AROMATIC SUBSTITUTION

PART II. THE REACTION OF VARIOUS 3-SUBSTITUTED PYRIDINE DERIVATIVES AND OF QUINOLINE WITH PHENYLLITHIUM[1]

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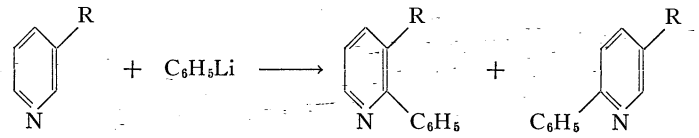
Received March 7, 1963

ABSTRACT

Phenyllithium and pyridine-3-*N*,*N*-diethylsulphonamide gave the expected 2-phenyl derivative exclusively. Contrary to a previous report some 2,3-diphenylpyridine is formed with 3-phenylpyridine. No pyridyne intermediate seems to be formed in the reaction of phenyllithium with 3-bromopyridine. The reactions of phenyllithium with quinoline and with *N*-benzylpyridinium chloride have also been studied and are discussed.

In previous papers in this series (1, 2, 3) the reaction of phenyllithium with a number of 3-substituted pyridines was examined. With a 3-alkylpyridine (I) the main product was the 3-alkyl-2-phenylpyridine (II) when the alkyl group was methyl, ethyl, or isopropyl, but it was the 5-alkyl-2-phenylpyridine when the substituent was *t*-butyl. With nicotine (I; R = 2-*N*-methylpyrrolidyl) the isomer ratio was approximately 1:1. Two further examples were studied: R = NH_2 and R = OCH_3. In both cases the only isomer detected was the 2,3-disubstituted pyridine. It was suggested (2) that in these last two cases the exclusive substitution at the 2-position might be explained by assuming some coordination of the lithium atom with a pair of electrons on the 3-substituent such that the phenyl group would be suitably oriented for attack at the 2-position. No 4-phenylpyridine could be detected gas chromatographically in the reaction of phenyllithium with pyridine. A number of possible explanations were considered (3) to account for the observed orientation with 3-alkylpyridines.



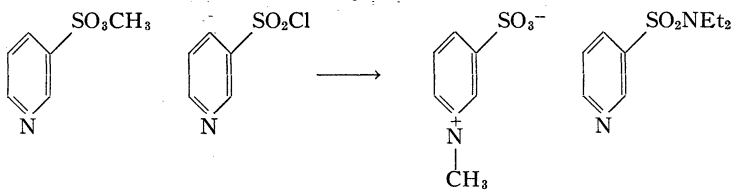
I II III

All the 3-substituents mentioned above are electron donating. The only reported example of such a reaction being carried out with a 3-substituted pyridine in which the 3-substituent may be considered to be electron attracting is that in which 3-phenylpyridine (I; R = C_6H_5) was the substrate used (4). In this case, and contrary to the expected electrical effect of a phenyl substituent group ($-I > +M$), it was reported that only 2,5-diphenylpyridine (III; R = C_6H_5) was isolated. It was postulated (1) that this might be attributed to steric inhibition of coplanarity in the transition state leading to the formation of the 2,3-isomer, whereas no such inhibition exists in the transition state for the 2,5-isomer. It seemed rather strange, though, that *no* 2,3-diphenylpyridine had been formed at all in this reaction. This has been reinvestigated. It was also important that the reaction of phenyllithium with 3-substituted pyridines in which the 3-substituent was electron attracting be studied: on the basis of simple electronic considerations (which fail to predict the correct behavior when R = CH_3, Et, or *i*-Pr (3)) it might be predicted that

