formed during the dithionite reduction of DPN was an addition product.

Experimental Section

1-Benzylnicotinamide chloride was prepared according to Karrer and Stare.[12] Found in the nmr spectrum in D_2O were benzyl CH protons as a singlet at 5.81, phenyl protons as a singlet at 7.41, H_5 as a pair of doublets ($J_{4,5}$ = 8.5 cps, $J_{5,6}$ = 6.3 cps) at 8.13, H_4 as a pair of triplets ($J_{4,5}$ = 8.5 cps, $J_{4,6}$ and $J_{2,4}$ = 1.6 cps) at 8.84, H_6 as a pair of partially resolved triplets ($J_{5,6}$ = 6.5 cps, $J_{2,6}$ and $J_{4,6}$ = 1.6 cps) at 9.02, H_2 as a broad "singlet" at 9.27; HDO as a singlet at 4.65.

1-Benzyl-1,4-dihydronicotinamide was prepared by reduction of the nicotinamide chloride with dithionite according to Mauzerall and Westheimer.[8] Nmr spectra in $CDCl_3$ agreed closely with the data reported previously.[13,14] Found were H_4 as a pair of doublets ($J_{4,5}$ = 3.3 cps, $J_{4,6}$ = 1.7 cps) at 3.15, benzyl CH_2 as a singlet at 4.28, H_5 as a pair of triplets ($J_{4,5}$ = 3.3 cps, $J_{5,6}$ = 7.9 cps) at 4.72, H_6 as a pair of quarters ($J_{5,6}$ = 7.9 cps, $J_{4,6}$ and $J_{2,6}$ = 1.7 cps) at 5.72 with amide protons on high-field side, H_2 as a doublet ($J_{2,6}$ = 1.7 cps) at 7.13, phenyl protons as a singlet at 7.28.

1-Benzyl-1,4-dideuterionicotinamide and 1-Benzyl-4-deuterionicotinamide Chloride.—To a solution of 1-benzyl-1,4-dihydronicotinamide (0.76 g, 3.5 mmoles) in dimethylformamide (5 ml) was added chloranil (0.91 g, 3.7 mmoles) in dimethylformamide (20 ml).[15] After 10 sec while mixing thoroughly, 10 ml of 1 *M* HCl was added. The aqueous phase, which contained benzylnicotinamide chloride, was washed three times with ethyl acetate and evaporated to dryness. Crystals were obtained from ethanol in 70–90% yield, mp 229–232°. After three cycles of oxidation with chloranil in dimethylformamide and reduction with dithionite in deuterium oxide, the nmr spectra obtained for both the oxidized and reduced compounds were consistent with the presence of only deuterium at the 4 position.

In the nmr spectrum for the reduced compound in $CDCl_3$ were found benzyl CH_2 protons as a singlet at 4.28, H_5 as a doublet ($J_{5,6}$ = 8.0 cps) at 4.72, H_6 as a pair of doublets ($J_{5,6}$ = 7.9 cps, $J_{2,6}$ = 1.7 cps) at 5.73, H_2 as a doublet ($J_{2,6}$ = 1.8 cps) at 7.13, phenyl protons as a singlet at 7.28. In the nmr spectrum for the oxidized compound in D_2O were found benzyl CH_2 protons as a singlet at 5.83, phenyl protons as a singlet at 7.42, H_5 as a doublet ($J_{5,6}$ = 6.2 cps) at 8.14, H_6 as a pair of doublets ($J_{5,6}$ = 6.3 cps, $J_{2,6}$ = 1.2 cps) at 9.03, H_2 as a doublet ($J_{2,6}$ = 1.1 cps) at 9.28, HDO as a singlet at 4.65.

Dithionite Addition Products.—For the nmr studies the 4-hydrogen and 4-deuterio derivatives were both prepared in the same manner. Sodium dithionite (93% pure,[16] 87 mg, 0.5 mmole) was dissolved in 0.5 ml of 2 *M* NaOD in D_2O under nitrogen. The benzylnicotinamide chloride (63 mg, 0.25 mmole) in 0.5 ml of D_2O was added dropwise to the alkaline dithionite solution over a period of 1 min and the nmr spectrum was observed. In the nmr spectrum for the solution from the 4-deuterio derivative were found benzyl CH_2 protons as a singlet at 4.35, H_5 as a doublet with the low-field peak at 4.98 (the high-field peak was hidden under the HDO peak), H_6 as a doublet ($J_{2,6}$ = 1.2 cps, $J_{5,6}$ = 7.8 cps) at 6.19, phenyl protons as a singlet at 7.23, H_2 as a doublet ($J_{2,6}$ = 1.2 cps) at 7.30. In the nmr spectrum for the solution from the 4-hydrogen derivative were found H_4 as a doublet corresponding to one proton ($J_{4,5}$ = 5.4 cps) at 3.97, benzyl CH_2 protons as a singlet at 4.34 cps, H_5 as a pair of doublets partially under HDO peak ($J_{4,5}$ = 5.5 cps, $J_{5,6}$ = 7.5 cps) at 4.92, H_6 as a pair of doublets ($J_{2,6}$ about 1.0 cps, $J_{5,6}$ = 7.5 cps) at 6.19, phenyl protons as a singlet at 7.23, H_2 as a doublet ($J_{2,6}$ = 1.0 cps) at 7.30. A solution of the 4-hydrogen derivative was prepared in the same manner except for the use of ordinary water in place of D_2O. This solution was transferred while minimizing exposure to oxygen *via* a syringe to an absorption cell with a 0.025-mm path length (Perkin-Elmer ultraviolet short path length cell no. 220-0070). With a 10% transmission neutral density screen in the reference beam, it was possible to observe a broad absorption band with ϵ 2800 at 375 mμ on a Perkin-Elmer Model 202 spectrophotometer (dithionite absorption in the reference cell amounted to an ϵ of 110 at 375 mμ). The spectra of more dilute solutions in cells of longer path lengths gave similar spectra. Thus when the original solution was diluted 1000-fold with either 1 or 0.05 *M* NaOH, a broad absorption band was observed with λ_{max} 372 mμ (ϵ 3000–3200).

