatography revealed that a very rapid reaction occurred; however, attempts to isolate the products according to the procedures previously employed with the epinephrine–acetaldehyde condensate[2] were unsuccessful. The norepinephrine–formaldehyde reaction products were found to be even more thermolabile and more polar than their previously encountered homologues. After some experimentation, however, a refinement of the earlier procedures successfully effected the isolation. As noted in the Experimental Section, high temperatures and strongly acidic conditions must be avoided during concentration of aqueous solutions.

In strongly acidic solution, the reaction of norepinephrine with formaldehyde afforded 1,2,3,4-tetrahydro-4,6,7-isoquinolinetriol (**2a**) almost exclusively. Thus at pH 0.7 under the conditions noted in the Experimental Section, the reaction half-life was 2 h at 24 °C. The yield before isolation was nearly quantitative, based on liquid chromatographic analysis, and the yield of **2a** isolated after 24 h was greater than 90%. In contrast, only a low yield of **2a** had been previously isolated after multiple recrystallizations to remove byproducts when this reaction was carried out at pH 2.2.[3b]

At pH 6–7 the reaction was essentially complete in less than 1 min, but a mixture comprised of 80% **2a** plus 20% **3a** was obtained. At pH 5, the half-life was 2.5 min at 24 °C, and a 88:12 mixture of **2a** and **3a** resulted. The combined yield of **2a** plus **3a** was 80–90% when the reaction at pH 6–7 was stopped after 5 min by acidification; however, the products disappeared over the course of several hours when maintained under the reaction conditions and formed an intractable presumably polymeric substance, evidently the product of further reaction with excess formaldehyde.

Isomeric tetrahydroisoquinolines **2a** and **3a** were separated by column chromatography on silica gel with a butanol–water–formic acid eluent. The ^{1}H NMR spectra of **2a** and **3a** matched the literature spectra,[3] and the ^{13}C NMR spectra exhibited the expected similarities with the spectra of the *N*-methyltetrahydroisoquinolines isolated from the epinephrine–formaldehyde reaction.[2]

Attention was now directed toward characterization of the more complex products resulting from the reaction of (−)-norepinephrine with acetaldehyde. At pH 0.7, this reaction with a 4-h half-life produced a 1:1 mixture of epimers **2b** and **2c** in essentially quantitative yield. These compounds had not been previously isolated in pure form and had eluded preparation by an independent synthesis.[3a] We found the two isomers to be inseparable by conventional thin-layer chromatography but separable by reverse-phase liquid chromatography. The stereochemistry in **2b** and **2c** was assigned as before by examination of the ^{1}H NMR chemical shifts and coupling constants. The 4-hydroxyl group preferentially occupies the pseudoaxial position; thus the deshielded (δ 1.70) pseudoequatorial 1-methyl group in **2b** is cis to the 4-hydroxyl while the shielded (δ 1.59) pseudoaxial 1-methyl group in **2c** is trans. These assignments are substantiated by the ^{1}H NMR chemical shift of the proton on C-1 and by the γ-gauche-induced upfield shift of the 1-methyl and C-3 signals in the ^{13}C NMR spectra.[2]

In neutral or slightly acidic solution, reaction between norepinephrine and acetaldehyde produced **3b** and **3c** as well as **2b** and **2c**. When a large excess of acetaldehyde (700 mol %) was utilized at pH 6.5, the half-life for disappearance of norepinephrine was approximately 10 min at 24 °C. Uncharacterizable, presumably polymeric material, however, was the main product of this reaction, and consequently the combined yield of tetrahydroisoquinolines **2b**, **2c**, **3b**, and **3c** was less than 10% on the basis of analytical liquid chromatography. Since the yield of tetrahydroisoquinolines from the analogous reaction between acetaldehyde and epinephrine under analogous conditions is essentially quantitative,[2] the lower yield realized with norepinephrine is presumably the consequence of further reactions of the secondary amine in **2b,c** and **3b,c** with excess acetaldehyde. Indeed, addition of excess acetaldehyde to mixtures of **2b,c** and **3b,c** at pH 6–7 rapidly led to substantial destruction of these compounds.

When less acetaldehyde was used, the reaction was slower and the norepinephrine was incompletely consumed, but the yield of tetrahydroisoquinolines improved. Thus when norepinephrine was treated with 200 mol % of acetaldehyde at pH 6.5, the chromatographically determined yields of **2b**, **2c**, **3b**, and **3c** stabilized at 21%, 22%, 6%, and 11% (60% total yield of tetrahydroisoquinolines) and 23% of the original norepinephrine remained unreacted after 2 h.

