166. *Kationoid Reactivity of Aromatic Compounds. Part I.*

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ONE of the advantages of the electrochemical theory of the reactions of unsaturated carbon compounds is that it accommodates not only the ordinary aromatic substitutions in which the nucleus exhibits anionoid reactivity but also those in which the reagent is anionoid.

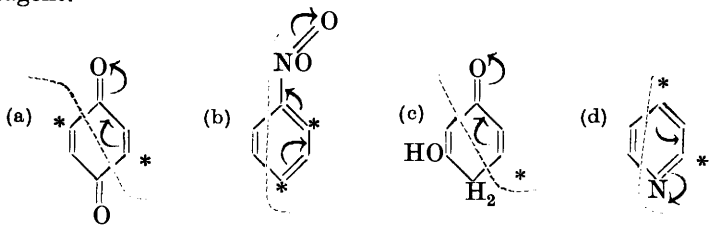
The natural character of benzene and naphthalene is to be electron-donors and it is only some special constitutional feature which can successfully oppose this tendency.

In every case the molecule will be found to contain a katio-enoid system (typified by C=C—C=O) in which the quality of reactivity of a carbonyl, nitroxyl or similar group is transmitted to an associated unsaturated centre, either ethenoid or polyenoid.

The four main classes of substances which contain such systems and manifest their characteristic reactions are : (a) quinones, using the term in its widest sense to include a great variety of types, (b) substances in which a kationoid group (NO_2, CO, etc.) is directly attached to the nucleus, (c) phenols (or amines) in which the katio-enoid system is apparent after isomeric change, and (d) heterocyclic substances, such as pyridine, in which the whole kationoid group (usually C : N) forms part of the ring structure. Examples are the direct introduction of hydroxyl and amino-groups into pyridine derivatives by means of alkali-metal hydroxides and sodamide respectively.

The annexed schemes show very simple examples of the four classes and the katio-enoid system is included in the dotted lines;

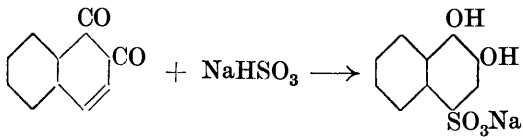
the asterisks indicate the alternative points of attack of the anionoid reagent.



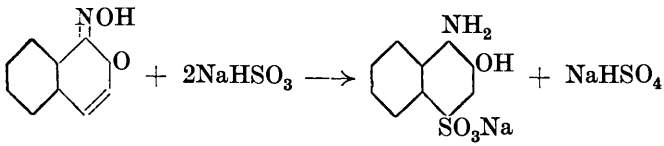
Class (c) is relatively unimportant, but in illustration the conversion of resorcinol into phloroglucinol by fusion with caustic alkalis may be cited. The replacement of hydroxyl by amino-groups and analogous reactions are doubtless the result of the independent kationoid reactivity of carbonyl groups in such tautomerides of phenols and naphthols.

The reactions attributable to the activation of the katio-enoid systems in class (a) are exceedingly numerous. Thus the action of alkaline hydroxides, amines, sulphinic acids, and cyanides leads to the formation of hydroxyquinones, amino-quinones, sulphones, and nitriles respectively.

In this category must be placed the action of sodium bisulphite on various quinones and, for example, β-naphthaquinone (F. Baeyer, D.R.-P., 70867; Friedländer, " Fortschritte," III, 503).



This again is clearly analogous to the action of the same reagent on nitroso-β-naphthol (Böniger, *Ber.*, 1894, **27**, 23; Schmidt, *J. pr. Chem.*, 1891, **44**, 522).



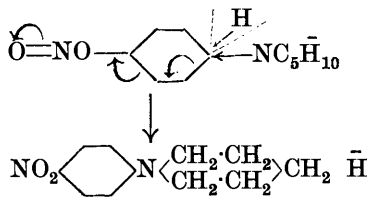
In class (b) of the aromatic substances containing katio-enoid systems, many kationoid reactions have already been observed, particularly when the process is facilitated by the fact that the group or atom displaced is ready to separate as an anion. In this group we find the hydrolysis of *p*-nitrochlorobenzenes and of nitroso-dimethylaniline and such reactions as the transposition of alkoxyl groups in 2 : 4-dinitrophenyl ethers, displacement of alkoxyl groups

and halogen atoms in nitro-compounds by amino-groups, and many others; the electronic mechanism of these processes has already been discussed by one of us (*inter alia*, *J. Soc. Chem. Ind.*, 1925, **44**, 456).

