(XII),[16] and *n*-butyl thiocyanate (XIII)[17] has been reported. The preparation of the other compounds used is described below.

Methyl 2-Thiocyanobenzoate.—Freshly distilled methyl anthranilate (10.0 g., 0.066 mole) in 100 ml. of water, to which 17 ml. of concentrated hydrochloric acid had been added, was diazotized by the addition of 5.24 g. (0.076 mole) of sodium nitrite in 20 ml. of water. The reaction flask was cooled in an ice bath during the diazotization. A suspension of cuprous thiocyanate was prepared by adding 8.75 g. of potassium thiocyanate to a solution of 20 g. of cupric sulfate pentahydrate and 37.5 g. of hydrous ferrous sulfate in 300 ml. of water. The grey precipitate of cuprous thiocyanate was filtered, washed with water, and suspended in 30 ml. of water containing 45 g. of potassium thiocyanate. The diazotized solution was added slowly to this suspension. Nitrogen evolution occurred and the reaction mixture turned dark brown. After standing at room temperature 1.5 hr., the mixture was heated on the steam bath for 15 min. and cooled. The solid was filtered and washed with water. Suspension of the solid in water and steam distillation gave 2.0 g. (16%) of a white solid. Two recrystallizations of the solid from methanol–water gave white needles: m.p. 75–76.5°, lit.[18] m.p. 76–77°; $\nu_{\max}^{\mathrm{KBr}}$ 2160, 1710 cm.$^{-1}$.

Methyl 4-Thiocyanobenzoate.—A solution of diazomethane was prepared[19] by adding in portions N-methyl-N-nitrosourea (1.0 g.) to a stirred suspension of 7 ml. of 40% potassium hydroxide in 15 ml. of ether at 0°. The mixture was stirred at 0° for 20 min. and then the yellow ether solution of diazomethane was decanted. The aqueous phase was rinsed once with 10 ml. of ether and again with 5 ml. of ether, and the ether washings were combined with the original ether solution. To the ether solution of diazomethane was added in portions 4-thiocyanobenzoic acid[20] (0.60 g., 3.33 mmoles) over a period of 5 min. The flask was loosely stoppered and allowed to stand for 42 hr. The ether solution was washed once with 10% sodium bicarbonate and once with water, and dried over magnesium sulfate. Filtration and removal of the solvent gave 0.55 g. of a yellow oil which slowly crystallized. An analytical sample was prepared by four recrystallizations from ether–petroleum ether (b.p. 30–60°), m.p. 61–63°.

Anal. Calcd. for $C_9H_7NO_2S$: C, 55.95; H, 3.65; N, 7.25. Found: C, 55.94; H, 3.62; N, 7.42.

---

[16] R. G. R. Bacon and R. G. Guy, *J. Chem. Soc.*, 2428 (1961).

[17] R. F. Kaufmann and R. Adams, *J. Am. Chem. Soc.*, **45**, 1744 (1923).

[18] P. Friedlander, *Ann.*, **351**, 400 (1907).

[19] F. Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 166.

[20] F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 854 (1956).

Reactions of Benzyne with Pyrroles

ENNO WOLTHUIS, DAVID VANDER JAGT, SHERMAN MELS, AND ANDREW DE BOER

Chemistry Department, Calvin College, Grand Rapids, Michigan

Received July 13, 1964

In contrast to furans, which react with benzyne to give 1,4-epoxy-1,4-dihydronaphthalenes, N-substituted pyrroles with alkyl or aryl groups in the 2- and 5-positions were found to give N-substituted 2-naphthylamines, not the expected 1,4-imines. Apparently the Diels–Alder reaction occurs to form the imine, but the latter immediately rearranges to the amine. The Grignard reagent, which is intermediate in the preparation of the benzyne, also seems to cause other reactions, such as the cleavage of the C–N bond in 1,4-dimethyl-N-benzyl-2-naphthylamine to give 1,4-dimethyl-2-naphthylamine.

