× 50 mL). The CH_2Cl_2 extracts were combined, washed with 25 mL of H_2O, and dried over Na_2SO_4. Removal of solvent in a rotary evaporator gave a solid that was recrystallized (twice) from heptane/toluene giving 56.3 mg (68%) of **7e** as light yellow needles: mp 179–180 °C; IR (Nujol) 1675, 1590, 1575, 1465, 1380, 1335, 1320, 1285, 1270, 1250, 1170, 1110, 1080, 1060, 1025, 990, 900, 855, 845, 830, 720 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.37 (s, 3 H), 5.05 (s, 2 H), 7.61–7.73 (m, 7 H), 8.11–8.30 (m, 3 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 17, 75, 122, 125 (q, J = 1250 Hz), 126 (3), 127 (2), 128, 129, 130 (2), 132, 134 (4), 142 (2), 158, 183 (2); MS, m/e (rel intensity) 396 (21), 378 (9), 250 (8), 237 (26), 222 (9), 159 (100), 152 (11), 109 (11). Anal. Calcd for $C_{23}H_{15}O_3F_3$: C, 69.70; H, 3.81. Found: C, 69.64; H, 4.11.

1-[(*p*-Cyanobenzyl)oxy]-2-methyl-9,10-anthraquinone (7d). A mixture of **2** (49.5 mg, 0.208 mmol), K_2CO_3 (2.2, 15.9 mmol), and *p*-cyanobenzyl bromide (2.17 g, 11.1 mmol) in 50 mL of 2-butanone was heated to reflux for 75 min. After cooling, the reaction mixture was diluted with 60 mL of H_2O and extracted with CH_2Cl_2 (2 × 50 mL). The CH_2Cl_2 extracts were combined, washed with H_2O (30 mL), and dried over Na_2SO_4. Removal of solvent in a rotary evaporator gave yellow crystals. Excess *p*-cyanobenzyl bromide was removed by sublimation (0.1 mmHg, ~70 °C). The residue was decolorized (norit) and recrystallized from toluene. Recrystallization gave 26.6 mg of **7d** (42%): mp 222–223 °C; IR (Diffuse reflectance in KBr) 2227, 1671, 1580, 1582, 1568, 1324, 1276, 1244, 1192, 1053, 985, 892, 824, 711 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 5.05 (s, 2 H), 7.65–7.78 (m, 7 H), 8.10–8.30 (m, 3 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 17, 73, 112, 118, 123, 126, 127 (2), 128, 129 (2), 132, 133 (2), 134 (4), 136, 139, 141, 156, 183. Anal. Calcd for $C_{23}H_{15}O_3N$: C, 78.18; H, 4.28; N, 3.96. Found: C, 77.89; H, 4.56; N, 3.97.

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Short, Enantiogenic Syntheses of (−)-Indolizidine 167B and (+)-Monomorine†

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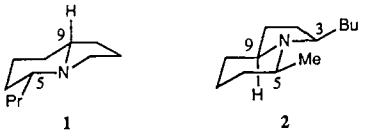
Abstract: The enantiogenic syntheses of (−)-indolizidine 167B (**1**) and (+)-monomorine (**2**) are described. D-Norvaline and L-alanine are converted into their 1-pyrrole derivatives by reaction with 2,5-dimethoxytetrahydrofuran. Thereafter, Arndt–Eistert homologation of the *N*-alkanoic acid substituent, followed by rhodium(II) acetate catalyzed decomposition of its α-diazo ketone derivative, provides the relevant bicyclic precursors, the vested chirality of which directs catalytic hydrogenation affording **1** and **2**. Provision for the 5-butyl side chain in **2** is made by prior Lewis acid catalyzed rearrangement of the mixed anhydride obtained from butyryl chloride and the pyrrole analogue of L-alanine.

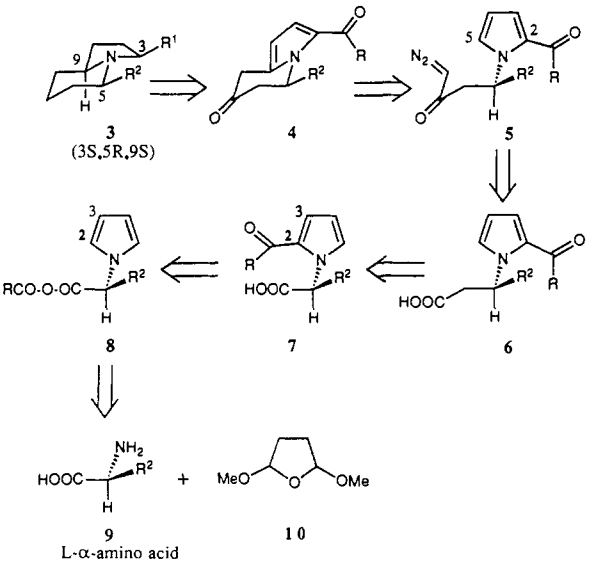
Introduction

Indolizidine alkaloids offer attractive targets for synthesis because of their exotic provenance, scarcity, and marked biological activity.[1] Two typical, but contrasting, examples are indolizidine 167B (**1**), a vanishingly minor constituent of the skin of a dendrobatid frog, caught on Isla de Colôn, Panamá,[2,3] and (+)-monomorine (**2**), a trail pheromone of the Pharaoh's ant (*Monomorium pharaonis* L.), a pest in heated buildings.[4] Although frogs of the genus *Dendrobates* were never used as a source of arrow poisons, unlike the Colombian genus *Phyllobates*,[2] several of the constituents contained in their skins and closely related to **1**, are noncompetitive blockers of neuromuscular transmission.[5] Consequently, the practical preparation of these rare and potent substances is of some importance. So far, indolizidine 167B has been synthesized twice in its racemic form[6,7] and once as its (−) enantiomer,[8] whereas many syntheses have been reported for racemic[9,10] and enantiomerically pure monomorine.[11] It might therefore appear that sufficient methods are available for preparing mono- and disubstituted indolizidines. Unfortunately, most are multistep procedures giving the product in poor overall yields. We



1 2

Scheme I



* To whom correspondence should be addressed.
† Dedicated to Professor W. Kirmse on the occasion of his 60th birthday.
‡ Ciba-Geigy SA, WFM, 1723 Marly, Switzerland.
§ Firmenich SA, P.O. Box 239, 1211 Geneva 8, Switzerland.

(1) Lamberton, J. A. *The Alkaloids*; Specialist Periodical Reports; The Royal Society of Chemistry: London, 1976–1983; Vol. 6–13. Gellert, E. *J. Nat. Prod.* **1982**, *45*, 50–73.

