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Octahydro-7(1*H*)-quinolones. III.[1] *cis-trans* Isomerization of Octahydro-7(1*H*)-quinolone Analogues[2]

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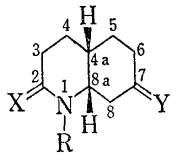
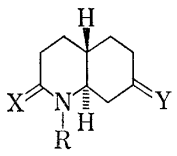
The isomerization reaction of N-nonsubstituted (**1** and **3**), N-benzylated (**4** and **5**), and N-benzoylated octahydro-7(1*H*)-quinolones (**6** and **7**) and decahydroquinoline-2,7-dione derivatives (**8**—**15**) was investigated under various acidic and basic conditions. Except for the N-benzoyl-7-ones (**6** and **7**), isomerization features were interpreted as the phenomenon associated both with the facility of the *cis*-isomers and the difficulty of the *trans*-ones in the retro-Michael ring opening to form amino enone intermediates and with predominance of the *cis*-ring junction over the *trans*-one in the subsequent recyclization of the intermediates. Isomerization of N-benzoyloctahydro-7(1*H*)-quinolone resulted in the exclusive formation of the *cis*-ketone (**6**) and in the successful isolation of the intermediate (**18**). The contrasting feature was interpreted by assuming both the facile ring opening of the *trans*-ketone (**7**) possibly *via* a cyclic process (**7'**) and the retarded recyclization of **18**, due to a reduced nucleophilicity of the amido nitrogen, resulting in a failure in the formation of **7**.

Keywords——*cis-trans* ring isomerization; retro-Michael ring opening; E_i mechanism; stereoelectronic requirement; kinetic effect; 1,3-diaxial interaction; AB type benzylic methylene signal; ^{1}H–NMR (PMR)

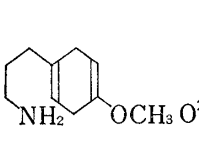
In the preceding paper,[1] we reported the exclusive formation of *cis*-octahydro-7(1*H*)-quinolone (**1**) from the enone precursor (**2**). This result seems to conflict with the prediction[4] that the cyclization would be reversible as a result of ring opening through the retro-Michael



	R	X	Y
1	H	H_2	O
4	CH_2Ph	H_2	O
6	COPh	H_2	O
8	CH_2Ph	O	O
10	H	O	O
12	H	O	
14	CH_2Ph	O	



	R	X	Y
3	H	H_2	O
5	CH_2Ph	H_2	O
7	COPh	H_2	O
9	CH_2Ph	O	O
11	H	O	O
13	H	O	
15	CH_2Ph	O	



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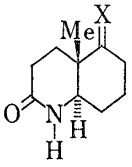
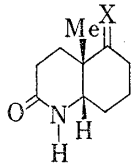
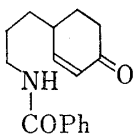


16a : X=O
b : X=H_2



17a : X=O
b : X=H_2



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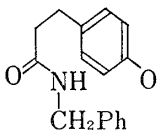

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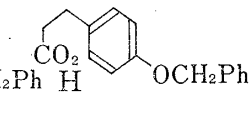

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Chart 1

1) Part II: T. Momose, S. Uchida, M. Kinoshita, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 1797 (1977).
2) *a*) A preliminary communication has appeared in *Heterocycles*, **3**, 713 (1975); *b*) This work was presented in part at the 97th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April 1977, Abstracts of papers, II, p. 62.
3) Location: *133–1, Yamada-kami, Suita, Osaka 565, Japan.*
4) C.A. Grob and H.J. Wilkens, *Helv. Chim. Acta*, **48**, 808 (1965).

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TABLE I. Isomerization Reaction of Octahydro-7(1*H*)-quinolone Analogues

Substrate	Method	Temperature (°C)	Time (hr)	Ratio *cis* : *trans*
1[a]	A	90	3	100 : 0
	B	Reflux	18.5	80 : 20
	C	Reflux	24	100 : 0
3[a]	B	Reflux	18.5	0 : 100
	C	Reflux	24	0 : 100
	D	Reflux	1.5	0 : 100
4[b]	B	Reflux	16	50 : 50
	C	Reflux	19	82 : 18
	D	Reflux	1.5	100 : 0
	E	r.t.	216	13 : 87
5[b]	B	Reflux	16	0 : 100
	D	Reflux	1.5	0 : 100
	E	r.t.	216	13 : 87
6[c]	B	Reflux	25	100 : 0
	C	Reflux	16	100 : 0
	E	r.t.	216	Decomposed
7[c]	B	Reflux	25	100 : 0
	C	Reflux	16	0 : 100
	E	r.t.	216	Decomposed

A: conc. HCl. B: *p*-TsOH-C_6H_6. C: K_2CO_3-acetone. D: 2N H_2SO_4. E: 1% KOH-EtOH. The isomer ratio was determined by *a*) benzoylation (see footnote 6 in the part II[1] of this series) and subsequent separation using preparative TLC on silica gel in ether, *b*) measurement of the signal intensity for benzylic methylene in its PMR spectrum, and *c*) separation using preparative TLC on silica gel in ether. r.t.: room temperature.