Fewer examples are available, however, in which hydrogen is replaced as the ultimate result of the attack of the aromatic nucleus by anionoid agents. Such processes do not usually give good yields of the products, because the hydrogen displaced along with an electron pair effects reduction of a part of the material.

Good examples are the oxidation of nitrobenzene to *o*-nitrophenol by the action of potassium hydroxide in air (Wohl, *Ber.*, 1899, **32**, 3486; 1901, **34**, 2444) and the formation of *p*-nitrophenylcarbazole from nitrobenzene and potassiocarbazole (G. and M. de Montmollin, *Helv. Chim. Acta*, 1923, **6**, 94). The direct introduction of hydroxyl groups into the anthraquinone molecule and the formation of indanthrone from β-aminoanthraquinone and of dibenzanthrone from benzanthrone are further typical cases of analogous reactions.

In an endeavour to find simpler cases of the direct introduction of amino-groups into the nitrobenzene molecule we have studied the behaviour of nitrobenzene towards amines under various conditions. In most cases the results have been negative or ambiguous, but it has been found that the piperidino-group can be directly introduced into the nucleus. The agent employed is the base itself in the presence of sodamide and we presume that the very active anion of sodium piperidine is actually responsible for the successful attack of the aromatic nucleus.



Similarly, α-nitronaphthalene yields a 4-piperidino-derivative and 8-nitroquinoline furnishes a piperidino-derivative the constitution of which has not yet been determined. 8-Nitroquinoline belongs both to class (b) and to class (d) (above) and the piperidino-group might therefore be in any of the positions 2, 4, 5, and 7. The most likely positions, namely, 2 and 5, have been excluded by the synthesis of the 2-piperidino- and 5-piperidino-8-nitroquinolines and apparently, therefore, the piperidine has attacked one of the positions 4 and 7.

The reactions described in the experimental section do not proceed entirely in one direction and the by-products may include members

of the phenazine group. The investigation is being continued in the hope of discovering the appropriate oxidising agent, but the problem of controlling these processes appears to be a difficult one. It may be noted that the required atom of oxygen may be introduced as part of the reagent, that is, hydroxylamine may be used instead of ammonia, and as an example the formation of 2-nitro-1-naphthylamine from α-nitronaphthalene and hydroxylamine in the presence of alcoholic sodium ethoxide (Meisenheimer and Patzig, *Ber.*, 1906, **39**, 2533) may be cited.

In accordance with our view this process is initiated by direct union of the nitrogen of the hydroxylamine with the nuclear carbon and the elimination of water occurs at a later stage; a scheme such as :C$\boxed{\text{H HO}}$NH$_2$, suggesting that the process is essentially a condensation, is simple but not acceptable.

EXPERIMENTAL.

p-*Nitrophenylpiperidine.*—A mixture of nitrobenzene (12·3 g.), piperidine (8·5 g.), and finely powdered sodamide (4 g.), shaken in a sealed bottle, rapidly became golden-brown and after 45 hours was an almost rigid mass, black in thick, but deep yellow in thin layers. There was a strong ammonia pressure. After a further 24 hours the product was decomposed by mixing it intimately with benzene and powdered ice and then adding dilute hydrochloric acid (containing 30 c.c., *d* 1·16). The liquid was filtered and the benzene layer was isolated, washed with 6% hydrochloric acid (60 c.c.), and extracted four times with 24% hydrochloric acid (30 c.c.); the aqueous extracts were combined, filtered, and basified with ammonia. The crude base was precipitated as a dark yellow, crystalline substance (5·53 g.), m. p. 92—94°. In a second preparation in which the product was kept for 34 days previous to isolation the yield was 6·45 g., m. p. 94—97°.

