

hydrazine. From the results in Table II it is seen that only acethydrazide has an effect. This effect is thought to be the result of disproportionation of acethydrazide yielding hydrazine and diacethydrazide.

TABLE II
EFFECT OF IMPURITIES

System	Absorbance	
	A	B
a. N ₂ H ₄ ·HOAc	0.318	0.612
b. a + 5.4 mM. AcNHNH ₂	0.322	0.618
c. b + 5.2 mM. AcNHNHAc	0.314	0.610
d. a + 1% water	0.316	0.611

A. N₂H₄·HOAc = 0.40 mg./ml., 4.35 mM.
B. N₂H₄·HOAc = 0.80 mg./ml., 8.70 mM.

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Mescaline Analogs IX. Tetra- and Pentamethyl- β -phenethylamines

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As part of a continuing study of the relationship between chemical structure and psychotomimetic activity, the effect of replacing the methoxyl groups in the hallucinogen mescaline with methyl groups has been examined.³ This series of ring-substituted polymethyl- β -phenethylamines has been extended to include all three possible tetramethyl- β -phenethylamines and pentamethyl- β -phenethylamine. The psychopharmacological properties of these compounds are to be compared with those of the corresponding tetra- and pentamethoxy- β -phenethylamines, which were described previously.⁴

The ring-substituted tetra- and pentamethyl- β -phenethylamines were all prepared by the same synthesis scheme as outlined by the following general equation, where Ar represents the appropriately polymethyl-substituted phenyl group: ArH \rightarrow ArCH₂Cl \rightarrow ArCH₂CN \rightarrow ArCH₂CH₂NH₂. This synthetic route was particularly well suited to this series of compounds, since all of the starting tetra- and pentamethylbenzenes are commercially available or are readily accessible, and the chloromethylation reaction can give only one monochloromethyl product in each case. Treatment of the substituted benzyl chlorides so obtained with sodium cyanide and reduction of the resulting substituted phenyl-

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(3) F. Benington, R. D. Morin, and L. C. Clark, *J. Org. Chem.*, **22**, 332 (1957).

(4) F. Benington, R. D. Morin, and L. C. Clark, *J. Org. Chem.*, **20**, 102 (1955).

acetonitriles with lithium aluminum hydride proceeded smoothly and afforded the desired ring-substituted polymethyl- β -phenethylamines, which were isolated as their hydrochlorides.

Results of psychopharmacological studies will be published elsewhere.

EXPERIMENTAL⁵

Preparation of polymethylbenzyl chlorides. All of the polymethylbenzyl chlorides were prepared by chloromethylation of the appropriate hydrocarbon by a procedure similar to that described by Aitken *et al.*⁶ In a typical run, a mixture of 25 g. (0.183 mole) of 1,2,3,4-tetramethylbenzene, 57 ml. of glacial acetic acid, 105 ml. of concentrated HCl, and 13 g. of 37% aqueous formaldehyde was stirred and heated at 60–70° for 6 hr., adding an additional 5.4 g. of formaldehyde solution at the end of the first 3 hr. When cool, the aqueous layer was decanted from the insoluble white solid reaction product, which was dissolved in benzene. The resulting solution was washed with aqueous Na₂CO₃, dried over anhydrous MgSO₄, and the solvent was removed by distillation under reduced pressure. Distillation of the residue gave 18.0 g. (52%) of pure 2,3,4,5-tetramethylbenzyl chloride; b.p. 140–150°/7–10 mm.; m.p. 44–45° (literature,⁷ m.p. 44–45°). By employing this procedure with other polymethylbenzenes, the following benzyl chlorides were prepared: pentamethylbenzyl chloride, m.p. 81–82° (literature,⁸ m.p. 82–84°), from pentamethylbenzene; 2,3,4,6-tetramethylbenzyl chloride, b.p. 133–137°/10 mm. (literature,⁸ b.p. 113–115°/5 mm.), from isodurene⁹; 2,3,5,6-tetramethylbenzyl chloride, b.p. 122–125°/5 mm. (literature,⁸ b.p. 140–148°/15 mm.), m.p. 70–71° (literature,⁹ m.p. 67–68°), from durene.

