(5%), and the solvent was removed by distillation. The product gave a distillate (30 g., 78%) boiling at 150–160° (3 mm.) which solidified on cooling and then melted at 148–150° alone or when mixed with II prepared as in A above.

5-Nitro-4,6,7-trimethylcoumarandione (VIII).—A cold (0°) solution of sodium nitrate (4.4 g.) in sulfuric acid (60 cc.) was added dropwise and with vigorous stirring to a cold (0°) solution of the coumarandione II (10 g.) in sulfuric acid (60 cc.). The solution was kept at 0° for 30 minutes and then poured over ice. The yellow solid (11 g., 92%, m.p. 165–170°) was removed and crystallized twice from a mixture of ethyl acetate and petroleum ether (b.p., 60–68°) when it melted at 178–178.5°.

Anal. Calcd. for $C_{11}H_9O_5N$: C, 56.17; H, 3.86; N, 5.96. Found: C, 56.31; H, 3.63; N, 6.17.

The nitro compound was stable at the melting point, but evolved gas at 210–220°. It was soluble in hot bicarbonate (5%) and in cold alkali (5%), but insoluble in cold bicarbonate. When the alkaline solutions were acidified, VIII was recovered unchanged.

4,6,7-Trimethylcoumaran-2-one (VII).—The coumarandione II (9.5 g.) was refluxed for 14 hours with amalgamated zinc (25 g.) and aqueous hydrochloric acid (200 cc., 1:1). The solid (2 g.) which sublimed into the condenser was removed and crystallized from petroleum ether (b.p., 60–68°) when it melted at 121–123°. This substance VII was not soluble in aqueous alkali (5%) even on warming, but it dissolved in boiling alkali. Acidification of the cooled solution regenerated unchanged VII.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.87. Found: C, 75.21; H, 7.22.

The non-volatile solid remaining in the flask was removed and dissolved in acetone. The solution was filtered to remove the zinc and the filtrate was evaporated. The residue (6 g.) was insoluble in ether, alcohol, benzene or dioxane. After several crystallizations from hot ethyl acetate, a product melting at 255° was isolated. This was insoluble in warm alkali, but dissolved when the suspension was boiled. The compound was not investigated further.

5-Hydroxy-4,6,7-trimethylcoumarandione (III). A.—A cold solution of diazotized sulfanilic acid (10.5 g.) was poured, with stirring, into a solution of the coumarandione II (9.5 g.) in water (100 cc.) containing potassium hydroxide (17 g.). The deep red solution was allowed to stand overnight at room temperature and was acidified with hydrochloric acid. The orange solid was not removed; stannous chloride (22.5 g.) and hydrochloric acid (20 cc.) were added, and the mixture was boiled gently until the solid dissolved (30 minutes). The solution was divided into two equal parts: to one part, ferric chloride (45 g.) was added and the mixture was distilled with steam. The distillate contained trimethylquinone (2 g.); the residue was a red tar from which no crystalline material could be isolated. To the other half of the solution ferric chloride (45 g.) was added and the mixture was allowed to stand at room temperature for two hours. It was then extracted with three 250-cc. portions of a mixture of benzene and ether (1:1), the persistent emulsion was broken by repeated filtration through Hi-Flo, the organic layer was removed, dried (sodium sulfate) and the solvent was removed by distillation under reduced pressure (100 mm.). The residue, when cooled, deposited a solid (2 g.) which, crystallized from a mixture of cyclohexane and ethyl acetate, formed scarlet needles melting at 188–190°.

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.24; H, 5.02.

B.—Trimethylhydroquinone (15 g.) and oxalyl chloride (38 g.) were dissolved in tetrachloroethane (150 cc.) and the solution was refluxed for 12 hours in a dry atmosphere. The solvent was removed by steam distillation; the red solid (12 g.) was removed from the cooled residue and boiled with aqueous sodium bicarbonate (5%, 300 cc.) and the insoluble trimethylhydroquinone (4 g.) was removed. The filtrate was acidified and the orange solid (2.5 g.) was removed. Concentration of the mother liquor yielded an additional 1 g. of product. The combined solids were recrystallized from hot water, yielding III melting at 188–190° alone or when mixed with the product from A above.

Substance III was unaffected by action of boiling ethanol, with or without inclusion of sulfuric acid. Likewise, cold aqueous or ethanolic ferric chloride had no effect upon III, nor was there any oxidation or any other change when a chloroform solution of III was shaken with aqueous ferric chloride. When III in ethanol was boiled for 30 minutes with ferric chloride, nothing could be recovered from the solution. Action of sodium dichromate in dilute sulfuric acid upon III at 50° for 30 minutes produced no change, but when the solution was boiled, III was completely destroyed.