TABLE II. Isomerization Reaction of Decahydroquinoline-2,7-dione Analogues

Substrate	Method	Temperature (°C)	Time (hr)	Ratio *cis* : *trans*
8	A	Reflux	24	100 : 0
	B	Reflux	76	65 : 35[a]
	C	r.t.	43	Decomposed
	D	30	76	100 : 0
9	A	Reflux	24	0 : 100
	B	Reflux	76	14 : 86[a]
	C	r.t.	43	Decomposed
	D	30	76	0 : 100
10	B	Reflux	76	100 : 0
	D	30	76	100 : 0
	E	Reflux	48	100 : 0
	F	r.t.→60[b]	216→10[b]	Decomposed
11	B	Reflux	76	0 : 100
	D	30	76	0 : 100
	E	Reflux	48	0 : 100
	F	r.t.→60[b]	216→10[b]	Decomposed
12	C	Reflux	14	Decomposed
13	C	Reflux	14	0 : 100
14	C	Reflux	14	100 : 0
15	C	Reflux	14	0 : 100

A: *p*-TsOH-C_6H_6. B: *p*-TsOH-toluene. C: 10% aq. KOH-dioxane. D: *t*-BuOK-*t*-BuOH. E: K_2CO_3-acetone. F: 1% KOH-EtOH. The isomer ratio determination or the detection of the isomeric counterparts was performed by TLC and IR spectrum measurements except for *a*. *a*) The ratio was determined *via* separation using column chromatography on silica gel in $CHCl_3$. *b*) Means initial treatment at room temperature for 216 hr and subsequent heating at 60° for 10 hr.
r.t.: room temperature.

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process and would result in formation of the thermodynamically more stable isomer, *trans*-octahydro-7(1*H*)-quinolone (**3**). However, there has been no reported examination on the ring isomerization of this system.[5] Thus, we investigated the behavior of several octahydro-7(1*H*)-quinolone analogues toward the ring isomerization.

Results of isomerization experiments on N-hydrogen (**1**[1] and **3**[6]), N-benzyl (**4** and **5**), and N-benzoyl (**6**[1] and **7**[6]) systems of octahydro-7(1*H*)-quinolone are summarizad in Table I, and those for decahydroquinoline-2,7-diones (**8**, **9**, **10**[1], **11**[1], **12**[1], **13**[1], **14**, and **15**) in Table II. As the results, in the acidic medium (tosylic acid in benzene) the relative stability of the *trans*-systems is found to be in the order, **3**≃**5**≃**9**>**7**, and that of the *cis*-series to be in the order, **6**≃**8**>**1**>**4**. Under the basic condition (aqueous potassium hydroxide in dioxane) which was used by Fedière and co-workers[7] for the transformation of the *trans*-lactams (**16a** and **16b**) into the *cis*-lactams (**17a** and **17b**), the *cis*- (**8**, **12**, and **14**) and *trans*-lactams (**9**, **13**, and **15**) were found unchanged (Table II).

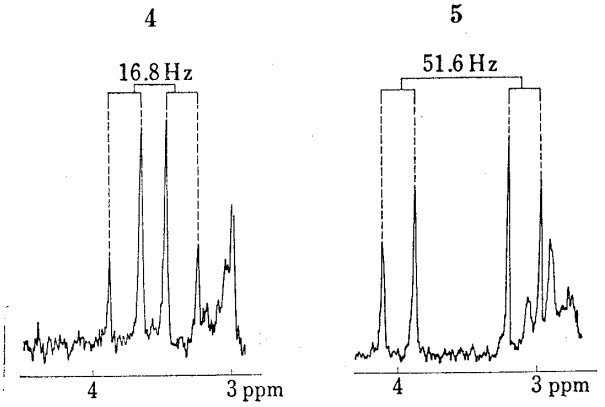

Fig. 1. The Benzyl Methylene Signals in ^{1}H–NMR Spectra of *cis*- and *trans*-N-Benzyloctahydro-7(1*H*)-quinolone (**4** and **5**) (60 MHz, in $CDCl_3$)

