$[\alpha]^{20}D$ −104.3° (c 0.79, benzene); tlc R_f 0.55 [silica gel G, absolute methanol–benzene (15:85), sprayed with 50% sulfuric acid and developed at 120°].

Anal. Calcd for $C_{14}H_{19}O_4N$: C, 63.29; H, 7.22; N, 5.28. Found: C, 62.95; H, 7.20; N, 5.60.

N-Benzoylristosamine. Methyl *N*-benzoylristosaminide (111 mg) was hydrolyzed in 6.0 ml of 0.1 *N* hydrochloric acid for 1 hr on a steam bath. The cooled solution was neutralized to pH 7.0 with about 1.0 ml of Dowex 2 (OH^-) resin, filtered, and evaporated to dryness. On standing in the refrigerator, the compound **5** crystallized as fleecy needles. Recrystallization from distilled water gave 53.9 mg (51.3%), mp 131–133°, $[\alpha]^{20}D$ −14° (c 1, ethanol), after 10 min $[\alpha]^{20}D$ −11°, tlc R_f 0.25 (conditions described above).

Anal. Calcd for $C_{13}H_{17}O_4N$: C, 62.14; H, 6.81; N, 5.57. Found: C, 61.56; H, 6.69; N, 5.50.

N-Benzoyl-D-aspartic Acid from N-Benzoylristosamine. *N*-Benzoylristosamine (130 mg) and 135 mg of sodium periodate were dissolved in 4.0 ml of distilled water. The reaction mixture was then allowed to stand for 20 hr at room temperature in the darkness. In the meantime the pH of the mixture was maintained at 4–5 with 0.5 mol of sodium bicarbonate. At the end of the reaction time the solution was evaporated to dryness at a temperature not exceeding 30°. The residue was taken up with 5.0 ml of absolute ethanol and filtered and the solvent was removed. This latter procedure was repeated three times. The residual gum was dissolved in 11 ml of distilled water, and 1 g of calcium carbonate and 14 ml of aqueous bromine were added. The reaction mixture was allowed to stand for 20 hr at room temperature and then filtered. The excess bromine was expelled from the solution by sweeping with nitrogen gas. The mixture was agitated with 1 g of silver carbonate for 5 min and again filtered. The filtrate was acidified to a pH of 1–2 with Dowex 50 (H^+) resin. The solvent was removed to yield a light yellow gum which crystallized from absolute ethanol, 12.0 mg (~10%). Recrystallization from distilled water gave mp 163–165° (lit.[24] mp 163–164°), $[\alpha]^{25}D$ −14.6° (c 1.28, H_2O containing 2 equiv of sodium hydroxide) [lit.[24] $[\alpha]^{23}D$ −22.3° (c 1.3, H_2O containing 2 equiv of potassium hydroxide)].

The R_f values of 0.34 and 0.76, respectively, on silica gel G tlc in solvent mixtures *n*-propyl alcohol–ammonium hydroxide (70:30) and *sec*-butylalcohol–formic acid–water (75:15:10) were in agreement with those obtained from the *N*-benzoyl-L-aspartic acid prepared by us. The ir spectra were likewise identical.

Acknowledgment. We wish to express our appreciation to Miss Katie Reimer of Arizona State University for the exploratory nmr work at 100 MHz, and to Dr. Frederick Antosz and Professor Kenneth L. Rinehart for their help in securing the 220-MHz spectrum. Helpful discussion with Professor Peter Brown is gratefully acknowledged. We express our gratitude to the Hungarian Academy of Sciences for support of this research and the Analytical Laboratory of the Institute of Organic Chemistry of the Kossuth University for the microanalyses.

Registry No.—**1**, 51869-30-8; **1** picrate, 51869-31-9; **1** HCl, 51869-32-0; **2**, 51869-33-1; **2** HCl, 51869-34-2; **3**, 51869-35-3; **4**, 51869-36-4; **5**, 51869-37-5; **6**, 4915-59-7; ristomycin A, 11021-66-2; ristomycin A sulfate, 51932-11-7.

References and Notes

(1) G. F. Gauze, E. S. Kudrina, R. S. Ukholina, and G. V. Gavrilina, *Antibiotiki*, **8**, 387 (1963).
(2) V. A. Shorin, N. S. Pevzner, and S. P. Shapovalova, *Antibiotiki*, **8**, 396 (1963).
(3) M. G. Brazhnikova, N. N. Lomakina, F. Sztaricskai, M. Puskás, S. Makleit, and R. Bognar, *Kem. Kozlem.*, **27**, 143 (1967).
(4) N. N. Lomakina, L. A. Szpiridonova, R. Bognar, M. Puskás, and F. Sztaricskai, *Antibiotikl*, **13**, 975 (1968).
(5) N. N. Lomakina, R. Bognar, M. G. Brazhnikova, F. Sztaricskai, and L. Muravyeva, Abstracts, Seventh International Symposium on the Chemistry of Natural Products, Zinate, Riga, 1970, p 625.
(6) J. S. Dixon and D. Lipkin, *Anal. Chem.*, **26**, 1092 (1954).
(7) No conflicting structural information derives from the mass spectra of **2** and **3**.
(8) T. Reichstein and E. Weiss, *Advan. Carbohyd. Chem.*, **17**, 65 (1962).
(9) F. Arcamone, G. Cassinelli, P. Orezzi, G. Franceschi, and R. Mondelli, *J. Amer. Chem. Soc.*, **86**, 5335 (1964).
(10) J. F. Stoddart, "Stereochemistry of Carbohydrates," Wiley-Interscience, New York, N. Y., 1971, p 129.
(11) A. W. Johnson, R. H. Smith, and R. D. Guthrie, *J. Chem. Soc., Perkin Trans. 1*, 2153 (1972).
(12) M. Miyamoto, Y. Kawamatsu, M. Shinohara, K. Nakanishi, Y. Nakadaira, and N. S. Bhacca, *Tetrahedron Lett.*, 2371 (1964).
(13) L. D. Hall and J. F. Manville, *Advan. Chem. Ser.*, **74**, 228 (1968).
(14) W. D. Celmer and D. C. Hobbs, *Carbohyd. Res.*, **1**, 137 (1965).
(15) J. S. Brimacombe and D. Portsmouth, *Carbohyd. Res.*, **1**, 128 (1965).
(16) W. Hofheinz, H. Grisebach, and H. Friebolin, *Tetrahedron*, **18**, 1265 (1962).
(17) T. D. Inch, J. R. Plummer, and H. G. Fletcher, Jr., *J. Org. Chem.*, **31**, 1825 (1966); D. Horton, J. B. Hughes, J. S. Jewell, K. D. Philips, and W. N. Turner, *ibid.*, **32**, 1073 (1973); D. Horton, W. E. Mast, and K. D. Philips, *ibid.*, **32**, 1471 (1967); R. J. Cushey, K. A. Watanabe, and J. J. Fox, *J. Amer. Chem. Soc.*, **89**, 394 (1967).
(18) E. A. Davidson, "Carbohydrate Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1967, p 73.
(19) Johnson, *et al.*,[11] found that the nmr spectrum of methyl α-L-vancosaminide in [$^2H_5$]-pyridine provided the *only* example from among ten vancosamine derivatives where H-2e appeared upfield of H-2a. This was also the *only* spectrum run in [$^2H_5$]-pyridine.
(20) In tri-*O*-acetyl-β-D-xylopyranosyl chloride, H-5e is reported to resonate at higher field than H-5a: C. V. Holland, D. Horton, and J. S. Jewell, *J. Org. Chem.*, **32**, 1818 (1967).
(21) R. U. Lemieux and J. C. Stevens, *Can. J. Chem.*, **43**, 2059 (1965).
(22) J. Euw and J. Reichstein, *Helv. Chim. Acta*, **31**, 883 (1948).
(23) J. C. Speck and A. A. Forest, *Anal. Chem.*, **26**, 1942 (1954).
(24) H. H. Baer and F. Kienzle, *Can. J. Chem.*, **43**, 3074 (1965).

