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Metabolites of the Marine Sponge *Laxosuberites* sp.

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The marine sponge *Laxosuberites* sp. contained a mixture of four 5-alkylpyrrole-2-carboxaldehydes **1**, (6′*Z*)-5-(12′-cyano-6′-dodecenyl)pyrrole-2-carboxaldehyde (**2**), and (6′*Z*)-5-(23′-cyano-23′-hydroxy-6′-tricosenyl)pyrrole-2-carboxaldehyde (**3**). The structures of the metabolites were determined by interpretation of spectral data and by chemical degradation. The cyanohydrin **3** is unusually stable to normal isolation and storage procedures.

In 1975, Cimino et al.[1] reported the isolation of a series of 3-alkylpyrrole-2-carboxaldehydes from the marine sponge *Oscarella lobularis*. During our studies on Indo-Pacific sponges, we obtained a group of alkylated pyrrole-2-carboxaldehydes from *Laxosuberites* sp. We have shown that these metabolites are pyrrole-2-carboxaldehydes substituted at the 5-position by various alkyl groups.

The sponge *Laxosuberites* sp. was collected from the inside of a pipe joining a seawater swimming pool to the lagoon at Canton Atoll. The sponge was kept frozen for about 1 year and then lyophilized. Extraction of the lyophilized sponge with cold ether gave an orange oil (1.4% dry weight) that was chromatographed on Florisil to obtain three fractions having interesting spectral data. The least polar fraction was crystallized from pentane to obtain a cocrystallizing mixture of four 5-alkylpyrrole-2-carboxaldehydes **1** (0.16% dry weight). More polar fractions contained the nitrile **2** (0.09% dry weight) and the cyanohydrin **3** (0.07% dry weight).

Although the mixture of 5-alkylpyrrole-2-carboxaldehydes **1** (Chart I) cocrystallized, the high-resolution mass spectrum indicated the presence of compounds having the molecular formulas $C_{20}H_{35}NO$, $C_{21}H_{37}NO$, $C_{22}H_{39}NO$, and $C_{24}H_{43}NO$. The mixture was not separated since the ^1H NMR spectrum indicated that the molecules differed only in the length of the alkyl side chain. The ^1H NMR spectrum contained an aldehyde proton signal at δ 9.29 (s, 1 H), two pyrrole proton signals at δ 6.82 (m, 1 H) and 5.99 (m, 1 H), both of which were coupled to a broad NH signal at 9.78 (br s, 1 H), and signals due to the alkyl side chain at δ 2.70 (t, 2 H, J = 7 Hz), 1.68 (m, 2 H), 1.25 (br s), 0.88 (t, 3 H, J = 7 Hz). Deuterium exchange of the NH proton converted the pyrrole proton signals to sharp doublets with a coupling constant of 3.7 Hz, a typical value for $J_{3,4}$ in pyrroles.[2a] The infrared (3400, 1640 cm^{-1}) and ultraviolet [297 nm (ϵ 16 000)] spectra were both typical of a pyrrole-2-carboxaldehyde.[2b] The ^{13}C NMR spectrum contained peaks at δ 178.1 (d), assigned to the aldehyde carbon, and at δ 145.0 (s), 132.5 (s), 123.9 (d), and 109.6 (d), assigned to the pyrrole carbons at C-5, C-2, C-3, and C-4, respectively.[3] The remaining ^{13}C NMR signals at δ 32.4 (t), 30.2 (many carbons), 29.8 (t), 28.1 (t), 23.1 (t), and 14.4 (q) were assigned to a combination of *n*-alkyl side chains. Combined gas chromatographic–mass spectral analysis indicated that the mixture consisted of approximately 46% 5-*n*-pentadecanylpyrrole-2-carboxaldehyde (**1**, n = 14), 12% 5-*n*-hexadecanylpyrrole-2-carboxaldehyde (**1**, n = 15), 23% 5-*n*-heptadecanylpyrrole-2-carboxaldehyde (**1**, n = 16), and 19% 5-*n*-nonadecanylpyrrole-2-carboxaldehyde (**1**, n = 18).