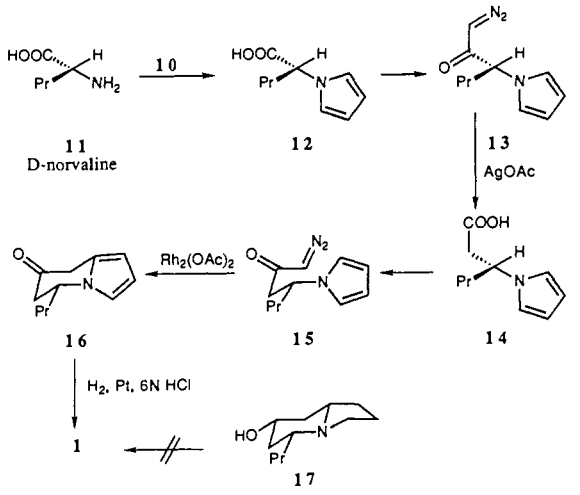
0002-7863/91/1513-3513$02.50/0

believed that substantial improvements could be made by exploiting the chemistry of pyrrole and appropriate substituents to obtain the requisite stereochemical control. Accordingly, we now describe short enantiogenic syntheses of **1** and **2** in which the necessary chirality is installed at the start and is used in the subsequent steps to induce the desired configuration in the final product.

General Synthetic Plan

Our design for synthesizing a *cis*-3,5-dialkylindolizidine (**3**) having, for example, the 3*S*,5*R*,9*S* configuration, where the substituents R^1 and R^2 are assigned a priority of 2, depends, as the disconnective analysis shows, on three critical steps (Scheme I). The creation of the bicyclic skeleton and the cis arrangement of the C3 and C5 substituents will be based on the technology recently developed for the syntheses of (±)-ipalbidine[12] and (±)-monomorine.[10] Rhodium(II) acetate catalyzed decomposition of the 1-diazo-4-(1′H-pyrrol-1′-yl)butan-2-one (**5**) should be effective for constructing the required dihydroindolizine (**4**). Cyclization should preferentially occur at the more nucleophilic C5 position in view of the electrophilic nature of the carbenoid intermediate involved. Removal of unsaturation by catalytic hydrogenation would put the incoming hydrogen atoms in an all-cis arrangement at the C3, C5, and C9 centers in **3**, since the bicyclic pyrrole derivative **4**, because of the bulk of the C5 substituent, should approach the catalytic surface from its least hindered side. The disconnections of the diazo ketone **5** to the pyrrole-protected α-amino acid **7** are straightforward as the intermediate acid **6** is simply the homologue. The logical disconnection of **7** would be C2 acylation. However, the intermolecular acylation of pyrrole derivatives is notoriously nonregioselective; both C2 and C3 substitution usually occur. Accordingly, intramolecular acylation by the mixed anhydride **8** ought to ensure the precise placement of the RCO group, the precursor to the R^1 substituent in **3**. The conditions used to effect this crucial step should not affect the chirality of **8** which will be introduced by the condensation of an α-amino acid of the appropriate configuration (**9**), here shown as R, with 2,5-dimethoxytetrahydrofuran (**10**). Lastly, the chirality of **9**, which becomes that of the C5 center in the indolizidine product **3**, is expected to completely control the genesis of the two other centers at C3 and C9, thereby affording a single product, namely the enantiomer having the 3*S*,5*R*,9*S* configuration.

Scheme II



Results and Discussion

The practicality of the aforementioned plan was first put to the test by selecting (5*R*,9*R*)-indolizidine 167B (**1**) as the target, since it only requires the establishment of one new asymmetric center. Although the configuration of the natural material was not determined, the configuration we chose for **1** (5*R*,9*R*) was inferred from that of the related alkaloid, (−)-indolizidine 223AB, which was shown to be (3*R*,5*R*,9*R*)-3-butyl-5-propylindolizidine by enantioselective synthesis.[13]

The point of departure was the condensation of 2,5-dimethoxytetrahydrofuran (**10**) with D-norvaline (**11**), which installed the desired enantiogenic chirality[14] (Scheme II). The resulting 1-pyrrolylacetic acid **12** was smoothly converted to the α-diazo ketone **13** in 74% yield by reaction of its mixed anhydride, obtained from isobutyl chloroformate, with diazomethane. Treatment of **13** with silver acetate brought about Wolff rearrangement, giving the homologous acid **14** in 80% yield. Repetition of the mixed anhydride–diazomethane procedure on **14** afforded the corresponding α-diazo ketone **15** in 81% yield. Decomposition of the latter with a catalytic amount of rhodium(II) acetate at room temperature was rapid and just as efficient as previously observed,[10,12] providing the dihydroindolizinone **16** in 93% yield. The hydrogenation of **16** was attempted with some trepidation since our experience with bicyclic pyrroles had shown that reduction was often incomplete.[10] However, submission of **16** to hydrogen under 15 atm of pressure with Adams catalyst under acid conditions[15] was entirely successful, giving analytically pure (5*R*,9*R*)-5-propyloctahydroindolizine (**1**) as the free base in 67% yield after neutralization with sodium carbonate. The ^{13}C NMR spectrum of **1** was identical with that of synthetic (5*RS*,9*RS*)-5-propylidnolizidine, while the ^1H NMR spectra broadly agreed.[16]

(2) The structure of indolizidine 167B has been tentatively assigned as a 5-propylindolizidine of unknown configuration on the basis of a GC–MS electron-impact mass spectrum, the observation that no hydrogen uptake (Pt/H_2) occurred, and the presence of a nonacetylatable nitrogen atom (Daly, J. W. *Fortschr. Chem. Org. Naturst.* **1982**, *41*, 205–340). Further data (NMR spectra, optical rotation, etc.) were not obtained. Alkaloid 167B was only detected once as a trace component in a complex mixture of alkaloids. It has not been subsequently detected in the original or in other extracts of frog skin until now (T. F. Spande and J. W. Daly, personal communication).

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(7) A good yield of (5*RS*,9*RS*)-5-*n*-propylindolizidine has been obtained by use of a classical procedure (Lions, F.; Willison, A. M. *J. Proc. R. Soc., N. S. W.* **1940**, *73*, 240–252; *Chem. Abstr.* **1940**, *34*, 5841). The 5*RS*,9*RS*-configuration was assigned by using the ratio of integrated areas of axial and equatorial protons in the ^1H NMR spectrum as measured in trifluoroacetic acid and the appearance of significant Bohlmann bands (2870, 2780, 2700, 2580 cm^{-1}) in the IR spectrum (T. F. Spande, private communication).

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(11) For nonnatural (−)-monomorine see: Royer, J.; Husson, H.-P. *J. Org. Chem.* **1985**, *50*, 670–673. Husson, H.-P. *J. Nat. Prod.* **1985**, *48*, 894–906. For (+)-monomorine see: Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1988**, *29*, 5767–5768. Momose, T.; Toyooka, N.; Seki, S.; Hirai, Y. *Chem. Pharm. Bull.* **1990**, *38*, 2072–2074. Ito, M.; Kibayashi, C. *Tetrahedron Lett.* **1990**, *31*, 5065–5068.

