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Reactions of Pyrazolo[1,5-*a*]pyrimidine Derivatives with Nucleophiles. IV.[1] Some Reactions of 1,4-Dihydrocyclopent[*b*]indoles

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4,7-Dihydro-4-methyl-7-(*N*-methyl-3-indolyl)pyrazolo[1,5-*a*]pyrimidine (**3**) obtained from pyrazolo[1,5-*a*]pyrimidine (**1**) was treated with indole in the presence of an excess of triethyloxonium fluoroborate to give a mixture of 1,4-dihydro-3-(3-indolyl)cyclopent[*b*]indoles (**5**, **6**, **7** and **8**). The reaction of **6** with potassium hydroxide in ethanol at room temperature gave the 1-hydroxy derivative (**10**), while under reflux **6** gave 1,4-dihydro-1-oxocyclopent[*b*]indole (**11**). Treatment of **6** with formaldehyde gave the 1-hydroxymethyl derivative (**13**). *m*-Chloroperbenzoic acid oxidation of **6** afforded the 3,4-dihydrocyclopent[*b*]indole (**14**). Furthermore, the reaction of **6** with activated olefins, such as maleic anhydride, maleimide, acrylonitrile and ethyl acrylate under reflux in benzene or acetonitrile gave [4+2] cycloadducts, bicyclo[2.2.1]hept[2,3-*b*]indoles (**17**, **18**, **20** and **21**), *via* the 2,4-dihydrocyclopent[*b*]indole intermediate (**6′**).

Keywords——pyrazolo[1,5-*a*]pyrimidine; indole; triethyloxonium fluoroborate; 1,4-dihydrocyclopent[*b*]indole; Diels–Alder reaction; maleic anhydride; acrylonitrile; bicyclo[2.2.1]-hept[2,3-*b*]indole

Nucleophilic additions of phenol, aniline, enamine of cyclohexanone, indole and their analogs to 6,7-diethoxycarbonylpyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**1**) in the presence of boron trifluoride (BF_3)-etherate[2] or triethyloxonium fluoroborate (Et_3OBF_4) have been reported. Recently, we reported[3] the synthesis and X-ray crystal structure derermination of novel 1,4-dihydrocyclopent[*b*]indole derivatives, which were obtained by the reaction of **1** with indole or N-methylindole in the presence of an excess of Et_3OBF_4. The present paper describes some reactions of 1,4-dihydrocyclopent[*b*] indoles, and also gives a full account of the work reported in a previous communication.[3]

Compound **1** was treated with one equivalent of N-methylindole in the presence of an excess of Et_3OBF_4 in dry dichloromethane to give a mixture of 6,7-diethoxycarbonyl-4,7-dihydro-4-ethyl-7-(*N*-methyl-3-indolyl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4**), mp 217—218 °C, and diethyl 1,4-dihydro-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (**6**), mp 169—174 °C, as orange needles in 17.1 and 24.6% yields, respectively. The structural assignment of **4** was achieved by an alternative synthesis of **4** by treatment of **2** with diethyl sulfate. The product **6**, $C_{27}H_{26}N_2O_4$ [mass spectrum (MS) *m/z*: 442 (M^+)], exhibited two carbonyl absorption bands (1720 and 1690 cm^{-1}) and no characteristic absorption band due to a CN group in the infrared (IR) spectrum. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed signals due to two N-methyl protons at δ 3.44 and 3.91 and the C_1-methine proton as a singlet at δ 4.84. These spectral data as well as the analytical data clearly indicate that compound **6** lacks an aminopyrazole moiety, and consists of two N-methylindoles and a three carbon unit as well as one hydrogen and two $CO_2C_2H_5$ groups from **1**. Treatment of **1** with two equivalents of N-methylindole under the same conditions as above increased the yield **6** to 69.6%. This result clearly demonstrates that **4** is an intermediate of this reaction.