Chart I

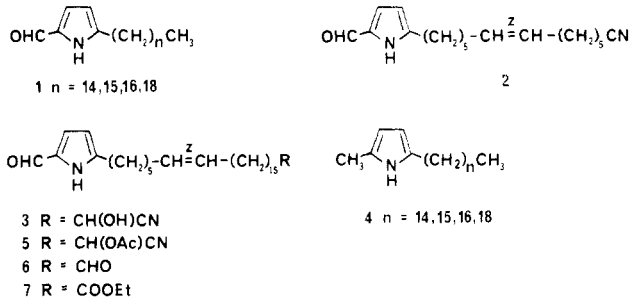
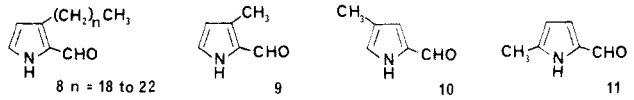


Table I. ^1H NMR Chemical Shift Data for Alkylated Pyrrole-2-carboxaldehydes[a]



	chemical shift, ppm					
compd	CHO	H-3	H-4	H-5	CH_3	J, Hz
1	9.29	6.82	5.99			3.7
8	9.22		5.94	6.76		2.4
9	9.53		6.02	7.04	2.40	1.9
10	9.32	6.69		6.96	2.13	
11	9.23	6.81	5.96		2.43	3.4

[a] The coupling constant (J) between the two pyrrole protons was measured in D_2O-exchanged spectra.

Reduction of the mixture of 5-alkylpyrrole-2-carboxaldehydes **1** with lithium aluminum hydride in ether at 25 °C gave the corresponding 5-alkyl-2-methylpyrroles **4**.[4] The ^1H NMR spectrum contained signals for the alkyl side chains together with signals at δ 5.75 (d, 2 H, J = 3 Hz), assigned to the protons on a 2,5-dialkyl pyrrole, and δ 2.24 (s, 3 H), due to a methyl group on the pyrrole ring. These data confirmed that the aldehydes **1** were 5-alkylpyrrole-2-carboxaldehydes and not the 3-alkylpyrrole-2-carboxaldehydes **8** reported to be isolated from *O. lubularis*.

Comparison of the spectral properties of the 5-alkylpyrrole-2-carboxaldehydes **1** with those of the 3-alkylpyrrole-2-carboxaldehydes **8** reported by Cimino et al.[1] revealed surprisingly few differences. The most significant difference was in the coupling constants between the pyrrole protons in the D_2O-exchanged ^1H NMR spectra, for Cimino et al.[1] had assigned the substitution pattern about the pyrrole ring on the basis of that coupling constant ($J_{4,5}$ = 2.4 Hz). We therefore prepared 3-methylpyrrole-2-carboxaldehyde (**9**), 4-methylpyrrole-2-carboxaldehyde (**10**), and 5-methylpyrrole-2-carboxaldehyde (**11**) and measured the ^1H NMR spectra (Table I). The chemical shift data for aldehyde **8** were closer to those of

(1) Cimino, G.; de Stefano, S.; Minale, L. *Experientia* **1975**, *31*, 1387.
(2) (a) Jones, R. A.; Bean, G. P. "The Chemistry of Pyrroles"; Academic Press: New York, 1977; p 473. (b) *Ibid.*, p 471. (c) *Ibid.*, p 477.
(3) ^{13}C NMR spectra were measured for model compounds **9**–**11** (see Experimental Section) and assigned by using the table in ref 2c. Corrections for the replacement of methyl by alkyl are +5.5 ppm for the carbon bearing the alkyl group and −1.5 ppm for the adjacent pyrrole carbon.
(4) Hinman, R. L.; Theodoropulos, S. *J. Org. Chem.* **1963**, *28*, 3052.

0022-3263/80/1945-4980$01.00/0

5-methylpyrrole-2-carboxaldehyde (11) than to those of the other two isomers, but the coupling constant between the pyrrole protons in 8 lay between those measured for 9 and 11. These data suggest that the metabolites of *O. lobularis* should be reinvestigated, for it would be remarkable if one sponge produced 3-alkylpyrrole-2-carboxaldehydes while the other produced 5-alkylpyrrole-2-carboxaldehydes.