Recrystallised from ethyl alcohol, the base was obtained in yellow or greenish-yellow plates, m. p. 103—103·5°, identical in all respects with the *p*-nitrophenylpiperidine prepared from *p*-chloronitrobenzene (Lellmann and Geller, *Ber.*, 1888, **21**, 2281, give m. p. 105°). The pure substance (Found: C, 64·2; H, 6·7; N, 13·5. Calc. for $C_{11}H_{14}O_2N_2$: C, 64·0; H, 6·8; N, 13·6%), mixed with a specimen (m. p. 103°) from *p*-chloronitrobenzene, had m. p. 103°. Success in the condensation is conditional on the use of active sodamide. Under all circumstances the base is accompanied by a relatively small amount of more strongly basic material, but nitrophenols and bases weaker than *p*-nitrophenylpiperidine are not formed.

Oxygen was absorbed at some phase of the reaction, but no

improvement in the yield of the base was effected by the introduction of oxidising agents or by carrying out the reaction in an atmosphere of oxygen. The crude base obtained in the last-mentioned experiment melted at 99—101°, a circumstance which indicated the absence of any isomeride.

It appeared probable that the observed evolution of ammonia was the result of interaction of sodamide with water formed in the reaction. Actually the use of 2 mols. of sodamide gave only a 14% yield of the crude base (m. p. 70—80°).

p-Nitrophenylpiperidine was also obtained from *p*-nitroanisole, although in smaller relative yield than from nitrobenzene under similar conditions.

1-*Nitro*-4-*piperidinonaphthalene*.—In the absence of a diluent the reaction between α-nitronaphthalene, piperidine, and sodamide gave varying results.

An equimolecular mixture of α-nitronaphthalene (8·6 g.), piperidine (4·3 g.), and sodamide (2·0 g.) was diluted with benzene (15 c.c.) and shaken in a sealed bottle during 84 hours. The product, a black tarry mass, was mixed with benzene and powdered ice and the dark alkaline aqueous layer was removed. The benzene layer was filtered and shaken with 6% hydrochloric acid (120 c.c.). A considerable brown precipitate separated and this was removed. The filtrate consisted of a red aqueous layer and a dark red benzene layer. The former, separated and basified with ammonia, gave a grey precipitate that darkened immediately (A, m. p. 50—100°; yield, 3·72 g.). The benzene layer was washed with 12% hydrochloric acid (60 c.c.) and then with concentrated hydrochloric acid (20 c.c.). The latter extract, washed with benzene, filtered, and basified with ammonia, afforded a greenish-yellow crystalline precipitate (B), m. p. 68—69° (yield, 3·25 g.).

The yield of (B) was increased (3·55 g., m. p. 70—71°) when only 5 c.c of benzene were added to the reactants, and again when 2 mols. of α-nitronaphthalene were used (2·1 g. from 8·6 g. of α-nitronaphthalene and 2·2 g. of piperidine).

The basic product (A) was far from homogeneous and was not obtained in a pure condition. It gave a colourless crystalline hydrochloride that dissolved in water to a red solution, and a colourless crystalline methiodide.

(B) was easily separable into a constituent readily soluble in methyl alcohol (C) and an almost insoluble portion (D).

(C) consisted of 1-*nitro*-4-*piperidinonaphthalene* and crystallised from the minimum volume of hot methyl alcohol, on cooling, in stout plates or tablets, m. p. 73—74°, and in slender, deep yellow prisms, m. p. 73·5—74°, on recrystallisation (Found : C, 70·4;

H, 6·2; N, 10·7. $C_{15}H_{16}O_2N_2$ requires C, 70·3; H, 6·3; N, 10·9%). *Reduction:* Granulated tin (5 g.) was added to the brown solution of the base (2 g.) in concentrated hydrochloric acid (40 c.c.); a colourless crystalline solid soon separated. After 1 hour the mixture was warmed and the colourless solution obtained was diluted and made strongly alkaline in the presence of ether. The extract was washed with 6% hydrochloric acid (30 c.c.), in which the nitro-base is insoluble, and the base again rendered to ether. The amber residue after evaporation of the dried ethereal solution solidified, in contact with light petroleum, to a colourless crystalline mass, m. p. 78—79° (Found: C, 79·3; H, 7·9; N, 12·4. $C_{15}H_{18}N_2$ requires C, 79·6; H, 8·0; N, 12·4%).

