vary widely; *e.g.*, depending on the side chain the figure for the p-N(CH$_3$)$_2$ group varies from −0.425 to −0.972.[4] Consequently the applicability of Hammett's value to reactions other than those of phenols seemed questionable.

We have redetermined the σ value for the m-N(CH$_3$)$_2$ group from the ionization constants of benzoic acid and m-N,N-dimethylaminobenzoic acid in 50% by volume ethanol. This solvent was chosen because the ρ value for the ionization of benzoic acids in it has been critically evaluated[5] and it can be shown that m-N,N-dimethylaminobenzoic acid in 50% ethanol is not more than 3% in the inner salt structure.

The result was -0.15 ± 0.04, a value quite close to the -0.211 calculated by Hammett and also within the range (-0.07−-0.20) assigned to the m-NH$_2$ group on the basis of pK_a' determinations in aqueous ethanol.[5]

Experimental Section[6]

Benzoic Acids.—National Bureau of Standards benzoic acid was used. The m-dimethylaminobenzoic acid was Eastman Practical Grade recrystallized from 95% ethanol to a constant melting point (calibrated electrically heated block) of 151.5–153.0° (lit.[6] 151°) and 100% purity by titration. Samples were dried to constant weight in a desiccator before use.

Acid Ionization Constants.—These were determined in duplicate by titration of the acids (2.00 mequiv dissolved in 190 ml of 50% by volume ethanol) with 0.100 N potassium hydroxide under nitrogen at 25 ± 0.03°. The pH was measured at each 0.2 mequiv by means of a Beckman Research Model 1010 pH meter equipped with a no. 41263 glass electrode with silver-silver chloride internal element and a Beckman No. 39071 frit-function calomel reference electrode. No significant differences were obtained with a Radiometer Model 4 pH meter equipped with a type GK 2021C combination calomel-glass electrode. The meter was calibrated before (and checked after) each titration with aqueous standard buffers. An amount of absolute ethanol equal to the volume of titrant increment was added before each measurement. The readings from 0.2 to 1.8 mequiv were converted to apparent pK_a (pK_a') values by the equation

$$\mathrm{p}K_a' = \mathrm{pH} + \log\frac{[\mathrm{HA}] - (\mathrm{H}^+)}{[\mathrm{A}^-] + (\mathrm{H}^+)}$$

These figures were converted to corresponding apparent ionization constants from which the mean values (and their standard deviations) were calculated and then reconverted to the following pK_a' values: benzoic acid, pK_a' 5.67 ± 0.03;[7] m-N,N-dimethylaminobenzoic acid, pK_{a_2}' 5.90 ± 0.03. These were substituted into the Hammett equation

$$\log K - \log K_0 = \sigma\rho \text{ with } \rho = 1.522^5$$

Basic Dissociation Constants.—The pK_1' for m-dimethylaminobenzoic acid (3.04 ± 0.08) was obtained by titration with 1.00 N hydrochloric acid of 4.00 mequiv of the compound in 200 ml of 50% ethanol. The pH at the beginning of the titration was 4.40 ± 0.04. The pH was measured at 1, 2, and 3 mequiv. The pK' (2.96 ± 0.08) of methyl m-N,N-dimethylaminobenzoate hydrochloride[8] (prepared from the acid chloride hydrochloride[9] and methanol) was obtained by titration of 2.00 mequiv of the salt in 190 ml of 50% ethanol. The pH was measured at 0.05, 0.10, and 0.15 mequiv. Both determinations were done in duplicate with an equivalent volume of ethanol added with each increment of titrant. The pH values were converted to apparent pK_a' values by the equation

$$\mathrm{p}K_a' = \mathrm{pH} + \log\frac{[\mathrm{ArN(CH_3)_2H^+}] - (\mathrm{H}^+)}{[\mathrm{ArN(CH_3)_2}] + (\mathrm{H}^+)}$$

Percentage of Inner Salt.—This can be shown to be not more than 3% by calculation of per cent ionization both as acid and base of m-dimethylaminobenzoic acid solutions in 50% ethanol. The fact that the pK_1' of the amino acid is almost identical with the pK' of its methyl ester is consistent with this result.[10]

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[4] H. H. Jaffé, *Chem. Rev.*, **53**, 229 (1953).

[5] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

[6] P. Griess, *Ber.*, **6**, 587 (1873).

