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A Synthesis of Isoquinuclidine Derivatives by the Diels–Alder Reaction of 2-Methylene-1,2-dihydropyridine Derivatives with Dienophiles

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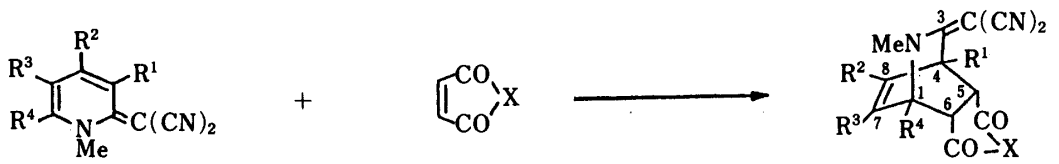
The Diels–Alder reaction of 2-methylene-1,2-dihydropyridines (Ia—f) with dienophiles such as maleic anhydride, maleimide, and *N*-phenylmaleimide proceeded in a stereoselective manner to give the *endo*-adducts (IIIa—i). This reaction provides a simple synthetic method for isoquinuclidines having a carbon side-chain at the 3-position.

Keywords——Diels–Alder reaction; 2-azabicyclo[2.2.2]octane; 2-dicyanomethylene-1,2-dihydro-1-methylpyridine; maleic anhydride; *N*-phenylmaleimide; maleimide

The Diels–Alder adducts from the reactions of 2(1*H*)-pyridone derivatives with dienophiles have an isoquinuclidine skeleton,[1] which is commonly found in many iboga alkaloids, and therefore the adducts have great potential as synthetic intermediates. Previously,[1-6] we have developed a synthetic route toward this heterocyclic ring system having various substituents by using the Diels–Alder reaction of 1-substituted 2(1*H*)-pyridones with dienophiles. In the present paper, we wish to report a simple synthetic method leading to 3-substituted isoquinuclidine derivatives by the Diels–Alder reaction of 2-methylene-1,2-dihydropyridines (Ia—f) with dienophiles (IIa—c).

The Diels–Alder reactions of 2-dicyanomethylene-1,2-dihydro-1-methylpyridine (Ia)[7] with maleic anhydride (IIa), maleimide (IIb), and *N*-phenylmaleimide (IIc) were carried out to produce the *endo*-adducts (IIIa—c) in 6%, 38%, and 78% yields, respectively (Chart 1). The structures of IIIa—c were confirmed in the following way. The products (IIIa—c) have the molecular formulae $C_{13}H_9N_3O_3$, $C_{13}H_{10}N_4O_2$, and $C_{19}H_{14}N_4O_2$, respectively, based on the elemental analyses and the mass spectra (MS). The infrared (IR) spectrum of IIIa showed absorptions due to the cyano and the carbonyl groups of the carboxylic anhydride, and furthermore, those of IIIb, c exhibited absorptions due to the cyano and the carbonyl groups of the imides (Table I). Moreover, the proton nuclear magnetic resonance (^{1}H-NMR) spectra of IIIa—c (Table I) were similar to those of 3-oxo-2-azabicyclo[2.2.2]octane derivatives,[2,8] which are the *endo*-adducts formed from 1-methyl-2(1*H*)-pyridone and IIa—c, respectively. Considering these results, IIIa—c are concluded to be the Diels–Alder adducts, namely, the isoquinuclidine derivatives having a carbon side-chain at the 3-position.

In order to perform the ^{1}H-NMR spectral assignments of IIIa—c, the deuterio-adduct (IIId) was synthesized by the reaction of 2-dicyanomethylene-3,5-dideuterio-1,2-dihydro-1-methylpyridine (Ib) and IIc (Chart 1). There were two protons less on the isoquinuclidine ring of IIId than in IIIa—c, as determined from the ^{1}H-NMR spectrum of IIId, and the deuterons must be located at the 4- and 7-positions in IIId. Consequently, considering the coupling constants (*J*), the one-proton signals at δ 3.43, 3.87, 5.05, and 6.61 in the ^{1}H-NMR spectrum of IIId could be unambiguously assigned to C_5-, C_6-, C_1- and C_8-H, respectively (Table I). Based on a comparison of the ^{1}H-NMR spectrum of IIId with those of IIIa—c, all the protons of IIIa—c could be assigned as shown in Table I.



