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Octahydro-7(1*H*)-quinolones. IV.[1] Construction of Decahydro-3*H*,10*H*-benzo[*i,j*]quinolizine-3,10-dione Systems from *cis*- and *trans*-Octahydro-7(1*H*)-quinolone[2]

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The cyclization of *N*-acrylyl-*trans*- and -*cis*-octahydro-7(1*H*)-quinolones (IXa and IXb) was examined under both acidic and basic conditions. Under kinetic conditions, the *trans*-isomer (IXa) gave two isomeric tricyclic lactams (X and XI) while the *cis*-isomer (IXb) gave no cyclized compounds. Under thermodynamic conditions, the *cis*-isomer (IXb) as well as the *trans*-isomer (IXa) gave the same lactams (X and XI). In the former case with kinetic conditions, the difference in behavior toward cyclization between IXa and IXb was interpreted by taking a stereoelectronic requirement for the Michael addition into consideration, and in the latter case with thermodynamic ones, unexpected formation of the lactams (X and XI) from the *cis*-isomer (IXb) was rationalized by assuming a reaction pathway *via* the intermediate enone (XXII) of which we succeeded in isolation from the reaction mixture.

Keywords——Lycopodium alkaloids; octahydro-7(1*H*)-quinolone systems; decahydrobenzo[*i,j*]quinolizinediones; *trans,trans*-perhydrojulolidine; intramolecular Michael addition; Bohlmann absorption; *cis*- and *trans*-quinolizine systems; stereoelectronic requirement for Michael addition; stereochemistry; ^{1}H-NMR (PMR)

Considerable efforts have been made to provide synthetic routes to the Lycopodium alkaloids,[4] as in the total synthesis of lycopodine (I) by Stork, *et al.*[5] and Ayer, *et al.*[6] A synthesis of 12-*epi*-lycopodine (II), by Wiesner, *et al.*,[7] *via* intramolecular Michael reaction of III to yield IV has provided another attractive route to these alkaloids. In our previous work[2b] on lycodoline (V) synthesis, the cyclization step from VI to VII was found unsuccessful under a variety of both acidic and basic conditions in contrast to the Wiesner's result, owing probably to the stereoelectronic control derived from the difference in ring junction of octahydro-7(1*H*)-quinolone moieties between III and VI. In order to explore the stereochemistry of this cyclization by use of model compounds, we prepared *trans*- and *cis*-amido ketone (IXa and IXb) and examined introduction of the third ring into each of them to yield decahydrobenzo[*i,j*]quinolizinone systems (X and XI).

Acylation of *trans*- and *cis*-amino ketone (VIIIa[8] and VIIIb[9]) with acrylyl chloride in the presence of triethylamine afforded the corresponding amides (IXa and IXb), respectively, in 70—90% yields. The proton magnetic resonance (PMR) spectrum of the *cis*-isomer (IXb)

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[1] Part III: T. Momose, S. Uchida, E. Hosoya, M. Kinoshita, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **26**, 620 (1978).

[2] *a*) This work was presented in part at the 94th Annual Meeting of Pharmaceutical Society of Japan, Sendai, April 1974, Abstracts of Papers, II, p. 147; *b*) A preliminary communication has appeared in *Heterocycles*, **6**, 1105 (1977).

[3] Location: *133-1, Yamada-Kami, Suita, Osaka 565, Japan.*

[4] D.B. MacLean, "The Alkaloid," Vol. XIV, ed. by R.H.F. Manske, Academic Press, New York, 1973, pp. 347—405.

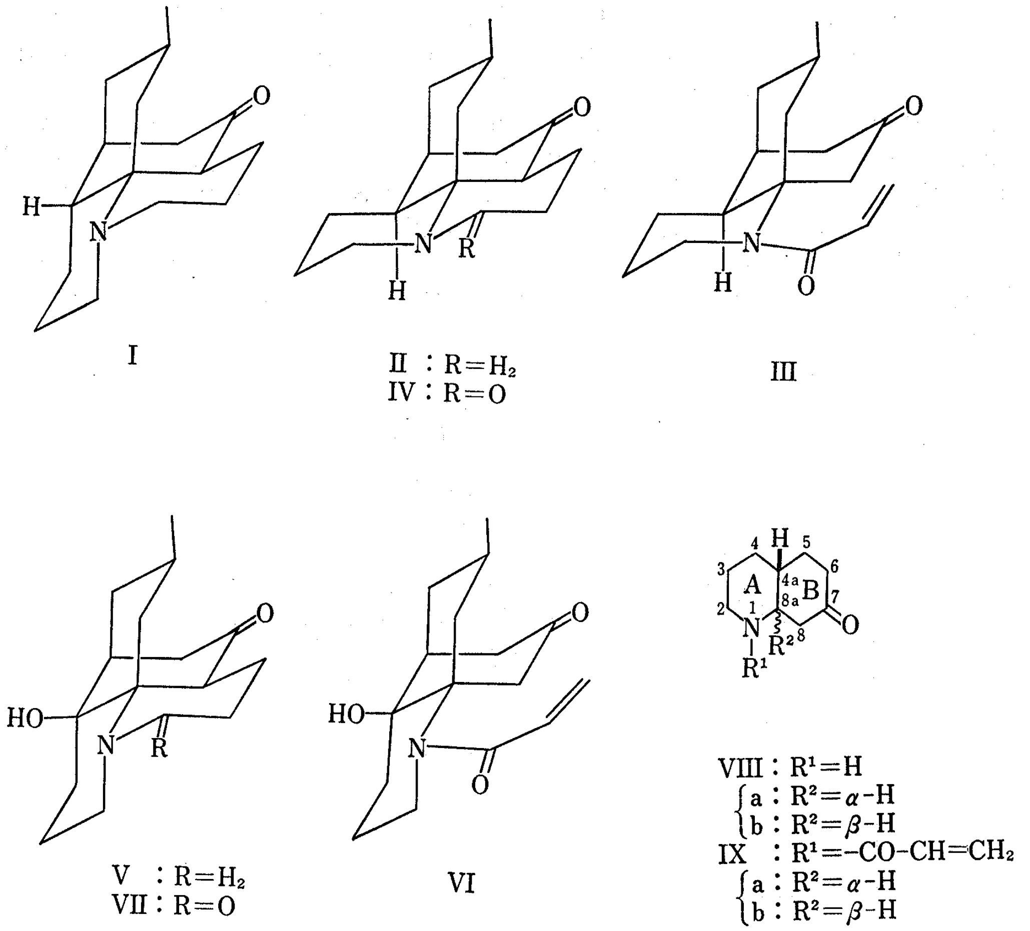
[5] G. Stork, R.A. Kretchmer, and R.H. Schlessinger, *J. Am. Chem. Soc.*, **90**, 1647 (1968).

