spectrometer[9] operating at an accelerating voltage of 8 kV. Electron ionization was carried out at 70 eV at a current of 100–500 μA. Other details have been described.[10] The preparative pyrolysis apparatus consisted of an electrically heated tubular oven, employing a 25 × 2 cm quartz tube, pumped at ca. 10^{-3} torr. In this case, the products were isolated in liquid N_2 traps. Melting points are uncorrected.

Diimidazo[3,4-*a*:3′,4′-*d*]pyrazine-5,10-dione (14). 5-(Anilinocarbonyl)imidazole (**9**) (250 mg) was sublimed at 130 °C and pyrolyzed at 800 °C (10^{-3} torr) in the course of 3 h. A yellow solid (20% yield) condensed at the exit of the oven, in the air-cooled part of the cold trap, and was identified as **14** on the basis of the following data: mp 250–253 °C (from dimethoxyethane) (lit.[11] mp 254–255 °C); IR (KBr) 3080 (m), 1730 (s), 1550 (s), 1450 (m), 1360 (s), 1320 (w), 1270 (s), 1210 (s), 1145 (w), 1100 (m), 1090 (m), 1015 (w), 880 (m), 730 (m), 630 (m) cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 8.87 (d, J = 0.7 Hz, 2 H), 8.23 (d, J = 0.7 Hz, 2 H); mass spectrum, m/z (relative intensity) 188 (M^+·, 100), 160 (15), 95 (40), 94 (41), 93 (57), 68 (60); high-resolution mass spectrum, M^+· 188.0336 (calcd for $C_8H_4N_4O_2$ 188.0334), 189.0339 (calcd for $^{12}C_7{}^{13}C_1H_4N_4O_2$ 189.0311). Anal. Calcd for $C_8H_4N_4O_2$: C, 51.07; H, 2.14; N, 29.78. Found: C, 51.03; H, 2.13; N, 29.49.

The same compound was obtained in 20% yield on pyrolysis of methyl imidazole-4-carboxylate (**8**) at 750 °C and identified as above.

Diimidazo[3,2-*a*:3′,2′-*d*]pyrazine-5,10-dione (16). Methyl imidazole-2-carboxylate (**12**) (50 mg) was sublimed at 100 °C and pyrolyzed at 750 °C in the course of 3 h. The yellow solid (20% yield) deposited in the air-cooled part of the cold trap was identified as **16** on the basis of the following data: mp 265–268 °C (from dimethoxyethane); IR (KBr) 3120 (m), 1740 (s), 1520 (m), 1445 (s), 1390 (s), 1330 (w), 1275 (s), 1160 (m), 1060 (m), 1020 (m), 800 (m), 750 (w), 700 (w), 650 (m) cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 8.14 (d, J = 1.5 Hz, 2 H), 7.50 (d, J = 1.5 Hz, 2 H); mass spectrum, m/z (relative intensity) 188 (M^+·, 8), 94 (55), 68 (100); high-resolution mass spectrum, M^+· 188.0332 (calcd for $C_8H_4N_4O_2$ 188.0334).

The same compound was obtained in 10% yield on pyrolysis of 2-(anilinocarbonyl)imidazole (**13**) at 700 °C and identified as above. In addition, *N*,*N*′-diphenylurea was isolated from the cold trap in 46% yield. No dimer **16** was isolable after pyrolysis of **13** at 800 °C; instead, the majority of the material polymerized at the exit of the pyrolysis tube.

Pyrolysis of Methyl Imidazole-1-carboxylate (4). (a) This was carried out at 750 °C (10^{-3} torr). The yellow substance condensing in the air cooled part of the cold trap was identified as a 1:2:1 mixture (20% yield) of **14**, **15**, and **16** by comparison of the IR and ^1H NMR spectra with those of **14** and **16** described above. Diimidazo[3,2-*a*:3′,4′-*d*]pyrazine-5,10-dione (**15**) had the following ^1H NMR spectrum: ($(CD_3)_2SO$) δ 8.90 (d, J = 0.7 Hz, 1 H), 8.20 (d, J = 0.7 Hz, 1 H), 8.13 (d, J = 1.5 Hz, 1 H), 7.54 (d, J = 1.5 Hz, 1 H). The dimers were virtually insoluble in all ordinary solvents of low and medium polarity and did not elute on thin-layer chromatography except when highly polar solvents (CH_3OH) were used. Therefore, a chromatographic separation of the dimers was not feasible.

(b) **4** was pyrolyzed at various temperatures between 300 and 720 °C. The IR and NMR spectra of the pyrolysate obtained at 630 °C demonstrated the presence of the starting material as well as 1-methylimidazole (**7**). The abovementioned mixture of dimers was obtained in 10% yield at 700 °C. At this temperature **4** was still detectable, but in none of these experiments was **8** or **12** detectable by ^1H NMR.

Registry No. **4**, 61985-23-7; **5**, 99560-58-4; **6**, 99560-59-5; **7**, 616-47-7; **8**, 17325-26-7; **9**, 13189-13-4; **10**, 99560-56-2; **11**, 99560-57-3; **12**, 17334-09-7; **13**, 63678-16-0; **14**, 53525-65-8; **15**, 99560-60-8; **16**, 79711-73-2; ethyl imidazole-1-carboxylate, 19213-72-0.

(9) Maquestiau, A.; Van Haverbeke, Y.; Flammang, R.; Abrassart, M.; Finet, D. *Bull. Soc. Chim. Belg.* **1979**, *87*, 765.
(10) Maquestiau, A.; Flammang, R.; Pauwels, P. *Org. Mass Spectrom.* **1983**, *18*, 547.
(11) Kasina, S.; Nematollahi, J. *Synthesis*, **1975**, *162*.

Nitrone Cycloaddition in the Stereoselective Synthesis of β-Carbolines from *N*-Hydroxytryptophan

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The cycloaddition chemistry of nitrone **6**, obtained by treatment of *N*-hydroxytryptophan ester **4** with methyl orthoformate, has been evaluated. 1,3-Dipolar cycloadditions with alkenes proceed with high or complete regioselectivity to yield 4′- or 5′-substituted isoxazolidines (Scheme II). Complete C(3) → C(1) trans induction as well as high or complete stereoselectivity at the other newly introduced chiral center C(4′) or C(5′) is observed. The regiochemical course of these reactions is as predicted by frontier molecular orbital theory.

Tryptophan derivatives having a functionality in addition to the amino and carboxy group in the α-amino acid fragment have been found as characteristic structural elements of several natural products.[1] Recently, we reported[2] a scheme in which *N*-hydroxytryptophan **4** links L-tryptophan to α- and/or β-functionalized tryptophan derivatives.