Hexamethyloxindigo (XII).—The diketone Ib (2.05 g.) was boiled for 2.5 hours with pyridine (75 cc.) containing iodine (2.5 g.) and the mixture was cooled to 40°. The solid (1.1 g.) was removed and boiled with pyridine (50 cc.) and the insoluble solid was removed by filtration of the hot mixture. The filtrate, on cooling, deposited unchanged Ib (0.4 g., m.p. and mixed m.p. 243–247°). The orange solid insoluble in hot pyridine was recrystallized from boiling nitrobenzene (100 cc.) when it formed tiny orange plates melting at 305–306° (dec.). The substance was insoluble in aqueous alkali (5%) and in Claisen alkali. It (0.5 g.) was insoluble in boiling pyridine (250 cc.) or in boiling acetic acid (800 cc.), or in any other organic solvent except nitrobenzene.

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.57; H, 6.17.

MINNEAPOLIS 14, MINNESOTA RECEIVED MARCH 15, 1951

[CONTRIBUTION FROM THE AVERY LABORATORY OF THE UNIVERSITY OF NEBRASKA]

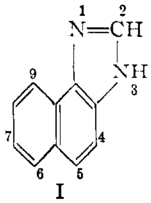
The Synthesis of Some Substituted Naphth[1,2]imidazole Derivatives

BY JOHN A. STEPHENS[1] AND CLIFF S. HAMILTON

The chemistry of certain naphth[1,2]imidazole derivatives which bear a substituent on the naphthalene nucleus has been investigated. Several new compounds of this class and various intermediates have been prepared and are reported along with some of their properties.

The present investigation was undertaken to study the chemistry of some naphth[1,2]imidazoles which bear a substituent on the naphthalene nucleus. The syntheses of a number of compounds based upon the naphth[1,2]imidazole nucleus (I) and some of their properties are reported.

Several new intermediates were prepared during the course of this work. Two of these, 1,5-diamino-2-acetamidonaphthalene and 1,6-diamino-2-acetamidonaphthalene, were found to possess an unexpected degree of stability since neither exhibited any evidence of deterioration upon exposure to the air.



I

Several methods for the preparation of naphth[1,2]imidazoles are extant and require suitable

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[1] Parke, Davis and Company Fellow.

derivatives of 1,2-naphthalenediamine, or immediate precursors, as the starting materials. The Phillips reaction[2] was utilized for the preparation of 6-amino- and 7-aminonaphth[1,2]imidazoles while a reductive ring closure reaction[3] proved more satisfactory for the preparation of 9-aminonaphth[1,2]imidazoles from the corresponding dinitronaphthylamine derivatives. 7-Bromo-2-methylnaphth[1,2]imidazole was obtained from 6-bromo-2-acetamido-1-naphthylamine by the method of Kelly and Day,[3] and a corresponding 4-bromo derivative was produced by catalytic hydrogenation of 3-bromo-1-nitro-2-acetamidonaphthalene. It appeared likely that, in the preparation of the latter, ring closure to produce 4-bromo-2-methylnaphth[1,2]imidazole occurred during the isolation procedure since other similar diamino derivatives, which were studied, offered no evidence that the conditions employed in catalytic hydrogenations could produce this desired reaction.

The compounds of the naphth[1,2]imidazole series were characterized by low solubility in organic solvents, with the exception of ethanol, and high solubility in both dilute acids and alkali.[4] The introduction of the amino group on the naphthalene nucleus appeared to enhance the basic properties of the naphth[1,2]imidazole nucleus and also its solubility in water. In general the naphth[1,2]-imidazoles studied formed rather insoluble hydrochloride salts, yellow picrates, and red copper complexes with ammoniacal cupric acetate.

Experimental[5]

4-Bromo-2-methylnaphth(1,2)imidazole (II).—A solution of 3-bromo-1-nitro-2-acetamidonaphthalene[6] (2 g., 0.007 mole) in 100 ml. of dry acetone was reduced with molecular hydrogen over Raney nickel catalyst at 46 lb. pressure. The catalyst was removed and the filtrate treated with dry hydrogen chloride to precipitate the product as the corresponding salt. The free base was liberated when the hydrochloride was treated with 5% aqueous solution of sodium bicarbonate and was recrystallized several times from dilute ethanol to give white microcrystals, m.p. 233–234°, in 59% yield.

Anal. Calcd. for $C_{12}H_9N_2Br$: C, 55.19; H, 3.47; N, 10.73. Found: C, 55.05; H, 3.48; N, 10.91.