[6] W.A. Ayer, W.R. Bowman, T.C. Joseph, and P. Smith, *J. Am. Chem. Soc.*, **90**, 1648 (1968).

[7] H. Dugas, M.E. Hazenberg, Z. Valenta, and K. Wiesner, *Tetrahedron Lett.*, **1967**, 4931.

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

[9] T. Momose, S. Uchida, M. Kinoshita, and T. Imanishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 1797 (1977).



I

II : $R=H_2$
IV : $R=O$

III

V : $R=H_2$
VII : $R=O$

VI

VIII : $R^1=H$
{a : $R^2=\alpha$-H
{b : $R^2=\beta$-H
IX : $R^1=-CO-CH=CH_2$
{a : $R^2=\alpha$-H
{b : $R^2=\beta$-H

Chart 1

displayed two deshielded protons as a broad signal in 3.60—5.19 ppm region, while that of the *trans*-isomer (IXa) exhibited no aliphatic proton signals in the region lower than 4.0 ppm. This behavior is consistent with our previous result concerning the assignment of stereochemistry of *N*-benzoyloctahydro-7(1*H*)-quinolone systems.[10]

Cyclization of IXa and IXb in the Presence of Potassium *tert*-Butoxide (*t*-BuOK)

As expected, cyclization of the *trans*-isomer (IXa) with *t*-BuOK in *t*-butanol at room temperature proceeded smoothly to give two isomeric tricyclic lactams, X (mp 135.5—137°) and XI (mp 119—121°), in 53% and 28% yields, respectively. Their infrared (IR) spectra showed ketone and lactam absorptions in the region of 1620—1715 cm^{-1}, and the PMR spectra exhibited one proton signal due to the C-5 equatorial proton at the lowest field and with a pattern characteristic of this system.[11] The stereochemistry of the main product (X) was determined as follows.

Reduction of X with lithium alanate afforded two isomeric amino alcohols, XII (64% yield; mp 131—135°) and XIII (30% yield; mp 148—151°), both displaying Bohlmann's absorptions in their IR spectra. Initial hydrogenation of X over platinum oxide in ethanol to lactam alcohols, XIV (34% yield) and XV (53% yield), and subsequent reduction of them with lithium alanate gave also XII (88% yield from XIV) and XIII (87% yield from XV), respectively. Tosylation of XII and XIII afforded the tosylates, XVI (mp 94—95.5°) and

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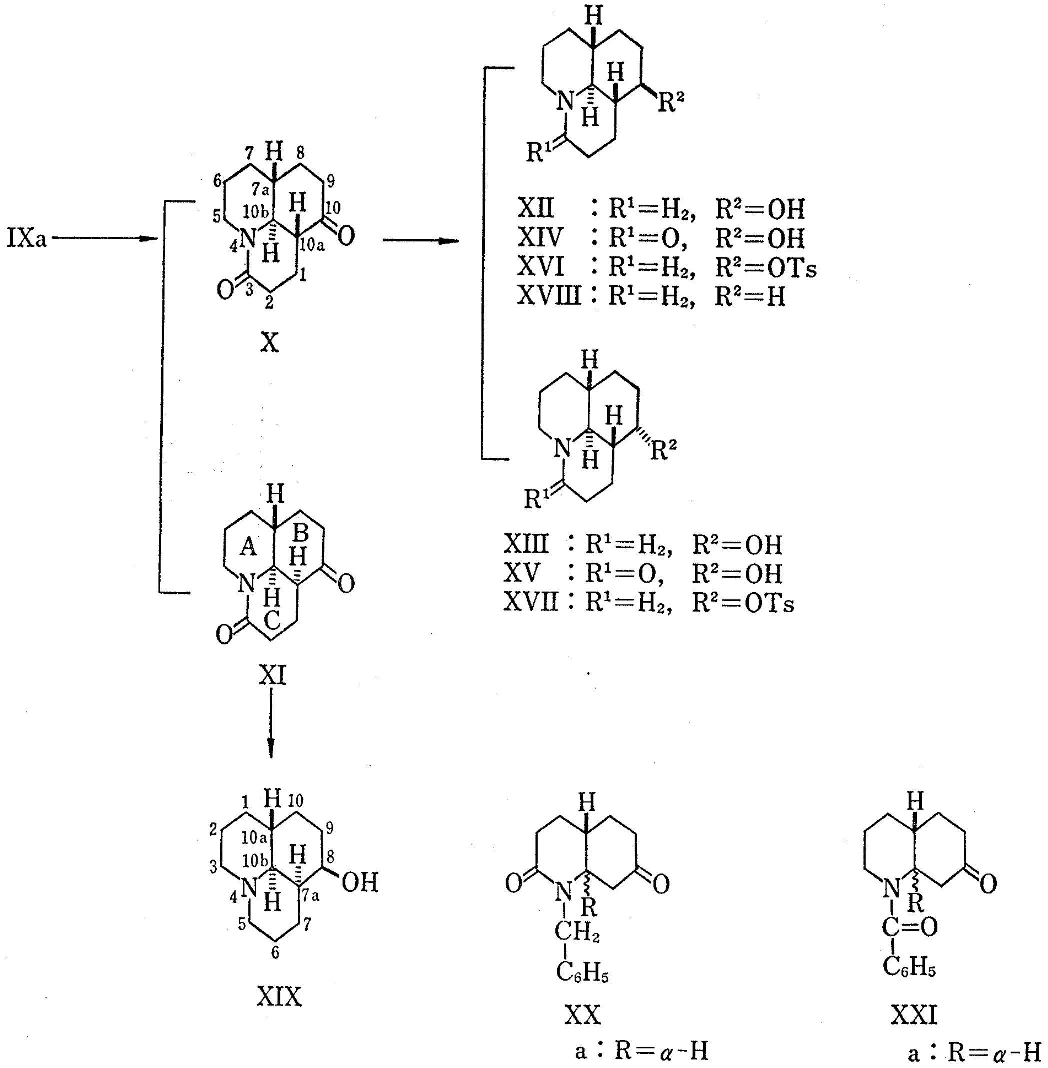
10) T. Momose, S. Uchida, N. Yamaashi, and T. Imanishi, *Heterocycles*, **3**, 713 (1975).
11) The stereochemistry of a similar system, 6a-ethyloctahydro-4*H*-pyrrolo[3,2,1-*i,j*]quinoline-2,9-dione, has been discussed: see Y. Ban, I. Iijima, I. Inoue, M. Akagi, and T. Oishi, *Tetrahedron Lett.*, **1969**, 2067.

