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FACILE DEHYDROGENATION AND AN UNEXPECTED CATALYTIC HYDROGEN TRANSFER REACTION OF 1,2,5,6,7,8-HEXAHYDROQUINAZOLIN-4(3H)-ONES

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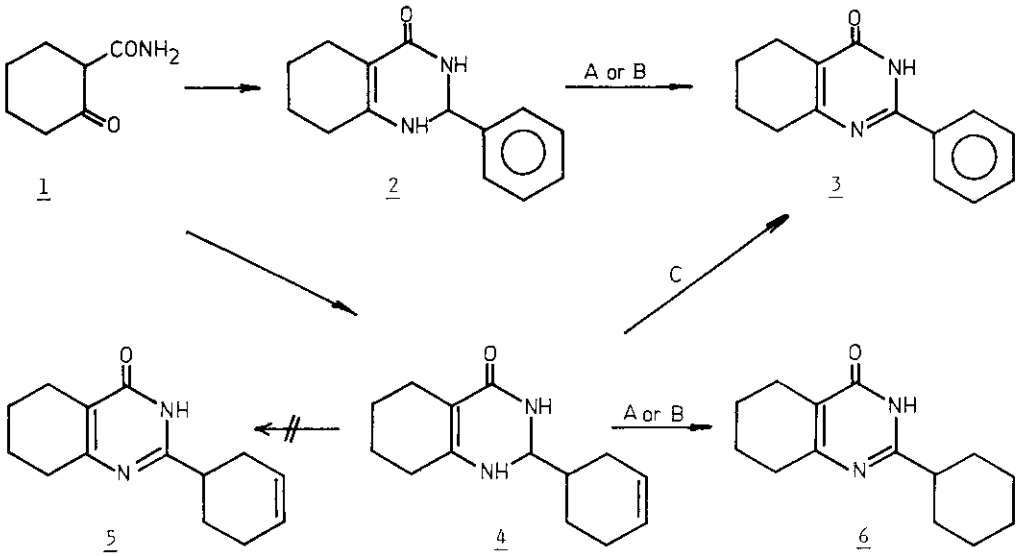
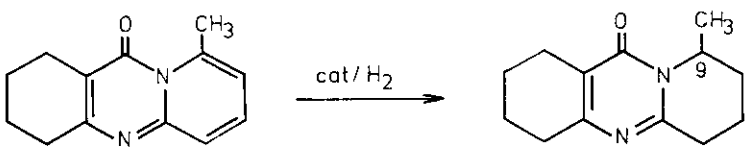
Abstract - 2-Phenyl-1,2,5,6,7,8-hexahydroquinazolin-4(3H)-one (2) and the related 2-(3'-cyclohexenyl) derivative (4) were observed to undergo a facile dehydrogenation and an intermolecular catalytic hydrogen transfer in the presence of Pd/C, even in a hydrogen atmosphere.

In a continuation of our work on bicyclic, fused-skeleton 1,3-heterocycles (see, e.g. refs.[2,3]), 2-phenyl-1,2,5,6,7,8-hexahydroquinazolin-4(3H)-one[7] (2) has been synthesized from 1[5,6] for the comparative polarographic investigation[4] of variously saturated pyrimidin-4-ones condensed with an alicyclic ring. When 2 (0.5 g) was stirred in ethanol for 10 h at ambient temperature and pressure under a hydrogen atmosphere in the presence of 5% palladium-on-charcoal (0.1 g) (Method A), instead of reduction an unexpected dehydrogenation was observed, which gave the 5,6,7,8-tetrahydroquinazoline derivative 3. Refluxing 2 in toluene with Pd/C for 30 min (Method B) also afforded 3, in nearly quantitative yield.

2-(3'-Cyclohexenyl)-1,2,5,6,7,8-hexahydroquinazolin-4(3H)-one (4) was synthesized from 1 with 1,2,5,6-tetrahydrobenzaldehyde in the presence of ammonium hydroxide, similarly as for the preparation of 2. Via Method A in 10 h, 4 gave 2-cyclohexyl-5,6,7,8-tetrahydroquinazolin-4(3H)-one (6). Interestingly, when Method B was used, the 2-cyclohexenyl derivative 4 was not dehydrogenated to 5, but a catalytic hydrogen transfer reaction occurred to give the 2-cyclohexyl derivative 6 again. This conversion belongs to the rare group of hydrogen transfer reactions[8] in which the transfer takes place in the same molecule, containing a hydrogen donor and an acceptor unit.