[1]*Part I. Can. J. Chem.* **40**, *213 (1962).*

the 2,3-isomer should be formed predominantly in these cases. The choice of such a substituent was made difficult by the fact that most of the common electron-attracting groups (e.g. NO_2, CO_2R) themselves react with the organolithium reagent. It was decided to examine the reactions when R = SO_3CH_3 and Br, and also to try and determine whether coordination of the organolithium reagent at the pyridine nitrogen atom was important in determining the preferential orientation of the entering nucleophile, as had been suggested (5). The latter seemed unlikely since it has been reported that the reaction of benzylmagnesium chloride with 3,4-lutidine methiodide (where further coordination at nitrogen is not possible) gives the 1,2-dihydro-2-benzyl derivative (6). Other examples of such reactions are known (7). To this end it was decided to study the reaction of phenyllithium with *N*-benzylpyridinium chloride and with 3-methyl-*N*-benzylpyridinium chloride. Finally, it was suggested by Brown and Harcourt (8) that a "strong" nucleophilic reagent would attack the quinoline ring preferentially at $C_{(2)}$, whereas a "weak" one would attack it at the position of lowest nucleophilic atom localization energy, namely $C_{(4)}$. Phenyllithium is considered to be a strong nucleophile and it was, consequently, of interest to determine the orientation of the entering phenyl group with greater certainty than had been done before. Ziegler and Zeiser (9) carried out this reaction and obtained 2-phenylquinoline together with a small amount of a lower-melting compound which, they suggested but did not prove, was 4-phenylquinoline. Gilman and Gainer (10) repeated the reaction and obtained 2-phenylquinoline and 2,2-diphenyl-1,2-dihydroquinoline, but no 4-phenylquinoline. It was decided to re-examine this reaction and to attempt to detect by gas chromatographic analysis any 4-phenylquinoline formed.

Methyl 3-pyridinesulphonate (IV) could not be prepared by any of the standard reactions. Pyridine-3-sulphonic acid was recovered unchanged on treatment with diazomethane. When the acid chloride (V) was treated with methanolic sodium methoxide the betaine (VI) was obtained, identical with that prepared from potassium pyridine-3-sulphonate and methyl iodide in the presence of aqueous sodium hydroxide (11). It is conceivable that the required ester may have been formed in this reaction but that it underwent self-alkylation in the working-up process. Pyridine-3-*N*,*N*-diethylsulphonamide (VII) was used instead of the ester in the reaction with phenyllithium. When VII

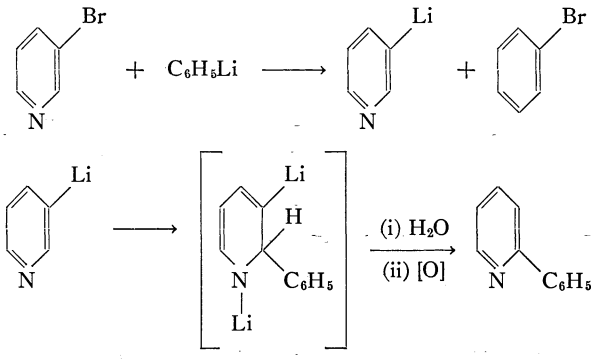


IV V VI VII

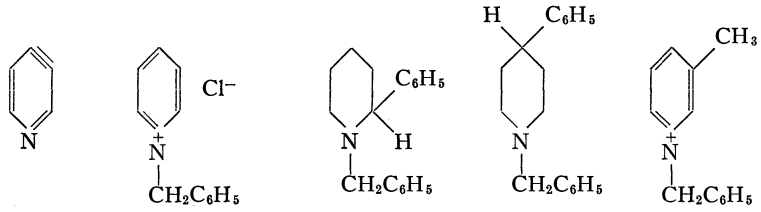
in excess was treated with phenyllithium and the product worked up by column chromatography only one product other than starting material was isolated, in low yield (20% based on phenyllithium). On the basis of its analysis and infrared spectrum (bands at 1578, 778, and 730 cm^{-1} (12, 13)) this is thought to be 2-phenylpyridine-3-*N*,*N*-diethylsulphonamide (II; R = SO_2NEt_2). No 2,5-isomer could be detected among the reaction products. The orientation observed is thus in accord with that expected on the basis of the electron-attracting character of the substituent.