The nitrile 2 had the molecular formula $C_{18}H_{26}N_2O$. The infrared spectrum indicated the presence of pyrrole-carboxaldehyde (3460, 1630 cm^{-1}) and nitrile (2250 cm^{-1}) functionalities. The ultraviolet spectrum [297 nm (ϵ 15 300)] was typical of a pyrrole-2-carboxaldehyde. The ^1H NMR spectrum contained signals at δ 9.35 (s, 1 H), 6.91 (m, 1 H), and 6.09 (m, 1 H), assigned to the pyrrole-2-carboxaldehyde moiety, two olefinic proton signals at δ 5.34 (m, 2 H) and signals at 2.68 (t, 2 H, J = 7 Hz), 2.32 (t, 2 H, J = 7 Hz), and 2.00 (m, 4 H) due to methylene groups adjacent to the pyrrole ring, the nitrile, and the olefin, respectively. The ^{13}C NMR spectrum confirmed the presence of the aldehyde [δ 178.1 (d)], pyrrole [δ 144.5 (s), 132.5 (s), 123.5 (d), 109.6 (d)], olefin [130.2 (2 d)], and nitrile [119.5 (s)] functional groups. The presence of signals at δ 27.6 (t) and 28.8 (t), with no signals in the range 31–35 ppm, indicated that the olefinic bond had the Z geometry.[5] The position of the olefinic bond was determined from the mass spectrum, which contained signals at m/e 150 and 204 that result from allylic cleavage of the side chain.

The cyanohydrin 3, obtained as a low-melting solid, had the molecular formula $C_{29}H_{48}N_2O_2$. The mass spectrum did not show a molecular ion due, presumably, to thermal elimination of hydrogen cyanide. However, the corresponding acetate 5, prepared by treatment of the cyanohydrin with acetic anhydride in pyridine, contained a strong molecular ion signal at m/e 498.383, corresponding to $C_{31}H_{50}N_2O_3$. The ultraviolet spectrum [297 nm (ϵ 16 100)] again indicated the presence of a pyrrole-2-carboxaldehyde moiety. The infrared spectrum contained bands at 3400 (OH and NH), 2250 (CN), and 1640 cm^{-1} (CHO). The presence of an α-cyanohydrin functionality was revealed by signals at δ 4.50 (t, 1 H, J = 7 Hz) in the ^1H NMR spectrum and at δ 120.9 (s) and 61.3 (d) in the ^{13}C NMR spectrum [cf. 2-hydroxynonyl cyanide: δ 4.46 (t, 1 H, J = 7 Hz); 120.8 (s), 61.2 (d)]. The ^{13}C NMR spectrum also contained signals at δ 178.4 (d), due to the aldehyde carbon, at δ 144.7 (s), 132.3 (s), 124.1 (d), and 109.8 (d), due to the pyrrole carbons, and at δ 130.3 (d), 130.2 (d), 27.6 (t), and 27.5 (t), assigned to the olefinic and allylic carbons of a Z-disubstituted olefin. Again the mass spectrum contained peaks at m/e 150 and 204, indicating that the olefinic bond was separated from the pyrrole ring by five methylene groups.

In order to confirm the position of the olefinic bond, we converted the cyanohydrin into a derivative suitable for degradation in an ozonolysis reaction. The corresponding dialdehyde 6 was prepared by treatment of the cyanohydrin 3 with sodium methoxide in methanol at 25 °C for 2 h. Oxidation of the dialdehyde 6 with Jones reagent gave an acid that was converted into the corresponding ethyl ester 7 with ethanolic hydrogen chloride. Ozonolysis of the ethyl ester at −78 °C, followed by hydrogenation of the ozonide, oxidation of the product with Jones reagent, and esterification with diazomethane, gave ethyl 16-(carbomethoxy)hexadecanoate as the only product isolated. The diester must have originated from the cyanohydrin side of the olefinic bond. The cyanohydrin 3 was therefore assigned the structure (6′Z)-5-(23′-cyano-23′-hydroxy-6′-tricosenyl)pyrrole-2-carboxaldehyde. The isolation of a stable cyanohydrin was unexpected, particularly since no especially mild conditions were employed.