9-Amino-2-methylnaphth(1,2)imidazole (III),—A suspension of 1,8-dinitro-2-acetamidonaphthalene[7] (4 g., 0.014 mole) and 50 g. of etched iron powder[8] (100 mesh) in 100 ml. of 90% aqueous ethanol was heated at reflux temperature for two hours with vigorous agitation. The insoluble material was removed from the hot mixture by filtration and the dark solution evaporated to near-dryness under reduced pressure. The residue was taken up in a solution of 0.5 g. of stannous chloride in 30 ml. of 5% hydrochloric acid, and the solution was warmed at 80° for five minutes. After the tin and any residual iron had been removed as the corresponding sulfides by treatment with hydrogen sulfide gas, concentrated hydrochloric acid (15 ml.) was added and the solution allowed to stand for 12 hours at 0°. The white crystals which separated were washed with ethanol and dried under reduced pressure. This salt did not melt when heated to 350°. When the solid was treated with a 5% aqueous solution of sodium bicarbonate, it was converted into a gray amorphous mass which was recrystallized from dilute ethanol and then from benzene as colorless needles; m.p. 205–207° (dec.). The yield was 1.3 g., 45%. The free base formed a yellow picrate, m.p. 228–231°, and a monoacetyl derivative, m.p. 322–323°, when treated with acetic anhydride in glacial acetic acid solution.

Anal. Calcd. for $C_{12}H_{11}N_3$: C, 73.06; H, 5.62; N, 21.31. Found: C, 72.81; H, 5.54; N, 21.09.

9-Aminonaphth(1,2)-imidazole (IV).—8-Nitro-2-naphthylamine was converted into the N-formyl derivative, m.p. 190–191°, by treatment with 88% formic acid, and the corresponding 1,8-dinitro compound, m.p. 222–224°, was prepared according to the method of Vesely and Jakes.[9] N-Formyl-1,8-dinitro-2-naphthalide (2 g., 0.008 mole), was subjected to a reductive ring closure reaction which was essentially the same as reported for III. The product was recrystallized from dilute ethanol as slate-colored needles, m.p. 199–200° (dec.), in 43% yield (0.6 g.).

Anal. Calcd. for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 71.87; H, 5.25; N, 23.19.

6-Bromo-1-nitro-2-acetamidonaphthalene (V).—6-Bromo-2-acetamidonaphthalene (5 g., 0.019 mole) was dissolved in a mixture of 60 ml. of glacial acetic acid and 10 ml. of acetic anhydride, and a solution of fuming nitric acid (3 ml., d. 1.5) in glacial acetic acid (7 ml.) was added dropwise during one hour with vigorous agitation. The product separated upon cooling and was recrystallized from ethanol as yellow needles, m.p. 157–159°, in 55% yield (3.2 g.). This material was characterized by hydrolysis in a mixture of ethanol and concentrated hydrochloric acid to 6-bromo-1-nitro-2-naphthylamine,[10] m.p. 189–191°, which had previously been obtained by a different method. The amine was further characterized by conversion to 6-bromo-1-nitro-2-naphthol, m.p. 122–123°, by heating in a dioxane–10% aqueous sodium hydroxide mixture.

6-Bromo-1-amino-2-acetamidonaphthalene (VI).—6-Bromo-1-nitro-2-acetamidonaphthalene (1 g., 0.003 mole) was hydrogenated in acetone solution (40 ml.) and the product isolated in the same manner as given for II. Recrystallization from 95% ethanol produced colorless needles, m.p. 219–221°, in 87% yield.

Anal. Calcd. for $C_{12}H_{11}ON_2Br$: C, 51.63; H, 3.97; N, 10.03. Found: C, 51.71; H, 4.05; N, 10.10.

7-Bromo-2-methylnaphth(1,2)imidazole (VII).—A solution of 6-bromo-1-amino-2-acetamidonaphthalene (0.5 g., 0.002 mole) in 100 ml. of xylene was heated under gentle reflux for one hour. The product separated as a tan powder when the solution was cooled in ice and was recrystallized from aqueous ethanol as nearly colorless needles, m.p. 216–218°.

Anal. Calcd. for $C_{12}H_9N_2Br$: N, 10.73. Found: N, 10.66.

1,6-Diamino-2-acetamidonaphthalene (VIII).—1,6-Dinitro-2-acetamidonaphthalene (3 g., 0.047 mole) was reduced in acetone solution (75 ml.) by catalytic hydrogenation over Raney nickel catalyst. The solvent was removed by evaporation under reduced pressure and the product recrystallized from a mixture of 1 part acetone and 1 part methanol as colorless needles, m.p. 205–206°, in 81% yield (1.9 g.).