1-*Amino*-4-*piperidinonaphthalene* is very easily soluble in the common solvents. Exposed to air and light, it becomes blue and then dissolves in ether to a strong blue-fluorescent solution. It can be diazotised and coupled with β-naphthol in the normal manner. The *benzoyl* derivative crystallised from ethyl alcohol in colourless pointed prisms, m. p. 213—214° (Found: C, 79·5; H, 6·8; N, 8·5. $C_{22}H_{22}ON_2$ requires C, 80·0; H, 6·7; N, 8·5%).

Oxidation of the base occurred smoothly when a solution in 10% sulphuric acid was shaken with powdered potassium dichromate in the presence of ice and benzene. The yellow benzene layer, washed with water, dried with sodium sulphate, and evaporated, gave a crystalline residue; this crystallised from light petroleum in lemon-yellow plates, m. p. 124—125°, easily volatile in steam and possessing the characteristic odour of quinones. The substance was thus α-naphthaquinone and its formation is the basis of the proposed constitution for the nitropiperidinonaphthalene.

The greenish-yellow residue (D) (0·13 g., m. p. 223—229°) that remained from 9 g. of the crude product (B) was digested with boiling ethyl alcohol (200 c.c.); less than 0·1 g. dissolved, and this separated on cooling. Repeated crystallisations gave slender yellow prisms, m. p. 257—258° (Found: C, 81·8, 81·8; H, 5·8, 5·7; N, 11·1, 11·6. $C_{25}H_{21}N_3$ requires C, 82·6; H, 5·8; N, 11·6%). The base is sparingly soluble in most organic solvents, the solutions in alcohol and acetic acid are faintly coloured and non-fluorescent, but the solution in benzene shows very intense yellow-green fluorescence. The base dissolves in concentrated sulphuric acid with a fine violet colour that remains unchanged in tone and intensity after 2 months. The yellow solution in concentrated hydrochloric acid deepens in colour on moderate dilution; further addition of water reprecipitates the base.

The composition and properties of the substance are approximately those of a *piperidino*-as.-αβ-*dinaphthazine* which might result

by reduction processes applied to a mixture of α-nitronaphthalene and 1-nitro-4-piperidinonaphthalene.

Action of Sodamide and Piperidine on p-*Nitrotoluene.*—A piperidinonitrotoluene was not formed but instead 4 : 4′-dinitrodibenzyl was obtained. A suspension of sodamide (4 g.) in a solution of *p*-nitrotoluene (28 g.) in piperidine (20 c.c.) was mechanically stirred in a bottle provided with a mercury seal. Absorption of oxygen occurred and after 7 days the product was a viscous black paste, deep red brown in thin layers. Addition of benzene, ice, and dilute hydrochloric acid (containing 60 c.c. of acid, *d* 1·16) caused the separation of an ochre-yellow solid, which was collected and washed with water and benzene. No other homogeneous material could be isolated. Extracted with hot water and 5% hydrochloric acid, and recrystallised from glacial acetic acid, the solid was obtained as a brick-red powder (8·3 g.), m. p. 173—176°. Repeated crystallisation from 95% alcohol and then from ethyl alcohol gave yellow needles or slender prisms, m. p. 179·5—180·5° (Found : C, 61·9; H, 4·5; N, 10·0. Calc. for $C_{14}H_{12}O_4N_2$: C, 61·8; H, 4·5; N, 10·3%), identical with 4 : 4′-dinitrodibenzyl in all properties. Oxidation with chromic anhydride in glacial acetic acid gave *p*-nitrobenzoic acid only.

