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Octahydro-7(1*H*)-quinolones. VII.[1] A Stereoselective Synthesis of *cis,trans*-Decahydro-3*H*,8*H*-benzo[*i*,*j*]quinolizine-3,8-dione

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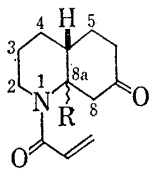
The conversion of 1-(3-chloropropyl)-*cis*-decahydroquinoline-2,7-dione (3) into decahydro-3*H*,8*H*-benzo[*i*,*j*]quinolizine-3,8-diones (**12a** and **12b**) was accomplished with retention of the parent stereochemistry. The stereochemistry of the tricyclic system was assigned from chemical and physical evidences. It was postulated that this successful ring closure in the *cis* ring system resulted from easy fulfilment of the stereoelectronic requirement, for intramolecular alkylation in 3, much reduced as compared to that for *N*-acrylyl-*cis*-octahydro-7(1*H*)-quinolone (**1b**).

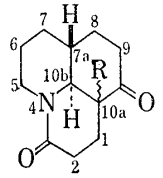
Keywords——*cis*-decahydroquinoline-2,7-dione; decahydrobenzo[*i*,*j*]quinolizinedione; 2-oxoquinolizidine system; intramolecular cyclization; stereoelectronic requirement; hydroboration; stereochemistry; Bohlmann absorption; ^{1}H-NMR

In the previous paper,[3] we described the ring closure of *N*-acrylyl-*cis*- and -*trans*-octahydro-7(1*H*)-quinolone (**1b** and **1a**) into tricyclic lactam ketones (**2a** and **2b**), and showed the failure for the *cis*-isomer (**1b**) of cyclization under basic conditions and of retention of the parent stereochemistry in cyclization under drastic acid conditions. For stereoselective construction of the *cis*-A/B-hexahydrojulolidine skeleton, a des-ring D model for Lycopodium alkaloids, an approach from the *cis*-perhydroquinolone system should be conducted with retention of the ring configuration. This paper describes an efficient route to the tricyclic system involving the stereochemistry required of the natural alkaloids, which was performed as exploratory experiments for the lycodoline synthesis.[4]

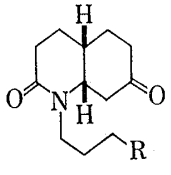
As a synthetic strategy, our attention was given to the incorporation of a saturated three-carbon functionality on the nitrogen in the *cis*-perhydroquinolone system with little tendency of isomerization to the *trans* system. An amide structure of the nitrogen in the octahydro-7(1*H*)-quinolone system has been shown[5] to be essential for prevention of the *cis* ring fusion from isomerization into *trans*, and the severe stereoelectronic requirement[3,4] for C–C bond formation in **1b** *via* the intramolecular Michael addition between the *N*-acrylyl and the enolate



1a : R=α-H
1b : R=β-H



2a : R=α-H
2b : R=β-H



3 : R=Cl
4 : R=OMs

Chart 1

1) Part VI: T. Momose, S. Uchida, T. Miyata, K. Chiamchittrong, K. Ohshima, and T. Imanishi, *Heterocycles*, **12**, No. 3 (1979) in press.
2) Location: *133-1, Yamada-kami, Suita, Osaka 565, Japan*; *a*) Present address: *Faculty of Pharmaceutical Sciences, Kanazawa University, 13-1 Takara-machi, Kanazawa 920, Japan.*
3) T. Momose, S. Uchida, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **26**, 972 (1978).
4) T. Momose, S. Uchida, T. Imanishi, S.W. Kim, N. Takahashi, and Z. Horii, *Heterocycles*, **6**, 1105 (1977).
5) T. Momose, S. Uchida, E. Hosoya, M. Kinoshita, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **26**, 620 (1978).

at C_7–C_8 is expected to be reduced by converting the mode of this step into a substitution reaction between the saturated carbon terminal of the *N*-alkyl moiety and the carbanion at C_8. For this purpose, we chose the decahydroquinoline-2,7-dione system (**3** or **4**)[6] bearing a saturated *N*-propyl moiety with ω-functionality.

Synthesis of 1-(3-Substituted propyl)-*cis*-decahydroquinoline-2,7-diones

Inspection of the Dreiding model indicates that the ω-carbon of the saturated *N*-propyl group in **3** or **4** could be linked to the C_8-position through an intramolecular S_N2 alkylation owing to its easy fulfilment of the stereoelectronic requirement.