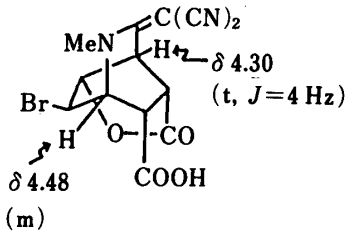
Ia: $R^1=R^2=R^3=R^4=H$
Ib: $R^1=R^3=D$, $R^2=R^4=H$
Ic: $R^1=Me$, $R^2=R^3=R^4=H$
Id: $R^2=Me$, $R^1=R^3=R^4=H$
Ie: $R^3=Me$, $R^1=R^2=R^4=H$
If: $R^4=Me$, $R^1=R^2=R^3=H$

IIa: X=O
IIb: X=NH
IIc: $X=NC_6H_5$

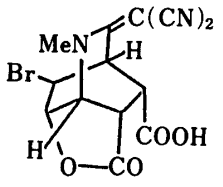
IIIa: $R^1=R^2=R^3=R^4=H$, X=O
IIIb: $R^1=R^2=R^3=R^4=H$, X=NH
IIIc: $R^1=R^2=R^3=R^4=H$, $X=NC_6H_5$
IIId: $R^1=R^3=D$, $R^2=R^4=H$, $X=NC_6H_5$
IIIe: $R^1=Me$, $R^2=R^3=R^4=H$, $X=NC_6H_5$
IIIf: $R^2=Me$, $R^1=R^3=R^4=H$, $X=NC_6H_5$
IIIg: $R^3=Me$, $R^1=R^2=R^4=H$, $X=NC_6H_5$
IIIh: $R^4=Me$, $R^1=R^2=R^3=H$, $X=NC_6H_5$
IIIi: $R^3=Me$, $R^1=R^2=R^4=H$, X=O

Chart 1

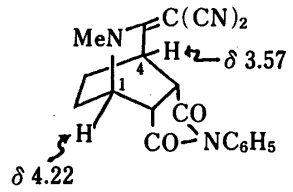
Next, the configurations of the two substituents at the 5- and 6-positions in IIIa—c were investigated as follows. Bromolactonization of the carboxylic acid (IV) obtained by hydrolysis of IIIa gave the bromolactone (V), the IR spectrum of which showed absorption due to the carbonyl group of the γ-lactone. The ^{1}H-NMR spectrum of V (Table I) was similar to that of the *endo*-lactone (VI)[2] (Chart 2). In the ^{1}H-NMR spectrum of V, the signals due to the two bridgehead protons were observed as a triplet at δ 4.30 (J=4 Hz) and a multiplet at δ 4.48. The signals due to the protons at the bases of bromine (Br–C<u>H</u>–) and oxygen in the lactone (–COOC<u>H</u>–) appeared at δ 4.85 (d, J=2 Hz) and δ 5.13 (d, J=4 Hz), respectively, and furthermore, those at the bases of the carbonyl groups in the lactone (–C<u>H</u>COO–) and the carboxylic acid (–C<u>H</u>COOH) appeared at δ 3.23 (dd, J=10, 4 Hz) and δ 3.60 (dd, J=10, 4 Hz), respectively. From the examination of the J values of all the signals, the triplet at δ 4.30 (J=4 Hz) could be assigned to the bridgehead proton on the γ-lactone side. From the above results, the structure of V should be either Va or Vb as shown in Chart 2. Ramey and others[9] reported that the signal due to C_1-H on the γ-lactone side was located at a lower magnetic field than that due to C_4-H owing to the deshielding effect resulting from the ring current associated with the lactone carbonyl group in the ^{1}H-NMR spectrum of VII (Chart 2), and also, our previous paper[2] showed that the signals due to C_1-H and C_4-H in the ^{1}H-NMR spectrum of VI appeared at 0.12 and 0.63 ppm lower magnetic field than those due to the corresponding protons of VIII (Chart 2). Based on the above paper and the chemical shifts of the two bridgehead protons in the 7,8-dihydro compound (XIa) (Chart 2 and Table I), the signals due to the bridgehead proton on the γ-lactone side and the other bridgehead proton in the ^{1}H-NMR spectrum of Vb would be expected to appear at around δ 4.85 (0.63 ppm lower magnetic field) and around δ 3.69 (0.12 ppm lower magnetic field) than those at δ 4.22 (C_1-H) and 3.57 (C_4-H) of XIa, respectively. This is not in agreement with the fact that the signal due to the bridgehead proton on the γ-lactone side (δ 4.30) appears at higher magnetic field than that due to the other bridgehead proton (δ 4.48) in the ^{1}H-NMR spectrum of V. On the other hand, the signals due to the bridgehead proton on the γ-lactone side and the other bridgehead proton in the ^{1}H-NMR spectrum of Va would be expected to appear at around δ 4.20 and around δ 4.34, respectively, which are close to the chemical shifts (δ 4.30 and 4.48) of the corresponding protons of V. From the above discussion, it can be deduced that the structure of V is not Vb but Va, which is produced from the carboxylic acid (IV) and bromine.