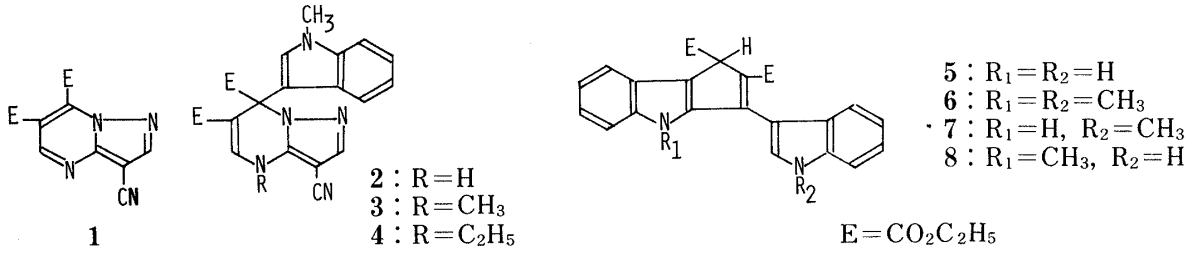


Chart 1

TABLE I. Spectral Data for 1,4-Dihydrocyclopent[*b*]indoles

Compd. No.	IR ν_{max}^{KBr} cm^{-1}	UV λ_{max}^{EtOH} nm (log ε)	^{1}H-NMR (DMSO-d_6) δ J, Hz	*Rf*-value[a]
5	3360, 3320 (NH)	360 (4.27)	1.03 and 1.23 (each 3H, each t, J=7, 2×$CO_2CH_2C\underline{H}_3$)	0.44
	1710, 1650 (CO)	255 (4.20)	3.90—4.40 (4H, m, 2×$CO_2C\underline{H}_2CH_3$)	
		210 (4.72)	4.80 (1H, s, C_1–H), 7.0—7.60 (8H, m, Ar–H)	
			7.95 (1H, d, J=2, C_2–H of indole ring)	
			11.60 (1H, s, NH), 11.90 (1H, br s, NH)	
6	1720, 1690 (CO)	369 (4.25)	0.97 and 1.24 (each 3H, each t, J=7, 2×$CO_2CH_2C\underline{H}_3$)	0.84
		260 (4.25)	3.44 and 3.91 (each 3H, each s, 2×NCH_3)	
		218 (4.73)	3.80—4.35 (4H, m, 2×$CO_2C\underline{H}_2CH_3$)	
			4.84 (1H, s, C_1–H), 7.0—7.70 (8H, m, Ar–H)	
			7.79 (1H, s, C_2–H of indole ring)	
7	3380 (NH)	365 (4.28)	1.03 and 1.23 (each 3H, each t, J=7, 2×$CO_2CH_2C\underline{H}_3$)	0.76
	1720, 1695 (CO)	255 (4.15)	3.90 (3H, s, NCH_3)	
		218 (4.70)	3.90—4.20 (4H, m, 2×$CO_2C\underline{H}_2CH_3$)	
			4.80 (1H, s, C_1–H), 7.0—7.60 (8H, m, Ar–H)	
			7.90 (1H, s, C_2–H of indole ring), 11.30 (1H, s, NH)	
8	3360 (NH)			
	1720, 1780 (CO)	355 (4.15)	0.95 and 1.25 (each 3H, each t, J=7, 2×$CO_2CH_2C\underline{H}_3$)	0.60
		260 (4.23)	3.43 (3H, s, NCH_3)	
		218 (4.68)	3.80—4.30 (4H, m, 2×$CO_2C\underline{H}_2CH_3$)	
			4.80 (1H, s, C_1–H), 6.90—7.60 (8H, m, Ar–H)	
			7.70 (1H, d, J=2, C_2–H of indole ring)	
			11.45 (1H, br s, H/W 4, NH)	
9	1720, 1690 (CO)	367 (4.25)	1.15 and 1.33 (each 3H, each t, J=7, 2×$CO_2CH_2C\underline{H}_3$)	
		260 (4.24)	3.40 and 3.90 (each 3H, each s, 2×NCH_3)	
		218 (4.72)	4.0—4.40 (4H, m, 2×$CO_2C\underline{H}_2CH_3$)	
			7.0—7.80 (9H, m, Ar–H)	
10	3400 (OH)	360 (4.20)	0.90 and 1.05 (each 3H, each t, J=7, 2×$CO_2CH_2C\underline{H}_3$)	
	1720, 1695 (CO)	255 (4.25)	3.45 and 3.90 (each 3H, each s, 2×NCH_3)	
		220 (4.70)	3.80—4.20 (4H, m, 2×$CO_2C\underline{H}_2CH_3$)	
			5.90 (1H, br s, OH)	
			7.0—7.60 (8H, m, Ar–H)	
			7.80 (1H, s, C_2–H of indole ring)	

a) $SiO_2/CHCl_3$: AcOEt (9 : 1).

Analogously, the reaction of **1** with two equivalents of indole gave **5** in 65% yield. Next, we investigated the reaction of **3**, prepared by methylation of **2** with dimethyl sulfate, with indole. A mixture of **3** with 1.2 eq of indole in the presence of an excess of Et_3OBF_4 in dichloromethane was allowed to stand at room temperature for 24 h, then the reaction mixture was washed with cold water to give a complex mixture from which four 1,4-dihydrocyclopent[*b*]indoles [**5** (19.1%), **6** (12.2%), **7** (7.5%), and **8** (7.8%)] were isolated by

silica gel column chromatography, together with three unidentified products. The IR, ultraviolet (UV), and ^{1}H-NMR spectral data as well as the *Rf*-value of these products (**5**, **6**, **7** and **8**) are summarized in Table I.

An X-ray crystallographic analysis of the compound **8** unambigously established that **5**—**8** have the 1,4-dihydrocyclopent[*b*]indole skeleton.[4] The ring transformation of **3** to 1,4-dihydrocyclopent[*b*]indoles can be rationalized as shown in Chart 2; namely, the N-methylindole adduct (**3**) forms an equilibrium mixture with the indole adduct (**3′**) *via* the intermediate A. The nucleophilic attack of the second indole or N-methylindole at the C_5-position of **3** or **3′** may form B. Subsequent intramolecular cyclization with loss of the aminopyrazole moiety followed by prototropy will finally yields a mixture of the compounds **5**—**8**.

Cyclopent[*b*]indole itself was first isolated by Paul and Weise[5] as the hydrobromide salt