Alkaloid Studies. LXVIII.[1] Novel Piperidyl Alkaloids from *Lupinus formosus*

William L. Fitch, Peter M. Dolinger, and Carl Djerassi*

Department of Chemistry, Stanford University, Stanford, California 94305

Received May 13, 1974

Three new alkaloids, (+)-*N'*-methylammodendrine (**3**), *N*-acetylhystrine (**4**), and the biogenetically intriguing smipine (**9**), have been isolated from *Lupinus formosus* and their structures determined. Other alkaloids identified were hystrine (**1**), (+)-ammodendrine (**2**), (−)-anabasine (**5**), (−)-*N*-methylanabasine (**6**), lupinine (**7**), and *N*-methylpelletierine (**8**).

In conjunction with an ecological study comparing the predation patterns and alkaloidal contents of several Colorado *Lupinus* species,[2] we undertook an investigation of the alkaloids of a local species, *L. formosus* Greene, collected within a few miles of the Stanford Chemistry Department.

The alkaloids were isolated and identified by standard techniques. The two major alkaloids were hystrine (**1**)[3] and (+)-ammodendrine (**2**).[4] To our knowledge this is the first report of the occurrence of these bipiperidyl alkaloids in a *Lupinus* species,[5] although they have been found together in the related legume genus *Genista*.[6] (+)-Ammodendrine and racemic ammodendrine have been encountered in several genera of the Leguminosae.[7]

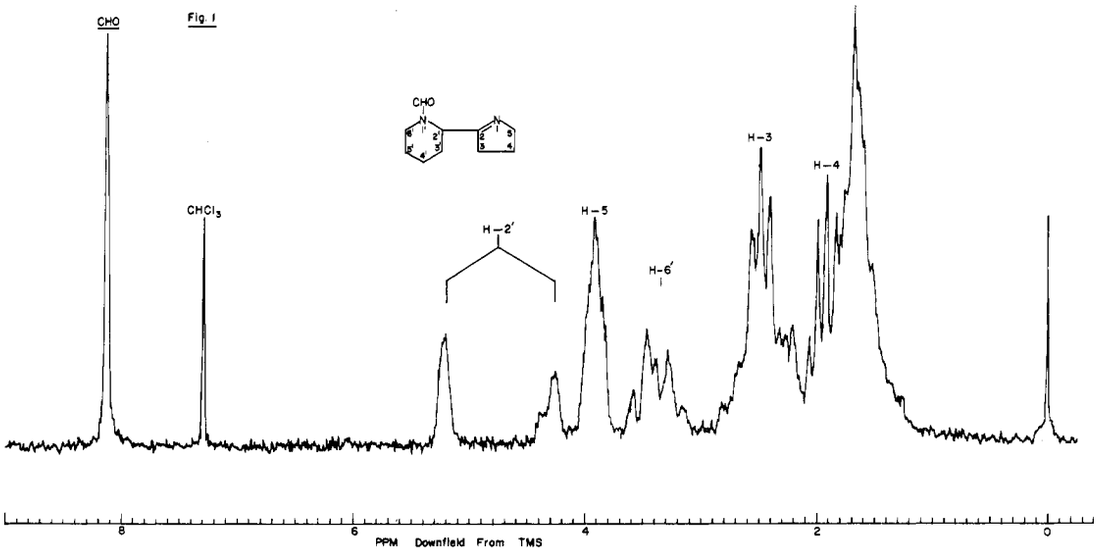


Figure 1. Nmr spectrum of smipine (**9**) at 100 MHz in $CDCl_3$.

The related compounds (+)-*N'*-methylammodendrine (**3**) and *N*-acetylhystrine (**4**) were also isolated from the

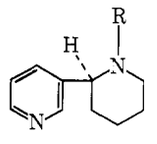
1, R = H
4, R = $COCH_3$

2, R = H
3, R = CH_3

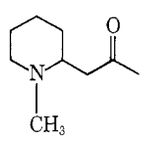
crude basic fraction in reasonable amounts. The former (**3**) was identified by its mass spectrum[8] (M^+ 222), and the similarity of its nmr spectrum with that of ammodendrine (**2**)[9] (excepting an *N*-methyl signal at δ 2.08). Confirmation of the structure was obtained by comparison with a sample prepared by methylation of (+)-ammodendrine.[10] The absolute configurations of (+)-**2** and (+)-**3** have been determined.[11] To our knowledge this is the first description of *N'*-methylammodendrine (**3**) as a natural product.

N-Acetylhystrine (**4**) was identified by its mass and nmr spectra. Confirmation was obtained by comparison with a sample synthesized by acetylation of hystrine (**1**).[3] In spite of a thorough search,[12] this fairly unstable alkaloid could not be found in the hystrine-containing plant *Genista hystrix*.