(5) Cf.: (*Z*)-6-dodecene, δ 14.3 (C-1), 23.4 (C-2), 32.1 (C-3), 30.4 (C-4), **28.0** (C-5); (*E*)-6-dodecene, 14.3 (C-1), 23.3 (C-2), 32.5 (C-3), 30.0 (C-4), **33.7** (C-5).

Experimental Section[6]

Collection and Extraction. *Laxosuberites* sp. (reference no. 78-018) was collected from the inside of a pipe (3 ft in diameter) joining a seawater swimming pool with the lagoon at Canton Island (2°50′S, 171°42′W). The sponge was immediately frozen and stored at −20 °C for approximately 1 year. The sponge was then lyophilized to obtain 400 g of dry material that was extracted with cold ether (2 L). The ether extract was filtered and the solvent evaporated to obtain an orange oil (5.5 g, 1.4% dry weight).

Chromatographic Separation. The crude extract (3.0 g) was applied to a column (55 × 3 cm diameter) of Florisil and fractions were eluted with solvent mixtures of increasing polarity from hexane through ether to ethyl acetate. Fractions eluted with 10% ether in hexane gave a solid that was recrystallized from pentane to obtain a mixture of alkylated pyrrole-2-carboxaldehydes 1 (350 mg, 0.16% dry weight). Fractions eluted with 30% ether in hexane were combined and rechromatographed on a column (20 × 2 cm diameter) of silica gel with 20% ether in hexane as the eluant to separate the nitrile 2 (200 mg, 0.09% dry weight) and the cyanohydrin 3 (150 mg, 0.07% dry weight).

5-Alkylpyrrole-2-carboxaldehydes 1: UV (CH_3CN) 297 nm (ϵ 16 000); IR (CCl_4) 3400, 2750, 1640, 1225, 920 cm^{-1}; ^1H NMR (CCl_4) δ 0.88 (t, 3 H, J = 7 Hz), 1.25 (br s, ~26.5 H), 1.68 (m, 2 H), 2.70 (t, 2 H, J = 7 Hz), 5.99 (m, 1 H), 6.82 (m, 1 H), 9.29 (s, 1 H), 9.78 (br s, 1H); addition of D_2O gave δ 5.99 (d, 1 H, J = 3.7 Hz), 6.82 (d, 1 H, J = 3.7 Hz); ^{13}C NMR (C_6D_6) δ 178.1 (d), 145.0 (s), 132.5 (s), 123.9 (d), 109.6 (d), 32.4 (t), 30.2 (~11 C), 29.8 (t), 28.1 (t), 23.1 (t), 14.4 (q); mass spectrum, m/e 361, 333, 319, 305, 122, 108; high-resolution mass measurement, calcd for $C_{24}H_{43}NO$ m/e 361.3344, $C_{22}H_{39}NO$ m/e 333.3031, $C_{21}H_{37}NO$ m/e 319.2875, $C_{20}H_{35}NO$ m/e 305.2719; found m/e 361.3368, 333.3009, 319.2879, 305.2711.

(6′*Z*)-5-(12′-Cyano-6′-dodecenyl)pyrrole-2-carboxaldehyde (2): UV (CH_3CN) 297 (ϵ 15 300); IR ($CHCl_3$) 3460, 2750, 2250, 1630, 1480, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (br s, 8 H), 1.66 (m, 4 H), 2.00 (m, 4 H), 2.32 (t, 2 H, J = 7 Hz), 2.68 (t, 2 H, J = 7 Hz), 5.34 (m, 2 H), 6.09 (m, 1 H), 6.91 (m, 1 H), 9.35 (s, 1 H); ^{13}C NMR (C_6D_6) δ 178.1 (d), 144.5 (s), 132.5 (s), 130.2 (d, 2 C), 123.5 (d), 119.5 (s), 109.6 (d), 30.1 (14 C), 29.7 (t), 29.1 (t), 28.8 (t), 27.6 (t), 25.5 (t), 16.7 (t); mass spectrum, m/e (relative intensity) 286 (<1), 260 (1.6), 204 (5.7), 150 (19), 122 (100), 108 (97); high-resolution mass measurement, calcd for $C_{17}H_{26}NO$ (M − CN) m/e 260.2014, found m/e 260.2014.

