Rearrangement of Isoxazoline-5-spiro Derivatives. 5.[1] Diastereofacial Selectivity in the Cycloaddition of Substituted Five-Membered Cyclic Nitrones and Methylenecyclopropanes. Stereoselective Synthesis of 3,5-Substituted Indolizidinones

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Substituted five-membered cyclic nitrones **1–3** cycloadd to substituted methylenecyclopropanes **4** and **5** with high diastereofacial selectivity, through anti–anti transition states, to produce regioisomeric hexahydrospiro-[cyclopropane-1,2′(and 3′)-pyrrolo[1,2-*b*]isoxazolidines] **6–11**. 2-Spirocyclopropane derivatives undergo thermal rearrangement in mild conditions to 3,5-substituted indolizidinones **14**, **16**, and **18**, by the regioselective cleavage of the cyclopropane ring leading to the more stabilized secondary radical. Isomeric enaminones **15**, **17**, and **19**, deriving from the same intermediate, are also formed in the rearrangement. Complete control of two out of the three stereocenters is achieved in the cycloaddition–rearrangement process for the disubstituted derivatives. This protocol is applied to a new synthesis of the skeleton of bicyclic indolizidine alkaloids (Gephyrotoxins).

The use of 1,3-dipolar cycloaddition reactions of nitrones in organic synthesis has developed quite rapidly in recent years. The high regio- and stereoselectivity exhibited by this reaction has made it especially attractive in incorporating multiple stereocenters in a single step.[2]

Recently another useful application of this reaction has been found with the synthesis of spiro[cyclopropane-5′-isoxazolidines] by cycloaddition of nitrones to methylenecyclopropanes.[3] These compounds undergo an easy thermal rearrangement resulting in the production of selectively substituted 4-piperidones (Scheme I). In particular, cyclic nitrones gave ultimately N-bridgehead bicyclic ketones, including some important precursors of alkaloids.[3b]

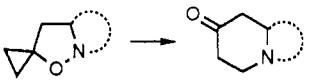
Our synthetic plans in alkaloid synthesis required that we have some knowledge of the regiochemical and stereochemical course of the cycloaddition of substituted cyclic nitrones with methylenecyclopropanes and of the rearrangement of the adducts. A new approach to the skeleton of bicyclic Gephyrotoxins[4] by this strategy is also reported.

Results and Discussion

Cycloadditions. The cycloaddition of 2,2-dimethyl-3,4-dihydro-2*H*-pyrrole *N*-oxide (DMPO, **1**) to 1-methylene-2-phenylcyclopropane (**4**) gives a mixture of four isomers (entry 1, Table I). The isomers were identified as two pairs of spiro[cyclopropane-2′-pyrroloisoxazolidines] **6a** and **6b** and spiro[cyclopropane-3′-pyrroloisoxazolidines] **7a** and **7b** in 2:2:1:1 molar ratio (see Table I, Experimental Section, and below). Although the regioselectivity of the cycloaddition is low, as already observed for the cycloaddition of methylenecyclopropane with the same nitrone,[3] the face diastereoselection of the reaction appears to be high. Of the four possible isomers expected for each regioisomer, only two are obtained, those derived from an anti transition state. A complete degree of face discrimination therefore exists in the approach of the reactants.

When only one methyl group is present (i.e. nitrone **2**; entry 2, Table I) the complexity of the reaction mixture should increase due to the added chiral center. On the contrary, the reaction of **2** and **4** gives once again almost exclusively two regioisomeric pairs of adducts, the 2-spirocyclopropane derivatives **8a** and **8b** and the 3-spirocyclopropane derivatives **9a** and **9b**, in 5:5:1:1 molar ratio.[5] The four isomers could only partially be separated by column chromatography. However, isolation of one 2-spiro isomer **8a** and one 3-spiro isomer **9a**, as well as NMR spectra of fractions enriched in the other isomers (see Experimental Section), allowed the complete assignment of the structure to all these compounds.

Scheme I



The assignment of the regiochemistry relies on the ^{13}C NMR chemical shifts of the spiro carbon atoms. In compounds **8a** and **8b** resonances at 68.51 and 68.03 ppm, respectively (see Table II), for the quaternary C-2 atom result from the deshielding of the adjacent oxygen and the shielding effect of the cyclopropane ring. In compounds **9a** and **9b** similar values, 66.78 and 69.07 ppm, respectively, are consistent with a methylene carbon deshielded by the

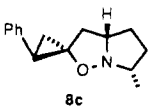
(1) Part 4: Cordero, F. M.; Goti, A.; De Sarlo, F.; Guarna, A.; Brandi, A. *Tetrahedron* **1989**, *45*, 5917.

(2) (a) Torssell, K. B. G. *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*; Feuer, H., Ed.; VCH Publishers: New York, 1988. (b) Tufariello, J. J. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley-Interscience: New York, 1984. (c) Desimoni, G.; Tacconi, G.; Barco, A.; Pollini, G. P. *Natural Products Synthesis Through Pericyclic Reactions*; ACS Monograph no. 180; Caserio, M. C., Ed.; American Chemical Society: Washington, 1983, and references cited therein.

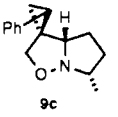
(3) (a) Brandi, A.; Guarna, A.; Goti, A.; De Sarlo, F. *Tetrahedron Lett.* **1986**, *27*, 1727. (b) Brandi, A.; Garro, S.; Guarna, A.; Goti, A.; Cordero, F.; De Sarlo, F. *J. Org. Chem.* **1988**, *53*, 2430.

(4) (a) Daly, J. W.; Spande, T. F. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley-Interscience: New York, 1986; Vol. 4, p 112, and references cited therein. (b) Brandi, A.; Cordero, F.; Querci, C. *J. Org. Chem.* **1989**, *54*, 1748.

(5) Minor amounts of another adduct for each regioisomer were detected in the fractions of the separated mixture. Each of these products (**8c** and **9c**) added up to about the tenth part of the major isomer (**8a**) and derived likely from a syn_{dipole}–$anti_{dipolarophile}$ exo transition state (see Discussion and Experimental Section).



8c



9c

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[§] Dipartimento di Chimica, Università della Basilicata.

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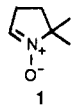
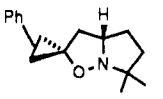
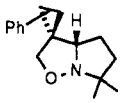
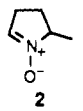
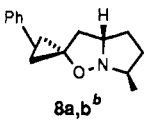
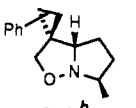
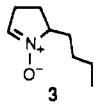
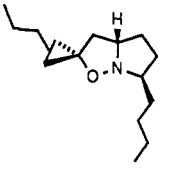
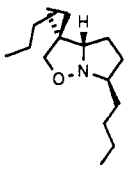
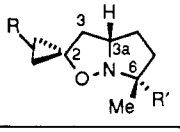
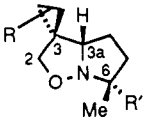
Table I. Cycloadditions of Five-Membered Cyclic Nitrones to Methylenecyclopropane

entry	nitrone	methylenecyclopropane	adducts[a] (regioisomeric ratio)	yield, %
1	 1	 4	 **6a,b** (2:1)  **7a,b**	76
2	 2	4	 **8a,b**[b] (5:1)  **9a,b**[b]	90
3	 3	 5	 **10a,b** (3:1)  **11a,b**	76

[a] Each regioisomer is made of a 1:1 mixture of diastereoisomers. [b] See ref 5.