First, we attempted the reaction sequence, a lactam (**5**)[6] →an olefin (**6**)→a primary alcohol (**8**)→the mesylate (**9**)→a lactam ketone (**4**). *N*-Allylation of **5** with allyl bromide in benzene containing sodium hydride (NaH) afforded the N-propenyllactam (**6**) in 88% yield. Hydroboration–oxidation of **6** afforded unexpectedly a mixture of two diastereomeric secondary alcohols, **7a** (13%) and **7b** (11%), along with a small amount of the primary alcohol (**8**: 7%). The proton magnetic resonance (PMR) spectra of the former two exhibit three proton signals due to their terminal methyls as a doublet (J=6 Hz) at 1.16 and 1.18 ppm, respectively, while that of the latter lacks a methyl signal. The inductive or through-space effect of the allylic amide functionality operating on the hydroboration would be responsible for the predominance of the secondary alcohol (**7**) over the primary one (**8**).[7]

Because of poor yield of the desired product (**8**) on this reaction, this route was abandoned,[8] and eventually, the sequence involving the alkylation with 2-(3-chloropropoxy)-tetrahydropyran[9] was shown to be promising. The alkylation in N,N-dimethylformamide (DMF) containing NaH to give the masked derivative (**10**) of **8** in moderate yield. Hydrolysis of **10** with 5% HCl–acetone at room temperature gave a keto alcohol (**11**) in 66% yield. Ketalization of **11** afforded the primary alcohol (**8**), which was identical with the sample obtained by the foregoing route *via* hydroboration–oxidation of **6**. Treatment of **11** with

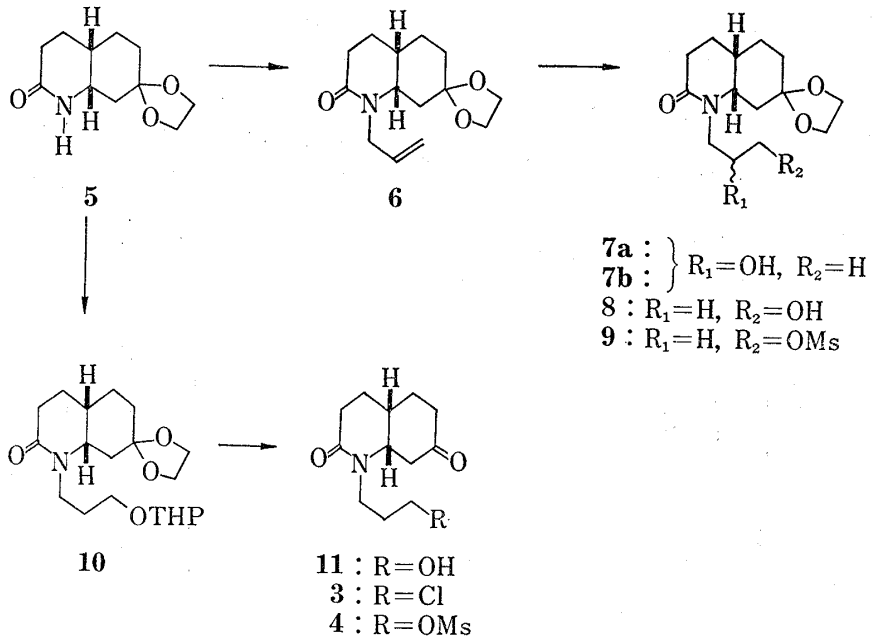


Chart 2

6) T. Momose, S. Uchida, M. Kinoshita, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 1797 (1977).
7) *Cf.* D.N. Butler and A.H. Soloway, *J. Am. Chem. Soc.*, **88**, 484 (1966).
8) Another approach to the ω-chloro compound *via* selective hydrogenation of 1-(3-chloro-2-propenyl)-*cis*-decahydroquinoline-2,7-dione 7-ethylene ketal, prepared in a similar way to that described for **6**, resulted in concurrent partial dehalogenation. *Cf.* G.E. Ham and W.P. Coker, *J. Org. Chem.*, **29**, 194 (1964).
9) W.E. Parham and E.L. Anderson, *J. Am. Chem. Soc.*, **70**, 4187, (1948).

methanesulfonyl chloride (MsCl) in pyridine with cooling gave the chloro ketone (**3**) in 60% yield without accompanying any O-mesylated product (**4**).[10] The structure of **3** was assigned from the combustion, PMR, and mass spectrum data.

Synthesis of Decahydro-3*H*,8*H*-benzo[*i*,*j*]quinolizine-3,8-diones (12a and 12b)

Cyclization of **3** was achieved by means of potassium *tert*-butoxide (*t*-BuOK) in *tert*-butanol (*t*-BuOH) at 45°. Careful chromatography of the product led to the isolation of two isomeric lactam ketones, **12a** (73% yield; mp 103—107°) and **12b** (4% yield; mp 130—135°). These lactam ketones were epimeric each other at the C-7a configuration,[3,5] and isomer **12a** was thermodynamically more stable because isomerization of each of **12a** and **12b** under a condition similar to that for the ring closure resulted in the equilibrium with predominance of **12a**.

