Sympathomimetics: 2,3-Diphenylpropylamines[1]

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The sympathomimetic group of drugs is composed largely of phenylethylamines with various substituents on both the aromatic and aliphatic portions of the molecule. It has often been found that the addition of a methyl group to either carbon of the aliphatic chain of phenethylamine derivatives yielded compounds with improved pressor activity (*i. e.*, amphetamine, propadrine, ephedrine), but the effect produced by introduction of radicals larger than methyl in these positions has not been extensively studied. It was believed important that such substitutions be investigated since it is possible that compounds with more prolonged pharmacological action might result.

For initial studies 2,3-diphenylpropylamines, compounds that may be regarded as 2-aralkylphenethylamines, were synthesized.

2,3-Diphenylacrylonitriles (prepared by the procedure of Knoevenagel[3] in glacial acetic acid solution were smoothly hydrogenated to diphenylpropylamines in a Parr low-pressure hydrogenator using platinum oxide catalyst. The products were isolated in yields varying from 58–72%. 2-Phenyl-3-(4-hydroxyphenyl)-propylamine and 2-phenyl-3-(3,4-dihydroxyphenyl)-propylamine were obtained from the corresponding methoxy and methylenedioxy amines by hydrolysis with hydriodic acid. These compounds were extracted as free bases and converted into hydrochlorides with alcoholic hydrogen chloride.

Experimental

2,3-Diphenylacrylonitriles.—One mole of benzyl cyanide, one mole of benzaldehyde, and 15 cc. of piperidine were mixed and heated at 100° for thirty-six hours. While hot, the mixture was poured into a beaker and stirred occasionally until it had crystallized. The crystals were washed free of unreacted materials on a filter and recrystallized from glacial acetic acid. The recrystallized product was air-dried. 2,3-Diphenyl-,[3] 2-phenyl-3-(4-methoxyphenyl)-,[4] and 2-phenyl-3-(3,4-methylenedioxyphenyl)-acrylonitriles were obtained in yields of 86, 42 and 43%, respectively. The latter compound, not previously synthesized, melted at 115–116°, and its empirical formula was proved by analysis.

Anal. Calcd. for $C_{16}H_{12}O_2N$: C, 73.90; H, 4.38. Found: C, 73.90, 74.11; H, 4.42, 4.40.

2,3-Diphenylpropylamines.—Five-hundredths mole of diphenylacrylonitrile was dissolved in 100–200 cc. of glacial acetic acid; 0.5 g. of platinum oxide catalyst was added and the mixture shaken in a Parr low-pressure hydrogenator at an initial pressure of 40 pounds. After the calculated amount of hydrogen was absorbed (usually after five to six hours), the reaction mixture was removed and filtered. Most of the acetic acid was distilled off under vacuum, and the residue was made strongly basic with 30% sodium hydroxide. The free amine was extracted with ether and fractionally distilled at reduced pressure through a Vigreux column.

TABLE I

DIPHENYLPROPYLAMINES, $RCH_2CH(C_6H_5)CH_2CH_2$

R	Yield, %	B. p. Free base °C.	Mm.	M. p. HCl, °C.	Form analyzed	Composition, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
C_6H_5-[a]	58	105–108	0.5	189–190	HCl					5.65	5.60, 5.57
3,4-$CH_2O_2C_6H_3$-	61	176–178	1		Base	75.27	74.86, 75.20	6.71	6.97, 6.99	5.49	5.44, 5.59
4-$CH_3OC_6H_4$-	72	168–172[b]	2		Base	79.63	79.62, 79.72	7.94	8.42, 7.86	5.80	5.65, 5.87
3,4-$(HO)_2C_6H_3$-	42			183–184	HCl	64.39	64.08, 64.04	6.49	6.30, 5.39	5.01	4.96, 5.03
4-HOC_6H_4-	55			212–214	HCl					5.31	5.34, 5.36

[a] Previously synthesized in 15% yield.[5] [b] M. p. 42°.

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Storage Effects on the Proteins of Peanuts

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Jones and Gersdorff[1] reported that after six months storage of soybean meal at 30° and 76° F. the solubility of the proteins in salt solution decreased. Other workers[2,3] found no change in solubility of the proteins in cottonseed after prolonged storage at a wide range of temperatures.

As the results reported on cottonseed and soybeans are in marked contrast and as practically all harvested peanuts, whether in the shell, shelled or as meal, are stored under variable conditions, a study was made in order to determine the effects of storage on peanut proteins. Protein solubilities were determined on whole, shelled, hydraulic pressed and solvent-extracted Spanish peanuts. The samples were air-dried and stored in the dark at 33°F. and both in the dark and light at 75 ± 10°F. At intervals up to three years the peanuts were shelled, extracted with Skellysolve F, finely ground, and the solubilities of the proteins in water were determined on all the samples using the Smith, Circle and Brother procedure.[4] After storing three years at 33°F. and in the dark and

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