N-Methylpyrrole has been reported[1] to condense with benzyne to give a small amount of imine (called endamine by these authors) isolated in the form of its quaternary iodide, but chiefly 1-methyl-10,11-dihydro-1,2-benzocarbazole. It was postulated that the basic imine nitrogen atom reacted with more benzyne to give the benzocarbazole. This observation has been supported recently by condensation of benzyne with N-phenyl and N-benzylpyrroles.[2] In both cases the reaction products were chiefly benzocarbazoles, especially when an excess of benzyne was used, but these investigators also reported the formation of N-phenyl and N-benzyl-1-naphthylamines. Supposedly these compounds were formed by rearrangement of the imines, although the latter were not isolated and characterized as such. It should be noted that the formation of the N-substituted 1-naphthylamines is entirely analogous to the conversion of the epoxides to 1-naphthols.[3]

Our previous work[4] has shown that, when the 1- and 4-positions in the 1,4-epoxides are blocked by alkyl groups, the epoxides are converted to substituted 2-naphthols or their ethers. Therefore, one of the objects of the present work was to see whether 1,4-naphthalene imines, substituted by alkyl or aryl groups in the 1- and 4-positions, would rearrange to substituted 2-naphthylamines. A further objective was to isolate if possible, and to characterize the imines, perhaps by reducing the basicity of the pyrrole nitrogen atom by proper substitution.

Two pyrroles were chosen such that the unshared nitrogen electron pair would be less available for secondary reaction with benzyne, making the isolation of the imine more likely. 2,5-Dimethyl-1-phenylpyrrole (**1**) possesses the N-phenyl group which obviously shares in the charge on the nitrogen atom, and 1-methyl-2,5-diphenylpyrrole (**2**) has an extensively conjugated system involving the phenyl and pyrrole groups and the nitrogen electron pair. One other compound, 1-benzyl-2,5-dimethylpyrrole (**3**), was also used for comparison with **1**.

These pyrroles were prepared by the usual method of condensing the appropriate 1,4-diketones with amines, with or without a solvent. A modification of the normal procedure was tried in the preparation of **3** and found to be a distinct improvement with respect to both yield and quality of product obtained. This method involves the azeotropic removal of the water formed, and is similar to that reported,[5] except that ligroin was substituted for benzene, thereby making isolation of the product easier owing to its lower solubility in ligroin.

The ultraviolet spectra of the pyrroles which were used have not been reported previously and provide an interesting comparison as shown in Figure 1. It has

---

[1] G. Wittig and W. Behnisch, *Ber.*, **91**, 2358 (1958).

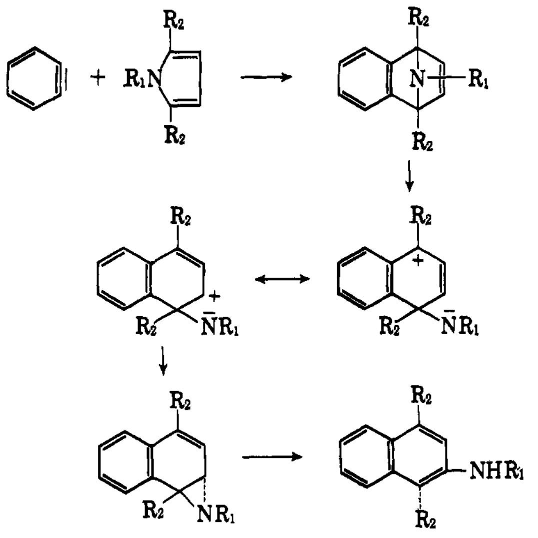
[2] G. Wittig and B. Reichel, *ibid.*, **96**, 2851 (1963).

[3] G. Wittig and L. Pohmer, *ibid.*, **89**, 1349 (1956).

[4] E. Wolthuis, B. Bossenbroek, G. DeWall, E. Geels, and A. Leegwater, *J. Org. Chem.*, **28**, 148 (1963).

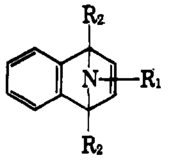
[5] W. S. Bishop, *J. Am. Chem. Soc.*, **67**, 2261 (1945).

