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Mild hydrogenation of quinoline 1. Role of reaction parameters

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Abstract

The hydrogenation of quinoline (Q) under mild conditions was studied using commercial Pd, Rh or Ru/Al_2O_3 catalysts. Using Pd and Rh/Al_2O_3, the main product obtained was the partially hydrogenated 1,2,3,4-tetrahdroquinoline (py-THQ), while Ru/Al_2O_3 was inactive. The synthesis of the fully hydrogenated decahydroquinoline (DHQ) was not observed, since the irreversible adsorption on the active sites of a reaction intermediate(s) formed in the step, Q → py-THQ. No modification was observed in this adsorption with increasing temperature and pressure or with the addition of a Brønsted acid or base. On the contrary, the addition of a strong and sterically hindered Lewis base allowed the partial formation of DHQ, hampering the irreversible adsorption of intermediate(s). © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Quinoline hydrogenation; Mild pressure and temperature; Rh/Al_2O_3; Pd/Al_2O_3; Catalyst poisoning; 1,2,3,4-Tetrahydroquinoline

1. Introduction

Hydrogenation of quinoline (Q) and its derivatives is of considerable industrial interest for the production of petrochemicals [1], fine chemicals and pharmaceuticals [2–4]. Different metals (Pd, Ni, Rh, Pt, Cu, etc.) supported on different solids (Al_2O_3, coal, keiselguhr, etc.) have been tested for the hydrogenation of Q to decahydroquinoline (DHQ) in the liquid phase. This reaction is essentially carried out in two steps [5] (Fig. 1). Mainly 1,2,3,4-tetrahydroquinoline (py-THQ) and a small amount of 5,6,7,8-tetrahydroquinoline (bz-THQ) are formed in the first step, while complete hydrogenation of both intermediates to DHQ occurs in the second step. The reaction conditions required for the first step include a reaction temperature of 373 K, hydrogen pressure from 0.1 to 7.0 MPa and the use of an alcohol as the solvent [6–8]. The complete hydrogenation is the most difficult step. Conversion of py-THQ to DHQ requires a longer reaction time and more drastic reaction conditions, typically at a temperature in the range 448–533 K, hydrogen pressure between 11.0 and 21.0 MPa and the use of an acid as the solvent [9,10].

However, these conditions are very far from those required in the production of pharmaceuticals to hydrogenate weak intermediates containing a Q ring [11]. Using boron-derived reducing agents, such as $Zn(BH_4)_2$ [12] or $NaCNBH_3$ [13], it is possible to obtain py-THQ only from Q. The objective of the present study was to investigate the hydrogenation of Q under mild conditions using a commercial catalyst.

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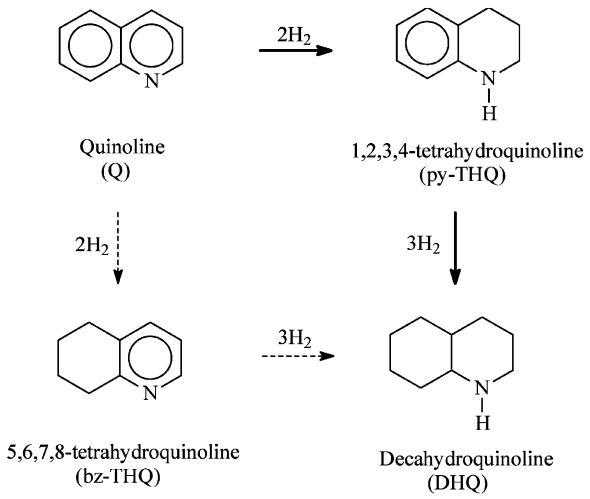

Fig. 1. Reaction pathway for Q hydrogenation.

