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OCTAHYDRO-7(1H)-QUINOLONES. VI.[1] ON THE INTERCONVERSION OF N-SUBSTITUTED CIS- AND TRANS-DECAHYDROQUINOLINE-2,5-DIONES

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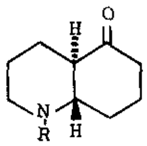
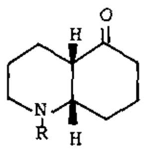
Abstract —— The equilibrium points for the isomerization of cis- and trans-decahydroquinoline-2,5-dione analogues (5 and 6) were investigated under basic and acidic conditions. The results can be explained by taking account of the equilibrium constant (K_2) for conformer 5′ (cis) ⇌ trans-isomer (6).

Two contrasting results have been reported concerning the isomerization experiments on decahydroquinolin-5-ones: in N-methyl compounds (1a and 2a) an equilibrium mixture with predominance of the trans-isomer (1a) was obtained while in N-benzoyl compounds (1b and 2b) the trans-isomer was irreversibly converted into the cis-isomer.[3,4] Such an interesting phenomenon has also been found in a series of



1 a: R=Me
b: R=COPh



2 a: R=Me
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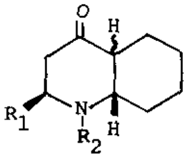
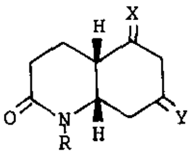
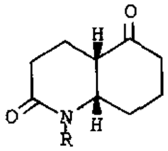


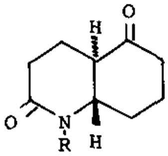
3 R_1=H, R_2=COPh
R_1=Me, R_2=H



4 R=H, Me, CH_2Ph
X=H_2, O, OCH_2CH_2O
Y=H_2, O, OCH_2CH_2O



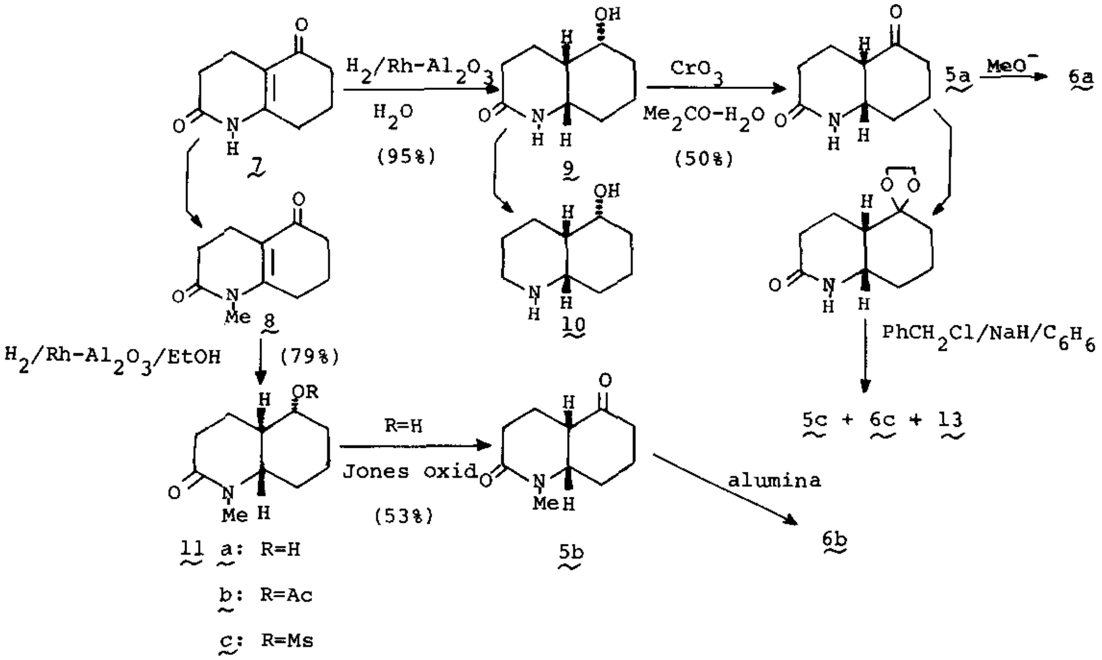
5 a: R=H
b: R=Me
c: R=CH_2Ph



6 a: R=H
b: R=Me
c: R=CH_2Ph

decahydroquinolin-4-ones (3).[5] In a previous report,[1] we have described the conformational equilibrium in *cis*-octahydrocarbostyrils (4), and, on the basis, we deal here with the systematic experiments on interconversion of N-substituted *cis*- and *trans*-decahydroquinoline-2,5-diones (5 and 6).[6]

The preparation of 5 and 6 was furnished starting from the readily available vinylogous imides (7 and 8)[3,7] as briefly depicted below.



The stereochemistry of 9 was confirmed by its transformation into a known compound (10), and that of 11 was assigned on the basis of ^{1}H-NMR spectral evidences on its O-acetyl and O-mesyl derivatives (11b and 11c).

Conditions employed for isomerization of 5 and 6 comprise their treatments with a) sodium methoxide in methanol at room temperature and b) p-toluenesulfonic acid in boiling benzene. Results of the interconversions are summarized in Table I. Determination of the *cis*/*trans* ratios was based on the integration of each C$_{8a}$-proton signal[8] for *cis*- and *trans*-isomers in ^{1}H-NMR spectra.