Their PMR spectra display a one-proton signal due to the C-5 equatorial proton at the lowest field, the pattern being characteristic of the 2-oxo-quinolizidine system.[3,11] The most significant difference is observed in the signal due to the C-10b proton. This signal for **12a** appears at 3.38 ppm with a half width ($W_{1/2}$) of 18 Hz while that of **12b** appears at 3.94 ppm ($W_{1/2}$=9 Hz). These observations are consistent with our previous result[12] that the C-8a proton signal for a so-called nonsteroid form (**13'**)[13] in perhydroquinolin-2-one analogues (**13**) appears with a narrow half width at the field lower than that for a steroid form (**13''**).[13] Furthermore, **12a** and the previously reported *trans*(7a*H*,10b*H*),*cis*(10a*H*,10b*H*)-3,10-dione

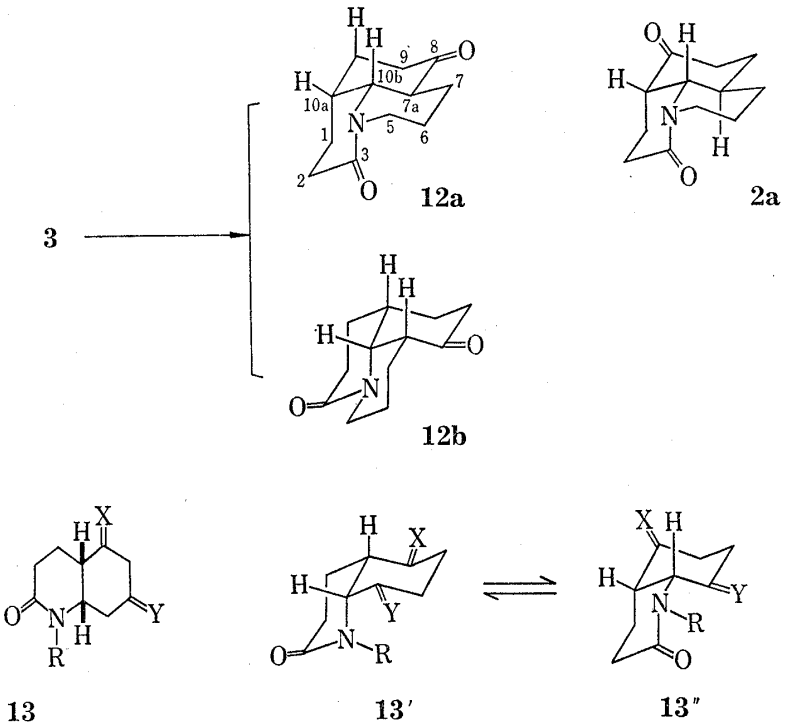


Chart 3

10) J. DeGraw and L. Goodman, *J. Org. Chem.*, **27**, 1395 (1962); M.E. Evans, L. Long, Jr., and F.W. Parrish, *ibid.*, **33**, 1074 (1968).
11) F. Bohlmann and D. Schumann, *Tetrahedron Lett.*, **1965**, 2435.
12) T. Momose, T. Miyata, and T. Imanishi, *Heterocycles*, **9**, 17 (1978).
13) Based on the designation by Aaron and Ferguson; H.S. Aaron and C.P. Ferguson, *Tetrahedron*, **30**, 803 (1974).

(**2a**) show close similarity in their PMR spectra in the region of 3.10—4.95 ppm, which is clearly a reflection of the same mode of ring junction between both compounds.

Chemical Evidence for the Stereochemistry of 12a

The stereochemistry of the main product (**12a**) was determined on the basis of the spectral properties of its transformation products and of an independent synthesis of the *trans*(7a*H*, 10b*H*),*cis*(10a*H*,10b*H*)-amino ketal (**19a**), which was also derived from **12a**.

Reduction of **12a** with lithium aluminum hydride (LAH) afforded two isomeric amino alcohols, **14a** (66%) and **14b** (18%), both displaying no Bohlmann's absorption in their infrared (IR) spectra. The PMR spectrum of **14b** displays a one-proton signal due to the C-8 proton at 3.76 ppm with a half width of 6 Hz while that of **14a** does not provide any information concerning the hydroxyl configuration at C_8 because of signal overlap. Consequently, the C-8 protons in **14a** and **14b** are situated axially and equatorially to the cyclohexane ring, respectively. They were found to be different on direct comparison from the previously reported *trans,trans*- (**15a** and **15b**),[3] *cis*(7a*H*,10b*H*),*trans*(10a*H*,10b*H*)- (**16**),[3] and *cis,cis*-amino alcohol (**17**).[14]