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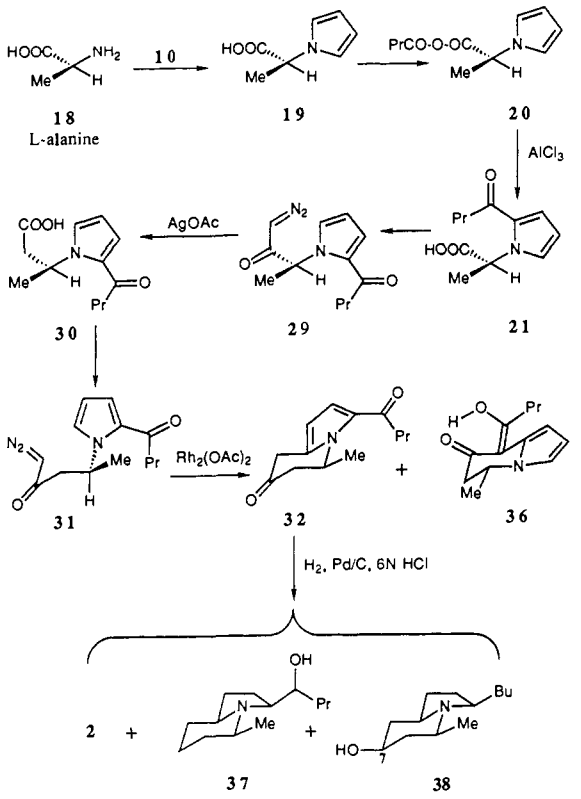
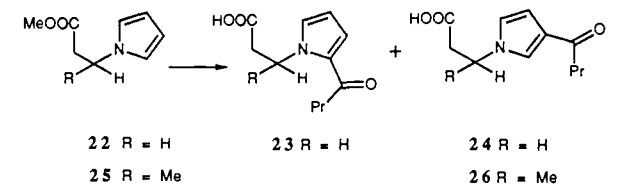
(14) 1-Pyrrole analogues of α-amino acids were prepared according to the modified Clauson–Kaas procedure: (a) Kashima, C.; Maruyama, T.; Harada, K.; Hibi, S.; Omote, Y. *J. Chem. Res., Miniprint* **1988**, 601–645. See also: (b) Gloede, J.; Poduška, K.; Rudinger, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1307–1314.

(15) The conditions chosen were those reported to be the best for ensuring complete hydrogenolysis of an isolated carbonyl group in azabicyclic ketones and in 2-indolizidone (Reiff, L. P.; Aaron, H. S. *Tetrahedron Lett.* **1967**, 2329–2332.

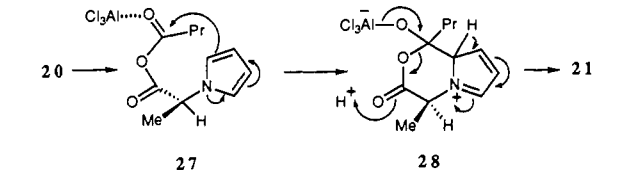
Scheme III



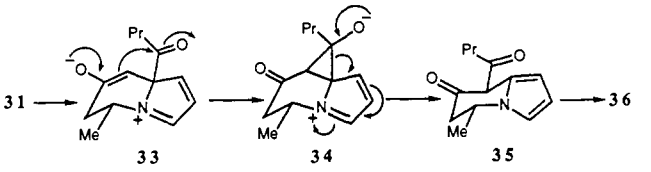
Scheme IV



Scheme V



Scheme VI



The NMR data of **1** were also essentially the same as those recently reported for **1** prepared by a different route starting from *S*-(−)-α-phenylethylamine.[8] The optical rotation, $[\alpha]^{20}_D$, of **1** was −106.3° (*c* = 0.800, *n*-hexane), which is gratifyingly close to the value of −111.3° (*c* 1.3, CH_2Cl_2) cited for the sample obtained by the aforementioned route.[8]

Since **1** in our hands was formed as a single product, it can be assumed that the operations of side-chain elongation, cyclization, and reduction, as well as the conditions employed, did not compromise the integrity of the primary enantiomeric element in **12**. It has been demonstrated elsewhere[14a] that the formation and even the subsequent destruction of the pyrrole ring causes essentially no racemization. Therefore, the vested chirality has completely determined the setting up of the new asymmetric center in the sense depicted by **1**, the reason being that hydrogen atom delivery at the developing tetrahedral center at C9 took the least hindered path with respect to the nearby propyl substituent.[17] Total reduction of the lone carbonyl group in **16** is highly unusual.[15] It is significant that the cyclohexanol **17** is not hydrogenolyzed under the reaction conditions and is not therefore an intermediate. The catalyst probably effects a Clemmensen-type deoxygenation[18] of the carbonyl group giving a cyclohexylidene–Pt derivative, which on double protonation gives the cyclohexane product.

Having demonstrated that the experimental plan in its important stereochemical aspects was realizable, the synthesis of (+)-monomorine, a disubstituted indolizidine, was next undertaken. This time the chiral foundation was laid by condensing L-alanine (**18**) with 2,5-dimethoxytetrahydrofuran[14a] (**10**) (Scheme III). The resulting pyrrole analogue of L-alanine **19** needed to be regioselectively acylated to form the required 2-butyryl derivative **21**. Originallly, it was thought that intermolecular acylation of **19** or its ester would be adequate. As a rule, Vilsmeier–Haack reagents bring about acylation at the 2-position of α-unsubstituted pyrroles.[19] In the present instance, a trial experiment with methyl 3-(1′-pyrrol-1-yl)propionate (**22**), which was treated with *N*,*N*-dimethylbutanamide and phosphorus oxychloride, gave, after saponification, moderate and equal amounts of the 2- and 3-butyryl derivatives of 3-pyrrolylpropionic acid (**23** and **24**) (Scheme IV). In another experiment, submission of the homologue of **22**, namely **25**, to the same conditions was equally unsuccessful in that only the 3-butyryl derivative **26** was obtained in a disappointingly poor yield.

These results reinforce the general finding that diversion toward C3 acylation occurs when the N-substitution is bulky.[20] Nevertheless, it occurred to us that this steric effect could be turned to advantage if the reagent itself were part of the group attached to the N atom. We reasoned that a suitably tethered electrophile, exemplified by the mixed anhydride **20**, would prefer to undergo intramolecular transfer through a six-membered transition state (**27**) to give the C2 derivative **21** via the dipolar intermediate **28** (Scheme V). Clearly, Lewis acid catalysis is indicated for such an acylation.[21] Operationally, the mixed anhydride **20** was prepared in situ from **19** and allowed to react with aluminum chloride, giving **21** in 76% yield. Thereafter, chain elongation via the α-diazo ketone derivative **29** to the homologous acid **30** according to the standard Arndt–Eistert procedure was accomplished in a combined yield of 75% (Scheme III). Conversion to the α-diazo ketone **31** was of similar efficiency (75% yield). Rhodium(II) acetate catalyzed decomposition of **31** proceeded smoothly and gave the bicyclic ketone intermediate **32** in 66% yield.

Contrary to expectation, a minor amount (15%) of the (*Z*)-hydroxybutylidene derivative **36** was also formed. Notwithstanding the weaker nucleophilicity of the pyrrole nucleus at the

(16) We thank Drs. A. B. Holmes (University Chemical Laboratory, Lensfield Road, Cambridge, U.K.) and T. F. Spande (Laboratory of Bioorganic Chemistry, NIDDK, NIH, Bethesda, MD) for kindly sending us unpublished ^{13}C and ^1H NMR data on synthetic, racemic **1** for comparison. We also thank Dr. M. J. Youssefi (Firmenich SA) for kindly determining the mass spectrum of **1**.

