Rhodium Sulfide Catalyzed Reductive Alkylation of 1,5-Naphthalenediamine

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The utility of metal sulfide hydrogenation catalysts for the reductive alkylation of primary aryl amines with aliphatic ketones has recently been disclosed.[1-5] Rhodium sulfide appears to be the most active of these catalysts for reductive alkylations. We now describe its use in the preparation of several new N,N′-dialkyl-1,5-naphthalenediamines.

Reactions of 1,5-naphthalenediamine with acetone, cyclohexanone, methyl ethyl ketone, and methyl isobutyl ketone went smoothly and resulted in high yields of the corresponding N,N′-dialkyl-1,5-naphthalenediamines. A preformed 5% rhodium sulfide on carbon catalyst was used in each case. In addition, a catalyst prepared *in situ* from 5% rhodium on carbon and hydrogen sulfide was used in one experiment with acetone.

Experimental Section

The 1,5-naphthalenediamine was purchased from Aldrich Chemical Co., Inc. The ketones used were reagent grade chemicals. The rhodium on carbon and rhodium sulfide on carbon catalysts were obtained from Engelhard Industries, Inc.

Yields of crude residue products were 96% or higher in each case. Yields of pure products were not determined but are estimated to be in excess of 90%.

A detailed description of one experiment is given to illustrate the procedure.

To a 600-ml stainless steel Magne-Dash autoclave were added 31.6 g (0.20 mole) of 1,5-naphthalenediamine, 200 ml (*ca.* 2.7 moles) of acetone, and 2.5 g of 5% rhodium on carbon. The autoclave was sealed, purged with nitrogen and then with hydrogen. Hydrogen sulfide was added to a pressure of 50 psig, followed by the addition of hydrogen to a pressure of 1300 psig. The reaction mixture was heated with agitation at 140° and 1200–1400 psig for 3 hr. The autoclave was cooled and depressurized and the reaction product removed. The reaction mixture was filtered to remove catalyst; the solvent was removed by distillation. The solid residue, crude N,N′-diisopropyl-1,5-naphthalenediamine, weighed 47 g and melted at 114–126°. The melting point was 130–132° after one recrystallization from acetone–water. Recrystallization from a mixture of benzene and hexane, followed by a recrystallization from hexane, gave white crystals, mp 134–135°. *Anal.* Calcd for $C_{16}H_{22}N_2$: C, 79.29; H, 9.15; N, 11.56. Found: C, 80.07; H, 9.26; N, 11.31. The dihydrochloride, prepared by reaction with concentrated hydrochloric acid in 95% ethanol, melted at 284° dec. *Anal.* Calcd for $C_{16}H_{24}N_2Cl_2$: Cl, 22.49. Found: Cl, 21.82.

The following experiments were run in a 2-l. stainless steel Magne-Dash autoclave with 94.9 g (0.60 mole) of 1,5-naphthalenediamine, 700 ml of ketone, and 5.0 g of 5% rhodium sulfide on carbon without added hydrogen sulfide.

N,N′-Diisopropyl-1,5-naphthalenediamine.—The reaction mixture containing *ca.* 9.5 moles of acetone was heated at 130–135° and 900–1100 psig for 2 hr. There was obtained 144 g of a crude residue of N,N′-diisopropyl-1,5-naphthalenediamine melting at 115–121° (mostly 118–121°).

N,N′-Dicyclohexyl-1,5-naphthalenediamine.—The reaction mixture containing *ca.* 6.7 moles of cyclohexanone was heated at 125–130° and 900–1100 psig for 3.5 hr. There was obtained 197 g of a crude residue melting at 159–194° (mostly 189–194°). Several recrystallizations from a mixture of benzene and 2-propanol gave a white powder, mp 195–196°. *Anal.* Calcd for $C_{22}H_{30}N_2$: C, 81.93; H, 9.38; N, 8.69. Found: C, 82.77; H, 9.54; N, 8.38.

N,N′-Di-*sec*-butyl-1,5-naphthalenediamine.—The reaction mixture containing *ca.* 7.8 moles of methyl ethyl ketone was heated at 120° and 900–1100 psig for 2.3 hr. There was obtained 161 g of a crude residue melting at 78–99° (mostly 95–99°). Several recrystallizations from hexane gave a pale yellow powder, mp 114–114.5°. *Anal.* Calcd for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.36. Found: C, 80.06; H, 9.65; N, 10.93.

