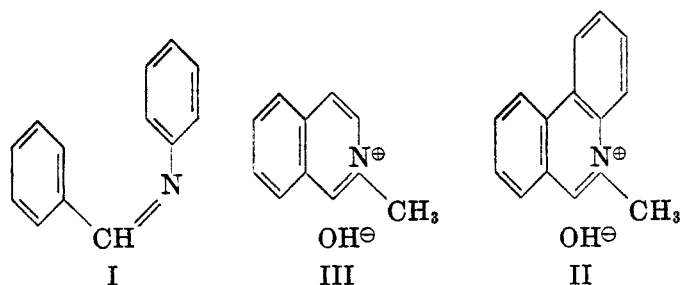


REACTIONS OF NITROPARAFFINS WITH IMINES AND PSEUDO BASES

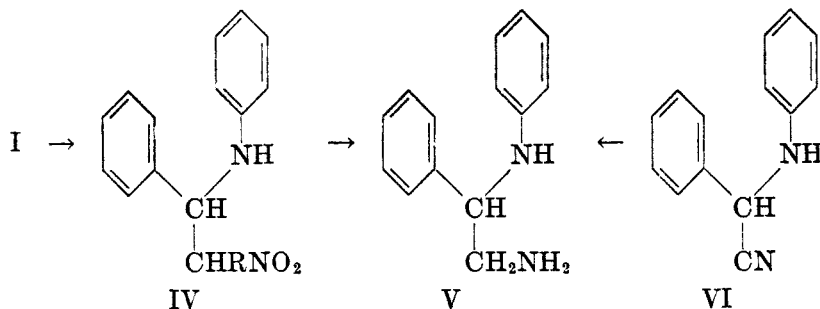
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As an adjunct to our study of the reactions of certain isoquinoline compounds (1, 2), the structural similarities of benzalaniline (I) and isoquinoline, 10-methylphenanthridinium hydroxide (II) and 2-methylisoquinolinium hydroxide (III) led us to investigate the condensation products of nitroparaffins with I and II. Optimum conditions have now been found for the condensation of nitroparaffins with benzalaniline (I), 10-methylphenanthridinium hydroxide (II), and the isomeric 10-methylacridinium hydroxide (IX).⁴



The addition of nitromethane to benzalaniline to give 1-anilino-2-nitro-1-phenylethane (IVa) was previously reported by Mayer (3), but the details of the preparation, such as proportion of reactants and yield obtained, were lacking. It has been possible to effect a 79% yield of the adduct IVa by heating an ethanol solution of benzalaniline with three mole-equivalents of nitromethane under reflux for six hours. The structure of the adduct (IVa) was established



a. R = H; b. R = CH₃;
c. R = C₂H₅

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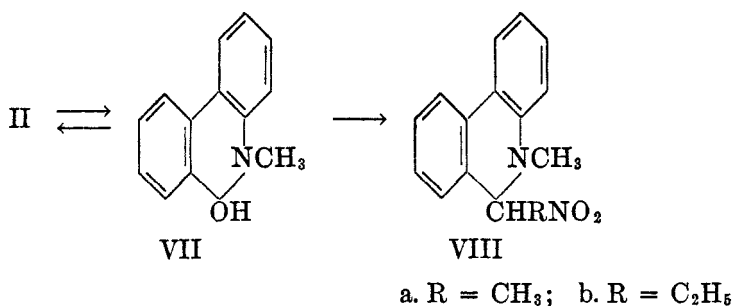
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⁴ The latter two probably as the pseudo base forms, VII and X.

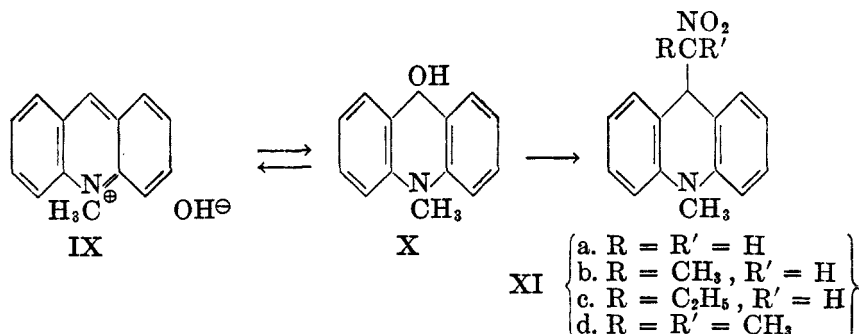
by its reduction, both by catalytic hydrogenation and by chemical means, to 2-anilino-2-phenylethylamine (V), identical with the product of similar reduction of anilinophenylacetonitrile (VI). Addition of the homologous nitroethane and 1-nitropropane to benzalaniline did not proceed very satisfactorily in the absence of a catalyst, and we were dissuaded from the use of an acidic catalyst since Snyder, Kornberg, and Romig (4) found, in a study of the addition of active methylene compounds to benzalaniline in the presence of boron trifluoride, that nitromethane failed to give a solid product. By contrast, the use of a basic catalyst such as diethylamine was found to facilitate the addition to benzalaniline of nitroethane to give 1-anilino-2-nitro-1-phenylpropane (IVb) and of 1-nitropropane to give 1-anilino-2-nitro-1-phenylbutane (IVc). The method employing diethylamine possesses an advantage over others in that the adducts are readily isolated in pure form.