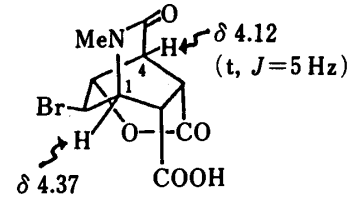
Va



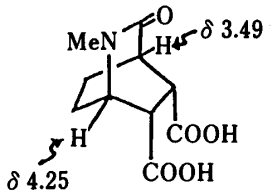
Vb



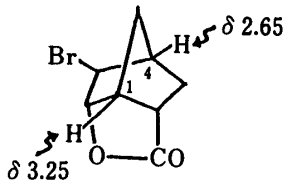
XIa



VI[2)]

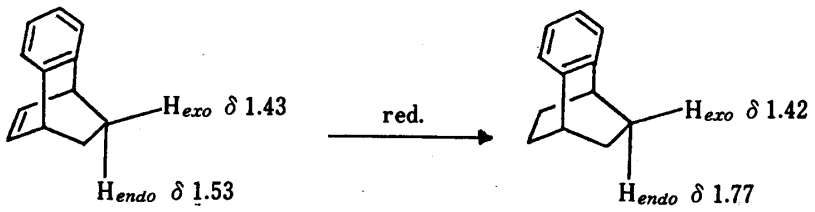


VIII[2)]

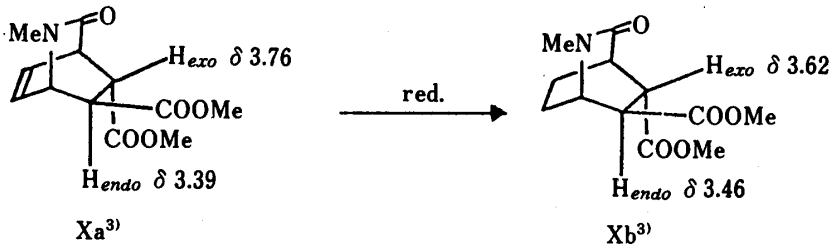


VII[9)]

Chart 2



IXa[10)] IXb[10)]



Xa[3)] Xb[3)]

Chart 3

Therefore, IV would be an *endo*-form, and so the adduct (IIIa) is determined to be an *endo*-form.

It has been reported that an interesting shift is observed, upon reduction of the double bond, in the signals of the *endo*- and *exo*-protons of the ethylene moiety in the ^{1}H-NMR spectra of the bicyclo[2.2.2]octane system as seen in IXa, b[10)] and Xa, b[3)] (Chart 3). Reduction of the aliphatic carbon–carbon double bonds in IXa and Xa caused a shift of the signal due to the *endo*-proton to a lower magnetic field, but a shift of that due to the *exo*-proton to a higher magnetic field. Catalytic reduction of IIIc was carried out to give the corresponding 7,8-dihydro compound (XIa). A comparison of the ^{1}H-NMR spectrum of IIIc with that of XIa showed that the signals due to C_5- and C_6-H in IIIc appeared at a lower magnetic field than those due to the corresponding protons in XIa (Table I). Thus, the stereochemistry of the hydrogens at the 5- and 6-positions in IIIc can be deduced as being in the *exo*-configuration, suggesting IIIc to be an *endo*-adduct. This conclusion was supported by the J values ($J_{16}=J_{45}=4$ Hz) in the ^{1}H-NMR spectrum of IIIc, which were the same as those of IIIa. The