N,N′-Di-1,3-dimethylbutyl-1,5-naphthalenediamine.—The reaction mixture containing *ca.* 5.6 moles of methyl isobutyl ketone was heated at 130° and 800–1200 psig for 9 hr. There was obtained 188 g of a semisolid, crude residue. Several recrystallizations from methanol gave white needles, mp 104.5–105°. *Anal.* Calcd for $C_{22}H_{34}N_2$: C, 80.92; H, 10.50; N, 8.58. Found: C, 81.42; H, 10.73; N, 8.80.

(1) F. S. Dovell and H. Greenfield, *J. Org. Chem.*, **29**, 1265 (1964).

(2) M. A. Ryashentseva, Kh. M. Minachev, and L. S. Geidysh, USSR Patent 170,998 (1965); *Chem. Abstr.*, **63**, 16259b (1965).

(3) U. S. Rubber Co., Belgian Patent 643,911 (1964).

(4) F. S. Dovell and H. Greenfield, *J. Am. Chem. Soc.*, **87**, 2767 (1965).

(5) H. Greenfield and F. S. Dovell, paper presented at 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965; Division of Petroleum Chemistry Preprint B-121.

Nuclear Magnetic Resonance Spectra of Some Polyphenyl-2,3-diazanaphthalenes and -2,3-diazaanthracenes

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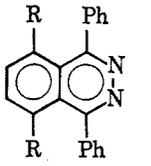
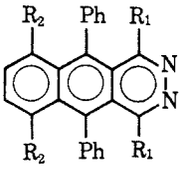
The geometry of fused-ring aromatic systems is such that substituents in the *peri* positions are forced into close proximity, giving rise to nonbonded interactions over unusually short distances. For example, phenyl substituents in the *peri* positions of naphthalene and anthracene are forced to rotate out of normal conjugation with the polycyclic ring,[1] one result being that protons in substituents *peri* to such phenyl rings are located in the diamagnetic shielding zone of the pendant phenyl ring,[2] and should resonate at higher field intensity than usual for the particular substituent. The nmr absorption of the pendant phenyl groups in the spectrum of 1,8-diphenylnaphthalene, for example, falls 0.5–0.6 ppm to higher field than the pendant phenyls of naphthalenes with nonadjacent phenyls.[3]

The preparation of some polyphenyl-substituted 2,3-diazanaphthalenes (**1** and **2**) and 2,3-diazaanthracenes (**3–5**) provides examples of *peri–peri* interaction in a



1, R = H
2, R = Ph



3, $R_1 = CH_3$; $R_2 = H$
4, $R_1 = Ph$; $R_2 = H$
5, $R_1 = R_2 = Ph$

(1) H. H. Jaffé and O. Chalvet, *J. Am. Chem. Soc.*, **85**, 1561 (1963).

(2) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., London, 1959, p 125.

(3) H. O. House, R. W. Magin, and H. W. Thompson, *J. Org. Chem.*, **28**, 2403 (1963).

different ring system and further provides an example of a phenyl ring sandwiched between two *peri*-phenyl rings.

Results and Discussion

The data for the nmr absorption of compounds **1–5** are given in Table I. The difference between the pendant phenyl resonance in the polyphenyl-substituted compound and that in the diphenyl compound is denoted $\Delta\ \delta$ and is tabulated for each compound.

TABLE I

NMR DATA FOR PHENYL-SUBSTITUTED 2,3-DIAZANAPHTHALENES AND 2,3-DIAZAANTHRACENES

	δ, ppm		
Compd	Phenyl	Other	Δδ, ppm
1	7.84	8.53[a] (m)	0[b]
2	7.17	8.45 (s)	0.53–0.67
	7.27		
	7.31		
3	7.75[c]	2.54[d] (s)	0[b]
4	7.30	8.06[a] (m)	0.44
5	6.80	7.91[a] (s)	0.95[e]

[a] The signal due to the diazanaphthalene or anthracene ring protons, either the singlet (s) for the A_2 cases or the center of the AA'BB' multiplet (m). [b] Used as a reference for the appropriate *peri*-phenyl-substituted compound. [c] Figure is for the sharp maximum of a complex multiplet extending from 7.5 to 8.0 ppm. [d] The methyl resonance. [e] Based on the assignment of the highest field peak to the 9,10-diphenyl groups.