Preparation of polymethylphenylacetone nitriles. All of the intermediate polymethylphenylacetone nitriles were prepared by treatment of the benzyl chlorides with NaCN in an aqueous alcohol solution and refluxing the mixture for a period of 3 hr. The phenylacetone nitriles were isolated and purified by the procedure outlined by Adams and Thal.¹⁰ The following polymethylphenylacetone nitriles were obtained by this procedure: 2,3,5,6-tetramethylphenylacetone nitrile, m.p. 85–87° (literature,⁶ m.p. 84–85°); 2,3,4,6-tetramethylphenylacetone nitrile, b.p. 148–164°/7 mm.; m.p. 49–50°¹¹; 2,3,4,5,6-pentamethylphenylacetone nitrile, b.p. 143–146°/1.2 mm., m.p. 103–104°.

Anal. Calcd. for C₁₃H₁₇N: C, 83.4; H, 9.1; N, 7.5. Found: C, 82.6; H, 9.0; N, 8.0.

Polymethyl- β -phenethylamines. The intermediate nitriles were reduced by means of lithium aluminum hydride using a procedure previously described for the preparation of pentamethoxy- β -phenethylamine by reduction of the corresponding nitrile.⁴ The β -phenethylamines were isolated by hydrolyzing the final reduction mixture with a limited quantity of water, filtering the ether solution of the product from inorganic matter, and drying the filtrate over anhydrous magnesium sulfate. In each instance, the product was

(5) All melting and boiling points are uncorrected.

(6) R. R. Aitken, G. M. Badger, and J. W. Cook, *J. Chem. Soc.*, 331 (1950).

(7) L. I. Smith and C. L. Agre, *J. Am. Chem. Soc.*, **60**, 648 (1938).

(8) R. C. Fuson and C. A. Sperati, *J. Am. Chem. Soc.*, **63**, 2643 (1941).

(9) Prepared from mesitylene as described by L. I. Smith, *Org. Syntheses*, **Coll. Vol. II**, 1st ed., 360 (1943).

(10) R. Adams and A. F. Thal, *Org. Syntheses*, **Coll. Vol. I**, 2nd ed., 107 (1948).

(11) Product was not further purified prior to use in next step. L. I. Smith, *J. Am. Chem. Soc.*, **60**, 648 (1938), reported a melting point of 57–58° for this nitrile.

isolated as the hydrochloride by treating the dry ether solution with anhydrous hydrogen chloride to obtain the following compounds:

2,3,4,5-Tetramethyl-β-phenethylamine hydrochloride (30%); m.p. 246–248°; colorless platelets (ethanol-ether).

Anal. Calcd. for C₁₂H₂₀ClN: Cl, 16.6; N, 6.55. Found: Cl, 16.4; N, 6.49.

2,3,4,6-Tetramethyl-β-phenethylamine hydrochloride (69%); m.p. 283–285° (dec.); colorless platelets (ethanol).

Anal. Calcd. for C₁₂H₂₀ClN: Cl, 16.6; N, 6.55. Found: Cl, 16.3; N, 6.54.

2,3,5,6-Tetramethyl-β-phenethylamine hydrochloride (79%); m.p. 360–365° (subl.); colorless plates (ethanol-water).

Anal. Calcd. for C₁₂H₂₀ClN: Cl, 16.6; N, 6.55. Found: Cl, 16.3; N, 6.45.

2,3,4,5,6-Pentamethyl-β-phenethylamine hydrochloride (40%); m.p. 340° (subl.); colorless needles (ethanol-water).

Anal. Calcd. for C₁₃H₂₂ClN: Cl, 15.6; N, 6.15. Found: Cl, 15.7; N, 6.0.