Determination of the stereochemistries and of the isomer compositions of the N-benzyl-7-one systems (**4** and **5**) was performed by use of the ^{1}H–NMR signals due to the benzyl methylene which appeared as an AB-type with signal separation of 16.8 Hz for **4** and 51.6 Hz for **5** (Fig. 1).[8]

On treatment with *p*-toluenesulfonic acid in boiling benzene, both of the N-benzoyl-7-ones (**6** and **7**) gave an α,β-unsaturated ketone (**18**) in 23% and 20% yields, respectively, along with the *cis*-ketone (**6**). Treatment of **18** under the condition mentioned above resulted in recyclization to *cis*-N-benzoyloctahydro-7(1*H*)-quinolone (**6**) with partial recovery of the starting material (**18**). A similar product, N-benzyl-3-(*p*-benzyloxyphenyl)propionamide (**19**), was obtained from both of *cis*- and *trans*-N-benzyldecahydroquinoline-2,7-diones (**8** and **9**) on treatment with the acid under a drastic condition. The structure of this anomalous product (**19**) was assigned from the spectral evidences (see Experimental) and confirmed by direct comparison with an authentic sample prepared from the acid (**20**)[9] and benzylamine.

Interpretation of Isomeriziaton of the N-Hydrogen- and N-Benzyloctahydro-7(1*H*)-quinolone System

There should be postulated two possible pathways for the isomerization reaction: one involves the cleavage and subsequent regeneration of the C_{8a}–N linkage *via* intermediate **21** (*i.e.* the retro-Michael and Michael process),[4] and the other involves the cleavage and regen-

5) In octahydro-4(1*H*)- or -5(1*H*)-quinolones, interconversions of *cis*- and *trans*-isomers have been reported: see R.A. Johnson, H.C. Murray, L.M. Reineke, and G.S. Fonken, *J. Org. Chem.*, **33**, 3207 (1968); C.A. Grob and H.R. Kiefer, *Helv. Chim. Acta*, **48**, 799 (1965); W.L.F. Armarego, "Stereochemistry of Heterocyclic Compounds," Vol. 1, John Wiley and Sons, Inc., New York, 1977, pp. 217—218.

6) T. Momose, S. Uchida, N. Yamaashi, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 1436 (1977).

7) J. Fedière, E. Guy, and F. Winternitz, *Ann. Chim.*, **10**, 337 (1975). They have not discussed about the pathway of these transformations.

8) The regularity that this signal separation for *trans*-decahydroquinolines is larger than that for the *cis*-counterparts has been described: see D.A. Walsh and E.E. Smissman, *J. Org. Chem.*, **39**, 3705 (1974). The feature is reversed in the decahydroquinoline-2,7-dione system (see Experimental).

9) D.G. Doherty, *J. Am. Chem. Soc.*, **77**, 4887 (1955).

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eration of the C_{8a}–C_8 linkage *via* intermediate **22** (*i.e.* the retro-Mannich and Mannich process).[10] Of these pathways, the latter could be ruled out on the basis of actual isolation of the enone intermediate (**18**) in the isomerization of the N-benzoyl-7-one system (**6** and **7**). Thus, the enone (**21**) is generated from conformer **24a** of the *cis*-7-ones (**1** and **4**) *via* an E_2 mechanism while conformer **24b** and the *trans*-7-ones (**23**) remain unchanged.[11] Owing to easy fulfilment of the stereoelectronic requirement for the pre-*cis* transition state (**25**),[12] recyclization of the enone (**21**) gives the *cis*-isomers as a main product accompanied by trace amounts of the *trans*-ones. Accumulation of the *trans*-ketones (**3** and **5**) is interpreted as a result of repeated retro-Michael and Michael processes.