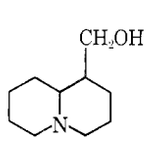
Several alkaloids present in *Lupinus formosus* in only trace amounts were identified by combined gas chromatography-mass spectrometry. These included the "tobacco" alkaloids (−)-anabasine (**5**)[13] and (−)-*N*-methylanabasine (**6**).[14] Also identified were the "pomegranate" alkaloid *N*-methylpelletierine (**7**)[13] and lupinine (**8**), the only conventional "lupine" alkaloid[7] isolated from this plant. These compounds were identified by comparison of their mass spectra and gas chromatographic retention times upon coinjection with authentic samples. It was possible to determine the ORD curves of **5** and **6** on small samples (*ca.* 0.5 mg) obtained by preparative gas chromatography. Unfortunately, sample limitations did not allow for comparable determinations on **7** or **8**. The identification of these trace components would have been impossible without the analytical power of gas chromatography–mass spectrometry.



5, R = H
6, R = CH_3



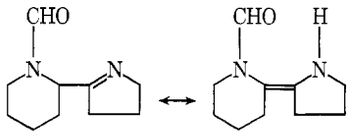
7



8

The most interesting alkaloid was named smipine (after the SMIP ranch near Stanford where some of the plant material was collected) and was assigned structure **9** on the basis of spectral evidence. High-resolution mass spectrometry and elemental analysis indicated the molecular formula $C_{10}H_{16}N_2O$. The mass spectrum displayed a small molecular ion (*m/e* 180) with significant peaks at *m/e* 163 (M − OH), 151 (M − CHO), 112 (M − C_4H_6N), 109 (base peak, M − C_3H_5NO), and 96 (M − C_4H_6NO). Diagnostically, the most informative peak was the one at *m/e* 112 which implied the loss of a five-membered nitrogen-containing ring (C_4H_6N) containing one degree of unsaturation. If that moiety and the formyl group (see M − CHO peak and appropriate nmr signal) are subtracted from the molecular formula, a piperidyl ring equivalent remains. Consequently, we started with the hypothesis that smipine was a bicyclic molecule consisting of a piperidine and a pyrroline ring.

Smipine was transparent in the ultraviolet above 210 nm, and optically inactive as evidenced by its optical rotatory dispersion curve. The equilibrium between the imine (**9**) and enamine (**10**) tautomeric forms would explain this lack of optical activity.[17] The infrared spectrum indicated

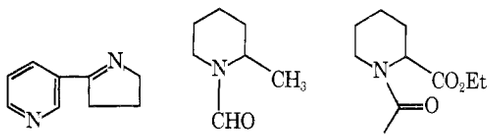


9 **10**

the presence of a tertiary amide (1670 cm^{-1}) and an isolated imine group (1645 cm^{-1}). No infrared absorption associated with NH, OH, or vinyl groups was observed.

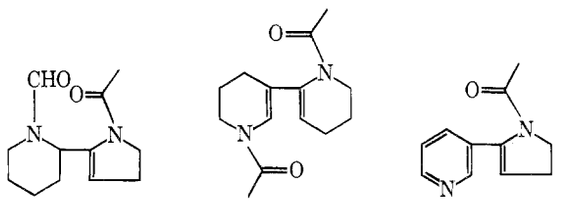
The nmr spectrum (Figure 1) of smipine indicated the presence of an *N*-formyl group (δ 8.15) as well as a 2-substituted 1-pyrroline [a two-hydrogen broad multiplet at δ 3.90, a broadened two-hydrogen triplet (J = 8 Hz) at δ 2.45, and a sharp two-hydrogen multiplet (J = 8 Hz) at δ 1.95]. The pyrroline assignment is supported by decoupling experiments as well as comparison with the nmr spectrum of myosmine (**11**).[18]

A complex set of broad peaks centered at δ 5.21, 4.25, and 3.35 and integrating for three protons is assigned to the α protons in a 2-substituted 1-acylpiperidine structure. This assignment is supported by comparison with the spectra of 1-formyl-2-methylpiperidine (**12**)[19] and ethyl 1-acetylpipecolinate (**13**) (see Experimental Section). The complex nature of these absorptions is due to restricted rotation about the amide bond.[19]



11 **12** **13**

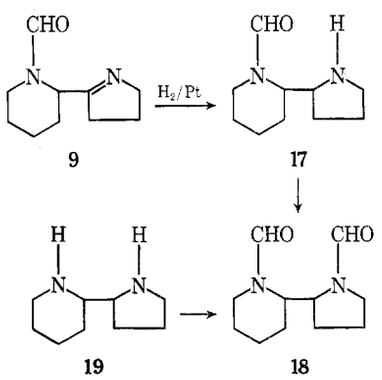
Acetic anhydride–pyridine acetylation of smipine yielded a monoacetyl derivative which was assigned structure **14** by analogy to the products **15** and **16** obtained by similar



14 **15** **16**

treatment of hystrine (**1**)[8] and myosmine (**11**).[20] The mass spectrum of acetylsmipine (**14**) (M^+ 222) displayed losses of 29 (M − CHO) and 43 (M − C_2H_3O) mass units. The ultraviolet spectrum (λ_{max} 244 nm, ϵ_{max} 7200) was indicative of a vinyl amide grouping [compare ammodendrine (**2**), λ_{max} 242 nm[9]]. The nmr spectrum indicated formyl (δ 8.15) and acetyl (δ 2.10) protons, the same diffuse peaks centered at δ 5.30, 4.10 and 3.50, and the resonances expected for a 2-substituted 1-acyl-2-pyrroline [a sharp one-proton triplet (J = 1–2 Hz) at δ 5.25, a two-proton triplet (J = 8 Hz) at δ 3.90, and a broadened two-proton triplet (J = 8 Hz) at δ 2.45]. These assignments are supported by comparison with the nmr spectrum (see Experimental Section) of acetylmyosmine (**16**).

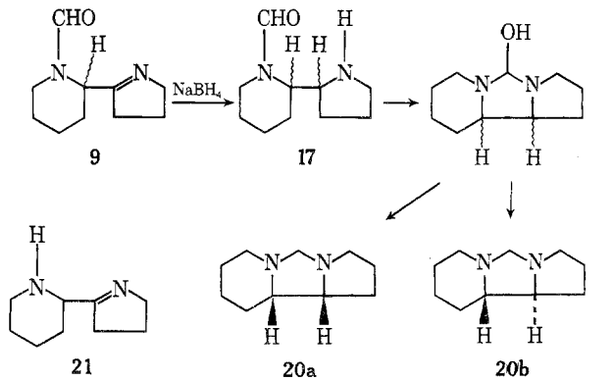
On catalytic hydrogenation (PtO_2–HOAc) smipine quickly took up 1 mol of hydrogen to give a dihydro derivative **17** which was difficult to isolate. It was characterized by formylation to **18**, which proved to be identical with a specimen prepared by diformylation of the known 2-(2-pyrrolidinyl)piperidine (**19**),[22] thus proving the skeletal structure of the alkaloid.