[7] This value of 5.67 ± 0.03 for the pK_a' of benzoic acid in 50% by volume ethanol at 25° is lower than those reported by several authors and assembled by McDaniel and Brown,[5] *i.e.*, 5.73, 5.75, and 5.80.

[8] A. C. Cumming, *Proc. Roy. Soc.* (London), **B78**, 103 (1906).

[9] G. Bramanti, G. DiPaco, and C. S. Tauro, *Boll. Chim. Farm.*, **99**, 517 (1960).

[10] L. Ebert, *Z. Physik. Chem.*, **121**, 385 (1926).

The Reaction of Aniline with 1,2,3,4-Tetrachloro-1,2,3,4-tetrahydronaphthalene

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The two benzyl-type chlorine atoms in 1,2,3,4-tetrachloro-1,2,3,4-tetrahydronaphthalene (I) should be reactive, and therefore I should have synthetic utility. Although it is reported[2] that the α isomer (Iα) may be hydrolyzed to a dichlorodihydroxytetrahydronaphthalene, no other replacement reactions of Iα are reported, and no replacement reactions of Iγ and Iϵ are known.

The reaction of aniline with benzene hexachloride to produce an N-(dichlorophenyl)aniline[3] suggested that aniline might be an ideal reagent for exploring replacement reactions of I. When each of three isomers was heated with excess aniline, it was found that Iα yielded a product containing four anilino groups, that Iγ gave a product containing two anilino groups, and that Iϵ did not react.

The product of the reaction of Iα with aniline consisted of isomeric 1,2,3,4-tetraanilino-1,2,3,4-tetrahydronaphthalenes. The reported geometric configuration of Iα[4,5] leads us to suggest that the replacement of the nonbenzylic chlorine atoms may occur by way of an aziridine-type intermediate (II) (Scheme I). Participation by neighboring nitrogen in the solvolysis of alkyl halides is well known.[6]

The reaction of Iγ with aniline gave a 63% yield of a material that appears to be a single isomer of 1,4-dianilino-2,3-dichloro-1,2,3,4-tetrahydronaphthalene (III). The product is a useful synthetic intermediate for the preparation of 1,4-dianilinonaphthalene (IV) and the dianil (V). Since the literature preparation[7] of IV and V is not straightforward, V was hydrolyzed to yield naphthoquinone and aniline as a proof of structure (Scheme II).

The tendency of the reaction of Iγ with aniline to stop after the replacement of the two benzylic chlorine atoms may be due to the configuration of Iγ.[5] Re-

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[2] M. E. Grimaux, *Compt. Rend.*, **75**, 351 (1872).

[3] W. E. Phillips, *Anal. Chem.*, **24**, 1976 (1952).

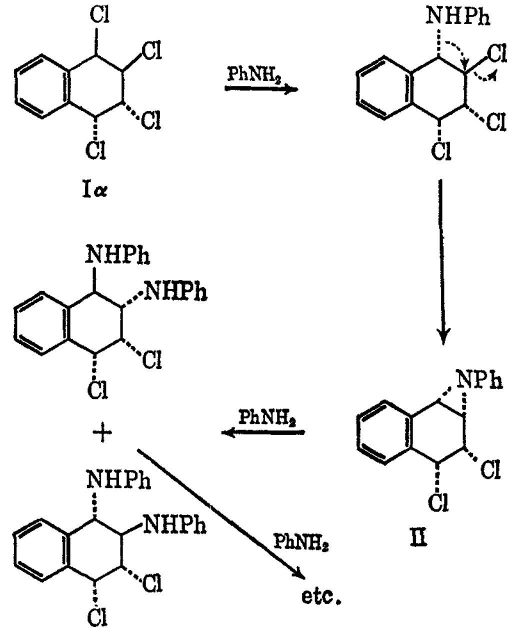
[4] M. A. Lasheen, *Acta Cryst.*, **5**, 593 (1952).

[5] P. B. D. de la Mare, M. D. Johnson, J. S. Lomas, and V. Sanchez del Olmo, *Chem. Commun.*, 483 (1965).