(17) For a closely related case of a substituent-directed hydrogenation of the pyrrole moiety of a chiral pyrrolizine see: Robins, D. J.; Sakdarat, S. *J. Chem. Soc., Perkins Trans. 1* **1981**, 909–913.

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C2 position, it had obviously suffered attack, albeit to a minor extent, to give presumably the dipolar species **33** (Scheme VI). Annihilation of the charges can be best achieved by rearrangement of the butyryl group through the formation of the cyclopropanolate entity **34** which, after ketonization to the 8-butyrylindolizone **35**, further enolizes to the hydrogen-bonded β-ketol **36**.

Apart from this partial loss of regioselectivity, the requisite ketone **32** was available in ample quantities for the decisive step of reduction. This time, a greater challenge is posed in that several different processes of hydrogenolysis would have to be called into play—the two implicated in the reduction of **16** to **1** and that needed for the butyryl substituent in **32**. It is essential to convert the latter into the butanol group while the pyrrole is still intact so that subsequent hydrogenolysis to the butyl substituent would be efficient. Consequently, palladium-on-charcoal under acid conditions, noted for favoring the reduction of benzyl ketones,[22] was used for the catalytic hydrogenation of **32**. The desired (+)-monomorine **2** was obtained in 51% yield, accompanied by the isomeric indolizinols **37** and **38** in yields of 21 and 8%, respectively (Scheme III). Both alcohols were resistant to further hydrogenation. The butanol derivative **37** presumably is an epimeric mixture as the side chain in **32** would be too flexible to be subject to much stereochemical control. On the other hand, the cyclohexanol **38** is formed as a single isomer of the 3*R*,5*S*,7*R*,9*R* configuration where the hydroxyl group is equatorial[23] as attested by the large ^3J coupling constants (each 11 Hz) displayed by the axial methine proton at C7 with the two vicinal axial protons.

The formation of these alcohols in no way defeats the purpose of the synthesis since both **37** and **38** could be easily converted, if so desired, to monomorine **2** by reduction of their thiocarbonylimidazole derivatives with tributyltin hydride. In fact, this procedure has been shown to work well with racemic **38**, which gave racemic monomorine in 63% yield.[10] The reduction of **32** gave (+)-monomorine **2** as a single product which exhibited ^{13}C and ^1H NMR spectra identical with those of the natural material. The optical rotation $[\alpha]^{20}_D$ was determined to be 35.7° (*c* 0.370, *n*-hexane). This value compares favorably with those obtained previously for synthetic (+)- and (−)-monomorines, namely 34.3° (*c* 1.02, hexane) and −35.8° (*c* 1.35, *n*-hexane), respectively.[11]

Conclusion

Starting from D-norvaline, (−)-indolizidine 167B (**1**) was prepared in six steps in an overall yield of 15%. Similarly, L-alanine was transformed into (+)-monomorine (**2**) in seven steps in a yield of 7–11%. Although most chiral syntheses of alkaloids make use of α-amino acids in one way or another,[24,25] the present route offers some particular advantages. The synthesis is short and economical, requiring no extraneous procedures to ensure the required stereochemistry. The chiral implant is retained as such and internally induces dissymmetry into the final product. It is worth noting that the directive chiral center lies outside the future pyrrolizidine moiety instead of being part of it, which is the case for the commoner proline-based technology.[26] This feature enables the configuration of ring fusion to be determined after cyclization. The *N*-pyrroleacetic acid function plays a dual role; it brings about selective intramolecular 2-acylation and is easily convertible in an iterative fashion to α-diazo ketones. When reaction of the latter is catalyzed by rhodium(II) acetate, cyclization with the pyrrole nucleus occurs regioselectively, in high yield, and under mild conditions.[27] Further applications of our procedure for preparing other scarce, chiral indolizidines and pyrrolizidines are under study, and the results will be disclosed in due course.

Experimental Section

General. All solvents were distilled prior to use. Et_2O and THF were dried over $LiAlH_4$ or sodium/potassium benzophenone and freshly distilled before use. CH_2Cl_2 was dried and distilled from P_2O_5. Pyrrole and *N*-methylmorpholine were distilled and stored over KOH pellets. Diazomethane was prepared from *N*-methyl-*N*-nitroso-4-toluenesulfamide by using a minimum amount of H_2O and ethoxyethanol as cosolvent and was dried over KOH pellets at −20 °C before use. All other liquids were distilled and stored under N_2. TLC: silica gel 60 F_{254} (Merck) or aluminum oxide F_{254} (Fluka). Column chromatography (CC): silica gel 60 (230–400 mesh ASTM, Merck), Florisil (100–200 mesh, Fluka), and aluminum oxide (neutral or basic, 70–230 mesh ASTM, Merck). mp: Reichert hot-stage microscope (uncorrected). IR spectra: CCl_4 solution; Perkin-Elmer 681 spectrometer. ^1H NMR spectra: $CDCl_3$ solution unless stated otherwise; chemical shifts in parts per million relative to internal TMS (=0 ppm), coupling constants (*J*) in hertz; Varian T-60 or XL-200 or Bruker WH 360 spectrometer. MS: Varian SM-1-B and Finnigan GC/MS 4023 using INCOS data system. Polarimeter: Perkin-Elmer 241. Elemental analyses were performed by Dr. H. Eder, Service de Microchimie, Institut de Chimie Pharmaceutique, Université de Genève.

Preparation of Pyrrole Analogues of α-Amino Acids.[14a] (2*R*)-2-(1*H*-Pyrrol-1-yl)pentanoic Acid (12) and (2*S*)-2-(1*H*-Pyrrol-1-yl)propionic Acid (19). To a solution of D-norvaline (**11**; 8.44 g, 72.1 mmol) or L-alanine (**18**; 17.8 g, 200 mmol) and NaOAc (6 equiv) in HOAc under gentle reflux was added 2,5-dimethoxytetrahydrofuran (**10**; 1.28 equiv). After 5 min, H_2O was added and the mixture was extracted continuously with Et_2O overnight. The ethereal extracts were evaporated. Bulb-to-bulb distillation of the resulting oil at 150 °C/0.15 Torr gave **12** (6.15 g, 36.8 mmol, 51% yield), whereas distillation at 120 °C/0.25 Torr afforded **19** (13.65 g, 97.9 mmol, 49% yield).

12. ^1H NMR δ 0.98 (t, *J* = 7.2 Hz, 3 H), 1.26–1.42 (m, 2 H), 2.02–2.22 (m, 2 H), 4.65 (dd, *J* = 9.5 and 6.5 Hz, 1 H), 6.25 (t, *J* = 2.2 Hz, 2 H), 6.80 (t, *J* = 2.2 Hz, 2 H), 11.05 (br s, 1 H); MS 167 (M^+, 20), 134 (14), 125 (13), 122 (37), 121 (50), 120 (11), 107 (11), 106 (19), 93 (14), 80 (81), 67 (25), 55 (100); IR 3000 (vbrs), 2967 (s), 2938 (m), 2878 (m), 2650 (vbrm), 1725 (vs), 1538 (vw), 1487 (s), 1467 (w), 1457 (w), 1445 (w), 1428 (w), 1395 (w), 1382 (vw), 1314 (w), 1282 (s), 1212 (m), 1107 (w), 1090 (s), 1068 (m), 967 (w), 930 (brw), 890 (w), 718 (vs), 688 (w), 612 cm^{-1} (vw); $[\alpha]^{20}_D$ = −7.5° (*c* 1.02, MeOH).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.42; H, 7.82; N, 8.33.