2. Experimental section

Three commercial catalysts supplied by Engelhard containing 5 wt.% of supported metal were employed: Rh, Pd and Ru/Al_2O_3. The catalysts were obtained in reduced form from the producer and used as received without any further treatment. Q (98%), py-THQ (98%), *N*,*N*-diisopropylethylamine (99%) and isopropanol (98%) were obtained from Aldrich Chemicals and used as received without any previous purification. The tests were carried out using a 300 ml stainless steel Parr reactor equipped with magnetic stirrer and digital oven temperature control instrument. The standard conditions for experiments were: 0.45 g catalyst, 15.0 ml Q or py-THQ, 135.0 ml isopropanol, 2.0 MPa hydrogen pressure and 373 K reaction temperature. Before heating, the autoclave was always purged three times with helium at 0.3 MPa. When the system reached the reaction temperature, hydrogen was introduced at the set pressure and the reaction started. The reaction mixtures were periodically sampled and analysed by gas chromatography using a Perkin-Elmer Autosystem XL equipped with a PE-5 column (30 m × 0.25 mm, film thickness 0.25 μm) and FID detector, while the qualitative analyses were carried out using a GC-MS Hewlett-Packard GCD 1800A system equipped with an HP-5 column (30 m × 0.25 mm, film thickness 0.25 μm) and mass spectrometer detector. The yields reported are referred to the starting Q or py-THQ, depending on the feed employed.

3. Results and discussion

Hydrogenation of Q carried out at standard reaction conditions (373 K and $P_{H_2} = 2.0$ MPa) showed

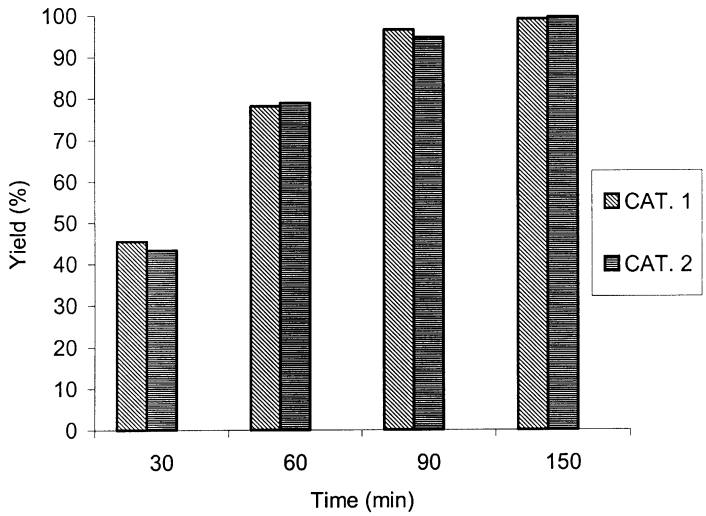

Fig. 2. Yield in py-THQ obtained with Rh/Al_2O_3 (Cat. 1) and Pd/Al_2O_3 (Cat. 2) catalysts ($W_{cat} = 0.45$ g, Q = 15.0 ml, isopropanol = 135.0 ml, $T = 373$ K, $P_{H_2} = 2.0$ MPa).

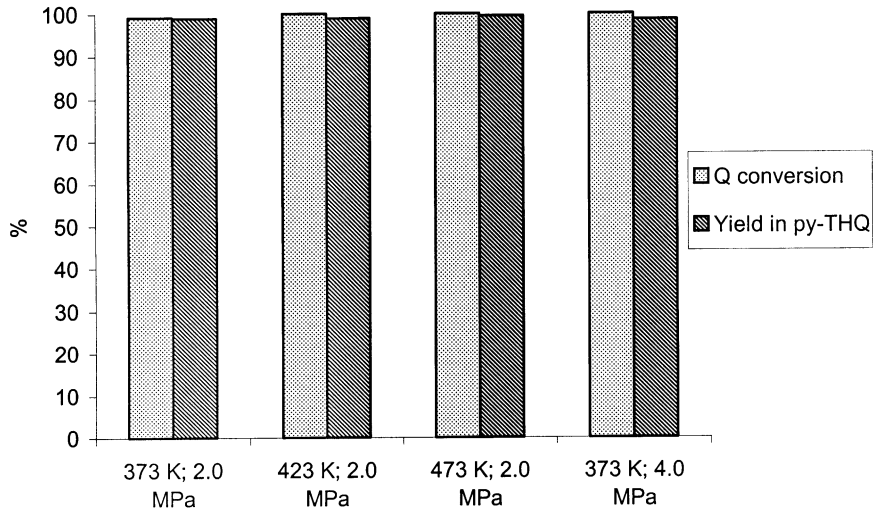

Fig. 3. Q conversion and yield in py-THQ obtained with the Rh/Al_2O_3 catalyst at different pressures and temperatures (W_{cat} = 0.45 g, Q = 15.0 ml, isopropanol=135 ml, reaction time = 150 min).

