

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

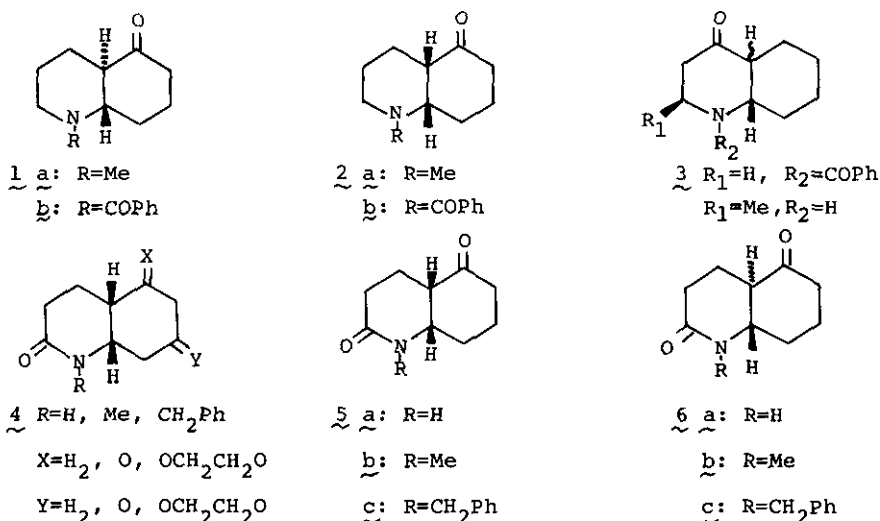
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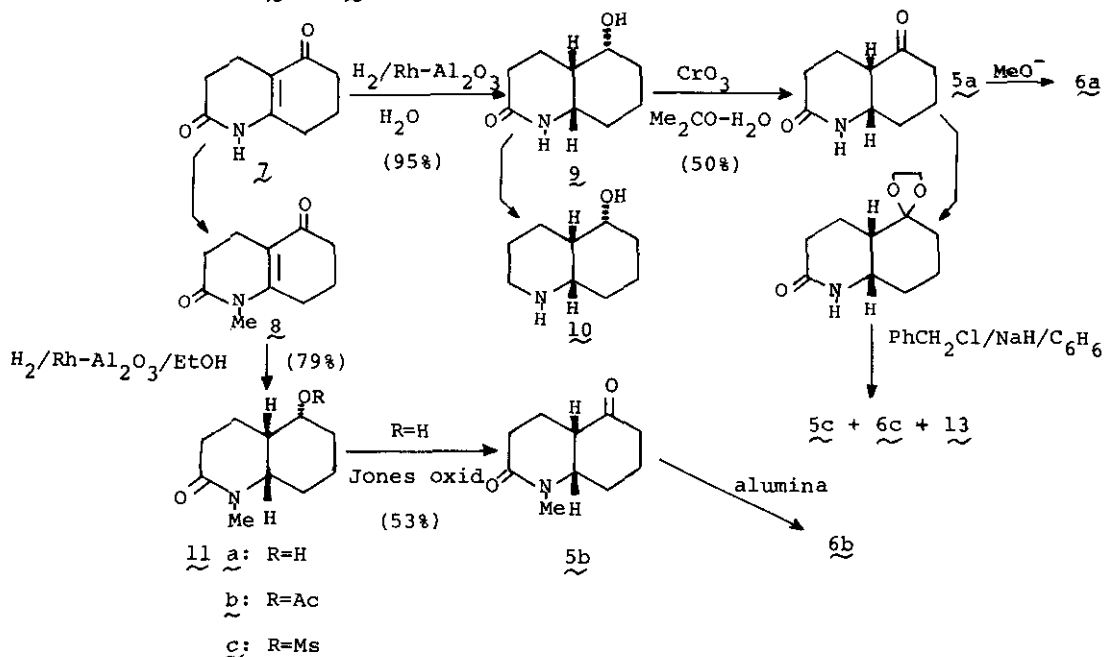
**Abstract** — The equilibrium points for the isomerization of cis- and trans-decahydroquinoline-2,5-dione analogues (5 and 6) were investigated under basic and acidic conditions. The results can be explained by taking account of the equilibrium constant ( $K_2$ ) for conformer 5' (cis)  $\rightleftharpoons$  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.<sup>3,4</sup> Such an interesting phenomenon has also been found in a series of



decahydroquinolin-4-ones (3).<sup>5</sup> In a previous report,<sup>1</sup> 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).<sup>6</sup>