The reaction of phenyllithium with 3-bromopyridine gave a mixture of neutral and basic products. Each of these fractions was analyzed by gas-phase chromatography. The neutral fraction was found to contain bromobenzene (43.4% of neutral components) together

with some biphenyl (some of which arises in the preparation of phenyllithium from bromobenzene) and an unknown product. No unreacted bromobenzene was present in the initial phenyllithium solution, however. The ether-soluble basic products were found to contain a small amount (1.8%) of 2-phenylpyridine together with a product which was different from 3-bromo-2-phenylpyridine (II; R = Br). A small amount of this substance was collected; its analysis was different from that expected for a bromophenylpyridine. Insufficient quantities were available to permit its structure to be investigated further at this time. Authentic 3-bromo-2-phenylpyridine could be prepared in low yield from 3-amino-2-phenylpyridine via the Sandmeyer reaction. A somewhat better yield (25.9%) was obtained by the use of Craig's perbromide hydrobromide method (14). Gilman and Spatz (15) similarly report (with L. Tolman) the isolation of 2-*p*-dimethylaminophenylquinoline from 3-bromoquinoline and *p*-dimethylaminophenyllithium. The reaction of 3-bromopyridine with butyllithium was shown (15) to give rise to a complex mixture of products. The 2-phenylpyridine and bromobenzene formed in the present reaction may arise as follows:



It is interesting to note that not only were no bromophenylpyridines isolated but neither was any 3- or 4-phenylpyridine detected gas chromatographically. This seems to rule out the formation of a 2- or 3-pyridyne intermediate in this case. In a recent report, Kauffmann and Boettcher (16) showed that the reaction of 3-chloro- or 3-bromo-pyridine with lithium piperidide and piperidine in ether involves the formation of a 3-pyridyne intermediate, with the resulting production of 3- (48%) and 4-piperidinopyridine (52%). Again, the formation of 4-phenacylpyridine and of 4-aminopyridine has been reported (17) in the reaction of 3-bromopyridine with sodioacetophenone and sodium in liquid ammonia, respectively, which has been postulated to take place by way of a pyridyne intermediate (VIII). Similarly, had a 2-pyridyne intermediate been formed one might have expected



VIII IX X XI XII

some 3-phenylpyridine to be formed, particularly in view of the −I effect of the pyridine ring nitrogen atom (which would direct the entering nucelophile mainly to $C_{(3)}$ (see, for example, reference 18)).

The procedure reported (4) for the reaction of phenyllithium with 3-phenylpyridine

(I; R = C_6H_5) was modified somewhat in that a larger proportion of I (R = C_6H_5) compared with phenyllithium was used. Column chromatographic separation of the mixture of products formed confirmed that 2,5-diphenylpyridine (III; R = C_6H_5) was the main product formed (29% yield). A second product, m.p. 216–216.5° (5.7% yield), was also isolated which analyzed for a diphenylpyridine. That this was the expected 2,3-diphenylpyridine was established by a study of its n.m.r. spectrum in carbon disulphide solution. It exhibited a single proton doublet ($J_{\alpha\beta}$ 5 c.p.s.) centered at 534 c.p.s. (relative to tetramethylsilane as internal standard and using an oscillator frequency of 60 Mc/s) corresponding to H_α (1, 19), and another single proton doublet centered at 461 c.p.s. due to H_γ ($J_{\beta\gamma}$ 5 c.p.s.), which is only consistent with a 2,3-disubstituted pyridine derivative (the resolution was not high enough to separate the bands due to splitting between the α- and γ-protons). The n.m.r. spectrum of 2,5-diphenylpyridine was more complex because of the overlap of some of the phenyl proton peaks with the H_γ peak. The H_α proton peak consisted of a singlet at 530 c.p.s. whose intensity corresponded to that expected for one proton. A third fraction was isolated from the column chromatographic separation but this could neither be purified properly for analysis nor characterized at this time.

An ethereal suspension of *N*-benzylpyridinium chloride (IX) was treated with phenyllithium and the reaction products reduced catalytically (to change any dihydropyridines to the corresponding piperidine derivatives) and analyzed by gas chromatography. Most of the reaction products were high-boiling polymeric tars, which is not unexpected since the 1,2-dihydropyridine adduct is essentially a *cis*-butadiene system, which in this case, cannot aromatize under the conditions of the reaction and is formed in the presence of an efficient Zielger-type polymerization catalyst. The gas chromatogram consisted of four minor peaks followed by a fifth larger one. The latter was found to be due to *N*-benzyl-2-phenylpiperidine (X) (5.2% yield based on total reduction products). No peak corresponding to *N*-benzyl-4-phenylpiperidine (XI) or to either of the debenzylated products was detected. This is in contrast with the reaction of cyclopentadienyllithium with IX, which is reported to give the 4-substituted derivative (20) (it should be noted that in this case aromatization of the adduct to give the zwitterion is favored). When the phenyllithium reaction was carried out with *N*-benzyl-3-picolinium chloride (XII) only high-boiling tars were obtained. The preparation of authentic samples of *N*-benzyl-2- and -4-phenylpiperidine and of *N*-benzyl-3-methyl-2-phenylpiperidine is described in the Experimental section.