Scheme I



been suggested[6] that the pyrrole and benzene rings are isoconjugate and show similar absorptions in the ultraviolet region of the spectrum. As expected, compound **3** has a spectrum comparable with that of 2,5-dimethylpyrrole.[7] On the other hand, compound **1** has a spectrum similar to that of **3** but shifted to the red owing to some conjugation of the pyrrole and phenyl rings. In contrast to both **1** and **3**, compound **2** shows the effect of much conjugation, and has essentially a 1,4-diphenylbutadiene structure with its many possible charged structures.[8]

The pyrroles described were treated with benzyne generated from 1-fluoro-2-bromobenzene and magnesium in tetrahydrofuran (THF) by the method previously described for the reaction of benzyne with furans.[4] In all cases the reactions were mildly exothermic, and a yellow-brown color appeared as the reaction proceeded. The products were isolated without difficulty, and were at first presumed to be imines with the general structure **4**. Although elementary



4

analyses and molecular weight determinations agreed with this structure, the ultraviolet spectra, shown in Figure 2, clearly showed that the compounds were really substituted 2-naphthylamines.[9] In compounds with structure **4**, it is obvious that conjugation is limited to the individual benzene rings, and absorption in the ultraviolet region should be no more than that for benzene itself. The identity of the substituted 2-naphthylamines was further established by n.m.r. spectra and by synthesis followed by infrared spectral comparison.

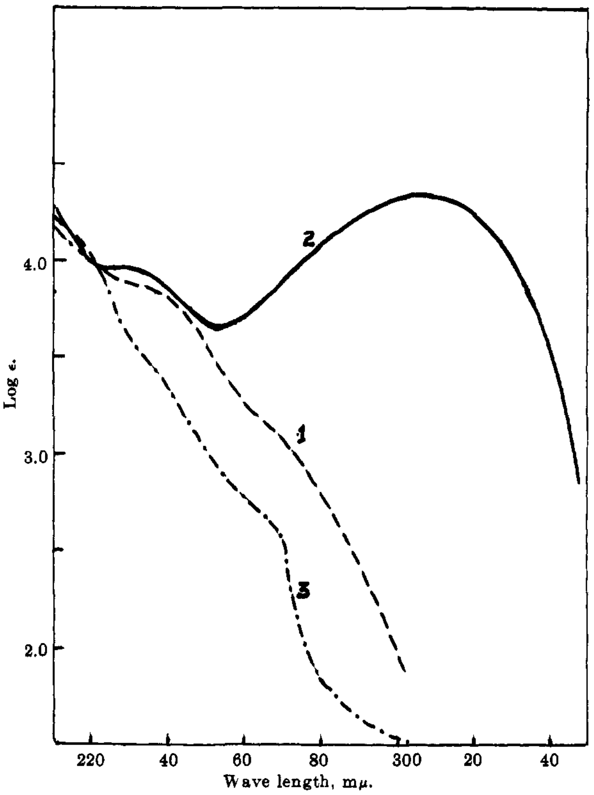


Figure 1.—Ultraviolet spectra of substituted pyrroles.

It is reasonably certain, therefore, that benzyne condensed with the pyrroles in normal Diels–Alder fashion to form the naphthalene skeleton, with R_2 groups (structure **4**) in the 1-and 4-positions. Many attempts were made to detect and isolate the imines resulting from such condensation, but failure to do so indicates they are short-lived and rearrange very readily to the more stable naphthalene structures, perhaps as shown in Scheme I.

These results, together with those reported earlier,[2-4] indicate a similarity between the condensations and condensation products of furans and pyrroles with benzyne. Normal 1,4-addition occurs in both cases, but the epoxides are far more stable than the imines. The epoxides and imines both rearrange to form substituted naphthols and naphthylamines, respectively, the former only when proton activated, the latter spontaneously. If the α-position is not occupied by an alkyl or aryl group, the products of rearrangement are substituted 1-naphthols or 1-naphthylamines. If both α-positions are occupied, the products are substituted 2-naphthols or 2-naphthylamines.

In the present work no evidence was found for a secondary reaction of the initially formed imine with more benzyne, such as was reported to occur when N-phenyl or N-benzylpyrroles were condensed with benzyne.[2] These authors showed that such secondary reaction is minimized by limiting the amount of benzyne generated. In our experiments no more than 1 mole of benzyne was used per mole of pyrrole, and it was generated slowly in the presence of the pyrrole, making an excess of benzyne unlikely at any time.