Column chromatography on silica gel separated **3b,c** from **2b,c**, and subsequent preparative reverse-phase liquid chromatography separated **3b** from **3c**. Assignment of stereochemistry to **3b** and **3c** followed from examination of the ^{1}H NMR and ^{13}C NMR spectra as described above.

Benzylic 4-hydroxy and 4-alkoxy substituents of tetrahydroisoquinolines such as **2** and **3** are extremely reactive toward nucleophilic substitution and epimerization.[2,6] Thus we previously demonstrated that *N*-methyl-**2b,c** and *N*-methyl-**3b,c** rapidly epimerize at pH 1.5.[2] Accordingly, preparations of tetrahydroisoquinolines **2a**, **2b**, and **2c** formed in strongly acidic solution are certainly racemic. In contrast, tetrahydroisoquinoline products of the condensations conducted under nearly neutral conditions would be expected to retain configurational integrity, but the acidic conditions employed for chromatographic separation on silica gel (formic acid–2-butanol) could potentially cause racemization.

In conclusion, norepinephrine (1) reacts with formaldehyde or acetaldehyde to produce tetrahydroisoquinolines **2** and **3**, the products of Pictet–Spengler condensations para and ortho, respectively, to the activating aromatic hydroxyl group. The products are thus analogous to those obtained from the reaction between epinephrine and formaldehyde or acetaldehyde,[2] although norepinephrine reacts somewhat more rapidly.[4] At low pH, cyclization occurs almost exclusively para to the activating hydroxyl group, in accord with the normally observed specificity of the Pictet–Spengler reaction.[5] Under neutral conditions, however, substantial cyclization ortho to the activating hydroxyl group also takes place. Occurrence of this abnormal cyclization was previously observed to an even greater extent in the reactions of epinephrine with formaldehyde and acetaldehyde and is apparently favored by the benzylic hydroxyl group since catecholamines lacking this functionality are reported to cyclize only para to the activating hydroxyl group.[5]

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(6) Jaques, B.; Deeks, R. H. L.; Shah, P. K. J. *J. Chem. Soc. D* **1969**, 1283.

We are currently examining the biological activities of the isomeric tetrahydroisoquinolines isolated in this study.

Experimental Section

General Procedures. Analytical TLC was performed on EM 5539 silica gel 60 plates eluted with 2-butanol–14 M formic acid (60:40), and preparative column chromatography was performed under nitrogen pressure with 230–400 mesh EM silica gel 60 (E. Merck). Compounds were visualized with 1% $FeCl_3$ in acetone–water (3:2). A Waters 6000-A pump and a Perkin-Elmer LC-55 variable-wavelength detector set at 282 nm were used for liquid chromatography. A 30 × 0.39 cm 10-μm Waters μBondapak C_{18} column was utilized for analytical chromatography, and two Waters 60 × 0.78 and 37–75-μm C_{18} Porasil columns in series were used for preparative chromatography. Elution was accomplished with 0.01 M KH_2PO_4 (pH 4.5) at a flow rate of 2.0 mL/min. The retention volumes (mL) on the analytical column were as follows: **1** (4.82), **2a** (6.28), **2b** (8.24), **2c** (10.92), **3a** (7.10), **3b** (7.08), **3c** (15.90).

^1H NMR were recorded at 80 MHz in D_2O containing DSS as an internal standard on a Varian CFT-20 spectrometer. ^{13}C NMR were recorded at 20 MHz in H_2O plus D_2O at pH 4–5, with dioxane (δ 67.39) as an internal standard on a Varian FT-20 spectrometer. UV spectra were recorded in aqueous solution with a Cary 118 spectrophotometer.

(–)-Norepinephrine was purchased from Sigma Chemical Co.; acetaldehyde was distilled and stored at 5 °C. Solutions were rotary evaporated at 50 °C or less under a vacuum of 2–5 mmHg. Substantial decomposition occurred when a weaker vacuum was utilized.

