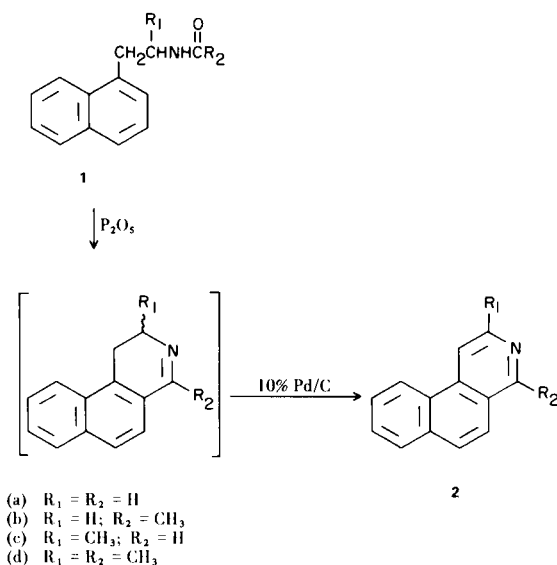


The Synthesis of Benz[*f*]isoquinoline

W. R. Schleigh

Research Laboratories, Eastman Kodak Company

The synthesis of benz[*f*]isoquinoline (**2a**) and a number of 6-, 8-, and 9-substituted derivatives by the photochemical cyclodehydrogenation of the appropriate 3-stilbazole has been reported (1-4). We wish to report a simple chemical synthesis of **2a** and three derivatives containing methyl substituents in the hetero ring.



An unsuccessful attempt to convert the formamide **1a** to **2a** by the Bischler-Napieralski reaction (5) has been reported (6). In our hands, the readily available amides **1a-1d** were converted to the corresponding benz[*f*]isoquinoline by the two-step sequence outlined. The physical properties of compound **2a** thus obtained (see Experimental) were identical with those reported (1,2,6) for benz[*f*]isoquinoline. The benz[*f*]isoquinolines **2b-2d** represent new compounds.

The combination of this simple chemical synthesis and the photochemical synthesis (1-3) should provide a convenient approach to a variety of benz[*f*]isoquinolines.

## EXPERIMENTAL (7)

## 2-(1-Naphthyl)ethylamine.

This compound was prepared by the method of Schleigh, *et al.* (8).

## 1-Methyl-2-(1-naphthyl)-1-nitroethylene.

A mixture of 1-naphthaldehyde (31.24 g., 0.2 mole), ammo-

nium acetate (12.8 g.), and nitroethane (22.5 g., 0.3 mole) in glacial acetic acid (90 ml.) was refluxed two hours. The mixture was cooled and poured onto ice. The oil that separated gradually solidified. The solid was collected, washed well with water, and dissolved in chloroform. The chloroform solution was washed once with a saturated sodium chloride solution and then passed through a short Florisil column. The eluate was concentrated and the residue recrystallized from ethanol-water (80%). The yellow crystals were collected and air-dried to yield the desired product, 26.0 g., 60%, m.p. 62-65°. A sample was recrystallized from ligroin (b.p. 35-60°) to yield pale yellow crystals, m.p. 66-69°.

*Anal.* Calcd. for  $C_{13}H_{11}NO_2$ : C, 73.2; H, 5.2; N, 6.6. Found: C, 73.5; H, 5.5; N, 6.2.

## 1-Methyl-2-(1-naphthyl)ethylamine.

A solution of 1-methyl-2-(1-naphthyl)-1-nitroethylene (21.52 g., 0.10 mole) in anhydrous ether (280 ml.) was added dropwise with stirring to a cooled (ice bath) suspension of lithium aluminum hydride (13.28 g., 0.35 mole) in anhydrous ether (700 ml.). After the addition was complete, the mixture was stirred at room temperature for one-half hour, refluxed for one-half hour, and cooled. The excess lithium aluminum hydride was destroyed by the successive addition of water (13.3 ml.), 20% sodium hydroxide solution (10.0 ml.), then water (46.5 ml.). The precipitate that separated was collected, washed well with ether, and the combined ether solutions were treated with hydrogen chloride gas. The solid that separated was washed with ether, air-dried, and taken up in water. After the resulting solution had been treated with solid sodium carbonate until alkaline, it was thoroughly extracted with ether. The extracts were dried (anhydrous sodium sulfate), concentrated, and the oil that was obtained was distilled *in vacuo* to yield the desired product, 11.84 g., 64%, b.p. 110-114°/0.09 mm, reported (9) b.p. 136°/4 mm.

*N*-Formyl-2-(1-naphthyl)ethylamine (**1a**).

A mixture of 2-(1-naphthyl)ethylamine (2.65 g., 0.016 mole) and formamide (0.77 g., 0.017 mole) was heated on a steam bath for 24 hours, cooled, and dissolved in ether. The ether solution was washed successively with 5% hydrochloric acid, water, and a saturated sodium chloride solution, after which it was concentrated and the residue distilled *in vacuo* to yield **1a**, 2.61 g., 85%, b.p. 180-184°/0.07 mm., m.p. 82-84°, reported (6) m.p. 86°.

*N*-Formyl-1-methyl-2-(1-naphthyl)ethylamine (**1c**).

This compound was prepared in a manner identical with that for the previous compound. From 5.00 g., 0.027 mole, of the amine was obtained **1c**, 4.72 g., 82%, b.p. 167°/0.15 mm., m.p. 80-83°.

*Anal.* Calcd. for  $C_{14}H_{15}NO$ : C, 78.8; H, 7.1; N, 6.6. Found: C, 79.0; H, 7.0; N, 6.6.