(6′*Z*)-5-(23′-Cyano-23′-hydroxy-6′-tricosenyl)pyrrole-2-carboxaldehyde (3): mp 38–40 °C; $[\alpha]_D$ 0°; UV (CH_3CN) 297 nm (ϵ 16 100), IR (CCl_4) 3400, 2750, 2250, 1640, 1510, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (br s, 32 H), 1.84 (m, 2 H), 2.01 (m, 4 H), 2.66 (t, 2 H, J = 7 Hz), 4.50 (t, 1 H, J = 7 Hz), 5.35 (m, 2 H), 6.09 (m, 1 H), 6.92 (m, 1 H), 9.34 (s, 1 H); ^{13}C NMR (C_6D_6) δ 178.4 (d), 144.7 (s), 132.3 (s), 130.3 (d), 130.2 (d), 124.1 (d), 120.9 (s), 109.8 (d), 61.3 (d), 35.5 (t), 30.1 (14 C), 29.7 (t), 29.3 (t), 28.0 (t), 27.6 (t), 27.5 (t), 24.9 (t); mass spectrum, m/e 429 (M − HCN), 204, 150, 122, 108; high-resolution mass measurement, calcd for $C_{28}H_{47}NO_2$ m/e 429.3607, found m/e 429.3623.

Reduction of Aldehydes 1 with Lithium Aluminum Hydride. Lithium aluminum hydride (20 mg) was added to a solution of the mixture of aldehydes 1 (20 mg, 0.07 mmol) in anhydrous ether (5 mL), and the reaction mixture was stirred at 25 °C for 10 min. Excess reagent was destroyed by dropwise addition of water followed by 5% hydrochloric acid. The ether layer was separated and dried over sodium sulfate, and the solvent was evaporated to obtain an oil (18 mg). The oil was chromatographed on a silica gel plate with 2:1 hexane–ether as the eluant to obtain a mixture of pyrroles 4: 6 mg (30% theoretical); UV (EtOH) 242 (ϵ 700); IR (CCl_4) 3450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, 3 H, J = 7 Hz), 1.25 (br s), 2.24 (s, 3 H), 2.53 (t, 2 H, J = 7

(6) For general procedures, see: Djura, P.; Stierle, D. B.; Sullivan, B.; Faulkner, D. J.; Arnold, E.; Clardy, J. *J. Org. Chem.* **1980**, *45*, 1435.

Hz), 5.75 (d, 2 H, J = 3 Hz); mass spectrum, m/e 347, 319, 305, 291.

Acetylation of the Cyanohydrin 3. A solution of the cyanohydrin **3** (20 mg, 0.05 mmol) in acetic anhydride (0.5 mL) and pyridine (1.0 mL) was stirred at 25 °C for 2 h. The solvents were removed under vacuum to obtain the cyanohydrin acetate **5**: 22 mg (quantitative); UV (MeOH) 298 (ϵ 14 500); IR ($CHCl_3$) 2750, 2260, 1720, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (br s, 28 H), 1.65 (m, 4 H), 1.91 (m, 2 H), 2.03 (m, 4 H), 2.14 (s, 3 H), 2.61 (t, 2 H, J = 7 Hz), 5.31 (t, 1 H, J = 7 Hz), 5.35 (br s, 2 H), 6.06 (m, 1 H), 6.90 (m, 1 H), 9.34 (s, 1 H), 9.55 (br s, 1 H); high-resolution mass measurement, calcd for $C_{31}H_{50}N_2O_3$ m/e 498.3821, found m/e 498.3830.