The shift to higher field of *ca.* 0.60 ppm for the phenyls of 1,4,5,8-tetraphenyl-2,3-diazanaphthalene (**2**) is very close to that observed for 1,8-diphenylnaphthalene; the effect of the two heteroatoms is minimal. In the case of 2,3-diazaanthracene, a shift value directly comparable to that in diazanaphthalene could not be obtained since the appropriate reference material, 9,10-diphenyl-2,3-diazaanthracene, was not available. We chose to use compound **3** as a reference. Even though its aromatic absorption is a very complex, only partially resolved multiplet, a sharp peak occurs at 7.75 ppm, near the center of the multiplet, and this value was used in computing $\Delta\delta$.

The pendant phenyl absorption of 1,4,9,10-tetraphenyl-2,3-diazaanthracene (**4**) falls at 7.30 ppm, a shift to higher field of 0.45 ppm. This is somewhat less than in the case of 2,3-diazanaphthalene but is subject to the uncertainty in the reference absorption. 1,4,5,8,-9,10-Hexaphenyl-2,3-diazaanthracene (**5**) exhibits three broadened maxima at 6.80, 6.92, and 7.08 ppm in addition to the diazaanthracene ring protons at 7.91 ppm. Taking the highest field maximum as that due to the 9,10-diphenyls gives an upfield shift of 0.95 ppm, appoximately twice the value for tetraphenyl. This observation indicates that there is little or no distortion of the molecular geometry of hexaphenyl compared to tetraphenyldiazaanthracene.

The use of trifluoroacetic acid as solvent for these spectra, necessitated by poor solubility in the more common solvents, requires some comment. In this strongly acidic system the diaza compounds are certainly protonated and if the rate of proton exchange were slow, this would lead to loss of symmetry and to nonequivalence of phenyls in analogous positions on opposite sides of the rings and thus to a confusion of the spectral assignments. That this is not the case is shown by the fact that the diazanaphthalene and anthracene ring protons appear as either sharp singlets (for the A_2 cases) or as symmetrical multiplets (for the AA'BB' cases). The appearance of the central ring proton absorption in the spectrum of 2-methyl-1,4,5,8-tetraphenyl-3-aza-2-azonianaphthalene iodide as a typical AB quartet (J_{ab} = 7.5 cps, δ_{ab} = 0.22 ppm) supports this conclusion.

Experimental Section

Spectra were determined by using a Varian Associates A-60 nmr spectrometer, with the probe at normal operating temperature (*ca.* 35°). Solutions were *ca.* 10% (w/v) in trifluoroacetic acid. Chemical shifts were determined relative to internal tetramethylsilane at δ = 0 ppm.

2,3-Dibenzoyl-1,4-diphenylnaphthalene.—A solution of 10.8 g (0.04 mole) of 1,3-diphenylisobenzofuran and 9.7 g (0.041 mole) of dibenzoylethylene in 200 ml of ethanol was refluxed for 2 hr. Removal of the solvent gave an oil which crystallized on boiling with methanol to yield 16.3 g of the Diels–Alder adduct, mp 155–155.5° (yellow at 130°, dark red melt).

A solution of 4.0 g of the adduct in 350 ml of methanol was saturated with hydrogen chloride. The mixture was then refluxed for 2 hr, while hydrogen chloride was slowly bubbled through the solution. Removal of the solvent and slurrying the resulting solid with methanol gave an off-white solid. Recrystallization from acetic acid and then ethanol gave pure 2,3-dibenzoyl-1,4-diphenylnaphthalene, mp 185–186.5°.

Anal. Calcd for $C_{36}H_{24}O_2$: C, 88.5; H, 4.9. Found: C, 88.5; H, 5.3.

2,3-Dibenzoyl-1,4,5,8-tetraphenylnaphthalene.—A suspension of 3 g of 2,3-dibenzoyl-1,4,5,8-tetraphenyl-1,4-dihydro-1,4-epoxynaphthalene[4] in 50 ml of acetic acid was heated to boiling. Zinc dust (3 g) was added, in portions, as fast as the resulting effervescence would permit. The mixture was stirred and boiled for 2 min and then filtered while hot. The residue was stirred with concentrated hydrochloric acid until the zinc metal dissolved. Filtration, followed by washing with water and ethanol, gave a gray solid. This solid was then boiled with ethyl acetate and filtered. This treatment was repeated with cyclohexane. Recrystallization from benzene–ligroin (bp 30–60°) and drying at 100° provided an analytical sample of the title compound, mp 309–311°.