8-*Nitroquinolylpiperidine.*—In purifying the 8-nitroquinoline prepared according to Knüppel (*Ber.*, 1896, **29**, 705), it was found advantageous to extract the dry crude product of the Skraup reaction with benzene and to recrystallise the recovered base from light petroleum. The material obtained in this manner melted at 87—88° as described in the literature. The base reacted very rapidly with piperidine and it was necessary to dilute the reactants with benzene. The whole of the product was soluble in dilute hydrochloric acid and no separation could be effected with this reagent. Several weaker acids were tried and of these 5% phosphoric acid gave the most satisfactory result.

A mixture of 8-nitroquinoline (7 g.), piperidine (3·4 g.), sodamide (1·6 g.) and benzene (10 c.c.) was shaken in a sealed bottle. There was only a gradual deepening of the colour and only a slight development of pressure during the first 3 days, but at this point the reaction commenced abruptly and within a few hours much ammonia had been liberated and a black pasty product formed. This was kept for 2 days, then mixed with benzene and ice, and acidified with dilute hydrochloric acid. The colourless benzene layer was separated from the deep red aqueous layer and this was filtered and basified in the presence of ether. A light-coloured substance separated during this process and was removed. The deep yellow ethereal solution was extracted with small successive volumes of 5% phosphoric acid and

the dissolved bases were recovered by addition to dilute alkali. The first fractions contained dark yellow material (0·13 g., m. p. 70—90°), the intermediate fractions almost all the nitroquinolylpiperidine (1·4 g., m. p. 100—110°), and unchanged 8-nitroquinoline was recovered from the last extracts (0·19 g., m. p. 70—120°).

The basic material from the intermediate fractions was extracted with 15—20 c.c. of boiling light petroleum, in which 8-nitroquinoline is readily soluble, and the bright yellow crystalline residue was dissolved in boiling light petroleum (b. p. 60—80°); on cooling, *8-nitroquinolylpiperidine* separated in an almost pure condition (yield, 0·8 g.; m. p. 126—129°). Recrystallised from light petroleum, the base formed lemon-yellow hexagonal tablets or prisms, m. p. 131·5—132·5° (Found: C, 65·5; H, 5·9; N, 16·1. $C_{14}H_{15}O_2N_3$ requires C, 65·3; H, 5·9; N, 16·3%). It dissolves in concentrated hydrochloric acid to a pale yellow solution which becomes deep orange on moderate dilution. An ethereal solution of the base affords with hydrogen chloride a colourless crystalline precipitate of a hydrochloride which is hygroscopic and becomes red when exposed for a short time to air.

8-Nitro-5-piperidinoquinoline.—5-Chloro-8-nitroquinoline was prepared by nitration of 5-chloroquinoline as described by Claus and Junghaus (*J. pr. Chem.*, 1893, **48**, 254).

A suspension of 5-chloro-8-nitroquinoline (2·44 g., m. p. 184°) in piperidine (6 c.c.) was boiled during 3 hours. The solid dissolved, the solution became deep yellow, and piperidine hydrochloride separated rapidly. The canary-yellow crystalline precipitate (2·94 g., m. p. 105—106°) obtained on addition of water was collected, washed with water, and crystallised from light petroleum (b. p. 60—80°), forming yellow needles, m. p. 105·5—106·5° (Found: C, 65·4; H, 5·8; N, 16·2. $C_{14}H_{15}O_2N_3$ requires C, 65·3; H, 5·9; N, 16·3%).

8-Nitro-2-piperidinoquinoline.—2-Chloro-8-nitroquinoline was obtained by nitration of 2-chloroquinoline (Fischer and Guthmann, *J. pr. Chem.*, 1916, **93**, 378); the base was most conveniently purified by steam-distillation of the crude nitration product without superheating. The residue, crystallised from alcohol, melted at 148—149° in agreement with Fischer and Guthmann.

2-Chloro-8-nitroquinoline (2·0 g.) was added to piperidine (6 c.c.), a rapid rise in temperature occurring after a few minutes. The brownish-yellow mass was heated at the boiling point during 1 hour and then poured into water. The yellow precipitate (2·36 g.) crystallised from light petroleum (b. p. 60—80°) in light yellow plates, m. p. 87° (Found: C, 65·1; H, 5·8; N, 16·3. $C_{14}H_{15}O_2N_3$ requires C, 65·3; H, 5·9; N, 16·3%). This substance becomes orange on keeping in a specimen tube.