relative configuration of two substituents at the 5- and 6-positions in IIIb was determined to be *endo* from the *J* values ($J_{16}=J_{45}=4$ Hz) in the ^{1}H-NMR spectrum of IIIb (Table I).

The reactions of the compounds (Ic—f)[11] with IIc, and Ie with IIa were carried out to afford the corresponding *endo*-adducts (IIIe—i) (Chart 1). The structures of IIIe—i were confirmed by their empirical formulae and spectral analyses (Table I). The configuration of the 5,6-*endo*-substituents in IIIe—g, i was supported by the *J* values ($J_{16}=4$—4.3 Hz) in the ^{1}H-NMR spectra, and that in IIIh was determined by ^{1}H-NMR spectral scrutiny and consideration of the corresponding 7,8-dihydro compound (XIb) (Table I) in the same way as described above for IIIc and XIa.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were measured with a Shimadzu IR-430 spectrometer in Nujol. ^{1}H-NMR spectra were recorded on JEOL JMN-PMX 60 and JEOL GX 270 spectrometers in dimethyl sulfoxide-d_6 with tetramethylsilane (TMS) as an internal standard. MS were taken on Hitachi RMU-6MG and JEOL JMN-DX 303 spectrometers.

Preparation of the Diels–Alder Adducts (IIIa, b, i)——A mixture of Ia[7] or Ie[11] (2 mmol) with IIa (40 mmol), or of Ia (2 mmol) with IIb (18 mmol) were heated in a sealed tube at 95—100 °C for 3 d. The reaction mixture was worked up in the following way to give the corresponding product, IIIa, b, i. IR and ^{1}H-NMR spectral data for IIIa, b, i are listed in Table I.

3-Dicyanomethylene-2-methyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboxylic Anhydride (IIIa): The reaction mixture was extracted with $CHCl_3$ (300 ml) under stirring at room temperature for 3 h and the extract was filtered. The filtrate was evaporated, and the residue was recrystallized from Ac_2O to give IIIa as colorless prisms, mp 248—249 °C (dec.) in 6% yield. High-resolution MS *m/z*: Calcd for $C_{13}H_9N_3O_3$ (M^+): 255.0644. Found: 255.0664.

3-Dicyanomethylene-2-methyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIIb): The reaction mixture was chromatographed on a column of silica gel. The fraction eluted with $CHCl_3$–Me_2CO (1 : 1) was evaporated, and the residue was recrystallized from Me_2CO to give IIIb as colorless prisms, mp 250—252 °C (dec.), in 38% yield. High-resolution MS *m/z*: Calcd for $C_{13}H_{10}N_4O_2$ (M^+): 254.0804. Found: 254.0799.

3-Dicyanomethylene-2,7-dimethyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboxylic Anhydride (IIIi): The reaction mixture was worked up as described above for the preparation of IIIa to give IIIi as colorless prisms, mp 245—246 °C (dec.) (Me_2CO), in 12% yield. High-resolution MS *m/z*: Calcd for $C_{14}H_{11}N_3O_3$ (M^+): 269.0801. Found: 269.0786.

Preparation of the Diels–Alder Adducts (IIIc—h)——A mixture of one of Ia,[7] b, c—f[11] (10 mmol) and IIc (80 mmol) was heated in a sealed tube at 100—110 °C for 3 d. The reaction mixture was stirred with Me_2CO (10 ml) at room temperature for 1 h. The precipitate formed was collected by filtration to give the corresponding product, IIIc—h. IR and ^{1}H-NMR spectral data for IIIc—h are listed in Table I.