Anal. Calcd for $C_{48}H_{32}O_2$: C, 90.0; H, 5.0. Found: C, 90.3; H, 5.4.

Preparation of 1, 2, 4, and 5.—Reaction of the appropriate 2,3-dibenzoyl compound[5] with hydrazine as outlined in Table II provided the title compounds characterized in Table III.

1,3-Dimethoxy-1,3-dimethyl-4,9-diphenyl-1,3-dihydronaphtho[2,3-*c*]furan.—A solution of 4.48 g (0.04 mole) of diacetylethylene in 100 ml of benzene was added to a solution of 10.8 g (0.04 mole) of 1,3-diphenylisobenzofuran in 100 ml of benzene. The fluorescence of the isobenzofuran solution was immediately quenched and a slight red color developed. The solution was refluxed for 3 hr and the clear yellow solution then stripped to yield a yellow oil. Addition of 100 ml of methanol, followed by stripping, gave a slurry. Filtration and washing with methanol gave 12.7 g (83%) of crude adduct, 2,3-diacetyl-1,4-diphenyl-1,4-epoxy-1,2,3,4-tetrahydronaphthalene, mp 127.5–129.0°.

To 500 ml of methanol saturated with hydrogen chloride was added 7.23 g of the adduct. The mixture was stirred for 1 hr at room temperature during which time the mixture became initially homogeneous and yellow and then solids formed. Stripping gave a dark solid which was slurried with cold methanol, filtered, and washed with cold methanol to yield a yellow solid, 4.54 g, mp 139–169°. Chromatography on alumina, recrystallization from methanol, and drying at 140° provided an analytical sample of a *cis–trans* mixture of the title compound, mp 152–166° dec (sintered at 143°). The nmr spectrum in addition to aromatic absorption exhibited singlets at 3.30 and 3.15 ppm (OMe)

(4) W. Reid and K. H. Bonnighausen, *Ann.*, **639**, 61 (1961).

(5) *o*-Dibenzoylbenzene was purchased from the Aldrich Chemical Co. 2,3-Dibenzoyl-1,4-diphenylbenzene was prepared as described in ref 4.

TABLE II

PREPARATION OF COMPOUNDS 1, 2, 4, AND 5

Compd	Hydrazine–Ketone	Solvent: Reaction	Solvent: Recrystn	Time, hr	Yield, %
1	8–1	EtOH	PhH	16	...
2	4–1	EtOH	C_5H_5N, $CHCl_3$–ligroin, $PhCH_3$	16	95 crude
4	10–1	*n*-PrOH–$PhCH_3$	PhH–ligroin	16	59 crude
5	10–1	*n*-PrOH–$PhCH_3$	Xylene	16	72 crude
					12 pure
				144	28 pure

TABLE III

2,3-DIAZANAPHTHALENES AND 2,3-DIAZAANTHRACENES

Compd	Mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
1	197.5–199.5 (lit.[a] 192)	85.1	5.0	9.9	85.4	5.2	9.8
2	338–341[b]	88.5	5.1	6.5	87.7	5.0	6.4
3	283 dec	86.7	5.6	7.8	86.8	5.4	7.8
4	277–279	89.3	5.0	5.8	88.9	4.9	5.7
5	384–386	90.6	5.0	4.4	90.6	5.1	4.2

[a] A. Guyot and J. Catel, *Compt. Rend.*, **140**, 1348 (1905). [b] A satisfactory analysis could not be obtained; characterized as a quaternary salt in the Experimental Section.

and at 1.45 and 1.30 ppm (C–Me). Integration indicated a 38/62 ratio of isomers.

Anal. Calcd for $C_{28}H_{26}O_3$: C, 82.0; H, 6.3. Found: C, 81.9; H, 6.3.

1,4-Dimethyl-9,10-diphenyl-2,3-diazaanthracene (3).—To a solution of 2.67 g of 1,3-dimethoxy-1,3-dimethyl-4,9-diphenyl-1,3-dihydronaphtho[2,3-c]furan in 20 ml of dioxane was added 5 ml of 5% hydrochloric acid. After 30 min, hydrazine was added to the solution until it was basic to litmus. Sufficient ethanol was added to homogenize the mixture which was then refluxed overnight. Stripping gave a yellow solid which, when recrystallized from ethanol, yielded 0.96 g (41%) of bright yellow crystals, mp 265° dec. A second recrystallization from ethanol provided an analytical sample, mp 283° dec.