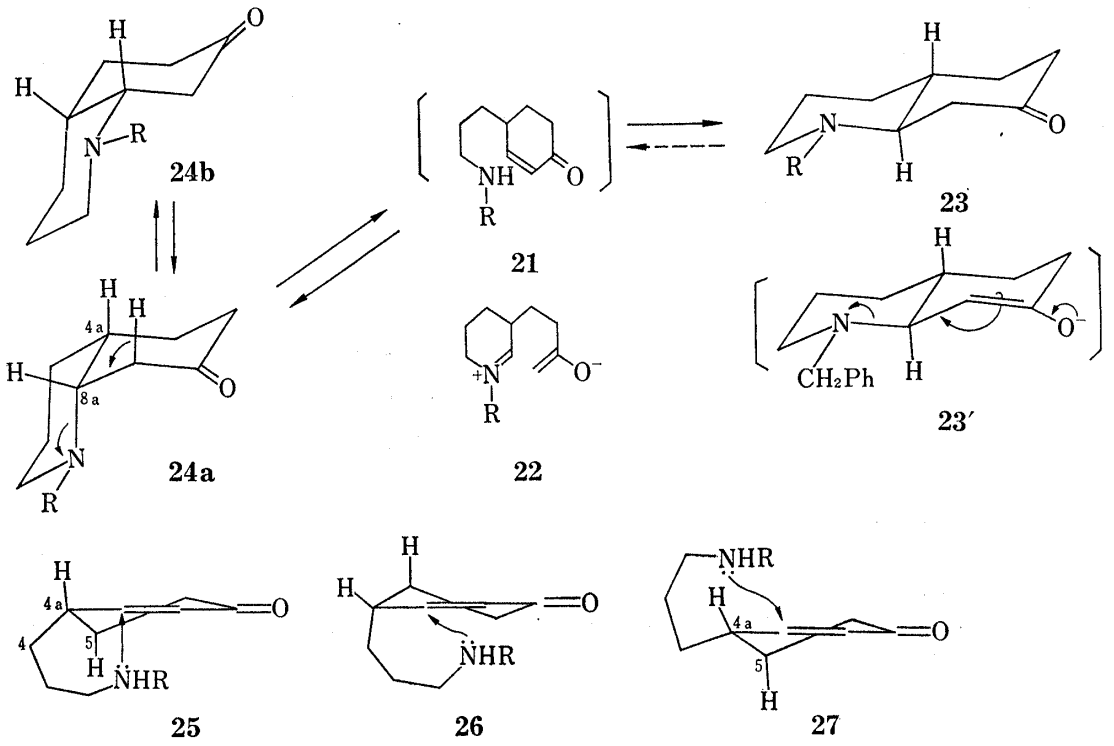

Chart 2

The apparent ease of isomeriztion of the N-benzyl-*cis*-7-one (**4**) compared to the N-hydrogen-*cis*-7-one (**1**) could be attributable to the favorable situation in the recyclization step of the enone intermediate (**21**; R=H) compared to that of **21**(R=benzyl).[13] Namely, in the recyclization step, the *trans*/*cis* ratio from **21** (R=benzyl) is expected to be higher than that from **21** (R=H) owing to the severe 1,3-diaxial interaction between the benzylamino group and the C-5 hydrogen in the transition state as depicted in **25** (R=benzyl).

Interpretation of Isomerization of the N-Benzoyloctahydro-7(1*H*)-quinolone System

It is noteworthy that the N-benzoyl-*trans*-7-one (**7**) isomerizes on acid treatment to the *cis*-ketone (**6**) exclusively. The N-benzyl-2,7-diones (**8** and **9**) having electronic environment

10) cf. H.J. Liu, Y. Sato, Z. Valenta, J.S. Wilson, and T.T.J. Yu, *Can. J. Chem.*, **54**, 97 (1976).
11) Only the treatment of **4** or **5** with potassium hydroxide in ethanol gave an equilibrium mixture, with a *cis-trans* ratio of 1:7.5, possibly derived from the contribution of an enolate (**23′** in Chart 2).
12) An alternative attack (**26** or **27**) would be of limited possibility, because in such an attack the nitrogen atom fails to come into an appropriate position to be cyclized, as suggested on inspection of the Dreiding model.
13) Conformer **24a** which fulfils a favorable steric requirement for the isomerization *via* the retro-Michael process is known to be favorable for **1** and less favorable for **4**: see H. Booth and D.V. Griffiths, *J.C.S. Chem. Commun.*, **1973**, 666; *idem*, *J.C.S. Perkin II*, **1975**, 111.

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at N-1 similar to the N-benzoyl-7-ones (**6** and **7**), however, are found to resemble the N-benzyl-7-ones (**4** and **5**) rather than the N-benzoyl-7-ones (**6** and **7**) in the behavior of isomerization. One of the possible factors to induce the difference in isomerization feature between these two systems would be a participation of the N-acyl carbonyl in the N-benzoyl-7-one system, possibly *via* a cyclic mechanism. Thus, the enone (**18**) is generated from both **6** and **7** as depicted in **6'**[14] and **7'** (Chart 3) and then recyclizes to the *cis*-N-benzoyl-7-one (**6**) under a severe stereoelectronic control associated with reduced nucleophilicity of the amido nitrogen.[15]