Table II. Selected ^{13}C NMR Chemical Shifts of Spiro[cyclopropane-2'(and 3')-pyrroloisoxazolidines]





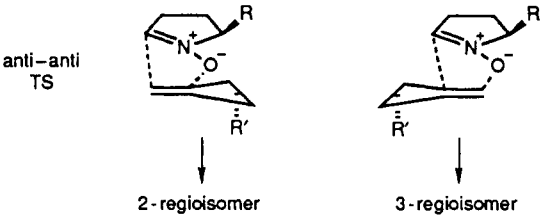
		C-2	C-3	Me[a]		C-2	C-3	Me[a]
R = H, R' = Me	**12**[b]	61.33	43.00	26.42	**13**[b]	73.08	31.51	27.02
R = Ph, R' = Me	**6a**	66.90	38.51	26.80	**7a**	68.83	39.16	27.05
	6b	67.98	37.69	26.58	**7b**	68.43	38.94	26.72
R = Ph, R' = H	**8a**	68.51	37.15	18.99	**9a**	66.78	38.02	19.11
	8b	68.03	37.89	18.99	**9b**	69.07	37.96	19.57

[a] Values for the methyl groups on the convex face are reported. [b] Reference 3b.

adjacent oxygen. The spiro C-3 carbon resonances lie, in these products, much more upfield, at 38.02 and 37.96 ppm, respectively.

The cis relationship between the methyl group at C-6 and the bridgehead proton rests on the ^{13}C NMR chemical shifts of the methyl groups (see Table II). The ^{13}C signals of the two methyl groups in the adduct **12** lie ca. 2.5 ppm apart: the value at lower field (δ 26.42) is ascribed to the methyl cis to the N lone pair and to the bridgehead proton, in agreement with an "unstrained"[6] condition, as that experienced by a methyl on the convex face in a cis-fused conformation of a bicyclic N-bridgehead compound.[6] The same argument applies to compound **6**, and to the regioisomers **13** and **7**. In the monomethyl adducts **8** and **9**, the signal at ca. δ 19 is consistent with the methyl cis to the bridgehead proton, if a standard allowance (7–8 ppm) is made for tertiary C-6.[7] The observation of a shielding (see Table II and Experimental Section) on the C-3 methylene in the ^{13}C NMR spectra of the 2-spiro derivatives **8** and on the C-2 methylene in those of the 3-spiro derivatives **9**, with respect to the unsubstituted isomers **12** and **13**, allowed the assignment of the relative stereochemistry to the substituted carbon atom of the cyclopropane ring. The phenyl ring is located, in all the four isomers, in a trans relationship with respect to the C–O or C–C bond formed in the cycloaddition.

Scheme II



An insight of the transition state trajectories of the two reagents is therefore apparent (Scheme II). The nitrone and the substituted methylenecyclopropane approach, in each of the two possible regioisomeric arrays, away from the nitrone substituent[8] and away from the methylenecyclopropane substituent. We call this favorable approach as occurring in an anti–anti type transition state. A high degree of diastereofacial selectivity, therefore, results in the cycloaddition. The only two isomers formed, for each regioisomeric mode, must derive from the anti–anti exo[9] and the anti–anti endo[9] approaches. No exo–endo selectivity is observed, as a consequence of the strong preference for the anti approach.

Finally, the stereochemistry of each compound at the spiro carbon atom, deriving from the exo or endo mode of cycloaddition, can also be assigned on the basis of the cyclopropane ^{13}C NMR resonances. Compounds **6–11a** present the cyclopropane substituted carbon atom more

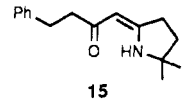
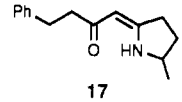
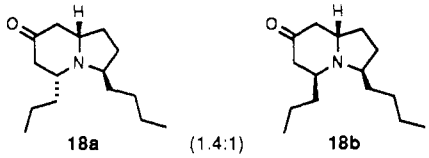
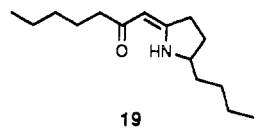
(6) Skvortsov, I. M.; Antipova, I. V. *Zh. Org. Khim.* **1979**, *15*, 868, 777 (Engl.).

(7) This assignment is confirmed by the ^{13}C NMR spectrum of compound **8c**. Indeed, its methyl carbon resonates at δ 15.83. A contemporary deshielding of the methyl protons is observed in the ^{1}H NMR spectrum. These data also support the assigned stereochemistry to the C-6 of **8c** and **9c**, with the methyl group directed toward the concavity of the bicyclic system.

(8) Tufariello, J. J.; Puglis, J. M. *Tetrahedron Lett.* **1986**, *27*, 1489.

(9) The endo–exo terminology is extended to indicate which of the two cyclopropane positions bears the substituent.

Table III. Thermal Rearrangements of Spiro[cyclopropane-2′-pyrroloisoxazolidines]

entry	isoxazolidine	indolizidinones (isomeric ratio)	enaminone	indolizidinones/enaminone	yield, %
1	6a	 **14a** (2:1) **14b**	 **15**	0.67	95
2	8a	 **16a** (1.2:1) **16b**	 **17**	3.6	97
3	10a	 **18a** (1.4:1) **18b**	 **19**	4.8	82

deshielded than compounds **6–11b** (3–7 ppm) and the unsubstituted ones more shielded of a similar value. Therefore compounds **6–11a** must derive from an exo transition state, with the cyclopropane-substituted carbons directed toward the convex face of the molecule.

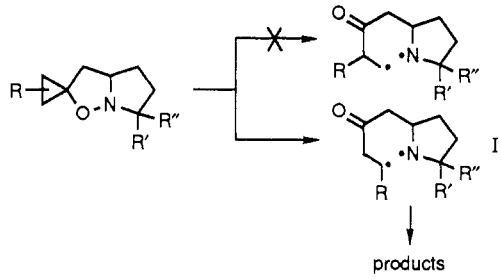
The remarkable difference in regioselectivity between the cycloadditions of nitrone **1** and nitrones **2** to **4** (Table I) also deserves some comment. Since the small difference between the two nitrones should only slightly affect the frontier orbitals parameters, a steric effect must play an important role at the transition state. The second methyl in nitrone **1** points right toward the approaching methylenecyclopropane in the transition state, thus hindering the approach that leads to the 2-spiro regioisomer more than the other regioisomeric mode. The energy gap between the transition states leading to 2-spiro and 3-spiro regioisomers is therefore reduced with nitrone **1**.

Thermal Rearrangements. The obtainment of the substituted pyrroloisoxazolidines **6**, **8**, and **10** allowed us to study their thermal rearrangement, in order to establish the regiochemistry and the stereochemistry of the process. Since the spiro[cyclopropane-3′-pyrroloisoxazolidines] are stable under the thermolysis conditions employed, the mixture of the cycloadducts can be used directly. The choice of the method to carry out the thermolysis was found to be troublesome. We had already observed[3] that FVT is the best way to perform the rearrangement, since rarefied conditions reduce the possibility of intermolecular hydrogen exchange. Indeed, thermal rearrangements in solution always gave a higher amount of isomeric enaminones and a lower selectivity between epimeric ketones. The low volatility of the starting materials is, however, an obstacle to the extensive use of FVT with our method. On the other hand, heating of the distilling bulb must be avoided, since rearrangement occurs, to some extent, even at room temperature. Attempts to run the FVT with different methods[10] gave nonreproducible or disappointing results. Eventually, the best conditions for the thermal rearrangements were found to be refluxing the adducts in toluene for several hours.