The nitroparaffins were found not to add readily to the analogous imine system of phenanthridine itself, but the combination of the two moieties was effected by condensation of 10-methylphenanthridinium iodide in ethanolic potassium hydroxide solution [essentially, therefore, the pseudo base form of II, 9-hydroxy-10-methyl-9,10-dihydrophenanthridine (VII) (5)] with nitroethane and with 1-nitropropane. The products, 9-(α -nitroethyl)-10-methylphen-



anthridan (VIIIa) and 9-(α -nitropropyl)-10-methylphenanthridan (VIIIb), were obtained in 54% yield in both examples.

The study of nitroparaffin condensation with a pseudo base (VII) was then extended to the vinylog of a pseudo base, as represented by the isomeric 9-hydroxy-10-methyl-9,10-dihydroacridine (X) (5). It was found that selected nitroparaffins (nitromethane, nitroethane, 1-nitropropane, and 2-nitropropane)



reacted readily with a solution of 10-methylacridinium iodide made alkaline with potassium hydroxide. The condensation products, which were assigned the general structure of 9-substituted-10-methylacridans (XI), were obtained in yields of 62% (XIa), 68% (XIb), 50% (XIc), and 35% (XI d).

EXPERIMENTAL⁵

1-Anilino-2-nitro-1-phenylethane (IVa). The method employed for the preparation of this compound was essentially that of Mayer (3), but since Mayer provided no details as to proportion of reactants used or yield obtained, the following directions are reported as giving the desired product in optimum yield. A solution of 100 g. (0.55 mole) of benzalaniline, 100 g. (1.64 mole) of nitromethane, and 50 ml. of absolute ethanol was heated at the reflux temperature for six hours. The solvent and excess nitromethane were evaporated at room temperature with the aid of a stream of dry air. The resulting mixture of rhombohedral prisms and oil was crushed and stirred with 95% ethanol, and the solid was collected. Several washings with cold 95% ethanol followed by air-drying gave 106 g. (79%) of product, m.p. 85–87°. Recrystallization from 95% ethanol raised the melting point of the light yellow prisms to 86–87.5° [reported by Mayer (3), 90°; reported by Worrall (6), who prepared it by a different method, 86–87°].

Anal. Calc'd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.82.

Found: C, 69.62; H, 5.91.

The *hydrochloride* was prepared by saturating an ether solution of the amine with anhydrous hydrogen chloride; m.p. 126–127° [reported (6), 126–127°]. The hydrochloride dissociated immediately on contact with water to give the free amine.

1-Anilino-2-nitro-1-phenylpropane (IVb). Five grams (27.6 millimoles) of benzalaniline was dissolved in 6.2 g. (82.6 millimoles) of nitroethane and 5 ml. of 95% ethanol. After the addition of 0.6 g. (8.2 millimoles) of diethylamine, the solution was heated at the reflux temperature for 15 minutes. Evaporation of the solution at room temperature with a stream of dry air gave an orange oil. Crystallization was induced by trituration with 95% ethanol, and the solid obtained was washed with ethanol; yield, 2.1 g. (30%); m.p. 100–102°. Recrystallization from absolute ethanol raised the melting point of the yellow prisms to 103–105°.

Anal. Calc'd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93.

Found: C, 70.30; H, 6.51; N, 10.70.

The employment of a longer reflux time with diethylamine led to impure product. The use of benzyltrimethylammonium hydroxide (Rohm and Haas Company) in 0.05 mole-equivalent quantity and with a reflux time of two hours gave a slightly higher yield (35%), but of less pure product (m.p. 96–100°). In the absence of a basic catalyst, the reactants produced a low-melting mixture (m.p. 78–83°).

