Dioxopyrrolines. XLVIII.[1] Regioselective Formation of Hydroindoles *via* Photochemical and Thermal Cycloaddition Reactions of 5-Aryl-4-ethoxycarbonyl-1*H*-pyrrole-2,3-dione with Isoprene

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Photocycloaddition of 5-aryl-4-ethoxycarbonyl-1*H*-pyrrole-2,3-dione 1 with isoprene and thermolysis of the resulting *exo*-vinyl cyclobutanes 6 caused a ring enlargement reaction due to a 1,3-shift, giving rise to the hydroindoles 9, which were found to be regioisomeric to the hydroindoles 14 obtained as a major cycloadduct by the Diels–Alder reaction of the same addends. Thus, the two-step hydroindole synthesis, *i.e.*, dioxopyrroline–diene photoannulation and thermolysis of the resulting vinyl cyclobutane, has a synthetic value in giving the product with the reverse regiochemistry to that of the Diels–Alder adduct.

Keywords dioxopyrroline; 1*H*-pyrrole-2,3-dione; isoprene; photocycloaddition; vinyl cyclobutane; thermolysis; 1,3-shift; Diels–Alder reaction; hydroindole; regioselectivity

In the preceding paper,[1] we demonstrated that thermolysis of the vinyl cyclobutanes **2** and **3** obtained by photocycloaddition of 5-aryl-4-ethoxycarbonyl-1*H*-pyrrole-2,3-dione **1** (dioxopyrroline) with butadiene caused two different types of skeletal rearrangements, depending on the stereochemistry of the 7-vinyl group. In the *exo*-vinyl cyclobutane **2**, ring enlargement of the cyclobutane due to the 1,3-shift of the C_1–C_7 bond to the vinyl group occurred to give the hydroindole **4**, while in the *endo*-isomer **3**, [3,3] sigmatropic shift occurred to give the aza-Cope product **5**. The hydroindole **4** was identical with the Diels–Alder (DA) adduct of **1** with butadiene. Since such hydroindole structures appear in various natural alkaloids,[2] we carried out the thermal reaction of the isoprene photo-adduct of **1**, and found that the hydroindole prepared by this photoannulation–thermolysis route is regioisomeric to the DA adduct of the same substrates. The results are presented here.

Results and Discussion

As reported previously,[3] photocycloaddition of the 5-phenyl dioxopyrroline **1a** with isoprene proceeded in a regio- and stereoselective manner to give the vinyl cyclobutane **6a** in which the vinyl group had *exo* and the methyl group had *endo* configurations. Similar photocycloaddition of the 5-methylenedioxyphenyl dioxopyrroline **1b** with isoprene gave two adducts, **6b** and **8b**, in yields of 16 and 19%, respectively. The cyclobutane structure of **6b** including the stereochemistry of the 7-vinyl group was confirmed by the spectral analogy with **6a**. The spectral characteristics of the other adduct **8b** were very similar to those of the aza-Cope product **5b**[1] obtained by the thermolysis of the *endo*-vinyl cyclobutane **3b**, except that **8b** had the additional methyl group on the double bond. This product was probably formed in a thermal process *via* the [3,3] sigmatropic shift of the *endo*-vinyl cyclobutane **7b**, a [2+2] photoadduct.

The vinyl cyclobutane **6a** on heating in toluene at 140 °C gave the hydroindole **9a** in 67% yield. The methylenedioxyphenyl analog **6b**, on similar thermolysis, gave two products, the hydroindole **9b** as a major (27%) and the dihydropyridone **10b** as a minor (10%) product. The spectral characteristics of the products **9a, b** were consistent with the assigned hydroindole structures. On the other hand, the structure of **10b** was elucidated from the molecular formula and the spectral analogy with known dihydropyridones,[3,4] whose formation had been observed in the thermolysis of some 2-azabicyclo[3.2.0]heptane-3,4-dione derivatives and rationalized in terms of a 1,3-sigmatropic rearrangement reaction followed by a cheletropic loss of CO of the intermediary 2-azanorbornene.[4]

The above thermolysis of **6a** indicated that the introduction of a methyl group at the C_7 position significantly increased the yield of **9a**, when compared with that of **2a** (30% yield).[1] Apparently, the additional methyl group facilitates the homolytic C_1–C_7 bond fission that

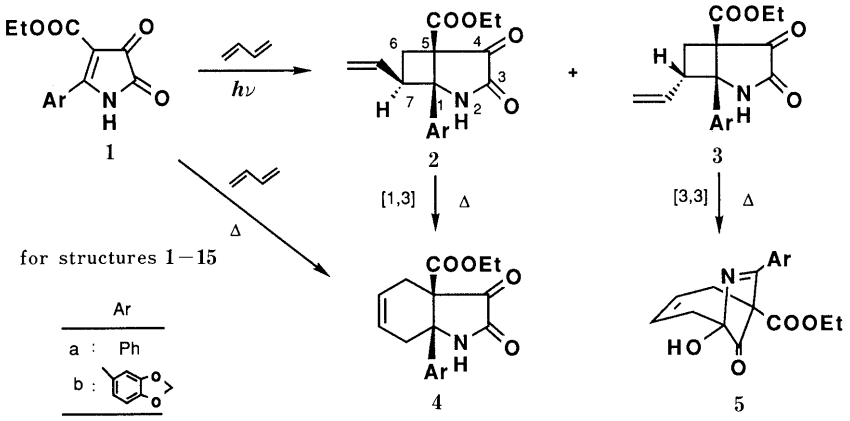

Chart 1

leads to the hydroindole derivative.