The results of the thermolyses are reported in Table III. The yields of ketones are fair, although, as expected, considerable quantities of enaminones **15**, **17**, and **19** are produced. Separation of the compounds by flash chromatography is not easy, and ketones tend to decompose on silica gel.

All the indolizidinones show ^{13}C NMR values for the C-5 carbon (see Experimental Section) in agreement with the

Scheme III



substitution α to the bridgehead nitrogen. The enaminones, moreover, show a pattern of NMR signals (see Experimental Section) in agreement with the assigned linear structure.

Both results confirm that the indolizidinones and the enaminones derive from a common diradical intermediate I[11] (Scheme III), which undergoes ring closure to the bicyclic base or 1,5-hydrogen shift to the enaminone.[3b] The common intermediate I originates from a highly regioselective cleavage of the cyclopropane bond with the carbon bearing the substituent, to form the more stabilized secondary radical.

The ring closure of the diradical I occurs with moderate selectivity to give two isomeric 3,5-substituted indolizidinones. As evidenced in Table III (entry 1), when two methyl groups are present on the C-3 the indolizidinone with the substituent on the C-5 cis with respect the H-8a prevails. On the contrary, when only one substituent is attached to the C-3, the steric hindrance at the transition state slightly favors the product with a trans relationship of the two substituents (entries 2 and 3, Table III), and consequently between groups on C-5 and H-8a.

Spectral data of the ketones in entry 2 (Table III) are discussed as representative for the stereochemical assignment to the ketones.

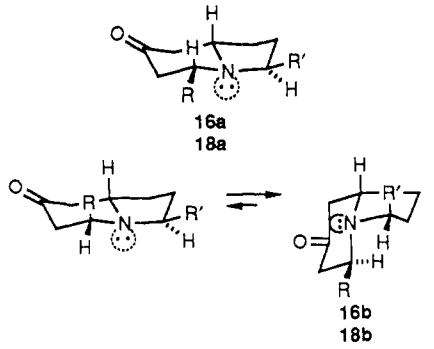
The benzylic proton in **16b** lies 0.62 ppm downfield with respect to **16a** in agreement with a proton on the α face of the molecule (Scheme IV). The H-5 on the β face in **16a**, in fact, experiences the shielding effect of the trans nitrogen doublet.[12] ^1H NMR data for H-8a and methyl

(10) Brown, R. F. C. *Pyrolytic Methods in Organic Chemistry*; Wasserman, H. H., Ed.; Academic Press: New York, 1980.

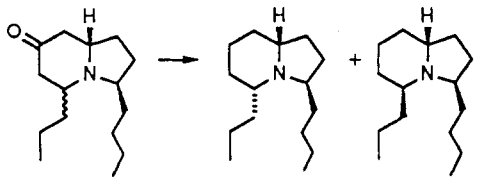
(11) Both isomeric isoxazolidines a and b give the same intermediate I, thus making useless their separation.

(12) Crabb, T. A.; Newton, R. F.; Jackson, D. *Chem. Rev.* **1971**, *71*, 109.

Scheme IV



Scheme V



in **16b** (δ 3.61 and 1.04, respectively) very closely resemble those of related protons in isoxazolidines 8 (see Experimental Section), attesting that a preference for a cis-fused conformation must exist in the *cis*-3-methyl-5-phenylindolizidinone **16b** (Scheme IV), due to the steric hindrance between the two 1,3-diaxial bulky groups in the less favorable trans-fused conformation. The rather different values of δ 2.95 and 0.72 for H-8a and methyl (also due to the trans relationship with the nitrogen lone pair) become therefore diagnostic for the assignment of the trans-fused conformation of **16a**. Further confirmation of the stereochemical assignment derives from the presence of Bohlmann bands[13] at 2800 and 2700 cm^{-1} in the IR spectrum of **16a**. The analysis confirms that the {C-3}–{C-8a} relative stereochemistry, as derived from the cycloaddition step, is not affected during the rearrangement, allowing the control of two out of the three chiral centers.

The protocol outlined in entries 3 (Tables I and III) represents a new synthesis of the octahydroindolizine skeleton of Amphibian alkaloids.[4] As a matter of fact, reduction of a mixture of the ketones, via the in situ formation of their (*p*-tolylsulfonyl)hydrazones, gave an unseparable mixture of (±)-Gephyrotoxin 223AB (**20**) and its C-5 epimer **21** (Scheme (V).[4]

Experimental Section

All the reactions were carried out under inert atmosphere (N_2), and the solvents were appropriately dried before the use. The R_f values refer to TLC on 0.25 mm silica gel plates (Merck F_{254}) obtained using the same eluant as in the column chromatographies. Melting points were observed with a microscope RCH Kofler apparatus. NMR spectra ($CDCl_3$ as solvent) were recorded on Varian XL 300 (^1H, 300 MHz), Varian M 390 (^1H, 90 MHz, where specified), and Varian FT-80A (^{13}C, 20 MHz) spectrometers; chemical shift values are reported in ppm downfield from tetramethylsilane: notations s, d, t, q, m, and br designate singlet, doublet, triplet, quartet, multiplet, and broad, respectively; the coupling constants J are given in hertz. IR spectra (in CCl_4 solution, unless otherwise stated) were recorded on a Perkin-Elmer 283 or a Perkin-Elmer 881 spectrophotometer. Mass spectra were recorded at 70 eV by GC inlet on a 5790A-5970A Hewlett-Packard instrument. Exact mass measurements were performed with a VG 70-70 EQ mass spectrometer at 70 eV. Combustion analyses were carried out with a Perkin-Elmer 240 C elemental analyzer.

2-Methyl-3,4-dihydro-2*H*-pyrrole 1-Oxide (2). 1,1-Dimethoxy-4-nitropentane (6.430 g, 34 mmol) was added to a solution of ammonium chloride (1.819 g, 34 mmol) in 50% aqueous tetrahydrofuran (40 mL). The mixture was cooled with an ice/water bath, and Zn powder (8.895 g, 136 mmol) was added in small portions over a period of 1 h while the reaction temperature was maintained below 10 °C. The mixture was then allowed to rise to room temperature, and the precipitate was filtered and washed with warm (50 °C) 50% aqueous tetrahydrofuran. The filtrate and washings were acidified with concentrated hydrochloric acid (3.7 mL) and stirred overnight at room temperature. The mixture was concentrated, neutralized with sodium carbonate solution, saturated with sodium chloride, and extracted with methylene chloride (6 × 20 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated. The resulting oil was distilled by Kugelrohr (80 °C, 0.08 mmHg) to give 1.523 g (45% yield) of the nitrone **2**. MS: *m/e* (rel intensity) 99 ($2^{\bullet+}$, 2), 98 (29), 97 (36), 43 (22), 42 (100), 41 (35), 39 (24). ^1H NMR (90 MHz): δ 6.86 (m, 1 H), 3.96 (m, 1 H), 2.73–1.54 (m, 4 H), 1.28 (d, J = 6, 3 H). ^{13}C NMR: 133.31 (d), 67.95 (d), 27.05 (t), 25.84 (t), 18.17 (q). IR ($CDCl_3$): 2980, 2870, 1590, 1460, 1250, 1205 cm^{-1}. HRMS: calcd for C_5H_9NO 99.0684, found (GC inlet) 99.0687.