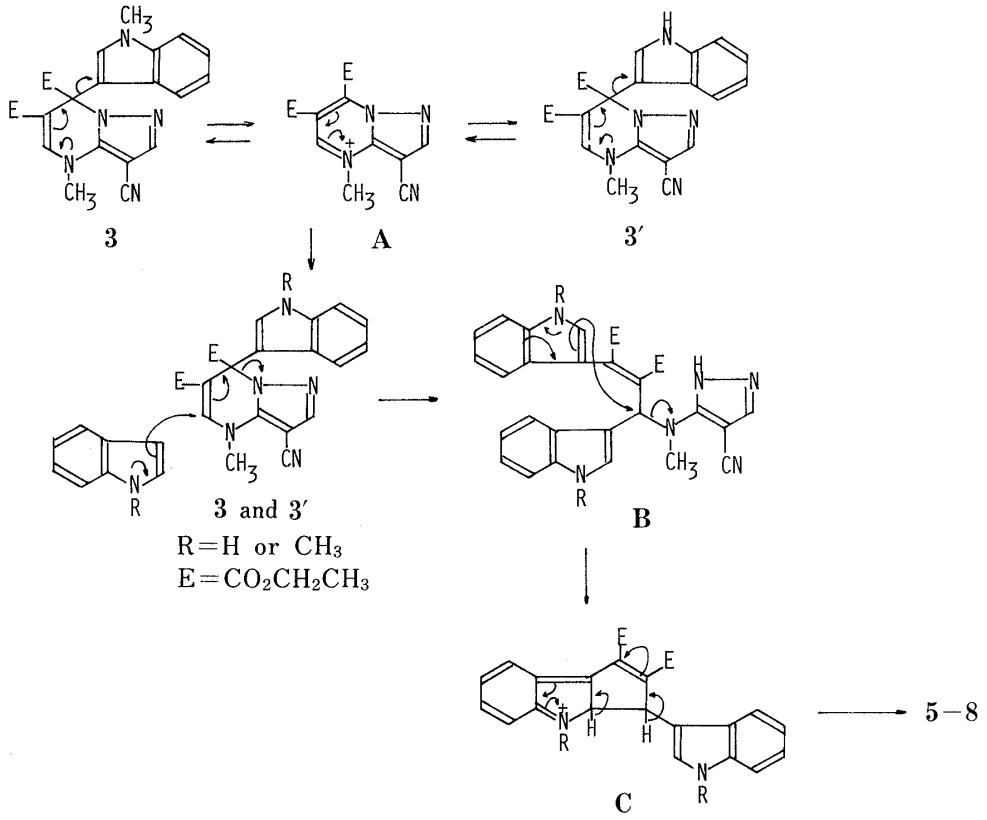


Chart 2

in 1963. However, to our knowledge, 1,4-dihydrocyclopent[*b*]indole and its derivatives have not previously been reported, probably because of the presence of an unstable cyclopentadiene moiety in the molecule. Thus, we were interested in investigating the chemical reactivity of these compounds, and our attention was focused on the compound **6**. Interestingly, it was found that the ^{1}H-NMR signal of the C_1-proton at δ 4.80 of **6** was exchangeable by the addition of deuterium oxide (D_2O) in deuteriodimethylsulfoxide (DMSO-d_6). Thus, compound **6** [MS *m/z*: 442 (M^+)] was treated with D_2O in DMSO to give **9**, whose MS showed a molecular ion peak at *m/z*: 443 (M^+). In addition, treatment of **6** with potassium hydroxide in ethanol at room temperature gave the 1-hydroxy-1,4-dihydrocyclopent[*b*]indole (**10**) in 70% yield as an unexpected product. The IR spectrum of **10** showed a strong absorption band at 3440 cm^{-1} due to the hydroxy group. Since the ^{1}H-NMR and UV spectra of **10** were similar to those of **6** or **9**, we assigned the C_1-hydroxy structure to

the product **10**. On the other hand, refluxing of **6** with three equivalents of potassium hydroxide in ethanol afforded 1,4-dihydro-3-(2,3-dihydro-*N*-methyl-3-indolyl)-4-methyl-1-oxocyclopent[*b*]indole (**11**), $C_{21}H_{18}N_2O$, mp 251—252 °C, in 30.3% yield. The IR spectrum of **11** showed a strong absorption band at 1670 cm^{-1} (CO). The ^{1}H-NMR spectrum showed signals at δ 2.98 (1H, dd, J=17 and 4 Hz) and δ 3.55 (1H, dd, J=17 and 8 Hz) as the AB part

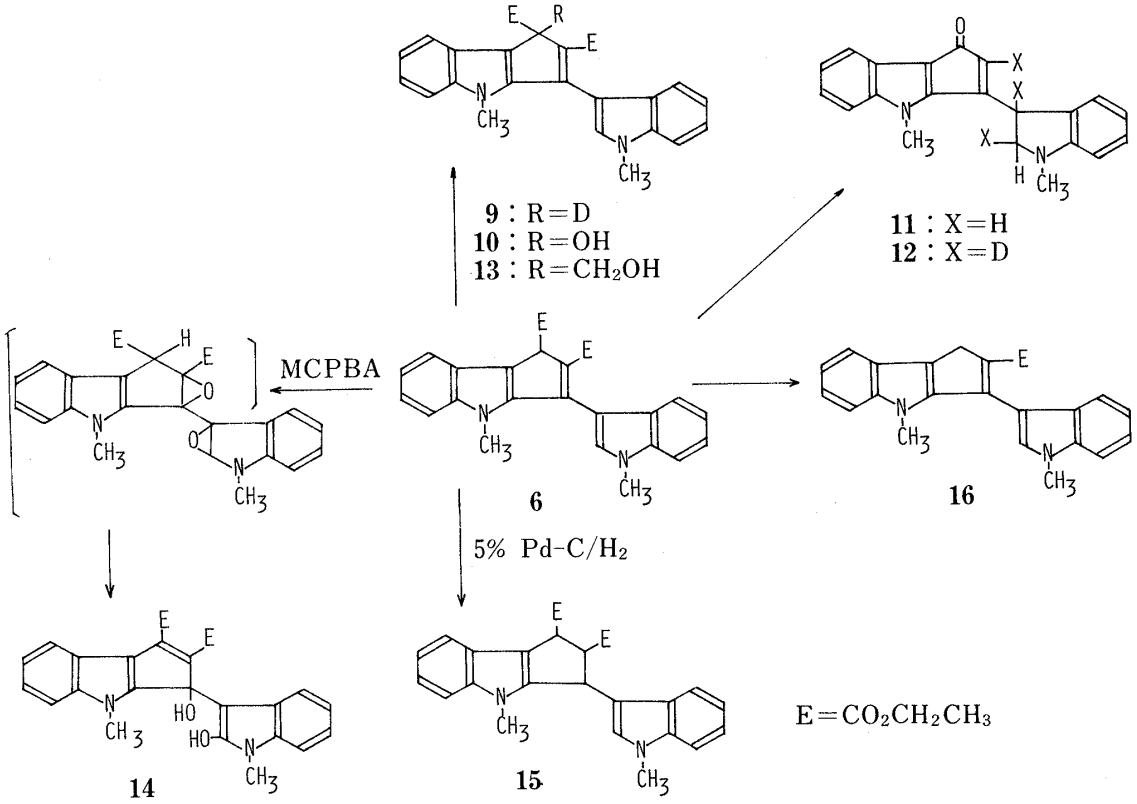


Chart 3

of an ABX pattern, and δ 4.82 (1H, dd, J=8 and 4 Hz) as the X part of an ABX pattern due to the $-CHCH_2-$ moiety. Based on these results, the 1,4-dihydro-1-oxocyclopentadiene structure was assigned to this product. Chart 4 shows a plausible mechanism for the formation of **11**.

In order to substantiate the mechanistic proposal in Chart 4, alkaline hydrolysis was

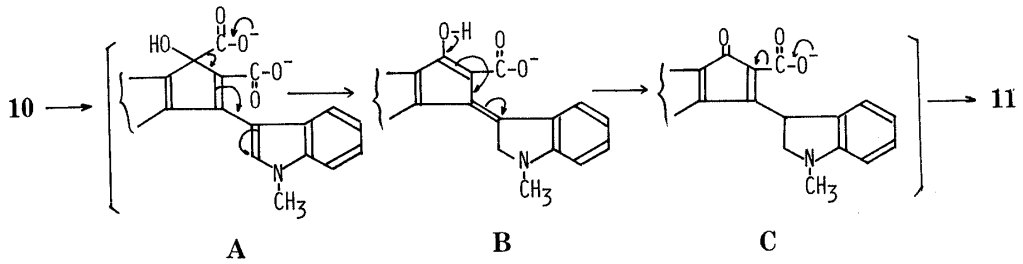


Chart 4

carried out in dry dioxane and D_2O. Namely, potassium hydroxide treatment of **6** in dry dioxane in the presence of 3% volume of D_2O (v/v) provided **12** in 4% yield; the MS of the product exhibited a molecular ion peak at m/z: 317 (M^+). The IR spectrum of **12** was in fair agreement with that of **11**. The ^{1}H-NMR spectrum [δ 3.30 (1H, s), 3.50 and 3.75 (each 3H,

