SELECTIVE HYDROGENATION OF NITRO DERIVATIVES OF HYDROQUINOLINES

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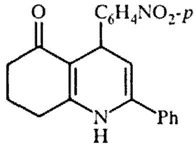
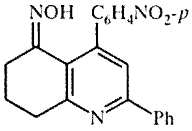
By catalytic hydrogenation of p-*nitrophenylhydroquinolines with 5-oxo- and 5-oxime functional groups in the presence of heterogeneous palladium complex catalysts, we have obtained the corresponding amino derivatives.*

Application of metal-complex catalysts in organic chemistry has made it possible to develop original and promising methods for synthesis of different nitrogen-containing derivatives [1, 2], including those having an amino group [3].

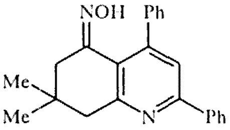
Earlier we [4, 5] described compounds of the tetrahydro- and hexahydroquinoline series with oxo-, nitro-, and oxime groups, the selective reduction of which provide a route for obtaining the corresponding amino derivatives. Accordingly, in this paper we have accomplished the hydrogenation of 5-oxo-2-phenyl-4-(4-nitrophenyl)-1,4,5,6,7,8-hexahydroquinoline (I), oximes of 2-phenyl-4-(4-nitrophenyl)- (II), 7,7-dimethyl-2,4-diphenyl- (III), and 7,7-dimethyl-2,3-diphenyl-5-oxo-5,6,7,8-tetrahydroquinolines (IV):



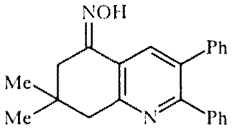
I



II

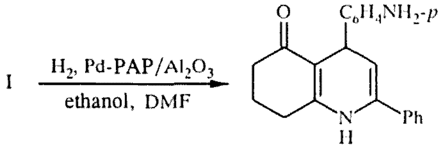


III

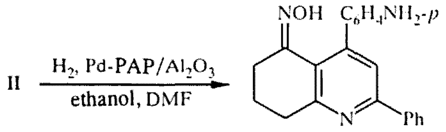


IV

As the catalysts, we used palladium(II) complexes with 4-(2-pyridylazo)resorcinol (Pd—PAR) and with 1-phenyl-3-methylpyrazol-5-one (Pd-PYR) supported on aluminum oxide, which have displayed effectiveness in reduction of the NO_2 group in aromatic and some heterocyclic compounds [3, 6]. Hydrogenation of the hydroquinoline derivatives I-IV was carried out at atmospheric pressure and a temperature of 25-50°C.



V



VI

Scientific—Research Institute of Chemistry at Saratov State University, Saratov 410026. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1138-1140, August, 1995. Original article submitted June 8, 1995.

Despite the presence in substrates I and II of several potential reduction centers (the nitro-, oxo-, and oxime functional groups and also the C=C and C=N multiple bonds of the phenyl and hydroquinoline rings), under our conditions (independently of the catalyst) only selective reduction of the nitro group to the amino group occurs, with formation of respectively 5-oxo-2-phenyl-4-(4-aminophenyl)-1,4,5,6,7,8-hexahydroquinoline (V) and 5-oxo-2-phenyl-4-(4-aminophenyl)-5,6,7,8-tetrahydroquinoline (VI). We should note that the reaction of hydrogenation of substrates I and II stops after absorption of the three moles of hydrogen required for reduction of the nitro group to the amino group.

In the IR spectra of products V and VI, bands appear for the stretching vibrations of the NH_2 group at 3360 and 3450 cm^{-1} (for V) or 3380 and 3460 cm^{-1} (for VI); the secondary amino group in compound V appears as a band at 3225 cm^{-1}. We also note the presence of absorption bands for stretching vibrations of the C=O group in the spectrum of the oxoquinoline V (1680 cm^{-1}) and the oxime functional group in the spectrum of the oxime VI (3150 cm^{-1}), and also the absence in both spectra of the characteristic bands for the stretching vibrations of the NO_2 group in the region 1240-1360 and 1500-1550 cm^{-1}.

In the PMR spectra of compounds V and VI, there are singlet signals from protons of the amino group at 4.52 and 4.41 ppm, which disappear upon deuteration.

Attempts to reduce the oxime group in substrates III and IV in the presence of complex catalysts did not meet with success — in all cases, we isolated the starting compounds.

Thus the use of metal complex catalysts allows us to accomplish selective reduction of nitro derivatives of heterocycles to the corresponding amines — potentially biologically active compounds and synthons in organic synthesis.

EXPERIMENTAL

The IR spectra were taken on a Specord IR-75 spectrometer (in Vaseline oil or hexachlorobutadiene). The PMR spectra were taken on a Varian-80A instrument (in DMSO-d_6), internal standard TMS.

The starting hydroquinolines I and II were synthesized using the familiar technique in [4, 5]. The metal complex catalysts were synthesized according to the techniques in [6, 7].

IR spectra and melting points were used to identify compounds V and VI. The course of the hydrogenation was monitored using TLC on Silufol UV-254 plates in the system hexane—chloroform—ether, 3:1:1 with detection in UV light or iodine vapor.

The elemental analysis data for C, H, and N in the hydrogenation products correspond to the calculated values.

Hydrogenation of 5-Oxo-2-phenyl-4-(4-nitrophenyl)-1,4,5,6,7,8-hexahydroquinoline (I). 0.3 g Pd-PAR/Al_2O_3 or Pd-PYR/Al_2O_3 catalyst (1 g catalyst contains 6 × 10^{-2} millimoles palladium) in 10 ml ethanol was placed in a thermostatted glass long-necked flask and 0.003 g (7 × 10^{-2} millimoles) sodium borohydride was added under a stream of hydrogen. After twenty-minute activation of the catalytic system with hydrogen, 0.35 g (1.0 millimoles) compound I in 10 ml DMF was added. Hydrogenation was carried out at a temperature of 25-50°C at atmospheric pressure with vigorous mixing on a laboratory shaker until absorption of hydrogen stopped. The catalyst was filtered off, the solvent was partially evaporated at reduced pressure, the residue of product was filtered off and recrystallized from ethanol. Yield, 0.27 g (85%). T_{mp} 232-235°C (decomp.). PMR spectrum: 7.03-7.52 (8H, m, H_{arom}); 6.60 (1H, d, 3-H); 6.23 (1H, d, 4-H); 4.52 (2H, s, NH_2); 2.03 ppm (6H, s, $3CH_2$). Found, %: C 79.31, H 6.74, N 8.95. $C_{21}H_{20}N_2O$. Calculated, %: C 79.71, H 6.37, N. 8.86.

Hydrogenation of the Oxime of 5-Oxo-2-phenyl-4-(4-nitrophenyl)-5,6,7,8-tetrahydroquinoline (II). Hydrogenation was carried out as described for compound I. Yield of product VI, 0.3 g (90%). T_{mp} 260-266°C. PMR spectrum: 10.93 (1H, s, OH); 7.66-8.20 (9H, m, H_{arom}); 7.43 (1H, d, 3-H); 5.15 (2H, s, NH_2); 2.75, 2.09 ppm (6H, s.s, $3CH_2$). Found, %: C 76.70, H 5.81, N 12.45. $C_{21}H_{21}N_3O$. Calculated, %: C 76.10, H 6.39, N 12.68.

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