XVII (mp 90—91°), respectively.[12] The PMR spectrum of XVI displays one proton signal due to the C-8 proton at 4.20 ppm with a half width ($W_{1/2}$) of 25 Hz while that of XVII displays the C-8 proton signal at 4.66 ppm ($W_{1/2}$=6 Hz). Apparently, the C-8 proton in XVI is an axial one, and that in XVII an equatorial one. The tosylate (XVI) was reduced with lithium alanate in boiling ether to afford *trans,trans*-perhydrojulolidine (XVIII).[13]

On the other hand, a clue to the stereochemistry of XI was given by the following observations: i) The minor product (XI) isomerized readily to the main product (X) during chromatography on basic alumina. This phenomenon rules out an A/B-*cis* ring junction for XI on taking the behavior of ring isomerization of XXa and XXb or of *N*-benzoyl analogues



XII : $R^1=H_2$, $R^2=OH$
XIV : $R^1=O$, $R^2=OH$
XVI : $R^1=H_2$, $R^2=OTs$
XVIII : $R^1=H_2$, $R^2=H$

XIII : $R^1=H_2$, $R^2=OH$
XV : $R^1=O$, $R^2=OH$
XVII : $R^1=H_2$, $R^2=OTs$

XX
a : R=α-H
b : R=β-H

XXI
a : R=α-H
b : R=β-H

Chart 2

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12) Wenkert, *et al.* have described both the preparation of a perhydrojulolidinol (mp 114—116°) corresponding to our present compound (XII) *via* reduction of the corresponding ketone and its conversion into *trans, trans*-perhydrojulolidine *via* reduction of its tosylate (mp 169—171°); E. Wenkert, K.G. Dave, and R.V. Stevens, *J. Am. Chem. Soc.*, **90**, 6177 (1968). Although neither of our alcohols, XII and XIII, or of the tosylates, XVI and XVII, showed close similarity in the melting characteristics to their compounds, alcohol XII was found almost identical in its IR spectrum (in CCl_4) with their alcohol by direct comparison of the spectra.

13) F. Bohlmann and C. Arndt, *Chem. Ber.*, **91**, 2167 (1958).

(XXIa and XXIb)[14] into consideration. ii) Reduction of XI with lithium alanate afforded the amino alcohol (XIX; mp 170—171°) as the only product,[15] which displayed no Bohlmann's absorption in its IR spectrum. From the fact, it is suggested that compound (XIX) involves a *cis*-quinolizidine system, that is, a B/C-*cis* ring junction. iii) The PMR spectrum of XI displays a downfield signal due to the C-10b proton at 3.28 ppm, which is absent in X. This feature is consistent with our previous results[9] that the C-8a proton signal for the *cis*-isomer of perhydroquinolin-2-one analogues[17] appears at the field lower than that for the *trans*-isomer in PMR spectra.

Meanwhile, the *cis*-isomer (IXb) afforded no cyclized compounds under a condition similar to that for the *trans*-isomer (IXa), but resulted in partial recovery (33%) of the starting material. Further treatment with the base gave only a complex mixture, probably of decomposed compounds.