Here we wish to report a reaction sequence that features the conversion of *N*-hydroxytryptophan **4** into the nitrone **6** which is used in a regio- and stereoselective cycloaddition to alkenes. The utility of the resulting cycloadducts for

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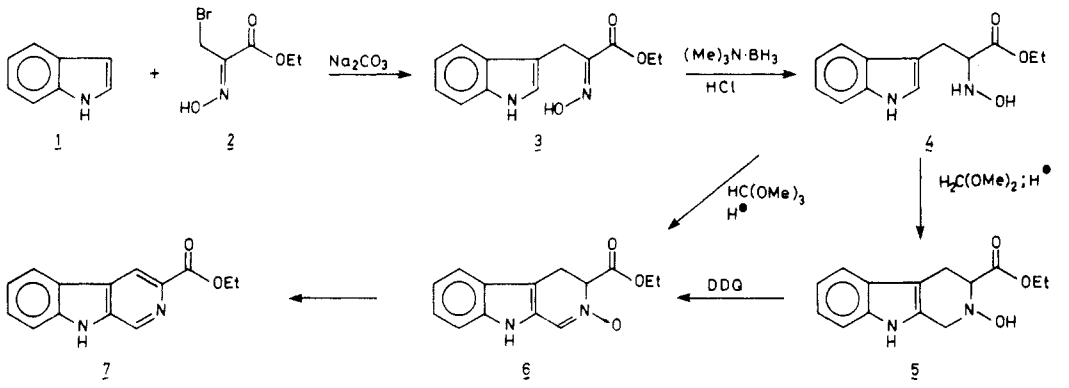
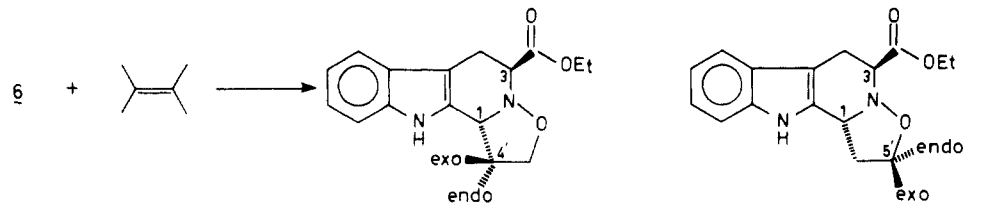
(1) E.g.: (a) Sporidesmin F: Jamieson, W. D.; Rahman, R.; Taylor, A. *J. Chem. Soc. C* **1969**, 1564. (b) TR-2: Cole, R. J.; Kirksey, J. W.; Cox, R. H.; Clardy, J. J. *J. Agric. Food Chem.* **1975**, *23*, 1015. (c) Neoechinulin B: Marchelli, R.; Dossena, A.; Pochini, A.; Dradi, E. *J. Chem. Soc., Perkin Trans. 1*, **1977**, 713. (d) Astechrome: Arai, K.; Sato, S.; Shimizu, S.; Nitta, K.; Yamamoto, Y. *Chem. Pharm. Bull.* **1981**, *29*, 1510.
(2) Ottenheijm, H. C. J.; Plate, R.; Noordik, J. H.; Herscheid, J. D. M. *J. Org. Chem.* **1982**, *47*, 2147.
(3) Sundberg, R. I., Ed. "The Chemistry of Indoles"; Academic Press: New York, 1970; p 236.
(4) In some cases small amounts of **9** were formed as side product.

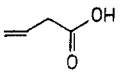
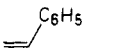
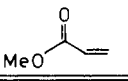
0022-3263/86/1951-0309$01.50/0

Scheme I



Scheme II



entry	alkene	overall yield [a] %	4'-isoxazolidine [b]	5'-isoxazolidine [b]
A		100		100
B		80		100 (exo)[c]
C		85	2 (exo)[e] 10 (endo)[e]	85 (exo)[c] 2 (endo)[d]
D		93	12 (exo)[c] 52 (endo)[c]	31 (exo)[c] 5 (endo)[d]
E		86	100 (exo)[e]	
F		93	100 (C=O at C-4')	

[a] These yields are based on the nitrone 6 and refer to isolated compounds.[4] [b] These ratios are based on isolated compounds. [c] This structure assignment is based on single-crystal X-ray crystallography. [d] Structure assignment made on the basis of NMR spectroscopy. [e] Tentative structure assignment.[5]

stereospecific syntheses of indole alkaloids is currently under investigation.

Synthesis of the Nitrone 6. The ethyl ester of *N*-hydroxytryptophan (4) was prepared from indole 1 and the oxime 2 as described by us previously[2] (Scheme I). Our first approach to 6 involves a modification of the Pictet–Spengler reaction:[3] reaction of 4 with formaldehyde dimethyl acetal yielded (91%) the 2-hydroxy-β-carboline 5. Selective DDQ oxidation of the hydroxylamine function of 5 could be achieved to yield (74%) the nitrone 6.

Subsequently, we reasoned that a one-step conversion of 4 into 6 might be possible if in the condensation reaction the acetal would be replaced by an ortho ester. This approach was found to be feasible indeed; treatment of 4 with methyl orthoformate gave 6 in excellent yield (85%). On occasion we observed that 6 is converted quantitatively to 3-(ethoxycarbonyl)-β-carboline (7) if kept in solution at room temperature for several weeks; during the cycloaddition reactions (vide infra) this β-carboline is formed in some cases as side product.

Cycloadditions. The cycloaddition reaction of the nitrone 6 to a variety of alkenes was investigated. The regio- and stereoselectivity of the reactions summarized in Scheme II are discussed below.

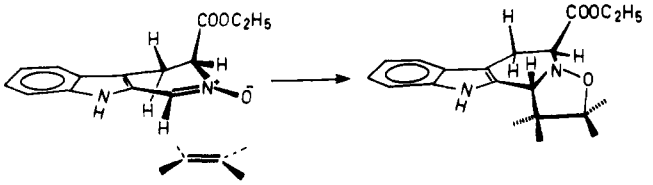
Regioselectivity. The concerted nature of cycloaddition reactions with nitrones as 1,3-dipoles has been generally accepted.[6] The regioselectivity in these reactions has been rationalized by use of the frontier-orbital theory.[7] Comparison of the values of the terminal coefficients of the interacting orbitals indicate that electron-rich dipo-

(5) The tentative assignment of the 4'-isoxazolidines' structures of entry C, i.e., 10 (endo) vs. 2 (exo) is based on ^{1}H NMR spectroscopy. The protons H(1) and H(4') have coupling constant values of 8.1 and 7.0 Hz, respectively. It is reasonable to assume that the compound with the higher value has the endo configuration, for in general $J_{endo} > J_{exo}$: Huisgen, R.; Grashey, R.; Hauck, H.; Seidl, H. *Chem. Ber.* **1968**, *101*, 2043.