comparable results for the Pd and Rh/Al_2O_3 catalysts, with complete Q conversion after 150 min mainly to py-THQ and only in small amounts to bz-THQ (yield < 1.5%) (Fig. 2). On the contrary, the Ru/Al_2O_3 catalyst was almost completely inactive. The conversion of Q was faster with Rh/Al_2O_3 than with Pd/Al_2O_3 at higher temperatures and thus, the investigation was continued using only Rh/Al_2O_3 as the catalyst. The formation of DHQ was not detected either when the temperature was increased to 473 K or when the pressure was increased to 4.0 MPa (Fig. 3). Formation of hydrogenolysis products was not detected; the only by-product observed was bz-THQ with a yield always lower than 1.5%.

It may be hypothesised that the formation mainly of py-THQ is due to a low activity of the catalyst in the hydrogenation of py-THQ to DHQ under these reaction conditions and/or to its deactivation due to a strong adsorption of py-THQ on the active sites. Thus, a new test at standard conditions was carried out, starting from py-THQ instead of Q. After 150 min of reaction conversion of the py-THQ feed to DHQ was complete. This result shows that Rh/Al_2O_3 is sufficiently active to give rise to DHQ under standard reaction conditions and that py-THQ is not responsible for catalyst deactivation. Thus, the different result obtained with Q has to be attributed to a reaction intermediate formed in the hydrogenation of Q to py-THQ, strongly adsorbed on the catalyst active sites. This hypothesis was confirmed by adding a fresh catalyst aliquot to the reaction mixture after the complete hydrogenation of Q to py-THQ. Formation of DHQ was detected, with a yield comparable to that obtained in the test with py-THQ as the feed (Fig. 4).

It is possible to hypothesise that the poisoning of active sites may be due to 1,4-dihydroquinoline, 1,2-dihydroquinoline or 3,4-dihydroquinoline (Fig. 5); although our results do not allow their discrimination. The intermediate(s) probably competes for active sites, hampering the adsorption of py-THQ but not completely that of Q. This last assumption was confirmed by feeding a new portion of Q after the total conversion of the previous Q feed to py-THQ, which resulted in a further conversion of 65.0% after 150 min. Hypothesising that acid or basic media may modify the adsorption equilibrium of intermediate(s) on the active sites, new tests were carried out with Q plus the addition of a Brønsted acid or base. The test in acid media was carried out by adding increasing amounts of acetic acid after the complete hydrogenation of Q to py-THQ (Table 1A). No formation of DHQ was observed even after the addition of excess acetic acid. On the other hand, the addition of a small amount of a 3 M NaOH solution completely inhibited

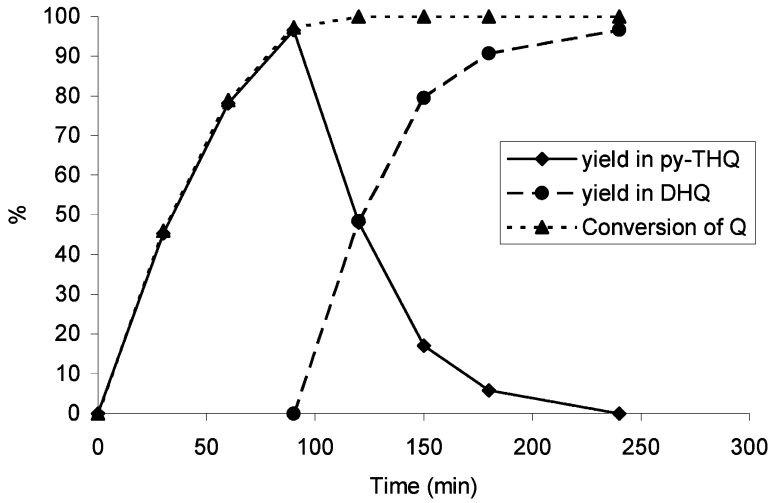

Fig. 4. Conversion of Q and yields in py-THQ and DHQ obtained under standard reaction conditions with the Rh/Al_2O_3 catalyst ($W_{cat} = 0.45$ g, Q = 15.0 ml, isopropanol = 135.0 ml, $T = 373$ K; $P_{H_2} = 2.0$ MPa). After 90 min of reaction time another 0.45 g of the Rh/Al_2O_3 catalyst was added.

the Q conversion (Table 1B). Thus, a Brønsted acid media does not affect the adsorption equilibrium on the active sites of the catalyst, while a base interacts with them too strongly.