19. mp 79–80 °C; ^1H NMR δ 1.78 (d, *J* = 7.5 Hz, 3 H), 4.81 (q, *J* = 7.5 Hz, 1 H), 6.22 (t, *J* = 2.2 Hz, 2 H), 6.75 (t, *J* = 2.2 Hz, 2 H), 11.18 (br s, 1 H); MS 139 (M^+, 51), 95 (9), 94 (100), 93 (12), 81 (6), 78 (16), 67 (15), 65 (7), 53 (8); IR 3000 (vbrs), 2630 (brm), 1737 (vs), 1538 (vw), 1487 (m), 1460 (w), 1420 (w), 1400 (w), 1375 (w), 1290 (brs), 1280 (s), 1250 (s), 1224 (s), 1096 (s), 1078 (w), 1062 (w), 1050 (w), 1000 (vw), 944 (s), 940 (brw), 870 (vw), 844 (vw), 715 (vs), 665 cm^{-1} (m); $[\alpha]^{20}_D$ = 20.6° (*c* 0.73, MeOH).

Anal. Calcd for $C_7H_9NO_2$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.33; H, 6.54; N, 10.13.

Acylations. 3-(2-Butyryl-1*H*-pyrrol-1-yl)propionic Acid (23) and 3-(3-Butyryl-1*H*-pyrrol-1-yl)propionic Acid (24). To a solution of *N*,*N*'-dimethylbutanamide (828 mg, 7.2 mmol) in benzene (1.5 mL) at −10 °C was added a solution of $POCl_3$ (0.6 mL, 6.6 mmol) in benzene (1 mL) during 10 min. After 30 min of stirring at 25 °C, the mixture was cooled to −10 °C and a solution of methyl 3-(1-pyrrol-1-yl)propionate (**22**)[28] (918 mg, 6 mmol) in benzene (0.5 mL) was added. The resulting solution was stirred at 25 °C overnight. After addition of aqueous $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Bulb-to-bulb distillation at 80 °C/0.01 Torr removed starting materials. Column chromatogra-

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phy (SiO_2, CH_2Cl_2) gave **23** (377 mg, 1.7 mmol, 28% yield) and **24** (379 mg, 1.7 mmol, 28% yield).

23. ^1H NMR δ 0.85 (t, J = 7 Hz, 3 H), 1.57 (sext, J = 7 Hz, 2 H), 2.40–2.80 (m, 4 H), 3.30 (s, 3 H), 4.43 (t, J = 6.5 Hz, 2 H), 5.80–6.00 (m, 1 H), 6.67–6.90 (m, 2 H).

24. ^1H NMR δ 0.85 (t, J = 7 Hz, 3 H), 1.62 (sext, J = 7 Hz, 2 H), 2.40–3.10 (m, 4 H), 3.57 (s, 3 H), 4.10 (t, J = 6.5 Hz, 2 H), 6.33–6.60 (m, 2 H), 7.10–7.27 (m, 1 H).

(3*RS*)-Methyl 3-(3-Butyryl-1*H*-pyrrol-1-yl)butanoate (26). (3*RS*)-Methyl 3-(1*H*-pyrrol-1-yl)butanoate (**25**)[28] (1 g, 6 mmol) was treated as previously described with *N*,*N*-dimethylbutanamide (828 mg, 7.2 mmol) and $POCl_3$ (0.6 mL, 6.6 mmol) in benzene. The mixture was stirred at 60 °C overnight and then treated with an aqueous solution of Na_2CO_3 at 25 °C during 3 h and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were washed with brine (2 × 15 mL), dried ($MgSO_4$), and evaporated. Column chromatography (SiO_2, $CHCl_3$/MeOH 9:1) of the residue gave crude product (470 mg) which was treated with aqueous KOH (10 mL, 20%) in MeOH (10 mL). After the usual workup, **26** (250 mg, 1.12 mmol, 19% yield) was obtained as a colorless oil.

26. ^1H NMR δ 0.92 (t, J = 7.2 Hz, 3 H), 1.51 (d, J = 7 Hz, 3 H), 1.69 (sext, J = 7.2 Hz, 2 H), 2.69 (t, J = 7.2 Hz, 2 H), 2.74 (ABd syst, J = 16 and 7 Hz, 1 H), 2.83 (ABd syst, J = 16 and 7 Hz, 1 H), 4.59 (sext, J = 7 Hz, 1 H), 6.57 (dd, J = 3 and 1.5 Hz, 1 H), 6.68 (dd, J = 3 and 2.5 Hz, 1 H), 7.38 (dd, J = 2.5 and 1.5 Hz, 1 H), 8.7 (br s, 1 H); IR 3000 (vbrs), 2964 (s), 2932 (m), 2872 (m), 2650 (vbrm), 1716 (brvs), 1648 (brvs), 1529 (vs), 1501 (w), 1450 (w), 1410 (s), 1395 (m), 1379 (m), 1345 (vw), 1287 (brm), 1262 (m), 1220 (vbrm), 1177 (vs), 1104 (w), 1087 (w), 1037 (vw), 974 (vw), 932 (w), 926 (vw), 884 (w), 628 cm^{-1} (w).

(2*S*)-2-(2-Butyryl-1*H*-pyrrol-1-yl)propionic Acid (21). A mixture of **19** (5.6 g, 40.3 mmol), *N*-methylmorpholine (4.65 mL, 42.3 mmol), and freshly distilled butyryl chloride (4.39 mL, 42.3 mmol) in dry ether (250 mL) was allowed to react. The resulting solution containing the mixed anhydride **20** was filtered through Celite into a solution of $AlCl_3$ (5.64 g, 42.3 mmol) in ether (20 mL). The mixture was strongly stirred at 25 °C overnight. After addition of H_2O (50 mL) and concentrated aqueous HCl (30 mL), the ethereal layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. The resulting brown oil was slowly distilled bulb-to-bulb at 130 °C/0.22 Torr to remove starting acid. Subsequent distillation at 150 °C/0.22 Torr gave **21** (6.4 g, 30.6 mmol, 76% yield): ^1H NMR δ 0.96 (t, J = 7.5 Hz, 3 H), 1.74 (sext, J = 7.5 Hz, 2 H), 1.78 (d, J = 7 Hz, 3 H), 2.77 (t, J = 7.5 Hz, 2 H), 5.83 (br q, J = 7 Hz, 1 H), 6.24 (dd, J = 4 and 3 Hz, 1 H), 7.07 (dd, J = 4 and 1.5 Hz, 1 H), 7.10 (dd, J = 3 and 1.5 Hz, 1 H), 10.81 (br s, 1 H); MS 209 (M^+, 16), 194 (1), 165 (10), 164 (11), 148 (4), 139 (10), 138 (46), 122 (25), 121 (29), 94 (100), 71 (24); IR 3000 (vbrs), 2965 (s), 2932 (m), 2872 (m), 2650 (vbrm), 1725 (brvs), 1650 (brvs), 1530 (m), 1465 (m), 1415 (vs), 1376 (w), 1353 (vw), 1330 (vw), 1310 (w), 1278 (m), 1230 (brs), 1190 (vw), 1107 (w), 1083 (m), 1066 (m), 1044 (w), 1005 (vw), 955 (w), 905 (vw), 890 cm^{-1} (vw); $[\alpha]^{20}_D$ = −51.3° (*c* 0.93, MeOH).