Another observation requires special comment. In addition to **7**, a by-product was obtained in the reaction of **3** with benzyne. This compound was identified as 1,4-dimethyl-2-naphthylamine (**8**). Diazotization

---

(6) J. R. Platt, *J. Chem. Phys.*, **19**, 101 (1951).

(7) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, Spectrum No. 2.

(8) K. W. Hausser, R. Kuhn, and A. Smakula, *Z. physik. chem.* (Leipzig), **B29**, 384 (1935).

(9) The authors thank Dr. J. R. Platt of the University of Chicago for valuable comments on the spectra.

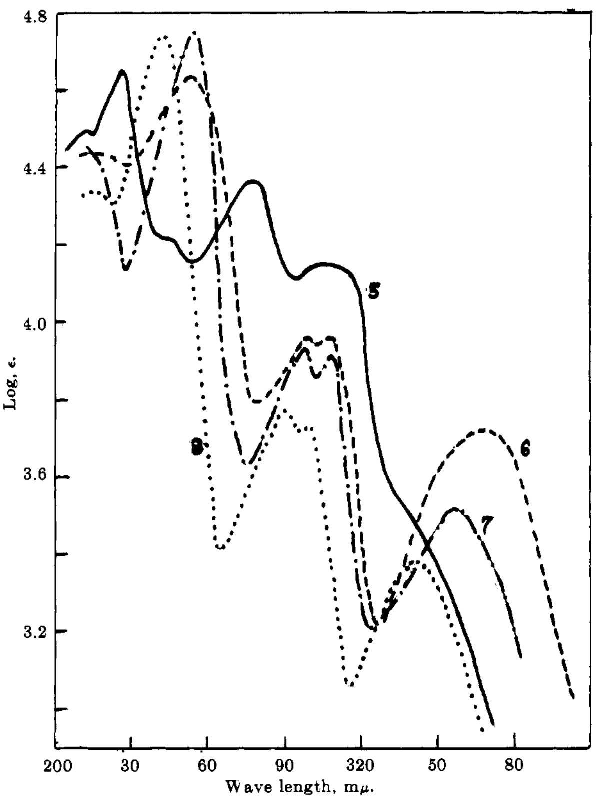


Figure 2.—Ultraviolet spectra of substituted 2-naphthylamines.

followed by coupling with a naphthol showed it to be a primary aromatic amine. Its identity was established by elementary analyses, titration of its hydrochloride, and finally by its synthesis from the corresponding naphthol.[4] Apparently the formation of compound **8** results from a C–N bond rupture. The amount of it formed probably increases with the amount of moisture in the THF, only a trace of it being detected when the THF was freshly distilled over lithium aluminum hydride. It was also found that the primary amine is formed in significant quantity when compound **7** is refluxed in THF with a Grignard reagent, such as phenyl magnesium bromide, or even with magnesium chloride. Since both a Grignard reagent and a magnesium halide are present during the condensation of benzyne with the pyrrole, it is likely that the acidic Grignard reagent attacks the basic N-atom in compound **7**, releasing the relatively stable benzyl carbonium ion, whereupon the moisture present may finish the reaction. However, it must be said that the use of gas chromatography failed to show the formation of any compound which could be derived from the benzyl ion. Investigations are being continued to clarify the course of this reaction.

Experimental[10]

2,5-Dimethyl-1-phenylpyrrole (**1**).—Prepared essentially by the method of Yanovskaya,[11] the crude product was obtained in 82% yield, m.p. 48–49.5°, and was recrystallized from acetic acid–water (5:1) to give 72% yield: m.p. 50–50.3°, lit. 53°,[11] 52–53°,[12] and 47–49°[13]; $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 238 sh (3.83) and 268 (3.14).

1-Methyl-2,5-diphenylpyrrole (**2**).—1,4-Dibenzoyl-2-butene was prepared by the method of Lutz,[14] and reduced to 1,4-diphenyl-1,4-butadione,[15] which was cyclized quantitatively to the pyrrole by the method used to make 1-methyl-2,3,5-triphenylpyrrole.[16] The product had m.p. 202.8–203°, lit.[1] 200.5–201.5°; $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 230 (3.97) and 307 (4.35).