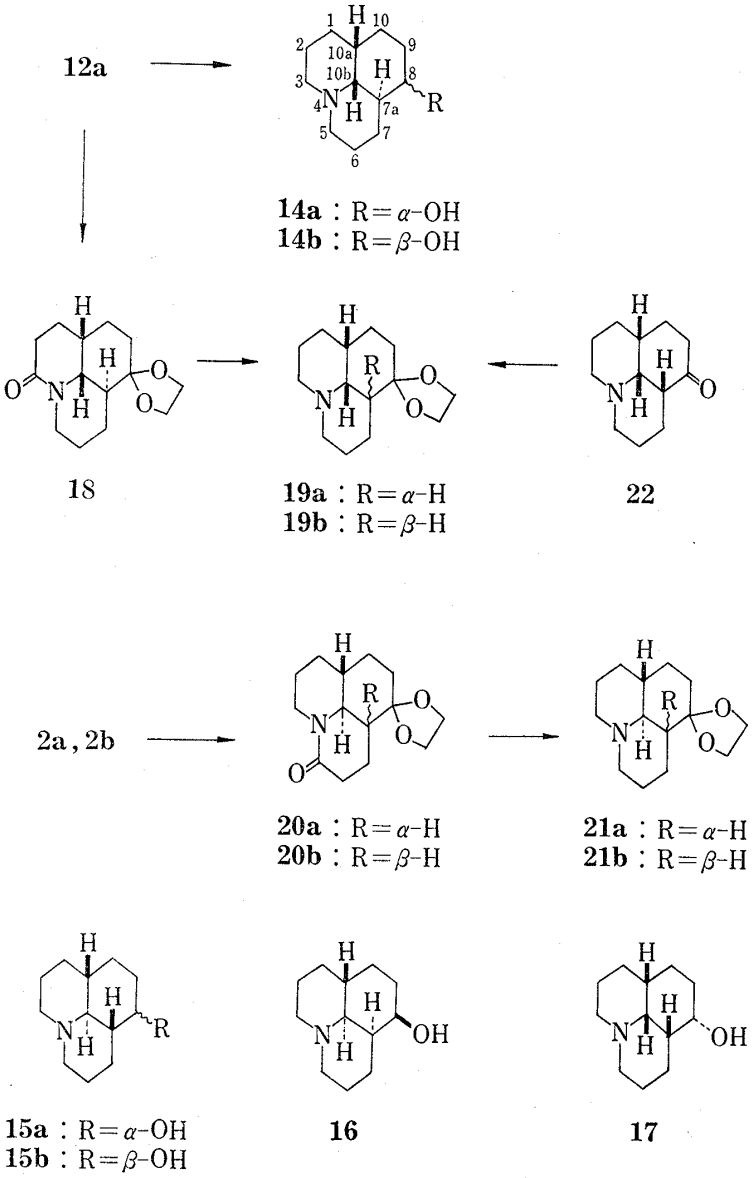


Chart 4

14) Prepared by the method reported: F. Bohlmann and O. Schmidt, *Chem. Ber.*, **97**, 1354 (1964).

Final and direct proof of the stereochemistry was obtained as follows. The main product (**12a**) was converted to the ketal (**18**), the PMR spectrum of which displayed a one-proton signal due to the C-10b proton at 3.35 ppm ($W_{1/2}$=18 Hz). Reduction of **18** with LAH gave the amino ketal (**19a**), which displayed no Bohlmann's absorption in its IR spectrum. Here, we undertook the synthesis of all of the four possible isomers of amino ketals starting from the *trans,trans*-3,10-dione (**2b**)[3] and *cis,cis*-amino ketone (**22**).[14,15] When the former (**2b**) was treated with *p*-toluenesulfonic acid (*p*-TsOH) in boiling toluene, a mixture of two isomers (**2a** and **2b**) in a ratio of *ca.* 1: 3 resulted. The mixture was converted to the ketal mixture (**20a** and **20b**), the isomer composition of which was estimated as *ca.* 1: 3 from integration of the C-10b proton for **20a** and of the C-5 equatorial proton for **20b** in its PMR spectrum. The ketal mixture was reduced with LAH to afford isomeric amino ketals [**21a** (16%) and **21b** (61%)] having the *trans*(10a*H*,10b*H*)-ring junction. On the other hand, ketalization of **22** resulted in isomerization at C-7a to give the isomeric amino ketals, **19a** (37%) and **19b** (53%), neither of which was identical with **21a** and **21b**. Thus, the amino ketal derived from **12a** was identical with **19a** obtained from the Bohlmann's ketone (**22**), and the stereochemistry of **12a** was established as *trans*(7a*H*,10b*H*),*cis*(10a*H*,10b*H*)-ring junction.