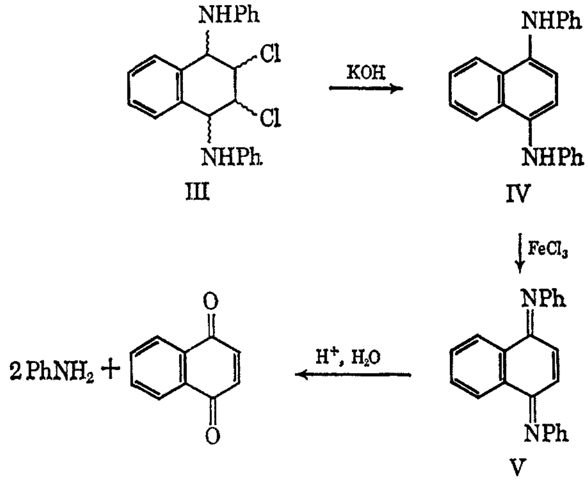
[6] A. Streitweiser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 105.

[7] O. Fischer and E. Hepp, *Ann.*, **256**, 233 (1890).

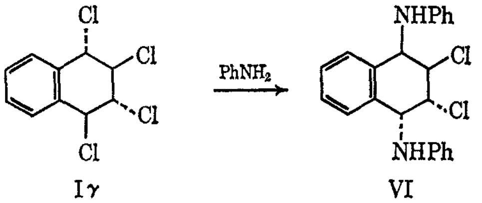
Scheme I



Scheme II

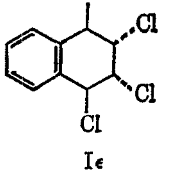


placement of the benzylic chlorine atoms with inversion by aniline would yield VI. In VI, the anilino group and the adjacent chlorine atom have a *cis* relationship which may prevent the aziridine ring formation postulated for Iα.



Iγ VI

Consideration of the configuration of Iε[5] does not suggest to us any sufficient reason for its lack of reactivity under these conditions.



Iε

Experimental Section

1,2,3,4-Tetrachloro-1,2,3,4-tetrahydronaphthalene.—Iα was purchased from Distillation Products Industries (mp 182°, lit.[5] mp 182°). Iγ (mp 133°, lit.[5] mp 134°) and Iε (mp 87°, lit.[5] mp 85–87°) were prepared by the same procedure as used by de la Mare and co-workers.[5]

Reaction of Aniline with Iα.—A side-arm test tube, equipped with thermometer and nitrogen line, was charged with 15 ml of aniline and 2.70 g (10 mmoles) of Iα. The tube was heated in an oil bath maintained at 110°. When the solution reached 105°, the mixture turned red and an exothermic reaction became apparent. The tube contents were maintained at 115° by raising and lowering the tube in the bath as required. After about 30 min the reaction no longer evolved heat, and the temperature of the oil bath was increased so that the tube contents could be maintained at 115° for an additional 15 min.

To the product was added 25 ml of benzene, and the aniline hydrochloride was extracted with water (three 10-ml portions). Titration of the water extract showed that 3.72 moles of hydrogen chloride had been produced per mole of Iα. The benzene and aniline were distilled from the product at reduced pressure. The residue was dissolved in 30 ml of benzene and treated with 50 ml of 1.0 *N* hydrochloric acid to extract any remaining aniline (the product was not soluble in dilute acid). After the mixture was washed in water, the benzene was removed by distillation (20 mm) and the residue then dissolved in ether. Distillation of the ether at reduced pressure yielded 4.35 g (88%) of an orange glassy residue. The infrared spectrum showed a single N–H stretching band indicating the material was a secondary amine.

Anal. Calcd for $C_{34}H_{32}N_4$: C, 82.22; H, 6.50; N, 11.28. Found: C, 82.13; H, 6.54; N, 11.10.

Reaction of Aniline with Iγ.—The reaction was carried out in the manner of the above experiment using 2.75 g (10.2 mmoles) of Iγ. There was produced 2.08 moles of aniline hydrochloride per mole of Iγ. After most of the aniline was distilled from the product by heating to 70° at 0.1 mm, the product was slurried with 15 ml. of boiling ethanol, cooled, and filtered. There was obtained 2.96 g of white crystals, mp 158–161.5°. Recrystallizations from a ethanol–benzene mixture gave 2.45 g of III, mp 164–165°.

Anal. Calcd. for $C_{22}H_{20}N_2Cl_2$: C, 69.29; H, 5.29; N, 7.35; Cl, 18.07. Found: C, 69.00; H, 5.41; N, 7.26; Cl, 18.43.