The hydroindole **9** has the structure of a 1,4-addition product of these addends in a formal sense. Thus, we carried out the DA reaction of **1** with isoprene. Heating of **1a** with isoprene in acetic anhydride at 160 °C gave three adducts, two N-acetyl compounds **11a** and **12a**, and one O-acetyl compound **13a**, in yields of 30, 7, and 8%, respectively. The DA reaction of **1b** with isoprene under similar conditions gave the N-acetyl compounds **11b** and **12b** as an inseparable mixture in 21% yield, and the O-acetyl compound **13b** in 10% yield.

The structure of the minor adduct **13** was assigned on the basis of the similarity of the spectral data to those of the aza-Cope product **8**, except that **13** has an OAc instead of OH. The adduct **13** may be produced by aza-Cope rearrangement from the *endo*-vinyl imidate **15**, which would be formed by a [2+2] cycloaddition followed by acetylation of the lactam oxygen, or may be directly formed from the O-acetyl pyrroline **1'** and isoprene by a [4+4] cycloaddition, although both cycloadditions are known to be forbidden under thermal conditions.

The structures of the N-acetyl adducts were confirmed

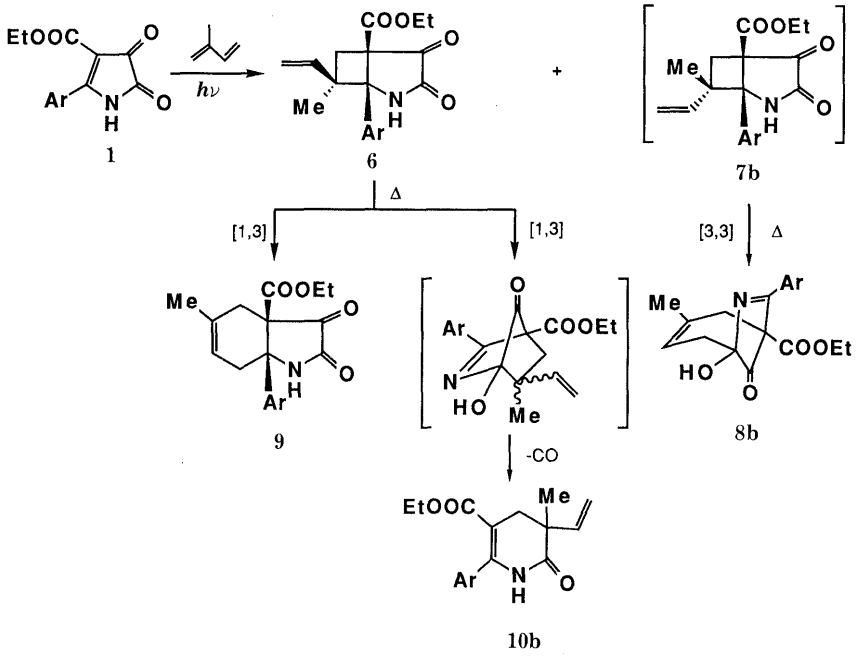

Chart 2

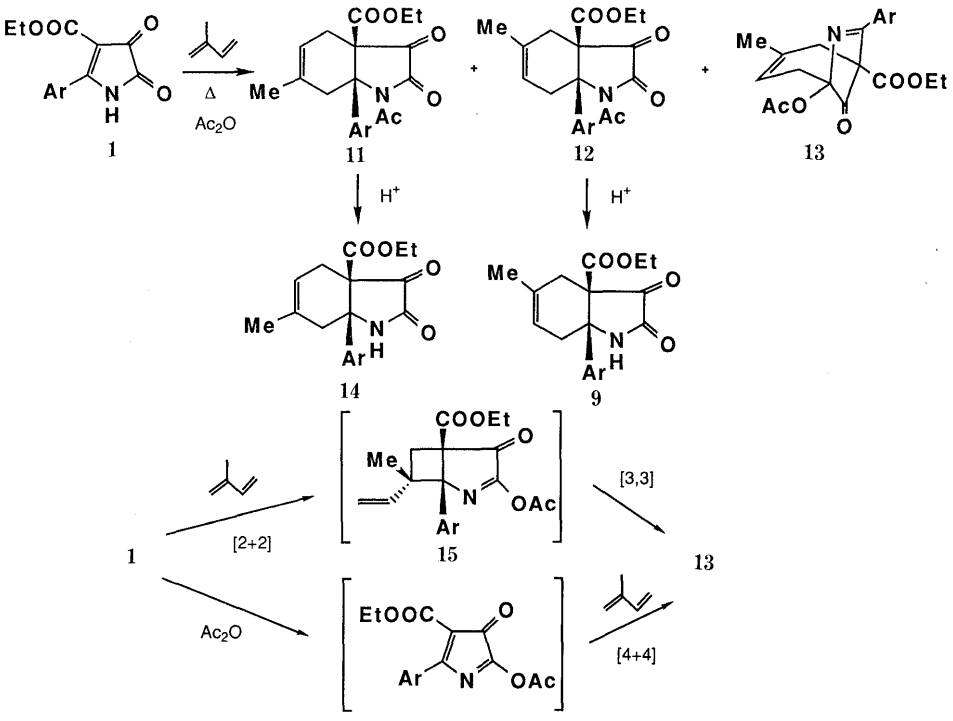

Chart 3

as follows. Hydrolysis of the major adduct **11** and minor adduct **12** with 5% hydrochloric acid gave the NH-derivatives **14** and **9**, respectively. The products **9a** and **9b** were identical with the hydroindoles obtained from the photoannulation route. The spectral characteristics of **14** showed that the major DA adduct was regioisomeric with the hydroindole **9**. Thus, these two different routes selectively provided the regioisomeric hydroindoles starting from the same addends.