It is reasonable to assume that the adsorption of the reaction intermediate(s) on the active sites is due to the aromatic ring and takes place mainly via the nitrogen electron doublet. Thus, addition of a Lewis base to the reaction mixture may modify the adsorption equilibrium of the reaction intermediate(s) by competitive adsorption, favouring the complete hydrogenation of Q to DHQ. The choice of the appropriate Lewis base was carried out considering that it had to be stable in reaction conditions and without any catalytic activity in the aromatic substitution of Q. A new test was carried out feeding a reaction mixture containing *N*,*N*-diisopropylethylamine (molar ratio Q/*N*,*N*-diisopropylethylamine = 1/1), i.e. a strong base [14] which has sufficient steric hindrance to avoid too strong adsorption on the active sites, as probably occurred when NaOH was added. Indeed, DHQ was formed, with a yield of 16.8% (Fig. 6), confirming the

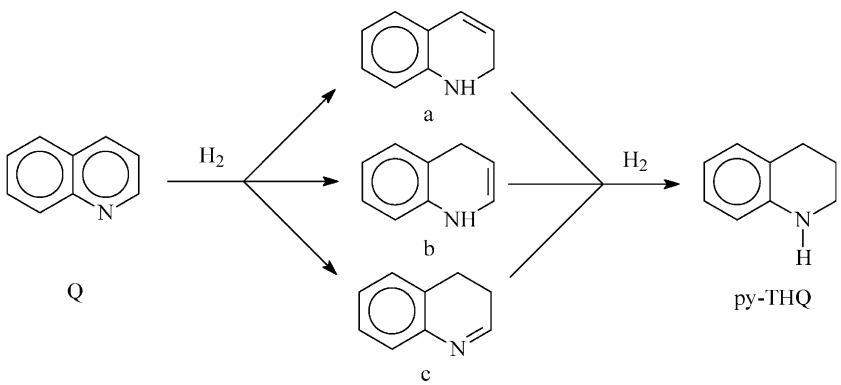

Fig. 5. Possible reaction intermediates responsible for deactivation of the catalyst during the hydrogenation of Q to py-THQ: 1,2-dihydroquinoline (a), 1,4-dihydroquinoline (b) and 3,4-dihydroquinoline (c).

Table 1
Q conversion and yield in py-THQ obtained by the addition of a Brønsted acid or base with the Rh/Al_2O_3 catalyst ($W_{cat} = 0.45$ g, Q = 15.0 ml, isopropanol = 135.0 ml, $T = 373$ K, $P_{H_2} = 2.0$ MPa)

Reaction time (min)	Acid or base/Q molar ratio	Q conversion (%)	Yield in py-THQ (%)
(A) Hourly additions of acetic acid after the first 150 min of reaction			
150	0.00	99.5	98.3
210	0.02	100.0	98.7
270	0.07	100.0	98.7
330	0.30	100.0	98.7
390	1.20	100.0	98.6
(B) Addition of a 3 M NaOH solution after the first 90 min of reaction			
90	0.00	84.8	83.7
120	0.02	84.8	83.7
150	0.02	85.2	84.1
180	0.02	85.2	84.1

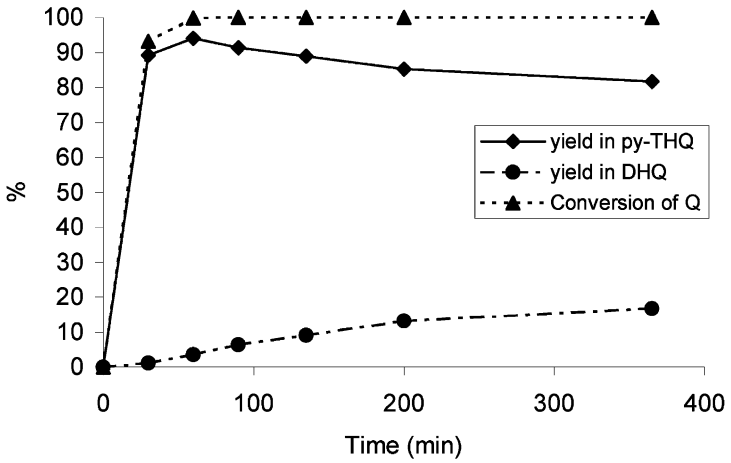

Fig. 6. Conversion of Q and yields in py-THQ and DHQ obtained, feeding *N,N*-diisopropylethylamine and Q ($W_{cat} = 0.45$ g, Q = 7.5 ml, *N,N*-diisopropylethylamine = 11.2 ml, isopropanol=135.0 ml, $T = 373$ K, $P_{H_2} = 2.0$ MPa).

hypothesis that a Lewis base may partially avoid the poisoning of the catalyst active sites.

