L(+)2-TROPINONE

Sir:

We wish to report the synthesis of L(+)2-tropinone, a key degradation product of the alkaloid dioscorine.[1] L-Cocaine hydrochloride[2] was hydrolyzed to ecgonine, which in turn was treated with phosphorus oxychloride to produce the unisolated acid chloride of anhydroecgonine.[3] Cold aqueous ammonia converted the chloride to L(−)-anhydroecgonine amide, m.p. 142.5–145°, $[\alpha]^{25}D$ −51.2° (1% in H_2O).

(*Anal.* Calcd. for $C_9H_{14}N_2O$: C, 65.03; H, 8.49; N, 16.86. Found: C, 65.27; H, 8.35; N, 16.66).[4] Treatment of the amide with sodium hypochlorite in aqueous methanol and then acid hydrolysis furnished L(+)2-tropinone, b.p. 60–61° (0.55 mm.), m.p. *ca.* 27°, $[\alpha]^{30}D$ +23.0° (1.6% in H_2O) (*anal.* Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.36; H, 9.46; N, 9.89).

The infrared spectrum showed carbonyl absorption at 5.82 μ ($CHCl_3$ solution and liquid film). The methiodide, m.p. >330°, (*anal.* Calcd. for $C_9H_{16}INO$: I, 45.14. Found: I, 45.28) absorbed at 5.76 μ (Nujol). The hydrobromide, m.p. 266–266.5°, reconvertible to the parent base, crystallized from methanol as a methanolate which was devoid of carbonyl absorption (KBr disc) and was therefore formulated as the hemiketal (*anal.* Calcd. for $C_8H_{13}NO\cdot HBr\cdot CH_4O$: C, 42.86; H, 7.19; Br, 31.69; CH_3O, 12.31. Found: C, 42.78; H, 6.84; Br, 32.20; CH_3O, 11.78).[5]

Apparently the proximity of the positively charged nitrogen in the 2-tropinone salts to the trigonal carbon is responsible for both the shift of ketonic absorption to lower wave lengths and the ready solvation of the carbonyl group.

Reduction of 2-tropinone with lithium aluminum hydride gave mainly 2α-tropanol, m.p. 73–76° (*anal.* Calcd. for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 67.61; H, 10.63; N, 9.88), (hydrochloride, m.p. 268–269.5° (dec.) (*anal.* Calcd. for $C_8H_{16}ClNO$: N, 7.88. Found: N, 7.81), and a small amount of the liquid 2β-tropanol isolated as the hydrochloride, m.p. 326–328° (dec.) (*anal.* Found: N, 7.70). Reduction of 2-tropinone by a slight modification of Dev's[6] sodium–propanol-2 method afforded in about 55% yield, 2β-tropanol substantially free of the alpha isomer (vapor phase chromatography and infrared spectrum). Since the intensity of the broad hydroxyl band in the spectrum of the solid isomer was concentration dependent and the intensity of the sharp hydroxyl band of the liquid isomer did not change on dilution, the latter alcohol shows intramolecular hydrogen bonding and must be 2β-tropanol. This is a case wherein metal–alcohol reduction of an unhindered ketone affords predominantly if not exclusively the axial alcohol.

(1) D. E. Ayer, G. Büchi, P. Reynolds Warnhoff and Dwain M. White, THIS JOURNAL, **80**, 6146 (1958).

(2) E. Hardegger and H. Ott, *Helv. Chim. Acta*, **38**, 312 (1955).

(3) A. Einhorn, *Ber.*, **20**, 1221 (1887).

(4) Analyses and spectral determinations were carried out under the supervision of M. E. Auerbach and F. C. Nachod, respectively.

(5) Earlier, R. E. Lyle, *et al.*, *J. Org. Chem.*, in press, found that 1-methyl-3-piperidone behaved similarly, *i.e.*, the base absorbed at 5.82 μ (liquid film) and the corresponding hydrochloride formed a stable hydrate that was transparent in the carbonyl region in the infrared. We wish to thank Dr. Lyle for supplying this information in advance of publication.

(6) S. Dev, *J. Ind. Chem. Soc.*, **33**, 769 (1956).

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HYDANTOIN-5-PROPIONIC ACID: A NEW URINARY METABOLITE OF UROCANIC ACID

Sir:

Some unidentified acidic metabolites have been found in urine after administration of radioactive histidine and urocanic acid (I) to mammals.[1] They could not be accounted for as intermediates in the known catabolic pathway of I which proceeds through breakage of the ring to formiminoglutamic acid (II) and finally glutamic acid.[2] Alternate pathways have been demonstrated in bacteria[3] and have been induced *in vitro* by the addition of oxidants (dichlorophenolindophenol (III) or ferricyanide) to I in the presence of purified liver urocanase.[4] It was suggested to us by Dr. B. Witkop that the hydantoin structure could account for the marked acidity of these unknown compounds.

Ring labelled (2-C^{14}) I was made enzymatically from L-histidine (Nuclear-Chicago),[5] and 4.8 μc. (9.3 mg.) were injected intraperitoneally into a 200-g. white male rat. Urine was collected under toluene; 10% of the injected radioactivity was excreted during the first 12 hours.

Urine was chromatographed directly on Dowex-1×8-acetate (100–200 mesh, 50 drops/tube). Samples were collected automatically, dried, and counted on a Packard Tri-Carb liquid scintillation counter after the addition of hyamine and phosphor.[6] Figure 1 shows the elution pattern. Un-

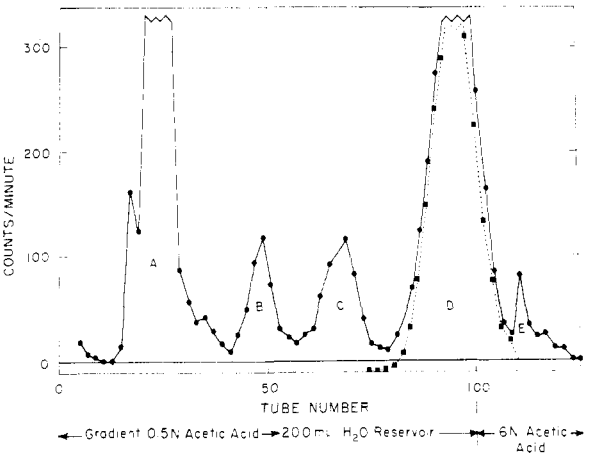

Fig. 1.—Urinary metabolites of 2-C^{14} urocanic acid in the rat.

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