

SATURATED HETEROCYCLES. 93¹.

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

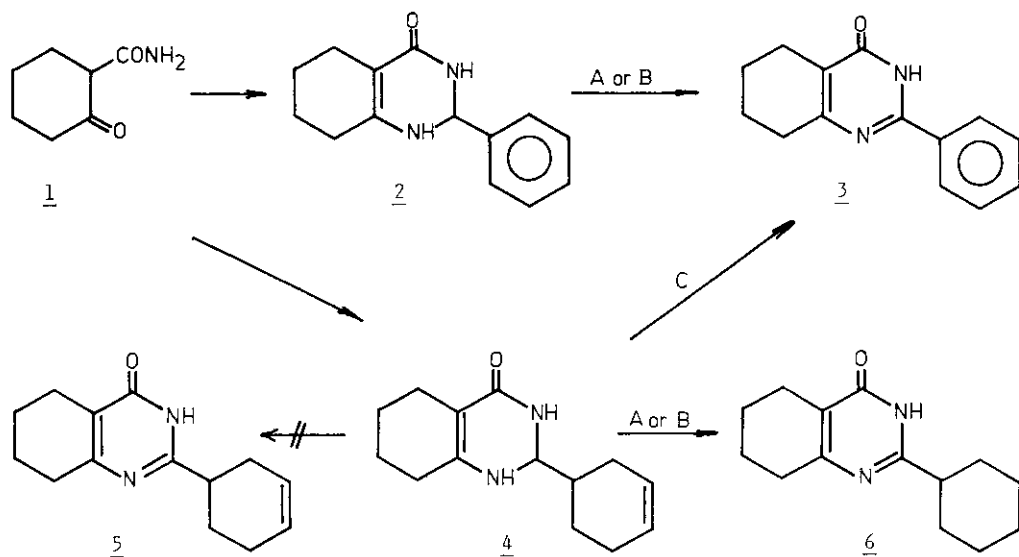
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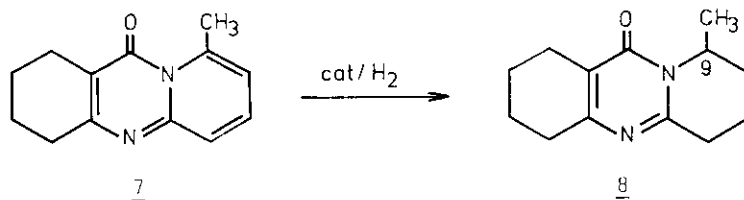
Abstract - 2-Phenyl-1,2,5,6,7,8-hexahydroquinazolin-4(3H)-one (2) and the related 2-(3'-cyclohexenyl) derivative (4) were observed to undergo a facile dehydrogenation and an intermolecular catalytic hydrogen transfer in the presence of Pd/C, even in a hydrogen atmosphere.

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)-one⁷ (2) has been synthesized from 1^{5,6} for the comparative polarographic investigation⁴ 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 reactions⁸ 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-one⁹ (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 ¹H 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 ($\delta = 4.9$ ppm) owing to the anisotropic effect of the C=O group,^{9,10} and also the doublet of the axial 9-CH₃ at $\delta = 1.35$ ppm ($J = 6$ Hz). When pure 8⁹ 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 \rightarrow 3 is in progress.

No. 12	Mp ($^{\circ}$ C) Solvent	Yield ^a (%)	¹ H NMR chemical shifts ($\delta_{TMS} = 0$ ppm)			
			Aliphatic protons	H(2)	m- and p- hydrogens	o-
<u>2</u>	153-155 $^{\circ}$ EtOH (lit. ¹¹ : 154-156 $^{\circ}$)	64	1.57, 1.76, 2.16, 2.31	5.70 (s, 1H)	7.40 (m, 3H)	7.52 (m, 2H)
	248-250 $^{\circ}$ EtOAc (lit. ⁹ : 246-247 $^{\circ}$)	80 (A) 94 (B) 72 (C)	1.81, 2.60 2.76 (3xm, 8H)	-	7.51 (m, 3H)	8.23 (m, 2H)
<u>4</u> ^b	172-174 $^{\circ}$ EtOH		1.24-2.7 (m, 14H)	4.58 (d, 1H $J \sim 5.5$ Hz)	-	-
<u>6</u>	199-201 $^{\circ}$ 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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12. All prepared compounds gave satisfactory microanalyses. IR spectra were recorded in KBr pellets with a SPECORD 75 IR instrument. ¹H NMR spectra were recorded in CDCl₃ solution at 250 MHz with a Bruker WM-250-FT spectrometer at room temperature, using TMS as internal standard.

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