each s), 6.80—7.80 (8H, m)] of **12** is consistent with the trideuterated structure in Chart 3. Treatment of **6** with 37% formaldehyde solution in tetrahydrofuran (THF) at 40 °C gave the 1-hydroxymethyl derivative (**13**) in 26.6% yield. *m*-Chloroperbenzoic acid (MCPBA) oxidation of **6** in dichloromethane gave **14** as pale orange needles, mp 224—226 °C, in 65% yield. The MS of **14** [*m/z*: 474 (M^+)] clearly demonstrates it to be an adduct of two oxygen atoms with **6**. The IR spectrum showed two ester carbonyl absorption bands at 1700 and 1650 cm^{-1} in addition to broad absorption band at 3400 cm^{-1}. The UV spectrum is very similar to that of **6**, while the ^{1}H-NMR spectrum revealed the disappearance of the C_1-proton and indole C_2-proton signals, and the presence of two hydroxy protons at δ 7.37 and 12.80 as singlets. Thus, **14** was assigned as diethyl 3,4-dihydro-3-hydroxy-4-methyl-3-(2-hydroxy-*N*-methyl-3-indolyl)cyclopent[*b*]indole-1,2-dicarboxylate, which would be formed *via* the diepoxide intermediate. Catalytic hydrogenation of **6** gave the tetrahydrocyclopent[*b*]indole (**15**) in 70% yield. When refluxed in xylene for 20 h, **6** afforded ethyl 1,4-dihydro-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-2-carboxylate (**16**) in 21% yield; the structure of the product was readily determined from the ^{1}H-NMR and UV spectral data given in the experimental section.

It was reported[6] that heating of indene resulted in the formation of isoindene intermediate by hydrogen rearrangement, and this reacted with maleic anhydride to yield the [4+2] cycloadduct, benzonorbornenedicarboxylic acid anhydride. Thus, we investigated the reaction of **6** with activated olefins under heating.

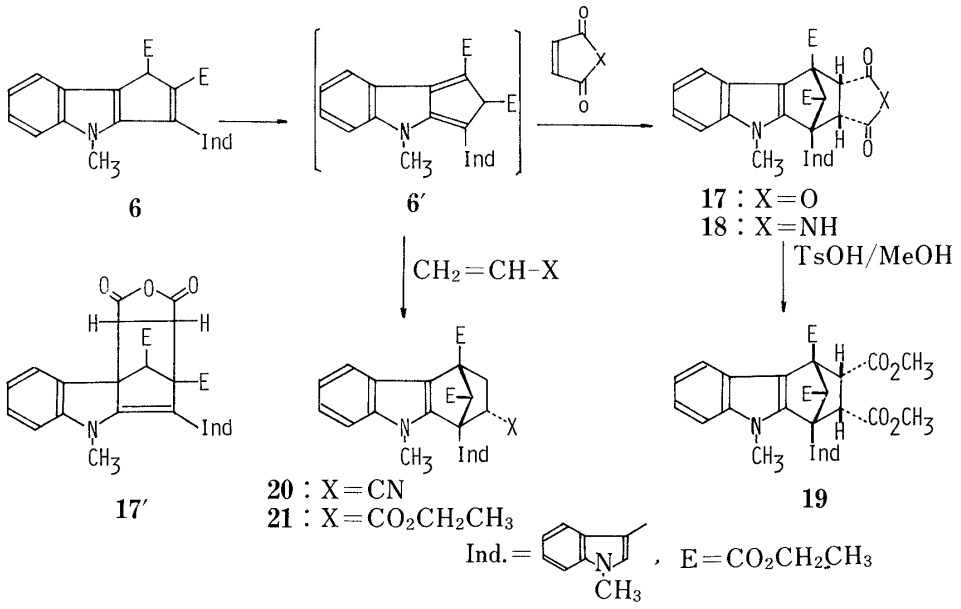
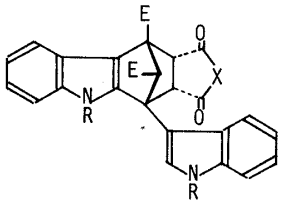


Chart 5

A solution of **6** and maleic anhydride in benzene was refluxed for 30 min to give colorless needles of mp 213—214 °C in quantitative yield; the structure of this product was determined to be 1,10-*anti*-diethoxycarbonyl-5-methyl-4-(*N*-methyl-3-indolyl)bicyclo-[2.2.1]hept[2,3-*b*]indole-2,3-*endo*-dicarboxylic acid anhydride (**17**), $C_{31}H_{28}N_2O_7$, as following spectral data; namely, the IR spectrum showed characteristic absorption bands of a carboxylic acid anhydride carbonyl group at 1860 and 1785 cm^{-1} in addition to an ester carbonyl group at 1725 cm^{-1}. The ^{1}H-NMR spectrum showed a pair of doublets (J=9 Hz) at δ 4.28 and 4.95 due to the C_2- and/or C_3-protons as well as a singlet at δ 3.68 due to the C_{10}-proton. Moreover, the UV spectrum showed absorption maxima at 287 (4.16) and 293 (4.16) nm, which are very similar to those of N-methylindole itself. Thus, the other possible structure (**17′**) for the [4+2] cycloadduct was ruled out. On the basis of the concept that the Diels–

TABLE II. Physical Property for Bicyclo[2.2.1]hept[2,3-*b*]indoles



E = $CO_2CH_2CH_3$

Product			Reaction solvent	Reaction time (h)	Yield (%)	Solvent for recrystallization	mp (°C)
No.	R	X					
17	CH_3	O	Benzene	0.5	100	AcOEt	213—214
18	CH_3	NH	CH_3CN	1	93	EtOH	213—214
22	H	O	Benzene	1	62	AcOEt	159—160
23	H	NH	CH_3CN	5	61	MeOH	269—271