The reaction of phenyllithium with an excess of quinoline was examined next. Two products were detected by gas chromatography. The major product was, as expected, 2-phenylquinoline. The first, and very minor, peak corresponded to a compound whose retention time was different from that of authentic 4-phenylquinoline (21). A very small amount could be collected: its infrared spectrum and melting point (84–85° as compared with 61–62° for 4-phenylquinoline) were different from those of 4-phenylquinoline, whose presence was not detected among the reaction products. Similarly, no 2,2-diphenyl-1,2-dihydroquinoline appeared to be formed under these conditions. Unfortunately, insufficient quantities of the unknown component were obtained to permit any further structural work to be carried out. Though the possibility of an addition across the —C(|)=N— cannot be ruled out to explain the lack of formation of 4-phenylquinoline, with acridine, in which such an addition is not possible, phenyllithium gives 9,10-dihydro-9-phenylacridine readily (22).

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were measured on a Perkin–Elmer Model 21 spectrometer equipped with sodium chloride optics (only the main peaks are reported), and n.m.r. spectra on a Varian

A60 instrument, using carbon disulphide solutions of the compounds and tetramethylsilane as the internal standard. The oscillator frequency was 60 Mc/s.

Pyridine-3-*N,N*-diethylsulphonamide, m.p. 49–50°, was prepared according to the method of Zienty (23). 4-Phenylquinoline was prepared from β-chloropropiophenone as described by Kenner and Statham (21). 2-Phenylpyridine was prepared from pyridine and phenyllithium (24). 3-Phenylpyridine was obtained from the reaction of 3-pyridyllithium with cyclohexanone followed by dehydration and dehydrogenation (25). 2,2-Diphenyl-1,2-dihydroquinoline was prepared from 2-phenylquinoline and phenyllithium (10). 3-Amino-2-phenylpyridine was obtained by the reaction of phenyllithium on 3-aminopyridine (2). Treatment of dry pyridine with benzyl chloride gave *N*-benzylpyridinium chloride as a highly hygroscopic solid (26).

N-Methyl Betaine of Pyridine 3-Sulphonic Acid

(*a*) A solution of pyridine 3-sulphonyl chloride (4.54 g) in dry methanol (10.5 ml) containing sodium methoxide (from 0.60 g of sodium) was boiled under gentle reflux for 1 hour and then treated with water. The mixture was extracted repeatedly with ether, the ether layer washed with aqueous sodium bicarbonate and then with water, and the solvent evaporated to give the betaine as a pale yellow solid (0.6 g) which did not melt below 330° and was sparingly soluble in ether. (Calc. for $C_6H_7NO_3S$: C, 41.62; H, 4.08. Found: C, 41.79; H, 4.18.)

(*b*) Cf. Meyer (11). Potassium pyridine-3-sulphonate (0.8 g), 10% aqueous sodium hydroxide (1 ml), and methyl iodide (2 ml) were heated under reflux for 12 hours. The solution was evaporated to dryness and the residue recrystallized from hot water to give the betaine, m.p. > 330°, whose infrared spectrum was identical with that of the sample prepared above. Infrared spectrum (Nujol mull): 1646 (s), 1505 (s), 1235 (vs), 1215 (vs), 1135 (s), 1045 (vs), 1032 (vs), 820 (m), 720 (s), and 675 cm^{-1} (s).