Cyclization of IXa and IXb in the Presence of *p*-Toluenesulfonic Acid (*p*-TsOH)

Treatment of the *trans*-isomer (IXa) with *p*-TsOH in benzene at room temperature for one hour odd gave XI (3%) and an α,β-unsaturated ketone (XXII; 1%), along with the starting material (IXa; 81%). The structure of XXII was assigned from the spectral evidences. Its IR spectrum showed a carbonyl absorption band at 1675 cm^{-1}, and the PMR spectrum displayed three olefinic proton signals in the region of 5.64—6.09 ppm and two olefinic proton signals at 5.98 and 6.82 ppm. The signal pattern of the latter resembles

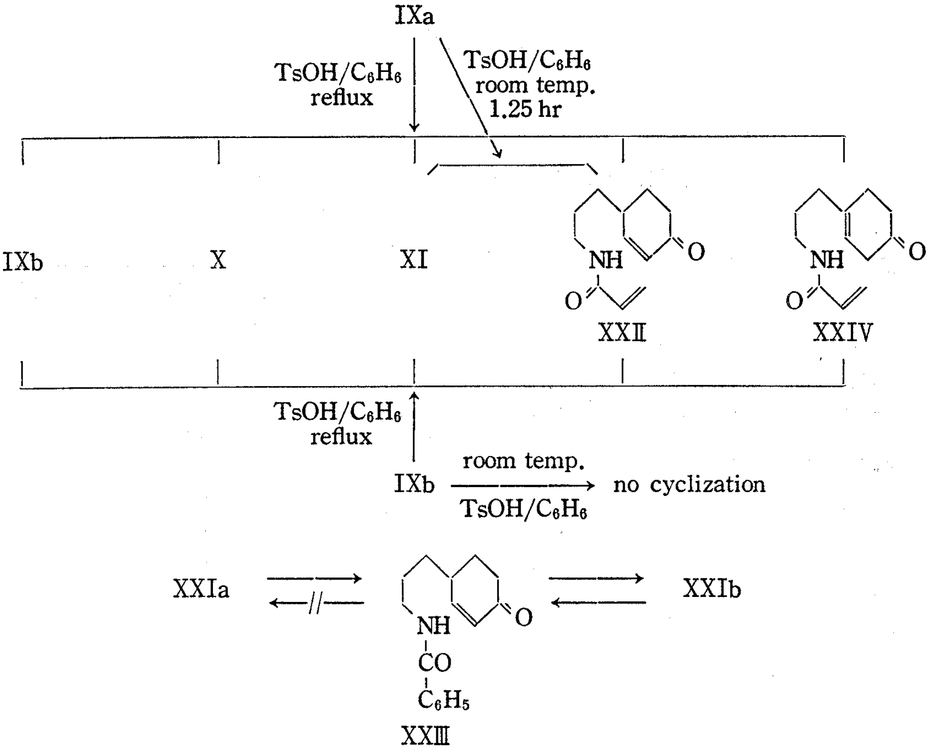

Chart 3

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[14] Under mild, basic conditions, the ring configuration in *cis*- and *trans*-octahydro-7(1*H*)-quinolones of amide structure has been demonstrated not to isomerize to any extent: see ref. 1.

[15] Hydrogenation of XI over platinum oxide in ethanol was accompanied by partial isomerization[16] of the ring configuration and resulted in formation of a mixture of XIV (28% yield), XV (29% yield), and a new lactam alcohol (21% yield; mp 75—78°), the last of which gave XIX on reduction with lithium alanate.

[16] See, for example, P. Deslongchamps, Z. Valenta, and J.S. Wilson, *Can. J. Chem.*, **44**, 2539 (1966).

[17] Corresponding to the B/C ring moiety in the present systems (X and XI).

that of the olefinic protons in the α,β-unsaturated ketone (XXIII).[1] The ultraviolet (UV) spectrum of XXII showed an absorption maximum at 227 nm. In addition, when the reaction was carried out under the same condition for 72 hr, the tricyclic lactams (X and XI) were formed in 43% and 10% yields, respectively, along with the *cis*-isomer (IXb; 9%) derived from partial isomerization of the starting material.[18]

Cyclization reaction of the *cis*-isomer (IXb) under the same condition as above resulted in complete recovery of the starting material.

On the other hand, when the *trans*-isomer (IXa) was treated with *p*-TsOH in boiling benzene for 2 hr, five components were found in the mixture: IXb (37%), X (42%), XI (9%), a β,γ-unsaturated ketone (XXIV; 2%), and XXII (3%). The IR spectrum of XXIV showed three absorption bands due to ketone, amide, and ethylenic groups at 1718—1630 cm^{-1}, and the PMR spectrum displayed three olefinic proton signals in the region of 5.60—6.30 ppm and one olefinic proton signal at 5.44 ppm. Lewis, *et al.*[19] have examined the acid-catalyzed equilibria between α,β- and β,γ-unsaturated ketones in a series of 4-alkyl-cyclohexenones. The observed trend of isomerization has been described as an increase in the equilibrium percentage of β,γ-unsaturated ketone as the 4-substituent increases in size. The percentage of the β,γ-isomer (XXIV) to the α,β-isomer (XXII) in the present system is reasonable as compared with the results of their investigation.

A similar reaction was carried out with the *cis*-isomer (IXb) for 6 hr to yield the same members of products: IXb (52%), X (10%), XI (3%), XXIV (3%), and XXII (5%).

Discussion

Results of the above experiments are summarized in Table I.

TABLE I. Cyclization Reaction of IXa and IXb

Substrate	Acid or base	Solvent	Temperature (°C)	Time (hr)	Products (%)					
					IXa	IXb	X	XI	XXIV	XXII
IXa	*t*-BuOK	*t*-BuOH	r.t.	0.25			53	28		
	p-TsOH	C_6H_6	r.t.	1.25	81			3		1
	p-TsOH	C_6H_6	r.t.	72		9	43	10		
	p-TsOH	C_6H_6	Reflux	2		37	42	9	2	3
	p-TsOH	Toluene	Reflux	25			60	9		
IXb	*t*-BuOK	*t*-BuOH	r.t.	0.25		33				
	t-BuOK	*t*-BuOH	r.t.	1		Decomposed				
	p-TsOH	C_6H_6	r.t.	72		80				
	p-TsOH	C_6H_6	Reflux	6		52	10	3	3	5
	p-TsOH	Toluene	Reflux	25			47	11		

r.t.: room temperature.