1-Benzyl-2,5-dimethylpyrrole (**3**).—The method of Hazlewood[17] was tried but some difficulty was encountered in obtaining a pure product. The following procedure proved to be better with respect to both yield and quality obtained.

Benzylamine (21.4 g.), ligroin (50 ml., b.p. 100–115°), and 2,5-hexanedione (22.8 g.) reacted in a flask fitted with a Barrett water trap and condenser. The temperature of the mixture rose to about 60°, after which it was heated at reflux temperature for 1.5 hr., or until 7.2 ml. of water had been collected. Cooling at 5° overnight and filtering gave 25 g. (67.5%) of product, m.p. 45–45.3°, lit.[17] 48°. Evaporation of the filtrate to one-half volume and cooling gave another 5.6 g. (15%), m.p. 44.5–45°. Recrystallization of the main fraction from hexane did not raise the melting point: $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 209 sh (4.22), 263 sh (2.73), and 269 sh (2.58).

General Procedure for Condensation of Benzyne with N-Substituted Pyrroles (**5–8**).—Magnesium turnings (2.9 g., 0.12 mole) and 20 ml. of dry THF were added to a flask fitted with an agitator and condenser previously evacuated and filled with dry nitrogen to a positive pressure. About 10% of a solution of 17.5 g. (0.1 mole) of 1-fluoro-2-bromobenzene in 50 ml. of THF was added to start the reaction, sometimes with warming to 35–40°. After the addition of 0.1 mole of pyrrole dissolved in 25 ml. of THF, or suspended in 100 ml. of THF, the remaining fluorobromobenzene solution was added slowly during 4–5 hr. while maintaining a temperature of 60–70°. After allowing the reaction mixture to stand overnight at a slow reflux, it was worked up variously as outlined below.

N-Phenyl-1,4-dimethyl-2-naphthylamine (**5**).—The reaction mixture from the general procedure was treated with a solution of 50 g. of ammonium chloride and 2 ml. of concentrated ammonium hydroxide in 200 ml. of water, the layers were separated, and the aqueous layer was extracted with ether. The ether solution was added to the THF layer and dried over potassium carbonate; the solvents were removed finally under reduced pressure, to leave a viscous oil, which was dissolved in cyclohexane; the solution was clarified with carbon and refrigerated to give 7.0 g. (28.3%), m.p. 92–94°. Recrystallization from 85% aqueous acetic acid gave 5.2 g. (21%): m.p. 95–95.3°; $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 211 (4.49), 226 (4.65), 246 sh (4.19), 273 sh (4.35), 278 (4.37), 303 (4.15), 312 (4.14), and 345 sh (3.45). The infrared spectrum showed a band of medium intensity at 3365 cm.$^{-1}$. The n.m.r. spectrum confirmed the structure, showing ten aryl, one NH, and six aromatic methyl hydrogen atoms; molecular weight averaged 249 for three determinations.

Anal. Calcd. for $C_{18}H_{17}N$ (247.2): N, 5.67. Found: N, 5.79.

The stability toward acids of compound **5** (first thought to be the imine) was tested as follows. A mixture of **5** (1 g.), methanol (30 ml.), and concentrated hydrochloric acid (25 ml.) was refluxed for 5 days (after 18 hr. only a trace of aniline was detected). After cooling, 50 ml. of water was added, and the precipitate was filtered and washed, first with dilute acid, then with water. The residue, insoluble in acid, was extracted with warm, dilute sodium hydroxide, the solution was clarified with carbon, and acid was added to the filtrate to give 0.2 g. of 1,4-dimethyl-2-naphthol: m.p. 132–133°, lit.[18] 135–136°; acetyl derivative, m.p. 78.5–79°, lit.[18] 77–78°. One-half of the acid filtrate was titrated with 0.1 *N* sodium nitrite, showing the presence of 0.09 g. of aniline; the other half was benzoylated, giving 0.20 g. of benzanilide, m.p. 155.5–156.5°.