Anal. Calcd for $C_{26}H_{20}N_2$: C, 86.7; H, 5.6; N, 7.8. Found: C, 86.8; H, 5.4; N, 7.8.

2-Methyl-1,4,5,8-tetraphenyl-3-aza-2-azonianaphthalene Iodide.—To a solution of 2 g of **2** in 50 ml of chloroform was added 10 ml of methyl iodide. After the solution had stood overnight, it was diluted with ether to give an orange solid. Recrystallization from ethanol and then methanol gave an orange solid which was solvated even after drying at 180°, mp 309–314° dec.

Anal. Calcd for $C_{33}H_{25}IN_2 \cdot CH_3OH$: C, 67.1; H, 4.8; I, 20.9. Found: C, 67.0; H, 4.6; I, 21.3.

Acknowledgment.—We thank Mr. R. L. Young for assistance in determining the nmr spectra.

Ten π-Electron Nitrogen Heterocyclic Compounds. IX. The Syntheses and Nuclear Magnetic Resonance Spectra of Some Methylnaphthyridines

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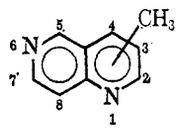
As part of a study of the chemistry of bicyclic heteroaromatic compounds[1] we have been interested in the chemistry of the various naphthyridines.[2]

Before a systematic study of these compounds could be undertaken, it became necessary to develop reasonable synthetic methods for the preparation of some of these substances.

The syntheses of the various parent and methyl-substituted naphthyridines generally involve multistep sequences, often affording the desired compounds only in low yields.[3] These tedious methods have considerably limited the study of naphthyridines. Our recent interest in 1,6-naphthyridines prompted us to study the applicability of the Skraup reaction to 4-aminopyridine. This was done despite the numerous comments in the literature[3] that this reaction does not occur with 4-aminopyridine. Since the over-all yields leading to the parent or methyl-1,6-naphthyridines (**1**) by the conventional procedures rarely exceed 4%, even a potentially low-yield, one-step Skraup synthesis would be a considerable synthetic improvement.



1.

Methyl-1,6-naphthyridines.—Rapaport and Batcho[4] have recently reported the preparation of 2-methyl- and of 4-methyl-1,5-naphthyridine by a modified Skraup reaction on 3-aminopyridine. We decided to apply this reaction to 4-aminopyridine in the hope of obtaining the 2-methyl- and the 4-methyl-1,6-naphthyridines. Neither one of these compounds had been prepared since they are not readily available by any of the known syntheses of 1,6-naphthyridines.

Two recent papers[5] describe the Skraup synthesis as applied to 4-aminopyridine N-oxide, a reaction which affords the corresponding 1,6-naphthyridine 6-oxide. No compounds substituted in the 2, 3, or 4 position were obtained. The use of the N-oxide starting material was predicated upon the assumption that the free amines would not undergo the cyclization reaction. Where the yields are reported for the Skraup reaction on the N-oxides, they are 5% or less.

The condensation of 4-aminopyridine with methyl vinyl ketone in the presence of Sulfo-mix afforded a low-melting solid $C_9H_8N_2$. The nmr spectrum of this material is reported in Table I and is clearly in agreement with the assigned structure of this compound, 4-methyl-1,6-naphthyridine (**2**). Similarly, the condensation of

(1) W. W. Paudler and H. L. Blewitt, *J. Org. Chem.*, **31**, 1295 (1966).
(2) W. W. Paudler and T. J. Kress, *J. Heterocyclic Chem.*, **2**, 393 (1965).
(3) R. C. Elderfield, "Heterocyclic Compounds," Vol. 7, John Wiley and Sons, Inc., New York, N. Y., 1961, pp 198–236.
(4) H. Rapaport and A. Batcho, *J. Org. Chem.*, **28**, 1753 (1963).
(5) T. Kato, F. Hamaguchi, and T. Oiwa, *Pharm. Bull.* (Tokyo), **4**, 178 (1956). S. Tamura, T. Kudo, and Y. Yanagishara, *Yakugaku Zasshi*, **80**, 562 (1960).