with methanol. The m.p. of this material, 16.3 g., was 67–72° (unsharp). Since repeated recrystallizations from methanol did not give a substance with sharp m.p., we dissolved the material in petroleum ether and chromatographed it on alumina, collecting fractions of 50 ml. Fractions 5–8 gave a crystalline residue of m.p. 86–87°, which upon recrystallization from isopropyl alcohol formed yellow cubes of m.p. 87°.

*Anal.* Calcd. for $C_{16}H_{11}OCl_3$: C, 59.0; H, 3.4. Found: C, 59.1; H, 3.4.

The ketone II did not react with any of the usual carbonyl reagents.

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## Reductions with Hydrazine Hydrate Catalyzed by Raney Nickel. I. Aromatic Nitro Compounds to Amines[1,2]

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Hydrazine, though a powerful reducing agent is not used extensively to reduce aromatic nitro compounds to amines. The rate of reaction is too slow. If employed in a sealed tube[3] or in high boiling solvents[4] almost all functional groups are reduced.

With the addition of a small amount of Raney nickel catalyst, hydrazine hydrate will selectively reduce an aromatic nitro compound to an amine at room or steam-bath temperature. Yields are excellent ranging from 80 to 99%. Under these conditions other functional groups, namely, carbonyls, will not be affected. To eliminate loss due to foaming a large excess of solvent alcohol is necessary. We have confirmed Kuhn's[5] observation that no reduction takes place even after 18 hours if no catalyst is added. The mechanism of the reaction is unknown, but hydrazine when catalytically decomposed liberates only water and gases[6] so that elimination of by-products is not a problem.

### Experimental

As all of the aromatic nitro compounds listed here were reduced by the same method, only a general procedure is given. In each case the amino compound listed was also obtained by the reduction of the nitro compound by a procedure obtained from the literature. Mixed melting points as well as fusion analysis[7] helped prove the identity of the amino compound. In some cases the hydrochloride rather than the free amine was isolated.

**Generalized Procedure.**—To the nitro compound dissolved in alcohol (10 ml./g.) was added 2–3 molar ratios of hydrazine hydrate 100%. The solution was placed on the steam-bath and when just warm a small amount of Raney Ni was added. The solution frothed. As the reaction proceeded (5 to 60 min.) the color changed from yellow to almost colorless. More catalyst was added to decompose the excess hydrazine and the solution was heated to boiling to drive off the dissolved gases. The hot solution was filtered to remove the Ni, boiled with decolorizing carbon and filtered again. The free amine was isolated by cooling the solution to *ca.* 50° and then pouring into a large excess of water; or the hydrochloride salt was obtained by evaporating the solvent to *ca.* 5–10 ml., adding *ca.* of 5 ml. ofconcentrated hydrochloric acid and cooling the mixture. The precipitates were isolated and dried.

**Amines.**—By this procedure *p*-aminobiphenyl ether[8] was obtained in 96.5% yield. Other amines obtained in yield between 80 and 99% were *p*-aminocinnamic acid,[9] *m*-aminobenzophenone,[10] 2-methyl-4′-aminobiphenyl,[11] 4,4′-diaminodiphenyl ether[12] and aniline.

**Biological Testing.**—These compounds were tested for their effect on the mouse Sarcoma-37. No inhibitory action was noted.[13]

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(2) This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service, and from the Catherine Stern Memorial Fund.

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## Preparation of 1-Methyl-3-phenyl-3-(γ-dimethylaminopropyl)-piperidine

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Phenyldi-(γ-dimethylaminopropyl)-acetonitrile, prepared from phenylacetonitrile, γ-dimethylaminopropyl chloride and sodamide, was hydrolyzed to the corresponding acetic acid. The latter compound was refluxed with thionyl chloride, the excess thionyl chloride removed and the residue heated until the evolution of methyl chloride stopped. The 1-methyl-3-phenyl-3-(γ-dimethylaminopropyl)-2-piperidone was reduced with lithium aluminum hydride to the corresponding piperidine.

### Experimental

**Phenyldi-(γ-dimethylaminopropyl)-acetonitrile.**—Phenylacetonitrile (35.2 g.) in 50 cc. of toluene was added, gradually, to a stirred mixture of 29.3 g. of sodamide in 100 cc. of toluene at 40–50°. The mixture was stirred for 1 hour, then 90 g. of γ-dimethylaminopropyl chloride[1] was added, dropwise, to the stirred mixture at 40–50°. The material was refluxed for 6 hours and treated in the usual manner. After fractionation 70.0 g. (81.3%) of nitrile was obtained, b.p. 155–158° (1 mm.).

The dihydrochloride, prepared from an ethereal solution of the base and hydrogen chloride, melted at 280–282° after recrystallization from absolute ethanol.

*Anal.* Calcd. for $C_{18}H_{31}N_3Cl_2$: N, 11.66; Cl, 19.72. Found: N, 11.55; Cl, 19.71.

**Phenyldi-(γ-dimethylaminopropyl)-acetic Acid.**—A mixture of 57.4 g. of the nitrile, 94 cc. of concd. sulfuric acid and 63 cc. of water was refluxed for 2 hours. The cold mixture was poured into water and sodium hydroxide was added until the mixture was only slightly acidic. It was then decolorized with Norite. The filtered solution was made alkaline whereupon an oil separated. A further amount of oil was obtained by extraction of the aqueous solution with chloroform and removal of the solvent. When the oil was warmed under 16 mm. pressure for some time, it be-

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