1-Chloro-1-methyl-2-propylcyclopropane. A solution of 1-pentene (26.288 g, 375 mmol) and 1,1-dichloroethane (24.751 g, 250 mmol) in anhydrous diethyl ether (80 mL) was cooled at −50 °C. A 1.48 M solution of *n*-butyllithium (141 mL) was added dropwise to the stirred mixture, during 2 h, while the reaction temperature was maintained below −35 °C. After the addition was complete, the temperature was allowed to rise to room temperature; the organic solution was washed with water (100 mL) and dried with anhydrous sodium sulfate. Removal of the solvent left a liquid, which was distilled to give the title compound, bp 123 °C (8.192 g, 30%). MS: *m/e* (rel intensity) 132 ($M^{\bullet+}$, 1), 97 (19), 96 (15), 89 (24), 76 (33), 56 (45), 55 (58), 53 (35), 41 (100). ^1H NMR (90 MHz): δ 1.86–0.68 (m, 10 H), 1.59 (s, 3 H).

1-Methylene-2-propylcyclopropane (5). A solution of *t*-BuOK (5.090 g, 45 mmol) in anhydrous DMSO (6 mL) was introduced into a flask equipped with a dropping funnel and a distillation apparatus. The solution was heated at 100–120 °C (bath temperature) while 1-chloro-1-methyl-2-propylcyclopropane (5.877 g, 44 mmol) was added dropwise. The colorless liquid distilled below 80 °C, consisting of **5** and *t*-BuOH in ca. 1:1 molar ratio, and was directly employed in the cycloaddition reaction. The distillate was washed with water to remove *t*-BuOH and gave pure **5** (2.390 g, 56%). MS: *m/e* (rel intensity) 96 ($5^{\bullet+}$, 1), 81 (91), 79 (25), 67 (36), 55 (34), 54 (30), 53 (41), 41 (100). ^1H NMR (90 MHz): δ 5.35 (m, 2 H), 1.68–0.60 (m, 7 H), 0.95 (t, J = 6, 3 H). ^{13}C NMR: 137.09 (s), 102.12 (t), 35.19 (t), 22.46 (t), 15.49 (d), 13.67 (q), 9.22 (t). IR ($CDCl_3$): 3080, 3050, 2970, 2880, 1750, 1465, 1250 cm^{-1}.

Cycloadditions of Nitrones and Methylenecyclopropanes: (i) (1*R,2*R**,3'a*S**)-2-Phenyl-6',6'-dimethylhexahydrospiro[cyclopropane-1,2'-pyrrolo[1,2-*b*]isoxazole] (Exo Adduct, 6a), (1*S**,2*S**,3'a*S**)-2-Phenyl-6',6'-dimethylhexahydrospiro[cyclopropane-1,2'-pyrrolo[1,2-*b*]isoxazole] (Endo Adduct, 6b), (1*S**,2*S**,3'a*S**)-2-Phenyl-6',6'-dimethylhexahydrospiro[cyclopropane-1,3'-pyrrolo[1,2-*b*]isoxazole] (Exo Adduct, 7a), and (1*R**,2*R**,3'a*S**)-2-Phenyl-6',6'-dimethylhexahydrospiro[cyclopropane-1,3'-pyrrolo[1,2-*b*]isoxazole] (Endo Adduct, 7b).** The nitrone 1 (236 mg, 2.09 mmol) and 1-methylene-2-phenylcyclopropane[14] (260 mg, 2.05 mmol) were reacted at room temperature for 15 days; the mixture was passed over a pad of silica gel and eluted with petroleum ether–ethyl acetate, 1:1. Concentration of the solution gave a mixture of the adducts **6a**, **6b**, **7a**, and **7b** in 2:2:1:1 molar ratio. The mixture was column chromatographed (eluant: petroleum ether–ethyl acetate, 70:30, and then 50:50) to give **6a** (R_f 0.44, 116 mg, 23%) containing impurities of the enaminone **15**, **7a** (R_f 0.31, 60 mg, 12%), and a mixture of **6b** and **7b** (R_f 0.11, 205 mg, 41%) (R_f values refer to the 70:30 eluant). Small amounts of pure **6b** were obtained by crystallization from *n*-pentane of an enriched fraction of the mixture **6b** + **7b**.

6a. MS: *m/e* (rel intensity) 243 ($6a^{\bullet+}$, 1), 228 (28), 124 (35), 104 (37), 82 (100), 55 (22), 41 (30). ^1H NMR: δ 7.29–7.03 (m, 5

(13) Bohlmann, F. *Chem. Ber.* **1958**, *91*, 2157.
(14) Arora, S.; Binger, P. *Synthesis* **1974**, 801.

H), 3.85 (dddd, J = 8.9, 7.7, 4.4, 2.8, 1 H), 2.40 (dd, J = 10.3, 7.2, 1 H), 2.30 (dd, J = 12.3, 7.7, 1 H), 2.11 (dq, J = 12.2, 8.9, 1 H), 1.94 (dt, J = 11.5, 9.4, 1 H), 1.78 (dd, J = 12.3, 2.8, 1 H), 1.67 (dddd, J = 12.2, 9.4, 4.4, 2.2, 1 H), 1.57 (ddd, J = 11.5, 8.5, 2.2, 1 H), 1.45 (dd, J = 10.3, 6.4, 1 H), 1.30 (s, 3 H), 1.13 (t, J = 6.8, 1 H), 1.04 (s, 3 H). ^{13}C NMR: δ 138.65 (s), 127.93 (d, 2 C), 127.46 (d, 2 C), 125.51 (d), 68.22 (s), 66.90 (s), 65.15 (d), 38.51 (t), 35.95 (t), 31.78 (t), 26.80 (q), 26.59 (d), 24.00 (q), 14.74 (t).

6b. White crystals, mp 81–83 °C, from *n*-pentane. MS: m/e (rel intensity) 243 (**6b**$^{\bullet+}$, 1), 228 (100), 131 (13), 124 (21), 104 (16), 103 (13), 82 (48). ^{1}H NMR: δ 7.32–7.24 (m, 2 H), 7.23–7.13 (m, 1 H), 7.10–7.02 (m, 2 H), 3.91 (dddd, J = 9.1, 7.3, 5.0, 1.9, 1 H), 2.47 (dd, J = 12.4, 7.3, 1 H), 2.36 (dd, J = 10.5, 7.1, 1 H), 2.02–1.88 (m, 2 H), 1.86 (dd, J = 12.4, 1.9, 1 H), 1.62–1.50 (m, 1 H), 1.51 (dd, J = 10.5, 6.5, 1 H), 1.44–1.35 (m, 1 H), 1.32 (s, 3 H), 1.11 (t, J = 6.8, 1 H), 1.03 (s, 3 H). ^{13}C NMR: δ 138.81 (s), 128.06 (d, 2 C), 126.69 (d, 2 C), 125.49 (d), 69.35 (s), 67.98 (s), 64.50 (d), 37.69 (t), 35.96 (t), 30.66 (t), 26.58 (q), 26.11 (d), 23.94 (q), 15.95 (t). IR: 3064, 3030, 2971, 2943, 2873, 1603, 1496, 1462, 1450, 1381, 1366, 1157 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.96; H, 8.88; N, 5.66%.