Consequently, the ring closure of **3** into **12** was shown to have proceeded with retention of the parent stereochemistry in the perhydroquinolone system. And easy fulfilment of the stereoelectronic requirement for cyclization of the present system (**3**) enabled the model system of the natural stereochemistry to be constructed, and it is hoped that the application of this method would provide an efficient route to the Lycopodium alkaloids.

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 solution in $CDCl_3$ with a Hitachi 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, dd=doublet of doublets, m=multiplet, dm=doublet of multiplets. Mass spectra (MS) 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*-Allyl-*cis*-decahydroquinoline-2,7-dione 7-Ethylene Ketal (6)**——A suspension consisting of *cis*-decahydroquinoline-2,7-dione 7-ethylene ketal[6] (**5**; 400 mg), NaH (50% in oil, 230 mg) and dry benzene (60 ml) was heated under reflux for 4 hr. After cooling, allyl bromide (0.7 ml) was added, and the resulting suspension was heated under reflux overnight. The suspension was washed with brine and evaporated under reduced pressure to give an oil, which was chromatographed on alumina. Elution with benzene–EtOH (10: 1) afforded 420 mg (88%) of **6** as an oil, which solidified on standing and was recrystallized from hexane to give colorless needles, mp 75—76°. IR ν_{max}^{KCl} cm^{-1}: 1620 (lactam). MS *m/e*: 251 (M^+, 50%), 99 (100%). PMR δ: 3.52 (1H, m, C_{8a}–H), 3.60 (1H, dm, A part of ABXY, J_{AB}=15, CH_2=CH–C$\underline{H}_2$–), 4.44 (1H, dm, B part of ABXY, J_{AB}=15, CH_2=CH–C$\underline{H}_2$–), 3.93 (4H, s, O–CH_2CH_2–O), 5.00—5.28 (2H, m, C$\underline{H}_2$=CH–), 5.58—6.05 (1H, m, CH_2=C$\underline{H}$–). *Anal.* Calcd. for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42; N, 5.57. Found: C, 66.98; H, 8.47; N, 5.58.

Hydroboration of 6 [1-(2-Hydroxypropyl)-*cis*-decahydroquinoline-2,7-dione 7-Ethylene Ketals (7a and 7b) and 1-(3-Hydroxypropyl)-*cis*-decahydroquinoline-2,7-dione 7-Ethylene Ketal (8)]——A mixture of **6** (350 mg) and $NaBH_4$ (80 mg) in dry THF (5.0 ml) was stirred at 0°. To this was added dropwise a solution of freshly distilled BF_3-etherate (0.4 ml) in dry THF (10 ml) over a period of 15 min at the same temperature, followed by stirring at room temperature for an additional one hr. After addition of H_2O (3.0 ml), and then of 3 N NaOH (10 ml) and 30% H_2O_2 (10 ml) at 0°, the mixture was stirred at room temperature for 1.5 hr. The THF layer was separated, evaporated under reduced pressure, and taken in $CHCl_3$. The aqueous phase was extracted with $CHCl_3$. The combined $CHCl_3$ extract was washed with 5% HCl, brine, satd. $NaHCO_3$ and brine, and evaporated to give an oil (210 mg), which was chromatographed on alumina in ether–EtOH

15) Our tricyclic *trans,trans*-amino ketone (mp 50—55°) prepared by oxidation (CrO_3–pyridine) of **15b** and the Bohlmann's ketone (**22**) were shown not to be identical by comparison of their IR spectra, though positive of the Bohlmann's absorption.

(10: 1). The first fraction gave 50 mg (13%) of **7a** as colorless needles (from acetone), mp 210—212°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370 (OH), 1610 (lactam). MS *m/e*: 269 (M^+, 1%), 124 (100%). PMR δ: 1.16 (3H, d, J=6, Me), 3.93 (4H, s, O–CH_2CH_2–O). *Anal.* Calcd. for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.44; H, 8.60; N, 5.18.

The second fraction gave 40 mg (11%) of **7b** as colorless crystals (from ether), mp 140—142°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3380 (OH), 1610 (lactam). MS *m/e*: 269 (M^+, 2%), 124 (100%). PMR δ: 1.18 (3H, d, J=6, Me), 3.93 (4H, s, O–CH_2CH_2–O). *Anal.* Calcd. for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.02; H, 8.59; N, 5.07.

The third fraction gave 26 mg (7%) of **8** as colorless needles (from hexane), mp 92.5—93.5°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3390 (OH), 1600 (lactam). MS *m/e*: 269 (M^+, 59%), 99 (100%). PMR δ: 3.95 (4H, s, O–CH_2CH_2–O). *Anal.* Calcd. for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.56; H, 8.58; N, 5.29.