Reaction of Phenyllithium with Pyridine-3-N,N-diethylsulphonamide

To a well-stirred solution of pyridine-3-*N,N*-diethylsulphonamide (18.2 g, 0.1 mole) in anhydrous ether (50 ml) and under nitrogen was added a solution of phenyllithium (0.05 mole, prepared from lithium and bromobenzene (3)) in dry ether (68 ml) at such a rate that the mixture boiled gently under reflux. At the end of the addition the ether was distilled off and simultaneously replaced with dry toluene. The solution was then boiled under reflux for 7.5 hours, cooled, treated with water, and extracted repeatedly with ether. The ether layer was extracted several times with hydrochloric acid, the acidic solution made strongly alkaline and extracted with several portions of ether. The dried (KOH) ether extract was evaporated and the residue chromatographed on a column of alumina (100 g). Elution with methanol (after preliminary elution with benzene and ether to remove unchanged VII) gave *2-phenylpyridine-3-N,N-diethylsulphonamide* as a waxy solid (2.8 g) which, after recrystallization from methanol, had m.p. 77–77.5°. (Calc. for $C_{15}H_{18}N_2O_2S$: C, 62.05; H, 6.25. Found: C, 62.12; H, 6.42.) Infrared spectrum (Nujol mull): 1578 (m), 1338 (s), 1155 (s), 778 (m), 730 (s), 700 (m), 690 (m), and 662 cm^{-1} (w).

3-Bromo-2-phenylpyridine

A solution of 3-amino-2-phenylpyridine (0.566 g) in 48% hydrobromic acid (2 ml) was cooled in an ice–salt mixture and bromine (0.8 ml) was added to it dropwise with stirring, when the solid orange perbromide separated. Sodium nitrite (1.0 g) in water (3 ml) was added with stirring at such a rate that the temperature remained at 0°. As the last of the sodium nitrite solution was added a vigorous evolution of gas occurred and the temperature rose to 10°. The reaction mixture was made strongly alkaline and steam-distilled, the distillate was extracted with ether, the ether extract dried (Na_2SO_4) and evaporated. The residue was distilled at 305–307° at 720 mm to give *3-bromo-2-phenylpyridine* (0.202 g) as a pale yellow liquid. (Calc. for $C_{11}H_8NBr$: C, 56.43; H, 3.44. Found: C, 56.74; H, 3.70.) Infrared spectrum (liquid film): 3030 (m), 1573 (s), 1432 (s), 1122 (s), 1088 (s), 1008 (s), 781 (s), 735 (s), and 682 cm^{-1} (s).

Reaction of Phenyllithium with 3-Bromopyridine

An ethereal solution of phenyllithium (28.5 ml, 0.0333 mole of phenyllithium, prepared from lithium and bromobenzene) was added dropwise under nitrogen to a stirred solution of 3-bromopyridine (15.8 g, 0.1 mole) in dry ether (100 ml). The mixture was stirred for another 2 hours, water was added followed by hydrochloric acid, the organic layer separated, and the aqueous layer extracted repeatedly with ether. The combined ether layers (A) containing the neutral products was concentrated and analyzed as described below. The acidic layer was basified with sodium hydroxide and extracted with ether. The ether extracts containing the basic material were evaporated, the residue distilled to remove unreacted 3-bromopyridine, and the residue (B) analyzed.

Fraction (A) was subjected to gas chromatography using a 3 ft×1/4 in. column packed with Apiezon N on Fluoropak (80–100 mesh) (1:10 by weight); the column temperature was 160° and the helium inlet pressure 30 p.s.i. Three peaks were observed, the first (retention time 1 min 20 sec) due to bromobenzene (43.4% of total neutral products), the second to biphenyl (retention time 12 min 40 sec), and the third to an unknown substance (retention time 29 min 20 sec).

Fraction (B) was subjected to gas chromatography on an 8 ft×1/4 in. column packed with ethylene glycol succinate on Chromosorb (1:10 by weight). The column temperature was 160° and helium inlet pressure 40 p.s.i. Two peaks were observed: the first (retention time 21 min 20 sec) was due to 2-phenylpyridine

(characterized by its retention time, infrared and ultraviolet spectra) (1.8% yield based on total amount of basic product); the second (retention time 44 min) was due to a compound of unknown structure. A small amount of the latter product was collected and analyzed: Found: C, 72.27; H, 5.94. Under these conditions the retention time of 3-bromo-2-phenylpyridine was 50 min. No 3- or 4-phenylpyridine could be detected.