(6) Huisgen, R. *J. Org. Chem.* **1976**, *41*, 403.

(7) Houk, K. N.; Sins, J.; Watts, C. R.; Luskus, L. J. *J. Am. Chem. Soc.* **1973**, *95*, 7302.

Scheme III



larophiles will yield 5′-substituted isoxazolidines due to a LUMO (nitrone)–HOMO (dipolarophile) interaction. The results of entries A and B agree with this theory. Partial reversal of this regioselectivity occurs with the electron-deficient dipolarophile methyl acrylate (entry D). Apparently the contribution of the HOMO (nitrone)–LUMO (dipolarophile) interaction is dominant in this entry, which leads to a ratio 4′- vs. 5′-isoxazolidine of 64:36. This is due to a crossover in the frontier orbital control.[7] A borderline case is the addition of styrene (entry C) where 12% of the two 4′-isoxazolidines is formed. With cyclohexenone (entry F) the cycloaddition proceeds with complete 4′-regiospecificity. Here the directing influences of the keto and alkyl substituents are cooperative.

The regioselectivity of entry D deserves further comment: it has been shown[8] that the amount of 4′-substituted isoxazolidine in general depends not only on the nature of the alkene but also on that of the nitrone. The proportion of the 4′-substituted product increases as the nitrone becomes more electron rich. A measure of this electron richness is the ionization potential, which can be determined by means of photoelectron spectroscopy. On the basis of this, one expects that the amount of 4′-substituted adduct increases as the value of the nitrone's IP decreases. However, this rule holds only with dipolarophiles having sufficient electron deficiency. Conversely, the cycloadduct's ratio (4′-vs. 5′-substitution) is thus a measure for the IP value of the nitrone used. The ratio 64:36 for the 4′-vs. 5′-substituted adduct of entry D points—according to Houk's calculation[8]—to an estimated IP value for nitrone **6** in the range of 8.35–8.40 eV. This consideration prompted us to study the photoelectron spectrum of **6**. The calculated value for the weighted average of the first two π-ionization potentials (8.40 eV)[9] is in good accordance with this estimated value.

Stereochemistry. As far as the relative stereochemistry at C(1) and C(3) is concerned it is noteworthy that the additions summarized in Scheme II proceed in a *completely stereocontrolled fashion*; the *C(1) and C(3) substituents* are in a trans orientation. This result may be rationalized as depicted in Scheme III.

In addition the relative stereochemistry at C(1) and C(4′) or C(5′) has to be discussed. For a given regioselective addition, the nitrone may approach the olefin in two, diastereoselective ways, resulting in an endo or exo adduct.

It is generally accepted that the exo approach is favored when only steric factors are to be considered.[10] The results of entries B–D agree with this rule as far as the 5′-isoxazolidines are concerned. On the basis of this we assign tentatively the exo structure to the adduct derived from cyclohexene (entry E).[11]

Entry D shows that this exo rule is not obeyed with the 4′-isoxazolidines derived from methyl acrylate, where the endo product is the major one (52 (endo) vs. 12 (exo)). This finding however, is in agreement with results reported[12] for nitrone additions with other α,β-dehydro carboxylates. These results have been rationalized by a secondary interaction of the frontier orbitals at the nitrone's nitrogen and at the alkene's carbonyl carbon atom.[12] However, CPK models indicate that an overlap geometry is not favorable. In addition, the low value of the calculated frontier orbital coefficient of the nitrone's nitrogen indicates that a possible secondary interaction must be located elsewhere in the nitrone.

The ratio 2 (exo) vs. 10 (endo) of the 4′-isoxazolidines of entry C might be rationalized by a similar secondary orbital interaction.

Finally, the endo/exo configuration of the adduct derived from cyclohexenone (entry F) has not been determined.[13]

In conclusion, the novel nitrone **6** can be used in 1,3-dipolar cycloadditions with alkenes, a reaction which proceeds in high or complete regioselectivity. In addition, this reaction is stereospecific: (i) the alkene approaches the nitrone exclusively from the side opposite the C(3) substituent (see Scheme III); this approach controls the C(1) stereochemistry; (ii) the configuration of the second newly formed chiral center, i.e., C(4′), or C(5′) in the isoxazolidine is determined by a preferential alkene facial selection by the nitrone. With some alkenes studied high endo or complete exo selectivity was observed.

Experimental Section

Melting points were taken on a Koefler hot stage (Leitz-Wetzlar) and are uncorrected. Ultraviolet spectra were measured with a Perkin-Elmer spectrometer, Model 555.

Proton magnetic resonance spectra were measured on a Varian Associates Model T-60 or a Bruker WH-90 spectrometer. Chemical shifts are reported as δ values (parts per million) relative to Me_4Si as an internal standard; $CDCl_3$ was used as the solvent unless stated otherwise. Mass spectra were obtained with a double-focusing VG 7070E spectrometer. Thin-layer chromatography (TLC) was carried out by using Merck precoated silica gel F-254 plates (thickness, 0.25 mm). Spots were visualized with a UV hand lamp, iodine vapor, Cl_2–TDM,[14] cinnimaldehyde/HCl for indole detection.[15] For column chromatography Merck silica gel H (Type 60) was used on preparative HPLC (Jobin Yvon).

Solvent systems used were as follows: system A, $MeOH/CH_2Cl_2$ (3/97 v/v); system B, $MeOH/CH_2Cl_2$ (7/93 v/v); system C, $MeOH/CHCl_3$ (7/93 v/v); system D, hexane/EtOAc (50/50 v/v); system E, hexane/EtOAc (10/90 v/v); system F, CH_2Cl_2/MeOH/HOAc (87/10/3 v/v).