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Phosphinemethylenes. IV. Coupling of Triphenylphosphoniumcyclopentadienylide with *p*-Diethylaminobenzediazonium Chloride

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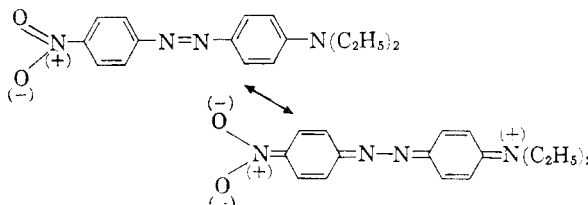
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We described recently^{2a} the preparation of the brightly colored phenylazophosphinemethylene (V) and *p*-nitrophenylazophosphinemethylene (VI), from the coupling reaction of triphenylphosphoniumcyclopentadienylide (I)^{2b} with the corresponding diazonium halide, II and III. In these reactions, a methylene chloride solution of the phosphine methylene I was added to an aqueous solution of the diazonium chloride, buffered with sodium acetate. Using the same procedure, we have prepared triphenylphosphonium-[2-(*p*-diethylaminophenylazo)cyclopentadienylide] (VII), a stable, crystalline substance, m.p. 199–200°, which is green in the form of large crystals and red-orange when powdered.

The *p*-diethylaminophenylazophosphinemethylene (VII) formed a crystalline *dihydrobromide*, which, as previously discussed,^{2a} has probably the structure of a cyclopentadienone phenylhydrazone (VIII).

It is of interest to compare the ultraviolet absorption spectra of the series of azophosphine-

methylenes having electron-attracting and electron-releasing groups in conjugation with the phosphorus. Table I shows the main absorption maxima of these substances in neutral and in acidic aqueous alcohol. In the azophosphinemethylenes (*neutral* medium), both types of groups exert a powerful bathochromic effect, although the *p*-nitro effect is considerably greater. We have suggested^{2a} that these bands are due to electronic transitions from ground states of type $a \leftrightarrow b$ (with little contribution from structures c and d) to electronically excited states of type $c \leftrightarrow d$. It may well be that operation of *d*-orbital resonance in phosphorus permits a significant contribution of structure VIIe to the excited state. Some of the electronic features of 4'-nitro-4-diethylaminoazobenzene³ can be recognized in the substituted azophosphinemethylenes VI and VII



Perhaps it is valid to regard the phosphoniumcyclopentadienylide moiety in the azophosphinemethylenes as both an electron-source and an electron sink, depending on the demands of the *p*-phenyl substituent X.

TABLE I

ULTRAVIOLET SPECTRA OF TRIPHENYLPHOSPHONIUM-[2-(X-PHENYLAZO)]CYCLOPENTADIENYLIDES

X	Neutral λ_{\max} , M μ (ϵ)	Acid λ_{\max} , M μ (ϵ)
<i>p</i> -H	455 (20,600)	440 (25,300)
<i>p</i> -N(C ₂ H ₅) ₂	483 (30,000)	423 (31,700)
<i>p</i> -NO ₂	537 (28,300)	436 (36,300)

In the hydrobromides, or in the azophosphinemethylenes in *acid* medium, both types of groups exert a weak hypsochromic effect, but now the *p*-diethylamino effect is somewhat greater. The bands in acid medium can be interpreted^{2a} in terms of electronic transitions from a ground state of type VIIc to an electronically excited state of type VIIIb. In this anomalous^{2a} phenylhydrazone absorption, the nature of the group X in the *p*-phenyl position is not very significant. In acid medium, the diethylammonium group is, as the nitro-group, strongly electron attracting, affecting adversely the stability of structure VIIIb.

It may be pointed out that, at least in some cases, the coupling reaction of the phosphinemethylene

(1) Texas Co. Fellow, 1956–1957.

(2) (a) F. Ramirez and S. Levy, *J. Am. Chem. Soc.*, **79**, 6167 (1957); (b) *J. Am. Chem. Soc.*, **79**, 67 (1957).

(3) (a) E. Sawicki, *J. Org. Chem.*, **21**, 605 (1956); (b) W. S. McGuire, T. F. Izzo, and S. Zuffanti, *J. Org. Chem.*, **21**, 632 (1956).