Dialdehyde 6. Sodium methoxide (30 mg) was added to a solution of the cyanohydrin **3** (60 mg, 0.16 mmol) in 1:1 chloroform–methanol (30 mL), and the mixture was stirred at 25 °C for 2 h under an atmosphere of nitrogen. The reaction mixture was poured into 5% hydrochloric acid (15 mL), the chloroform layer separated, and the aqueous phase was washed with chloroform (2 × 10 mL). The combined extracts were dried over sodium sulfate, and the solvent was evaporated to obtain an oil (60 mg). Chromatography of the oil on a silica gel plate with ether as eluant gave the dialdehyde **6** (30 mg, 60% theoretical) and recovered cyanohydrin (10 mg). For dialdehyde **6**: UV (MeOH) 297 nm (ϵ 14 000); IR (CCl_4) 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (br s, 24 H), 1.62 (br s, 8 H), 2.02 (m, 4 H), 2.42 (dt, 2 H, J = 7,2 Hz), 2.65 (t, 2 H, J = 7 Hz), 5.34 (m, 2 H), 6.07 (m, 1 H), 6.88 (m, 1 H), 9.20 (br s, 1 H), 9.35 (s, 1 H), 9.75 (t, 1 H, J = 2 Hz); high-resolution mass measurement, calcd for $C_{28}H_{47}NO_2$ m/e 429.3607, found m/e 429.3591.

Ethyl Ester 7. Jones reagent was added dropwise to a stirred solution of the dialdehyde **6** (30 mg, 0.09 mmol) in acetone (5 mL) at 0–5 °C until the solution remained orange. After 5 min, excess reagent was destroyed by addition of 2-propanol (1 drop). The solution was filtered through silica gel and the solvent evaporated. The crude product was dissolved in anhydrous ethanol (10 mL) containing hydrogen chloride, and the solution was stirred for 24 h at 25 °C. The solvent was evaporated under vaccum and the product purified by chromatography on a silica gel plate with 1:1 ether–hexane as the eluant to give the ethyl ester **7**: 22 mg (65% theoretical); IR ($CHCl_3$) 1740, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (br s, 30 H), 1.66 (m, 4 H), 2.02 (m, 4 H), 2.30 (t, 2 H, J = 7 Hz), 2.67 (t, 2 H, J = 7 Hz), 4.15 (q, 2 H, J = 7 Hz), 5.35 (m, 2 H), 6.10 (m, 1 H), 6.91 (m, 1 H), 9.48 (s, 1 H); mass spectrum, m/e 473.

Ozonolysis of Ester 7. A stream of ozone in oxygen was bubbled through a solution of the ester **7** (20 mg, 0.07 mmol) in ethyl acetate (10 mL) at −78 °C until a blue solution was obtained. After 5 min, excess ozone was removed in a stream of nitrogen while the solution warmed to ~0 °C. Palladium on carbon catalyst (10%, 5 mg) was added, and the solution was stirred under an atmosphere of hydrogen for 2 h. The catalyst was removed by filtration and the solvent evaporated to obtain an oil. The oil was oxidized by using Jones reagent as outlined above. The crude product was dissolved in ether, and ethereal diazomethane solution was added until a pale yellow solution resulted. The solvent was evaporated under vacuum and the product chromatographed on a silica gel plate with 25% ether in hexane as the eluant to obtain ethyl 16-(carbomethoxy)hexadecanoate: 4 mg (50% theoretical); IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (m, 25 H), 1.61 (m, 4 H), 2.28 (m, 4 H), 3.70 (s, 3 H), 4.12 (q, 2 H, J = 7 Hz); mass spectrum, m/e 342.

Cyanohydrin of Nonanal.[7] Nonanal (3.3 g, 25 mmol) was dissolved in 1 N sodium bisulfite solution (30 mL) at 50 °C, and the solution was cooled to −5 °C by using an ice–salt bath. The solution was covered with ether (20 mL), and a solution of sodium cyanide (4.75 g, 28 mmol) in water (8 mL) was added dropwise, keeping the temperature of the reaction mixture below 0 °C. The mixture was stirred at 0 °C for 40 min. The organic layer was separated, washed with 1 N sodium bisulfite solution (5 mL) and water (10 mL), and dried over anhydrous sodium sulfate, and the solvent was evaporated to give the cyanohydrin: 2.5 g (70% theoretical) as an oil; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3 H, J = 7 Hz), 1.31 (br s, 10 H), 1.84 (m, 2 H), 4.46 (t, 1 H, J = 7 Hz); ^{13}C NMR (C_6D_6) δ 120.8 (s), 61.2 (d), 35.4 (t), 32.2 (t), 29.7 (t), 29.6 (t), 29.3 (t), 24.9 (t), 23.0 (t), 14.2 (q).