Next, thermolysis of the 4-oxo imidate **16B** was examined. Pyrolysis of **16A**, as shown in the preceding paper,[1] caused two rearrangement reactions competitively; the major path was the 1,3-shift leading to the dihydropyridone **17A** (60%), and the minor one was the 1,3-shift leading to the hydroindole **19A** (4%). However, the imidate **16B**, when heated in toluene at 200 °C, gave two products, **19B** and **17B**, in yields of 46 and 52%. The product **19B** was identical with the hydroindole obtained by alkylation of **9a** with triethyloxonium fluoroborate and the other product **17B** was proved to have the dihydropyridone structure from its spectral features.[3] This result again indicates that the introduction of a methyl group at C_7 facilitates the homolytic cleavage of the C_1–C_7 bond and increases the ratio of rearrangement to the hydroindole.

Interestingly, these reaction pathways were profoundly affected by the stereochemistry of the substituent at C_4. The stereoisomeric acetoxy imidates **22** and **24** were prepared from **6a** by reduction with tetra-*n*-butylammonium borohydride, acetylation, and imidation (Chart 5). The stereochemistry of the 4-acetoxy group was assigned by the observation of the γ-effect in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum.[5] The acetoxy lactam **20** exhibited the C_6-signal at higher field (δ 30.3, $\Delta -4.3$ ppm) than that of the 4-oxo isomer **6a** (δ 34.6),[3] while the C_6-signal of the isomer **21** appeared at lower field (δ 38.2, $\Delta +3.6$ ppm), the facts indicating that the 4-acetoxy group of **20** and **21** has *endo*- and *exo*-configuration, respectively.

Heating of the 4-*endo*-acetoxy imidate **22** at 180 °C gave the hydroindole **23** in 88% yield, while the 4-*exo*-isomer **24** on heating at 140 °C gave the 2-azanorbornene **25**, although in low yield (20%). The structure **25** was deduced by comparison of the spectral data with those of the 6-vinyl[1] and the 6-phenyl[4] analogs. It has already been observed that the 4-*endo*-acetoxy group retards the 1,3-shift leading to azanorbornene owing to the steric hindrance between the *endo*-OAc and the 7-migrating group.[4] This steric effect in the case of **22** blocked the azanorbornene formation, thus leading to exclusive formation of the hydroindole.

In summary, the above results indicate that dioxopyrroline-1,3-diene photoannulation and thermolysis of the

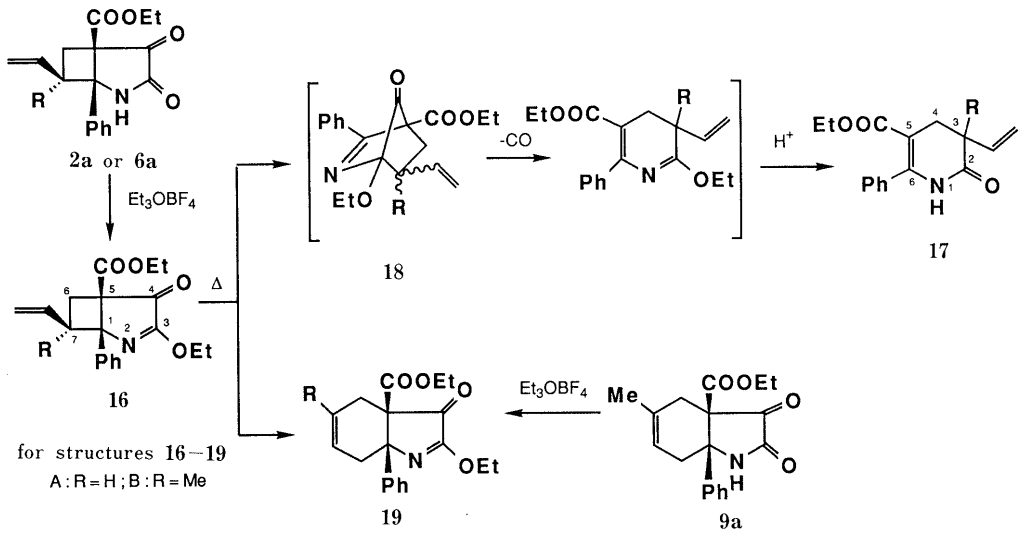

Chart 4

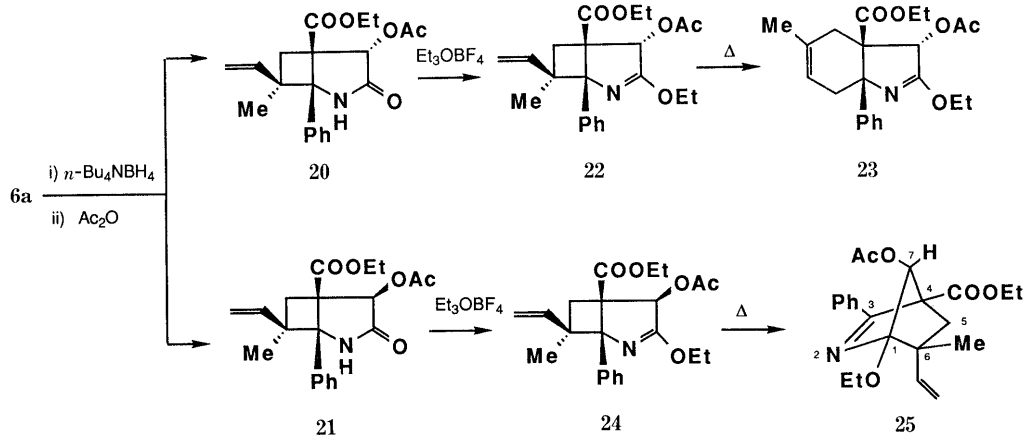

Chart 5

resulting vinyl cyclobutanes provide a valuable synthetic route to hydroindoles, although the total yields are sometimes not satisfactory. The results also show that this is not only a complimentary method to the DA reaction but also has an independent synthetic value in giving the product of reverse regioselectivity to the DA reaction.

