Synthesis of a 4-Hydroxyisoquinolin-1-one and a Related Dibenzo[a,g]quinolizin-8-one

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Aqueous acid converts the imidazo[4,3-a]isoindol-5-one 2 to a 4-hydroxyisoquinolin-1-one (3). A related imidazoisoindolone 6, obtained by photochemical cyclization of the Mannich base from 1,2,3,4-tetrahydro-isoquinoline, formaldehyde and phthalimide, gives a dibenzo[a,g]quinolizin-8-one (7) in a similar reaction.

J. Heterocyclic Chem., 17, 1131 (1980).

N-Substituted phthalimides can take part in a variety of photochemical reactions (1), and photochemical cyclization by way of hydrogen transfer to the oxygen atom of the excited imide group provides a useful route to a variety of heterocyclic systems (2). We have reported (3) that photocyclisation of N-(dibenzylaminomethyl)phthalimide (1) gives an imidazo[4,3-a]isoindol-5-one derivative (2), and that the mechanism probably involves initial electron transfer in the $(n,\pi)^*$ singlet state (4). We now report that treatment of the photoproduct 2 with aqueous acid gives rise to a 4-hydroxyisoquinolin-1-one (3), whose structure is amply confirmed by analytical and spectral data.

The reaction with acid involves formal loss of formaldimine; several plausible mechanisms can be written to account for this process, each of which begins with ringopening to form a fused 1,3-diazocine-4,7-dione system 4. The mechanism that we favour involves a subsequent retro-Mannich reaction followed by a ring-closure step to give a protonated tautomer of the isolated product.

As part of a study of multicyclic heterocycles we prepared the Mannich base 5 from phthalimide, formaldehyde and 1,2,3,4-tetrahydroisoguinoline. Photo-

chemical cycylisation of this compound gives the pentacyclic isoindolo[2',1':3,4]imidazo[5,1-a]isoquinolin-5-one 6 in good yield. The orientation of ring-closure corresponds to initial abstraction of a hydrogen atom from a benzylic methylene group (C-1 of the tetrahydroisoquinoline ring in 5) rather than from a non-benzylic group. Only one stereoisomer of 6 was produced, to which we assign the structure shown. This assignment is made on the basis of molecular models (which show quite severe steric strain in the other isomer) and by a comparison of spectral data with those from the two stereoisomers of 2 (the imidazo ring CH₂ protons appear at δ 4.13 and 4.46 for 6, compared with δ 4.05 and 4.42 for the corresponding stereoisomer of 2, and δ 3.66 and 4.75 for the opposite stereoisomer of 2).

Acid treatment of 6 leads to a reaction analogous to that of 2, and the product is a dibenzo[a,g]quinolizin-8-one (7). The ring system in this compound is the same as that in the naturally occurring dibenzoquinolizinium ion coralyne.

EXPERIMENTAL

2-Benzyl-2,3,5,9b-tetrahydro-1-phenyl-1H-imidazo[4,3-a]isoindol-5-one (2).

The preparation of this compound has been described (3).

2-Benzyl-4-hydroxy-3-phenylisoquinolin-1-one (3).

Photoproduct 2 (1.9 g.) was heated under reflux for 2 hours with aqueous hydrochloric acid (2M, 100 cm³). The residual solid (1.2 g.) was filtered and recrystallised from ethanol to give 0.54 g. (31%) of 3 as white crystals, m.p. 122° dec.; ir (Nujol): 3300 (m), 1645 (m), 1580 (s) cm⁻¹; nmr (DMSO-d₆): 8.6-6.7 (m, 14H), 5.13 (s, 2H); ms: m/e 327, 236, 222, 91.

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.70; H, 5.24; N, 4.28. Found: C, 80.73; H, 5.49; N, 4.25.

N(1,2,3,4-Tetrahydroisoquinolin-2-ylmethyl)phthalimide (5).

Finely ground phthalimide (20.0 g.), 1,2,3,4-tetrahydroisoquinoline (15.0 g.) and formalin (40%, 11 ml.) were warmed in ethanol (175 ml.) until solution occurred. The precipitate obtained on cooling was recrystallised from ethanol to give 23.0 g. (70%) of 5, m.p. 132-134°; ir (Nujol): 1765 (m), 1700 (s) cm⁻¹; nmr (deuteriochloroform): 8.0-7.2 (m, 4H), 7.03 (s, 4H), 4.75 (s, 2H), 3.8 (s, 2H), 2.92 (s, 4H).

Anal. Calcd. for C₁₈H₁₆N₂O₂: C, 73.94; H, 5.53; N, 9.58. Found: C, 74.04; H, 5.39; N, 9.50.

9,10,14b,14c-Tetrahydro-14c-hydroxy-7*H*-isoindolo[2',1':3,4]imidazo[5,1-a]isoquinolin-5-one (6).

Mannich base 5 (5.0 g.) was irradiated (Hanovia 450 watt medium pressure mercury arc, Pyrex filter) in Analar benzene (300 ml.) for 10 hours. The solvent was partially removed and the residual solid recrystallised from benzene to give 2.62 g. (52%) of 6, m.p. 182-183°; ir (Nujol): 3000 (m, broad), 1695 (s) cm⁻¹; nmr (deuteriochloroform): 8.0-6.7 (m, 8H), 4.43 (s, 1H), 4.46 and 4.13 (two d, 2H), 3.8 (broad, 1H), 3.0-1.8 (m, 4H)

Anal. Calcd. for C₁₈H₁₆N₂O₂: C, 73.94; H, 5.53; N, 9.58. Found: C, 73.92; H, 5.48; N, 9.59.

5,8-Dihydro-13-hydroxy-6H-dibenzo[a,g]quinolizin-8-one (7).

Compound 6 (0.81 g.) was heated under reflux with aqueous hydrochloric acid (2M, 100 ml.) for 2 hours. Recrystallisation of the residual solid from ethanol gave 0.41 g. (55%) of 7 as pale yellow crystals, m.p. $\sim 200^{\circ}$ dec.; ir (Nujol): 3100 (m), 1635 (s), 1615 (s) cm⁻¹; nmr (DMSO-d₆): 9.5-7.0 (m, 8H), 4.24 (t, J = 6, 2H), 2.95 (t, J = 6, 2H); ms: m/e 263, 248, 184, 124, 105, 91.

Anal. Calcd. for C₁₇H₁₈NO₂: C, 77.54; H, 4.99; N, 5.33. Found: C, 77.51; H, 5.10; N, 5.28.

REFERENCES AND NOTES

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