TABLE III. Analytical and Spectral Data for Bicyclo[2.2.1]hept[2,3-*b*]indoles

Compd. No.	Formula	Analysis (%) Calcd (Found)			IR (KBr) cm^{-1}	^{1}H-NMR (DMSO-d_6) δ *J*, Hz
		C	H	N		
17	$C_{31}H_{28}N_2O_7$	68.88	5.22	5.18	1860	0.40 and 1.37 (each 3H, each t, $J=7$, $2\times CO_2CH_2C\underline{H}_3$)
		(68.90	5.27	5.10)	1785	3.13 and 3.93 (each 1H, each s, $2\times NCH_3$)
					1720	3.70 (1H, s, C_{10}–H)
						4.28 and 4.95 (each 1H, each d, $J=9$, C_2– and/or C_3–H)
						4.20—4.50 (4H, m, $2\times CO_2C\underline{H}_2CH_3$)
						6.90—7.70 (8H, m, Ar–H)
						7.80 (1H, s, C_2–H of indole ring)
18	$C_{31}H_{29}N_3O_6$	69.00	5.42	7.79	3450	0.40 and 1.35 (each 3H, each t, $J=7$, $2\times CO_2CH_2C\underline{H}_3$)
		(69.25	5.59	8.00)	1770	3.10 and 3.90 (each 3H, each s, $2\times NCH_3$)
					1720	3.47 (1H, s, C_{10}–H)
						3.20—3.45 (2H, m, $CO_2C\underline{H}_2CH_3$)
						3.85 and 4.55 (each 1H, each d, $J=8$, C_2– and/or C_3–H)
						4.40 (2H, q, $J=7$, $CO_2C\underline{H}_2CH_3$)
						6.90—7.50 (8H, m, Ar–H)
						7.75 (1H, s, C_2–H of indole ring), 10.30 (1H, s, NH)
22	$C_{29}H_{24}N_2O_4$	67.96	4.72	5.47	3400	0.60 and 1.40 (each 3H, each t, $J=7$, $2\times CO_2CH_2C\underline{H}_3$)
		(68.15	4.88	5.42)	1860	3.60 (2H, q, $J=7$, $CO_2C\underline{H}_2CH_3$)
					1780	4.23 (1H, s, C_{10}–H)
					1720	4.10 and 4.70 (each 1H, each d, $J=9$, C_2– and/or C_3–H)
						4.40—4.60 (2H, m, $CO_2C\underline{H}_2CH_3$)
						7.0—7.90 (9H, m, Ar–H)
						11.30 (1H, br s, NH), 11.60 (1H, s, NH)
23	$C_{29}H_{25}N_3O_6$	68.09	4.93	8.22	3450	0.60 and 1.40 (each 3H, each t, $J=7$, $2\times CO_2CH_2C\underline{H}_3$)
		(68.30	5.10	8.30)	3360	3.55 (2H, q, $J=7$, $CO_2C\underline{H}_2CH_3$)
					1770	4.0 (1H, s, C_{10}–H)
					1720	4.10 (1H, d, $J=8$, C_2– and/or C_3–H)
					1700	4.30 (3H, m, $CO_2C\underline{H}_2CH_3$ and C_2– and/or C_3–H)
						6.90—7.90 (9H, m, Ar–H)
						10.20, 11.20, and 11.45 (each 1H, each br s, $3\times NH$)

Alder adduct generally has *endo-cis* substituents originating from the dienophiles, the stereostructure of **17** was assigned as shown in Chart 5. Treatment of **17** with *p*-toluenesulfonic acid in methanol gave the 2,3-dicarboxylic acid ester (**19**) in 30.6% yield.

Similarly, the reaction of **6** with maleimide in acetonitrile afforded the corresponding cycloadduct **18** in 93% yield. Elemental analysis and spectroscopic data were consistent with the assigned structure. Analytical and spectroscopic data for the Diels–Alder adducts of **5** (and **6**) with maleic anhydride or maleimide are summarized in Tables II and III.

These experiments revealed that heating of 1,4-dihydrocyclopent[*b*]indole (**6**) resulted in isomerization to 3,4-dihydrocyclopent[*b*]indole (**6'**) in [4+2] cycloaddition with olefins.

Refluxing of a solution of **6** and acrylonitrile in acetonitrile for 2 d gave colorless needles (**20**), $C_{30}H_{29}N_3O_4$, mp 209—211 °C, in 46.7% yield. The ^{1}H-NMR spectrum showed signals due to the C_2-proton (*exo*) as a double-doublet at δ 1.77 with $J=15$ and 5 Hz, and the C_2-proton (*endo*) as a double-doublet at δ 2.82 ($J=15$ and 12 Hz) coupled with the C_3-proton (*exo*), together with a singlet signal due to the C_{10}-proton at δ 3.13. The UV spectrum was very similar to that of **19**. Thus, **20** was assigned as diethyl 3-*endo*-cyano-5-methyl-4-(*N*-methyl-3-indolyl)bicyclo[2.1.1]hept[2,3-*b*]indole 1,10-*anti*-dicarboxylate. It is well known that the dienes are generally the electron donor and dienophiles the electron acceptor in the Diels–Alder reaction.Thus, it seems reasonable to assume that the cyano group is attached to the C_3-position. The reaction of **6** with ethyl acrylate was rather slow, and afforded the adduct **21**, $C_{32}H_{34}N_2O_6$, mp 192—194 °C in 19.6% yield.

The reaction of **6** with dimethyl acetylenedicarboxylate under thermal conditions is currently under investigation.

Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were recorded on a JASCO model IRA-1 spectrophotometer and the UV spectra on a JASCO UVIDEC-505 spectrophotometer. The ^{1}H-NMR spectra were taken at 90 MHz with a Hitachi R-24A spectrometer and chemical shifts are expressed in ppm downfield from tetramethylsilane (TMS) as an internal standard. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. The MS were recorded with Hitachi RMU-7L and Hitachi M-80 instruments.