7a. White crystals, mp 102–103 °C, from *n*-pentane. MS: m/e (rel intensity) 243 (**7a**$^{\bullet+}$, 8), 228 (30), 157 (100), 152 (55), 129 (80), 128 (52), 115 (73), 114 (78), 104 (28), 91 (73), 81 (36), 77 (36), 55 (50), 41 (91). ^{1}H NMR: δ 7.28–7.08 (m, 5 H), 3.59 (d, A part of an AB system, J = 8.0, 1 H), 3.57 (dd, J = 9.0, 4.2, 1 H), 3.39 (d, B part of an AB system, J = 8.0, 1 H), 2.36 (dd, J = 8.9, 6.2, 1 H), 2.10–1.49 (m, 4 H), 1.32 (s, 3 H), 1.23 (dd, X part of an AXY system, J = 8.9, 6.0, 1 H), 1.15 (t, Y part of an AXY system, J = 6.1, 1 H), 1.06 (s, 3 H). ^{13}C NMR: δ 137.94 (s), 128.08 (d, 2 C), 127.87 (d, 2 C), 126.00 (d), 72.09 (d), 68.89 (s), 68.83 (t), 39.16 (s), 35.81 (t), 29.86 (t), 29.02 (d), 27.05 (q), 23.67 (q), 12.40 (t). IR ($CDCl_3$): 3070, 3040, 2980, 2870, 1610, 1500, 1460, 1370 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.91; H, 8.72; N, 5.37%.

7b. ^{1}H NMR: δ 7.32–7.02 (m, 5 H), 3.60 and 3.49 (AB system, J = 7.9, 2 H), 3.47 (dd, J = 9.2, 5.3, 1 H), 2.26 (dd, J = 9.0, 6.4, 1 H), 2.20–2.05 (m, 1 H), 1.32 (s, 3 H), 1.17 (t, J = 6.2, 1 H), 1.05 (s, 3 H). ^{13}C NMR: δ 138.33 (s), 128.06 (d, 2 C), 127.22 (d, 2 C), 125.90 (d), 71.47 (d), 68.53 (s), 68.43 (t), 38.94 (s), 35.54 (t), 29.80 (t), 26.72 (q), 24.69 (d), 23.50 (q), 17.75 (t).

(ii) (1*R,2*R**,3′a*S**,6′*R**)-2-Phenyl-6′-methylhexahydrospiro[cyclopropane-1,2′-pyrrolo[1,2-*b*]isoxazole] (Exo Adduct, 8a), (1*S**,2*S**,3′a*S**,6′*R**)-2-Phenyl-6′-methylhexahydrospiro[cyclopropane-1,2′-pyrrolo[1,2-*b*]isoxazole] (Endo Adduct, 8b), (1*R**,2*R**,3′a*S**,6′*S**)-2-Phenyl-6′-methylhexahydrospiro[cyclopropane-1,2′-pyrrolo[1,2-*b*]isoxazole] (8c), (1*S**,2*S**,3′a*S**,6′*R**)-2-Phenyl-6′-methylhexahydrospiro[cyclopropane-1,3′-pyrrolo[1,2-*b*]isoxazole] (Exo Adduct, 9a), (1*R**,2*R**,3′a*S**,6′*R**)-2-Phenyl-6′-methylhexahydrospiro[cyclopropane-1,3′-pyrrolo[1,2-*b*]isoxazole] (Endo Adduct, 9b), and (1*S**,2*S**,3′a*S**,6′*S**)-2-Phenyl-6′-methylhexahydrospiro[cyclopropane-1,3′-pyrrolo[1,2-*b*]isoxazole] (9c).** The nitrone **2** (222 mg, 2.24 mmol) and 1-methylene-2-phenylcyclopropane (**4**, 264 mg, 2.03 mmol) were reacted and worked up as described in (i), to give a mixture of the adducts **8a**, **8b**, **8c**, **9a**, **9b**, and **9c** (10:10:1:2:2:1 molar ratio, 418 mg, 90%). Attempted separation by column chromatography (eluant: petroleum ether–ethyl acetate, 70:30, and then pure ethyl acetate) gave a mixture of **8b** and the rearranged enaminone **17** (R_f 0.47, 124 mg, 27%), **9a** (R_f 0.40, 34 mg, 7%), **8a** (R_f 0.27, 172 mg, 37%), and a mixture of **9b**, **9c**, and **8c** (R_f 0.15, 60 mg, 13%). The latter mixture was further fractionated to allow a complete NMR characterization of the components.

8a. White crystals, mp 82–83 °C, from petroleum ether. MS: m/e (rel intensity) 229 (**8a**$^{\bullet+}$, 12), 214 (93), 152 (25), 110 (100), 104 (82), 103 (34), 84 (32), 82 (47), 77 (33), 68 (98), 55 (29), 41 (57). ^{1}H NMR: δ 7.38–7.24 (m, 2 H), 7.24–7.17 (m, 1 H), 7.11–7.02 (m, 2 H), 3.89 (tt, J = 8.7, 4.9, 1 H), 3.36 (d quintet, J = 9.3, 6.4, 1 H), 2.39 (dd, J = 10.4, 7.2, 1 H), 2.33 (dd, J = 12.5, 8.7, 1 H), 1.93 (m, 2 H), 1.71 (dd, J = 12.5, 4.9, 1 H), 1.50 (dd, J = 10.4, 6.9, 1 H), 1.39 (m, 2 H), 1.21 (d, J = 6.4, 3 H), 1.16 (t, J = 7.0, 1 H). ^{13}C NMR: δ 138.59 (s), 128.25 (d, 2 C), 126.75 (d, 2 C), 125.67 (d), 68.51 (s), 64.63 (d), 60.68 (d), 37.15 (t), 30.64 (t), 28.84 (d), 28.79 (t), 18.99 (q), 12.44 (t). IR: 3080, 3064, 3029, 2968, 2872, 1604, 1497, 1452, 1376, 1173, 1112 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.77; H, 8.40; N, 6.09%.

8b. MS: m/e (rel intensity) 229 (**8b**$^{\bullet+}$, 15), 214 (100), 186 (26), 110 (75), 104 (69), 82 (39), 68 (75). ^{1}H NMR: δ 7.30–7.05 (m, 5 H), 3.78 (dq, J = 5.8, 7.6, 1 H), 3.42 (d quintet, J = 8.5, 6.3, 1 H), 2.37 (dd, J = 10.4, 7.2, 1 H), 2.12 (dd, J = 12.3, 8.2, 1 H), 2.10–1.96 (m, 2 H), 1.78 (dd, J = 12.3, 5.8, 1 H), 1.75–1.60 (m, 1 H), 1.50 (dd, J = 10.4, 6.5, 1 H), 1.47–1.39 (m, 1 H), 1.19 (t, J = 6.9, 1 H), 1.15 (d, J = 6.3, 3 H). ^{13}C NMR: δ 138.28 (s), 128.05 (d, 2 C), 127.37 (d, 2 C), 125.67 (d), 68.03 (s), 64.37 (d), 62.01 (d), 37.89 (t), 30.94 (t), 29.40 (t), 24.88 (d), 18.99 (q), 15.79 (t).