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 62.76; H, 7.22; N, 6.89.

Preparation of α-Diazo Ketones. (3*R*)-1-Diazo-3-(1*H*-pyrrol-1-yl)-2-hexanone (13), (4*R*)-1-Diazo-4-(1*H*-pyrrol-1-yl)-2-heptanone (15), (3*S*)-3-(2-Butyryl-1*H*-pyrrol-1-yl)-1-diazo-2-butanone (29), and (4*S*)-4-(2-Butyryl-1*H*-pyrrol-1-yl)-1-diazo-2-pentanone (31). A mixture of the corresponding acid **12** (6 g, 35.9 mmol), **14** (3.23 g, 17.8 mmol), **21** (6 g, 28.7 mmol), or **30** (3.6 g, 16.1 mmol), *N*-methylmorpholine (1.33 equiv), and freshly distilled isobutyl chloroformate (1.26 equiv) in Et_2O was allowed to react. The resulting solution after filtration through Celite was treated at 0 °C with an ethereal solution of diazomethane (10 equiv). N_2 evolved vigorously, and the mixture was allowed to warm to 25 °C overnight. Removal of the solvent left an orange oil which was purified by chromatography (SiO_2) to give **13** (5.08 g, 26.6 mmol, 74% yield), **15** (2.96 g, 14.4 mmol, 81% yield), **29** (5.5 g, 23.6 mmol, 82% yield), or **31** (3 g, 12.1 mmol, 75% yield).

13. ^1H NMR δ 0.95 (t, J = 7.5 Hz, 3 H), 1.28–1.40 (m, 2 H), 1.90–2.02 (m, 1 H), 2.18–2.28 (m, 1 H), 4.46 (dd, J = 10.5 and 4.5 Hz, 1 H), 4.72 (s, 1 H), 6.24 (t, J = 2.2 Hz, 2 H), 6.70 (t, J = 2.2 Hz, 2 H); MS 163 (9), 135 (6), 134 (22), 122 (32), 121 (70), 120 (15), 106 (25), 93 (16), 80 (75), 55 (100); IR 3110 (m), 2962 (s), 2935 (m), 2875 (m), 2108 (vs), 1647 (brvs), 1488 (m), 1467 (w), 1395 (vw), 1352 (brvs), 1320 (m), 1278 (s), 1260 (w), 1158 (m), 1106 (w), 1086 (m), 1064 (w), 1010 (brvw), 962 (vw), 722 (vs), 635 cm^{-1} (w); $[\alpha]^{20}_D$ = 107.9° (*c* 1.035, MeOH).

Anal. Calcd for $C_{10}H_{13}N_3O$: C, 62.81; H, 6.85; N, 21.97. Found: C, 62.71; H, 6.87; N, 21.76.

15. ^1H NMR δ 0.90 (t, J = 7.5 Hz, 3 H), 1.08–1.32 (m, 2 H), 1.64–1.86 (m, 2 H), 2.65 (br ABd syst, J = 14 and 5 Hz, 1 H), 2.76 (br ABd syst, J = 14 and 8 Hz, 1 H), 4.36–4.48 (m, 1 H), 4.97 (s, 1 H), 6.14 (t, J = 2.2 Hz, 2 H), 6.67 (t, J = 2.2 Hz, 2 H); MS 177 (14), 149 (8), 135 (55), 134 (88), 120 (14), 107 (48), 106 (80), 94 (14), 93 (20), 81 (13), 80 (100), 79 (52), 67 (35), 55 (75); IR 3110 (w), 2962 (s), 2935 (m), 2875 (m), 2108 (vs), 1647 (brvs), 1488 (m), 1467 (w), 1457 (vw), 1415 (w), 1368 (brvs), 1330 (m), 1274 (m), 1260 (w), 1142 (m), 1115 (w), 1086 (m), 1067 (m), 962 (vw), 720 (vs), 645 (vw), 630 cm^{-1} (w); $[\alpha]^{20}_D$ = −163.6° (*c* 1.04, MeOH).

Anal. Calcd for $C_{11}H_{15}N_3O$: C, 64.37; H, 7.37; N, 20.47. Found: C, 64.12; H, 7.32; N, 20.26.

29. ^1H NMR δ 0.93 (t, J = 7.5 Hz, 3 H), 1.59 (d, J = 7.5 Hz, 3 H), 1.65 (sext, J = 7.5 Hz, 2 H), 2.70 (t, J = 7.5 Hz, 2 H), 5.00 (s, 1 H), 5.99 (br q, J = 7.5 Hz, 1 H), 6.19 (dd, J = 4 and 3 Hz, 1 H), 7.00 (dd, J = 4 and 1.5 Hz, 1 H), 7.06 (dd, J = 3 and 1.5 Hz, 1 H); MS 206 (17), 205 (6), 177 (6), 176 (6), 164 (36), 136 (8), 135 (71), 134 (42), 120 (13), 106 (34), 94 (29), 71 (100), 69 (64); IR 3117 (w), 2968 (s), 2938 (m), 2878 (m), 2108 (vs), 1660 (brvs), 1527 (w), 1457 (m), 1416 (s), 1375 (s), 1356 (brs), 1312 (m), 1274 (vw), 1230 (w), 1185 (vw), 1145 (w), 1110 (vw), 1088 (w), 1065 (w), 1054 (brw), 1000 (brvw), 953 (w), 890 (vw), 610 cm^{-1} (vw); $[\alpha]^{20}_D$ = −171.2° (*c* 0.815, MeOH).

Anal. Calcd for $C_{12}H_{15}N_3O_2$: C, 61.79; H, 6.48; N, 18.01. Found: C, 61.77; H, 6.56; N, 17.52.

31. mp 42–44 °C; ^1H NMR δ 0.98 (t, J = 7.5 Hz, 3 H), 1.53 (d, J = 7 Hz, 3 H), 1.74 (sext, J = 7.5 Hz, 2 H), 2.58 (br dd, 1 H), 2.77 (t, J = 7.5 Hz, 2 H), 2.89 (br dd, 1 H), 5.48 (br s, 1 H), 5.67 (br sext, 1 H), 6.16 (dd, J = 4 and 3 Hz, 1 H), 7.01 (dd, J = 4 and 1.5 Hz, 1 H), 7.08 (dd, J = 3 and 1.5 Hz, 1 H); MS 219 (1), 191 (1), 176 (1), 164 (4), 149 (8), 148 (8), 143 (27), 125 (10), 107 (100), 91 (27), 79 (99), 77 (70), 71 (17), 51 (22); IR 3105 (w), 2968 (s), 2935 (m), 2875 (m), 2104 (vs), 1646 (brvs), 1523 (w), 1461 (m), 1450 (brw), 1412 (s), 1359 (brvs), 1332 (m), 1310 (m), 1294 (w), 1268 (vw), 1227 (m), 1187 (w), 1163 (vw), 1140 (brw), 1113 (w), 1085 (s), 1044 (brw), 1025 (vw), 965 (vw), 955 (w), 888 (vw), 645 (brvw), 603 cm^{-1} (w); $[\alpha]^{20}_D$ = −32.9° (*c* 1.085, MeOH).