To obtain a sample for elemental analyses a preparation was carried out in nondeuterated solvent and with tenfold larger amounts. The intermediate spontaneously crystallized from such solutions on standing at 3–4° overnight. The crystals were isolated by centrifugation and pressed dry on unglazed porcelain followed by drying under vacuum at room temperatue for 12 hr. The yellow crystals turned brown on standing exposed to air and the material underwent decomposition during attempts at recrystallization. The yield was 53%.

Anal. Calcd for $C_{13}H_{13}N_2NaO_{13}S$: C, 51.99; H, 4.36; N, 9.33; Na, 7.66; S, 10.68. Found: C, 47.75; H, 4.67; N, 8.93; Na, 7.54; S, 10.74.

The low value for carbon could result from sodium carbonate formation during combustion (as is frequently encountered with sodium salts) or from lack of purity. The absorption spectra of a 0.25 m*M* solution of the crystalline material in 1 *M* NaOH exhibited a broad band with λ_{max} 372 mμ (ϵ 3100). The yellow crystals were insoluble in ethanol and freely soluble in water; a yellow oil, possibly the dihydropyridine, separated from the water solution a few minutes after mixing. When heated in a sealed evacuated capillary, the crystals shrank and turned brown at 114–117°; further heating (to 200°) did not result in melting. Both solubility and melting characteristics were consistent with the crystals being a salt. In contrast, the dihydropyridines were readily soluble in ethanol and sparingly soluble in water.

Nmr Spectra.—All nmr spectra were obtained with a Varian Model A-60 spectrometer. Data in $CDCl_3$ are reported as parts per million from tetramethylsilane as internal standard (δ values). Chemical shifts for the D_2O solutions were estimated by the method of tube replacement; these values are thus only approximate as no internal or external reference was used. More precise chemical shifts were not considered necessary to support the conclusions of this paper.

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Dihydropyran Derivatives of Secondary Aromatic Amines

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Although dihydropyran has been used in numerous synthetic sequences as a blocking group for alcohols and acids, recent reviews indicate its use has not been extended to amines.[2–4] The sole work in this area is that of Glacet, who prepared 2-tetrahydropyranylamines by the addition of aniline and N-methylaniline to dihydropyran.[5,6]

We have now extended the scope of this reaction to five secondary aromatic amines. Since the tetrahydropyranyl group can be easily removed to regenerate the original amine, it offers promise as a base-stable blocking group for these amines.

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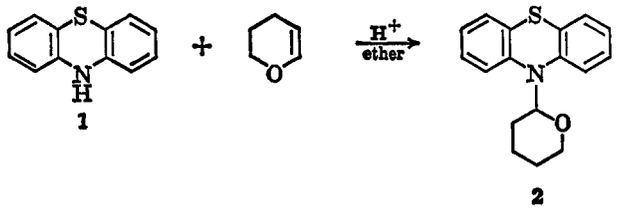
TABLE I

N-(2-TETRAHYDROPYRANYL)AMINES

Starting amine	Yield, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % O	Found, % C	Found, % H	Found, % O
Diphenylamine	60	89–90[a]	$C_{17}H_{17}NO$	80.6	7.6	6.3	80.3	7.6	6.4
Phenoxazine	85	140–141[b]	$C_{17}H_{17}NO_2$	76.4	6.4	12.0	76.3	6.2	12.0
Phenyl-α-naphthylamine	42	115–116[c]	$C_{21}H_{21}NO$	83.1	7.0	5.3	83.1	7.2	5.3
Phenothiazine	72	156–157[b]	$C_{17}H_{17}NOS$	72.1	6.1	*d*	72.1	5.8	*d*
4-Methyl-4′-nitrodiphenylamine	85	99–100[e]	$C_{18}H_{20}N_2O_3$	69.2	6.5	*f*	69.2	6.5	*f*

[a] Recrystallized from methanol. [b] Recrystallized from acetonitrile. [c] Recrystallized from petroleum ether (bp 30–60°). [d] *Anal.* Calcd: S, 11.3. Found: S, 11.4. [e] Recrystallized from cyclohexane. [f] *Anal.* Calcd: N, 9.0, Found: N, 8.9.