1,2,3,4-Tetrahydro-4,6,7-isoquinolinetriol Hydrochloride (2a). (–)-Norepinephrine (100 mg, 0.59 mmol) was dissolved in 1 M HCl such that the final pH was 0.4. After purging with nitrogen, aqueous formaldehyde (0.2 mL, 39%, 2.66 mmol, 450 mol %) was added. After 24 h at 24 °C, the solution was extracted three times with ethyl acetate, basified to pH 4 with 1 M $NaHCO_3$, and the water evaporated. The residue was dissolved in water (0.4 mL) plus absolute ethanol (6 mL). The precipitate was removed, and the solvent was evaporated from the filtrate. In the same manner, the filtrate was sequentially triturated with 97% and then 100% ethanol to yield 119 mg (92% yield) of a light yellow solid: mp 165–170 °C dec (lit. mp[3b] 172 °C). UV λ_{max} 283 nm; ^{13}C NMR (H_2O) δ 44.35 (t), 49.00 (t), 62.94 (d), 114.03 (d), 117.00 (d), 120.61 (s), 125.65 (s), 144.94 (s), 145.82 (s); ^1H NMR[3] (D_2O) δ 3.55 (2 H, m), 4.26 (2 H, s), 4.95 (1 H, t, J = 3 Hz), 6.68 (1 H, s), 6.91 (1 H, s); mass spectrum, m/e 181 (13, M^+), 164 (67), 162 (75), 152 (58), 151 (65), 136 (100).

***cis*- and *trans*-1,2,3,4-Tetrahydro-1-methyl-4,6,7-isoquinolinetriol Hydrochloride (2b,c).** (–)-Norepinephrine (100 mg, 0.59 mmol) was dissolved in sufficient 1 M HCl to produce a final pH of 0.7 and treated under nitrogen with acetaldehyde (140 mg, 3.18 mmol, 537 mol %) for 36 h. Extraction with ethyl acetate, adjustment to pH 4, and sequential trituration with 95% and 100% ethanol as described for **2a** afforded 137 mg (100% yield) of a 48:52 mixture of **2b** and **2c** as a lemon yellow solid.

A portion of this mixture (22 mg) was chromatographed on C_{18} Porasil B. Compound **2b** was eluted with 43–56 mL of phosphate buffer and **2c** eluted with 56–85 mL of the buffer. To remove the potassium phosphate, each eluate was passed through Dowex 2-X8 Cl^- (1 mL resin for each 50 mL of eluate) and evaporated; then the residue was sequentially triturated with 95% and 100% ethanol. The final filtrates were evaporated to dryness to afford **2b** (11 mg, 50% yield) and **2c** (11 mg, 50% yield).

***cis*-1,2,3,4-Tetrahydro-1-methyl-4,6,7-isoquinolinetriol hydrochloride (2b)** was obtained as a pale yellow solid: mp 130 °C dec; UV λ_{max} 283 nm; ^{13}C NMR (H_2O) δ 19.27 (q), 48.50 (t), 52.51 (d), 63.24 (d), 113.50 (d), 117.16 (d), 125.72 (s), 126.16 (s), 144.96 (s), 146.09 (s); ^1H NMR (D_2O) δ 1.70 (3 H, d, J = 6.7 Hz), 3.52 (2 H, t), 4.49 (1 H, q, J = 6.7 Hz), 4.90 (1 H, t, J = 3 Hz), 6.80 (1 H, s), 6.92 (1 H, s); mass spectrum, m/e 195 (3, M^+), 180 (79), 164 (100), 162 (94). Anal. ($C_{10}H_{14}NO_3Cl$) C, H.

***trans*-1,2,3,4-Tetrahydro-1-methyl-4,6,7-isoquinolinetriol hydrochloride (2c)** was obtained as a very pale yellow solid: mp 131–133 °C dec; UV λ_{max} 283 nm; ^{13}C NMR (H_2O) δ 19.58 (q), 44.83 (d), 51.23 (t), 63.02 (d), 114.15 (d), 116.92 (d), 125.41 (s), 126.43 (s), 145.08 (s), 146.04 (s); ^1H NMR (D_2O) δ 1.59 (3 H, d, J = 6.7 Hz), 3.59 (2 H, m), 4.65 (1 H, q, J = 6.7 Hz), 4.93 (1 H, t, J = 3 Hz), 6.77 (1 H, s), 6.95 (1 H, s); mass spectrum, see **2b**. Anal. ($C_{10}H_{14}NO_3Cl$) C, H.