1-(3-Tetrahydropyranyloxypropyl)-*cis*-decahydroquinoline-2,7-dione 7-Ethylene Ketal (10)——A mixture of **5** (6.0 g), NaH (50% in oil, 2.7 g), 2-(3-chloropropoxy)tetrahydropyran[9] (15.3 g) and dry DMF (100 ml) was heated under reflux for 5 hr. The resulting mixture was diluted with H_2O (80 ml) and extracted with $CHCl_3$. The solvent was removed *in vacuo*, and the residue (12.3 g) was chromatographed on alumina in ether–EtOH (10: 1). The first fraction gave 7.3 g (73%) of **10** as a semi-solid, bp 190° (0.015 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1620 (lactam). MS *m/e*: 353 (M^+, 1%), 268 (100%). PMR δ: 3.93 (4H, s, O–CH_2CH_2–O), 4.55 (1H, m, anomeric H). *Anal.* Calcd. for $C_{19}H_{31}NO_5 \cdot 1/4H_2O$: C, 63.75; H, 8.87; N, 3.91. Found: C, 63.58; H, 8.82; N, 4.04.

The second fraction gave 520 mg of the starting material (**5**).

1-(3-Hydroxypropyl)-*cis*-decahydroquinoline-2,7-dione (11)——A mixture of **10** (3.8 g), 5% HCl (20 ml) and acetone (20 ml) was stirred at room temperature overnight. 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 (2.4 g), which was triturated with ether to give a crystalline solid. Recrystallization from benzene afforded 1.2 g (50%) of **11** as colorless plates, mp 111—112°. The mother liquor was chromatographed on alumina in ether–EtOH (10: 1) to give additional **11** (400 mg, 16%). IR ν_{max}^{KCl} cm^{-1}: 3330 (OH), 1718 (CO), 1610 (lactam). MS *m/e*: 225 (M^+, 8%), 83 (100%). PMR δ: 1.35—2.80 (12H, m), 2.80—3.32 (2H, m), 3.32—4.10 (5H, m). *Anal.* Calcd. for $C_{12}H_{19}NO_3$: C, 63.97; H, 8.50; N, 6.22. Found: C, 64.10; H, 8.50; N, 6.15.

1-(3-Chloropropyl)-*cis*-decahydroquinoline-2,7-dione (3)——A mixture of **11** (700 mg), MsCl (460 mg) and dry pyridine (7.0 ml) was allowed to stand in a refrigerator for ten days. The reaction mixture was diluted with ice-water and extracted with $CHCl_3$. The extract was evaporated to give an oil (590 mg), which was chromatographed on alumina. Elution with ether–EtOH (100: 7.5) gave 460 mg (60%) of **3** as an oil which solidified on standing. mp 55—57°. IR ν_{max}^{KCl} cm^{-1}: 1718 (CO), 1635 (lactam). MS *m/e*: 245 (M^+, 5%), 243 (M^+, 13%), 186 (100%). PMR δ: 1.40—2.78 (12H, m), 2.78—3.25 (2H, m), 3.25—4.00 (4H, m). *Anal.* Calcd. for $C_{12}H_{18}ClNO_2$: C, 59.13; H, 7.44; N, 5.75. Found: C, 58.80; H, 7.46; N, 5.94.

Cyclization of 3 [*cis*,*cis*-Decahydro-3*H*,8*H*-benzo[*i*,*j*]quinolizine-3,8-dione (12b) and *trans*(7a*H*,10b*H*),*cis*-(10a*H*,10b*H*)-Decahydro-3*H*,8*H*-benzo[*i*,*j*]quinolizine-3,8-dione (12a)]——A solution of **3** (460 mg) in *t*-BuOH (4.0 ml) was added to a solution of *t*-BuOK in *t*-BuOH (prepared from 75 mg of potassium and 20 ml of *t*-BuOH), and the mixture was heated at 45° for 2 hr. The reaction mixture was neutralized with AcOH, and the solvent was removed under reduced pressure to give an oily residue, which was taken in $CHCl_3$. The $CHCl_3$ layer was washed with satd. $NaHCO_3$ and brine, and evaporated to give an oil (400 mg), which was chromatographed on silica gel in $CHCl_3$. The first fraction gave 15 mg (4%) of **12b** as colorless needles (from isopropyl ether), mp 130—135°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1628 (lactam). MS *m/e*: 207 (M^+, 100%), 206 (45%). PMR δ: 3.94 (1H, m, $W_{1/2}$=9, C_{10b}–H), 4.58 (1H, dm, J=13, C_5-equatorial H). High resolution MS *m/e*: Found: 207.124; Calcd. for $C_{12}H_{17}NO_2$ (M^+) 207.126.