Reaction of Compound 1 with N-Methylindole——Et_3OBF_4 (5.7 g, 0.03 mol) was added in one portion to a solution of **1** (2.88 g, 0.01 mol) and N-methylindole (1.31 g, 0.01 mol) in CH_2Cl_2 (45 ml), and the mixture was stirred at room temperature overnight. The CH_2Cl_2 solution was washed with cold water (20 ml × 5), and dried over anhyd. Na_2SO_4. After removal of the solvent by evaporation, benzene (10 ml) was added to the residue. The resulting precipitate was collected by filtration and recrystallized from acetonitril to give 6,7-diethoxycarbonyl-4,7-dihydro-4-ethyl-7-(*N*-methyl-3-indolyl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4**) (765 mg, 17.1%) as prisms, mp 217—218 °C. IR ν_{max}^{KBr} cm^{-1}: 2220 (CN), 1760, 1690 (CO). ^{1}H-NMR (DMSO-*d*) δ: 1.10 (6H, t, $J=7$ Hz, 2 × $CO_2CH_2C\underline{H}_3$), 1.40 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 3.73 (3H, s, NCH_3), 3.85—4.30 (6H, m, 3 × $C\underline{H}_2CH_3$), 6.80—7.10 (3H, m, Ar–H), 7.30 (1H, m, C_7–H of indole ring), 7.55 (1H, s, C_2–H of indole ring), 7.75 and 7.85 (each 1H, each s, C_2– and/or C_5–H). *Anal.* Calcd for $C_{24}H_{25}N_5O_4$: C, 64.41; H, 5.63; N, 15.65. Found: 64.38; H, 5.45; N, 15.37. The filtrate was concentrated *in vacuo* to give a tarry residue, which was subjected to silica gel column chromatography. Elution with $CHCl_3$ gave a crystalline product (1.09 g, 24.6%), which was recrystallized from EtOH to give diethyl 1,4-dihydro-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (**6**), mp 171—173 °C (Table I). MS *m/z*: 442 (M^+). *Anal.* Calcd for $C_{27}H_{26}N_2O_4$: C, 73.28; H, 5.92; N, 6.33. Found: C, 73.22; H, 5.95; N, 6.25. The reaction of **1** with two equivalents of N-methylindole gave **6** in 69.6% yield.

Reaction of Compound 2 with Diethyl Sulfate——A mixture of **2** (411 mg, 1 mmol), diethyl sulfate (308 mg, 2 mmol) and K_2CO_3 (415 mg, 3 mmol) in acetone (30 ml) was refluxed for 5 h under vigorous stirring, then cooled. After removal of K_2CO_3 by filtration, the filtrate was concentrated *in vacuo*. The residue was recrystallized from acetonitrile to give the product **4** (405 mg, 92%), mp 217—218 °C, which was identical with an authentic sample.

Reaction of 1 with Indole——Et_3OBF_4 (5.7 g, 0.03 mol) was added in one portion to a solution of **1** (2.88 g, 0.01 mol) and indole (2.3 g, 0.02 mol) in CH_2Cl_2 (45 ml), and the mixture was stirred at room temperature overnight. The CH_2Cl_2 solution was washed with cold water (20 ml × 5), and dried over anhyd. Na_2SO_4. After removal of the solvent by evaporation, the residue was recrystallized from EtOH to give diethyl 1,4-dihydro-3-(3-indolyl)cyclopent[*b*]indole-1,2-dicarboxylate (**5**) (2.69 g, 65%), mp 223—225 °C (Table I). MS *m/z*: 414 (M^+). *Anal.* Calcd for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76. Found: C, 72.50; H, 5.25; N, 6.50.

6,7-Diethoxycarbonyl-4,7-dihydro-4-methyl-7-(*N*-methyl-3-indolyl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (3)——Compound **2** (411 mg, 0.01 mol) was treated with dimethyl sulfate (2.52 g, 0.02 mol) and K_2CO_3 (4.15 g, 0.03 mol) under a procedure similar to that given for **4** to provide the product **3** (4.03 g, 99%), mp 172—173 °C, as

prisms, which were recrystallized from EtOH. IR ν_{max}^{KBr} cm^{-1}: 1760, 1690 (CO). ^{1}H-NMR (DMSO-d_6) δ: 1.15 (6H, t, J=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 3.77 (6H, s, 2×NCH_3), 3.90—4.30 (4H, m, 2×$CO_2C\underline{H}_2CH_3$), 6.90—7.40 (4H, m, Ar–H), 7.60 (1H, s, C_2–H of indole ring), 7.80 and 7.95 (each 1H, each s, C_2– and/or C_5–H). *Anal.* Calcd for $C_{23}H_{23}N_5O_4$: C, 63.73; H, 5.35; N, 16.16. Found: C, 63.53; H, 5.22; N, 16.21.

Reaction of Compound 3 with Indole——A solution of **3** (7.52 g, 17.4 mmol) and indole (2.34 g, 20 mmol) was treated with Et_3OBF_4 as described for the reaction of **1** with N-methylindole. After usual work-up, the residual oil obtained was subjected to silica gel column chromatography. The fractions eluted with $CHCl_3$ provided **6** (1.463 g, 19.1%), **7** (552 mg, 7.5%), **8** (580 mg, 7.8%), and **5** (880 mg, 12.2%) in that order (Table I).

Diethyl 1,4-Dihydro-3-(*N*-methyl-3-indolyl)cyclopent[*b*]indole-1,2-dicarboxylate (**7**): mp 205—207 °C (EtOH). MS *m/z*: 428 (M^+). *Anal.* Calcd for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.68; H, 5.69; N, 6.40.

Diethyl 1,4-Dihydro-3-(3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (**8**): mp 190—191 °C (EtOH). MS *m/z*: 428 (M^+). *Anal.* Calcd for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 73.01; H, 5.52; N, 6.62.

Elution with $CHCl_3$–ethyl acetate mixture (1 : 1) gave three crystalline products, $C_{31}H_{28}N_6O_3$ [mp 291—292 °C, 202 mg (2.2%)], $C_{30}H_{26}N_6O_3$ [mp >300 °C, 576 mg (6.4%)], and $C_{29}H_{24}N_6O_3$ [mp 250—251 °C, 234 mg (2.7%)]. The structural determinations of these products are in progress.

Diethyl 1-Deuterio-1,4-dihydro-4-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (9)——A solution of **6** (44.2 mg, 0.1 mmol) in DMSO (1 ml) was diluted with D_2O (2 ml). The resulting precipitate was collected by filtration and recrystallized from EtOH to give **9** (26 mg), mp 172—173 °C. MS *m/z*: 443 (M^+).

Diethyl 1,4-Dihydro-1-hydroxy-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (10)——A solution of **6** (360 mg, 0.82 mmol) and KOH (120 mg, 2 mmol) in EtOH (160 ml) was allowed to stand overnight. After removal of the solvent by evaporation, the residue was recrystallized from EtOH to give **10** (264 mg, 70%), mp 197—198 °C. (Table I). MS *m/z*: 458 (M^+). *Anal.* Calcd for $C_{27}H_{28}N_2O_5$: C, 70.42; H, 6.13; N, 6.08. Found: C, 70.28; H, 5.87; N, 6.03.