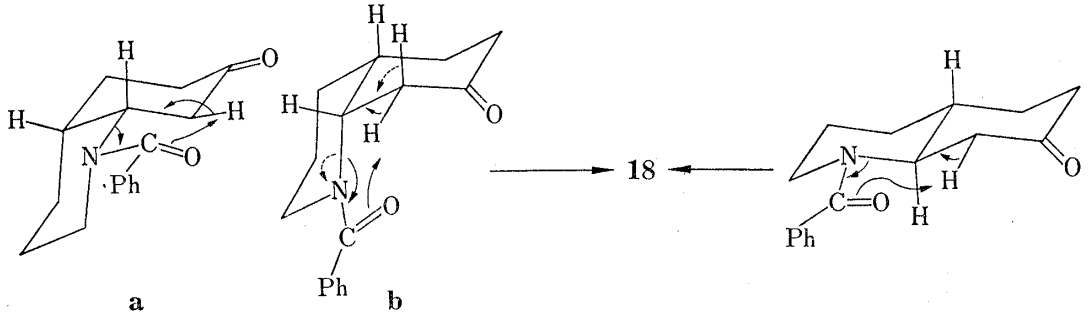

Chart 3

Interpretation of Isomerization of the N-Benzyldecahydroquinoline-2,7-dione System

N-Benzyldecahydroquinoline-2,7-dione system (**8** and **9**) is found to be the most stable toward the ring isomerization. However, under the drastic condition (tosylic acid in boiling toluene), the mutual **8**⇄**9** isomerization was found to take place. The actual isolation of **19** suggests that the enone (**28**) is formed and takes part in the isomerization as an intermediate. Furthermore, a ratio (more than 8/1) of the yields of **19** from **8** and **9** might be proportional to the relative rates of formation of **28** from **8** and **9**. The question of the origin of the O-benzyl group have remained unsolved.

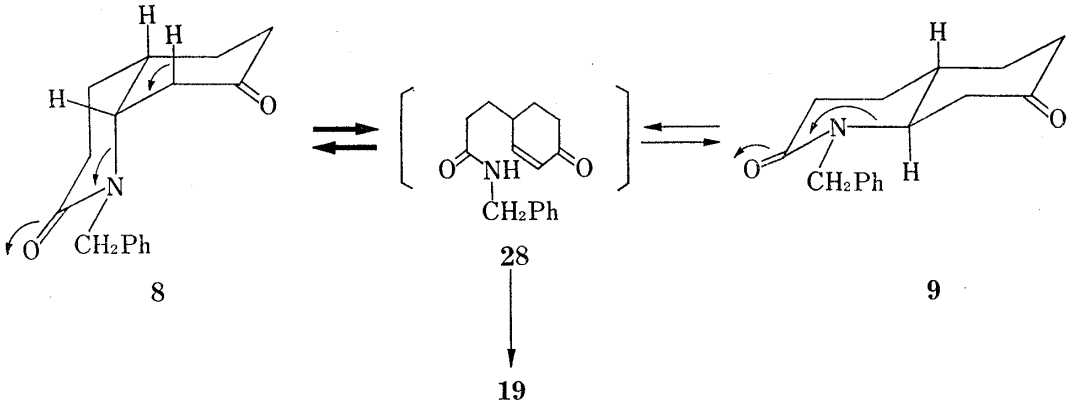

Chart 4

It is noteworthy that the substituents on N-1 govern the behavior of ring isomerization of octahydro-7(1*H*)-quinolones, and this feature suggested the importance of the kinetic effects rather than the thermodynamic ones on the configurational stability of this system.

14) For the *cis*-ketone (**6**), an E_2 elimination also may occur *via* conformer **6'b**.
15) The reduced nucleophilicity of the amido nitrogen seems to be responsible also for the successful isolation of the enone intermediate (**18**).

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Experimental

All melting points are uncorrected. IR spectra were taken on a Hitachi EPI-G3 grating spectrophotometer. ^{1}H-NMR (PMR) spectra were measured for the solutions in $CDCl_3$ with a Hitachi R-20A (60 MHz) or R-22 (90 MHz) spectrometer with tetramethylsilane as an internal standard. Coupling constants (J) and half widths ($W_{1/2}$) are given in Hz, and the following abbreviations are used; s=singlet, d=doublet, t=triplet, m=multiplet, dd=doublet of doublets, dm=doublet of multiplets. Mass spectra were taken on a Hitachi RMU-6E mass spectrometer. All the organic extracts were dried over anhydrous magnesium sulfate prior to evaporation. Column chromatography was performed on Merck Aluminiumoxid (Aktivitätsstufe II—III) or Mallinckrodt silicic acid. Thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 PF_{254} or Merck Aluminiumoxid PF_{254} (Typ T).