N-Phenyl-3-dicyanomethylene-2-methyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIIc): Yield 78%, colorless prisms, mp 279—280 °C (Me_2CO). *Anal.* Calcd for $C_{19}H_{14}N_4O_2$: C, 69.08; H, 4.27; N, 16.96. Found: C, 68.98; H, 3.95; N, 16.99. MS *m/z*: 330 (M^+).

N-Phenyl-3-dicyanomethylene-4,7-dideuterio-2-methyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIId): Yield 78%, colorless prisms, mp 279—280 °C (Me_2CO). MS *m/z*: 332 (M^+). The melting point of IIId coincided with that of IIIc (mp 279—280 °C).

N-Phenyl-3-dicyanomethylene-2,4-dimethyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIIe): Yield 63%, colorless prisms, mp 212—213 °C (Me_2CO). *Anal.* Calcd for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.47; H, 4.49; N, 16.01. MS *m/z*: 344 (M^+).

N-Phenyl-3-dicyanomethylene-2,8-dimethyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIIf): Yield 66%, colorless prisms, mp 260—261 °C (Me_2CO). *Anal.* Calcd for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.77; H, 4.49; N, 16.38. MS *m/z*: 344 (M^+).

N-Phenyl-3-dicyanomethylene-2,7-dimethyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIIg): Yield 98%, colorless prisms, mp 277—278 °C (Me_2CO). *Anal.* Calcd for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.60; H, 4.37; N, 16.27. MS *m/z*: 344 (M^+).

N-Phenyl-3-dicyanomethylene-1,2-dimethyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboximide (IIIh): Yield 38%, colorless prisms, mp 236—237 °C (Me_2CO). *Anal.* Calcd for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68, N; 16.27. Found: C, 69.71; H, 4.49; N, 16.29. MS *m/z*: 344 (M^+).

Preparation of IV——A mixture of IIIa (0.2 mmol) and H_2O (20 ml) was stirred at 70—80 °C overnight. The reaction mixture was evaporated, and the residue was recrystallized from H_2O to give 3-dicyanomethylene-2-methyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboxylic acid (IV) as colorless prisms, mp 247—248 °C (dec.), in 93% yield.

