flux to give 2-(N-methylphenethylamino)-propionanilide (III), m.p. 65–67°, in 81% yield. The reduction of III with lithium aluminum hydride in tetrahydrofuran afforded 80% of N^2-methyl-N^2-phenethyl-N^1-phenyl-1,2-propanediamine (IV), b.p. 138–144° (0.2 mm.), $n^{27}D$ 1.564. When IV was acylated with propionic anhydride N-[2-(methylphenethylamino)-propyl]-propionanilide (Ib), b.p. 174–178° (0.5 mm.), $n^{26}D$ 1.546, was obtained in 83% yield. The sulfate, m.p. 110–111°, crystallized from ethanol–ether in 85% yield. *Anal.* Calcd. for $C_{21}H_{30}N_2O_5S$: C, 59.7; H, 7.2; N, 6.6; S, 7.6. Found: C, 59.4; H, 7.4; N, 6.6; S, 7.4.

A benzene solution of aniline and 1-(2-bromopropionyl)-piperidine[7] was heated under reflux to give 1-(2-anilinopropionyl)-piperidine (V), m.p. 90–91° in 81% yield. The reduction of V with lithium aluminum hydride in tetrahydrofuran yielded 86% of 1-(2-anilinopropyl)-piperidine (VI), b.p. 108–112° (0.4 mm.), $n^{29}D$ 1.537. Acylation of VI with propionic anhydride gave N-(1-methyl-2-piperidinoethyl)-propionanilide (Ic), b.p. 124–128° (0.2 mm.), $n^{28}D$ 1.518, in 88% yield. The hydrochloride, m.p. 201–202°, was obtained in 88% yield by treating Ic with ethanolic hydrogen chloride and ether. *Anal.* Calcd. for $C_{17}H_{27}ClN_2O$: C, 65.8; H, 8.8; Cl, 11.4; N, 9.0. Found: C, 65.7; H, 8.7; Cl, 11.4; N, 9.3.

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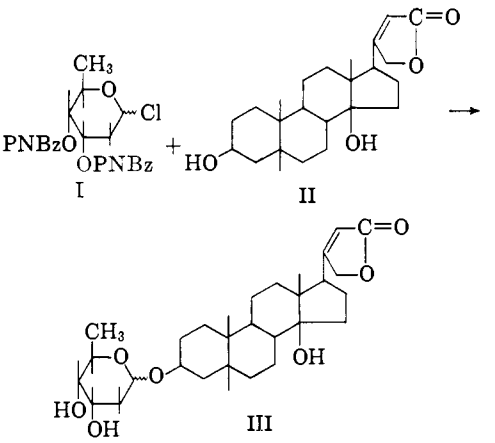
THE PARTIAL SYNTHESIS OF A MONODIGITOXOSIDE OF DIGITOXIGENIN[1]

Sir:

We wish to report the partial synthesis of a monodigitoxoside of digitoxigenin (II) which represents, to our knowledge, the first partial synthesis of a 2′-deoxycardenolide.

By coupling 3,4-di-*O*-*p*-nitrobenzoyl-2,6-dideoxy-D-*ribo*-hexosyl chloride (I)[2] with digitoxigenin (II) in the absence of an acid acceptor, there was obtained an *O*-acylated glycoside which was not isolated; instead, the crude reaction products were saponified *in toto* to give material which, by fractional crystallization, yielded a small quantity of the digitoxoside III, m.p. 253.5–258.5°, $\lambda_{max}^{Me\ alc}$ 218 mμ (characteristic of the α,β-butenolide ring at C_{17}); (*Anal.* Calcd. for $C_{29}H_{44}O_7$: C, 69.00; H, 8.79. Found: C, 68.67; H, 8.74). The compound gave a positive Kedde reaction.

The glycoside III differs from the "natural" monodigitoxoside obtained by Kaiser and coworkers[3]; the infrared spectra of the two compounds, although not identical in all respects, bear



a striking similarity. Paper chromatography in a system designed to separate closely related cardenolides[3] proved III to be homogeneous. It has an R_f value midway between digitoxigenin (II) and Kaiser's monodigitoxoside.[4] Splitting of 0.5 mg. of III in methanol under conditions of transglycosidation and paper chromatography of the resulting material in the same system gave a single spot, coincident in position with digitoxigenin (II). A similar quantity of III (0.4 mg.) was hydrolyzed in a manner to yield the free sugar rather than its methyl glycoside. This was likewise chromatographed, but in a system suitable for sugars only. The result again was a single spot (detected by a reagent employed for deoxy sugars[5]) coinciding exactly with digitoxose (2,6-dideoxy-D-*ribo*-hexopyranose).

The securing of a monodigitoxoside of digitoxigenin different from the "natural" compound is not unexpected, and our III may well be the alternate anomeric form. Since the structure of the "natural" glycoside has not been adduced with certainty, either with respect to the size of the lactol ring of the bound digitoxose or as to anomeric configuration, it is felt that the synthesis reported herein will, ultimately, have an important bearing on these two yet unresolved questions.

Noteworthy also is the fact that our synthesis was accomplished in a classical, yet simple and direct, method, *i.e.*, by converting the 2-deoxy sugar under consideration to an acylglycosyl halide and coupling the latter to the genin II. This obviates the more cumbersome methodology as employed in the synthesis of 2′-deoxyuridine,[6] and of 2′-deoxyadenosine.[7]

Details of this work, which will include configurational assignments, will be published in full at a later date.

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