Ethyl α-(hydroxyimino)-β-indol-3-ylpropanoate (**3**) was prepared by the literature procedure.[16]

Ethyl α-(Hydroxyamino)-β-indol-3-ylpropanoate (4). A solution of HCl in ethanol (60 mL of a 7 N solution) was added dropwise to a stirred solution of **3** (9.0 g, 36.6 mmol) and $(C_2H_5)_3N{\cdot}BH_3$ (Aldrich Chemical Co., 2.9 g, 40.2 mmol) in EtOH (150 mL) at room temperature under argon atmosphere. Stirring was continued for 5 h. The mixture was then concentrated to dryness; the residue was dissolved in CH_2Cl_2; the solution was neutralized with $NaHCO_3$ and filtered. The resulting solution was washed with 0.1 N HCl and dried over Na_2SO_4. Evaporation of the solvent in vacuo gave crystalline material. Recrystallization from

(8) (a) Houk, K. N.; Bimand, J. A.; Mukkerjee, D.; Sims, J.; Chang, Y.; Kaufman, D. C.; Domelsmith, L. N. *Heterocycles* **1977**, *7*, 293. (b) Bimand, A. Z.; Houk, K. N. *Tetrahedron Lett.* **1983**, 435.

(9) According to Houk (ref 8a) this value is calculated as follows: $0.7IP^1 + 0.3IP^2 = (0.7)(7.98\text{ eV}) + (0.3)(9.38\text{ eV}) = 8.40\text{ eV}$.

(10) Mulzer, J. *Nachr. Chem. Tech. Lab.* **1984**, *32*, 882. Tufariello, J. J.; Asrof Ali, Sk. *Tetrahedron Lett.* **1978**, 4647.

(11) This assignment is supported by the comparatively low ^1H NMR coupling constant $J_{H(1),H(4')} = 4.1$ Hz (see also ref 5).

(12) Joucla, M.; Tonnard, F.; Gme, D.; Hamelin, J. *J. Chem. Res.* **1978**, 240.

(13) The value of $J_{H(1),H(4')} = 7.5$ Hz does not permit a structure assignment.

(14) Arx, E. V.; Faupel, M.; Bruggen, M. *J. Chromatogr.* **1976**, *120*, 224.

(15) Merck, Fa. "Anfaerbereagentien fuer Duennschichtchromatographie"; 1979; p 108.

(16) Gilchrist, T. L.; Roberts, T. G. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1283.

CH_2C_2/MeOH (99/1)–*n*-hexane gave 7.5 g (83%): mp 118–119 °C; R_f 0.40, solvent system B; high-resolution mass spectrum, exact mass calcd for $C_{13}H_{17}N_2O_3$ (M + 1) *m/e* 249.1239, found *m/e* 249.1238; electron-impact mass spectrum, *m/e* 248 (M^+); UV (methanol) λ_{max} 218, 272, 278, 287 nm; ^1H NMR δ 8.1 (br s, 1 H, NH), 7.60–7.10 (m, 4 H, indole C(4)C(7)H), 7.00 (s, 1 H, indole C(2)H), 5.20 (br s, 2 H, HNOH), 4.15 (q, 2 H, OCH_2CH_3), 3.95 (X part of ABX spectrum, 1 H, J_{XA} = 5.4 Hz, J_{XB} = 7.8 Hz, indole C(3)CH_2CH), 3.20 and 3.00 (AB part of ABX spectrum, 2 H, J_{AB} = 15.0 Hz, J_{AX} = 5.4 Hz, J_{BX} = 7.8 Hz, indole C(3)CH_2CH), 1.20 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.88; H, 6.43; N, 11.20.

2-Hydroxy-3-(ethoxycarbonyl)-1,2,3,4-tetrahydro-β-carboline (5). To a stirred solution of *N*-hydroxytryptophan ethyl ester (**4**, 250 mg, 1 mmol) in dry CH_2Cl_2 (15 mL) at room temperature was added an excess of formaldehyde dimethyl acetal (10 mL). The reaction mixture was acidified with trifluoroacetic acid (0.5 mL). The reaction was monitored by TLC, solvent system B. After the mixture was stirred for 3 h, the solvents were removed in vacuo. The residue was dissolved in CH_2Cl_2 and the resulting solution washed with 5% $NaHCO_3$ and brine, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. Recrystallization of the residue (CH_2Cl_2/*n*-hexane) gave 235 mg (91%) of **5**: mp 147–150 °C; high-resolution mass spectrum, exact mass calcd for $C_{14}H_{16}N_2O_3$ *m/e* 260.1161, found *m/e* 260.1156; electron-impact mass spectrum, *m/e* (relative intensity) 260 (31, M^+), 243 (42, M^+ – OH), 187 (50, $M^+ - COOC_2H_5$), 143 (100, $C_{10}H_9N^+$); UV (methanol) λ_{max} 222, 281, 288 (sh) nm; ^1H NMR (CD_2Cl_2) δ 7.90 (s br, 1 H, NH), 7.50–7.00 (m, 4 H, indole C(5)-C(8)H), 4.35 and 4.15 (AB spectrum, 2 H, J_{AB} = 16 Hz, 2 H, C(1)H_2), 4.25 (q, 2 H, OCH_2CH_3), 3.80 (X part of ABX spectrum, 1 H, J_{AX} = 7.2 Hz, J_{BX} = 8.1 Hz, C(3)H), 3.15 and 3.05 (AB part of ABX spectrum, 2 H, C(4)H_2); 1.35 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.80; H, 6.20; N, 10.79.

2-Oxo-3-(ethoxycarbonyl)-3,4-dihydro-β-carboline (6). Procedure A. 2-Hydroxy-3-(ethoxycarbonyl)-1,2,3,4-tetrahydro-β-carboline (**5**, 130 mg, 0.5 mmol) was dissolved in dry CH_2Cl_2 (25 mL). To this stirred solution was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (115 mg, 0.5 mmol) portionwise at room temperature. The reaction was monitored by TLC. After stirring for 4 h the reaction mixture was concentrated to dryness and subjected to flash chromatography (silica gel 60; MeOH/CH_2Cl_2 (4/96)) to yield 96 mg (74%) of **6**: mp 193–195 °C; R_f 0.31, solvent system B; high-resolution mass spectrum, exact mass calcd for $C_{14}H_{14}N_2O_3$ *m/e* 258.1004; found *m/e* 258.0995; electron-impact mass spectrum, *m/e* (relative intensity) 258 (33, M^+), 240 (12, $M^+ - H_2O$), 168 (100, $C_{11}H_8N_2^+$); UV (methanol) λ_{max} 212, 260, 353 nm; ^1H NMR (CD_2Cl_2) δ 10.40 (s br, 1 H, NH), 8.75 (s, 1 H, C(1)H), 7.60–7.05 (m, 4 H, C(5)C(8)H), 5.10 (X part of ABX spectrum, 1 H, J_{AX} = 3.6 Hz, J_{BX} = 7.3 Hz, C(3)H), 4.20 (q, 2 H, OCH_2CH_3), 3.85 and 3.60 (AB part of ABX spectrum, 2 H, J_{AB} = 17.7 Hz, J_{AX} = 3.6 Hz, J_{BX} = 7.3 Hz, C(4)H_2), 1.25 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 64.55; H, 5.45; N, 10.74.