1,4-Dihydro-3-(2,3-dihydro-*N*-methyl-3-indolyl)-4-methyl-1-oxocyclopent[*b*]indole (11)——A solution of **6** (442 mg, 1 mmol) and KOH (198 mg, 3 mmol) in 98% EtOH (150 ml) was refluxed for 36 h. After removal of the solvent by evaporation, the residue was extracted with water (50 ml) and $CHCl_3$ (50 ml). The $CHCl_3$ layer was separated, washed with water, and dried over anhyd. Na_2SO_4. Removal of the solvent by evaporation gave a crystalline product, which was recrystallized from MeOH to give **11** (95 mg, 30.3%), mp 251—252 °C. IR ν_{max}^{KBr} cm^{-1}: 1670 (CO). ^{1}H-NMR ($CDCl_3$) δ: 2.98 (1H, dd, J=17, 4 Hz, CH_2), 3.55 (1H, dd, J=17, 8 Hz, CH_2), 3.45 and 3.75 (each 3H, each s, 2×NCH_3), 4.82 (1H, dd, J=8, 4 Hz, CH), 6.84 (1H, s, vinyl-H), 6.90—8.10 (8H, m, Ar–H). MS *m/z*: 314 (M^+). *Anal.* Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.08; H, 5.75; N, 8.98.

2-Deuterio-1,4-dihydro-3-(2,3-dideuterio-*N*-methyl-3-indolyl)-4-methyl-1-oxocyclopent[*b*]indole (12)——A solution of **6** (442 mg, 1 mmol) and KOH (198 mg, 3 mmol) in dry dioxane (300 ml) containing D_2O (10 ml) was refluxed for 36 h. After removal of the solvent by evaporation, the residue was extracted with water (50 ml) and $CHCl_3$ (50 ml). The $CHCl_3$ layer was separated, washed with water, and dried over anhyd. Na_2SO_4. Removal of the solvent by evaporation gave a crystalline residue, which was recrystallized from MeOH to give **12** (17.8 mg, 4%), mp 252—254 °C. IR ν_{max}^{KBr} cm^{-1}: 1690 (CO). ^{1}H-NMR (DMSO-d_6) δ: 3.30 (1H, s, C_2–H of indole ring), 3.50 and 3.75 (each 3H, each s, 2×NCH_3), 6.80—7.80 (8H, m, Ar–H). MS *m/z*: 317 (M^+).

Diethyl 1,4-Dihydro-1-hydroxymethyl-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (13)——A solution of **6** (884 mg, 2 mmol) and 37% formaldehyde solution (530 mg, 6 mmol) in THF (30 ml) was stirred at 40 °C for 20 h. After removal of the solvent by evaporation, the residue was subjected to silica gel column chromatography. Elution with benzene–ethyl acetate (20 : 1) gave a crystalline product, which was recrystallized from ethyl acetate to give **13** (252 mg, 26.2%) as yellow needles, mp 180—183 °C. IR ν_{max}^{KBr} cm^{-1}: 3260 (OH), 1730, 1650 (CO). ^{1}H-NMR ($CDCl_3$) δ: 0.93 and 1.21 (each 3H, each t, J=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 3.41 and 3.91 (each 3H, each s, 2×NCH_3), 4.0—4.40 (6H, m, CH_2 and 2×$CO_2C\underline{H}_2CH_3$), 7.10—7.80 (9H, m, Ar–H). *Anal.* Calcd for $C_{28}H_{28}N_2O_5$: C, 71.17; H, 5.97; N, 5.93. Found: C, 70.90; H, 6.19; N, 5.86.

Diethyl 3,4-Dihydro-3-hydroxy-4-methyl-3-(2-hydroxy-*N*-methyl-3-indolyl)cyclopent[*b*]indole-1,2-dicarboxylate (14)——A solution of **6** (180 mg, 0.4 mmol) and MCPBA (260 mg, 1.2 mmol) in CH_2Cl_2 (30 ml) was stirred with ice-cooling for 20 h. The CH_2Cl_2 solution was washed with saturated $NaHCO_3$ solution and water, then dried over anhyd. Na_2SO_4. After removal of the solvent by evaporation, the residue was recrystallized from EtOH to give **14** (124 mg, 65%), mp 224—226 °C. IR ν_{max}^{KBr} cm^{-1}: 3540 (OH), 1700, 1670 (CO). UV λ_{max}^{EtOH} nm (log ε): 345 (4.16), 260 (sh), 220 (4.64). ^{1}H-NMR (DMSO-d_6) δ: 0.60 and 1.27 (each 3H, each t, J=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 3.20 and 3.77 (each 3H, each s, 2×NCH_3), 3.70 and 4.30 (each 2H, each m, 2×$CO_2C\underline{H}_2CH_3$), 6.70—7.50 (8H, m, Ar–H), 7.40 and 12.80 (each 1H, each s, 2×OH, exchangeable with D_2O). MS *m/z*: 474 (M^+). *Anal.* Calcd for $C_{27}H_{26}N_2O_6$: C, 68.34; H, 5.52; N, 5.90. Found: C, 68.31; H, 5.79; N, 6.04.

Diethyl 1,2,3,4-Tetrahydro-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-1,2-dicarboxylate (15)——A solution of **6** (442 mg, 1 mmol) in MeOH (50 ml) was shaken with hydrogen over 5% Pd–C (300 mg) for 10 h in a Skita apparatus. The mixture was filtered and concentrated *in vacuo*. The residue was recrystallized from EtOH to give **15** (333 mg, 75%), mp 175—176 °C. IR ν_{max}^{KBr} cm^{-1}: 1740 (CO). ^{1}H-NMR (DMSO-d_6) δ: 0.45 and 1.17 (each 3H, each t, J=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 3.30 and 3.70 (each 3H, each s, 2×NCH_3), 3.20—3.50 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.10 (2H,

q, $J=7$ Hz, $CO_2C\underline{H}_2CH_3$), 4.30—4.45 (2H, m, C_2– and C_3–H), 5.25 (1H, dd, $J=3.5$, 2 Hz, C_1–H), 6.90—7.60 (9H, m, Ar–H). MS *m/z*: 444 (M^+). *Anal.* Calcd for $C_{27}H_{28}N_2O_4$: C, 72.95; H, 6.35; N, 6.30. Found: C, 72.76; H, 6.62; N, 6.41.