In order to prove the intermolecular character of the observed hydrogen transfer, an equivalent amount of 9-methyl-1,2,3,4-tetrahydropyrido[2,1-b]quinazolin-11-one[9] (7) was added to 4; ring C of 7 can readily be reduced, and thus it may act as a proton acceptor in the reaction. The crude product obtained by Method B from the mixture of 4+7 contained, according to ^{1}H NMR evidence, about 20% of the octahydro compound[9,10] 8. The latter was identified by the H(9) signal, which appears in a comparatively low field (δ = 4.9 ppm) owing to the anisotropic effect of the C=O group,[9,10] and also the doublet of the axial 9-CH_3 at δ = 1.35 ppm (J = 6 Hz). When pure 8[9] was added to the crude product, these signals unequivocally increased. Formation of the octahydro derivative 8 unambiguously proves that the catalytic hydrogen transfer 4 → 6 is an intermolecular process.



When 4 was refluxed in the presence of Pd/C for 30 min in the strongly proton acceptor solvent nitrobenzene (Method C), the product was surprisingly neither the expected cyclohexenyl derivative 5 nor 6, but the 2-phenyl derivative 3; hence, both dehydrogenation of the hetero ring and aromatisation of the cyclohexenyl ring took place.

Further study of the aromatisation reaction 2 → 3 is in progress.

No.[12]	Mp (°C) Solvent	Yield[a] (%)	^{1}H NMR chemical shifts (δ_{TMS} = 0 ppm) Aliphatic protons	H(2)	ArH m- and p-hydrogens	ArH o-hydrogens
2	153-155° EtOH (lit.[11]: 154-156°)	64	1.57, 1.76, 2.16, 2.31	5.70 (s, 1H)	7.40 (m, 3H)	7.52 (m, 2H)
3	248-250° EtOAc (lit.[9]: 246-247°)	80 (A) 94 (B) 72 (C)	1.81, 2.60 2.76 (3xm, 8H)	-	7.51 (m, 3H)	8.23 (m, 2H)
4[b]	172-174° EtOH		1.24-2.7 (m, 14H)	4.58 (d, 1H J ~5.5 Hz)	-	-
6	199-201° EtOAc	77 (A) 84 (B)	1.35, 1.79, 2.52, 2.64 (4xm, 19H)	-	-	-

[a] The method used is given in brackets. [b] $\delta_{CH=CH}$ = 5.70 ppm (s, 2H).

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REFERENCES AND NOTES

1. Part 92: S. Stankovic, Á. Kapor, B. Ribár, L. Karanovic, A. Kálmán, Gy. Argay, G. Stájer and G. Bernáth, J. Mol. Structure, accepted for publication.
2. F. Fülöp, G. Bernáth, Gy. Argay, A. Kálmán and P. Sohár, Tetrahedron, 1984, 40, 2053.
3. F. Fülöp, G. Bernáth, P. Sohár and I. Pelczer, J. Chem. Soc. Perkin Trans. 1, 1984, 2043.
4. P. Pflegel, Ch. Kühmstedt, F. Fülöp and G. Bernáth, Pharmazie, 1983, 38, 373; 1984, 39, 106; P. Pflegel, Ch. Kühmstedt, J. Lázár and G. Bernáth, Pharmazie, 1984, 39, 39.
5. G. Zigeuner and G. Gübitz, Monatsh., 1970, 101, 1547 and references cited therein.
6. C. Bischoff and H. Herma, J. Prakt. Chem., 1976, 318, 773; C. Bischoff, E. Schröder and E. Gründemann, J. Prakt. Chem., 1984, 326, 849.
7. C. Bischoff, H. Herma and E. Schröder, J. Prakt. Chem., 1976, 318, 895.
8. G. Brieger and T. J. Nestrick, Chem. Rev., 1974, 74, 567.
9. G. Bernáth, F. Fülöp, I. Hermecz, Z. Mészáros and G. Tóth, J. Heterocyclic Chem., 1979, 16, 137.
10. I. Hermecz, B. Podányi, Z. Mészáros, J. Kökösi, Gy. Szász and G. Tóth, J. Heterocyclic Chem., 1983, 20, 92.
11. G. Bernáth, T. Janáky, Gy. Göndös, J. Lázár and Z. Ecsery, Pharmazie, 1983, 38, 270.
12. All prepared compounds gave satisfactory microanalyses. IR spectra were recorded in KBr pellets with a SPECORD 75 IR instrument. ^{1}H NMR spectra were recorded in $CDCl_3$ solution at 250 MHz with a Bruker WM-250-FT spectrometer at room temperature, using TMS as internal standard.

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