Experimental

Unless otherwise stated, the following procedures were adopted. Melting points were taken on a Yanagimoto micro hot-stage melting point apparatus, and are uncorrected. Infrared (IR) spectra were taken in Nujol mulls with a Hitachi 260-10 spectrophotometer and data are given in cm^{-1}. Ultraviolet (UV) spectra were taken in a dioxane solution with a Hitachi 200-10 spectrophotometer and data are given in λ_{max} nm (ε). ^{1}H-NMR (100 MHz) and ^{13}C-NMR (25.0 MHz) spectra were taken in $CDCl_3$ solution with tetramethylsilane (TMS) as an internal standard on a JEOL FX-100 spectrometer. Chemical shifts are reported in ppm (δ), and signals are described as a (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). High-resolution mass spectra (MS) were recorded on a JEOL JMS-D300 mass spectrometer. Thin layer chromatography (TLC) was performed on precoated Silica gel 60 F_{254} plates (Merck). Medium-pressure liquid chromatography (MPLC) was performed on Kusano CIG prepacked silica gel columns. The photolysis solution was irradiated internally using a 300 W high-pressure mercury lamp (Eikosha Halos PIH 300) with a Pyrex filter.

Photocycloaddition of 1b with Isoprene A solution of **1b** (1.90 g) and isoprene (2.45 g) in dimethoxyethane (200 ml) was irradiated at 0 °C for 50 min. After evaporation of the solvent *in vacuo*, the residue was chromatographed over SiO_2. Elution with benzene–CH_2Cl_2 (1 : 1) gave *dl*-(1*R**,6*R**)-1-ethoxycarbonyl-6-hydroxy-3-methyl-8-(3′,4′-methylenedioxyphenyl)-7-azabicyclo[4.2.1]nona-3,7-dien-9-one (**8b**) (480 mg, 19%), colorless prisms from CH_2Cl_2–Et_2O, mp 164—167 °C. IR: 3150, 1740, 1580. UV: 230 (1500), 275 (9000), 309 (9900). ^{1}H-NMR: 1.06 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.69 (3H, s, C-Me), 2.50—2.90 (4H, m, C_2-H and C_5-H), 4.15 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.27 (1H, m, C=CH), 6.03 (2H, s, OCH_2O), 6.80 (1H, d, J=8 Hz, ArH), 7.16 (1H, dd, J=2, 8 Hz, ArH), 7.48 (1H, d, J=2 Hz, ArH). *Anal.* Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.64; H, 5.35; N, 3.68.

Further elution with CH_2Cl_2 gave *dl*-(1*R**,5*S**,7*S**)-5-ethoxycarbonyl-7-methyl-1-(3′,4′-methylenedioxyphenyl)-7-vinyl-2-azabicyclo[3.2.0]-heptane-3,4-dione (**6b**) (390 mg, 16%), colorless needles from CH_2Cl_2–Et_2O, mp 130—133 °C. IR: 1775, 1750, 1720. ^{1}H-NMR: 0.88 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.18 (3H, s, C-Me), 2.11 (1H, d, J=13 Hz, C_6-H), 3.35 (1H, d, J=13 Hz, C_6-H), 3.95 (2H, qd, J=1, 7 Hz, $COOC\underline{H}_2CH_3$), 5.11 (1H, d, J=10 Hz, CH=C$\underline{H}_2$), 5.12 (1H, d, J=18 Hz, CH=C$\underline{H}_2$), 5.65 (1H, dd, J=10, 18 Hz, C$\underline{H}$=CH_2), 5.95 (1H, d, J=1 Hz, OCH_2O), 5.98 (1H, d, J=1 Hz, OCH_2O), 6.80 (3H, s, ArH). *Anal.* Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.58; H, 5.33; N, 3.70.

Pyrolysis of 6a A solution of **6a** (200 mg) in xylene (10 ml) was heated under reflux for 5 h. After evaporation of the solvent *in vacuo*, the residue was chromatographed over SiO_2. Elution with CH_2Cl_2 gave *dl*-(1*R**,6*S**)-1-ethoxycarbonyl-3-methyl-6-phenyl-7-azabicyclo[4.3.0]non-3-ene-8,9-dione (**9a**) (134 mg, 67%) as colorless prisms from methanol, mp 218—219 °C. IR: 1775, 1760, 1730. ^{1}H-NMR: 0.70 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.77 (3H, s, C-Me), 2.51 (1H, dd, J=7, 16 Hz, C_2-H), 2.80—3.00 (3H, m, C_2-H and C_5-H), 3.47 (2H, m, J=1, 7 Hz, $COOC\underline{H}_2CH_3$), 5.51 (1H, m, C=CH), 7.29—7.42 (5H, m, ArH). *Anal.* Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.67; H, 6.22; N, 4.38.