9 **17** **19** **18**

Further chemical support for the structure of smipine was provided by sodium borohydride reduction of the alkaloid, which led to a mixture of isomers shown to be identical with the syn and anti isomers of perhydropyrido[1,2-*c*]pyrrolo[2,1-*e*]imidazole (**20a** and **20b**).[21] As shown in Scheme I, these isomers can be formed by hydride attack on smipine (**9**) followed by cyclization and further reduction.

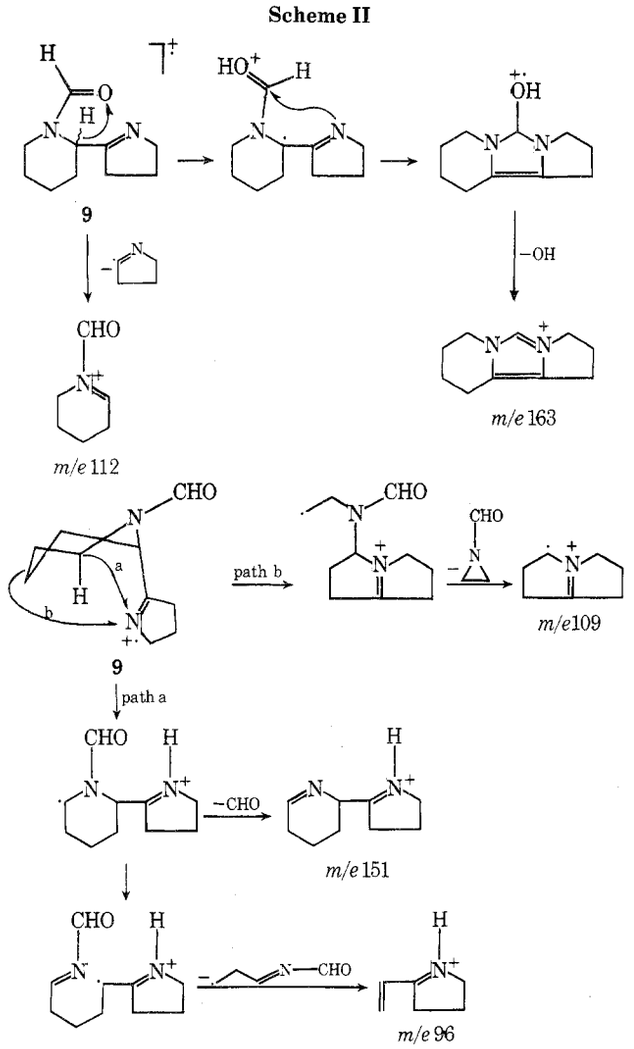
Scheme I



9 **17** **21** **20a** **20b**

With the structure of smipine (**9**) established, it is now possible to rationalize the mass spectral fragmentation in terms of the ion structures listed in Scheme II.

Scheme II

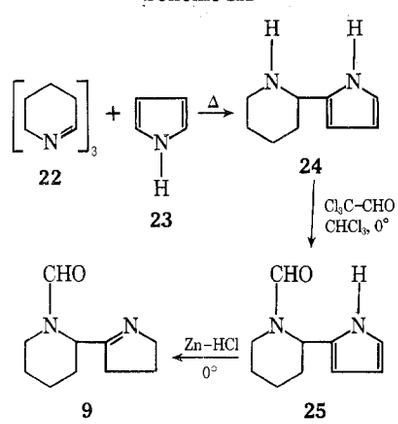


m/e 112 *m/e* 163 *m/e* 109 *m/e* 151 *m/e* 96

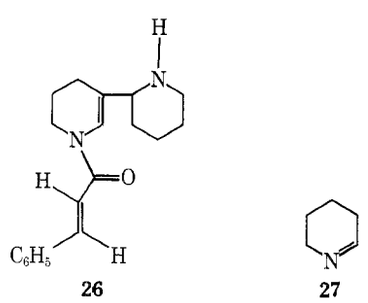
Owing to the unusual chemistry and unprecedented skeleton of smipine a total synthesis was undertaken to confirm the structure. The logical intermediates **17** and **21** proved too unstable to be converted to smipine. Smipine was finally synthesized by the reactions depicted in Scheme III. Condensation[22] of α-tripiperidine (**22**) with pyrrole (**23**) gave 2-(2-piperidyl)pyrrole (**24**), which on

chloral formylation[23] yielded the formyl derivative **25**. Zinc–hydrochloric acid reduction of pyrroles is known[24] to give mixtures of 1- and 3-pyrrolines. Unfortunately, the strong acid conditions necessary for the reduction also led to considerable hydrolysis of the amide function, and the best yield obtainable was only 10%. This synthetic material was identical in all respects with naturally occurring smipine, thus providing final confirmation for structure **9**.

Scheme III

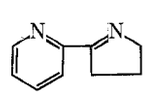


The alkaloids of *Lupinus formosus* all possess a common 2-substituted piperidine ring. In the well-studied cases, including anabasine (**5**),[25] *N*-methylpelletierine (**7**),[26] lupinine (**8**),[27] and the bipiperidyl alkaloid adenocarpine (**26**),[28] these structural units have been shown to arise from lysine, most likely *via* Δ^1-piperideine (**27**).[29] The co-occurrence of



bipiperidyl and lupine alkaloids is well precedented from several plants.[30,31]

How the unusual alkaloid smipine fits into this scheme is not clear. To our knowledge the only other naturally occurring compound possessing the 2-(2-pyrrolidinyl)piperidine skeleton is the bacterial metabolite, apoferrorosamine (**28**).[32]

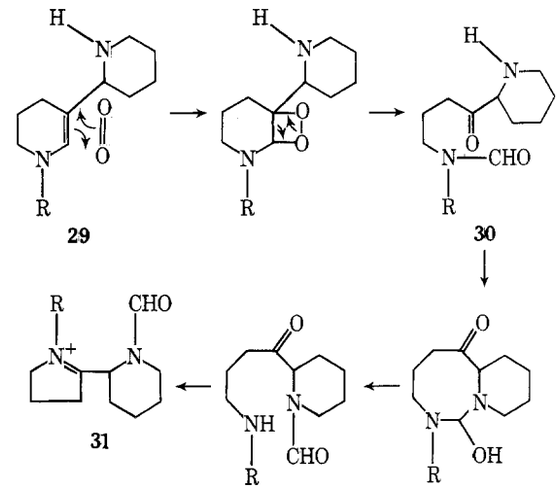


28

As smipine does not easily fit into the common Δ^1-piperideine biosynthetic scheme and considering that its molecular formula, $C_{10}H_{16}N_2O$, corresponds to a hystrine oxide or partially oxidized tetrahydroanabasine, we believe that smipine arises from an oxidative rearrangement of one of the major alkaloids.

