The addition reactions involving the nitrile imines and their formation by thermolysis of I and dehydrochlorination of VIII are novel in that they represent examples of 1,3-addition and elimination reactions. Apparently, the only nitrile imine described previously is "isodiazomethane,"[4] prepared by de- and reprotonation of diazomethane.

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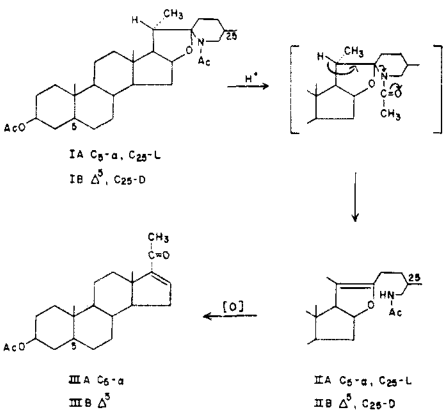
Improvement in the Preparation of 3β-Acetoxy-5α-pregn-16-en-20-one and 3β-Acetoxypregna-5,16-dien-20-one from the Steroidal Alkaloids, Tomatidine and Solasodine

Sir:

The degradation of the steroidal alkaloids, tomatidine and solasodine into 3β-hydroxy-5α-pregn-16-en-20-one[1] (yield: *ca.* 60%) and 3β-acetoxypregna-5,16-dien-20-one[2,3] (yield: *ca.* 10%) has been previously reported. A recent article,[4] using a modification of the original method, reports a marked improvement in the yield of pregnadienolone from solasodine. We wish to report our findings on the conversion of the steroidal alkaloids which lead to a further substantial increase in the production of allopregnenolone and pregnadienolone from tomatidine and solasodine, respectively.

O,N-Diacetyltomatidine[5] (IA) and *O,N*-diacetylsolasodine[6] (IB) in an acidic medium undergo a remarkably facile prototropic rearrangement to yield the unsaturated *O,N*-diacetyl derivatives IIA and IIB. Thus, O,N-diacetyltomatidine (IA) can be converted in an almost quantitative manner (95–98%) to IIA, m.p. 128–132°,[7] $[\alpha]_D^{20}$ +1.5°, λ_{max}^{chlf} 2.89, 2.97μ (N—H); 5.78μ (3-acetoxy); 5.99, 6.59μ (NH-acetyl) (*Anal.* Calcd. for $C_{31}H_{49}O_4N$: C, 74.51; H, 9.88. Found: C, 74.66; H, 10.02), by the treatment of IA with a solution of mineral acid in acetic acid at room temperature or more conveniently by the direct introduction of IA into boiling acetic acid followed by brief refluxing (15 min.). The partially hydrolyzed alcohol of IIA has been previously obtained by the alkaline hydrolysis of the so-called unsaturated triacetyltomatidine.[8]

Upon carefully controlled oxidation of IIA with chromic acid in acetic acid and subsequent cleavage of the side chain moiety with acetic acid[9] 3β-acetoxy-5α-pregn-16-en-20-one (IIIA) is obtained in excellent yields (*ca.* 80% based on IA), m.p. 165–167°, $[\alpha]_D^{20}$ + 42° ($CHCl_3$), λ_{max} 239 mμ, log ε 3.98, (*Anal.* Calcd, for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.32; H, 9.58). It agreed in all properties with an authentic sample of allopregnenolone.



In a similar manner the treatment with acetic acid of *O,N*-diacetylsolasodine (IB) yielded IIB (95–98%), m.p. 135–138°, $[\alpha]_D^{20}$ −23°, λ_{max}^{chlf} 2.90, 2.98μ (N—H); 5.78μ (3-acetoxy); 5.98, 6.60μ (NH-acetyl), (*Anal.* Calcd. for $C_{31}H_{47}O_4N$: C, 74.81; H, 9.52. Found: C, 75.09; H, 9.36) which has also been previously obtained from the alumina chromatography of the unsaturated triacetylsolasodine[3] (pseudosolasodine A). Oxidation and removal of the consequent 16β-ester side chain of IIB resulted in a good yield (75–80% based on IB) of 3β-acetoxypregna-5,16-dien-20-one (IIIB) m.p. 173–175.5°, $[\alpha]_D^{20}$ −35°, λ_{max} 239 mμ, log ε 4.0, (*Anal.* Calcd. for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.45; H, 9.11), identical in all respects with an authentic specimen. In a continuous operation from solasodine without isolation and purification of intermediates, an over-all yield of 65% of IIIB was obtained.