The second fraction gave 285 mg (73%) of **12a** as colorless plates (from ether), mp 103—107°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1628 (lactam). MS *m/e*: 207 (M^+, 100%), 206 (45%). PMR δ: 3.38 (1H, dd, $W_{1/2}$=18, C_{10b}–H), 4.68 (1H, dm, J=13, C_5-equatorial H). *Anal.* Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.27; H, 8.23; N, 6.28.

***trans*(7a*H*,10b*H*),*cis*(10a*H*,10b*H*)-Decahydro-1*H*,5*H*-benzo[*i*,*j*]quinolizin-8-ols (14a and 14b)**——A suspension consisting of **12a** (210 mg), $LiAlH_4$ (600 mg) and dry ether (50 ml) was heated under reflux overnight. After decomposing the excess reducing agent with AcOEt, an aqueous solution of sodium potassium tartarate was added to the reaction complex, and the supernatant was decanted. The precipitate was washed with ether. The combined ethereal layer was evaporated to give an oil (210 mg), which was chromatographed on alumina in $CHCl_3$–EtOH (20: 1). The first fraction gave 130 mg (66%) of the 8α-ol (**14a**) as colorless needles (from benzene), mp 123—125°. IR ν_{max}^{KCl} cm^{-1}: 3100 (OH), no Bohlmann band. MS *m/e*: 195 (M^+, 30%), 194 (100%). PMR δ: 2.79 (1H, s, disappeared with D_2O, OH). *Anal.* Calcd. for $C_{12}H_{21}NO$: C, 73.79; H, 10.84; N, 7.17. Found: C, 73.53; H, 10.77; N, 7.19.

The second fraction gave 35 mg (18%) of the 8β-ol (**14b**) as colorless needles (from benzene), mp 150—153°. IR ν_{max}^{KCl} cm^{-1}: 3100 (OH), no Bohlmann band. MS *m/e*: 195 (M^+, 30%), 194 (100%). PMR δ: 2.32 (1H, broad s, disappeared with D_2O, OH), 3.76 (1H, m, $W_{1/2}$=6, C_8–H). High resolution MS *m/e*: Found: 195.161; Calcd. for $C_{12}H_{21}NO$ (M^+) 195.162.

***trans*(7a*H*,10b*H*),*cis*(10a*H*,10b*H*)-Decahydro-3*H*,8*H*-benzo[*i*,*j*]quinolizine-3,8-dione 8-Ethylene Ketal (18)**——A mixture of **12a** (30 mg), ethylene glycol (0.2 ml), *p*-TsOH (trace) and benzene (15 ml) was heated under reflux by use of a Dean–Stark water separator for 1.5 hr. The reaction mixture was washed with satd. $NaHCO_3$, brine, and evaporated to give a solid, which was recrystallized from hexane to give 33 mg of **18** as colorless plates, mp 135—137°. IR ν_{max}^{KCl} cm^{-1}: 1630 (lactam). MS *m/e*: 251 (M^+, 28%), 99 (100%). PMR δ: 3.35 (1H, $W_{1/2}=18$, C_{10b}–H). *Anal.* Calcd. for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42; N, 5.57. Found: C, 66.79; H, 8.41; N, 5.51.

***trans*(7a*H*,10b*H*),cis(10a*H*,10b*H*)-Decahydro-1*H*,8*H*-benzo[*i*,*j*]quinolizin-8-one 8-Ethylene Ketal (19a)**——A suspension consisting of **18** (30 mg), $LiAlH_4$ (60 mg) and dry ether (30 ml) was heated under reflux for 12 hr. The reaction mixture was worked up as usual to afford 20 mg of **19a** as colorless crystals, mp 85—100°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1098. MS *m/e*: 237 (M^+, 55%), 236 (100%). PMR δ: 3.93 (4H, m, O–CH_2CH_2–O). The picrolonate: mp 250—252° (dec.). *Anal.* Calcd. for $C_{14}H_{23}NO_2 \cdot C_{10}H_8N_4O_5$: C, 57.47; H, 6.23; N, 13.97. Found: C, 57.43; H, 6.29; N, 13.94.

Equilibration of *trans*,*trans*-Decahydro-3*H*,10*H*-benzo[*i*,*j*]quinolizine-3,10-dione (2b)——A mixture of **2b** (50 mg), *p*-TsOH (15 mg) and dry toluene (5.0 ml) was heated under reflux for 15 hr. The reaction mixture was washed with satd. $NaHCO_3$, brine, and evaporated under reduced pressure to give the crude product, which was chromatographed on silica gel in $CHCl_3$–EtOH (100: 1). The first fraction gave 36 mg (72%) of **2b**.