Pyrolysis of 6b A solution of **6b** (175 mg) in toluene (5 ml) was heated in a sealed tube at 160 °C for 2 h. After evaporation of the solvent *in vacuo*, the residue was chromatographed over SiO_2. Elution with CH_2Cl_2–benzene (1 : 1) and preparative TLC (developed with CH_2Cl_2) of the eluate gave *dl*-5-ethoxycarbonyl-3-methyl-6-(3′,4′-methylenedioxyphenyl)-3-vinyl-3,4-dihydropyridin-2(1*H*)-one (**10b**) (16 mg, 10%), colorless needles from Et_2O–hexane, mp 145—147 °C. IR: 3200, 1700, 1670, 1640. UV: 288 (13000). ^{1}H-NMR: 1.05 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.35 (3H, s, C-Me), 2.63 (1H, d, J=17 Hz, C_4-H), 2.92 (1H, d, J=17 Hz, C_4-H), 4.02 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.18 (1H, d, J=18 Hz, CH=C$\underline{H}_2$), 5.18 (1H, d, J=10 Hz, CH=C$\underline{H}_2$), 5.93 (1H, dd, J=10, 18 Hz, C$\underline{H}$=CH_2), 5.99 (2H, s, OCH_2O), 6.70—6.87 (3H, m, ArH). *Anal.* Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.39; H, 5.86; N, 4.25.

Further elution with CH_2Cl_2 gave *dl*-(1*R**,6*S**)-1-ethoxycarbonyl-3-methyl-1-(3′,4′-methylenedioxyphenyl)-7-azabicyclo[4.3.0]non-3-ene-8,9-dione (**9b**) (48 mg, 27%), colorless needles from CH_2Cl_2–Et_2O, mp 210—211 °C. IR: 1780, 1745, 1730. ^{1}H-NMR: 0.83 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.76 (3H, br s, C-Me), 2.46 (1H, dd, J=6, 15 Hz, C_2-H), 2.76 (2H, m, C_5-H), 2.85 (1H, m, C_2-H), 3.62 (2H, m, $COOC\underline{H}_2CH_3$), 5.50—5.56 (1H, m, C=CH), 5.96 (2H, s, OCH_2O), 6.73—6.96 (3H, m, ArH). *Anal.* Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.65; H, 5.57; N, 3.67.

Diels–Alder Reaction of 1a with Isoprene A mixture of **1a** (3 g) and isoprene (3 g) in Ac_2O (15 ml) was heated in a sealed tube at 160 °C for 3 h. After evaporation of the solvent *in vacuo*, the residue was chromatographed over SiO_2. Elution with CH_2Cl_2–benzene (1 : 1) and fractional crystallizations of the eluate from CH_2Cl_2–Et_2O gave **11a** (1.285 g, 30%) and **12a** (315 mg, 7%).

dl-(1*R**,6*S**)-7-Acetyl-1-ethoxycarbonyl-4-methyl-6-phenyl-7-azabicyclo[4.3.0]non-3-ene-8,9-dione (**11a**): Colorless prisms, mp 148—150 °C. IR: 1775, 1750, 1730. ^{1}H-NMR: 0.91 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.72 (3H, br s, C-Me), 2.69 (3H, s, $COCH_3$), 2.78—2.84 (2H, m, C_2-H), 3.17 (2H, br s, C_5-H), 3.52 (2H, m, $COOC\underline{H}_2CH_3$), 5.56—5.61 (1H, m, C=CH), 7.09—7.33 (5H, m, ArH). *Anal.* Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.42; H, 6.11; N, 3.87.

dl-(1*R**,6*S**)-7-Acetyl-1-ethoxycarbonyl-3-methyl-6-phenyl-7-azabicyclo[4.3.0]non-3-ene-8,9-dione (**12a**): Colorless prisms, mp 143—145 °C. IR: 1780, 1750, 1730. ^{1}H-NMR: 0.92 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.75 (3H, br s, C-Me), 2.70 (3H, s, $COCH_3$), 2.80 (2H, m, C_5-H), 3.17 (2H, br s, C_2-H), 3.52 (2H, m, $COOC\underline{H}_2CH_3$), 5.59 (1H, m, C=CH), 7.10—7.35 (5H, m, ArH). *Anal.* Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.78; H, 6.03; N, 4.27.

Further elution with CH_2Cl_2 gave *dl*-(1*R**,6*R**)-6-acetoxy-1-ethoxycarbonyl-3-methyl-8-phenyl-7-azabicyclo[4.2.1]nona-3,7-dien-9-one (**13a**) (350 mg, 8%), colorless prisms from CH_2Cl_2–Et_2O–hexane, mp 121—122 °C. IR: 1760, 1740, 1580. UV: 277 (18500). ^{1}H-NMR: 1.14 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.68 (3H, br s, C-Me), 2.04 (3H, s, $OCOCH_3$), 2.52—2.91 (3H, m, C_2-H and C_5-H), 3.16—3.30 (1H, m, C_5-H), 4.19 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.20 (1H, m, C=CH), 7.30—7.78 (3H, m, ArH), 7.98 (2H, m, ArH). *Anal.* Calcd for $C_{20}H_{21}NO_5$: C, 67.59; N, 3.94. Found: C, 67.46; H, 6.08; N, 3.78.