Piperidinobenzanthrone.—A suspension of equimolecular amounts of benzanthrone (2·3 g.) and sodamide (0·4 g.) in piperidine (10 c.c.) was boiled during 1 hour. The brown solution obtained was poured into water. The oily precipitate was collected and extracted with hot 20% hydrochloric acid. The filtered, orange solution, when basified, afforded a yellow precipitate (0·66 g., m. p. 145—151°), which crystallised from light petroleum (b. p. 60—80°), in which it was easily soluble, in yellow plates, m. p. 176·5—178° (Found: C, 84·1; H, 5·9; N, 4·5. $C_{22}H_{19}ON$ requires C, 84·3; H, 6·1; N, 4·5%), soluble in concentrated hydrochloric acid to a golden-yellow solution, from which the *base* was reprecipitated on dilution with water. The solution in concentrated sulphuric acid was deep orange. The base was unaffected by warm alkaline sodium hydrosulphite, but the yellow solution in glacial acetic acid was almost decolorised by reduction with zinc powder.

Products of the Interaction of Nitrobenzene, Liquid Ammonia, and Sodamide.—A mixture of nitrobenzene (40 g.) and sodamide (10 g.) with a considerable excess of liquid ammonia was kept in an enamelled steel cylinder at the ordinary temperature during 10 months. The dark tarry product was mixed with benzene and water, and the large quantity of dark oily solid that remained undissolved was collected (R). The orange benzene layer was separated, washed with water, filtered, and extracted with 15% hydrochloric acid. The acid extracts were basified and gave a yellow precipitate (0·68 g.), m. p. 215—220°. After several crystallisations from light petroleum (b. p. 60—80°), long yellow needles, m. p. 215° (decomp.), were obtained (Found: C, 73·4; H, 4·2; N, 14·4. $C_{12}H_8ON_2$ requires C, 73·4; H, 4·1; N, 14·3%). The *base* is fairly readily soluble in light petroleum but is insoluble in 10% aqueous potassium hydroxide. The solution in concentrated hydrochloric acid is deep yellow. Heated gradually to 270°/15 mm., the substance evolves gas and affords a yellow crystalline basic sublimate, m. p. 185—200°; in this respect it differs from phenazine oxide (m. p. 226·5°), which yields phenazine (m. p. 171°) under the same conditions (Wohl and Aue, *Ber.*, 1901, **34**, 2442; Wohl, *Ber.*, 1903, **36**, 4139).

The dark oily residue (R) was extracted twice with boiling methyl alcohol (300 c.c.) and was thus obtained as an orange-yellow crystalline powder, apparently a sodium salt. It crystallised from a large volume of methyl alcohol in pale orange needles that did not melt below 300°, and was much more readily soluble in water to an orange solution, from which acetic acid precipitated a yellow solid that redissolved on the addition of hydrochloric acid.

The free phenolic *base* was prepared by dissolving the recrystallised

sodium salt in hydrochloric acid and neutralising the solution with aqueous sodium bicarbonate. The canary-yellow precipitate crystallised from light petroleum (b. p. 60—80°) in yellow prisms, m. p. 230—231° (Found : C, 59·8; H, 2·8; N, 17·3; *M*, in camphor, 274, 299. $C_{12}H_7O_3N_3$ requires C, 59·7; H, 2·9; N, 17·4%; *M*, 241).

The phenolic base is moderately easily soluble in light petroleum and is easily soluble in benzene. It dissolves in concentrated sulphuric acid to a greenish-violet dichroic solution that becomes yellow on dilution with water. The solution in concentrated hydrochloric acid is orange-yellow; dilution reprecipitates the base. In warm 10% aqueous potassium hydroxide it dissolves to a deep yellow solution, from which yellow needles (potassium salt ?) separate on cooling. Addition of zinc dust to a solution of the base in dilute hydrochloric acid causes the development of a violet colour, and this changes through green to yellow; ultimately the solution becomes colourless. Exposed to air, the colourless solution becomes yellow and finally violet.

This phenolic base is possibly a nitrohydroxyphenazine.

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