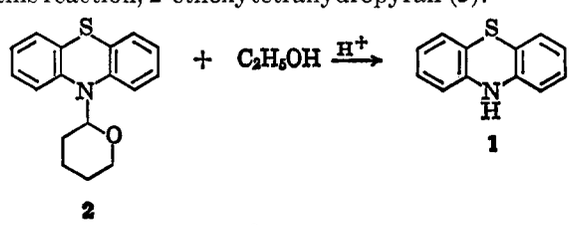
The course of the reaction is illustrated by phenothiazine (1), which reacts with dihydropyran to give 10-(2-tetrahydropyranyl)phenothiazine (2) in 72% yield. The proposed structure of this derivative is in



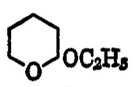
1 2

agreement with spectral data. The infrared spectrum showed no N–H stretching band in the 3400-cm.$^{-1}$ region (present in phenothiazine at 3390 cm.$^{-1}$) but contained two strong bands attributed to C–O stretching[7] at 1025 and 1070 cm^{-1}. The ultraviolet spectrum (acetonitrile) of the product, λ_{max} 251 mμ (ε 31,000) and 298 mμ (ε 3240), was similar to that of phenothiazine, λ_{max} 253 mμ (ε 31,900) and 312 mμ (ε 5640). In the nmr spectrum, complex multiplets occurred at 7.1, 4.9, 4.0, and 1.7 ppm. The signal at 7.1 ppm is attributed to the eight aromatic protons, that at 4.9 ppm to the methine proton, the signal at 4.0 ppm to the methylene protons adjacent to oxygen, and that at 1.7 ppm to the remaining six methylene protons. The integrated strengths of these peaks were in the expected ratio of 8:1:2:6.

All derivatives could be easily decomposed in alcohol to regenerate the starting amine in high yield. No attempt was made to identify the other expected product of this reaction, 2-ethoxytetrahydropyran (3).



2 1



3

Data on derivatives of five secondary aromatic amines are summarized in Table I. The yields are based on single reactions and may be capable of significant improvement.

The sole failure encountered to date has been with 2,4-dinitrodiphenylamine, and is probably due to the combined resonance effects of the two nitro groups and steric hindrance by the *ortho* nitro group.

Experimental Section

Methods.—Analyses were performed by the Analytical Research Branch of the Chemical Research and Development Laboratories. Infrared spectra were recorded using a Perkin-Elmer 521 or a Beckman IR-5A infrared spectrophotometer. All compounds were run as 5% solutions in chloroform. Nmr spectra were recorded using a Varian Associates A-60 nmr spectrometer, and all chemical shifts are given in parts per million downfield from tetramethylsilane. Deuteriochloroform was used as the solvent in all cases. A Beckman DK-2 recording spectrophotometer was used to record ultraviolet spectra. For thin layer chromatography, silica gel G, Merck, was used. Melting points were taken on a Thomas–Hoover melting point apparatus and are uncorrected. 3,4-Dihydropyran was distilled and stored over anhydrous potassium carbonate prior to use. All experimental procedures were similar to that described for phenothiazine, with the exception of phenyl-α-naphthylamine. Tetrahydrofuran was used as the solvent with this amine, since no reaction occurred in diethyl ether.

10-(2-Tetrahydropyranyl)phenothiazine (2).—To a slurry of 15.0 g (0.0755 mole) of phenothiazine in 20 ml of anhydrous ether was added 13.8 g (0.164 mole) of dihydropyran and 1 drop of concentrated sulfuric acid (sp gr 1.84). The phenothiazine dissolved completely within 30 sec and a mildly exothermic reaction continued for 2 min. After 4 min, the adduct began to precipitate. It was then filtered and washed with 250 ml of 5% sodium carbonate solution. The adduct was dissolved in boiling acetonitrile and recrystallized as the solution cooled to room temperature. A total of 15.1 g (72% yield) was obtained. After two additional recrystallizations from acetonitrile, an analytical sample had mp 156–157°.

Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; S, 11.31. Found: C, 72.1; H, 5.8; S, 11.4.

Regeneration of Phenothiazine.—A total of 15.1 g (0.0533 mole) of 10-(2-tetrahydropyranyl)phenothiazine was partially dissolved in 50 ml of boiling ethanol. When 1 drop of concentrated sulfuric acid (sp gr 1.84) was added, the solution turned dark brown and the compound dissolved completely. As the solution cooled, yellow crystals of phenothiazine precipitated. A total of 10.6 g (quantitative yield) was obtained. After drying, the crystals had mp 183–184.5°, lit.[8] mp 183–185°. A mixture melting point with an authentic sample of phenothiazine showed no depression.

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Substituent Effects in Photochromic Nitrobenzylpyridines

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Previous investigations showed that many derivatives of 2-(2-nitrobenzyl)pyridine[1–3] and related compounds[4]

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