One hypothetical scheme for such a transformation (Scheme IV) involves light-induced singlet oxygen cycloaddition to ammodendrine (**2**) or a tetrahydroanabasine analog **29**. Although the singlet oxygen reaction with enamides such as ammodendrine (**2**) has not been studied, $^1O_2$ is known to react with enamines to give dicarbonyl products in high yield.[33] The product from such an oxidative cleavage (**30**) after formyl transfer and recyclization would yield directly a smipine derivative (**31**).

Scheme IV



Experimental Section

Low-resolution mass spectra were recorded on Atlas CH-4 and AEI MS-9 mass spectrometers and are reported as *m/e* values with intensities in parentheses. High-resolution mass spectra were recorded on a Varian MAT-711 mass spectrometer. Combined gas chromatography–mass spectrometry was carried out on a Hewlett-Packard 7610 gas chromatograph (3% OV-17 on Gas-Chrom Q) interfaced through a Watson-Biemann dual stage separator to a Varian MAT-711 mass spectrometer. For infrared spectra, a Perkin-Elmer Model 700 spectrophotometer was used. Nmr spectra were obtained with either a Varian Model T-60 or HA-100 spectrometer, and are recorded in δ values with $CDCl_3$ as solvent unless otherwise stated.

Thin layer chromatograms on silica gel HF-254 as adsorbent were developed with ethyl acetate–hexane–diethylamine (7:7:2). Gas chromatography was carried out on OV-17 (3% on Gas-Chrom Q).

Authentic samples of alkaloids were obtained as follows. (±)-Ammodendrine was a gift from Professor R. R. Arndt, Rand Africaans University, Johannesburg, South Africa. (−)-Anabasine was obtained from Aldrich Chemical Co. (−)-*N*-Methylanabasine,[16] (+)-*N'*-methylammodendrine,[10] hystrine,[3] *N*-acetylhystrine,[3] and (±)-*N*-methylpelletierine[26] were synthesized by standard procedures.

Detailed mass spectral analyses of several of these alkaloids have been published elsewhere.[8]

Extraction and Isolation of Alkaloids. The plant material was collected in September 1971. The dried, ground, whole plants (3.3 kg) were extracted for 1 week with EtOH–CH_2Cl_2 (1:1) at room temperature. After removal of the solvents *in vacuo*, the extract was treated with 1 *N* HCl and washed with several portions of CH_2Cl_2. The aqueous layer was then basified to pH 12 and extracted first with ether and then with $CHCl_3$. The ether extract was evaporated to dryness and treated with acetone to give 7.5 g of a crude precipitate of hystrine hydrochloride (**1**). Purification by chromatography on alumina and recrystallization from MeOH–acetone gave pure hystrine hydrochloride. Chromatography of the acetone-soluble portion of the ether extract on alumina gave 5.5 g of fairly pure *N'*-methylammodendrine (**3**), 12 g of pure ammodendrine (**2**), and an additional 2 g of hystrine hydrochloride. Vacuum distillation of the impure *N'*-methylammodendrine failed to separate it from the contaminating ammodendrine but collection of the first drop of distillate gave a sample enriched in several volatile alkaloids. *N'*-Methylammodendrine could be obtained in a pure state by preparative tlc on silica gel.

N-Acetylhystrine (**4**) was not stable to any extended procedures and was isolated from the fresh crude ether extract by preparative tlc on silica gel followed by preparative gc.

Alumina chromatography of the chloroform extract gave an additional 1.2 g of hystrine hydrochloride as well as a new alkaloid smipine, which was purified by preparative gc.

Hystrine (**1**) was isolated as the hydrochloride (9.2 g, 0.23%), prisms from MeOH–acetone, mp 206–208°. *Anal.* Calcd for

$C_{10}H_{17}N_2Cl$: C, 59.84; H, 8.54; N, 14.00; Cl, 17.66. Found: C, 59.54; H, 8.39; N, 14.00; Cl, 17.71. It was identical with a synthetic sample[3] by mixture melting point and tlc.

(+)-Ammodendrine (2, 13 g, 0.39%) was a colorless oil, $C_{12}H_{20}N_2O$ (calcd mol wt 208.157, obsd 208.159 by high-resolution mass spectrum): $[\alpha]D$ +6.6° (*c* 3.9, EtOH); nmr δ 2.10, 2.14 (singlets split by conformation about N-1, 3 H, $COCH_3$), 2.64 [triplet (J = 11 Hz) of doublets (J = 3 Hz), 1 H, H-6′ axial], 3.05 (m, 2 H, H-2′, -6′ equatorial), 3.60 (m, 2 H, H-2), 6.55, 7.19 (singlets, vinyl hydrogen, two conformations). The perchlorate (from H_2O) had mp 210–211°. **2** was identical by ir, tlc, gc, and mass spectrum with an authentic sample.[9]

(+)-*N′*-Methylammodendrine (3, 2.5 g, 0.08%) was a colorless oil, $C_{13}H_{22}N_2O$ (calcd mol wt 222.173, obsd 222.173 by high-resolution mass spectrum): $[\alpha]D$ −40.5° (*c* 2.0, EtOH); ir (neat) 1640 cm^{-1} (C=O); nmr δ 2.08 (s, 3 H, NCH_3), 2.17, 2.14 (s, 3 H, $COCH_3$), 2.95 [doublet (J = 11 Hz) of triplets (J = 2–3 Hz), 1 H, H-6′ equatorial], 3.65 (m, 2 H, H-2), 6.56, 7.21 (s, 1 H, H-6). It was identical by ir, tlc, gc, and mass spectrum with a synthetic sample.[10]

***N*-Acetylhystrine (4)** (*ca.* 0.01% by gc analysis) was a colorless oil which rapidly yellowed in air, $C_{12}H_{18}N_2O$ (calcd mol wt 206.141, obsd 206.142 by high-resolution mass spectrum), nmr δ 2.20 (s, 3 H, $COCH_3$), 3.65 (m, 4 H, H-2, -6′), 7.18, 7.78 (s, 1 H, H-6). It was identical by gc, mass spectrum, and tlc with a synthetic sample.[3]

Analysis of Volatile Alkaloid Fraction. This fraction (20 mg) obtained as described above, was analyzed by combined gas chromatography–mass spectrometry. Compounds were identified by comparison of mass spectra and coinjection on gc with authentic samples. Small amounts of anabasine and *N*-methylanabasine were present in the crude *N′*-methylammodendrine fraction. By exhaustive preparative gas chromatography small samples (*ca.* 0.5 mg) of these alkaloids were obtained in a pure state. The amounts of lupinine and *N*-methylpelletierine did not allow for similar isolations.