Diels–Alder Reaction of 1b with Isoprene A mixture of **1b** (1.4 g) and isoprene (2 g) in Ac_2O (15 ml) was heated in a sealed tube at 160 °C for 2 h. After evaporation of the solvent *in vacuo*, the residue was chromatographed over SiO_2. Elution with CH_2Cl_2–benzene (1 : 1) gave a 2 : 1 mixture of **11b** and **12b** as a gum. The ratio was calculated from the intensities of the methyl signals of COOEt in the ^{1}H-NMR. ^{1}H-NMR: 1.00 and 1.01 (t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.72 (br s, C-Me), 2.00—2.53 (m, CH_2), 2.67 (s, $COCH_3$), 2.76—2.81 and 3.10 (m, CH_2), 3.70 (m, $COOC\underline{H}_2CH_3$), 5.57 (m, C=CH), 5.94 (s, OCH_2O), 6.56—6.76 (m, ArH).

Further elution with CH_2Cl_2 gave *dl*-(1*R**,6*S**)-6-acetoxy-1-ethoxycarbonyl-3-methyl-8-(3′,4′-methylenedioxyphenyl)-7-azabicyclo[4.2.1]nona-3,7-dien-9-one (**13b**) (183 mg, 9.5%) as a colorless gum. IR (CH_2Cl_2): 1740, 1720. UV: 242 (11900), 292 (6300), 341 (8000). ^{1}H-NMR: 1.17 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.67 (3H, br s, C-Me), 2.10 (3H, s, $OCOCH_3$), 2.20—3.03 (4H, m, C_2-H and C_5-H), 4.08 (2H, qd, J=2, 7 Hz, $COOC\underline{H}_2CH_3$), 5.13 (1H, m, C=CH), 6.07 (2H, s, OCH_2O), 6.77 (2H, m, ArH), 7.61 (1H, m, ArH). MS *m/z*: M^+ Calcd for $C_{21}H_{21}NO_7$ 399.1319. Found: 399.1321.

Hydrolysis of the N-Acetyl compounds 11 and 12 (General Procedure) A solution of the N-acetyl compound **11a** or **12a** in 5% HCl—EtOH was heated under reflux for 30 min. After evaporation of the solvent *in vacuo*, the residue was taken up in CH_2Cl_2 and the solution was washed with H_2O, dried over Na_2SO_4 and concentrated. The product **14a** or **9a** was purified by crystallizations. In the case of **11b** and **12b**, the mixture was used for hydrolysis and the products **14b** and **9b** were separated by MPLC using CH_2Cl_2 as eluent. The compounds **9a** [114 mg (63%) from **12a** (200 mg)] and **9b** were identical with the hydroindoles described above, respectively.

dl-(1*R**,6*S**)-1-Ethoxycarbonyl-4-methyl-6-phenyl-7-azabicyclo[4.3.0]non-3-ene-8,9-dione (**14a**): Yield, 833 mg (94%) from **11a** (1.0 g). Colorless needles from methanol, mp 253—255 °C. IR: 1780, 1755, 1740, 1700. ^{1}H-NMR: 0.68 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.73 (3H, s, C-Me), 2.40 (1H, d, J=15 Hz, C_5-H), 2.83—2.89 (2H, m, C_2-H), 2.98 (1H, br d, J=15 Hz, C_5-H), 3.45 (2H, m, $COOC\underline{H}_2CH_3$), 5.69 (1H, m, C=CH), 7.29—7.30 (5H, m, ArH). *Anal.* Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.87; H, 6.03; N, 4.27.

dl-(1*R**,6*S**)-1-Ethoxycarbonyl-4-methyl-6-(3′,4′-methylenedioxyphenyl)-7-azabicyclo[4.3.0]non-3-ene-8,9-dione (**14b**): Colorless needles from CH_2Cl_2–Et_2O, mp 193—195 °C. IR: 3050, 1770, 1745. ^{1}H-NMR:

0.81 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.72 (3H, br s, C-Me), 2.39 (1H, d, $J=15$ Hz, C_5-H), 2.78—2.84 (2H, m, C_2-H), 2.93 (1H, d, $J=15$ Hz, C_5-H), 3.60 (2H, m, $COOC\underline{H}_2CH_3$), 5.66—5.74 (1H, m, C=CH), 5.97 (2H, s, OCH_2O), 6.73—6.96 (3H, m, ArH). *Anal.* Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.64; H, 5.52; N, 3.77.

Imidation of 6a with Triethyloxonium Tetrafluoroborate A solution of **6a** (200 mg) and excess Et_3OBF_4 in CH_2Cl_2 (10 ml) was allowed to stand overnight at room temperature. The mixture was diluted with CH_2Cl_2, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$, and concentrated. The residue in benzene was passed through a short SiO_2 column to give *dl*-(1*R**,5*S**,7*S**)-3-ethoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-7-vinyl-2-azabicyclo[3.2.0]hept-2-en-4-one (**16B**) (190 mg, 87%), as colorless prisms from Et_2O–hexane, mp 95—97 °C. IR: 1750, 1730, 1640, 1630. ^{1}H-NMR: 0.77 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 0.98 (3H, s, C-Me), 1.50 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$), 1.85 (1H, d, $J=14$ Hz, C_6-H), 3.33 (1H, d, $J=14$ Hz, C_6-H), 3.87 (2H, q, $J=7$ Hz, $COOC\underline{H}_2CH_3$), 4.62 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 4.90—5.87 (3H, m, $C=CH_2$), 7.4 (5H, m, ArH). *Anal.* Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.46; H, 6.81; N, 4.11.