Behavior of the *trans*- and *cis*-isomers (IXa and IXb) toward cyclization under kinetic condition (*p*-TsOH in benzene or *t*-BuOK in *t*-BuOH at room temperature) is consistent with the assumption that this intramolecular Michael addition should proceed under the severe stereoelectronic control which enables the π-electrons of both reaction centers to come into the maximum overlap, that is, *via* a perpendicular attack of the electrophilic center on the enolate.[20]

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[18] An anomalous feature in isomerization of this system has been discussed in the preceding paper; see ref. 1.
[19] K.G. Lewis and G.J. Williams, *Tetrahedron Lett.*, **1965**, 4573.
[20] F.E. Ziegler and E.B. Spitzner, *J. Am. Chem. Soc.*, **95**, 7146 (1973).

Thus, the *trans*-isomer (IXa) could easily maintain the complete overlap of the π-orbitals in the transition state, while the *cis*-isomer (IXb) would be forced in ring A to be in a boat conformation such as IXb′ in order to furnish the overlap and thereby would be forced to produce severe steric interactions both between C_2–H and C_{4a}–H and between C_4–H and $C_{3'}$–H.

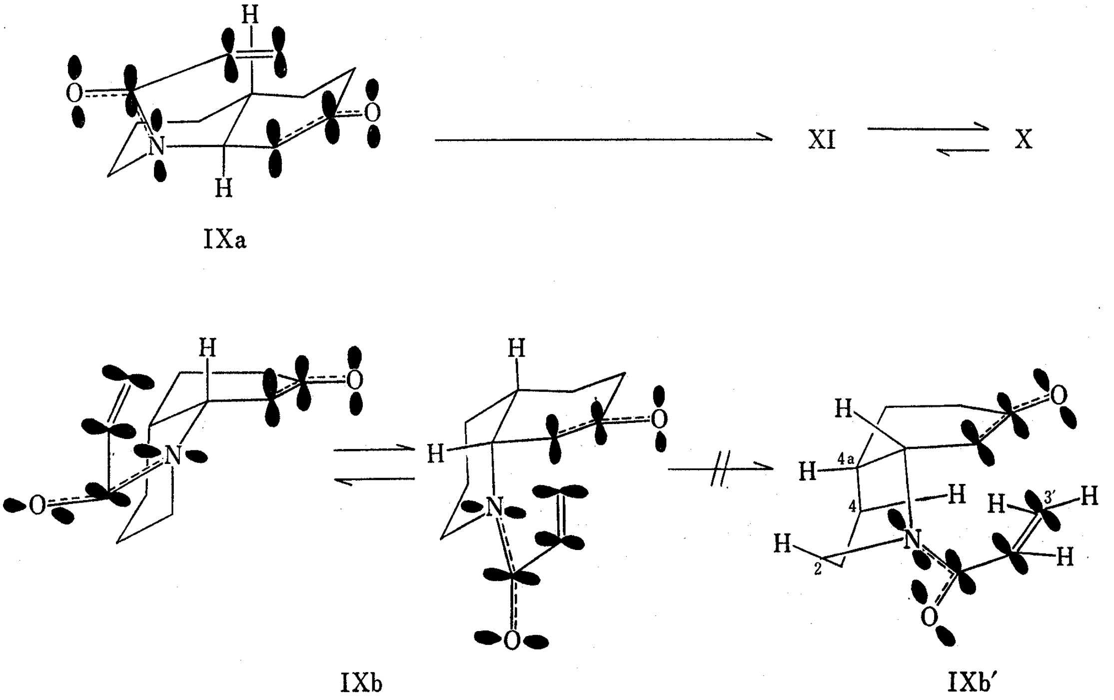

Chart 4

There arises the question as to which product, X or XI, resulted from the kinetic control. Inspection of the Dreiding model indicates a stereoelectronic preference for approach from the β-side over that from the other side. Indeed, we found that the acid-catalyzed cyclization of IXa under a mild condition gave initially the minor product (XI) and was followed by its isomerization to the main product (X) terminating in the equilibrium with predominance of X.

Our another point of interest was the reason why the *cis*-isomer (IXb) cyclized to yield only the "*trans*" tricyclic lactams (X and XI) under a drastic condition (*p*-TsOH in boiling toluene).21) We examined in detail the mechanistic pathway by substituting toluene for benzene as the solvent system. When the reactions were carried out in boiling benzene containing *p*-TsOH for a short time, the possible intermediate (XXII) could be obtained from both IXa and IXb. In the case of the *trans*-isomer (IXa), the main route to the tricyclic lactams would be a direct cyclization *via* Michael-type reaction owing to its easy fulfilment of the stereoelectronic requirement mentioned above. However, in the case of the *cis*-isomer (IXb), cyclization to yield the tricyclic lactams would be realized only *via* recyclization of the intermediate (XXII) because of its unfavorable situation in the orbital overlap. Upon comparing the behavior of the present intermediate (XXII) with the one (XXIII) in the previous study,1) it is quite interesting that the former recyclizes to the tricyclic lactams having an A/B-*trans* ring juncture while the latter, it is known, recyclizes exclusively to the *cis*-juncture. The acid-induced recyclization of the former (XXII) to the *trans*-system (IXa) also seems to be difficult, as suggested by eventual accumulation of only the *cis*-isomer (IXb)

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21) This condition was described in the previous communication: see ref. 2*b*.

on the run performed by using the *trans*-isomer (IXa) 'in boiling benzene.' Thus, it is suggested that the cyclization pathway (XXII→IXa→X and XI) would be ruled out. As one of the possible explanations, a mechanism involving a thermal Diels-Alder cyclization of XXII has been proposed for the present results.[2b)] Under the condition using *p*-TsOH 'in boiling toluene,' the *cis*-isomer (IXb) would be consumed *via* the retro-Michael cleavage followed by this highly temperature-dependent thermal cyclization, and hence would fail to accumulate in the reaction of the *trans*-isomer (IXa). The marked accumulation of the *cis*-isomer (IXb) on the run performed by using the *trans*-isomer (IXa) 'in boiling benzene' would be derived both from poor participation of this thermal cyclization and from the markedly increased rate of the retro-Michael cleavage of IXa prior to its direct cyclization to the tricyclic system (X and XI).

