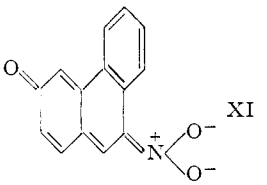
The conclusion of the last paragraph, that the nitro group in the 5-position of the naphthalene ring system is acting only inductively, makes it necessary to search for the reason why resonance structure VI is more effective than VII in stabilizing the anions. On close examination it will be noted that in structure VI one ring of the naphthalene system is quinoid while the other is still benzenoid. In VII, however, both rings are quinoid. This means that VII represents a structure of higher energy than VI and therefore its contribution to the resonance hybrid is considerably smaller. Eastman[1] advanced a similar explanation for the absence of enhanced acidity in 4'-nitro-4-hydroxybiphenyl.

The observation that the nitro group in the 4-position of 1-naphthol is about 30 times more acidifying than the same group in the *para* position of phenol can be explained by considering the difference in the ease of formation of a *para*-quinoid system between benzene and naphthalene. The formation of the *para*-quinoid form is energetically more favorable in II than in III, and, therefore, structure VI contributes more to the resonance hybrid of the II anion than resonance structure IV to the hybrid of III anion.

Included in Table II are also data for 3-phenanthrol and 9-nitro-3-phenanthrol (X). The latter compound is another representative of the class of compounds in which the two functional groups are attached to different rings of a fused ring system. Again in X as in V it is possible to write a resonance structure for the anion, shown in XI, where the



XI

negative charge can be stabilized by the oxygen of the nitro group. The experimental data indicate that this system is similar to V, in which there is little resonance interaction between the nitro and the hydroxy group.

Summarizing, it has been shown that the nitro group in the 4-position of 1-naphthol is more acidifying than in the *para* position of phenol, while a nitro group in the 5-position of 1-naphthol acts essentially only inductively.

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PITTSBURGH 19, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NORTH CAROLINA]

Mechanisms for the Formation of Naphthylpiperidines from Naphthyl Bromides[1]

BY J. F. BUNNETT AND T. K. BROTHERTON[2]

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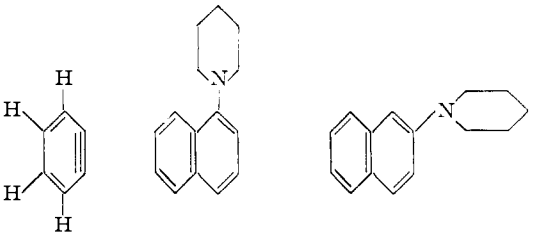
Both α- and β-bromonaphthalene react with piperidine at 230° to form the corresponding N-naphthylpiperidine. However, each bromonaphthalene reacts with sodium amide and refluxing piperidine to form a mixture of the two naphthylpiperidines (II and III). The latter reactions presumably involve the "benzyne" type of mechanism, and the former definitely do not.

For some time it has been recognized that unactivated aryl halides, such as tolyl and unsubstituted phenyl and naphthyl halides, differ from activated aryl halides, such as *o*- and *p*-nitrophenyl halides, in their mode of reaction with nucleophilic reagents. The difference is more profound than mere dependence of reaction rate on the presence or absence of activating groups. It is most evident in the orders of replaceability of the four halogens: in activated aryl halides, the order is F >> Cl ~ Br ~ I, while in unactivated phenyl halides the order is I > Br > Cl > F, as in alkyl halides.[3,3a]

One of the reactions of unactivated aryl halides formerly regarded as a straightforward replacement is now recognized to involve a special and unique mechanism. This is the reaction with alkali metal amides to form amines; for example, the reaction of chlorobenzene with potassium amide to form aniline. Roberts and co-workers[5] have presented evidence that in this reaction the elements of hydrogen chloride are split out to form a symmetrical intermediate resembling "benzyne" (I), and that this intermediate then adds ammonia to form aniline. The formation of rearranged products from substituted phenyl halides, such as *m*-anisidine from *o*-iodoanisole and sodium amide,[6] is explicable in terms of this mechanism.



I II III

In the reactions of phenyl and naphthyl halides

(1) Presented to the XIVth International Congress of Pure and Applied Chemistry, Zurich, July, 1955.