Anal. Calcd. for $C_{12}H_{13}ON_3$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.74; H, 6.32; N, 19.39.

7-Amino-2-methylnaphth(1,2)imidazole (IX).—This substance was prepared successfully by the methods of (a) Phillips[2] and (b) Fischer.[11]

a.—When a solution of 1,6-diamino-2-acetamidonaphthalene (2 g., 0.009 mole) in 25 ml. of 10% hydrochloric acid was heated at reflux temperature for one hour, lustrous gray crystals separated during the course of the reaction. A second crop of solid was obtained by cooling the mixture in an ice-bath, and the two specimens were combined. The free base was liberated by treatment with a concentrated aqueous solution of sodium bicarbonate and then with a suspension of solid sodium bicarbonate in hot aqueous ethanol. The product was decolorized with Nuchar in dilute ethanol solution and recrystallized from the same solvent as colorless needles, m.p. 109–110°. The m.p. was raised to 126.5–128° after a specimen had been dried in a pistol over phosphorus pentoxide for six hours at 108–110°. The

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[2] Phillips, *J. Chem. Soc.*, 172 (1928).

[3] Kelly and Day, THIS JOURNAL, **67**, 1074 (1945).

[4] Compare Malmberg and Hamilton, *ibid.*, **70**, 2415 (1948).

[5] Melting points are uncorrected for stem emergence.

[6] Consden and Kenyon, *J. Chem. Soc.*, 1585 (1935).

[7] Bell, *ibid.*, 2784 (1929).

[8] Clemo and Legg, *ibid.*, 548 (1947).

[9] Vesely and Jakes, *Bull. soc. chim.*, **33**, 949 (1923).

[10] Davis, *Chem. News*, **74**, 302 (1896).

[11] Fischer, *Ber.*, **34**, 934 (1901).

yield was 1.6 g. (87%). An orange picrate, m.p. 259–260°, and an acetyl derivative, m.p. 354–357°, were prepared from the free base.

b.—Ring closure and acetylation of the amino group in the 7-position were effected by heating 1,6-diamino-2-acetamidonaphthalene (3 g., 0.014 mole) with 15 ml. of glacial acetic acid and 0.3 g. of fused sodium acetate for one hour. When the reaction mixture was made just alkaline to litmus paper with concentrated ammonium hydroxide at 0°, the product separated as a pink gum which was gradually converted to the solid state. It was recrystallized from 95% ethanol as fine pink needles, m.p. 355–356°. No depression of the m.p. was noted when this material was mixed with a specimen of the acetyl derivative reported under (a) above.

Anal. Calcd. for $C_{14}H_{13}ON_3$: N, 17.56. Found: N, 17.44.

The product from the reaction was heated with 20 ml. of concentrated hydrochloric acid for one hour, and 7-amino-2-methylnaphth(1,2)imidazole separated as a hydrochloride. The solid was treated with a concentrated aqueous solution of sodium bicarbonate and the resulting free base recrystallized from dilute ethanol as fine white needles, m.p. 109–110°. The m.p. was raised to 126–128° as in (a) by prolonged drying and no depression was observed when the solid was mixed with a specimen prepared in (a).

An analytical sample was prepared by combining equal weights of 7-amino-2-methylnaphth(1,2)imidazole from (a) and (b) and the mixture dried as outlined. This substance was found to be hygroscopic and special precautions were taken to avoid absorption of moisture during the various analytical manipulations.

Anal. Calcd. for $C_{12}H_{11}N_3$: C, 73.06; H, 5.62; N, 21.31. Found: C, 72.93; H, 5.53; N, 21.12.

7-Chloro-2-methylnaphth(1,2)imidazole (X).—A cold solution of sodium nitrite (0.3 g.) in 1 ml. of water was added dropwise to a suspension of 7-amino-2-methylnaphth(1,2)-imidazole (1 g., 0.004 mole) in 4 ml. of water containing 1 ml. of concentrated hydrochloric acid. The addition which was carried out at 0° required approx. 20 minutes, and vigorous stirring was maintained at all times. The diazonium mixture was slowly poured into a solution of cuprous chloride (0.008 mole) in concentrated hydrochloric acid (8 ml.). The dark mixture was stirred for one hour while the temperature was allowed to rise to 29°, and it was then warmed at 80° for an additional hour. The solid which separated was treated with a warm saturated solution of sodium bicarbonate and the resulting free base recrystallized from dilute ethanol as faintly pink crystals, m.p. 235.5–236.5° in 43% yield (0.4 g.).