The preparation of 5 and 6 was furnished starting from the readily available vinylogous imides (7 and 8)<sup>3,7</sup> 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 <sup>1</sup>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<sub>8a</sub>-proton signal<sup>8</sup> for cis- and trans-isomers in <sup>1</sup>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.<sup>9</sup> 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	
		<i>cis</i>	<i>trans</i>
<u>5a</u>	A, 24 hr	42	58
	B, 15 hr	45	55
<u>5b</u>	A, 24 hr	77	23
	B, 3 hr	75	25
<u>5c</u>	A, 24 hr	85	15
	B, 3 hr	67	33
<u>6a</u>	A, 24 hr	46	54
	B, 15 hr	39	61
<u>6b</u>	A, 24 hr	73	27
	B, 5 hr	74	26
<u>6c</u>	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 ( $\underline{5''} \rightleftharpoons \underline{5}'$ ) are given from our previous report,<sup>1</sup> and the equilibrium constants ( $K_0$ ) for the whole isomerization ( $\underline{5} \rightleftharpoons \underline{6}$ ) are calculated on the basis of the values in Table I. Thereby, the values of the equilibrium constant ( $K_2$ ) for equilibrium II ( $\underline{5}' \rightleftharpoons \underline{6}$ ) are calculated according to the equation:

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

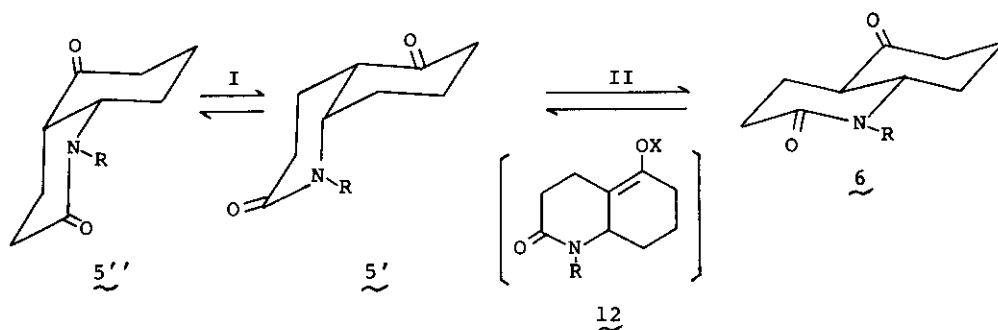


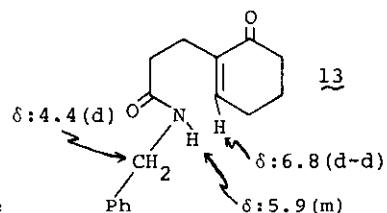
Table II. The values of equilibrium constants

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 <sub>2</sub> Ph	0.19	0.176	1.1

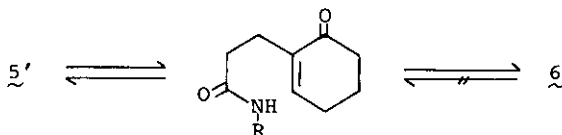
These values are summarized in Table II. The difference in  $K_2$  values reflects the conformational situation where the severe steric interaction between the N-substituent (R) and  $C_8$ -methylene operates for R=Me or  $CH_2Ph$  in both 5' and 6 while small for R=H.<sup>1</sup> And as a result, the 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,<sup>3,4</sup> i.e. 1 and 2.

Under the acidic condition, a small amount of an  $\alpha,\beta$ -unsaturated ketone (13) was isolated when the N-substituent is benzyl.<sup>10</sup> 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.<sup>6</sup> 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.



#### REFERENCES AND NOTES

1. The previous paper entitled "Conformational Equilibrium in cis-Octahydrocarbo-styryls." [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  $\rightleftharpoons$  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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