(−)-Anabasine (5), mass spectrum *m/e* (rel intensity) 162 (M^+, 49), 161 (38), 133 (54), 119 (40), 105 (51), 84 (100), 80 (24), ORD (*c* ~0.01, EtOH) $[\alpha]_{275}$ −490°, $[\alpha]_{255}$ +1050°,[34] was identical by gc, mass spectrum, and ORD with an authentic sample.

(−)-*N*-Methylanabasine (6), mass spectrum *m/e* (rel intensity) 176 (M^+, 19), 175 (12), 147 (9), 133 (9), 119 (21), 98 (100), 42 (11), ORD (c ~0.01, EtOH) $[\alpha]_{275}$ −700°, $[\alpha]_{255}$ + 670°,[34] was identical by gc, mass spectrum, and ORD with a synthetic sample.[16]

***N*-Methylpelletierine (7),** mass spectrum *m/e* (rel intensity) 155 (M^+, 7), 112 (9), 98 (100), 96 (25), 82 (10), 70 (42), 41 (41), was identical by gc and mass spectrum with a synthetic sample.[26]

Lupinine (8), mass spectrum *m/e* (rel intensity) 169 (M^+, 60), 168 (52), 152 (100), 138 (74), 124 (30), 110 (49), 97 (64), 96 (50), 83 (88), 55 (40), 41 (32), was identical by gc and mass spectrum with an authentic sample. In an earlier paper,[2] the lupinine from *Lupinus bakeri* was thought to be epilupinine. However, it has since been shown by optical ($[\alpha]D$ −18.1° (*c* 0.27, EtOH)) and infrared (ν_{max} 3250 cm^{-1} for a dilute $CHCl_3$ solution) measurements to be (−)-lupinine.[36]

Smipine (9) (*ca.* 0.003%) was a colorless oil which rapidly yellowed on standing, $C_{10}H_{16}N_2O$ (calcd mol wt 180.126, obsd 180.126 by high-resolution mass spectrum). *Anal.* Calcd: C, 66.64; H, 8.95; N, 15.54. Found: C, 66.30: H, 8.98; N, 15.26.) Smipine showed no ultraviolet absorption above 230 nm and no optical activity to 200 nm by ORD measurements: ir 1660 (tertiary amide), 1640 cm^{-1} (shoulder, C=N); mass spectrum *m/e* (rel intensity) 180 (M^+, 3), 163 (2), 151 (14), 112 (11), 109 (100), 96 (74); nmr ($CHCl_3$, see Figure 1) (C_6D_6) 1.2–1.8 (8 H), 2.04 (t, 2 H, H-3′), 2.80 (m, 2 H, H-6′), 3.68 (br, 2 H, H-5), 4.44. 5.30 (br, 1 H, H-2′), 7.89 7.92 (s, 1 H, CHO).

Acetylation of Smipine. Treatment of smipine with excess acetic anhydride–pyridine at room temperature for 1 hr gave a monoacetyl derivative isolated by preparative gas chromatography. The colorless oil was assigned structure **14** [1-acetyl-2-(1-formyl-2-piperidyl)-2-pyrroline] on the basis of the spectral evidence: mass spectrum *m/e* (rel intensity) 222 (M^+, 24), 193 (M − CHO, 12), 179 (M − C_2H_3O, 44), 163 (71), 151 (100), 43 (55); ir 1665 cm^{-1}; uv (EtOH) λ_{max} 244 nm (ϵ_{max} 7200); nmr δ 8.15 (s, 1 H, CHO), 5.30 (t, J = 2 Hz, 1 H, H-3), 5.25, 4.10 (br, 1 H, H-2′), 3.90 (t, J = 8 Hz, 2 H, H-5), 3.50 (br, 2 H, H-6′), 2.55 (t, J = 8 Hz, 2 H, H-4), 2.10 (s, 3 H, $COCH_3$), 1.4–1.8 (6 H).

Borohydride Reduction of Smipine. Smipine (65 mg) was dissolved in absolute EtOH (20 ml), sodium borohydride (100 mg) was added, and the solution was refluxed overnight. After removal of the EtOH *in vacuo*, the residue was dissolved in 10% KOH, extracted with CH_2Cl_2, dried ($MgSO_4$), and evaporated to yield 45 mg of a colorless oil. Gas chromatography indicated a 3:2 mixture of two products which could be separated on a preparative scale. The two products showed identical mass spectra, *m/e* (rel intensity) 166 (M^+, 18), 165 (14), 97 (67), 96 (10), 83 (100); ir 2800, 2750 cm^{-1} (typical Bohlmann bands[36]), no carbonyl, imine, or NH peaks observed; nmr ($CHCl_3$ solution of the isomer mixture) distinctive doublets at δ 2.82 (J = 4 Hz), 3.10 (J = 7 Hz), 3.60 (J = 7 Hz), and 4.12 (J = 4 Hz), no vinyl peaks present. These products were shown to be identical with the syn and anti isomers of perhydropyrido[1,2-*c*]-pyrrolo[2,1-*e*]imidizoles **20a** and **20b** by comparison (gc, mass spectrum, nmr, ir) with a synthetic mixture of the isomers.[21]

Catalytic Hydrogenation of Smipine. Smipine (8.4 mg) was hydrogenated at 1 atm with PtO_2 in acetic acid at room temperature. After 1 hr 0.92 ml (0.88 equiv) of H_2 had been absorbed. Filtration and evaporation gave a colorless oil which was dissolved in formic acid (1 ml) and treated with acetic anhydride (0.5 ml). After 2 hr at 60°, the mixture was evaporated to dryness and the product was isolated by preparative gc. This material was identical by ir, gc, and mass spectrum with a sample synthesized as follows. 2-(2-Pyrrolidinyl)piperidine[21] (100 mg) was stirred at 60° for 2 hr with formic acid and acetic anhydride. Evaporation yielded the diformyl derivative **18** as a colorless oil: mass spectrum *m/e* (rel intensity) 210.137 (M^+, calcd for $C_{11}H_{18}N_2O_2$, 210.137, 10), 112 (100), 99 (59), 98 (25), 84 (35), 70 (23); nmr δ 1.3–2.2 (br, 10 H), 3.0–4.5 (complex, 6 H), 8.10 (br, 2 H).

