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STUDIES ON POLYCYCLIC AZAARENES—1

SYNTHESIS OF ACENAPHTHO[1,2-*b*]QUINOLINES

JAYANTA K. RAY,* GANDHI K. KAR and BASANTA G. CHATTERJEE
Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India

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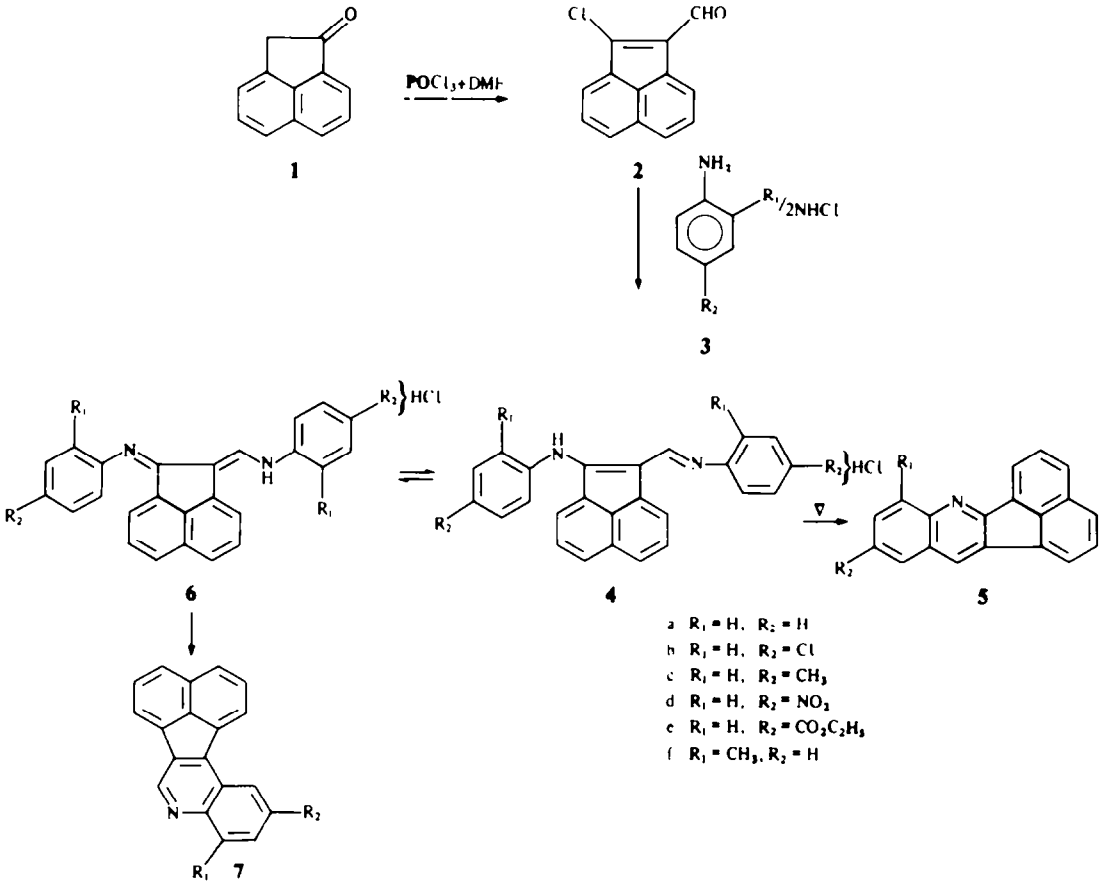
Abstract—A simple synthesis of acenaphthoquinolines by thermal cyclization of anils is described.

Polycyclic aromatic hydrocarbons and their oxidized metabolites are long known for their carcinogenic properties.[1,2] However polycyclic aza-arenes were not investigated for their biological activities until Jerina *et al.*[3] showed that benzoacridines and other poly-azaarenes are potential carcinogens. Aza-arenes are widely spread in the biosphere,[4] stimulating further interest in this group of heterocycles. An acenaphthoquinoline possess a region in its structure which is likely to be the cause for carcinogenic activity as in related polycyclic aromatic hydrocarbons.[5]

We present here a simple three steps synthesis of acenaphthoquinolines from acenaphthenone, by Vilsmeier-Haack reaction[6] (phosphoryl chloride–dimethylformamide) to produce the chloroaldehyde **2** in 75% yield, treatment with aniline or substituted anilines **3(a–f)** in ethanol to afford the corresponding anil derivatives **4(a–f)** as red crystals (90–97%). Finally, **4(a–f)** on brief heating slightly above their m.p. produced acenaphtho quinolines **5(a–f)** in good yields (46–80%). The alternative thermal cyclization[7] of the anil derivatives to produce **7** via **6** was not achieved as confirmed by spectral data, synthesis[8] and by analogy[9] with other systems. The mass spectral fragmentation pattern proves the stability of the molecules as reported by Koch *et al.*[10]

This method also provides a simple and facile entry into azabenzofluoranthrene systems.



EXPERIMENTAL

Preparation of the chlorocaldehyde (**2**)

To a stirred mixture of $POCl_3$ (2.6 g, 16 mmol) and DMF (2 ml) at 0° a soln of acenaphthenone (**1**; 1.8 g, 11 mmol) in DMF (10 ml) was added dropwise during 10 min. The mixture was allowed to attain room temp, and then stirred for 1 h and finally at 60–70° for 6 h. Then it was cooled and poured over crushed ice. Sat. soln of aq NaOAc was added to pH 5–6 giving a yellow solid which was extracted with $CHCl_3$ (2 × 50 ml), washed successively with 5% $NaHCO_3$ (1 × 100 ml) and water (2 × 250 ml). The organic layer was separated and dried (Na_2SO_4). Removal of solvent furnished an orange yellow solid (2.2 g). This on repeated crystallization from ethanol afforded 1.7 g yellow crystals (74%) m.p. 157–158°, IR ($CHCl_3$) ν_{max} 1610, 1640 and 1680 cm^{-1}, NMR δ ($CDCl_3$) 7.2–8.3 (m, 6H) 10.3 (s, 1H) ppm. UV λ_{max} (EtOH) 335 (11368), 246 (15015) nm. (Found: C, 72.43; H, 3.19%. Calc for $C_{13}H_7OCl$ C, 72.73; H, 3.26%).