1,2,3,4-Tetrahydro-4,7,8-isoquinolinetriol Hydrochloride (3a). (–)-Norepinephrine (200 mg, 1.18 mmol) was dissolved in 1 M HCl (1.3 mL) and adjusted to pH 6.5 with 1 M $NaHCO_3$. Aqueous formaldehyde (0.1 mL, 37%, 1.33 mmol, 112 mol %) was added under nitrogen. After 10 min, 1 M HCl was added to pH 5, the water was evaporated, and the residue was sequentially triturated as before with 90%, 97%, and 100% ethanol. The final filtrate was dissolved in 2-butanol–14 M formic acid (75:25), applied to a 3 × 15 cm silica gel column, and eluted with the same solvent. Compound **3a** was eluted in a pale yellow fraction after 80–110 mL of solvent, while compound **2a** eluted after 120–150 mL. The solvent was evaporated from the eluate containing **3a**, and the residue was dissolved in water, basified to pH 6 with 1 M $NaHCO_3$, filtered through Dowex 2-X8 Cl^- (1 mL, 20–50 mesh) acidified to pH 4 with 1 M HCl, and extracted twice with ethyl acetate. The water was evaporated from the aqueous phase, and the residue was sequentially triturated as before with 90%, 95%, and 100% ethanol to afford 23 mg (9% yield) as a clear solid that eventually became tan colored: UV λ_{max} 280 nm; ^{13}C NMR (H_2O) δ 41.44 (t), 48.42 (t), 62.94 (d), 116.67 (d), 117.21 (s), 122.45 (d), 128.01 (s), 141.37 (s), 145.14 (s); ^1H NMR[3b] (D_2O) δ 3.51 (2 H, m), 4.33 (2 H, AB quartet), 4.99 (1 H, t, J = 3 Hz), 6.95 (2 H, s); mass spectrum, m/e 181 (19, M^+), 164 (42), 162 (77), 152 (82), 151 (100), 136 (50).

***cis*- and *trans*-1,2,3,4-Tetrahydro-1-methyl-4,7,8-isoquinolinetriol Hydrochloride (3b,c).** (–)-Norepinephrine (200 mg, 1.18 mmol) was dissolved in 1 M HCl, adjusted to pH 6.5 with 1 M $NaHCO_3$, and diluted to 7.0 mL with water. Acetaldehyde (125 mg, 2.84 mmol, 240 mol%) was added under nitrogen. The yield of **2** and **3** reached a plateau after 2 h, but the concentration of norepinephrine continued to fall. After 18 h, the deep orange polymeric precipitate was removed by centrifugation and the supernatant was adjusted to pH 4.2 with 1 M HCl, extracted with ethyl acetate, evaporated, and sequentially triturated with 95% and 100% ethanol as before to afford 280 mg of an orange residue.

Chromatography on silica gel (3 × 15 cm column) as described for **3a**, afforded **3b,c** after 60–85 mL of 2-butanol–14 M formic acid (80:20) and **2b,c** after 85–200 mL of the same solvent. The solvent was evaporated from the eluate containing **3b,c**, and the residue was redissolved in water, basified to pH 5 with 1 M $NaHCO_3$, and processed as described for **3a** to afford 43 mg of an impure olive green solid containing **3b,c**. This mixture was chromatographed on C_{18} Porasil B as described above. Compound **3b** eluted after 45–70 mL of solvent and **3c** eluted after 95–130 mL. Removal of the potassium phosphate with Dowex 2-X8 and trituration as described above furnished 8 mg (3% yield) of **3b** and 13 mg (5% yield) of **3c**.

***cis*-1,2,3,4-Tetrahydro-1-methyl-4,7,8-isoquinolinetriol hydrochloride (3b)** was obtained as a light orange solid: mp 184–188 °C dec; UV λ_{max} 280 nm; ^{13}C NMR (H_2O) δ 18.64, 44.94, 49.32, 63.42, 116.53, 121.34, 122.57, 126.60, 141.62, 145.38; ^1H NMR (D_2O) δ 1.73 (3 H, d, J = 6.7 Hz), 3.44 (2 H, d, J = 5.2 Hz), 4.81 (1 H, q, J = 6.7 Hz), 5.02 (1 H, t, J = 5 Hz), 6.98 (2 H, s); mass spectrum, m/e 195.0891 (2, M^+; calcd m/e 195.0896), 180 (100), 175 (27), 172 (77).

***trans*-1,2,3,4-Tetrahydro-1-methyl-4,7,8-isoquinolinetriol hydrochloride (3c)** was obtained as a light orange solid: mp 190–195 °C dec; UV λ_{max} 280 nm; ^{13}C NMR (H_2O) δ 16.62, 43.88, 48.09, 62.98, 116.83, 122.50, 122.95, 124.88, 141.31, 145.59; ^1H NMR (D_2O) δ 1.60 (3 H, d, J = 6.8 Hz), 3.59 (2 H, m), 4.90 (1 H, q, J = 6.8 Hz), 4.95 (1 H, t, J = 3 Hz), 6.96 (2 H, s); mass spectrum, see **3b**.

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Registry No. 1, 51-41-2; **2a**, 41462-32-2; **2b**, 85507-48-8; **2c**, 85507-49-9; **3a**, 85507-50-2; **3b**, 85507-51-3; **3c**, 85507-52-4; formaldehyde, 50-00-0; acetaldehyde, 75-07-0.