Compound **5** was also synthesized as follows. A mixture of 0.215 g. of 1,4-dimethyl-2-naphthol, 0.107 g. of potassium pyro-

---

[10] Melting points are corrected. The authors thank Dr. G. Slomp and his associates at the Upjohn Co. in Kalamazoo, Mich., for obtaining the spectra, the infrared on the Perkin-Elmer 21 spectrophotometer, the ultraviolet on the Cary 14 spectrophotometer, and the n.m.r. on the Varian A-60 spectrometer operating at 60 Mc. on solutions in chloroform.

[11] L. A. Yanovskaya, *Akad. Nauk SSSR, Inst. Organ. Khim. Sintezy Organ. Soedin. Sb.*, **1**, 152 (1950).

[12] A. P. Terent'ev and M. A. Volodina, *Dokl. Akad. Nauk SSSR*, **88**, 845 (1953).

[13] H. H. Schlubach, V. Franzen, and E. Dahl, *Ann.*, **587**, 124 (1954).

[14] R. E. Lutz, *Org. Syn.*, **20**, 29 (1940).

[15] J. P. Schaefer, *J. Org. Chem.*, **25**, 2027 (1960).

[16] A. Lespagnol, J. M. Dumont, J. Mercier, and P. Etzensperger, *Bull. soc. pharm. Lille*, 87 (1955).

[17] S. J. Hazlewood and G. K. Hughes, *J. Proc. Roy. Soc., N. S. Wales*, **71**, 92 (1937).

[18] S. Cannizzaro and A. Carnelutti, *Gazz. chim. ital.*, **12**, 407 (1882).

sulfate, and 1.028 g. of aniline was heated at 190° overnight. The cooled mixture was extracted with warm, dilute acid to leave a dark oil which was dissolved in 5 ml. of hot acetic acid, the solution was clarified with carbon, and water was added in equal volume to give 0.152 g., m.p. 86–95°. Recrystallization from hexane gave m.p. 94.5–95°, m.m.p. (with **5**) 94.5–95°. Infrared spectra of the two were identical.

N-Methyl-1,4-diphenyl-2-naphthylamine (**6**).—The reaction mixture from the general procedure was distilled under reduced pressure to remove all solvent, the residue was extracted several times with boiling hexane, and the extracts were clarified with carbon and cooled to give, first, 1.64 g. of the pyrrole (**2**) and then 6.96 g. (23%) of **6**, m.p. 146–151°. Recrystallization from methanol gave m.p. 162.9–163.5°; $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε): 220 (4.43), 253 (5.64), 298 (3.96), 308 (3.95), and 366 (3.72). Infrared spectrum showed a band of medium intensity at 3280 cm.$^{-1}$. The n.m.r. spectrum confirmed the structure, showing fifteen aryl, one NH, and three methyl hydrogen atoms.

Anal. Calcd. for $C_{23}H_{19}N$ (309.4): N, 4.53. Found: N, 4.81.

1,4-Dimethyl-N-benzyl-2-naphthylamine (**7**) **and 1,4-Dimethyl 2-naphthylamine** (**8**).—After the condensation by the general procedure, the solvents were removed under reduced pressure, the residue was extracted thoroughly with boiling benzene, and the benzene was removed to leave 27 g. of an oil, which was dissolved in hexane and put through a column of neutral alumina. When hexane was used as eluent, there was eluted, first, **7**, 7.2 g. (27.6%), m.p. 66–67°. Adding 0.5% methanol to the hexane eluted 1 g. of compound **8**, m.p. 65–66°. Mixture melting point and infrared spectra showed these two compounds to be different, and they were characterized as follows.

Compound 7.—Recrystallization from methanol (fluorescent solution) gave m.p. 70–70.3°; $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε): 211.5 (4.45), 254 (4.75), 285 sh (3.77), 296 (3.94), 309 (3.92), and 356 (3.52). Infrared spectrum showed a band at 3430 cm.$^{-1}$. The n.m.r. spectrum confirmed the structure, showing ten aromatic, two methylene, one NH, and six methyl hydrogen atoms.

Anal. Calcd. for $C_{19}H_{19}N$ (261.4): C, 87.50; H, 7.28; N, 5.36. Found: C, 87.67; H, 7.41; N, 5.49.