TABLE I. IR and ^{1}H-NMR Spectral Data for IIIa—i, IV, Va, and XIa, b

Compd. No.	IR (cm^{-1})	^{1}H-NMR δ (ppm, J=Hz)
IIIa	2200, 1860, 1780	3.43 (3H, s, N-Me), 3.70 (1H, dd, J_{56}=9, J_{45}=4, C_5-H), 4.08 (1H, dd, J_{56}=9, J_{16}=4, C_6-H), 4.43 (1H, m, C_4-H), 5.07 (1H, m, C_1-H), 6.57—6.97 (2H, m, C_7,C_8-H)
IIIb	2250, 1795, 1700	3.77 (3H, s, N-Me), 3.25 (1H, dd, J_{56}=8, J_{45}=4, C_5-H), 3.67 (1H, dd, J_{56}=8, J_{16}=4, C_6-H), 4.43 (1H, m, C_4-H), 5.02 (1H, m, C_1-H), 6.35—6.95 (2H, m, C_7,C_8-H), 11.15—11.63 (1H, m, NH)
IIIc	2230, 1780, 1710	3.53 (3H, s, N-Me), 3.45 (1H, dd, J_{56}=8, J_{45}=4, C_5-H), 3.90 (1H, dd, J_{56}=8, J_{16}=4, C_6-H), 4.53 (1H, m, C_4-H), 5.10 (1H, m, C_1-H), 6.40—6.98 (2H, m, C_7,C_8-H), 7.02—7.77 (5H, m, C_6H_5)
IIId	2230, 1780, 1710	3.54 (3H, s, N-Me), 3.47 (1H, d, J_{56}=8, C_5-H), 3.87 (1H, dd, J_{56}=8, J_{16}=4, C_6-H), 5.05 (1H, d, J_{16}=4, C_1-H), 6.61 (1H, br s, C_8-H), 7.17—7.52 (5H, m, C_6H_5)
IIIe	2200, 1770, 1700	2.10 (3H, s, C-Me), 3.52 (3H, s, N-Me), 3.26 (1H, d, J_{56}=8.0, C_5-H), 3.88 (1H, dd, J_{56}=8.0, J_{16}=4.0, C_6-H), 5.04 (1H, ddd, J_{17}=6.0, J_{16}=4.0, J_{18}=1.4, C_1-H), 6.29 (1H, dd, J_{78}=7.5, J_{18}=1.4, C_8-H), 6.77 (1H, dd, J_{78}=7.5, J_{17}=6.0, C_7-H), 7.17—7.20 (2H, m, C_6H_5), 7.40—7.53 (3H, m, C_6H_5)
IIIf	2200, 1780, 1710	1.90 (3H, s, C-Me), 3.52 (3H, s, N-Me), 3.50—3.54 (1H, C_5-H), 3.84 (1H, dd, J_{56}=8.0, J_{16}=4.0, C_6-H), 4.28 (1H, dd, J_{45}=3.4, J_{47}=1.8, C_4-H), 4.96 (1H, dd, J_{17}=5.5, J_{16}=4.0, C_1-H), 6.40 (1H, dd, J_{17}=5.5, J_{47}=1.8, C_7-H), 7.14—7.18 (2H, m, C_6H_5), 7.41—7.54 (3H, m, C_6H_5)
IIIg	2200, 1770, 1710	1.92 (3H, s, C-Me), 3.55 (3H, s, N-Me), 3.43 (1H, dd, J_{56}=8.0, J_{45}=3.4, C_5-H), 3.89 (1H, dd, J_{56}=8.0, J_{16}=4.3, C_6-H), 4.44 (1H, dd, J_{48}=6.1, J_{45}=3.4, C_4-H), 4.85 (1H, dd, J_{16}=4.3, J_{18}=1.8, C_1-H), 6.15 (1H, dd, J_{48}=6.1, J_{18}=1.8, C_8-H), 7.14—7.18 (2H, m, C_6H_5), 7.49—7.54 (3H, m, C_6H_5)
IIIh	2200, 1780, 1710	2.01 (3H, s, C-Me), 3.41 (3H, s, N-Me), 3.50 (1H, dd, J_{56}=7.9, J_{45}=3.1, C_5-H), 3.54 (1H, d, J_{56}=7.9, C_6-H), 4.55 (1H, ddd, J_{48}=6.1, J_{45}=3.1, J_{47}=1.8, C_4-H), 6.52 (1H, dd, J_{78}=7.6, J_{47}=1.8, C_7-H), 6.61 (1H, dd, J_{78}=7.6, J_{48}=6.1, C_8-H), 7.18—7.22 (2H, m, C_6H_5), 7.43—7.53 (3H, m, C_6H_5)
IIIi	2200, 1865, 1785	1.90 (3H, s, C-Me), 3.45 (3H, s, N-Me), 3.63 (1H, dd, J_{56}=9, J_{45}=4, C_5-H), 4.13 (1H, dd, J_{56}=9, J_{16}=4, C_6-H), 4.33 (1H, dd, J_{48}=6, J_{45}=4, C_4-H), 4.88 (1H, dd, J_{16}=4, J_{18}=2, C_1-H), 6.23 (1H, m, C_8-H)
IV	2230, 1750, 1725	3.70 (3H, s, N-Me), 3.13 (1H, dd, J_{56}=10, J_{45}=2, C_5-H), 3.50 (1H, dd, J_{56}=10, J_{16}=3, C_6-H), 4.17 (1H, m, C_4-H), 4.72 (1H, m, C_1-H), 6.25—6.85 (2H, m, C_7,C_8-H)
Va	2230, 2210, 1780, 1740	3.53 (3H, s, N-Me), 3.23 (1H, dd, J_{56}=10, J_{45}=4, C_5-H), 3.60 (1H, dd, J_{56}=10, J_{16}=4, C_6-H), 4.30 (1H, t, J_{45}=J_{48}=4, C_4-H), 4.48 (1H, m, C_1-H), 4.85 (1H, d, J_{17}=2, C_7-H), 5.13 (1H, d, J_{48}=4, C_8-H)
XIa	2200, 1770, 1700	3.57 (3H, s, N-Me), 1.67—1.95 (4H, m, C_7,C_8-H), 3.38 (1H, m, C_5-H), 3.57 (1H, m, C_4-H), 3.66 (1H, m, C_6-H), 4.22 (1H, m, C_1-H), 7.32—7.36 (2H, m, C_6H_5), 7.44—7.57 (3H, m, C_6H_5)
XIb	2200, 1780, 1710	1.71 (3H, s, C-Me), 3.45 (3H, s, N-Me), 1.75—1.83 (4H, m, C_7,C_8-H), 3.38—3.40 (2H, m, C_5,C_6-H), 3.61 (1H, m, C_4-H), 7.33—7.36 (2H, m, C_6H_5), 7.47—7.57 (3H, m, C_6H_5)