N-Benzyl-*trans*-octahydro-7(1*H*)-quinolone (5)——A suspension consisting of *trans*-octahydro-7(1*H*)-quinolone[6] (3; 94 mg), benzyl chloride (82 mg), K_2CO_3 (130 mg) and acetone (10 ml) was heated under reflux for 18 hr. The inorganic material was removed, and the solution was evaporated. The resulting residue was taken in $CHCl_3$, and the $CHCl_3$ layer was washed with brine and evaporated to give an oil, which was chromatographed on alumina. Elution with $CHCl_3$ gave 100 mg (67%) of **5** as an oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (CO). MS *m/e*: 243 (M^+). PMR (60 MHz) δ: 7.25 (5H, s, $C_6\underline{H}_5$), 3.99 and 3.13 (each 1H, AB type, J=14, $C\underline{H}_2$–Ph). *Anal.* Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.58; H, 8.73; N, 6.05.

N-Benzyl-*cis*-octahydro-7(1H)-quinolone (4)——A suspension consisting of *cis*-octahydro-7(1*H*)-quinolone[1] (1; 170 mg), benzyl chloride (160 mg), K_2CO_3 (300 mg) and acetone (10 ml) was heated under reflux for 20 hr. Usual working-up as described above gave an oil, which was chromatographed on alumina in benzene. The first fraction gave 72 mg (27%) of **4** as an oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (CO). MS *m/e*: 243 (M^+). PMR (60 MHz) δ: 7.26 (5H, s, C_6H_5), 3.70 and 3.42 (each 1H, AB type, J=14, $C\underline{H}_2$–Ph). *Anal.* Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.75; H, 8.69; N, 6.00. The second one gave 67 mg (25%) of **5**. Its IR spectrum was identical with that of **5** obtained from **3**. PMR (60 MHz) of the crude product [δ: 3.42 (1/2H, d, J=14, one of $C\underline{H}_2$–Ph for **4**), 3.13 (1/2H, d, J=14, one of $C\underline{H}_2$–Ph for **5**)] indicated a 1:1 mixture of **4** and **5**.

N-Benzyl-*trans*-decahydroquinoline-2,7-dione 7-Ethylene Ketal (15)——A suspension consisting of *trans*-decahydroquinoline-2,7-dione 7-ethylene ketal[1] (13; 290 mg), NaH (50% in oil, 200 mg) and dry toluene (50 ml) was heated under reflux for 4 hr. After cooling, benzyl chloride (500 mg) was added, and the resulting suspension was heated under reflux for another 4 hr. The suspension was washed with brine and evaporated under reduced pressure to give a yellow oil (940 mg), which was triturated with hexane to give a crystalline product (330 mg). Recrystallization from isopropyl ether afforded 310 mg (75%) of **15** as colorless plates, mp 150—151.5°. IR ν_{max}^{KCl} cm^{-1}: 1645 (lactam). MS *m/e*: 301 (M^+). PMR (90 MHz) δ: 6.85—7.38 (5H, m, $C_6\underline{H}_5$), 4.99 and 4.37 (each 1H, AB type, J=15, $C\underline{H}_2$–Ph), 3.68—3.98 (4H, m, O–$C\underline{H}_2C\underline{H}_2$–O), 2.98—3.31 (1H, m, $W_{1/2}$=24, C_{8a}–$\underline{H}$). *Anal.* Calcd. for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.77; N, 4.65. Found: C, 71.65; H, 7.70; N, 4.78.

N-Benzyl-*cis*-decahydroquinoline-2,7-dione 7-Ethylene Ketal (14)——A suspension consisting of *cis*-decahydroquinoline-2,7-dione 7-ethylene ketal[1] (12; 420 mg), NaH (50% in oil, 240 mg) and dry benzene (50 ml) was heated under reflux for 3 hr. After cooling, benzyl chloride (760 mg) was added, and the resulting suspension was heated under reflux for another 3 hr. Usual working-up as described above gave a colorless oil (1.70 g), which was chromatographed on alumina. Elution with benzene afforded 550 mg (91%) of **14** as colorless plates (from benzene–hexane), mp 114—115°. IR ν_{max}^{KCl} cm^{-1}: 1620 (lactam). MS *m/e*: 301 (M^+). PMR (90 MHz) δ: 7.24 (5H, s, $C_6\underline{H}_5$), 5.17 and 4.02 (each 1H, AB type, J=15, $C\underline{H}_2$–Ph), 3.90 (4H, s, O–CH_2CH_2–O), 3.28—3.67 (1H, m, $W_{1/2}$=21, C_{8a}–H). *Anal.* Calcd. for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.77; N, 4.65. Found: C, 71.86; H, 7.69; N, 4.64.