Reaction of Aniline with Iε.—No exotherm was apparent and no aniline hydrochloride was produced when Iε was heated with aniline for 20 min at 120°.

Dehydrohalogenation of III.—A mixture of 1.08 g (2.83 mmoles) of III and 20 ml of 1.32 *N* potassium hydroxide in ethanol was stirred and refluxed under a nitrogen atmosphere for 3 hr. The mixture was cooled, 50 ml of water added, and the alcohol removed by distillation. After the product was separated with benzene, the benzene was distilled (20 mm) from the extract, and the residue was recrystallized from an isooctane–benzene mixture to yield 0.691 g (79%) of 1,4-dianilinonaphthalene (IV). A second recrystallization did not raise the melting point (0.667 g, mp 141.5–142.5°, lit.[7] mp 144°). The infrared spectrum indicated that the product was a secondary amine.

Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.84; N, 9.03. Found: C, 85.33; H, 6.06; N, 9.13.

Oxidation of IV.—A solution of 0.222 g (0.71 mmole) of IV in 25 ml of benzene was added to a solution of 1.0 g (6 mmoles) of anhydrous ferric chloride in 25 ml of ethanol. The solution was allowed to stand for 1 min at room temperature and was then treated with 200 ml of water. Extraction of the product with four 60-ml portions of benzene gave an orange extract, which was washed with water, with 1.0 *N* sodium hydroxide solution, and again with water. The benzene was removed by distillation (20 mm), and the residue was recrystallized twice from an isooctane–benzene mixture to yield 0.180 g (80%) of the dianil (V), mp 184.5–185° (lit.[7] mp 187°).

Anal. Calcd for $C_{22}H_{16}N_2$: C, 85.68; H, 5.23; N, 9.09. Found: C, 85.92; H, 5.28; N, 9.39.

Hydrolysis of the Dianil (V).—A 0.356-g (1.15 mmoles) sample of V (prepared as in the above experiment) was dissolved in 5 ml of 50% (by volume) sulfuric acid. After the solution was allowed to stand for 20 min at room temperature, 5 ml of water was added dropwise. The mixture was then partially neutralized by pouring it into 100 ml of 0.25 *N* aqueous sodium hydroxide solution, and the product was extracted with ether. (The amount of base used was not sufficient to neutralize the aniline sulfate.) The ether was distilled from the extract, after which the residue was sublimed at 80° and high vacuum. Recrystallization of the sublimate from ethanol gave 0.139 g (76%) of yellow prisms, mp 123–125°. The infrared spectrum of this material was identical with that of an authentic sample of 1,4-naphthoquinone.

To the aqueous solution presumed to contain the aniline sulfate was added 5 *N* sodium hydroxide solution until the phenolphthalein end point was reached. The oil layer was then removed by benzene extraction, and the extract was dried by distilling the water–benzene azeotrope. To the hot benzene solution was then added 10 ml of acetic anhydride. The solution was distilled at reduced pressure until a white crystalline residue remained. The residue was recrystallized from a benzene-isooctane solution to yield 0.266 g (85%) of acetanilide, mp 113.5–114.5°, mmp 113–114°.

Acknowledgment.—The authors are indebted to Mr. John E. Graham for the determination and interpretation of the infrared spectra.

The Catalytic Methylation of Pyridine and Its Derivatives in the Vapor Phase

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A number of methods have been used to introduce an alkyl group into the pyridine ring. Ladenburg[1] obtained a mixture of 2- and 4-picolines by heating methylpyridinium iodide at 300°. Rieger[2] obtained 2- and 4-picolines by heating pyridine at 80–100° with acetic acid and lead tetraacetate. Propionic acid and lead tetrapropionate gave 2- and 4-ethylpyridine. Goldschmidt and Minsinger[3] heated pyridines with diacyl peroxides and the corresponding acids at 100° and obtained mixtures of 2- and 4-alkylpyridines. 4-Alkylpyridines have been synthesized directly from pyridine by the Wibaut–Arens alkylation[4] which involves the reaction of pyridine with an acid anhydride. Cullinane, *et al.*,[5] passed a mixture of methanol and pyridine vapors over alumina or aluminum silicate catalysts obtaining small yields of 2-, 3-, and 4-picolines and lutidines. Ziegler and Zeiser[6] obtained only 2-butylpyridine by decomposing the addition product of butyllithium and pyridine at 100°. Daniels and Salerni[7] obtained only 2-picoline from the irradiation of diazomethane in pyridine. Recently, Reinecke and Kray[8] have described the α-alkylation of pyridine by heating the base with an alcohol in the presence of W-5 Raney nickel in the liquid phase.