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-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, dd = doublet of doublets, ddt = doublet of doublets of triplets, dm = doublet of multiplets, qn = quintet, m = multiplet. 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} (Type T).

***N*-Acrylyl-*trans*-octahydro-7(1*H*)-quinolone (IXa)**——A mixture of *trans*-octahydro-7(1*H*)-quinolone[8)] (VIIIa; 1.2 g), acrylyl chloride (1.0 g), triethylamine (4.0 ml) and dry $CHCl_3$ (80 ml) was stirred at room temperature overnight. The reaction mixture was washed with 5% HCl, brine, satd. $NaHCO_3$ and brine, and evaporated to give an oil (2.1 g), which was chromatographed on silica gel. Elution with $CHCl_3$–EtOH (100: 1) gave 1.4 g (86%) of IXa as an oil. Attempted vacuum distillation, at 0.006 mmHg and 140°, resulted in partial decomposition of IXa. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1710 (CO), 1640 (amide), 1605 (C=C). MS *m/e*: 207 (M^+). PMR (90 MHz) δ: 3.11—3.98 (3H, m), 5.62 (1H, dd, $J=10$, 3, $_{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 6.20 (1H, dd, $J=17$, 3, $^{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 6.50 (1H, dd, $J=17$, 10, $_{\underline{\mathrm{H}}}{>}\mathrm{C{=}CH_2}$).

***N*-Acrylyl-*cis*-octahydro-7(1*H*)-quinolone (IXb)**——A mixture of *cis*-octahydro-7(1*H*)-quinolone[9)] (VIIIb; 400 mg), acrylyl chloride (270 mg), triethylamine (475 mg) and dry $CHCl_3$ (20 ml) was stirred at room temperature overnight. The reaction mixture was worked up as described for IXa to give 380 mg (70%) of IXb as an oil. Attempted vacuum distillation, at 0.006 mmHg and 140°, resulted in partial decomposition of IXb. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1710 (CO), 1635 (amide), 1610 (C=C). MS *m/e*: 207 (M^+). PMR (90 MHz) δ: 3.60—5.19 (2H, m, C_2-equatorial H and C_{8a}–H), 5.65 (1H, dd, $J=10$, 3, $_{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 6.20 (1H, dd, $J=17$, 3, $^{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 6.53 (1H, dd, $J=17$, 10, $_{\underline{\mathrm{H}}}{>}\mathrm{C{=}CH_2}$).

Cyclization Reaction of the Amido Ketone (IXa and IXb)——A) In the Presence of Potassium *t*-Butoxide (*t*-BuOK): i) To a stirred solution of *t*-BuOK in *t*-BuOH (prepared from 110 mg of potassium and 50 ml of *t*-BuOH) was added a solution of IXa (680 mg) in *t*-BuOH (10 ml) all at once, and the stirring was continued for 15 min at room temperature. 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 $CHCl_3$ solution was washed with satd. $NaHCO_3$, brine, and evaporated to give an oil (680 mg), which was chromatographed on silica gel. The first fraction eluted with $CHCl_3$–EtOH (100: 1) gave 360 mg (53%) of *trans, trans*-decahydro-3*H*,10*H*-benzo[*i,j*]quinolizine-3,10-dione (X) as colorless needles (from hexane), mp 135.5—137°. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 1715 (CO), 1628 (lactam). MS *m/e*: 207 (M^+). PMR (90 MHz) δ: 4.76 (1H, ddt, $J=13$, 4, 2, C_5-equatorial H). *Anal.* Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.37; H, 8.19; N, 6.76. The second fraction gave 190 mg (28%) of *trans*(7a*H*, 10b*H*), *cis*(10a*H*, 10b*H*)-decahydro-3*H*, 10*H*-benzo[*i,j*]quinolizine-3,10-dione (XI) as colorless needles (from hexane), mp 119—121°. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 1709 (CO), 1620 (lactam). MS *m/e*: 207 (M^+). PMR (90 MHz) δ: 4.79 (1H, ddt, $J=13$, 4, 2, C_5-equatorial H), 3.28 (1H, dd, $J=11$, 6, C_{10b}–H). *Anal.* Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.46; H, 8.28; N, 6.85.

ii) To a stirred solution of *t*-BuOK in *t*-BuOH (prepared from 10 mg of potassium and 2.5 ml of *t*-BuOH) was added a solution of IXb (33 mg) in *t*-BuOH (0.6 ml) all at once, and the stirring was continued for 15 min at room temperature. The reaction mixture was worked up as described in i) to give 11 mg (33%) of the starting material (IXb).

iii) To a stirred solution of *t*-BuOK in *t*-BuOH (prepared from 30 mg of potassium and 9.0 ml of *t*-BuOH) was added a solution of IXb (120 mg) in *t*-BuOH (2.0 ml) all at once, and the stirring was continued for one hr at room temperature. The reaction mixture was worked up as described in i) to give a residue (45 mg) which showed many spots on TLC.

