OXIDATIVE AMINATION OF 6-HYDROXYQUINAZOLINE

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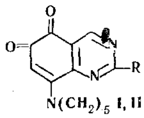
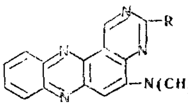
In connection with the search for physiologically active compounds, the synthesis of the first representative of a new class of heterocyclic quinones – quinazoline-5,8-quinone – was described in 1970 [1]. In order to develop an accessible method for the preparation of substituted quinazolinequinones, we studied the oxidation of 6-hydroxyquinazoline by oxygen in the presence of a Cu^{2+}–piperidine complex. Having the oxidation of 6-hydroxybenzothiazole under these conditions in view [2] as well as the ease with which nucleophilic attack of quinazoline at the 4-position is realized [3], we assumed that one of the piperidine residues in the quinone obtained was situated at C_8 and that the second was situated at C_2 or C_4. The PMR spectrum of the quinone confirms this but does not make it possible to unambiguously determine the position of the second piperidine residue. To establish the structure of the quinone we oxidized 2-phenyl-6-hydroxyquinazoline [4], which gave 2-phenyl-8-piperidinoquinazoline-5,6-quinone (II). On the basis of this, the product of oxidation of 6-hydroxyquinazoline was assigned the 2,8-dipiperidinoquinazoline-5,6-quinone structure (I). The o-quinoid structure of quinones I and II is confirmed by the formation of derivatives III and IV with o-phenylenediamine. Derivatives III and IV are the first representatives of the heretofore undescribed heterocyclic pyrimido[5,4-a]phenazine system.



I, II



III, IV

I, III $R = N(CH_2)_5$; II, IV $R = C_6H_5$

EXPERIMENTAL

2,8-Dipiperidinoquinazoline-5,6-quinone (I). This was obtained in 88% yield and had mp 206-208 deg (from benzene). IR spectrum: 1668, 1625, 1590, 1564, 1538, 1516 cm^{-1}. UV spectrum (in ethanol), λ_{max}, nm (log ε): 246 (4.32), 294 (3.90), 342 (4.18), 390 (4.22). PMR spectrum in $CDCl_3$ (δ, ppm): 1.75 (singlet, β, γ-CH_2), 3.93 (doublet, J 14 Hz, α-CH_2), 6.20 (singlet, H-7), 9.07 (singlet, H-4). Found %: C 66.6; H 6.8; N 17.4. $C_{18}H_{22}N_4O_2$. Calc. %: C 66.3; H 6.8; N 17.2.

2-Phenyl-8-piperidinoquinazoline-5,6-quinone (II). This was obtained in 84% yield and had mp 179-181 deg [from chloroform–hexane (2:1)]. IR spectrum, cm^{-1}: 1693, 1618, 1576, 1553, 1538 (shoulder). UV spectrum (in ethanol), λ_{max} (log ε): 230 (4.20), 280 (4.31), 324 (4.31). PMR spectrum in $CDCl_3$ (δ, ppm): 1.90 (singlet, β, γ-CH_2), 3.93 (singlet, α-CH_2), 6.29 (singlet, H-7). Found %: C 71.7; H 5.5; N 13.2. $C_{19}H_{17}N_3O_2$. Calc. %: C 71.5; H 5.4; N 13.2.

3,5-Dipiperidinopyrimido[5,4-a]phenazine (III). This compound had mp 241-242 deg (from benzene). Found %: C 72.5; H 6.7; N 21.1. $C_{24}H_{26}N_6$. Calc. %: C 72.3; H 6.7; N 21.1.

3-Phenyl-5-piperidinopyrimido[5,4-a]phenazine (IV). This compound had mp 225-226 deg [from acetone–water (3:1)]. Found %: C 76.5; H 5.5; N 17.7. $C_{25}H_{21}N_5$. Calc. %: C 76.7; H 5.4; N 17.9.

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