1-Anilino-2-nitro-1-phenylbutane (IVc). A method similar to that for 1-anilino-2-nitro-1-phenylpropane was used, with the difference that a two-hour reflux time was employed. The product was obtained in 55% yield as yellow prisms, m.p. 128–130°.

Anal. Calc'd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.37.

Found: C, 70.93; H, 6.86; N, 10.33.

Anilinophenylacetonitrile (VI). This compound was prepared by the method of Bucher and Grolée (7). The *N-acetyl derivative* was best prepared as follows. Anilinophenylacetonitrile with four mole-equivalents of acetic anhydride and a few drops of sulfuric acid was heated at 100° for one hour or at the reflux temperature for one-half hour. The reaction mixture was poured into water, giving a light yellow solid in quantitative yield (in small runs). Recrystallization from petroleum ether gave colorless prisms, m.p. 75–76°.

Anal. Calc'd for $C_{14}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.20.

Found: C, 76.57; H, 5.69; N, 11.08.

⁵ All melting points are corrected.

2-Anilino-2-phenylethylamine (V). The method of catalytic reduction employed was that used with analogous compounds by Reihlen and coworkers (8). The most satisfactory results were achieved when 30-g. batches of anilinophenylacetonitrile dissolved in 60 ml. of acetic anhydride were pretreated with Raney nickel at 25° and then hydrogenated over 1.0 g. of platinum oxide catalyst at 2-3 atm. and 60°. Even under these conditions, the usual yield was not over 20% of 2-anilino-2-phenylethylamine. Separation from the by-products of aniline (60%), identified as the picrate, and N-benzylaniline (*ca.* 10%), identified as the phenylthiourea derivative, was accomplished by fractional distillation *in vacuo*; b.p. 119-128° (0.13-0.20 mm.); n_D^{20} 1.6069.

Anal. Calc'd for $C_{14}H_{16}N_2$: C, 79.20; H, 7.60; N, 13.20.

Found: C, 79.42; H, 7.43; N, 12.96.

The *monohydrochloride* of 2-anilino-2-phenylethylamine was formed in ethanol-ether and was recrystallized from 95% ethanol; m.p. 245-248°.

Anal. Calc'd for $C_{14}H_{17}ClN_2$: C, 67.59; H, 6.89; N, 11.26.

Found: C, 67.74; H, 6.88; N, 10.98.

The yield of 2-anilino-2-phenylethylamine was not improved by using N-acetylanilino-phenylacetonitrile in the hydrogenation over platinum oxide. When lithium aluminum hydride was employed for the reduction of anilinophenylacetonitrile using the conditions which Nystrom (9) applied for the conversion of nitriles to amines, a 25% yield of 2-anilino-2-phenylethylamine was realized, but N-benzylaniline was the major product (41% yield).

Reduction of 1-anilino-2-nitro-1-phenylethane. The structure of 1-anilino-2-nitro-1-phenylethane was related to that of anilinophenylacetonitrile by reduction to the same product: 2-anilino-2-phenylethylamine. The diamine, b.p. 124-125° (*ca.* 0.3 mm.), n_D^{20} 1.6064, was obtained, but only in low yield, by the hydrogenation of 1-anilino-2-nitro-1-phenylethane over platinum oxide catalyst (8) or by reduction with lithium aluminum hydride (9). Aniline and N-benzylaniline were again formed in larger amount than that of the desired diamine.

9-(α -Nitroethyl)-10-methylphenanthridan (VIIIa). A solution of 1.3 g. (23 millimoles) of potassium hydroxide in 20 ml. of absolute ethanol was added to a boiling suspension of 4.6 g. (14 millimoles) of 10-methylphenanthridinium iodide (5) in 15 ml. of absolute ethanol. To the resulting solution, 7.0 g. (93 millimoles) of nitroethane was added, and the light orange reaction mixture was heated under reflux for 30 minutes. After saturation with carbon dioxide, the reaction mixture was allowed to stand 12 hours at 25°. The solid which separated was recrystallized from 95% ethanol. Yellow rhombic crystals of 9-(α -nitroethyl)-10-methylphenanthridan, m.p. 112.5-113.5°, were thereby obtained; yield, 2.03 g. (54%).

Anal. Calc'd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.45.

Found: C, 71.60; H, 6.25; N, 10.29.