In this paper, we report a convenient method for introducing methyl groups into the pyridine ring by direct reaction with an alcohol or other compound in the vapor phase. Of special significance is the fact that the reaction gives only products substituted in the α positions. The reaction has been applied to pyridine, mono- and disubstituted pyridines, and quinoline.

The method consists of passing a mixture of the pyridine compound and the alkylating agent over a nickel catalyst in the vapor phase. A variety of compounds will serve as methylating agents. A list of those evaluated is found in Table I along with reaction conditions and yields. All of the methylating reagents used gave only substitution on the 2-position with the exception of methanol which gave substitution on both the 2- and 6-positions. This apparently anomalous result may be related to the higher molar ratio of methanol to pyridine than was employed with the other reagents.

The results of a number of experiments on pyridine with different methylating agents are given in Table I.

Table I
Methylation of Pyridine[a]

Methylating agent	Temp, °C	Mole ratio, methylating agent–pyridine	Contact time, sec	2-Picoline, % yield
Methanol	295	15:1	11.5	57[b]
Ethanol	263	3:1	11.6	61
1-Propanol	300	2.5:1	11.4	52
2-Propanol	295	2.5:1	12.2	38
1-Butanol	298	2.1:1	14.0	48
2-Methyl-1-propanol	298	2.1:1	14.0	25
Acetone	325	2.5:1	12.2	38
Methylal	258	2.3:1	14.0	55
Ethyl orthoformate[c]	256	1.3:1	20.6	57
Ethyl acetate	298	1.6:1	16.2	58
Methane	260	3.8:1	9.8	10
Carbon monoxide–hydrogen	270	2:1:1[d]	11.0	30

[a] Harshaw catalyst Ni-0104T was used in all experiments reported in this table. [b] 2,6-Lutidine formed in 24% yield as coproduct. [c] By-products from this reaction were diethyl ether, carbon monoxide, carbon dioxide, and methane. [d] Mole ratio of H_2–CO–pyridine.

Table II lists results from methylation of substituted pyridines and quinoline with methanol.

Table II
Alkylation of Pyridine Compounds with Methanol[a]

Pyridine compd	Temp, °C	Mole ratio, methanol–pyridine compd	Contact, time, sec	Product	Yield, %
2-Picoline	260–265	3.6:1	12.2	2,6-Lutidine	11
3-Picoline	265–269	3.7:1	12.2	2,5-Lutidine	54
4-Picoline	260	3.6:1	11.5	2,4-Lutidine	21
Quinoline	260	4.0:1	13.4	2-Methylquinoline	65
2,4-Lutidine	260	4.0:1	12.2	*s*-Collidine	5

[a] Harshaw catalyst Ni-0104T was used in all experiments reported in this table.

The methylation reactions described in Table II do not proceed in the absence of a nickel catalyst. A study of the behavior of some of the alkylating agents over the catalyst in the absence of pyridine revealed that a fairly large number of gaseous products is formed

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[1] A. Ladenburg, *Ann.*, **247**, 1 (1888).

[2] W. H. Rieger, U. S. Patent 2,502,174 (March 28, 1950).

[3] S. Goldschmidt and M. Minsinger, German Patent 952,807 (Nov. 22, 1956); *Chem. Abstr.*, **53**, 16160 (1959).

[4] J. P. Wibaut and J. F. Arens, *Rec. Trav. Chim.*, **60**, 119 (1941); **61**, 59, (1942).

[5] N. M. Cullinane, S. J. Chard, and R. J. Meatyard, *J. Soc. Chem. Ind.* (London), **67**, 142 (1948).

[6] K. Ziegler and H. Zeiser, *Ber.*, **63**, 1847 (1930).

[7] R. Daniels and O. L. Salerni, *Proc. Chem. Soc.*, 286 (1960)

[8] M. G. Reinecke and L. R. Kray, *J. Am. Chem. Soc.*, **86**, 5355 (1964).