8c. ^{1}H NMR: δ 7.32–7.24 (m, 2 H), 7.21–7.13 (m, 1 H), 7.11–7.02 (m, 2 H), 3.77 (ddt, J = 8.8, 1.7, 7.3, 1 H), 3.12 (d quintet, J = 9.8, 6.8, 1 H), 2.48 (dd, J = 12.4, 7.5, 1 H), 2.38 (dd, J = 10.4, 7.4, 1 H), 1.85 (dd, J = 12.4, 1.7, 1 H), 1.83–1.70 (m, 3 H), 1.51 (dd, J = 10.4, 6.4, 1 H), 1.44–1.34 (m, 1 H), 1.33 (d, J = 6.8, 3 H), 1.12 (t, J = 6.9, 1 H). ^{13}C NMR: δ 139.12 (s), 128.18 (d, 2 C), 126.93 (d, 2 C), 125.59 (d), 67.87 (s), 66.49 (d), 64.95 (d), 38.03 (t), 31.95 (t), 31.28 (t), 26.75 (d), 16.34 (t), 15.83 (q).

9a. MS: m/e (rel intensity) 229 (**9a**$^{\bullet+}$, 4), 212 (20), 157 (18), 138 (43), 129 (40), 115 (42), 100 (100), 91 (46), 77 (22), 55 (20), 41 (40). ^{1}H NMR: δ 7.31–7.11 (m, 5 H), 3.76 (d, J = 8.6, 1 H), 3.65 (t, J = 7.0, 1 H), 3.30 (d, J = 8.6, 1 H), 3.24 (d quintet, J = 9.8, 6.5, 1 H), 2.26 (dd, J = 8.3, 6.7, 1 H), 2.04–1.90 (m, 4 H), 1.66 (dd, J = 8.3, 6.7, 1 H), 1.21 (d, J = 6.5, 3 H), 1.11 (t, J = 6.7, 1 H). ^{13}C NMR: δ 137.90 (s), 128.21 (d, 4 C), 126.19 (d), 70.23 (d), 66.78 (t), 61.76 (d), 38.02 (s), 30.95 (t), 28.87 (d), 28.08 (t), 19.11 (q), 10.33 (t). IR ($CDCl_3$): 3095, 3085, 3018, 2972, 2879, 1609, 1500, 1455 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.22; H, 8.55; N, 6.39%.

9b. ^{1}H NMR: δ 7.34–7.05 (m, 5 H), 3.59 and 3.52 (AB system, J = 8.4, 2 H), 3.53 (t, J = 6.6, 1 H), 3.21 (d quintet, J = 8.1, 6.5, 1 H), 2.26 (dd, J = 9.0, 6.1, 1 H), 2.13–1.98 (m, 2 H), 1.88–1.72 (m, 1 H), 1.50–1.15 (m, 3 H), 1.17 (d, J = 6.5, 3 H). ^{13}C NMR: δ 70.33 (d), 69.07 (t), 61.38 (d), 37.96 (s), 30.83 (t), 27.80 (t), 24.02 (d), 19.57 (q), 16.95 (t).

9c. ^{1}H NMR: δ 7.33–7.24 (m, 2 H), 7.21–7.14 (m, 1 H), 7.10–7.02 (m, 2 H), 3.58 and 3.48 (AB system, J = 7.9, 2 H), 3.35 (dd, J = 8.2, 6.3, 1 H), 3.20 (d quintet, J = 11.0, 6.7, 1 H), 2.26 (dd, J = 9.1, 6.4, 1 H), 2.02–1.65 (m, 4 H), 1.38 (dd, J = 9.1, 5.2, 1 H), 1.32 (d, J = 6.7, 3 H), 1.30–1.10 (m, 1 H).

(iii) (1*R,2*S**,3′a*S**,6′*R**)-2-Propyl-6′-butylhexahydrospiro[cyclopropane-1,2′-pyrrolo[1,2-*b*]isoxazole] (Exo Adduct, 10a), (1*S**,2*S**,3′a*S**,6′*R**)-2-Propyl-6′-butylhexahydrospiro[cyclopropane-1,2′-pyrrolo[1,2-*b*]isoxazole] (Endo Adduct, 10b), (1*S**,2*R**,3′a*S**,6′*R**)-2-Propyl-6′-butylhexahydrospiro[cyclopropane-1,3′-pyrrolo[1,2-*b*]isoxazole] (Exo Adduct, 11a), and (1*R**,2*S**,3′a*S**,6′*R**)-2-Propyl-6′-butylhexahydrospiro[cyclopropane-1,3′-pyrrolo[1,2-*b*]isoxazole] (Endo Adduct, 11b).** The nitrone **3**[4b] (705 mg, 5 mmol) and 1-methylene-2-propylcyclopropane (**5**, 480 mg, 5 mmol) were dissolved in benzene (4 mL) and heated at 50 °C in a sealed tube for 15 days. The solvent was then removed in vacuo, and the residue was passed over a pad of silica gel and eluted with ethyl acetate. Concentration of the solution gave a mixture of the adducts **10a**, **10b**, **11a**, and **11b** in 3:3:1:1 molar ratio (900 mg, 76%). The mixture was column chromatographed (eluant: petroleum ether–ethyl acetate, 4:1) to give **11a** (R_f 0.56, 134 mg, 11%), a mixture of **10b** and **11b** (R_f 0.41, 306 mg, 26%), and **10a** (R_f 0.36, 276 mg, 23%). The adducts **10a** and **10b** underwent a partial isomerization to the rearranged products during the separation.

10a. MS: m/e (rel intensity) 237 (**10a**$^{\bullet+}$, 2), 180 (72), 124 (20), 110 (27), 82 (63), 69 (36), 68 (97), 55 (58), 42 (35), 41 (100); ^{1}H NMR: δ 3.85 (m, 1 H), 3.15 (m, 1 H), 2.27 (dd, J = 12.2, 8.5, 1 H), 2.09–1.91 (m, 2 H), 1.96 (dd, J = 12.2, 5.3, 1 H), 1.74–1.52 (m, 3 H), 1.48–0.78 (m, 18 H). ^{13}C NMR: δ 65.87 (d), 65.78 (s), 64.70 (d), 35.75 (t), 34.12 (t), 32.75 (t), 29.68 (t), 29.35 (t), 28.97 (t), 22.68 (t), 22.02 (t), 21.82 (d), 14.25 (t), 13.85 (q), 13.78 (q). IR: 3080, 2970, 2880, 1470, 1380 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NO$: C, 75.90; H, 11.46; N, 5.90. Found: C, 76.01; H, 11.39; N, 5.89.

10b. ^{1}H NMR: δ 3.82 (m, 1 H), 3.20 (m, 1 H), 2.50 (dd, J = 8.7, 3.4, 1 H), 2.40–1.85 (m, 3 H). ^{13}C NMR: δ 66.75 (d), 65.64 (s), 64.67 (d), 38.36 (t), 34.21 (t), 32.53 (t), 30.12 (t), 29.48 (t), 28.98 (t), 22.71 (t), 22.19 (t), 18.40 (t), 16.55 (d), 13.86 (q), 13.68 (q).