2-(2-Piperidyl)pyrrole (24). Condensation of α-tripiperidine and pyrrole as described[22] gave 2-(2-piperidyl)pyrrole, which was obtained pure after vacuum sublimation and recrystallization from ethyl acetate: mp 96.5–97.5°; mass spectrum *m/e* (rel intensity) 150 (M^+, 100), 134 (34), 121 (86), 107 (38), 94 (96), 93 (67), 80 (38), 67 (30); nmr δ 1.4–2.0 (7 H), 2.5–3.2 (br, 2 H, H-6′), 3.80 (br, 1 H, H-2′), 5.95 (m, 2 H, H-3, -4), 6.52 (m, 1 H, H-5), 10.0 (br, 1 H, H-1).

2-(1-Formyl-2-piperidyl)pyrrole (25). A solution of pure **24** (2.5 g) in $CHCl_3$ (25 ml) was treated dropwise at 0° with chloral (3.0 g).[23] When the addition was complete, the mixture was allowed to warm to room temperature and stirred for 3 hr. It was then evaporated below 40° to a gum which crystallized on addition of a small amount of ether. Filtration and washing with cold ether gave 2.7 g (90%) of crude **25.** After recrystallization from ethyl acetate–hexane the pure material was obtained as colorless needles, mp 113–114°. *Anal.* Calcd for $C_{10}H_{14}N_2O$: C, 67.39; H, 7.92; N, 15.71. Found: C, 67.19; H, 7.83; N, 15.75. Mass spectrum *m/e* (rel intensity) 178 (M^+, 100), 161 (17), 149 (46), 134 (14), 121 (14), 93 (34), 80 (24); ir 3470, 3300 (NH), 1665 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.5–2.5 (6 H), 2.8–3.6, 4.05 (broad multiplets, 2 H, H-6′), 4.75, 5.60 (br, 1 H, H-2′), 6.05 (m, 2 H, H-3, -4), 6.65 (m, 1 H, H-5), 7.90 (s, 1 H, CHO), 9.7 (br, 1 H, H-1); nmr (C_6D_6) 4.35, 5.75 (br, 1 H, H-2′), 7.70, 7.85 (s, 1 H, CHO).

2-(1-Formyl-2-piperidyl)-1-pyrroline (Smipine 9). Zinc dust (200 mg) was added at 0–5° to 2 ml of 20% HCl. Then **25** (50 mg) was added and the solution was stirred for 0.5 hr, at which time concentrated HCl (2 ml) was added. Stirring at 0° was continued for an additional 4 hr. The cold solution was filtered, neutralized to pH 12 with K_2CO_3 and 30% KOH, and extracted with CH_2Cl_2. After drying and evaporation, 20 mg of reddish oil was obtained. Gc analysis indicated roughly equal amounts of starting material, an unstable product which could not be isolated (possibly the 3-pyrroline), and a peak which corresponded to smipine. Chromatography on neutral alumina (activity II) gave 5 mg of pure 2-(1-formyl-2-piperidyl)-1-pyrroline identical in all respects (gc, tlc, ir, mass spectrum, nmr) with natural smipine.

Acetylmyosmine (16). Myosmine[38] (30 mg) was stirred at room temperature overnight with acetic anhydride and pyridine. Evaporation and normal work-up gave 26 mg of a monoacetyl derivative **16**:[20] mass spectrum *m/e* (rel intensity) 188.095 (M^+, calcd for $C_{11}H_{12}N_2O$, 188.095, 29), 146 (71), 145 (100), 43 (19); nmr δ 1.95 (s, 3 H, $COCH_3$), 2.75 [triplet (J = 8 Hz) of doublets (J = 3 Hz), 2 H, H-4], 4.2 (t, J = 8 Hz, 2 H, H-5), 5.55 (t J = 3 Hz, 1 H, H-3), 7.25 [doublet (J = 8 Hz) of doublets (J = 4 Hz), 1 H, H-5′], 7.54 [doublet (J = 8 Hz) of triplets (J = 2 Hz), 1 H, H-4′], 8.4 (br, 2 H, H-2′, -6′).

Ethyl 1-Acetylpipecolinate (13). This compound was prepared as previously described:[37] nmr δ 2.6–3.9, 4.48, 5.25 (broad, complex, 3 H, H-2, -6), 4.16 (q, 2 H, CH_2CH_3), 1.25 (t, 3 H, CH_2CH_3), 2.05, 2.10 (singlets, 3 H, $COCH_3$); nmr (C_6D_6) 5.45, 4.57, 2.8–3.5 (complex, 3 H).

Acknowledgments. Financial support from the National Institutes of Health (Grants AM-04257 and RR 00612-05Al) is gratefully acknowledged. We also thank the proprietor of the SMIP Shorthorn Ranch (Woodside, Calif.) for facilitating the plant collection on his ranch.

Registry No.—1 HCl, 18017-52-2; **2**, 494-15-5; **3**, 52196-10-8; **4**, 52195-93-4; **5**, 494-52-0; **6**, 24380-92-5; **7**, 40199-45-9; **8**, 486-70-4; **9**, 52196-11-9; **13**, 52195-94-5; **14**, 52196-12-0; **16**, 52195-95-6; **18**, 52195-96-7; **20a**, 23972-23-8; **20b**, 23972-24-9; **24**, 52196-13-1; **25**, 52196-14-2.