9-(α -Nitropropyl)-10-methylphenanthridan (VIIIb). This product was obtained in the same manner as the lower homolog by the use of 1-nitropropane; m.p. 102-103.5°; yield, 54%.

Anal. Calc'd for $C_{17}H_{18}N_2O_2$: C, 72.31; H, 6.43; N, 9.92.

Found: C, 72.32; H, 6.55; N, 9.65.

9-Dimethylaminomethylphenanthridine. A solution of 4.0 g. (17 millimoles) of 9-chloromethylphenanthridine (10) and 6.80 g. (150 millimoles) of dimethylamine in 20 ml. of 95% ethanol was placed in a pressure bottle and allowed to stand at 25° for four days. When the reaction mixture was added to 60 ml. of 5% aqueous sodium hydroxide, an oil separated which was extracted with ether. The ether extracts were evaporated and the crude 9-dimethylaminomethylphenanthridine was distilled at 160-170° (2 mm.). The distillate crystallized on cooling and was recrystallized from aqueous methanol; m.p. 86-87°; yield, 2.1 g. (50%).

Anal. Calc'd for $C_{16}H_{18}N_2$: C, 81.32; H, 6.83; N, 11.85.

Found: C, 81.23; H, 6.87; N, 11.81.

9-Diethylaminomethylphenanthridine. A solution of 10.6 g. (140 millimoles) of diethylamine and 10 g. (44 millimoles) of 9-chloromethylphenanthridine in 20 ml. of 95% ethanol

was heated under reflux for two hours. The reaction mixture was worked up in the same manner as that used for the dimethylamine product. The 9-diethylaminomethylphenanthridine was recrystallized from petroleum ether; m.p. 72.5–73°.

Anal. Calc'd for $C_{13}H_{20}N_2$: C, 81.77; H, 7.63; N, 10.59.

Found: C, 81.70; H, 7.90; N, 10.44.

9-(N-Piperidinomethyl)phenanthridine. Prepared by the same method using piperidine, the product crystallized from aqueous methanol as colorless needles, m.p. 98–99° [reported (11), 90–93°]; yield, 57.2%.

Anal. Calc'd for $C_{15}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.14.

Found: C, 82.43; H, 7.23; N, 10.18.

9-Nitromethyl-10-methylacridan (XIa). A solution of 0.45 g. (8 millimoles) of potassium hydroxide in 10 ml. of absolute ethanol was added to a suspension of 2.4 g. (7.5 millimoles) of 10-methylacridinium iodide in 15 ml. of absolute ethanol. To the resulting clear solution was added 2.93 g. (48 millimoles) of nitromethane. The reaction mixture was heated to boiling and then was allowed to stand at 25° for three days. The resulting suspension was saturated with carbon dioxide, heated to boiling, and filtered to remove inorganic salts. Upon cooling, 9-nitromethyl-10-methylacridan separated and was recrystallized from absolute ethanol; plates, m.p. 131–132°; yield, 1.18 g. (62%).

Anal. Calc'd for $C_{15}H_{14}N_2O_2$: C, 70.84; H, 5.55; N, 11.02.

Found: C, 70.80; H, 5.35; N, 10.96.

9-(α -Nitroethyl)-10-methylacridan (XIb). This compound was prepared in 68% yield by the same method, using nitroethane; plates from ethanol, m.p. 144.5–145.5°.

Anal. Calc'd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.45.

Found: C, 71.72; H, 6.20; N, 10.45.

9-(α -Nitropropyl)-10-methylacridan (XIc). This compound was prepared in 50% yield by the same method, using 1-nitropropane; plates from ethanol, m.p. 134–135°.

Anal. Calc'd for $C_{17}H_{18}N_2O_2$: C, 72.31; H, 6.43; N, 9.92.

Found: C, 72.27; H, 6.65; N, 9.79.

9-(α -Methyl- α -nitroethyl)-10-methylacridan (XIId). This compound was prepared in 35% yield by the same method, using 2-nitropropane; needles from ethanol, m.p. 198°.

Anal. Calc'd for $C_{17}H_{18}N_2O_2$: C, 72.31; H, 6.43; N, 9.92.

Found: C, 72.17; H, 6.44; N, 10.06.

SUMMARY

Optimum conditions have been found for the addition of representative nitroparaffins to the imino linkage of benzalaniline and for the condensation of nitroparaffins with the pseudo bases derived from 10-methylphenanthridinium hydroxide and 10-methylacridinium hydroxide.

URBANA, ILLINOIS

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