(2) American Enka Fellow, 1954–1955.

(3) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 333 (1951).

(3a) The order of replaceability from activated halides depends somewhat on the nucleophilic reagent.[4]

(4) G. S. Hammond and L. R. Parks, THIS JOURNAL, **77**, 340 (1955).

(5) J. D. Roberts, H. E. Simmons, L. A. Carlsmith and C. W. Vaughan, *ibid.*, **75**, 3290 (1953); J. D. Roberts, private communications.

(6) H. Gilman and S. Avakian, THIS JOURNAL, **67**, 349 (1945).

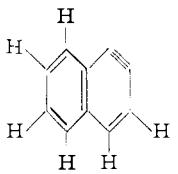
with alkali metal amides, fluorides are less reactive than chlorides, and chlorides less reactive than bromides.[7] This is similar to the order of reactivity of these halides with nucleophilic reagents such as piperidine and sodium methoxide, and Hammond and Parks[4] have suggested that reactions of the latter type also involve the "benzyne" type of mechanism. By their suggestion, the difference between activated and unactivated displacements is fundamentally a difference in mechanism, the activated halides (from which fluorine is most easily displaced) reacting by direct displacement, and the unactivated halides (from which fluorine is least easily displaced) reacting by the elimination–addition ("benzyne") mechanism.

In this paper we show that the attractive hypothesis of Hammond and Parks cannot be accepted as universally applicable. Specifically, we show that intermediates of the "benzyne" type are not involved in the formation of naphthylpiperidines by the reaction of naphthyl bromides with piperidine at elevated temperatures.

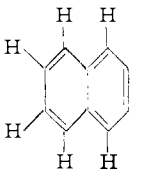
Reactions with Sodium Amide and Piperidine.—The reaction of α-bromonaphthalene with sodium amide and piperidine produces a mixture of α-naphthylpiperidine (II) and β-naphthylpiperidine (III) in high yield. This mixture comprises 32% of the α-isomer (II) and 68% of the β-isomer (III),[7a] as determined by a procedure of direct crystallization of much III followed by infrared spectrophotometric analysis of the mixture of II and III remaining in the mother liquor. The reaction of β-bromonaphthalene with sodium amide and piperidine also produces a mixture of II and III in high yield. The percentage of β-naphthylpiperidine (III) in this mixture is somewhat higher, the composition being 26% II and 74% III. The difference in the compositions of the mixtures of II and III obtained from α- and β-bromonaphthalenes is reproducible and significant.

The foregoing reactions probably involve intermediates of the "benzyne" type. In the formation of II and III from α-bromonaphthalene, "α-naphthalyne" (IV) is probably generated, and the proportions of II and III formed probably reflect the relative rates of addition of piperidine to the "triple bond" of IV.

The formation of a substantial amount of II from the reaction of β-bromonaphthalene with sodium amide and piperidine is an indication that IV is also a dominant intermediate in this process. However, the fact that significantly more III is formed from β-bromonaphthalene than from its α-isomer suggests that "β-naphthalyne" (V) is also generated to some extent. It should be noted that addition of piperidine to V can form only III, and no II. From our data we estimate that IV and V are formed from β-bromonaphthalene in a ratio of four parts of IV per one part of V.[8]



IV



V

Huisgen and Rist[9] have obtained from α-fluoronaphthalene, by treatment with phenyllithium and then with carbon dioxide, a mixture of 1-phenyl-2-naphthoic acid and 2-phenyl-1-naphthoic acid. From β-fluoronaphthalene, they obtained the foregoing two acids plus 2-phenyl-3-naphthoic acid. They postulate "naphthalyne" intermediates for their reactions, and the ratios of their products indicate that the phenyl group of phenyllithium attaches preferentially but not exclusively to the 2-position of IV, and that IV is formed in greater proportion than V from β-fluoronaphthalene. Their experiences in "naphthalyne" chemistry are thus in qualitative agreement with ours.[10]