Ethyl 1,4-Dihydro-3-(*N*-methyl-3-indolyl)-4-methylcyclopent[*b*]indole-2-carboxylate (16)——A solution of **6** (1 g, 2.26 mmol) in xylene (50 ml) was refluxed for 20 h. After removal of the solvent by evaporation, the residue was subjected to silica gel column chromatography. Elution with benzene gave a crystalline product, which was recrystallized from EtOH to give **16** (176 mg, 21%), mp 201—202 °C. IR ν_{max}^{KBr} cm^{-1}: 1680 (CO). UV λ_{max}^{EtOH} nm (log ε): 367 (4.20), 260 (4.22), 220 (4.71). ^{1}H-NMR (DMSO-d_6) δ: 1.02 (3H, t, $J=7$ Hz, $CO_2CH_2C\underline{H}_3$), 3.42 and 3.93 (each 3H, each s, NCH_3), 3.77 (2H, s, CH_2), 4.0 (2H, q, $J=7$ Hz, $CO_2C\underline{H}_2CH_3$), 7.0—7.68 (8H, m, Ar–H), 7.70 (1H, s, C_2–H of indole ring). *Anal.* Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.66; H, 6.06; N, 7.51.

Reaction of 5 and 6 with Maleic Anhydride and Maleimide: General Procedure——A solution of **5** or **6** (1 mmol) and an olefin (1.2 mmol) in dry benzene or acetonitrile was refluxed. The reaction mixture was concentrated *in vacuo*, and the residue was recrystallized to give the corresponding 1,10-*anti*-diethoxycarbonyl-4-(3-indolyl)bicyclo-[2.2.1]hept[2,3-*b*]indole-2,3-*endo*-dicarboxylic acid anhydrides (**17** or **22**) and 1,10-*anti*-diethoxycarbonyl-4-(3-indolyl)bicyclo[2.2.1]hept[2,3-*b*]indole-2,3-*endo*-dicarboximide (**18** or **23**) (Tables II, III).

Dimethyl 1,10-*anti*-Diethoxycarbonyl-5-methyl-4-(*N*-methyl-3-indolyl)bicyclo[2.2.1]hept[2,3-*b*]indole-2,3-*endo*-dicarboxylate (19)——A solution of **17** (540 mg, 1 mmol) and *p*-toluenesulfonic acid (30 mg) in MeOH (30 ml) was refluxed for 3 d. After removal of the solvent by evaporation, the residue was recrystallized from ethyl acetate to give **19** (179 mg, 30.6%), mp 217—218 °C. IR ν_{max}^{KBr} cm^{-1}: 1760—1720 (CO). ^{1}H-NMR (DMSO-d_6) δ: 0.34 and 1.36 (each 3H, each t, $J=7$ Hz, $2\times CO_2CH_2C\underline{H}_3$), 3.26 (6H, s, $2\times CO_2CH_3$), 3.36 and 3.86 (each 3H, each s, $2\times NCH_3$), 3.50 (1H, s, C_{10}–H), 3.50—3.73 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.20—4.50 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.23 and 4.70 (each 1H, each d, $J=9$ Hz, C_2– and/or C_3–H), 6.90—7.90 (8H, m, Ar–H), 7.42 (1H, s, C_2–H of indole ring). *Anal.* Calcd for $C_{33}H_{34}N_2O_8$: C, 67.56; H, 5.84; N, 4.78. Found: C, 67.29; H, 5.94; N, 4.65.

Reaction of 6 with Acrylonitrile (or Ethyl Acrylate): General Procedure——A soluion of **6** (0.5 mmol) and acrylonitrile (or ethyl acrylate) (0.7 mmol) in acetonitrile (30 ml) was refluxed for 48 h (or 96 h), then cooled. The resulting precipitate was collected by filtration and recrystallized.

Diethyl 3-*endo*-Cyano-5-methyl-4-(*N*-methyl-3-indolyl)bicyclo[2.2.1]hept[2,3-*b*]indole-1,10-*anti*-dicarboxylate (**20**): Yield: 46.7%, mp 209—212 °C (MeOH). IR ν_{max}^{KBr} cm^{-1}: 2210 (CN), 1725—1700 (CO). ^{1}H-NMR ($CDCl_3$) δ: 0.48 and 1.44 (each 3H, each t, $J=7$ Hz, $2\times CO_2CH_2C\underline{H}_3$), 1.77 (1H, dd, $J=15$, 5 Hz, C_2–H *exo*), 2.82 (1H, dd, $J=15$, 12 Hz, C_2–H *endo*), 3.13 (1H, s, C_{10}–H), 3.28 and 3.86 (each 3H, each s, $2\times NCH_3$), 3.55 (1H, m, C_3–H *exo*), 3.80 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.45 (2H, q, $J=7$ Hz, $CO_2C\underline{H}_2CH_3$), 7.0—7.40 (8H, m, Ar–H), 8.10 (1H, m, Ar–H). MS *m/z*: 495 (M^+). *Anal.* Calcd for $C_{30}H_{29}N_3O_4$: C, 72.70; H, 5.90; N, 8.48. Found: C, 72.60; H, 5.97; N, 8.30.

Triethyl 5-Methyl-4-(*N*-methyl-3-indolyl)bicyclo[2.2.1]hept[2,3-*b*]indole-1,10-*anti*-3-*endo*-tricarboxylate (**21**): Yield: 19.2%, mp 192—194 °C (EtOH). IR ν_{max}^{KBr} cm^{-1}: 1740 (CO). ^{1}H-NMR ($CDCl_3$) δ: 0.55, 1.50 and 1.49 (each 3H, each t, $J=7$ Hz, $3\times CO_2CH_2C\underline{H}_3$), 2.12 (1H, dd, $J=15$, 5 Hz, C_2–H *exo*), 2.90 (1H, dd, $J=15$, 12 Hz, C_2–H *endo*), 3.20 and 3.83 (each 3H, each s, $2\times NCH_3$), 3.30 (1H, s, C_{10}–H), 3.40—3.80 (5H, m, $2\times CO_2C\underline{H}_2CH_3$ and C_4–H *exo*), 4.45 (2H, q, $J=7$ Hz, $CO_2C\underline{H}_2CH_3$), 6.90—7.50 (8H,m, Ar–H), 7.90 (1H, m, Ar–H). MS *m/z*: 542 (M^+). *Anal.* Calcd for $C_{32}H_{34}N_2O_6$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.65; H, 6.55; N, 5.10.

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References and Notes

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