The hydrochloride of **7** was formed as follows. A mixture of 0.520 g. of **7**, 25 ml. of water, and 10 drops of concentrated hydrochloric acid was refluxed 2 hr., during which time crystals formed. Cooling to 10° and filtering gave 0.50 g. (84%), m.p. 200–202°. The infrared spectrum showed a broad band at 2500–2700 cm.$^{-1}$, indicating an amine salt. Titration of the salt, under hexane, with standard alkali gave equiv. wt. 306, and the base (**7**), m.p. 68–70°, was recovered from the hexane layer.

Anal. Calcd. for $C_{19}H_{20}ClN$ (297.9): Cl, 12.25; N, 4.70. Found: Cl, 12.43; N, 4.63.

Compound **7** was also synthesized as follows. A mixture of 0.155 g. of 1,4-dimethyl-2-naphthol, 0.200 g. of potassium pyrosulfate, and 0.885 g. of benzylamine was heated for 10 hr. at 190°, cooled, and extracted with warm, dilute alkali to remove naphthol, then with warm, dilute acid to remove benzylamine. The residue was taken up in hexane and passed through a column of neutral alumina to give 0.100 g., m.p. 63–64°, identical with **7** as shown by mixture melting point and infrared spectra.

Compound 8.—Recrystallization from hexane gave m.p. 71–71.3°; $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε): 215 (4.34), 243 (4.74), 279 sh (3.65), 289 (3.78), 300 (3.74), and 343 (3.39). **8** gave a positive test for primary amine. Derivatives of **8** were acetyl, m.p. 221–221.5°; benzoyl, m.p. 207.2–207.6°.

Anal. of acetyl derivative of **8**. Calcd. for $C_{14}H_{15}NO$ (213.2): C, 78.9; H, 7.1; N, 6.57. Found: C, 78.8; H, 7.2; N, 6.67.

Compound **8** was also synthesized as follows. A mixture of 0.89 g. of 1,4-dimethyl-2-naphthol, 12 ml. of 40% ammonium sulfite, and 12 ml. of concentrated ammonium hydroxide was sealed in a small iron pipe, and heated with shaking for 60 hr. at 145–150°. After cooling, the contents were rinsed with water; the precipitate was filtered off, washed, and extracted with hot methanol. The methanol was removed, and the residue was extracted with warm, dilute acid, leaving 0.8 g. of unchanged naphthol. The acid extract, made alkaline, gave a precipitate which was recrystallized from hexane to give 0.040 g., m.p. 71–71.5°, identical with **8** as shown by mixture melting point and ultraviolet and infrared spectra.

Compound 8 from Compound 7 and a Grignard Reagent.—Magnesium turnings (0.35 g.) were added to a flask, which was then evacuated and filled with dry nitrogen to a positive pressure. THF (10 ml.), freshly distilled over lithium aluminum hydride, was added, and then 10% of a solution of 1.96 g. of bromobenzene in 12 ml. of THF. After the reaction was started with a little heat, there was added a solution of 0.500 g. of compound **7** in 10 ml. of THF. While maintaining a gentle reflux, the remaining bromobenzene solution was added in 1.5 hr., during which time the color of the mixture changed from colorless to greenish brown. The solvent was removed under reduced pressure, the residue was extracted twice with warm, dilute acid, the acid extracts were combined and made alkaline, and the resulting precipitate was dissolved in hexane. Passing dry hydrogen chloride through the dried hexane solution gave the hydrochloride of **8** (0.033 g.), which was converted to the base, m.p. 65–66°, whose ultraviolet spectrum was identical with that of **8** prepared by benzyne condensation. An additional 0.052 g. of the product was obtained by further extraction of the alkalized acid extracts with methanol, and it was converted to its benzoyl derivative, m.p. 204–205°, identical with the benzoyl derivative of **8**.

A similar reaction of phenyl magnesium bromide with N-phenyl-2-naphthylamine gave a product which contained a small amount of primary amine as shown by diazotization and coupling, but the yield was uncertain owing to difficulties in separating it from unchanged starting material.

Acknowledgment.—We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.