Pyrolysis of 16B A solution of **16B** (100 mg) in toluene (5 ml) was heated under reflux for 1 h. After evaporation of the solvent, the residue was chromatographed over SiO_2. Elution with benzene gave *dl*-5-ethoxycarbonyl-3-methyl-6-phenyl-3-vinyl-3,4-dihydropyridin-2(1*H*)-one (**17B**) (43 mg, 52%) as colorless needles from Et_2O–hexane, mp 117—121 °C. IR: 3200, 1680, 1660, 1630. UV (EtOH): 225 (7300), 283 (7900). ^{1}H-NMR: 0.97 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.33 (3H, s, C-Me), 2.60 (1H, d, $J=17$ Hz, C_4-H), 2.97 (1H, d, $J=17$ Hz, C_4-H), 3.93 (2H, q, $J=7$ Hz, $COOC\underline{H}_2CH_3$), 5.17 (2H, each d, $J=10$, 18 Hz, $CH=C\underline{H}_2$), 5.93 (1H, dd, $J=10$, 18 Hz, $C\underline{H}=CH_2$), 7.3 (5H, m, ArH). MS *m/z*: M^+ Calcd for $C_{17}H_{19}NO_3$ 285.1363. Found: 285.1348.

Further elution with benzene–CH_2Cl_2 gave *dl*-(1*R**,5*S**)-3-ethoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-2-azabicyclo[4.3.0]nona-2,7-dien-4-one (**19B**) (46 mg, 46%), as colorless prisms from Et_2O–hexane, mp 130—132 °C. IR: 1755, 1735, 1640. ^{1}H-NMR: 0.63 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.47 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$), 1.70 (3H, br s, C-Me), 2.3—2.85 (4H, m, C_6-H and C_9-H), 3.43 (2H, m, $COOC\underline{H}_2CH_3$), 4.52 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 5.37 (1H, m, CH=C), 7.3 (5H, m, ArH). MS m/z: M^+ Calcd for $C_{20}H_{23}NO_4$ 341.1628. Found: 341.1636.

Imidation of 9a with Triethyloxonium Tetrafluoroborate A solution of **9a** (20 mg) and excess Et_3OBF_4 in CH_2Cl_2 (5 ml) was allowed to stand overnight at room temperature. The product isolated in a usual way was identical with the imidate **19B** described above.

Reduction of 6a with Tetra-*n*-butylammonium Borohydride A solution of **6a** (100 mg) in CH_2Cl_2 (10 ml) was treated with *n*-Bu_4NBH_4 (0.5 molar eq) at 0 °C for 30 min. The reaction mixture was diluted with CH_2Cl_2, washed with water and 5% $NaHCO_3$, dried over $MgSO_4$, and concentrated. The residue was treated with Ac_2O (1 ml) and pyridine (2 ml) at room temperature overnight. The acetates obtained by a usual work-up were separated by MPLC using hexane–AcOEt (3 : 1) as an eluent to give **20** (69 mg, 60%) and **21** (20 mg).

dl-(1*R**,4*R**,5*S**,7*S**)-4-Acetoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-7-vinyl-2-azabicyclo[3.2.0]hept-3-one (**20**): Colorless prisms from Et_2O–hexane, mp 197—201 °C. IR: 1750, 1730, 1710. ^{1}H-NMR: 0.97 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.32 (3H, s, C-Me), 2.16 (1H, d, $J=13.5$ Hz, C_6-H), 2.18 (3H, s, OAc), 2.95 (1H, s, $J=13.5$ Hz, C_6-H), 3.98 (2H, m, $COOC\underline{H}_2CH_3$), 5.08 (1H, dd, $J=1$, 10.5 Hz, $CH=C\underline{H}_2$), 5.19 (1H, $J=1$, 17.5 Hz, $CH=C\underline{H}_2$), 5.92 (1H, s, C_4-H), 5.98 (1H, dd, $J=10.5$, 17.5 Hz, $C\underline{H}=CH_2$), 7.27 (5H, br s, ArH), 7.90 (1H, s, NH). ^{13}C-NMR: 13.6 (q, $COOCH_2\underline{C}H_3$), 20.4 (q, $OCO\underline{C}H_3$), 23.2 (q, CH_3), 30.3 (t, C_6), 48.3 (s, C_7), 54.0 (s, C_5), 61.6 (t, $COO\underline{C}H_2CH_3$), 71.0 (s, C_1), 74.8 (d, C_4), 112.5 (t, $CH=\underline{C}H_2$), 127.2 (d, 2C, Ph), 127.7 (d, 3C, Ph), 136.5 (s, Ph), 143.1 (d, $\underline{C}H=CH_2$), 169.7 (s, C_3), 170.7 (s, $\underline{C}OOCH_2CH_3$), 171.8 (s, $O\underline{C}OCH_3$). MS *m/z*: M^+ Calcd for $C_{20}H_{23}NO_5$ 357.1576. Found: 357.1576.

dl-(1*R**,4*S**,5*S**,7*S**)-4-Acetoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-7-vinyl-2-azabicyclo[3.2.0]hept-3-one (**21**) was obtained as a gum which was contaminated with a small amount of **20**. ^{1}H-NMR: 1.03 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.04 (3H, s, C-Me), 2.15 (3H, s, OAc), 2.17 (1H, d, $J=13$ Hz, C_6-H), 2.75 (1H, d, $J=13$ Hz, C_6-H), 3.98 (2H, q, $J=7$ Hz, $COOC\underline{H}_2CH_3$), 5.05 (1H, dd, $J=1$, 11 Hz, $CH=C\underline{H}_2$), 5.19 (1H, dd, $J=1$, 17 Hz, $CH=C\underline{H}_2$), 5.64 (1H, s, C_4-H), 6.11 (1H, dd, $J=11$, 17 Hz, $C\underline{H}=CH_2$), 7.27 (5H, br s, ArH), 7.81 (1H, br s, NH). ^{13}C-NMR: 13.7 (q, $COOCH_2\underline{C}H_3$), 20.6 (q, $OCO\underline{C}H_3$), 21.7 (q, CH_3), 39.2 (t, C_6), 47.3 (s, C_7), 53.8 (s, C_5), 61.0 (t, $COO\underline{C}H_2CH_3$), 72.6 (s, C_1), 75.0 (d, C_4), 112.6 (t, $CH=\underline{C}H_2$), 127.5 (d, 2C, Ph), 127.6 (d, 3C, Ph), 137.4 (s, Ph), 143.3 (d, $\underline{C}H=CH_2$), 168.9 (s, C_3), 169.0 (s, $\underline{C}OOCH_2CH_3$), 171.5 (s, $O\underline{C}OCH_3$).

