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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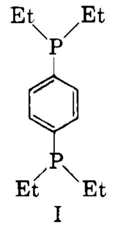
P,P,P′,P′-Tetraethyl-*p*-phenylenediphosphine

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 $1M$ 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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Spectral Data on New Compounds

	Ultraviolet: Wave lengths of maxima and inflections (*) in 95% ethanol are given in mμ with intensities in (log ε)					Infrared Frequencies in Cm.$^{-1}$		
						Medium	NH	NO_2 (Aliphatic)
I	275	296*		307*		$CHCl_3$	3520	1558, 1387
	(3.83)	(3.70)		(3.54)		Nujol	3380	1553, 1385
II	275	295*		308*		$CHCl_3$	3440	1552, 1380
	(3.85)	(3.74)		(3.60)		Nujol	3400	1550, 1380
III	275	295*		309*		$CHCl_3$	3450	1550, 1387 or 1360
	(3.81)	(3.73)		(3.57)		Nujol	3390	1547, 1385 or 1355
Ia	275*	297		309	357	Nujol	3400	
	(3.92)	(3.85)		(3.85)	(4.20)			
IIa	277*	297	302*	309	357	Nujol	3360	
	(3.91)	(3.87)	(3.87)	(3.87)	(4.20)			
IIIa	277*	298	304*	309	357	Nujol	3400	
	(3.90)	(3.88)	(3.87)	(3.89)	(4.20)			

232° dec., calcd. for $C_{23}H_{21}N_5O_8$ (495.44): C, 55.75; H, 4.27; N, 14.14; found: C, 55.69; H, 4.58; N, 14.07; IIa (94% yield from II), red crystals from ethanol, m.p. 176–176.5°, calcd. for $C_{29}H_{25}N_5O_8$ (571.53): C, 60.94; H, 4.41; N, 12.25; found: C, 60.96; H, 4.74; N, 12.08; IIIa (62% yield from III), bright red crystals from ethanol, m.p. 213–215°, calcd. for $C_{30}H_{27}N_5O_8$ (585.56): C, 61.53; H, 4.65; N, 11.96; found: C, 61.83; H, 4.91; N, 12.09. The tryptamine from I was also characterized as the hydrochloride, which had m.p. 245–247° dec., in agreement with that reported, 248–250°.[6]

Hydrogenation of I at 2 atm. over 10% palladium on charcoal catalyst, resulting in concomitant reduction of the nitro group and debenzylation, gave serotonin in 69% yield as the hygroscopic creatinine sulfate monohydrate salt, m.p. 212–214°, mixed m.p. with an authentic sample (of m.p. 214–216°), 212–216°. The infrared spectra of the two samples in Nujol were identical and in agreement with the spectrum described in the literature[6]—λ_{max} in water: 220 mμ (log ε 4.40), 274 (3.72), 293 inflection (3.63). Reported λ_{max} in water: 275 mμ and 293 inflection.[7] Calcd. for $C_{14}H_{23}N_5O_7S$ (405.43): C, 41.47; H, 5.72; N, 17.28; S, 7.91; found: C, 41.43; H, 5.73; N, 17.54; S, 8.14. This new synthesis of serotonin in two steps from 5-benzyloxyindole is simpler than previously described methods. The over-all yield (31%) from 5-benzyloxyindole appears to be higher than that reported for all other methods except those of Speeter and Anthony[8] (probably greater than 60%) and Young (34%).[9]

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Formylation of Aromatic Amines with Dimethylformamide[1]

Sir:

A variety of methods are available for the preparation of formamides.[2] However, only several procedures exist for the direct formylation of amines with more readily available formamides.

In 1886, Just described the formylation of phenylhydrazine with formamide at 130°.[3] Several years later Hirst and Cohen obtained formanilides from a number of aromatic amines using formamide in glacial acetic acid.[4] A more recent procedure employs the amine hydrochloride and formamide.[5]

We now wish to report the facile formylation of aromatic amines with dimethylformamide in the presence of sodium methoxide. Conversion to the formanilide is accomplished by heating a mixture of sodium methoxide (0.3 mole), the aniline (0.15 mole) and dimethylformamide (150 ml.) at reflux for 30 min. The reaction is accompanied by the evolution of dimethylformamine. Generally, the formanilide, obtained by diluting the reaction mixture with water, does not require further purification. Typical examples include 2-iodoformanilide, colorless needles, m.p. 113–113.5°, 68% yield (*Anal.* Calcd. for C_7H_6INO: C, 34.04; H, 2.45; N, 5.67.

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[1] Support of this investigation by a Frederick Gardner Cottrell grant from the Research Corporation is gratefully acknowledged.

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