Reaction of Phenyllithium with 3-Phenylpyridine

A solution of phenyllithium (0.0182 mole) in dry ether (47 ml) was added dropwise under nitrogen to a well-stirred solution of 3-phenylpyridine (3 g, 0.0193 mole) in ether (150 ml). The mixture was stirred for a further 24 hours and oxygen was then bubbled through the reaction mixture for 30 minutes. An excess of water was added and the mixture extracted exhaustively with ether. The dried (Na_2SO_4) ether extract was evaporated and the residue chromatographed on a column of alumina (110 g). Elution with light petroleum (b.p. 40–60°) – benzene mixture (4:1 v/v) gave 2,5-diphenylpyridine (0.947 g), m.p. 174–175° after recrystallization from alcohol. Wiley *et al.* (25) report m.p. 174–175° for this compound. Elution with light petroleum – benzene (1:1 v/v) gave unreacted 3-phenylpyridine (1.003 g). Elution with benzene – ether (4:1 v/v) brought down *2,3-diphenylpyridine* (0.169 g), which gave a bluish fluorescence in this solvent mixture. It was recrystallized from a benzene – light petroleum (b.p. 40–60°) mixture and had m.p. 216–216.5°. (Calc. for $C_{17}H_{13}N$: C, 88.28; H, 5.60. Found: C, 88.40; H, 5.61.) Infrared spectrum (KBr disk): 3060 (m), 1600 (m), 1538 (m), 1500 (m), 1457 (m), 1428 (m), 1121 (s), 903 (m), 800 (m), 767 (s), 748 (s), 698 (s), 678 cm^{-1} (m). Elution with ether and ethyl acetate gave a yellow powder (0.531 g), m.p. 112–113°, which could not be purified further. Infrared spectrum (KBr disk): 3090 (m), 1684 (s), 1610 (m), 1505 (s), 1465 (s), 758 (s), 698 cm^{-1} (s). The n.m.r. spectrum of this compound exhibited none of the peaks usually associated with pyridine ring protons.

2-Phenylpiperidine (27)

2-Phenylpyridine (1 g) in 1.1 *N* hydrochloric acid (6.6 ml) and 95% ethanol (50 ml) was reduced at atmospheric pressure in the presence of platinic oxide (50 mg). The catalyst was filtered off, the solvent evaporated, and the residue treated with dilute sodium hydroxide solution and extracted with ether. The dried (Na_2SO_4) ether extract was evaporated and the residue distilled to give 2-phenylpiperidine (0.855 g), b.p. 246–248° at 726 mm. Ushakov and Promyslov (27) give b.p. 255–256° at 766 mm for this compound.

4-Phenylpiperidine

This was prepared similarly by the reduction of 4-phenyl-1,2,3,4-tetrahydropyridine (28). The yield of product, b.p. 250–252° at 720 mm, was 74%. It had previously been prepared by the reduction of 4-phenylpyridine (29) and the reported boiling point was 255–257° at 727 mm.

N-Benzyl-2-phenylpiperidine

2-Phenylpiperidine (0.683 g) and benzyl chloride (0.53 g) were heated at 120–160° for 1/2 hour, the mixture was cooled, treated with dilute sodium hydroxide solution, and extracted with ether. The dried (Na_2SO_4) ether extract was evaporated, yielding *N-benzyl-2-phenylpiperidine* (0.728 g), which crystallized from ethanol and had m.p. 93–93.5°. (Calc. for $C_{18}H_{21}N$: C, 86.01; H, 8.42. Found: C, 86.00; H, 8.60.)

N-Benzyl-4-phenylpiperidine

Prepared in the same way as the 2-isomer it was obtained as a yellow oil, b.p. 149–150° at 0.4 mm. Boggiano, Petrov, Stephenson, and Wild (30), who prepared this compound by the reduction of *N*-benzyl-4-phenyl-4-propionoxypiperidine, report its b.p. as 151° at 0.4 mm.