Reactions with Piperidine Alone.—Lellman and Büttner[11] reported that α- and β-bromonaphthalene react with piperidine at *ca.* 250° to form, respectively, II and III. Since their yields were not stated, their II was possibly impure and they did not examine their reaction mixtures for by-products, we have re-examined these reactions. We find indeed that each bromonaphthalene gives the corresponding unrearranged naphthylpiperidine, with no rearranged products being detectable by infrared spectrophotometry or elution chromatography. The reaction of α-bromonaphthalene with excess piperidine for 48 hours at 230° afforded II in 49% yield, while the reaction of β-bromonaphthalene with piperidine under the same conditions furnished 79% of pure III.[12]

Since cine-substitution[15] (substitution with rearrangement) did not occur during the reactions of the naphthyl bromides with piperidine at 230°,

(7) F. W. Bergstrom and C. H. Horning, *J. Org. Chem.*, **11**, 334 (1946).

(7a) NOTE ADDED IN PROOF.—In the abstract of our paper in the "Congress Handbook" of the International Congress, the percentage of III was incorrectly given as 86.6%, owing to a typographical error.

(8) This estimate involves the assumption that no direct replacement of bromine by piperidino groups occurs in the reactions with sodium amide–piperidine, in other words that these reactions go wholly *via* "naphthalyne" intermediates. Such direct replacements, occurring to a maximum extent of 19%, are not excluded by evidence now available.

(9) R. Huisgen and H. Rist, *Naturwissenschaften*, **41**, 358 (1954).

(10) Huisgen and Rist[9] detected about the same ratio (1:2) of α- to β-attachment to IV as we did, but they got considerably more V (40%) from β-fluoronaphthalene than we got (19%) from β-bromonaphthalene. The ratio of IV to V generated from a 2-halonaphthalene will depend on the relative rates of proton removal from the 1- and 3-positions. It can be anticipated that a large base, such as phenyllithium, will experience more steric interference from the *peri*-position in approaching the 1-hydrogen than will a small base, such as the amide ion, whereas both may approach the 3-hydrogen freely. Thus one should obtain a larger proportion of V when a large base is used.

We presume that sodium amide is the effective base in our experiments since we have observed no ammonia evolution or change in the appearance of the solid phase when sodium amide is combined with boiling piperidine, in which it is insoluble. R. A. Seibert and F. W. Bergstrom, *J. Org. Chem.*, **10**, 544 (1945), reported that they had never succeeded in preparing sodium salts of primary or secondary amines by heating the amines with sodium amide.

(11) E. Lellman and M. Büttner, *Ber.*, **23**, 1383 (1890).

(12) These observations are of incidental interest in verifying that Berliner, *et al.*,[13] and Brower and Amstutz,[14] who studied kinetics of the reactions of the bromonaphthalenes with piperidine, were indeed dealing with the reactions they assumed to be occurring.

(13) E. Berliner, M. J. Quinn and P. J. Edgerton, THIS JOURNAL, **72**, 5305 (1950).

(14) K. R. Brower and E. D. Amstutz, *J. Org. Chem.*, **18**, 1075 (1953).

(15) Reference 3, p. 382.

these reactions must have a mechanism different from that of the reactions with sodium amide and piperidine. Specifically, "naphthalyne" intermediates are excluded from consideration for these reactions furnishing unrearranged naphthylpiperidines.[16]

Since the high-temperature reactions of the halonaphthalenes with piperidine show the order of halogen replaceability[13] typical of unactivated aromatic nucleophilic substitutions, and since we have shown that "benzyne" type intermediates are not involved in the reactions of the bromonaphthalenes with piperidine, we conclude that the explanation for the difference between activated and unactivated substitutions is not to be found in Hammond and Parks' suggestion that the unactivated substitutions involve the elimination–addition (benzyne) mechanism.

This is a negative conclusion, and leaves unanswered the questions: what is the mechanism of the unactivated substitutions, and why does the order of halogen replaceability vary according to the presence or absence of activating groups? Our belief, which will be discussed and supported in a forthcoming publication, is that in the reactions of activated halides with strong nucleophilic reagents the rate-determining step is the formation of a metastable adduct intermediate, and that the various halogens affect the rate by affecting the rate of attachment of reagent to substrate. We further believe that in the reactions of unactivated aryl halides with these reagents such metastable adducts play little or no part and there is partial breaking of the C–X bond in the transition state, so that rates reflect the ease of expulsion of the halogen atoms. We have held this belief since 1950,[17] and are pleased to acknowledge that Dr. G. S. Hammond has postulated, in private correspondence, a similar interpretation based on his independent consideration of the problem.