Under kinetic control, enol or enolate is known to be formed by removal of an axial proton attached to the carbon atom adjacent to the carbonyl group.[9] Therefore, the *trans*-isomer (6) or conformer 5' of the *cis*-isomer (5) gives the isomerization intermediate (12) *via* enolization while conformer 5'' remains unchanged. And the interconversion under the basic condition is interpreted as a result of sum of

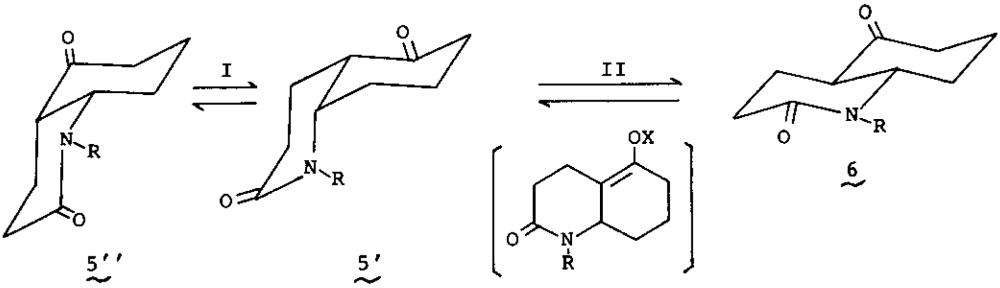
Table I. Interconversion of cis- and trans-decahydroquinoline-2,5-diones

Compounds	Conditions	Relative Ratio cis	: trans
5a	A, 24 hr	42	58
	B, 15 hr	45	55
5b	A, 24 hr	77	23
	B, 3 hr	75	25
5c	A, 24 hr	85	15
	B, 3 hr	67	33
6a	A, 24 hr	46	54
	B, 15 hr	39	61
6b	A, 24 hr	73	27
	B, 5 hr	74	26
6c	A, 24 hr	71	29
	B, 7 hr	67	33

A: MeONa in MeOH at room temperature.
B: p-TsOH in boiling benzene.

equilibriums I and II: equilibrium I is the one between conformer 5'' and 5', and equilibrium II is the other between conformer 5' and the trans-isomer (6). The equilibrium constants (K_1) for equilibrium I ($5'' \rightleftharpoons 5'$) are given from our previous report,[1] and the equilibrium constants (K_0) for the whole isomerization ($5 \rightleftharpoons 6$) are calculated on the basis of the values in Table I. Thereby, the values of the equilibrium constant (K_2) for equilibrium II ($5' \rightleftharpoons 6$) are calculated according to the equation:

$$K_0 = \frac{[6]}{[5'] + [5'']} = \frac{K_2[5']}{[5'] + [5']/K_1} = \frac{K_2}{1 + 1/K_1}$$



5''

5'

12

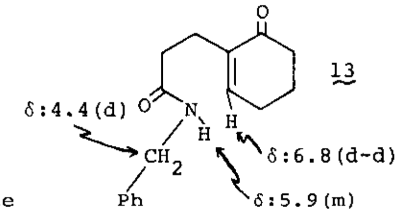
6

Table II. The values of equilibrium constants

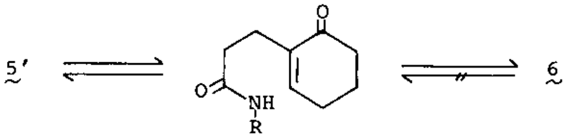
N-Substituent (R)	K_1	K_0	K_2
R=H	2.1	1.38	2.0
R=Me	0.41	0.299	1.0
R=CH_2Ph	0.19	0.176	1.1

These values are summarized in Table II. The difference in K_2 values reflects the conformational situation where the severe steric interaction between the N-substituent (R) and C_8-methylene operates for R=Me or CH_2Ph in both 5' and 6 while small for R=H.[1] And as a result, the *trans*-isomer is favored for R=H while the *cis*-isomer is favored for R=Me, CH_2Ph. This concept is widely applicable to other related systems,[3,4] i.e. 1 and 2.

Under the acidic condition, a small amount of an α,β-unsaturated ketone (13) was isolated when the N-substituent is benzyl.[10] Formation of 13 indicates the concomitant alternative route for the isomerization. This route involves the retro-Michael cleavage of the N-C_{8a} bond similarly to the isomerization of the octahydro-7(1H)-quinolone system.[6] The *trans*-isomer seems to be accumulated *via* this route under the acidic condition, and thereby the proportions of the *trans*-isomers (5c and 6c) are somewhat higher than those under the basic condition.



13



REFERENCES AND NOTES

1. The previous paper entitled "Conformational Equilibrium in *cis*-Octahydrocarbostyrils." [T. Momose, T. Miyata, and T. Imanishi, *Heterocycles*, 1978, 9, 17] constitutes Part V of this series.
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6. In Part III [T. Momose, S. Uchida, E. Hosoya, M. Kinoshita, and T. Imanishi, *Chem. Pharm. Bull.*, 1978, 26, 620], we reported the *cis* ⇄ *trans* isomerization of octahydro-7(1H)-quinolone and decahydroquinoline-2,7-dione analogues.
7. E.H.M. Böhme, Z. Valenta, and K. Wiesner, *Tetrahedron Lett.*, 1965, 2441.
8. The signal appears in good separation between both isomers and in the region remote from the other ring protons.
9. H.O. House,"Modern Synthetic Reactions," W.A. Benjamin, Inc. Menlo Park, California, 1972, Chapter 9.
10. When R is methyl, a similar intermediate seems to be also formed but fails to be isolated.

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