Reaction of Phenyllithium with N-Benzylpyridinium Chloride

To a well-stirred suspension of *N*-benzylpyridinium chloride (15.87 g, 0.154 mole) in dry ether under nitrogen was added an ethereal solution of phenyllithium (0.077 mole) during 1/2 hour. The reaction mixture was stirred for 24 hours under nitrogen, treated with water, and extracted repeatedly with ether. The dried (Na_2SO_4) ether extract was evaporated to give a viscous dark red residue (11.82 g). A portion of this (1.18 g) was dissolved in a mixture of 95% ethanol (60 ml) and 1.1 *N* hydrochloric acid (4.8 ml) and hydrogenated at room temperature and pressure over platinic oxide. Uptake of hydrogen was very slow. The hydrogenated product was subject to gas chromatographic analysis on a 3 ft×1/4 in. Apiezon N on Fluoropak (80–100 mesh) (1:10 w/w) column operated at 220° and with a helium inlet pressure of 30 p.s.i. Five peaks were observed, the last one (retention time 15 min 15 sec) being due to *N*-benzyl-2-phenylpiperidine (5.2% yield based on reduced products) (retention time and infrared spectrum). The retention times and spectra of the compounds giving rise to the first four peaks were quite different from those of 2- and 4-phenylpiperidine and *N*-benzyl-4-phenylpiperidine. These substances were not investigated further.

3-Methyl-2-phenylpiperidine

This was prepared by catalytic reduction of 2-phenyl-3-picoline (1). The *product* (76.2% yield), b.p. 256–257° at 724 mm, was purified for analysis by gas chromatography using a 5 ft×1/4 in. 10% Apiezon N on Fluoropak column, followed by redistillation, but could not be obtained in an analytically pure state. (Calc. for $C_{12}H_{17}N$: C, 82.23; H, 9.78. Found: C, 80.55; H, 9.26.) Infrared spectrum (liquid film) 1497 (m), 1457 (s), 1383 (m), 1277 (m), 1130 (m), 1088 (m), 875 (m), 827 (s), 696 cm^{-1} (s).

N-Benzyl-3-methyl-2-phenylpiperidine

3-Methyl-2-phenylpiperidine (0.876 g; redistilled) and benzyl chloride at 120–160° for 1 hour gave, in a manner similar to that described for the unmethylated compound, *N-benzyl-3-methyl-2-phenylpiperidine* (0.8 g), b.p. 176–180° at 6 mm, m.p. 69–69.5° (after recrystallization from absolute alcohol). (Calc. for $C_{19}H_{23}N$: C, 85.92; H, 8.75. Found: C, 85.71; H, 8.92.) Infrared spectrum (KBr disk): 1610 (m), 1502 (s), 1462 (s), 1379 (m), 1272 (m), 1230 (m), 1142 (s), 738 (s), and 694 cm^{-1} (s).

Reaction of Phenyllithium with Quinoline

A solution of phenyllithium (0.024 mole) in dry ether (150 ml) was added dropwise under nitrogen to quinoline (9.29 g, 0.072 mole; purified via the zinc chloride complex) in dry ether (20 ml). When the addition was complete the ether was distilled off and simultaneously replaced by dry toluene (60 ml). The mixture was then boiled under reflux for 6 1/2 hours, the solution cooled and treated with water, and the toluene layer separated and extracted with hydrochloric acid. The acid layer was basified, extracted with ether, and the dried (NaOH) ether extract evaporated. The excess quinoline was distilled at 80° at 0.35 mm and the residue (1.434 g) analyzed by gas chromatography. A 3 ft × 1/4 in. 10% Apiezon N on Fluoropak column was used at a temperature of 220° and a helium inlet pressure of 45 p.s.i. Only two peaks, with retention times of 9.9 and 14.4 min, were observed. The latter (major peak) was due to 2-phenylquinoline (retention time and infrared spectrum). The first peak had a retention time and infrared spectrum different from that of 4-phenylquinoline. A small sample was collected and had m.p. 84–85°. Infrared spectrum (KBr disk): 1587 (s), 1494 (s), 1393 (s), 850 (m), 766 (s), and 698 cm^{-1} (s). This substance was not investigated further at this time.

ACKNOWLEDGMENTS

The authors are grateful to the National Research Council for financial support of this work and for the award of a studentship to C-S. G.

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