Procedure B. Trifluoroacetic acid (2 mL) was added to a stirred solution of **4** (3.9 g, 15.7 mmol) in $HC(OMe)_3$ (60 mL) at room temperature under an argon atmosphere. Stirring was continued for 1 h. The mixture was then concentrated to near dryness, dissolved in CH_2Cl_2, and again concentrated. The residue was dissolved in CH_2Cl_2, and the resulting solution was washed with 0.1 N $NaHCO_3$ and water and finally dried over Na_2SO_4. Evaporation gave crystalline material which was recrystallized from CH_2Cl_2/MeOH, 3.45 g (85%).

3-(Ethoxycarbonyl)-β-carboline (7). When a solution of **6** (150 mg, 0.58 mmol) in CH_2Cl_2/MeOH (3/1, 150 mL) was stored at room temperature for 3 weeks, compound **7** was formed quantitatively. Evaporation of the solvent gave a residue, which was recrystallized from EtOAc/*n*-hexane to yield **7**: mp 222–224 °C (lit.[17] mp 224–229 °C). Anal. Calcd for $C_{14}N_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.82; H, 5.00; N, 11.61.

Spectroscopic data are identical with those reported previously.[18]

2,2-Dimethyl-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline (Entry A). A stirred solution of **6** (1.81 g, 7 mmol) in dry toluene (120 mL) and isobutene (80 mL) was heated for 4 h at 120 °C in a 250-mL pressure vessel. The pressure increased up to 9 bar. Evaporation of the solvent gave the adduct of entry A quantitatively. The compound was recrystallized from CH_2Cl_2: mp 248–250 °C; R_f 0.53, solvent system C; high-resolution mass spectrum, exact mass calcd for $C_{18}H_{22}N_2O_3$ *m/e* 314.1630, found *m/e* 314.1624; electron-impact mass spectrum, *m/e* (relative intensity) 314 (54, M^+), 241 (100, M^+ – (COOEt), 169 (28); UV (methanol) λ_{max} 220, 270, 276, 279, 287 nm; ^1H NMR (CD_2Cl_2) δ 8.05 (br s, 1 H, N(11)H), 7.45–7.00 (m, 4 H, C(7)C(10)H), 4.85 (X part of ABX spectrum, 1 H, J_{XA} = 7.0 Hz, J_{XB} = 10.0 Hz, C(11b)*H*C(1)H_2), 4.23 and 4.20 (2 q from diastereotopic protons, 2 H, OCH_2CH_3), 4.05 (X part of ABX spectrum, 1 H, J_{XA} = 5.0 Hz, J_{XB} = 8.5 Hz, C(5)*H*C(6)H_2), 3.10 and 2.90 (AB part of ABX spectrum, 2 H, J_{AB} = 15.0 Hz, J_{AX} = 5.0 Hz, J_{BX} = 8.5 Hz, C(6)H_2C(5)H), 2.50 and 2.30 (AB part of ABX spectrum, 2 H, J_{AB} = 12.0 Hz, J_{AX} = 7.0 Hz, J_{BX} = 10.0 Hz, C(1)H_2C(11b)H), 1.40 and 1.36 (2 × s, 6 H, 2 × CH_3), 1.28 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 68.68; H, 7.02; N, 8.89.

***exo*-2-(Carboxymethyl)-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline (Entry B).** This structure has been secured by single-crystal X-ray crystallography.[19] A stirred solution of **6** (1.04 g, 4 mmol) and vinylacetic acid (Aldrich Chemical Co., 3.8 g, 44 mmol) in dry toluene (40 mL) under argon atmosphere was heated at 80 °C. Stirring was continued for 24 h. Crystals separated upon cooling of the reaction mixture to room temperature. The crystals were filtered off and washed with *n*-hexane. Recrystallization from CH_2Cl_2 gave 1.10 g, 80% of the adduct: mp 217–218 °C; R_f 0.35, solvent system F; high-resolution mass spectrum, exact mass calcd for $C_{18}H_{19}N_2O_5$ (M^+ – 1) *m/e* 343.1294, found *m/e* 343.1295; chemical-ionization mass spectrum, *m/e* (relative intensity) 343 (80, M^+ – 1), 281 (100, M^+ – ($COOC_2H_5$)); UV methanol) λ_{max} 220, 272, 276, 280, 288 nm; ^1H NMR δ 9.85 (br s, 1 H, N(11)H), 7.45–7.00 (m, 4 H, C(7)C-(10)H), 4.95–4.65 (X part of ABX spectrum, 1 H, C(11b)C(1)H_2, and X part of ABXA'B' spectrum, 1 H, C(1)H_2C(2)*H*CH_2COOH), 4.30 (q, 2 H, OCH_2CH_3), 3.95 (X part of ABX spectrum, 1 H, J_{XA} = 5.5 Hz, J_{XB} = 8.5 Hz, C(5)*H*C(6)H_2), 3.20–3.00 (AB part of ABX spectrum, 2 H, J_{AX} = 5.5 Hz, J_{BX} = 8.5 Hz, C(6)H_2C(5)H), 2.75–2.45 (AB part of ABX spectrum, 2 H, HOOCCH_2C(2)H, and AB part of MABX spectrum, 2 H, C(11b)HC(1)H_2C(2)H), 1.30 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{18}N_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13. Found: C, 62.76; H, 5.83; N, 8.16.

Entry C. A stirred solution of **6** (0.26 g, 1 mmol) and styrene (1.04 g, 10 mmol) in dry toluene (10 mL) under argon atmosphere was heated at 110 °C for 1.5 h. The residue obtained after evaporation of the solvent was subjected to HPLC (silica gel 60H), eluent hexane/EtOAc (75/25 v/v), to yield (320 mg, 85%) four stereomers in a ratio 10:3:85:2.