4. Conclusions

The liquid phase hydrogenation of Q in mild conditions is only partial and gives rise mainly to py-THQ, probably due to of the formation of reaction intermediate(s) strongly adsorbed on catalyst active sites. The addition of a Brønsted acid does not allow complete hydrogenation to DHQ to be obtained, while with the addition of a Brønsted base, the catalytic activity is completely lost. On the contrary, the complete hydrogenation of Q was partially obtained by addition of a Lewis base (*N,N*-diisopropylethylamine). Probably, an aromatic amine could give better results. The presence of an sp^3 hybridised nitrogen and an aromatic ring provides aromatic amines with proprieties intermediate between those of py-THQ and the reaction intermediate(s) responsible for catalyst deactivation.

Another means to avoid deactivation of the catalyst may be to increase the metal dispersion, analogous to that observed for Pt-cinchonidine heterogeneous catalysts, used for the stereoselective hydrogenation of methyl pyruvate [15]. In fact, for a platinum particle

size smaller than 4 nm, a decrease in enantioselectivity has been observed [16–18] due to lower adsorption onto the metal surface and/or hydrogenation of the Q ring of cinchonidine. Work is presently in progress to verify this hypothesis as well as to extend the results obtained with *N*,*N*-diisopropylethylamine to aromatic amines to study the effects of steric hydrance, basicity and electronic properties.

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References

[1] G. Perot, Catal. Today 10 (1991) 447.
[2] R.T. Shuman, P.L. Ornstein, J.W. Paschal, P.D. Gesellchem, J. Org. Chem. 55 (1990) 738.
[3] J.M. Schaus, D.L. Huser, R.D. Titus, Synth. Commun. 20 (1990) 3553.
[4] P. Bouyssou, C. Le Goff, J. Chenault, J. Heterocycl. Chem. 29 (1992) 895.
[5] C.W. Curtis, D.R. Cahela, Energy Fuels 3 (1989) 168.
[6] H. Adkins, H.R. Billica, J. Am. Chem. Soc. 70 (1948) 695.
[7] J.E. Shaw, P.R. Stapp, J. Heterocycl. Chem. 24 (1987) 1477.
[8] F. Santangelo, C. Casagrande, G. Miragoli, V. Vecchietti, Eur. J. Med. Chem. 20 (1994) 877.
[9] M. Freifelder, Adv. Catal. 14 (1963) 203.
[10] S. Tsushima, S. Sudzuki, J. Chem. Soc. Jpn. 64 (1943) 1295; Chem. Abstr. 41 (1947) 3801c.
[11] J.F. Gerster, S.R. Rohlfing, S.E. Pecore, R.M. Winandy, R.M. Stern, J.E. Landmesser, R.A. Olsenand, W.B. Gleason, J. Med. Chem. 30 (1987) 839.
[12] B.C. Ranu, U. Jana, A. Sarkar, Synth. Commun. 28 (1998) 485.
[13] A. Srikrishna, T.J. Reddy, R. Viswajanani, Tetrahedron 52 (1996) 1631.
[14] L.A. Carpino, A. El-Faham, J. Org. Chem. 59 (1994) 695.
[15] Y. Orito, S. Imai, S. Niwa, Nippon Kagaku Kaishi 8 (1979) 1118; Chem. Abstr. 91 (1979) 192483h.
[16] G. Webb, P.B. Wells, Catal. Today 12 (1992) 319.
[17] J.T. Wehrli, A. Baiker, D.M. Monti, U. Blaser, J. Mol. Catal. 61 (1990) 207.
[18] S.D. Jackson, M.B.T. Keegan, G.D. McLellan, P.A. Meheux, R.B. Moyes. G. Webb, P.B. Wells, R. Whyman, J. Willis, in: G. Poncelet, P.A. Jacobs, P. Grange, B. Delmon (Eds.), Preparation of Catalysts V, Elsevier, Amsterdam, 1991, p. 135.