Though we have shown that the suggestion of Hammond and Parks lacks general validity, we nevertheless regard it as valuable and quite likely applicable in some instances. It appears that for the present each case of unactivated nucleophilic displacement will have to be considered separately, to see whether a mechanism of direct displacement or one of the "benzyne" type is operating.

Experimental

Materials.—Commercial **piperidine** (mostly from Matheson, Coleman and Bell) was refluxed over sodium for six hours and then distilled. **β-Bromonaphthalene**, m.p. 55–56°, was prepared by a standard method.[18] In reactions with sodium amide and piperidine, and in the early reactions with piperidine alone, **α-bromonaphthalene** (from bromination of naphthalene) of f.p. 4.7°, indicating[19] the presence of 3.0% of β-bromonaphthalene, was used. In the later reactions with piperidine alone, α-bromonaphthalene of f.p. 6.1°, freed from the β-isomer by the procedure of Jones and Lapworth,[20] was used.

Authentic II from 1-Naphthylamine.—The reaction of 1-naphthylamine with 1,5-dibromopentane according to method B of Sommers and Aaland[21] furnished II in obviously impure form: a small amount of crystalline solid separated from the reduced pressure distillate. A more pure product was obtained by treating the combined toluene solutions (method B[21]) with *p*-toluenesulfonyl chloride, heating 30 minutes on the steam-bath, extracting the cooled toluene solution with dilute hydrochloric acid, and then recovering the amine from the acid solution by conventional means. This treatment was designed to remove unreacted 1-naphthylamine from the product. After vacuum distillation, the N-1-naphthylpiperidine (II) was dissolved in ether and treated with dry hydrogen chloride. The resulting hydrochloride had, after two recrystallizations from absolute ethanol, m.p. 200–202°, not raised by further recrystallization. This compares with m.p. 178–179° reported by Abel[22] and m.p. 184–186° reported by Sommers and Aaland.[21]

Anal. Calcd. for $C_{15}H_{18}ClN$: Cl, 14.32. Found: Cl, 14.39.

From the hydrochloride, II was regenerated by standard means; it had b.p. 142–145° (3 mm.), $n^{23}D$ 1.6178.

Authentic III from 2-Naphthylamine.—The above procedure was followed except that the product, being a solid, was recrystallized thrice from ethanol and twice from petroleum ether (30–60°) instead of being distilled. There resulted a fluffy white powder, m.p. 58–58.5°, in agreement with literature[11,23,24] values. The hydrochloride had m.p. 214.5–217°, in agreement with Roth.[24]

Infrared Analytical Technique.—The infrared spectra of authentic samples of the two N-naphthylpiperidines were determined, carbon tetrachloride solutions of the amines being examined in a Baird double-beam recording spectrophotometer. The spectra differed in several respects. The α-isomer II absorbed much more strongly than III at 9.13, 9.95 and 10.94 μ, while the β-isomer III had characteristic strong absorption peaks at 6.18, 6.3, 6.67, 8.27, 8.5, 10.47 and 11.9 μ. A Beckman IR-2 spectrophotometer was used for most quantitative determinations, with measurements being made at 10.47 μ (a peak for III) and at 10.94 μ (a peak for II). There was good agreement between analyses based on measurements at these wave lengths. It was shown, by measurements on solutions of both II and III at several wave lengths, that Beer's law is obeyed and that optical density for synthetic mixtures of the two amines is linearly related to concentration.