B) In the Presence of *p*-Toluenesulfonic Acid (TsOH): i) A mixture of IXa (830 mg), TsOH (240 mg) and dry benzene (60 ml) was stirred at room temperature for 1.25 hr. The reaction mixture was washed with satd. $NaHCO_3$, brine, and evaporated to give a residue, which was chromatographed on silica gel. The first fraction eluted with $CHCl_3$–EtOH (100: 1) gave 670 mg (81%) of the starting material (IXa). The second fraction gave 25 mg (3%) of XI. The third fraction gave 10 mg (1%) of 4-(3-acrylamidopropyl)-2-cyclohexenone (XXII) as an oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1675 (enone, amide), 1630 (C=C). MS *m/e*: 207 (M^+). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (ε): 227 (12800). PMR (90 MHz) δ: 5.64 (1H, dd, $J=10, 3$, ${}_{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 5.98 (1H, dd, $J=10, 3$, $-\mathrm{CH{=}C\underline{H}{-}}\overset{|}{\mathrm{C}}\mathrm{{=}O}$), 6.09 (1H, dd, $J=17, 10$, ${}_{\underline{\mathrm{H}}}{>}\mathrm{C{=}CH_2}$), 6.31 (1H, dd, $J=17, 3$, ${}^{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 6.82 (1H, dm, $J=10$, $-\mathrm{C\underline{H}{=}CH{-}}\overset{|}{\mathrm{C}}\mathrm{{=}O}$).

ii) A mixture of IXa (610 mg), TsOH (180 mg) and dry benzene (30 ml) was stirred at room temperature for 72 hr. The reaction mixture was worked up as described in i) to give a residue (390 mg), which was chromatographed on silica gel. The first fraction eluted with $CHCl_3$–EtOH (100: 1) gave 55 mg (9%) of IXb. The second fraction gave 260 mg (43%) of X. The third fraction gave 60 mg (10%) of XI.

iii) A mixture of IXb (68 mg), TsOH (20 mg) and dry benzene (6.0 ml) was stirred under the same condition as described in ii) to result in recovery of the starting material (IXb).

iv) A mixture of IXa (430 mg), TsOH (130 mg) and dry benzene (43 ml) was heated under reflux for 2 hr. The reaction mixture was worked up as described in i) to give 160 mg (37%) of IXb (from the 1st fraction), 180 mg (42%) of X (from the 2nd one), 40 mg (9%) of XI (from the 3rd one), 15 mg (3%) of XXII (from the 5th one), and 10 mg (2%) of 4-(3-acrylamidopropyl)-3-cyclohexenone (XXIV) as an oil (from the 4th one). Compound XXIV: IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1718 (CO), 1670 (amide), 1630 (C=C). MS *m/e*: 207 (M^+). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (ε): 222 (4800). PMR (90 MHz) δ: 5.44 (1H, m, $>\mathrm{C{=}C\underline{H}{-}}$), 5.60 (1H, dd, $J=10, 3$, ${}_{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$), 6.02 (1H, dd, $J=17, 10$, ${}_{\underline{\mathrm{H}}}{>}\mathrm{C{=}CH_2}$), 6.30 (1H, dd, $J=17, 3$, ${}^{\mathrm{H}}{>}\mathrm{C{=}C}{<}^{\mathrm{H}}_{\underline{\mathrm{H}}}$).

v) A mixture of IXb (420 mg), TsOH (120 mg) and dry benzene (40 ml) was heated under reflux for 6 hr. The reaction mixture was worked up as described in i) to give 220 mg (52%) of IXb, 44 mg (10%) of X, 12 mg (3%) of XI, 11 mg (3%) of XXIV, and 20 mg (5%) of XXII.

vi) A mixture of IXa (0.10 g), TsOH (30 mg) and dry toluene (10 ml) was heated under reflux for 25 hr. The reaction mixture was worked up as described in i) to give 60 mg (60%) of X and 9 mg (9%) of XI. A similar treatment of IXb (0.10 g) gave 47 mg (47%) of X and 11 mg (11%) of XI.

***trans,trans*-Decahydro-1*H*,5*H*-benzo[*i,j*]quinolizin-8-ols (XII and XIII)**——A suspension consisting of X (0.30 g), $LiAlH_4$ (900 mg) and dry ether (80 ml) was heated under reflux overnight. After decomposing the excess reducing agent with AcOEt, an aqueous solution of sodium potassium tartrate was added to the reaction complex, and the supernatant was decanted. The precipitate was washed with ether. The combined ethereal layers were evaporated to give crystals (310 mg), which was chromatographed on alumina in ether. The first fraction gave 85 mg (30%) of the 8α-ol (XIII) as colorless needles (from hexane), mp 148—151°. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3120 (OH). MS *m/e*: 195 (M^+). PMR (90 MHz) δ: 2.10 (1H, broad s, disappeared with D_2O, OH), 3.94 (1H, m, $W_{1/2}=6$, C_8–H). *Anal.* Calcd. for $C_{12}H_{21}NO$: C, 73.79; H, 10.84; N, 7.17. Found: C, 73.65; H, 10.84; N, 7.03. The second fraction gave 180 mg (64%) of the 8β-ol (XII) as colorless needles (from hexane), mp 131—135° (lit.[12] 114—116°). IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3120 (OH). MS *m/e*: 195 (M^+). PMR (90 MHz) δ: 2.35 (1H, s, disappeared with D_2O, OH), 3.17 (1H, m, $W_{1/2}=20$, C_8–H). *Anal.* Calcd. for $C_{12}H_{21}NO$: C, 73.79; H, 10.84; N, 7.17. Found: C, 73.79; H, 10.80; N, 6.96.