High-resolution MS m/z: Calcd for $C_{13}H_9N_3O_3$ ($M^+ - H_2O$): 255.0644. Found: 255.0651. IR and ^{1}H-NMR (Table I).

Preparation of Va——A solution of IV (0.18 mmol) dissolved in 10% $NaHCO_3$ (0.5 ml) was maintained at 0—5 °C and Br_2 was added dropwise until a faint yellow color remained. The mixture was stirred at room temperature overnight and was acidified with concentrated HCl. The precipitate formed was collected by filtration, and was recrystallized from H_2O to give 7-*exo*-bromo-6-*endo*-carboxy-3-dicyanomethylene-8-*endo*-hydroxy-2-methyl-2-azabicyclo[2.2.2]octane-5-*endo*-carboxylic acid γ-lactone (Va) as colorless prisms, mp 228—229 °C (dec.) in 90% yield. High-resolution MS m/z: Calcd for $C_{13}H_{11}BrN_3O_4$ ($M^+ + 1$): 351.9933. Found: 351.9913. IR and ^{1}H-NMR (Table I).

Preparation of XIa, b——A mixture of IIIc or IIIh (0.58 mmol), PtO_2 (30 mg) and *N*,*N*-dimethylformamide (DMF (20 ml)) was stirred at room temperature until the mixture stopped absorbing H_2. The catalyst was filtered off, and the filtrate was evaporated to give XIa or XIb, respectively. IR and ^{1}H-NMR spectral data for XIa, b are shown in Table I.

N-Phenyl-3-dicyanomethylene-2-methyl-2-azabicyclo[2.2.2]octane-5,6-*endo*-dicarboximide (XIa): Yield 88%, colorless prisms, mp >300 °C (Me_2CO). *Anal.* Calcd for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.85. Found: C, 68.20; H, 4.63; N, 16.88. MS m/z: 332 (M^+).

N-Phenyl-3-dicyanomethylene-1,2-dimethyl-2-azabicyclo[2.2.2]octane-5,6-*endo*-dicarboximide (XIb): Yield 80%, colorless prisms, mp 285—286 °C (Me_2CO). *Anal.* Calcd for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.18. Found: C, 69.07; H, 4.90; N, 16.20. MS *m/z*: 346 (M^+).

Preparation of Ib——A mixture of 3,5-dideuterio-1-methyl-2(1*H*)-thiopyridone[12] (23.6 mmol) and MeI (96 mmol) was refluxed for 48 h. The resulting precipitate was collected by filtration to give 3,5-dideuterio-1-methyl-2-methylthiopyridinium iodide (XII) as pale yellow prisms, mp 154—155 °C (Me_2CO), in 87% yield. The melting point of XII coincided with that of 1-methyl-2-methylthiopyridinium iodide[13] (mp 156 °C). A mixture of malononitrile (12 mmol), NaH (12 mmol) and DMF (14 ml) was stirred at room temperature for 10 min, and XII (10 mmol) was added. After being stirred at the same temperature for 3 h, the reaction mixture was treated with H_2O (80 ml), and the precipitate formed was collected by filtration to give Ib as yellow needles, mp 204—205 °C (MeOH), in 88% yield. MS *m/z*: 157 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 2200, 2180 (CN). ^{1}H-NMR δ: 4.03 (3H, s, N–Me), 7.73 (1H, br s, C_4-H), 8.05 (1H, br s, C_6-H). The melting point of Ib coincided with that of Ia[7] (mp 203.5—204.5 °C).

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