***endo*-1-Phenyl-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** Recrystallization from EtOAc/*n*-hexane gave 30 mg (10%): mp 172–173 °C; R_f 0.61, solvent system D; high-resolution mass spectrum, exact mass calcd for $C_{22}H_{22}N_2O_3$ *m/e* 362.1630, found *m/e* 362.1620; electron-impact mass spectrum, *m/e* (relative intensity) (12, M^+), 362, 289 (17, M^+ – ($COOC_2H_5$)), 258 (81), 185 (94), 169 (100); UV (methanol) λ_{max} 204, 218, 272, 278, 288 nm; ^1H NMR δ 7.50–7.15 (m, 10 H, N(11)H and C(7)N(11)H and C_6H_5), 4.70 and 4.62 (AB part of ABX spectrum, 2 H, J_{AB} = 8.5 Hz, J_{AX} = 3.6 Hz, J_{BX} = 4.5 Hz, C(2)H_2C(1)H), 4.30 (q, 2 H, OCH_2CH_3), 4.10 (d, 1 H, C(11b)-*H*C(1)H, J = 8.1 Hz), 4.05 (X part of ABX spectrum, 1 H, C-(5)*H*C(6)H_2), 3.70 (X part of ABXM spectrum, 1 H, C(2)H_2C-(1)*H*C(11)H), 3.15–3.00 (AB part of ABX spectrum, 2 H, C-(6)H_2C(5)H), 1.30 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73. Found: C, 72.47; H, 6.12; N, 7.56.

***exo*-1-Phenyl-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** This compound has been isolated as an oil: 10 mg (3%); R_f 0.38, solvent system D; high-resolution mass spectrum, exact mass calcd for $C_{22}H_{22}N_2O_3$ *m/e* 362.1630, found *m/e* 362.1624; electron-impact mass spectrum

(17) Moody, Ch. J.; Ward, J. G. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2899.

(18) Braestrup, C.; Nielsen, M.; Olsen, C. E. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 2288.

m/e (relative intensity) 362 (26, M^+), 289 (49, $M^+ - (COOC_2H_5)$), 258 (71), 185 (88), 169 (47.7); UV (methanol) λ_{max} 204, 218, 272, 278, 288 nm; ^1H NMR δ 8.0 (br s, 1 H, N(11)H), 7.50–7.00 (m, 9 H, C(7)C(10)H and C_6H_5), 4.90–4.70 (AB part of ABX spectrum, 2 H, C(2)H_2C(1)H), 4.25 (q, 2 H, OCH_2CH$_3$), 4.05–3.80 (X part of ABX spectrum, 1 H, C(5)*H*C(6)H_2, and d, 1 H, C(11b)*H*C(1)H, J = 7.0 Hz), 3.45–3.20 (X part of ABXM spectrum, 1 H, C(2)H_2C(1)*H*C(11b)H), 3.10–3.00 (AB part of ABX spectrum, 2 H, C(6)H_2C(5)H), 1.30 (t, 3 H, OCH$_2$CH_3).

***exo*-2-Phenyl-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** This structure has been secured by single-crystal X-ray crystallography.[19] Recrystallization from CH_2Cl_2/*n*-hexane gave 275 mg (85%) of the adduct; mp 212–215 °C; R_f 0.56, solvent system D; high-resolution mass spectrum, exact mass calcd for $C_{22}H_{22}N_2O_3$ *m/e* 362.1630, found *m/e* 362.1624; electron-impact mass spectrum, *m/e* (relative intensity) 362 (46, M^+), 289 (70), 258 (37), 185 (100), 169 (34); UV (methanol) λ_{max} 204, 220, 272, 276, 280, 288 nm; ^1H NMR δ 7.80 (br s, 1 H, N(11)H), 7.50–7.10 (m, 9 H, C(7)C(10)H and C_6H_5), 5.30 (X part of ABX spectrum, 1 H, J_{XA} = 3.6 Hz, J_{XB} = 8.4 Hz, C(2)*H*C(1)H_2), 4.95 (X part of ABX spectrum, 1 H, $J_{XA} = J_{XB}$ = 5.0 Hz, C(11b)*H*C(1)H_2), 4.30 and 4.27 (2 q from diastereotopic protons, 2 H, OCH_2CH$_3$), 4.05 (X part of ABX spectrum, 1 H, J_{XB} = 3.3 Hz, J_{XA} = 4.5 Hz, C(5)*H*C(6)H_2), 3.20 and 3.00 (AB part of ABX spectrum, 2 H, J_{AX} = 4.5 Hz, J_{BX} = 3.3 Hz, J_{AB} = 10.0 Hz, C(6)H_2C(5)H), 2.80–2.45 (AB part of MABX spectrum, 2 H, C(11b)HC(1)H_2C(2)H), 1.20 (t, 3 H, OCH$_2$CH_3). Anal. Calcd for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73. Found: C, 72.92; H, 6.06; N, 7.56.

***endo*-2-Phenyl-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** This compound has been isolated as an oil: 5 mg, (2%); R_f 0.32, solvent system D; high-resolution mass spectrum, exact mass calcd for $C_{22}H_{22}N_2O_3$ *m/e* 362.1630, found *m/e* 362.1624; electron-impact mass spectrum, *m/e* (relative intensity) 362 (32, M^+), 289 (58, $M^+ - (COOC_2H_5)$), 258 (37), 185 (100), 169 (39); UV (methanol) λ_{max} 204, 220, 272, 276, 280, 288 nm; ^1H NMR δ 8.65 (br s, 1 H, N(11)H), 7.45–7.00 (m, 9 H, C(7)C(10)H and C_6H_5), 5.00–4.70 (X part of ABX spectrum, 1 H, C(11b)*H*C(1)H_2, and X part of ABX spectrum, 1 H, C(2)*H*C(1)H_2), 4.45–4.40 (2 q from diastereotopic protons, 2 H, OCH_2CH$_3$, and X part of ABX spectrum, 1 H, C(5)*H*C(6)H_2), 3.20–3.00 (AB part of ABX spectrum, 2 H, C(6)H_2C(5)H), 2.90–2.00 (AB part of MABX spectrum, 2 H, C(11b)HC(1)H_2C(2)H), 1.30 (t, 3 H, OCH$_2$CH_3).

Entry D. A solution of **6** (0.26 g, 1 mmol) and methyl acrylate (0.86 g, 10 mmol) in toluene/methanol (9/1 v/v, 10 mL) was stirred for 5 h at room temperature under an argon atmosphere. The residue obtained after evaporation of the solvent was subjected to HPLC, eluent hexane/EtOAc (60/40 v/v), to yield four stereoisomers, 325 mg (93%), in a ratio 12:52:31:5. The structures of the first three compounds were secured by single-crystal X-ray crystallography.[19]