11a. MS: m/e (rel intensity) 237 (**11a**$^{\bullet+}$, 11), 180 (100), 142 (15), 121 (25), 55 (24), 41 (52). ^{1}H NMR: δ 3.81 and 3.68 (AB

system, J = 8.3, 2 H), 3.35 (t, J = 7.3, 1 H), 3.11–2.92 (m, 1 H), 2.09–1.03 (m, 15 H), 1.03–0.75 (m, 8 H); ^{13}C NMR: δ 70.43 (d), 66.97 (t), 66.35 (d), 34.70 (t), 34.41 (s), 32.51 (t), 29.14 (t), 29.00 (t), 27.64 (t), 23.12 (d), 22.73 (t), 22.31 (t), 13.81 (q, 2 C), 12.30 (t). IR ($CDCl_3$): 3068, 2960, 2880, 1605, 1468, 1380 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NO$: C, 75.90; H, 11.46; N, 5.90. Found: C, 75.59; H, 11.40; N, 6.24.

11b. ^{1}H NMR: δ 3.95 (d, J = 8.1, 1 H), 3.53 (d, J = 8.1, 1 H), 3.25 (t, J = 7.2, 1 H), 3.04 (m, 1 H). ^{13}C NMR: δ 70.61 (d), 68.68 (t), 66.68 (d), 34.69 (t), 33.41 (s), 29.44 (t), 29.06 (t), 28.31 (t), 28.02 (t), 22.91 (t), 22.77 (t), 19.05 (t), 18.27 (d), 13.92 (q, 2 C).

Rearrangement of the Adduct 6a: (5*R,8a*S**)-3,3-Dimethyl-5-phenyloctahydroindolizin-7-one (14a), (5*S**,8a*S**)-3,3-Dimethyl-5-phenyloctahydroindolizin-7-one (14b), and 1-(5,5-Dimethyl-2-pyrrolidinylidene)-4-phenyl-2-butanone (15).** A solution of **6a** (116 mg, 0.47 mmol) in toluene (9 mL) was refluxed for 4 h, and then the solvent was removed in vacuo to give an oil. By passing through a pad of silica gel (eluant ethyl acetate), it afforded a 2:1:4.5 mixture of **14a**, **14b**, and **15** (110 mg, 95%). Attempted chromatographic separation (eluant: petroleum ether–ethyl acetate, 70:30) gave only pure **15** (R_f 0.38, 25 mg, 21%) and a mixture of **14a**, **14b**, and **15** (R_f 0.43–0.38, 47 mg, 40%).

14a. MS: m/e (rel intensity) 243 (**14a**$^{\bullet+}$, 1), 228 (53), 124 (39), 104 (25), 82 (100), 55 (18), 41 (27). ^{1}H NMR: δ 7.44–7.16 (m, 5 H), 4.57 (t, J = 6.0, 1 H), 3.75 (m, 1 H), 1.28 (s, 3 H), 0.87 (s, 3 H). ^{13}C NMR: δ 210.81 (s), 60.58 (s), 55.67 (d), 55.34 (d), 48.44 (t), 47.19 (t), 39.71 (t), 31.76 (t), 29.18 (q), 26.11 (q).

14b. MS: m/e (rel intensity) 243 (**14b**$^{\bullet+}$, 2), 228 (79), 166 (7), 124 (46), 104 (24), 82 (100), 41 (21). ^{1}H NMR: δ 7.44–7.16 (m, 5 H), 3.76 (dd, J = 10.2, 4.1, 1 H), 3.02 (m, 1 H), 0.98 (s, 3 H), 0.54 (s, 3 H). ^{13}C NMR: δ 208.77 (s), 61.70 (d), 61.38 (d), 60.58 (s), 50.47 (t), 48.26 (t), 40.47 (t).

15. MS: m/e (rel intensity) 243 (**15**$^{\bullet+}$, 20), 138 (100), 111 (47), 96 (54), 91 (24), 55 (11), 41 (13). ^{1}H NMR: δ 9.79 (br s, 1 H), 7.38–7.18 (m, 5 H), 5.05 (s, 1 H), 3.00–2.92 (m, 2 H), 2.70 (t, J = 7.6, 2 H), 2.65–2.57 (m, 2 H), 1.84 (t, J = 7.6, 2 H), 1.35 (s, 6 H). ^{13}C NMR: δ 196.34 (s), 165.60 (s), 142.06 (s), 128.10 (d, 4 C), 125.49 (d), 88.40 (d), 62.28 (s), 43.07 (t), 35.44 (t), 31.75 (t, 2 C), 28.39 (q, 2 C). IR: 3285, 3070, 3040, 2980, 2880, 1630, 1550 cm^{-1}.

Rearrangement of the Adduct 8a: (3*R,5*S**,8a*S**)-3-Methyl-5-phenyloctahydroindolizin-7-one (16a), (3*R**,5*R**,8a*S**)-3-Methyl-5-phenyloctahydroindolizin-7-one (16b), and 1-(5-Methyl-2-pyrrolidinylidene)-4-phenyl-2-butanone (17).** A solution of **8a** (62 mg, 0.27 mmol) in toluene (5 mL) was refluxed for 3 h, and then the solvent was removed in vacuo to give an oil, which was passed over a pad of silica gel. By elution with ethyl acetate, it afforded 60 mg (97%) of a 2:1.6:1 mixture of **16a**, **16b**, and **17**. This mixture was column chromatographed (eluant: petroleum ether–ethyl acetate, 70:30) to give **16a** (R_f 0.63, 22 mg, 35%), **16b** (R_f 0.42, 13 mg, 21%), and **17** (R_f 0.37, 10 mg, 16%).

16a. MS: m/e (rel intensity) 229 (**16a**$^{\bullet+}$, 17), 214 (100), 152 (24), 110 (87), 104 (70), 82 (41), 77 (28), 68 (74), 55 (33), 41 (57). ^{1}H NMR: δ 7.43–7.25 (m, 5 H), 3.71 (dd, J = 10.1, 4.5, 1 H), 3.30 (d quintet, J = 1.2, 6.6, 1 H), 2.95 (dddd, J = 10.7, 9.1, 6.9, 3.0, 1 H), 2.60 (dt, J = 13.3, 2.6, 1 H), 2.52–2.33 (m, 3 H), 2.11 (m, 2 H), 1.60 (m, 1 H), 1.38 (m, 1 H), 0.72 (d, J = 6.6, 3 H). ^{13}C NMR: δ 208.75 (s), 142.04 (s), 128.46 (d, 2 C), 127.28 (d), 127.16 (d, 2 C), 60.92 (d), 57.88 (d), 53.07 (d), 50.64 (t), 48.23 (t), 30.32 (t), 30.01 (t), 13.64 (q). IR: 3060, 3030, 2960, 2870, 2800, 2700, 1725, 1605, 1495, 1455, 1380, 1170 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.48; H, 8.22; N, 5.99.

16b. MS: m/e (rel intensity) 229 (**16b**$^{\bullet+}$, 14), 210 (100), 186 (27), 110 (62), 104 (54), 82 (30), 68 (47). ^{1}H NMR: δ 7.47–7.37 (m, 2 H), 7.36–7.20 (m, 3 H), 4.33 (t, J = 5.9, 1 H), 3.61 (dddd, J = 10.2, 7.1, 4.5, 3.2, 1 H), 3.18 (sextet, J = 6.5, 1 H), 2.77 (ddd, J = 15.2, 6.4, 1.1, 1 H), 2.63 (ddd, J = 15.2, 5.3, 0.7, 1 H), 2.37 (ddd, J = 15.2, 10.2, 0.7, 1 H), 2.25 (ddd, J = 15.2, 4.5, 1.1, 1 H), 2.12 (m, 2 H), 1.51 (m, 2 H), 1.04 (d, J = 6.1, 3 H). ^{13}C NMR: δ 210.14 (s), 143.49 (s), 128.16 (d, 2 C), 127.12 (d, 2 C), 126.80 (d), 59.79 (d), 57.08 (d), 56.23 (d), 43.89 (t), 42.92 (t), 31.14 (t), 29.51 (t), 21.37 (q).