3-Methylpyrrole-2-carboxaldehyde (9) and 4-Methylpyrrole-2-carboxaldehyde (10).[8] Phosphorus oxychloride (2.07 g, 12.3 mmol) was added dropwise to dimethylformamide (0.98 g, 12.3 mmol) at 0 °C, and the mixture was stirred at 0–20 °C for 15 min. Ethylene chloride (5 mL) was added, and the solution was cooled to 5 °C. A solution of 3-methylpyrrole[9] (1.0 g, 12.3 mmol) in ethylene dichloride (2 mL) was added dropwise, and the mixture was then boiled under reflux for 15 min. Aqueous sodium acetate solution (6 g in 10 mL) was added to the cooled solution, and the mixture was again boiled under reflux for 15 min. The cooled reaction mixture was extracted with ether (3 × 30 mL), the combined organic layers were washed with saturated sodium bicarbonate solution and dried over sodium sulfate, and the solvent was evaporated to give an oil (600 mg). The oil was chromatographed by LC on μ-Porasil with 20% ether in hexane as the eluant to give 3-methylpyrrole-2-carboxaldehyde (**9**; 200 mg, 18% theoretical) and 4-methylpyrrole-2-carboxaldehyde (**10**; 30 mg, 3% theoretical).

3-Methylpyrrole-2-carboxaldehyde (9): mp 86–88 °C; UV (MeOH) 293 nm (ϵ 17 500); IR ($CHCl_3$) 3350, 1640 cm^{-1}; ^1H NMR (CCl_4), see Table I; ^{13}C NMR (C_6D_6) δ 177.7 (d), 133.2 (s), 130.0 (s), 126.9 (d), 112.6 (d), 10.3 (q).

4-Methylpyrrole-2-carboxaldehyde (10): mp 47–48 °C; UV (MeOH) 250 nm (ϵ 6300), 301 (13 700); IR ($CHCl_3$) 3350, 1640 cm^{-1}; ^1H NMR (CCl_4), see Table I; ^{13}C NMR (C_6D_6) δ 179.1 (d), 133.1 (s), 126.1 (d), 122.4 (d), 121.5 (s), 11.4 (q).

5-Methylpyrrole-2-carboxaldehyde (11). 2-Methylpyrrole, prepared by the method of Hinman and Theodoropulos,[4] was formylated by using the procedure above to obtain 5-methylpyrrole-2-carboxaldehyde (**11**, quantitative): mp 68–69 °C; UV (MeOH) 300 nm (ϵ 19 800); IR ($CHCl_3$) 3350, 1640 cm^{-1}; ^1H NMR (CCl_4), see Table I; ^{13}C NMR (C_6D_6) δ 178.2 (d), 140.2 (s), 132.5 (s)), 124.2 (d), 110.7 (d), 12.9 (q).

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Registry No. **1** (n = 14), 75233-97-5; **1** (n = 15), 75233-98-6; **1** (n = 16), 75233-99-7; **1** (n = 18), 75234-00-3; **2**, 75234-01-4; **3**, 75234-02-5; **4** (n = 14), 75234-03-6; **4** (n = 15), 75234-04-7; **4** (n = 16), 75234-05-8; **4** (n = 18), 75234-06-9; **5**, 75234-07-0; **6**, 75234-08-1; **7**, 75234-09-2; **9**, 24014-18-4; **10**, 24014-19-5; **11**, 1192-79-6; ethyl 16-(carbomethoxy)-hexadecanoate, 75234-10-5; nonanal, 124-19-6; 2-hydroxydecanenitrile, 75234-11-6; dimethylformamide, 68-12-2; 3-methylpyrrole, 616-43-3; 2-methylpyrrole, 636-41-9; (*E*)-6-dodecene, 7206-17-9; (*Z*)-6-dodecene, 7206-29-3.

(7) Cf. preparation of acetone cyanohydrin: "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. 3, p 324.

(8) Silverstein, R. M.; Ryskiewicz, E. E.; Willard, C. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, p 831.

(9) Prepared by the method of: M. E. Garst and D. Lukton (personal communication) after: Ichimura, K. *Japan Kokai Tokkyo Koho* **1975**, *75 18 462*; *Chem. Abstr.* **1975**, *83*, 492.