Reaction of β-Bromonaphthalene with Piperidine Alone.—A mixture of 12.5 g. (0.06 mole) of β-bromonaphthalene and 30 cc. of piperidine was heated, in a nitrogen-filled sealed tube, 48 hours at 230°. The cooled contents were combined with 100 cc. of 25% sodium hydroxide solution, and the mixture was extracted with benzene. The benzene extract was extracted with four 35-cc. portions of 10% hydrochloric acid, the aqueous extract was made basic with sodium hydroxide, and the amines were taken up in ether. Distillation of the ether solution furnished 11.8 g. of semi-solid material which boiled at about 100–140° (2–4 mm.). An equal volume of petroleum ether (b.p. 30–60°) was added, and the white crystals which formed when the resulting solution was cooled in an acetone–solid carbon dioxide-bath were collected on a suction filter. These crystals weighed 9.53 g. and had m.p. 55–55.5°, not depressed on admixture with authentic III. Evaporation of the mother liquor yielded 1.89 g. of light yellow oil which was chromatographed on an alumina column using benzene as eluent. There was no trace of II in fractions of eluate which would contain II if it were present, that is, the fractions immediately preceding the fractions containing III. A total of 0.47 g. of III, m.p. 50–53°, was recovered by chromatography, raising the yield of III to 10.00 g. (79%).

From the later benzene fractions and from a final washing

(16) The exclusive formation of II from α-bromonaphthalene is most conclusive. *A priori*, it is conceivable (though most unlikely) that the base piperidine might, for some unsuspected reason, extract only the 3-hydrogen from 2-bromonaphthalene so as to form V as the sole "naphthalyne" intermediate; the addition of piperidine to V would of necessity form III. Only IV could be formed from α-bromonaphthalene, and our work indicates that IV adds piperidine to form both II and III.

(17) (a) J. F. Bunnett, Absts. of Chicago Am. Chem. Soc. Meeting, Sept., 1950, p. 98-N; (b) reference 3, p. 297.

(18) M. S. Newman and P. H. Wise, THIS JOURNAL, **63**, 2847 (1941).

(19) J. F. Suyver and J. P. Wibaut, *Rec. trav. chim.*, **64**, 65 (1945).

(20) M. Jones and A. Lapworth, *J. Chem. Soc.*, **105**, 1804 (1914); these authors report f.p. 6.20° for pure α-bromonaphthalene.

(21) A. H. Sommers and S. E. Aaland, THIS JOURNAL, **75**, 5280 (1953).

(22) J. Abel, *Ber.*, **28**, 3106 (1895).

(23) M. Scholtz and E. Wassermann, *ibid.*, **40**, 856 (1907).

(24) W. Roth, *ibid.*, **29**, 1175 (1896).

of the column with methanol, a total of 1.55 g. of oil of $n^{25}D$ varying from 1.4798 to 1.5001 was obtained. Since oils of similarly low refractive index (*e.g.*, $n^{23}D$ 1.4769) were produced when piperidine hydrobromide and piperidine were heated together (in the absence of aryl halides) at 230°, but not when piperidine alone was heated at that temperature, we believe the by-product oils do not come primarily from any reaction of β-bromonaphthalene. Similar low refractive index by-products were obtained from reactions of piperidine with α-bromonaphthalene. We have not yet determined their identity.

Reaction of α-Bromonaphthalene with Piperidine Alone.—A mixture of 29.4 g. of α-bromonaphthalene, f.p. 6.1°, and 45 cc. of piperidine was heated 48 hours at 230°. The reaction mixture was treated as described above through the distillation at reduced pressure, which furnished 17.49 g. of clear, blue-fluorescent oil of b.p. 90–135° (2–4 mm.), $n^{23}D$ 1.5819. Ten grams of this oil was chromatographed on alumina using benzene as eluent; there were obtained several fractions of blue-fluorescent oil of $n^{23}D$ 1.6129 to 1.6137, whose weight totalled 8.32 g. This refractive index approaches that of pure II, and the weight indicates a yield of 49%. The combined fractions of II were treated with benzenesulfonyl chloride in boiling pyridine solution, and 6.71 g. of pure II was recovered as a clear, blue-fluorescent oil, $n^{23}D$ 1.6174, identical in infrared spectrum with authentic pure II. The above chromatographic separation yielded no solid materials in fractions that would contain III were it present. Methanol stripping of the column furnished 1.88 g. of oils of low refractive index (*e.g.*, $n^{23}D$ 1.4919).