*N*-Acetyl-2-(1-naphthyl)ethylamine (**1b**).

A mixture of 2-(1-naphthyl)ethylamine (8.68 g., 0.05 mole) and isopropenyl acetate (6.00 g., 0.06 mole) was heated two hours on a steam bath. The mixture was cooled and treated with ligroin (b.p. 63-75°). The solid that separated was collected, washed with

a small volume of ligroin (b.p. 64-75°), and air-dried to yield **1b**, 8.51 g., 80%, m.p. 86-88°. A sample was recrystallized from ligroin (b.p. 63-75°), affording colorless crystals, m.p. 89-92°, reported (10) m.p. 91°.

*N*-Acetyl-1-methyl-2-(1-naphthyl)ethylamine (**1d**).

This compound was prepared in a manner identical with that for the previous compound. From 5.55 g., 0.03 mole, of the amine was obtained **1d**, 5.29 g., 78%, m.p. 108-110°. Recrystallization of a sample from acetone-ligroin (b.p. 35-60°) yielded colorless crystals, m.p. 112-114°, reported (9) m.p. 114°.

Benz[*f*]isoquinoline (**2a**).

A solution of *N*-formyl-2-(1-naphthyl)ethylamine (1.58 g., 0.008 mole) in tetralin (10 ml.) was added in small portions to a refluxing suspension of phosphorus pentoxide (6.0 g.) in tetralin (40 ml.) that was protected from the atmosphere by nitrogen. After one-half hour, an additional portion (7.0 g.) of phosphorus pentoxide was added and refluxing was continued for another one-half hour. The mixture was cooled and the tetralin removed by decantation. The residue was added cautiously in small portions to a large volume of ice. After treatment of the tetralin in the same fashion, the resulting aqueous acidic solutions were combined and washed with ether. The acidic solutions were brought to pH 8-9 with a 20% sodium hydroxide solution, then extracted with ether. The extracts were dried over anhydrous sodium sulfate and concentrated. The residue was taken up in tetralin (10 ml.) and 10% palladium on charcoal (0.5 g.) was added. The mixture was refluxed one hour, cooled, and the catalyst was removed by filtration and washed with tetralin. The combined tetralin solutions were extracted with 10% hydrochloric acid solution. The aqueous extracts were treated with 20% sodium hydroxide solution until alkaline, then extracted with chloroform. The extracts were dried over anhydrous sodium sulfate and concentrated to yield a pale yellow oil that crystallized, yielding **2a**, 315 mg., 21%, m.p. 92-95°. A portion was sublimed to yield nearly colorless crystals, m.p. 97-99°, reported (2) m.p. 98-99.5°. The spectral properties were identical with those reported in the literature (2).

In the same manner, the compounds **2b-2d** were obtained.

4-Methylbenz[*f*]isoquinoline (**2b**), 56%, m.p. 130-131°; uv,  $\lambda$  max nm (log  $\epsilon$ ) 210 (4.45), 220 (4.72), 249 (4.39), 276 (4.07), 287 (4.14), 299 (4.19), 316 (inf) (3.02), 319 (3.13), 327 (inf) (3.00), 334 (3.40), 345 (3.09), 347 (3.14), 350 (3.50); nmr  $\delta$  8.56 (D,  $J_{1,2}$  6 Hz, H-2), 8.52 (M, H-10), 8.15 (D,  $J_{1,2}$  6 Hz, H-1), 7.77 (M, 5 protons, aromatic H), 2.97 (S, C<sub>4</sub>-CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>14</sub>H<sub>11</sub>N: C, 87.0; H, 5.7; N, 7.2. Found: C, 86.9; H, 5.7; N, 7.1.

2-Methylbenz[*f*]isoquinoline (**2c**), 44%, m.p. 93-95°; uv,  $\lambda$  max nm (log  $\epsilon$ ) 211 (4.44), 213 (4.44), 215 (4.42), 220 (4.41), 242 (4.68), 244 (4.69), 250 (4.72), 273 (4.09), 284 (4.08), 296 (4.16), 308 (inf) (2.91), 315 (2.81), 318 (2.91), 322 (3.14), 330

(2.99), 333 (3.13), 337 (3.45), 345 (3.02), 349 (3.18), 354 (3.57); nmr  $\delta$  9.08 (S, H-4), 8.55 (M, H-10), 8.15 (S, H-1), 7.74 (M, 5 protons, aromatic H), 2.78 (S, C<sub>2</sub>-CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>14</sub>H<sub>11</sub>N: C, 87.0; H, 5.7; N, 7.2. Found: C, 86.6; H, 6.0; N, 7.5.

2,4-Dimethylbenz[*f*]isoquinoline (**2d**), 30%, m.p. 129-132°; uv,  $\lambda$  max nm (log  $\epsilon$ ) 214 (4.42), 222 (4.39), 228 (4.33), 249 (4.67), 270 (inf) (4.11), 280 (4.03), 291 (4.13), 304 (4.17), 319 (inf) (3.04), 321 (inf) (3.10), 323 (3.17), 332 (inf) (3.11), 334 (inf) (3.18), 335 (inf) (3.21), 338 (3.44), 350 (inf) (3.22), 354 (3.53); nmr  $\delta$  8.53 (M, H-10), 8.02 (S, H-1), 7.69 (M, 5 protons, aromatic H), 2.92 (S, C<sub>4</sub>-CH<sub>3</sub>), 2.72 (S, C<sub>2</sub>-CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>15</sub>H<sub>13</sub>N: C, 86.9; H, 6.3; N, 6.8. Found: C, 87.1; H, 6.5; N, 6.8.

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Rochester, New York 14650