17. MS: m/e (rel intensity) 229 (**17**$^{\bullet+}$, 14), 124 (100), 97 (32), 91 (13), 82 (19). ^{1}H NMR: δ 9.82 (br s, 1 H), 7.34–7.08 (m, 5 H), 5.00 (s, 1 H), 3.96 (sextet, J = 6.6, 1 H), 2.96–2.88 (m, 2 H), 2.66–2.58 (m, 4 H), 2.14 (dddd, J = 12.5, 8.0, 7.0, 5.4, 1 H), 1.52 (ddt, J = 12.5, 7.0, 9.0, 1 H), 1.26 (d, J = 6.3, 3 H). ^{13}C NMR: δ 196.41 (s), 166.59 (s), 142.02 (s), 128.08 (d, 4 C), 125.49 (d), 88.66 (d), 55.41 (d), 43.11 (t), 32.07 (t), 31.79 (t), 29.44 (t), 21.30 (q). IR: 3270, 3090, 3060, 3030, 2970, 2870, 1635, 1550, 1305 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.72; H, 8.43; N, 6.14.

Rearrangement of the Adduct 10a: (3*R,5*R**,8a*S**)-3-Butyl-5-propyloctahydroindolizin-7-one (18a), (3*R**,5*S**,8a*S**)-3-Butyl-5-propyloctahydroindolizin-7-one (18b), and 1-(5-Butyl-2-pyrrolidinylidene)-2-heptanone (19).** A solution of **10a** (170 mg, 0.72 mmol) in toluene (15 mL) was refluxed for 6 h, and then the solvent was removed in vacuo. The oil obtained was passed over a pad of silica gel (eluant: methanol + 2% ammonia solution–chloroform, 12:88) to give a mixture of the products **18a**, **18b**, and **19** in 2.8:2:1 molar ratio (140 mg, 82%). Separation of this mixture by flash chromatography (eluant: methanol + 12% ammonia solution–chloroform, 2:98) gave the enaminone **19** (R_f 0.36, 17 mg, 10%), a mixture of **18a** and **19** (40 mg, 23%), and a mixture of **18a** and **18b** (65 mg, 38%).

18a. MS: m/e (rel intensity) 237 (**18a**$^{\bullet+}$, 2), 194 (56), 180 (100), 152 (33), 110 (16), 68 (31), 41 (26). ^{1}H NMR: δ 3.58 (quintet, J = 5.3, 1 H), 3.37 (m, 1 H), 3.03 (m, 1 H), 2.66 (dd, J = 13.1, 6.0, 1 H), 2.20–1.98 (m, 5 H), 1.75–1.20 (m, 12 H), 0.92 (t, J = 6.8, 3 H), 0.88 (t, J = 7.1, 3 H). ^{13}C NMR: δ 210.96 (s), 58.21 (d), 57.81 (d), 56.12 (d), 44.67 (t), 40.89 (t), 36.40 (t), 35.36 (t), 29.44 (t), 28.06 (t), 27.96 (t), 22.97 (t), 17.57 (t), 14.06 (q), 13.71 (q). IR ($CDCl_3$): 2965, 2880, 1705, 1470, 1460 cm^{-1}. HRMS: calcd for $C_{15}H_{27}NO$ 237.2092, found (GC inlet) 237.2074.

18b. MS: m/e (rel intensity) 237 (**18b**$^{\bullet+}$, 1), 194 (100), 180 (86), 152 (58), 110 (21), 82 (28), 68 (47), 55 (34), 41 (48). ^{1}H NMR: δ 3.37 (m, 1 H), 3.16 (m, 1 H), 2.18 (m, 1 H). ^{13}C NMR: δ 209.69 (s), 58.64 (d), 57.71 (d), 54.69 (d), 48.17 (t), 45.59 (t).

19. MS: m/e (rel intensity) 237 (**19**$^{\bullet+}$, 16), 181 (71), 166 (100), 139 (48), 124 (23), 82 (42). ^{1}H NMR: δ 9.95 (br s, 1 H), 5.05 (s, 1 H), 3.79 (quintet, J = 6.7, 1 H), 2.65–2.55 (m, 2 H), 2.25 (t, J = 7.6, 2 H), 2.10 (m, 2 H), 1.73–1.25 (m, 12 H), 0.91 (t, J = 6.7, 3 H), 0.89 (t, J = 6.7, 3 H). ^{13}C NMR: δ 198.21 (s), 166.59 (s), 88.82 (d), 60.19 (d), 41.75 (t), 35.72 (t), 31.91 (t), 31.70 (t), 28.44 (t), 27.70 (t), 25.77 (t), 22.49 (t), 22.48 (t), 13.88 (q), 13.84 (q). IR ($CDCl_3$): 3300, 2970, 2880, 1620, 1535, 1300, 1250 cm^{-1}.

Reduction of 18a and 18b to (3*R,5*R**,8a*R**)-3-Butyl-5-propyloctahydroindolizine (GTX 223AB, 20) and (3*R**,5*S**,8a*R**)-3-Butyl-5-propyloctahydroindolizine (21).** A solution of (*p*-tolylsulfonyl)hydrazine (110 mg, 0.58 mmol) and of the mixture of **18a**, **18b**, and **19** (95 mg, 0.4 mmol) in absolute ethanol (8 mL) was refluxed for 5 h. $NaBH_4$ (313 mg, 8.27 mmol) was added during 1 h under cooling (0 °C), and then the mixture was refluxed for 3.5 h and worked up routinely. The oily residue was purified by passing through a short pad of silica gel (eluant: methanol + 12% ammonia solution–chloroform, 2:98) to give 76 mg (85%) of a 1.4:1 mixture of GTX 223AB (**20**) and its C-5 epimer **21** as an oil. Their mass spectra were identical with those of ref 4b.

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Registry No. **1**, 3317-61-1; **2**, 124583-15-9; **3**, 118798-54-2; **4**, 124571-36-4; **5**, 124583-16-0; **6a**, 124583-19-3; **6b**, 124648-38-0; **7a**, 124583-22-8; **7b**, 124648-39-1; **8a**, 124583-20-6; **8b**, 124648-40-4; **8c**, 124648-44-8; **9a**, 124583-23-9; **9b**, 124648-41-5; **9c**, 124648-45-9; **10a**, 124583-21-7; **10b**, 124648-42-6; **11a**, 124583-24-0; **11b**, 124648-43-7; **14a**, 124583-25-1; **14b**, 124583-27-3; **15**, 124583-26-2; **16a**, 124583-28-4; **16b**, 124648-46-0; **17**, 124583-29-5; **18a**, 124583-31-9; **18b**, 124648-47-1; **19**, 124583-30-8; **20**, 81076-50-8; **21**, 81076-53-1; 1,1-dimethoxy-4-nitropentane, 124583-17-1; 1-pentene, 109-67-1; 1,1-dichloroethane, 75-34-3; 1-chloro-1-methyl-2-propylcyclopropane, 124583-18-2.