From a similar reaction, 33% of pure II was obtained and 55% of pure α-bromonaphthalene was recovered.

The reaction of α-bromonaphthalene of f.p. 4.7° with piperidine at 230° furnished yields of II comparable to those above plus small amounts of pure III, the separation being made by chromatography.

Reaction of α-Bromonaphthalene with Sodium Amide and Piperidine.—Sodium amide (5.9 g., 0.15 mole) was added to 20 cc. of piperidine, and the mixture was refluxed for ten minutes. α-Bromonaphthalene, f.p. 4.7° (10.4 g., 0.05 mole), was added through the condenser during ten minutes, and refluxing was continued for two hours. Water (25 cc.) was added cautiously to the cooled reaction mixture, which was then extracted with 25 cc. of benzene. The benzene extract was extracted with 10% hydrochloric acid (four 25-cc. portions), the aqueous extract was made basic by addition of sodium hydroxide, and the oil which separated was taken up in ether. Distillation of the ether solution yielded 9.77 g. (92% of theory) of yellow oil, b.p. 120–140° (2 mm.), which partially solidified on cooling. An equal weight of petroleum ether (30–60°) was added, and the resulting solution was cooled by a mixture of acetone and solid carbon dioxide. The white solid which separated was collected on a suction filter, weighed 5.23 g., had m.p. 55–56° and did not depress the melting point of authentic III. The mother liquor from the crystallization was distilled, furnishing 4.17 g. of yellow liquid distillate and 0.3 g. of a dark, oily residue. Analysis by infrared measurements showed the yellow liquid to contain 68% II (measurement at 10.47 μ, Beckman spectrophotometer) or 72% II (at 10.94 μ, Beckman) or 72% II (at 9.15 μ, Baird); average, 70.6% II. The dark residue contained 36.5% of II (measurement at 9.15 μ, Baird spectrophotometer). Summing all fractions, the product was 68.6% III and 31.4% II.

Another run, under identical conditions, gave 89% of mixed naphthylpiperidines of which 68.6% was III. In this second run, it should be noted, the weight of the various product fractions and their individual analyses differed from those in the first run, but on summation the same overall result was obtained.

The α-bromonaphthalene used in the above runs contained, as judged from its freezing point, 3.0% of β-bromonaphthalene. Taking account of the composition of the mixture of II and III obtained from β-bromonaphthalene and sodium amide–piperidine (see below), the composition of the above mixture is adjusted to 68.4% III and 31.6% II, identical within experimental error with the original result.

Reaction of β-Bromonaphthalene with Sodium Amide and Piperidine.—The reaction was carried out as described above, except that the reaction mixture was mechanically stirred during refluxing. In one run, there was obtained 88.4% of mixed II and III of which 73.6% was the β-isomer III. In a second run, 94.1% of mixed II and III, of which 73.2% was III, was obtained.

Although the infrared spectra of the oily mixtures recovered from the mother liquors after crystallization of III clearly indicated the presence of II, it was felt desirable to isolate II as a product from β-bromonaphthalene and sodium amide–piperidine. For this purpose, a mixture of amines from this reaction was chromatographed on alumina, using benzene as eluent. Pure II, $n^{25}D$ 1.6172, and identical in infrared spectrum with authentic II, was isolated.

The Action of Sodium Amide and Piperidine on II.—This experiment was performed to check the possibility that III might be produced from α-bromonaphthalene and sodium amide–piperidine by an initial direct substitution to form II followed by isomerization of II to III. Chromatographically-purified II was refluxed with sodium amide and piperidine under the conditions of concentration and time used for the reactions of the naphthyl halides with these reagents. The resulting mixture of amines was chromatographed on alumina, and less than 1% of III was obtained. This may have been an impurity in the II used in this experiment, or it may have been an actual product of isomerization, but in any case the amount is totally insufficient to account for the production of III from α-bromonaphthalene.

Acknowledgments.—We thank the Office of Ordnance Research, U. S. Army, for financial assistance, and Dr. R. L. McKee for stimulating discussions and helpful suggestions.

CHAPEL HILL, N. C.