***trans,trans*-3-Oxo-10-hydroxy-decahydro-3*H*,10*H*-benzo[*i,j*]quinolizines (XIV and XV)**——The keto lactam (X; 50 mg) was hydrogenated over PtO_2 (20 mg) in EtOH (6 ml) at room temperature and an atmospheric pressure until the uptake of hydrogen ceased. The catalyst was filtered off, and the filtrate was evaporated under reduced pressure to give a residue (50 mg), which was chromatographed on alumina. The first fraction eluted with ether–MeOH (100: 4) gave 27 mg (53%) of XV as colorless crystals (from acetone), mp 169—170°. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3300 (OH), 1600 (lactam). MS *m/e*: 209 (M^+). PMR (60 MHz) δ: 4.06 (1H, m, $W_{1/2}=6$, C_{10}–H), 4.72 (1H, dm, C_5–equatorial H). *Anal.* Calcd. for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.60; H, 9.17; N, 6.55. The second fraction gave 17 mg (34%) of XIV as colorless crystals (from acetone), mp 158—162°. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3300 (OH), 1605 (lactam). MS *m/e*: 209 (M^+). PMR (60 MHz) δ: 3.38 (1H, m, $W_{1/2}=15$, C_{10}–H), 4.75 (1H, dm, C_5-equatorial H). *Anal.* Calcd. for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.80; H, 9.17; N, 6.37.

An Alternative Synthesis of XII and XIII——A suspension consisting of the lactam alcohol (XIV; 56 mg), $LiAlH_4$ (110 mg) and dry ether (30 ml) was heated under reflux for 20 hr. The mixture was worked up as usual to afford 46 mg (88%) of XII. Its IR spectrum was identical with that of XII obtained from the reduction of X with $LiAlH_4$.

A suspension consisting of the lactam alcohol (XV; 54 mg), $LiAlH_4$ (110 mg) and dry ether (30 ml) was heated under reflux for 20 hr. The mixture was worked up as usual to afford 44 mg (87%) of XIII. Its IR spectrum was identical with that of XIII obtained from the reduction of X with $LiAlH_4$.

***cis*(7a*H*,10b*H*),*trans*(10a*H*,10b*H*)-Decahydro-1*H*,5*H*-benzo[*i*,*j*]quinolizin-8β-ol (XIX)**——A suspension consisting of XI (86 mg), $LiAlH_4$ (256 mg) and dry ether (50 ml) was heated under reflux overnight. The reaction mixture was worked up as usual to afford crystals (74 mg), which were chromatographed on alumina. Elution with ether gave 65 mg (74%) of XIX as colorless plates (from hexane), mp 170—171°. IR $\nu_{\max}^{\text{KCl}}$ cm^{-1}: 3175 (OH). MS *m/e*: 195 (M^+). PMR (90 MHz) δ: 3.20 (1H, broad s, disappeared with D_2O, OH), 3.68 (1H, qn, $W_{1/2}=23$, C_8–H). *Anal.* Calcd. for $C_{12}H_{21}NO$: C, 73.79; H, 10.84; N, 7.17. Found: C, 73.56; H, 10.80; N, 7.24.

***trans*,*trans*-Decahydro-8β-tosyloxy-1*H*,5*H*-benzo[*i*,*j*]quinolizine (XVI)**——A mixture of XII (65 mg), *p*-toluenesulfonyl chloride (100 mg) and dry pyridine (1.0 ml) was allowed to stand in a refrigerator for 40 hr. Removal of the solvent afforded an oily residue, which was chromatographed on alumina. Elution with ether gave 80 mg (69%) of XVI as colorless needles (from hexane), mp 94—94.5° (lit.[12] 169—171°). IR $\nu_{\max}^{\text{KCl}}$ cm^{-1}: 1598 (arom.), 1365 and 1178 (SO). MS *m/e*: 349 (M^+). PMR (90 MHz) δ: 4.20 (1H, m, $W_{1/2}=25$, C_8–H), 7.54 (4H, AB type, arom.). *Anal.* Calcd. for $C_{19}H_{27}NO_3S$: C, 65.31; H, 7.79; N, 4.01. Found: C, 65.16; H, 7.80; N, 4.21.

***trans*,*trans*-Decahydro-8α-tosyloxy-1*H*,5*H*-benzo[*i*,*j*]quinolizine (XVII)**——A mixture of XIII (146 mg), *p*-toluenesulfonyl chloride (300 mg) and dry pyridine (1.0 ml) was allowed to stand in a refrigerator for 70 hr. Removal of the solvent afforded an oily residue, which was chromatographed on alumina. The first fraction eluted with $CHCl_3$ gave 85 mg (33%) of XVII as colorless needles (from petr. ether), mp 90—91°. IR $\nu_{\max}^{\text{KCl}}$ cm^{-1}: 1596 (arom.), 1355 and 1178 (SO). MS *m/e*: 349 (M^+). PMR (90 MHz) δ: 4.66 (1H, m, $W_{1/2}=6$, C_8–H), 7.54 (4H, AB type, arom.). *Anal.* Calcd. for $C_{19}H_{27}NO_3S$: C, 65.31; H, 7.79; N, 4.01. Found: C, 65.41; H, 7.80; N, 4.13. The second fraction gave 80 mg of the starting material.

***trans*,*trans*-Perhydrojulolidine (XVIII)**——A suspension consisting of XVI (65 mg), $LiAlH_4$ (100 mg) and dry ether (20 ml) was heated under reflux for 10 hr. The reaction mixture was worked up as usual to give an oil (41 mg), which was chromatographed on alumina. Elution with ether gave 33 mg (100%) of XVIII as an oil, which was identical in its IR spectrum with XVIII reported by Bohlmann.[13] The picrate, mp 185—187.5° (EtOH) (lit.[13] 186°). *Anal.* Calcd. for $C_{12}H_{21}N \cdot C_6H_3N_3O_7$: C, 52.93; H, 5.92; N, 13.72. Found: C, 52.69; H, 5.92; N, 13.68.

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