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This method of production of pregnadienolone appears to be superior to the hitherto published methods[3,4] where some by-product[10] formation is involved. The successful degradation of these steroidal alkaloids in high yields, particularly solasodine to pregnadienolone, a biologically important hormone intermediate, may be of considerable industrial importance.

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[10] The stucture and the various chemical manifestations of this substance will be published in the full report.

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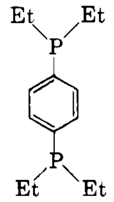
P,P,P',P'-Tetraethyl-*p*-phenylenediphosphine

Sir:

A recent preliminary report by Clifford and Olsen[1] prompts us to record at this time our preparation of *P,P,P',P'*-tetraethyl-*p*-phenylenediphosphine (I). This substance is the phosphorus analog of the tetraalkyl-*p*-phenylenediamines, which are the precursors of the highly colored Wurster radical ions. Our studies on the behavior toward oxidizing agents of the diphosphine I and of the corresponding N-P system, will be published elsewhere.



I

The diphosphine I was obtained in *ca.* 20% yield from the reaction of diethylchlorophosphine[2] with *p*-phenylenedilithium[3] in petroleum ether at temperatures below 30°, in a nitrogen atmosphere. I was isolated by extraction into hydrochloric acid followed by the usual alkaline treatment and fractional distillation. The diphosphine I had b.p. 172–174° (9 mm.), n_D^{25} 1.5666, bands at 6.85, 7.00, 7.22, 8.1, and 8.90 μ. Calcd. for $C_{14}H_{24}P_2$: C, 66.2; H, 9.5; P, 24.4. Found: C, 66.2; H, 9.4; P, 23.9.

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A New Synthesis of Serotonin

Sir:

The nitroethylation of indoles and substituted indoles, yielding 3-(2-nitroethyl)indoles has been previously described.[1-3] Catalytic hydrogenation of the 3-(2-nitroethyl)indoles provides a general synthetic route to tryptamine and substituted tryptamines. We wish to record the successful application of this procedure to the synthesis of serotonin.

Dropwise addition of a 1*M* excess of nitroethylene[4,5] to molten 5-benzyloxyindole at steam-bath temperature (total time 1.83 hr.) gave 3-(2-nitroethyl)-5-benzyloxyindole (I, hygroscopic white crystals from methylene chloride-light petroleum (b.p. 60–68°), m.p. 93.5–95°, calcd. for $C_{17}H_{16}N_2O_3$ (296.31): C, 68.90; H, 5.44; N, 9.45; found: C, 68.62; H, 5.58; N, 9.13) in 45% yield. Use of excess nitroethylene is desirable since unreacted 5-benzyloxyindole (36% by wt.) and I (64%) form a eutectic mixture, m.p. 81–81.5°. Similar reactions of 5-benzyloxyindole with equimolar portions of β-nitrostyrene (6 hr., 72% yield) and β-methyl-β-nitrostyrene (22 hr., 37% yield), both at steam bath temperature, gave 3-(1-phenyl-2-nitroethyl)-5-benzyloxyindole (II, white platelets from ethanol, m.p. 117–118°, calcd. for $C_{23}H_{20}N_2O_3$ (372.41): C, 74.17; H, 5.41; N, 7.52; found: C, 74.36; H, 5.40; N, 7.36) and 3-(1-phenyl-2-nitropropyl)-5-benzyloxyindole (III, white rod-like crystals from ethanol, m.p. 152–152.5°, calcd. for $C_{24}H_{22}N_2O_3$ (386.43): C, 74.59; H, 5.74; N, 7.25; found: C, 74.80; H, 5.61; N, 7.26).

Hydrogenation at 2 atm. over platinic oxide catalyst of the adducts I–III gave in high yields the corresponding tryptamines, isolated as the picrates: Ia (84% yield from I), very hygroscopic reddish orange crystals from ethanol, m.p. 231.5–

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