***exo*-1-(Methoxycarbonyl)-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** Recrystallization from EtOAc/*n*-hexane gave 40 mg (12%): mp 162–163 °C; R_f 0.38, solvent system E; high-resolution mass spectrum, exact mass calcd for $C_{18}H_{20}N_2O_5$ *m/e* 344.1372, found *m/e* 344.1375; electron-impact mass spectrum, *m/e* (relative intensity) 344 (23, M^+), 271 (100, $M^+ - (COOC_2H_5)$), 185 (56); UV (methanol) λ_{max} 220, 272, 278, 288 nm; ^1H NMR δ 8.50 (br s, 1 H, N(11)H), 7.45–7.05 (m, 4 H, C(7)C(10)H), 4.90 (d, 1 H, J = 9.0 Hz, C(11b)*H*C(1)H), 4.60–4.20 (q, 2 H, OCH_2CH$_3$, and X part of ABX spectrum, 1 H, C(5)*H*C(6)H_2, and X part of ABXM spectrum, 1 H, C(2)H_2C(1)*H*C(11b)H), 3.90 (s, 3 H, OCH$_3$), 3.85–3.40 (AB part of ABX spectrum, 2 H, C(2)H_2C(1)H), 3.20–3.00 (AB part of ABX spectrum, 2 H, C(6)H_2C(5)H), 1.20 (t, 3 H, OCH$_2$CH_3). Anal. Calcd for $C_{18}N_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13. Found: C, 62.57; H, 5.75; N, 7.98.

***endo*-1-(Methoxycarbonyl)-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** Recrystallization from EtOAc/*n*-hexane gave 170 mg (52%): mp 180–182 °C; R_f 0.15, solvent system E; high-resolution mass spectrum, exact mass calcd for $C_{18}H_{20}N_2O_5$ *m/e* 344.1372, found *m/e* 344.1375; electron-impact mass spectrum, *m/e* 344 (18, M^+), 271 (33, $M^+ - (COOC_2H_5)$), 185 (100), 169 (47); UV (methanol) λ_{max} 220, 272, 278, 288 nm; ^1H NMR δ 8.10 (br s, 1 H, N(11)H), 7.45–7.05 (m, 4 H, C(7)C(10)H), 5.00 (d, 1 H, J = 9.2 Hz, C(11b)*H*C(1)H), 4.60–4.10 (q, 2 H, OCH_2CH$_3$, and AB part of ABX spectrum, 2 H, C(2)H_2C(1)H, and X part of ABX spectrum, 1 H, C(5)*H*C(6)H_2), 3.85 (X part of MXAB spectrum, 1 H, C(11b)HC(1)*H*C(2)H_2), 3.40 (s, 3 H, OCH$_3$), 3.15–3.05 (AB part of ABX spectrum, 2 H, C(6)H_2C(5)H), 1.30 (t, 3 H, OCH$_2$CH_3). Anal. Calcd for $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13. Found: C, 62.72; H, 5.79; N, 8.13.

***exo*-2-(Methoxycarbonyl)-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** Recrystallization from EtOAc/*n*-hexane gave 100 mg (31): mp 165–167 °C; R_f 0.24, solvent system E; high-resolution mass spectrum, exact mass calcd for $C_{18}H_{20}N_2O_5$ *m/e* 344.1372, found *m/e* 344.1375; electron-impact mass spectrum, *m/e* (relative intensity) 344 (10, M^+), 271 (53, $M^+ - (COOC_2H_5)$), 258 (38), 185 (90), 169 (82), 168 (100); UV (methanol) λ_{max} 220, 272, 278, 280, 288 nm; ^1H NMR δ 8.0 (br s, 1 H, N(11)H), 7.55–7.05 (m, 4 H, C(7)C(10)H), 5.05–4.75 (X part of ABX spectrum, 1 H, C(11b)*H*C(1)H_2, and X part of ABX spectrum, 1 H, C(2)*H*C(1)H_2), 4.27 and 4.25 (2 q from diastereotopic protons, 2 H, OCH_2CH$_3$), 4.05 (X part of ABX spectrum, 1 H, J_{XA} = 3.3 Hz, J_{XB} = 4.5 Hz, C(4)*H*C(5)H_2), 3.80 (s, 3 H, OCH$_3$), 3.20–3.10 (AB part of ABX spectrum, 2 H, J_{XA} = 3.3 Hz, J_{BX} = 4.5 Hz, C(6)H_2C(5)H), 3.05–2.40 (AB part of MABX spectrum, 2 H, C(11b)HC(1)H_2C(2)H), 1.30 (t, 3 H, OCH$_2$CH_3). Anal. Calcd for $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13. Found: C, 62.48; H, 5.48; N, 8.07.

***endo*-2-(Methoxycarbonyl)-5-(ethoxycarbonyl)-4,5,6,11b-tetrahydroisoxazolidino[2,3-*a*]-β-carboline.** Recrystallization from EtOAc/*n*-hexane gave 15 mg (5%): mp 163–167 °C; R_f 0.11, solvent system E; high-resolution mass spectrum, exact mass calcd for $C_{18}H_{20}N_2O_5$ *m/e* 344.1372, found *m/e* 344.1375; electron-impact mass spectrum, *m/e* (relative intensity) 344 (32, M^+), 271 (70, $M^+ - (COOC_2H_5)$), 185 (48), 169 (100); UV (methanol) λ_{max} 220, 272, 278, 280, 288 nm; ^1H NMR δ 7.85 (br s, 1 H, N(11)H), 7.50–7.05 (m, 4 H, C(7)C(10)H), 5.00–4.65 (X part of ABX spectrum, 1 H, C(11b)*H*C(1)H_2, and X part of ABX spectrum, 1 H, C(2)*H*C(1)H_2), 4.30 (q, 2 H, OCH_2CH$_3$), 4.15 (X part of ABX spectrum, 1 H, J_{XA} = 3.0 Hz, J_{XB} = 4.8 Hz, C(5)*H*C(6)H_2), 3.65 (s, 3 H, OCH$_3$), 3.20–3.05 (AB part of ABX spectrum, 2 H, J_{AX} = 3.0 Hz, J_{BX} = 4.8 Hz, C(6)H_2C(5)H), 2.95–2.40 (AB part of MABX spectrum, 2 H, C(11b)HC(1)H_2C(2)H), 1.30 (t, 3 H, OCH$_2$CH_3). Anal. Calcd for $C_{18}H_{20}N_2O_5 \cdot {}^1/_7 n$-$C_6H_{14}$: C, 63.50; H, 6.22; N, 7.85. Found: C, 63.44; H, 6.22; N, 7.82.