Anal. Calcd. for $C_{12}H_9N_2Cl$: C, 66.45; H, 4.19; N, 12.93. Found: C, 66.52; H, 4.02; N, 13.19.

1,5-Diamino-2-acetamidonaphthalene (XI).—1,5-Dinitro-2-acetamidonaphthalene[9] (2.0 g., 0.007 mole) was reduced in acetone solution (75 ml.) by catalytic hydrogenation over Raney nickel catalyst. The solvent was removed by evaporation under reduced pressure and the product recrystallized from 90% ethanol as fine white needles, m.p. 215–217° (dec.), in 70% yield (1.1 g.). The substance failed to undergo ring closure when heated in xylene solution and was recovered unchanged.

Anal. Calcd. for $C_{12}H_{13}ON_3$: N, 19.52. Found: N, 19.39.

The product reacted readily with acetic anhydride in glacial acetic acid solution to give 1,2,5-triacetamidonaphthalene, m.p. 313–314°.

Anal. Calcd. for $C_{16}H_{17}O_3N_3$: N, 14.04. Found: N, 14.18.

6-Amino-2-methylnaphth(1,2)imidazole Hydrochloride (XII).—1,5-Dinitro-2-acetamidonaphthalene (2 g., 0.007 mole) was reduced as above and the product heated at reflux temperature with 10% hydrochloric acid (18 ml.) for one hour. A gray solid separated during the course of the reaction and a second crop of material was obtained by allowing the mixture to stand for 12 hours. The yield of the hydrochloride salt was 1.7 g. When a sample of this substance was treated with an aqueous sodium bicarbonate solution, it was converted into a red gum which failed to solidify even upon prolonged standing. After the salt was recrystallized from 95% ethanol and dried under reduced pressure at 108–110°, it was found that a fraction of the hydrogen chloride had been removed. Results obtained from analyses for nitrogen content corresponded approximately to values required for $C_{12}H_{11}N_3\cdot{}^1/_2HCl$. This material was then crystallized from 95% ethanol containing a small amount of dry hydrogen chloride and dried under reduced pressure at room temperature. The hydrochloride salt was used to provide an analytical sample.

Anal. Calcd. for $C_{12}H_{11}N_3\cdot HCl$: C, 61.66; H, 5.13; N, 17.98. Found: C, 61.39; H, 5.35; N, 18.18.

LINCOLN, NEBRASKA RECEIVED MARCH 12, 1951

[CONTRIBUTION FROM THE SHELL DEVELOPMENT COMPANY]

The Alkaline Cleavage of Isophorone

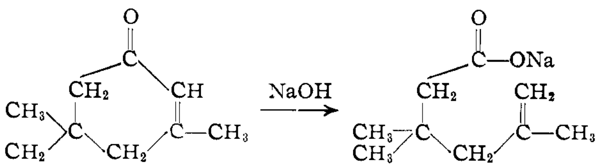
BY H. FINCH, KENNETH E. FURMAN AND SEAVER A. BALLARD

Treatment of isophorone with fused alkali metal hydroxides has been found to yield salts of 3,3,5-trimethyl-5-hexenoic acid in 49% yield. Other products of the reaction include methane, isobutene, acetone, acetic acid and carbonates.

Although a fairly extensive literature is available on the treatment of saturated cyclic ketones with fused alkali,[1,2] relatively little has been reported on the alkaline cleavage of conjugated unsaturated cyclic ketones. Weizmann reported the isolation of 2-cyclohexyl-2-hexenoic acid from the high temperature treatment of cyclohexanol with sodium hydroxide.[3] Pelton[2] isolated 1-cyclohexene-1-caproic acid from the reaction of cyclohexanone with fused sodium–potassium hydroxide. The intermediate in both cases was believed to be a cyclohexenecyclohexanone, or an isomer of this C_{12} unsaturated ketone; however, the material was not isolated nor was the location of the double bond in the C_{12} ketone established.

With the idea of determining whether cleavage at the carbonyl group in the cyclic conjugated unsaturated ketones would occur next to the adjacent saturated or unsaturated carbon atoms, experiments were carried out with isophorone.

The main product obtained by treatment of isophorone with a molten mixture of sodium and potassium hydroxides at 300° was the alkali metal salt of 3,3,5-trimethyl-5-hexenoic acid.



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(1) Guerbet, *Compt. rend.*, **148**, 720 (1909); *Bull. soc. chim.*, **5**, 420 (1909).

(2) Pelton, Starnes and Shrader, THIS JOURNAL, **72**, 2039 (1950).

(3) Weizmann, *J. Chem. Soc.*, 772 (1947).