N-Benzyl-*trans*-decahydroquinoline-2,7-dione (9)——A mixture of **15** (257 mg), 1 N HCl (3.0 ml) and acetone (5.0 ml) was allowed to stand for 36 hr. After being made alkaline with K_2CO_3, the mixture was evaporated to give a residue, which was taken in $CHCl_3$. The $CHCl_3$ layer was washed with brine and evaporated to afford an oil (240 mg), which was chromatographed on alumina. Elution with benzene–EtOH (10:1) afforded 210 mg (96%) of **9** as a highly viscous, hygroscopic paste, $bp_{0.005}$ 180° (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710 (CO), 1629 (lactam). MS *m/e*: 257 (M^+). PMR (90 MHz) δ: 7.00—7.30 (5H, m, C_6H_5), 4.39 and 5.00 (each 1H, AB type, J=15, $C\underline{H}_2$–Ph), 3.00—3.45 (1H, m, $W_{1/2}$=27, C_{8a}–H). *Anal.* Calcd. for $C_{16}H_{19}NO_2 \cdot 1/4H_2O$: C, 73.39; H, 7.51; N, 5.35. Found: C, 73.20; H, 7.46; N, 5.71.

N-Benzyl-*cis*-decahydroquinoline-2,7-dione (8)——A mixture of **14** (0.40 g), 1N HCl (5.0 ml) and acetone (5.0 ml) was allowed to stand for 36 hr. Usual working-up as described above gave an oily residue (345 mg), which was chromatographed on alumina. Elution with benzene–EtOH (10:1) afforded 330 mg (96%) of **8** as colorless plates (from isopropyl ether), mp 105.5—106.5°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1630 (lactam). MS *m/e*: 257 (M^+). PMR (90 MHz) δ: 7.05—7.35 (5H, m, $C_6\underline{H}_5$), 3.90 and 5.31 (each 1H, AB type, J=15, $C\underline{H}_2$–Ph), 3.43—3.90 (1H, m, $W_{1/2}$=27, C_{8a}–H). *Anal.* Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.60; H, 7.43; N, 5.42.

Isomerization Reaction of Octahydro-7(1H)-quinolone Analogues——General Procedure: A) In Acidic Media: i) A mixture of the substrate (0.1 mmol) and a mineral acid (1.0 ml of 2 N H_2SO_4 or 1.0 ml of

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conc. HCl) was heated under reflux for 1.5—3 hr. After cooling, the reaction mixture was made alkaline with K_2CO_3 and extracted with $CHCl_3$. The extract was washed with brine and evaporated to give the product. ii) A mixture of the substrate (0.1 mmol), *p*-TsOH (trace) and dry benzene (3.0 ml) was heated under reflux for 16—25 hr. The reaction mixture was washed with satd. $NaHCO_3$ and brine and evaporated to give the product.

B) In Basic Media: i) A suspension consisting of the substrate (0.4 mmol), K_2CO_3 (100 mg) and acetone (5.0 ml) was heated under reflux for 16—24 hr. After the inorganic material was removed, the solution was evaporated to give a residue, which was taken in $CHCl_3$. The $CHCl_3$ solution was washed with brine and evaporated to give the product. ii) A solution of the substrate (0.4 mmol) and 1% KOH–EtOH (2.0 ml) was allowed to stand for nine days. The reaction mixture was acidified with AcOH and extracted with $CHCl_3$. The extract was washed with brine and evaporated to give the product.

4-(3-Benzamidopropyl)-2-cyclohexenone (18)——A mixture of N-benzoyl-*trans*-octahydro-7(1*H*)-quinolone (**7**; 25 mg), *p*-TsOH (trace) and dry benzene (3.0 ml) was heated under reflux for 25 hr. The reaction mixture was worked up in a usual manner to give an oil, which was chromatographed on silica gel in $CHCl_3$. The first fraction gave 12 mg (48%) of N-benzoyl-*cis*-octahydro-7(1*H*)-quinolone (**6**). The second one gave 5 mg (20%) of **18** as colorless needles (from benzene), mp 90.5—91.5°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (NH), 1665 (enone). MS *m/e*: 257 (M^+). UV λ_{max}^{EtOH} nm (ε): 227 (19700). PMR (90 MHz) δ: 6.82 (1H, dm, $J=10$, C_3–H), 5.97 (1H, dd, $J=10$, 2, C_2–H). *Anal.* Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44, N, 5.44. Found: C, 74.28; H, 7.35; N, 5.28. Treatment of **6** (23 mg) under a similar condition to that described above gave an oil, which was worked up as usual to give 11.5 mg (50%) of the starting material (**6**) from the first fraction of the chromatography and 5.3 mg (23%) of **18** from the second one.