Entry E. A stirred solution of **6** (0.26 g, 1 mmol) and freshly distilled cyclohexene (4.1 g, 50 mmol) in dry toluene (10 mL) was heated at 110 °C in an argon atmosphere. Stirring was continued for 6 days. Evaporation of the solvent gave crystalline adduct. Recrystallization from EtOAc/*n*-hexane gave the adduct in 86% yield (290 mg): mp 208–209 °C; R_f 0.61, solvent system C; high-resolution mass spectrum, exact mass calcd for $C_{20}H_{24}N_2O_3$ *m/e* 340.1787, found *m/e* 340.1795; electron-impact mass spectrum, *m/e* (relative intensity) 340 (32, M^+), 267 (100, $(M^+ - (COOC_2H_5))$, 185 (26), 169 (23); UV (methanol) λ_{max} 220, 272, 278, 288 nm; ^1H NMR δ 7.80 (br s, 1 H, N(13)H), 7.50–7.00 (m, 4 H, C(9)C(12)H), 4.65 (d, 1 H, C(13b)H, J = 4 Hz), 4.30 (X part of ABX spectrum, 1 H, $J_{XA} = J_{XB}$ = 5.5 Hz, C(7)*H*C(8)H_2), 4.15 and 4.10 (2 q from diastereotopic protons, 2 H, OCH_2CH$_3$), 4.20–4.00 (X part of MXAB spectrum, 1 H, C(13c)HC(4a)*H*C(4)H_2), 3.10 (AB part of ABX spectrum, 2 H, $J_{AX} = J_{BX}$ = 5.5 Hz, C(8)H_2C(7)H), 2.50 (m, 1 H, C(13c)H), 2.00–1.40 (m, 8 H, C(1)C(4)H_2), 1.20 (t, 3 H, OCH$_2$CH_3). Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.61; H, 7.20; N, 8.25. Found: C, 70.57; H, 7.11; N, 8.23.

Entry F. A stirred solution of **6** (0.26 g, 1 mmol) and 2-cyclohexen-1-one (Aldrich Chemical Co., 0.96 g, 10 mmol) in dry toluene (10 mL) was heated at 70 °C for 1 h under an argon atmosphere. Evaporation of the solvent and excess 2-cyclohexen-1-one gave quantitatively the adduct (354 mg). The analytical sample was obtained from recrystallization from THF/*n*-hexane: mp 180–182 °C; R_f 0.77, solvent system C; high-resolution mass spectrum, exact mass calcd for $C_{20}H_{22}N_2O_4$ *m/e* 354.1580, found *m/e* 354.1570; electron-impact mass spectrum, *m/e* (relative intensity) 354 (10, M^+), 281 (25, M^+ –

(19) The X-ray crystallography data will be published in *J. Crystallogr. Spectrosc. Res.*

($COOC_2H_5$)), 258 (38), 185 (100), 169 (53); UV (methanol) λ_{max} 220, 272, 278, 288 nm; ^1H NMR δ 8.70 (br s, 1 H, N(13)H), 7.45–7.05 (m, 4 H, C(9)C(12)H), 4.95 (X part of MXAB spectrum, 1 H, C(13c)H)C(4a)*HC*(4)H_2); 4.70 (d, 1 H, C(13b)H, J = 7.5 Hz), 4.40 (q, 2 H, OCH_2CH_3), 3.80 (X part of ABX spectrum, 1 H, J_{XA} = 4.5 Hz, J_{XB} = 8.2 Hz, C(7)*HC*(8)H_2), 3.30–3.05 (AB part of ABX spectrum, 2 H, C(8)H_2C(7)H, and X part of AXM spectrum, 1 H, C(13b)HC(13c)*HC*(4a)H), 2.60–2.30 (m, 2 H, C(2)H_2), 2.20 (m, 4 H, C(3)H_2C(4)H_2), 1.30 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.80; H, 6.25; N, 7.79.

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Thermal Cycloaddition Reactions of Thiocarbonyl Compounds. 4.[1] Synthesis of Novel Adamantane-2-spirothiaheterocycles via [4 + 2] Cycloaddition Reactions of Adamantanethione with Conjugated Dienes

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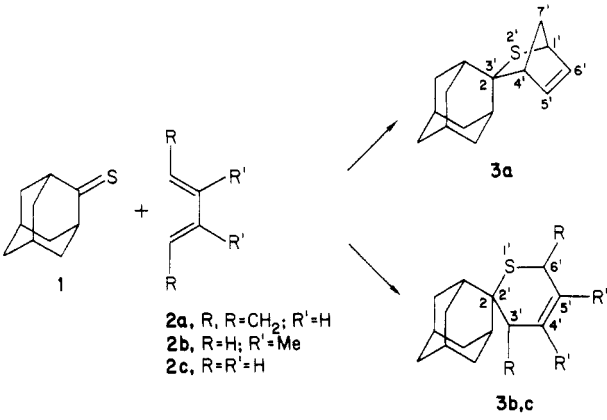
Thermal cycloaddition reactions of adamantanethione (1) with conjugated dienes such as cyclopentadiene, 2,3-dimethyl-1,3-butadiene, piperylene, isoindole, and isobenzofuran occurred smoothly at 20–110 °C to afford [4 + 2] cycloadducts (**3a**, **3b**, **3d**, **23a**, and **23b**) in good yields. On the other hand, similar treatment of 1 with isoprene gave a 45:55 mixture of regioisomers **3e** and **4e**. Furthermore, reaction of 1 with Danishefsky's diene (**2f**) occurred at 110 °C to afford regioselectively adamantane-2-spiro-(2′-thiacyclohex-5′-en)-4′-one (**9**) in a good yield after desilylative elimination of the initial adduct. On the other hand, reaction of thiobenzophenone (11) with **2f** gave 2,2-diphenyl-6-methoxythiacyclohexan-4-one (14) and 2,2-diphenylthiacyclohex-3-en-5-one (17) in 16% and 52% yields, respectively. The nature of these cycloadditions is discussed on the basis of FMO and steric effects.

The use of thiocarbonyl compounds as a cycloaddition component in organic synthesis has developed quite rapidly in recent years.[3-5] Numerous studies based on quantum theoretical calculations about [4 + 2] cycloaddition reactions have been reported,[6] and the methanistic aspect has been discussed at length.[7] Recently, the interest in cycloaddition reaction of thiocarbonyl compounds has grown significantly.[8] However, only a few reports are available on the cycloaddition reaction involving adamantanethione (1).[9] In this paper, we describe thermal [4 + 2] cycloaddition reactions of 1, a stable alicyclic thiocarbonyl compound, with conjugated dienes, which provided a facile route to some novel adamantane-2-spirothiaheterocycles.

Scheme I



Results and Discussion

Cycloaddition Reaction of 1 with Cyclic Polyenes. Reaction of 1 with an 8-fold excess of cyclopentadiene (**2a**) in dry benzene at 80 °C gave cycloadduct **3a** and thione dimer **5**[10] in 91% and 4% yields, respectively (Scheme I

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