The second fraction gave 12 mg (24%) of *trans*(7a*H*,10b*H*),*cis*(10a*H*,10b*H*)-decahydro-3*H*,10*H*-benzo-[*i*,*j*]quinolizine-3,10-dione (**2a**). Their IR spectra were identical with those of authentic samples.[3]

***trans*,*trans*- and *trans*(7a*H*,10b*H*),*cis*(10a*H*,10b*H*)-Decahydro-3*H*,10*H*-benzo[*i*,*j*]quinolizine-3,10-dione 10-Ethylene Ketals (20b and 20a)**——A mixture of the crude product (**2**; 970 mg) obtained above, ethylene glycol (2.0 ml), *p*-TsOH (50 mg) and dry benzene (100 ml) was heated under reflux by use of a Dean–Stark water separator for 10 hr. The mixture was worked up as usual to afford a solid (1.0 g), which showed two close spots on TLC and was subjected to the next step without further purification. The PMR analysis of the crude product showed an isomer composition of *ca.* 1: 3 [δ: 3.18 (1/4H, m, C_{10b}–H for **20a**) and 4.74 (3/4H, dm, C_5-equatorial H for **20b**)]. A sample, mp 115—122°, was analyzed after recrystallization from benzene–hexane. IR ν_{max}^{KCl} cm^{-1}: 1630 (lactam). MS *m/e*: 251 (M^+, 43%), 151 (100%). PMR δ: 3.18 (1/11H, m, C_{10b}–H), 4.74 (10/11H for **20b** and 1/11H for **20a**, dm, C_5-equatorial H). *Anal.* Calcd. for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42; N, 5.57. Found: C, 66.82; H, 8.38; N, 5.63.

***trans*,*trans*- and *cis*(7a*H*,10b*H*),*trans*(10a*H*,10b*H*)-Decahydro-1*H*,8*H*-benzo[*i*,*j*]quinolizin-8-one 8-Ethylene Ketals (21b and 21a)**——A suspension consisting of the crude product (**20**; 520 mg) obtained above, $LiAlH_4$ (1.0 g) and dry ether (100 ml) was heated under reflux overnight. The reaction mixture was worked up as usual to afford an oil (460 mg), which was chromatographed on alumina in ether. The first fraction gave 300 mg (61%) of **21b** as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2820—2750 (Bohlmann bands), 1110, 1085. MS *m/e*: 237 (M^+, 48%), 236 (100%). PMR δ: 3.93 (4H, m, O–CH_2CH_2–O). The picrolonate: mp 213—215° (dec.). *Anal.* Calcd. for $C_{14}H_{23}NO_2 \cdot C_{10}H_8N_4O_5$: C, 57.47; H, 6.23; N, 13.97. Found: C, 57.37; H, 6.25; N, 13.86.

The second fraction gave 80 mg (16%) of **21a** as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1110, 1080. MS *m/e*: 237 (M^+, 76%), 236 (100%). PMR δ: 3.93 (4H, m, O–CH_2CH_2–O). The picrolonate: mp 232—237° (dec.). *Anal.* Calcd. for $C_{14}H_{23}NO_2 \cdot C_{10}H_8N_4O_5$: C, 57.47; H, 6.23; N, 13.97. Found: C, 57.35; H, 6.27; N, 13.92.

Ketalization of *cis*,*cis*-Decahydro-1*H*,8*H*-benzo[*i*,*j*]quinolizin-8-one (22) [*cis*,*cis*-Decahydro-1*H*,8*H*-benzo[*i*,*j*]quinolizin-8-one 8-Ethylene Ketal (19b) and 19a]——A mixture of the all-*cis* amino ketone[14] (**22**; 70 mg), ethylene glycol (0.1 ml), *p*-TsOH (trace) and dry benzene (30 ml) was heated under reflux by use of a Dean–Stark water separator overnight. After addition of additional ethylene glycol (0.4 ml) and *p*-TsOH (trace), the mixture was further heated under reflux in a same manner to that described above overnight. The reaction mixture was worked up as usual to give an oil (84 mg), which was chromatographed on alumina in $CHCl_3$. The first fraction gave 46 mg (53%) of **19b** as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2810—2750 (Bohlmann bands), 1118. MS *m/e*: 237 (M^+, 42%), 236 (100%). PMR δ: 3.93 (4H, m, O–CH_2CH_2–O). The picrate: mp 158—160° (dec.). *Anal.* Calcd. for $C_{14}H_{23}NO_2 \cdot C_6H_3N_3O_7$: C, 51.50; H, 5.62; N, 12.01. Found: C, 51.67; H, 5.74; N, 11.99.

The second fraction gave 32 mg (37%) of **19a**. Its IR spectrum was identical with that of **19a** obtained from the reduction of **18**.

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