References and Notes

(1) For part LXVII see L. J. Durham, C. Djerassi, and J. N. Shoolery, *Proc. Nat. Acad. Sci.*, in press.
(2) P. M. Dolinger, P. R. Ehrlich, W. L. Fitch, and D. E. Breedlove, *Oecologia*, **13**, 191 (1973).
(3) E. Steinegger and P. Weber, *Helv. Chim. Acta*, **51**, 206 (1968).
(4) C. Schöpf and F. Braun, *Naturwissenschaften*, **36**, 377 (1949).
(5) (±)-Ammodendrine was found as the major alkaloid in one of the Colorado species, *Lupinus bakeri*.[2]
(6) E. Steinegger and C. Moser, *Pharm. Acta Helv.*, **42**, 177 (1967).
(7) J. A. Mears and T. J. Mabry in "Chemotaxonomy of the Leguminosae," J. B. Harborne, D. Boulten, and B. L. Turner, Ed., Academic Press, New York, N. Y., 1971, Chapter 3.
(8) The unusual mass spectra of 1–4 and several related molecules have been discussed by W. L. Fitch and C. Djerassi, *J. Amer. Chem. Soc.*, in press.
(9) R. R. Arndt and L. M. DuPlessis, *J. S. Afr. Chem. Inst.*, **21**, 54 (1968).
(10) A. Orechoff and N. Proskurnina, *Chem. Ber.*, **68**, 1807 (1935).
(11) I. Ribas and A. Blanco, *An. Real Soc. Espan. Fis. Quim., Ser. B*, **57**, 781 (1961); *Chem. Abstr.*, **55**, 5738c (1961).
(12) E. Steinegger and E. Schnyder, *Pharm. Acta Helv.*, **45**, 156 (1970).
(13) R. F. Raffauf, "A Handbook of Alkaloids and Alkaloid-Containing Plants," Wiley-Interscience, New York, N. Y., 1970.
(14) *N*-Methylanabasine (**6**) appears to be a somewhat elusive compound. The only report of its isolation[15] could not be confirmed.[16]
(15) E. Späth and F. Kesztler, *Chem. Ber.*, **70**, 2450 (1937).
(16) E. Leete and M. R. Chedekel, *Phytochemistry*, **11**, 2751 (1972).
(17) K. Bláha and O.Cervinka, *Advan. Heterocycl. Chem.*, **6**, 0000 (1966).
(18) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, p 281.
(19) L. A. LaPlanche and M. T. Rogers, *J. Amer. Chem. Soc.*, **85**, 3728 (1963).
(20) F. Kuffner and T. Kirchenmayer, *Monatsh. Chem.*, **92**, 701 (1961).
(21) P. J. Chivers, T. A. Crabb, and R. O. Williams, *Tetrahedron*, **25**, 2921 (1969).
(22) D. W. Fuhlhage and C. A. VanderWerf, *J. Amer. Chem. Soc.*, **80**, 6249 (1958).
(23) F. F. Blicke and C. J. Lu, *J. Amer. Chem. Soc.*, **74**, 3933 (1952).
(24) G. G. Evans, *J. Amer. Chem. Soc.*, **73**, 5230 (1951).
(25) E. Leete, *J. Amer. Chem. Soc.*, **91**, 1697 (1969).
(26) M. F. Keough and D. G. O'Donovan, *J. Chem. Soc. C*, 1792 (1972).
(27) H. R. Schütte, H. Hindorf, K. Mothes, and G. Hubner, *Justus Liebigs Ann. Chem.*, **680**, 93 (1964).
(28) H. R. Schütte, K. L. Kelling, D. Knofel, and K. Mothes, *Phytochemistry*, **3**, 249 (1964).
(29) E. Leistner and I. D. Spenser, *J. Amer. Chem. Soc.*, **95**, 4715 (1973).
(30) G. Faugeras, *Ann. Pharm. Fr.*, **29**, 241 (1971).
(31) E. Steinegger and E. Schlunegger, *Pharm. Acta Helv.*, **45**, 369 (1970).
(32) M. Pouteau-Thouvenot, A. Gaudemer, and M. Barbier, *Bull. Soc. Chim. Biol.*, **47**, 2085 (1965).
(33) C. S. Foote and J. Wei-Ping Lin, *Tetrahedron Lett.*, 3267 (1968).
(34) Owing to the small sample size, these values are not accurate, but they compare qualitatively with the published ORD data for anabasine[35] and *N*-methylanabasine.[16]
(35) J. C. Craig and S. K. Roy, *Tetrahedron*, **21**, 401 (1965).
(36) N. J. Leonard in "The Alkaloids," Vol. 7, R. H. F. Manske, Ed., Academic Press, New York, N. Y., 1960, Chapter 14.
(37) F. P. Doyle, M. D. Mehta, G. S. Sach, R. Ward, and P. S. Sherman, *J. Chem. Soc.*, 578 (1963).
(38) F. Korte and H. Schulze-Steiner, *Chem. Ber.*, **95**, 2444 (1962).

Diamantane. I.[1] Preparation of Diamantane. Physical and Spectral Properties

Tamara M. Gund,[2a] Eiji Osawa,[2b] Van Zandt Williams, Jr.,[2c] and P. v. R. Schleyer*

Department of Chemistry, Princeton University, Princeton, New Jersey 08540

Received October 30, 1973

The preparation of diamantane (I) by Lewis acid catalyzed rearrangements of various pentacyclic tetradecanes has been examined. The best yield (84%) was obtained from *trans*-tetrahydro-Binor-S (XXXV). However, the most convenient synthetic procedure involves rearrangement of hydrogenated Binor-S (XXVII/XXVIII), which gives I in ~70% yield. Other more highly strained precursors give I in lower yield (1–47%) owing to disproportionation. The diamond lattice structure of diamantane, confirmed by X-ray analysis, is consistent with high thermodynamic stability. However, I, like adamantane, is not strain free. Molecular mechanics calculations show that this is due to an excess of repulsive over attractive nonbonded interactions in comparison with noncage hydrocarbons. The spectral properties of diamantane are characterized by a single-line proton nmr spectrum, resistance toward mass spectral fragmentation, and a simplified ir spectrum due to high symmetry.

The beautiful three-dimensional array of the diamond lattice has provided many structural insights and synthetic challenges.[3–5] Prelog[4] recognized that cyclodecane in conformation II is such a diamond lattice hydrocarbon and can be deduced from the pentacyclotetradecane I by replacing two CH and two CH_2 by six hydrogens.[6,7] At Prelog's suggestion, I (pentacyclo[7.3.1.1^{4,12}.0^{2,7}.0^{6,11}]tetradecane) was chosen as the Congress Emblem of the 1963 London IUPAC meeting, and was featured as a decoration on the cover of abstracts, program, and publicity material. The *Handbook* challenged the Congress participants to synthesize I, and this challenge was reiterated by Cram and Hammond on the end papers of their popular text.[4c] The first preparation of "Congressane" was achieved at Princeton in 1965 in 1% yield by aluminum halide catalyzed isomerization of a mixture of norbornene [2 + 2] photodimers.[8]

Adamantane (IV) is the first and "Congressane" only the second member of an entire family of compounds "whose ultimate is diamond."[7] The synthesis of the third member of the series (V) in 1966[9] emphasized the need for a more general scheme of semitrivial nomenclature. Following the suggestion of Vogl and Anderson,[7] I was renamed "diamantane" and V designated triamantane.[7] The synthesis of tetramantane (three isomers are possible)[10] and of higher "amantanes" has not yet been achieved.

The year 1966 also marked the isolation of diamantane (I) from the high-boiling fractions of the crude oil of Hodonin (from which adamantane was discovered)[11] and the