General method for the preparation of anil derivatives (**4a–f**)

To a stirred soln of 6 mmol of aniline (or substituted aniline) in 25–30 ml ethanol, 2.5–3.0 ml of 2N HCl was added, then 2.5 mmol of the chloroaldehyde (**2**) in one portion. Stirring was continued for 2 h at room temp and then for 15 min under reflux. The reaction mixture was cooled in an ice bath and filtered; the solid washed with little cold ethanol and dried in air.

4A Bright red solid, m.p. 215–216° (d), yield 90%, IR (Nujol) ν_{max} 1615, 1635 and 3190 cm^{-1}. **4b** Dark red solid, m.p. 220–221° (d), yield 95–96%, IR (Nujol) ν_{max} 1618, 1632 and 3150 cm^{-1}. **4c** Dark red solid, m.p. 227–228° (d), yield 98%, IR (Nujol) ν_{max} 1615, 1640 and 3175 cm^{-1}. **4d** Bright red solid, m.p. 335–336° (d), yield 91%, IR (Nujol) ν_{max} 875, 1340, 1562, 1600, 1655, 3100 and 3200 cm^{-1}. **4e** Dark red solid, m.p. 180–181° (d) yield 61%, IR (Nujol) ν_{max} 1612, 1640, 1670, 1725 and 3450 cm^{-1}. **4f** Bright red solid, m.p. 219–220° (d) yield 96%, IR (Nujol) ν_{max} 1616, 1635 and 3150 cm^{-1}.

General method for the preparation of acenaphthoquinolines (**5a–f**)

The anil derivative was heated slightly above its m.p. for 5–10 min in a large test-tube. Aniline (or substituted aniline) hydrochloride deposited in the cooler part of the test-tube. The cooled mass was extracted with CH_2Cl_2 and passed through a short column of neutral alumina. Removal of CH_2Cl_2 afforded the desired solid which was purified from CH_2Cl_2–pet ether or benzene–pet ether.

5a Colourless solid, m.p. 180° (lit[8] 180–181°) yield 50–55%, NMR δ($CDCl_3$) 7.36–8.59 (m, 11H) ppm, MS, *m/e* 253 (M^+, 100%) other peaks are less than 10%. UV λ_{max} ($CHCl_3$) 380 (2685), 300 (10998), 254 (10894) nm. **5b** Colourless solid, m.p. 195°, yield 58%, NMR δ($CDCl_3$) 7.24–8.40 (m, 10H) ppm, MS, *m/e* 287.1 (M^+, 100%). UV λ_{max} ($CHCl_3$) 384 (2543), 314 (26980), 285 (23442) and 255 (24216) nm. (Found: C, 79.15; H, 3.18; N, 4.75. Calc for $C_{19}H_{10}NCl$ C, 79.30; H, 3.48; N, 4.87%). **5c** Colourless solid, m.p. 176° yield 46%, NMR δ($CDCl_3$) 7.24–8.36 (m, 10H) 2.44 (s, 3H) ppm, MS, *m/e* 267 (M^+, 100%). UV λ_{max} ($CHCl_3$) 383 (2368), 303 (13198), 258 (12594) nm. (Found: C, 89.72; H, 4.65; N, 5.11. Calc for $C_{20}H_{13}N$ C, 89.89; H, 4.87; N, 5.25%). **5d** Bright yellow solid, m.p. 280° yield 80%, IR (Nujol) ν_{max} 1340 and 1577 cm^{-1}, NMR δ(DMSO-d_6 + $CDCl_3$) 7.52–8.96 (m, 10H) ppm, MS, *m/e* 298 (M^+, 100%) 252 (63%). UV λ_{max} ($CHCl_3$) 367 (9628), 300 (12894), 253 (12836) nm. (Found: C, 76.29; H, 3.15; N, 9.42. Calc for $C_{19}H_{10}N_2O_2$ C, 76.51; H, 3.36; N, 9.40%). **5e** Colourless solid, m.p. 176–177°, yield 61%, IR ($CHCl_3$) ν_{max} 1710 cm^{-1}, NMR δ ($CDCl_3$) 7.24–8.46 (m, 10H) 4.46 (q, 2H) 1.44 (t, 3H) ppm, MS, *m/e* 325 (M^+, 100%), 280 (66%), 252 (63%). UV λ_{max} ($CHCl_3$) 340 (16250), 315 (21369), 275 (21044), 256 (19175) nm. (Found: C, 81.11; H, 4.45; N, 4.19. Calc for $C_{22}H_{15}NO_2$ C, 81.23; H, 4.62; N, 4.31%). **5f** Colourless solid, m.p. 168° yield 42%, NMR δ ($CDCl_3$) 7.30–8.49 (m, 10H) 2.97 (s, 3H) ppm. UV λ_{max} ($CHCl_3$) 388 (2206), 368 (3250), 317 (25771), 305 (25539), 256 (27860) nm. (Found: C, 89.69; H, 4.52; N, 5.17. Calc for $C_{20}H_{13}N$ C, 89.89; H, 4.87; N, 5.24%).

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