Cyclization of 18——A mixture of **18** (33 mg), *p*-TsOH (trace) and dry benzene (6 ml) was heated under reflux for 25 hr. The reaction mixture was worked up as usual to give an oil, which was subjected to preparative TLC on silica gel in $CHCl_3$–EtOH (20: 1) to afford 13 mg (38%) of **6** and 4 mg (12%) of the starting material (**18**).

Isomerization Reaction of Decahydroquinoline-2,7-dione Analogues——General Procedure: A) In Acidic Media: A mixture of the substrate (0.4 mmol), *p*-TsOH (trace) and dry benzene or toluene (20 ml) was heated under reflux for 24—76 hr. The reaction mixture was washed with satd. $NaHCO_3$ and brine, and evaporated to give the product.

B) In Basic Media: i) A suspension consisting of the substrate (0.4 mmol), K_2CO_3 (220 mg) and acetone (10 ml) was heated under reflux for 48 hr. The inorganic material was removed, and the solution was evaporated. The resulting residue was taken in $CHCl_3$, and the $CHCl_3$ layer was washed with brine and evaporated to give the product. ii) A solution of the substrate (0.4 mmol) and 1% KOH–EtOH (2.0 ml) was allowed to stand at room temperature for nine days and subsequently heated at 60° for 10 hr. The reaction mixture was acidified with AcOH and extracted with $CHCl_3$. The extract was washed with brine and evaporated to give the product. iii) A mixture of the substrate (0.4 mmol), 10% aq. KOH (5.0 ml) and dioxane (5.0 ml) was allowed to stand at room temperature for 43 hr or heated under reflux for 14 hr. After the reaction mixture was acidified with AcOH, the solvent was removed under reduced pressure to give a residue, which was taken in $CHCl_3$. The $CHCl_3$ solution was washed with brine and evaporated to give the product. iv) A mixture of the substrate (0.4 mmol) and *t*-BuOK (trace) in *t*-BuOH (20 ml) was heated on a water bath at 30° for 76 hr. After the reaction mixture was neutralized with AcOH, the solvent was removed under reduced pressure to give a residue, which was taken in $CHCl_3$. The $CHCl_3$ solution was washed with satd. $NaHCO_3$, brine, and evaporated to give the product.

N-Benzyl-3-(*p*-benzyloxyphenyl)propionamide (19)——A mixture of **8** (93 mg), *p*-TsOH (10 mg) and dry toluene (20 ml) was heated under reflux for 76 hr. The reaction mixture was worked up as usual to give an oil (160 mg), which was chromatographed on silica gel in $CHCl_3$. The first fraction gave a crystalline solid, which was recrystallized from benzene to give 8 mg (6%) of **19** as colorless needles, mp 133—134.5°. IR ν_{max}^{KCl} cm^{-1}: 1640 (amide). MS *m/e*: 345 (M^+). PMR (90 MHz) δ: 6.79—7.55 (14H, m, $C_6\underline{H}_5$), 5.50—5.68 (1H, m, NH), 5.00 (2H, s, O–C$\underline{H}_2$–Ph), 4.38 (2H, d, $J=5.2$, NH–C$\underline{H}_2$–Ph), 2.92 (2H, t, $J=7$, NH–CO–C$\underline{H}_2$–CH_2), 2.45 (2H, t, $J=7$, NH–CO–CH_2–C$\underline{H}_2$). *Anal.* Calcd. for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71; N, 4.06. Found: C, 79.73; H, 6.71; N, 4.32. The second one gave 11 mg (12%) of **9**. The third one gave 20 mg (22%) of the starting material (**8**). Treatment of **9** (96 mg) under a similar condition to that described above gave a trace of **19**, 58 mg (60%) of the starting material (**9**) and 10 mg (10%) of **8**.

An Alternative Synthesis of 19——A mixture of *p*-benzyloxyhydrocinnamic acid[9] (**20**; 205 mg), ethyl chloroformate (87 mg), triethylamine (1.1 ml) and $CHCl_3$ (5.0 ml) was stirred at room temperature for 20 min. Benzylamine (0.1 ml) was added dropwise during 10 min, and the resulting mixture was further stirred at room temperature overnight. The mixture was washed with brine and 1% HCl, and evaporated to give an oily residue (590 mg), which was chromatographed on alumina. Elution with benzene–EtOH (15: 1) gave 230 mg (83%) of **19** as colorless needles (from benzene), which was identical with the sample obtained from **8** or **9** with respect to TLC, IR, and mixed mp.

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