Anal. Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.93; N, 16.99. Found: C, 62.89; H, 6.88; N, 16.94.

Arndt–Eistert Reactions. (3*R*)-3-(1*H*-Pyrrol-1-yl)hexanoic Acid (14) and (3*S*)-3-(2-Butyryl-1*H*-pyrrol-1-yl)butyric Acid (30). A solution of the α-diazo ketone **13** (4.5 g, 23.6 mmol) or **29** (4.43 g, 19 mmol) in THF/H_2O (2:1) was treated with AgOAc (0.3 equiv) at 25 °C for 30 min. A saturated aqueous solution of $NaHCO_3$ was added, and the mixture was washed with Et_2O. The aqueous layer was acidified with concentrated aqueous HCl and extracted again with Et_2O. The combined Et_2O extracts were washed with brine, dried ($MgSO_4$), and evaporated. The resulting brown oil was distilled bulb-to-bulb at 125 °C/0.3 Torr and at 175 °C/0.2 Torr giving **14** (3.4 g, 18.8 mmol, 80% yield) and **30** (3.86 g, 17.3 mmol, 91% yield), respectively.

14. ^1H NMR δ 0.95 (t, J = 7.5 Hz, 3 H), 1.12–1.36 (m, 2 H), 1.70–1.90 (m, 2 H), 2.80 (ABd syst, J = 16 and 6.5 Hz, 1 H), 2.85 (ABd syst, J = 16 and 7.5 Hz, 1 H), 4.37–4.48 (m, 1 H), 6.20 (t, J = 2.2 Hz, 2 H), 6.73 (t, J = 2.2 Hz, 2 H), 11.38 (br s, 1 H); MS 181 (M^+, 53), 139 (50), 122 (34), 94 (100), 80 (21), 68 (26), 67 (50), 55 (13); IR 3020 (vbrs), 2965 (s), 2938 (m), 2878 (m), 2650 (vbrm), 1715 (vs), 1488 (m), 1467 (w), 1418 (brm), 1382 (vw), 1332 (w), 1310 (w), 1280 (brm), 1260 (m), 1235 (w), 1214 (vw), 1190 (vw), 1116 (vw), 1088 (s), 1068 (w), 962 (vw), 933 (w), 719 (vs), 640 (w), 630 cm^{-1} (w); $[\alpha]^{20}_D$ = −20.0° (*c* 0.96, MeOH).

Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.05; H, 8.34; N, 7.69.

30. mp 55–57 °C; ^1H NMR δ 0.97 (t, J = 7.5 Hz, 3 H), 1.55 (d, J = 7 Hz, 3 H), 1.74 (sext, J = 7.5 Hz, 2 H), 2.70 (ABd syst, J = 16 and 7.5 Hz, 1 H), 2.76 (t, J = 7.5 Hz, 2 H), 2.92 (ABd syst, J = 16 and 6 Hz, 1 H), 5.75 (br sext, 1 H), 6.17 (dd, J = 4 and 3 Hz, 1 H), 7.00 (dd, J = 4 and 1.5 Hz, 1 H), 7.09 (dd, J = 3 and 1.5 Hz, 1 H), 10.46 (br s, 1 H); MS 223 (M^+, 19), 208 (2), 195 (3), 180 (6), 164 (10), 153 (12), 152 (8), 138(56), 137 (8), 136 (54), 120 (11), 109 (11), 94 (100), 71 (17), 66 (40); IR 3000 (vbrs), 2965 (s), 2932 (m), 2872 (m), 2650 (vbrm), 1714 (brvs), 1653 (brvs), 1523 (w), 1460 (m), 1413 (vs), 1377 (w), 1357 (w), 1330 (w), 1310 (m), 1285 (w), 1270 (w), 1225 (brm), 1206 (m), 1180 (vw), 1095 (brw), 1073 (w), 1043 (brw), 957 (w), 930 (vw), 888 (vw), 719 (vw), 640 (vw), 607 cm^{-1} (w); $[\alpha]^{20}_D$ = −25.2° (*c* 1.075, MeOH).

Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.37; H, 7.51; N, 6.25.

Cyclizations.[10,12] Decomposition of Diazo Ketones 15 and 31. (5*R*)-5,6-Dihydro-5-propyl-7(8*H*)-indolizinone (16) and (5*S*)-3-Butyryl-5,6-dihydro-5-methyl-7(8*H*)-indolizinone (32). To a solution of the corresponding α-diazo ketone **15** (0.41 g, 2 mmol) or **31** (0.37 g, 1.5

mmol) in CH_2Cl_2 was added $Rh_2(OAc)_4$ (0.004 g). A rapid evolution of N_2 was observed. After 30 min, the reaction mixture was concentrated by evaporation to 2 mL and purified by chromatography (Florisil) to give **16** (0.33 g, 1.86 mmol, 93% yield) or **32** (0.217 g, 0.99 mmol, 66% yield) accompanied by (5*S*)-8-[(*Z*)-1-hydroxybut-1-ylidene]-5-methyl-5,6-dihydro-7(8*H*)-indolizinone (**36**; 49 mg, 0.22 mmol, 15% yield).

16. ^1H NMR δ 0.96 (t, J = 7.2 Hz, 3 H), 1.30–1.50 (m, 2 H), 1.60–1.82 (m, 2 H), 2.65 (ABd syst, J = 16 and 4 Hz, 1 H), 2.90 (ABd syst, J = 16 and 5.5 Hz, 1 H), 3.63 (AB syst, J = 20 Hz, 1 H), 3.72 (AB syst, J = 20 Hz, 1 H), 4.32–4.41 (m, 1 H), 5.98 (br dd, J = 3 and 1 Hz, 1 H), 6.17 (t, J = 3 Hz, 1 H), 6.70 (dd, J = 3 and 1 Hz, 1 H); MS 177 (M^+, 56), 176 (3), 148 (20), 135 (27), 134 (16), 120 (22), 107 (78), 106 (100), 80 (37); $[\alpha]^{20}_D$ = 103.3° (*c* 0.97, MeOH).

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.32; H, 8.52; N, 7.94.