Imidation of 20 with Triethyloxonium Tetrafluoroborate A solution of **20** (100 mg) in CH_2Cl_2 (5 ml) was treated with excess Et_3OBF_4 at room temperature overnight. The mixture was diluted with CH_2Cl_2, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$, and evaporated. The product was passed through a short column of SiO_2 to give *dl*-(1*R**,4*R**,5*S**,7*S**)-4-acetoxy-3-ethoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-7-vinyl-2-azabicyclo[3.2.0]hept-2-ene (**22**) (101 mg) as a colorless gum. IR (CH_2Cl_2): 1740, 1720, 1660. ^{1}H-NMR: 0.95 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.14 (3H, s, C-Me), 1.44 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$), 1.93 (1H, d, $J=13$ Hz, C_6-H), 2.16 (3H, s, OAc), 2.99 (1H, d, $J=13$ Hz, C_6-H), 3.97 (2H, q, $J=7$ Hz, $COOC\underline{H}_2CH_3$), 4.48 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 5.00 (1H, dd, $J=10$, 15 Hz, $CH=C\underline{H}_2$), 5.12 (1H, dd, $J=15$, 18 Hz, $CH=C\underline{H}_2$), 5.81 (1H, dd, $J=10$, 18 Hz, $C\underline{H}=CH_2$), 6.07 (1H, s, C_4-H), 7.1—7.4 (5H, m, ArH). MS *m/z*: M^+ Calcd for $C_{25}H_{27}NO_5$ 385.1889. Found: 385.1891.

Imidation of 21 with Triethyloxonium Tetrafluoroborate A solution of **21** (20 mg) in CH_2Cl_2 (5 ml) was treated with excess Et_3OBF_4 as described above to give *dl*-(1*R**,4*S**,5*S**,7*S**)-4-acetoxy-3-ethoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-7-vinyl-2-azabicyclo[3.2.0]hept-2-ene (**24**) as a gum. This was contaminated with a small amount of **22**. ^{1}H-NMR: 1.00 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.32 (3H, s, C-Me), 1.50 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$), 2.20 (3H, s, OAc), 2.22 (1H, d, $J=13$ Hz, C_6-H), 2.73 (1H, d, $J=13$ Hz, C_6-H), 6.34 (1H, s, C_4-H).

Pyrolysis of 22 A solution of **22** (50 mg) was heated in a sealed tube at 180 °C for 2 h. The product was purified by MPLC using hexane–EtOAc (3 : 1) as an eluent to give *dl*-(1*R**,4*R**,5*S**)-4-acetoxy-3-ethoxy-5-ethoxycarbonyl-7-methyl-1-phenyl-2-azabicyclo[4.3.0]nona-2,7-diene (**23**) (44 mg, 88%) as a colorless gum. IR (CH_2Cl_2): 1750, 1725, 1675. ^{1}H-NMR: 0.80 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.38 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$), 1.87 (2H, br s, C_6-H or C_9-H), 1.88 (3H, br s, C-Me), 2.5—2.7 (2H, m, C_6-H or C_9-H), 3.44 (2H, m, $COOC\underline{H}_2CH_3$), 4.36 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 5.5—5.7 (1H, m, CH=C), 6.30 (1H, s, C_4-H), 7.15—7.4 (5H, m, ArH). MS *m/z*: M^+ Calcd for $C_{22}H_{27}NO_5$ 385.1889. Found: 385.1900.

Pyrolysis of 24 A solution of **24** (50 mg) in toluene (5 ml) was heated in a sealed tube at 140 °C for 20 min. The product was purified by MPLC using hxane–AcOEt (3 : 1) as an eluent to give *dl*-(1*R**,4*R**,7*R**)-7-acetoxy-1-ethoxy-4-ethoxycarbonyl-6-methyl-3-phenyl-6-vinyl-2-azabicyclo[2.-2.1]hept-2-ene (**25**) (10 mg, 20%) as a colorless gum. IR (CH_2Cl_2): 1745, 1725. UV: 248 (9100). ^{1}H-NMR: 1.07 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 1.27 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$), 1.40 (3H, s, C-Me), 1.96 (1H, d, $J=13$ Hz, C_{5endo}-H), 2.03 (3H, s, OAc), 2.30 (1H, d, $J=13$ Hz, C_{5exo}-H), 4.0—4.3 (2H, m, $COOC\underline{H}_2CH_3$), 4.07 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 4.86 (1H, dd, $J=1$, 17 Hz, $CH=C\underline{H}_2$), 4.92 (1H, dd, $J=1$, 11 Hz, $CH=C\underline{H}_2$), 5.47 (1H, s, C_7-H), 5.89 (1H, dd, $J=11$, 17 Hz, $C\underline{H}=CH_2$), 7.3—7.7 (5H, m, ArH). MS *m/z*: M^+ Calcd for $C_{22}H_{27}NO_5$ 385.1889. Found: 385.1878.

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