32. ^1H NMR δ 0.96 (t, J = 7.5 Hz, 3 H), 1.37 (d, J = 6.5 Hz, 3 H), 1.73 (sext, J = 7.5 Hz, 2 H), 2.61 (ABd syst, J = 16 and 2 Hz, 1 H), 2.75 (t, J = 7.5 Hz, 2 H), 2.89 (ABd syst, J = 16 and 6.5 Hz, 1 H), 3.63 (AB syst, J = 20 Hz, 1 H), 3.77 (AB syst, J = 20 Hz, 1 H), 5.88 (quin d, J = 6.5 and 2 Hz, 1 H), 6.00 (d, J = 4 Hz, 1 H), 7.00 (d, J = 4 Hz, 1 H); MS 219 (M^+, 37), 191 (14), 176 (69), 163 (15), 148 (44), 134 (20), 106 (100), 93 (9), 78 (44), 69 (28), 51 (39); IR 2964 (s), 2935 (m), 2902 (w), 2875 (m), 1738 (vs), 1647 (vs), 1480 (vs), 1442 (s), 1396 (s), 1378 (m), 1358 (vw), 1340 (vw), 1321 (m), 1262 (m), 1250 (brm), 1189 (m), 1158 (vw), 1127 (w), 1095 (vw), 1068 (m), 1056 (w), 1038 (w), 990 (vw), 948 (vw), 937 (vw), 885 cm^{-1} (vw); $[\alpha]^{20}_D$ (an accurate value could not be obtained owing to decomposition during the determination).

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.11; H, 7.94; N, 6.26.

36. ^1H NMR δ 1.02 (t, J = 7.5 Hz, 3 H), 1.44 (d, J = 6.5, 3 H), 1.67 (sext, J = 7.5 Hz, 2 H), 2.71 (ABt syst, J = 12.5 and 7.5 Hz, 1 H), 2.76 (ABt syst, J = 12.5 and 7.5 Hz, 1 H), 2.99 (ABd syst, J = 16 and 6.5 Hz, 1 H), 3.11 (ABd syst, J = 16 and 2.5 Hz, 1 H), 4.41 (quin d, J = 6.5 and 2.5 Hz, 1 H), 6.19 (dd, J = 4 and 2.5 Hz, 1 H), 6.58 (dd, J = 4 and 1.5 Hz, 1 H), 6.77 (s, 1 H), 6.79 (dd, J = 2.5 and 1.5 Hz, 1 H); MS 219 (M^+, 100), 191 (49), 190 (11), 176 (25), 174 (10), 163 (16), 162 (74), 148 (40), 134 (19), 120 (42), 92 (35), 77 (24), 65 (39); IR 3400 (brs), 2964 (s), 2935 (m), 2876 (m), 1641 (vs), 1591 (vs), 1460 (brw), 1370 (vs), 1350 (s), 1320 (vs), 1306 (s), 1288 (w), 1268 (w), 1255 (w), 1239 (vw), 1230 (vw), 1218 (w), 1179 (w), 1143 (m), 1120 (w), 1107 (vw), 1088 (m), 1074 (vw), 1050 (w), 1032 (vw), 923 (vw), 910 (vw), 713 (vs), 605 cm^{-1} (vw).

Hydrogenations. (5*R*,9*R*)-5-Propyloctahydroindolizine [(−)-Indolizine 167B] (1). A solution of **16** (60 mg, 0.34 mmol) in aqueous HCl (6 N, 20 mL) containing HOAc (2 mL) was hydrogenated over PtO_2 (77 mg, 0.34 mmol) at an initial pressure of 15 bar for 16 h.[15] The solution was filtered through Celite, neutralized by adding Na_2CO_3, and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (2 × 10 mL), dried ($MgSO_4$), and evaporated by distillation. The product was purified by chromatography (Al_2O_3, pH 9.5, pentane/Et_2O 10:1) to give **1** as a volatile oil (38 mg, 0.23 mmol, 67% yield). ^1H NMR δ 0.92 (t, J = 7.2 Hz, 3 H), 1.14–1.58 (m, 7 H), 1.58–2.10 (m, 10 H), 3.31 (td, J = 8.7 and 2 Hz, 1 H); δ (CF_3COOD) 1.05 (t, J = 7.2 Hz, 3 H), 1.34–1.85 (m, 6 H), 1.85–2.02 (m, 2 H), 2.10–2.36 (m, 5 H), 2.36–2.50 (m, 1 H), 3.06–3.26 (m, 3 H), 3.94 (ddd, J = 11.5, 8.7 and 4.2 Hz, 1 H); ^{13}C NMR δ 14.39, 19.03, 20.26, 24.47, 30.31, 30.40, 30.54, 36.52, 51.26, 63.76, 65.21; MS 167 (M^+, 1), 166 (2), 125 (10), 124 (100), 96 (23), 70 (8); $[\alpha]^{20}_D$ = −106.3° (*c* 0.800, *n*-hexane).

Anal. Calcd for $C_{11}H_{21}N$: C, 78.98; H, 12.65; N, 8.37. Found: C, 78.88; H, 12.68; N, 8.18.

(3*R*,5*S*,9*S*)-3-Butyloctahydro-5-methylindolizine [(+)-Monomorine] (2). A solution of **32** (30 mg, 0.137 mmol) in aqueous HCl (6 N, 10 mL) containing AcOH (1 mL) was hydrogenated over Pd/C (10%, 16 mg) at 10 bar for 20 h.[22] The resulting solution was filtered through Celite, basified by adding Na_2CO_3, and thereafter extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (2 × 10 mL), dried ($MgSO_4$), and evaporated. The residue was purified by chromatography (Al_2O_3, pH 9.5, pentane/Et_2O 10:1) to give **2** (13.6 mg, 0.07 mmol, 51% yield) accompanied by (1*RS*,3*S*,5*S*,9*S*)-3-(1-hydroxybutyl)octahydro-5-methylindolizine (**37**, 6.1 mg, 0.029 mmol, 21% yield) and (3*R*,5*S*,7*R*,9*R*)-3-butyloctahydro-5-methylindolizin-7-ol (**38**, 2.4 mg, 0.011 mmol, 8% yield).

2. ^1H NMR δ 0.82 (t, J = 7 Hz, 3 H), 1.07 (d, J = 6.5 Hz, 3 H), 1.10–1.80 (m, 16 H), 1.96–2.06 (m, 1 H), 2.12–2.22 (m, 1 H), 2.38–2.48 (m, 1 H); ^{13}C NMR δ 14.12, 22.64, 22.86, 24.85, 29.36, 29.71, 30.31, 30.86, 35.79, 39.72, 60.20, 62.82, 67.11; MS 195 (M^+, 1), 194 (1), 180 (2), 139 (9), 138 (100); $[\alpha]^{20}_D$ = 35.7° (*c* 0.370, *n*-hexane).

37. ^1H NMR δ 0.82 (t, J = 7 Hz, 3 H), 1.08 (d, J = 6.5 Hz, 3 H), 1.10–1.80 (m, 14 H), 2.10–2.26 (m, 1 H), 2.26–2.42 (m, 1 H), 2.65–2.77 (m, 1 H), 3.50–3.65 (m, 1 H).

38. ^1H NMR δ 0.84 (t, J = 7 Hz, 3 H), 1.11 (d, J = 6.5 Hz, 3 H), 1.14–1.34 (m, 7 H), 1.38–1.52 (m, 2 H), 1.56–1.67 (m, 2 H), 1.78–1.94 (m, 2 H), 2.05 (ddt, J = 11.5, 5.2 and 2 Hz, 1 H), 2.14 (tdd, J = 11, 5, and 2 Hz, 1 H), 2.28 (dqd, J = 8.5, 6.5, and 2.5 Hz, 1 H), 2.46 (tt, J = 9.5 and 2.5 Hz, 1 H), 3.64 (tt, J = 11 and 5 Hz, 1 H).

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