Synthesis of Prostaglandin Synthetase Substrate Analogues. 1. (Z)-14-Hydroxy-12,13-methano-8-nonadecenoic Acid

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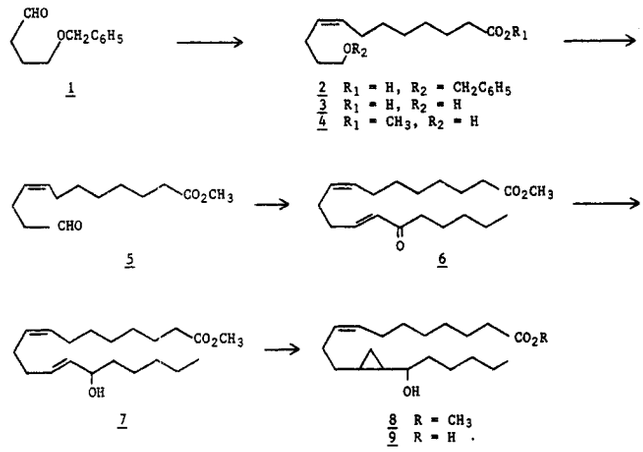
As part of our program to prepare (8Z,11Z,14Z)-8,11,14-eicosatrienoic acid analogues[1] with potential prostaglandin synthetase inhibitory activity, (Z)-14-hydroxy-12,13-methano-8-nonadecenoic acid (**9**) was synthesized. This acid, which was envisioned as either a substrate or transition-state analogue, was prepared in seven steps from 4-benzyloxybutanal.



Wittig reaction of 4-benzyloxybutanal (**1**) with the ylide derived from treatment of 7-carboxyheptyltriphenylphosphonium bromide with sodio methylsulfinylmethide in dimethyl sulfoxide afforded (Z)-12-benzyloxy-8-dodecenoic acid (**2**) in 87% yield. Reduction of benzyl ether **2** with sodium in liquid ammonia–tetrahydrofuran, followed by esterification, provided a 74% yield of methyl (Z)-12-hydroxy-8-dodecenoate (**4**). None of the *E* isomer was detected by NMR or VPC.

Oxidation of the hydroxyl group with Collins reagent[2] afforded the aldehyde **5** in 69% yield. The aldehyde was converted to the conjugated enone in 89% yield by reaction with the sodio derivative of dimethyl 2-oxoheptylphosphonate. To prevent aldol condensation of the aldehyde, it was necessary to run the reaction at 0–5 °C and add hexamethylphosphoric triamide to solubilize the phosphonate salt.

The *E:Z* isomer ratio for the enone was 12.5:1. The *E*-enone **6** was isolated in 69% yield after chromatography. The stereochemistry of the C-12 double bond was verified by comparison of the NMR spectrum with that of known 15-keto prostaglandins.

Because enone **6** is not as sterically hindered as the 15-keto prostaglandin intermediates, standard reduction methods [$Zn(BH_4)_2$ or $LiAl(OtBu)_3H$] afforded appreciable reduction to the saturated ketone. However, reduction with lithium triethylborohydride at −78 °C afforded the allylic alcohol **7** in 80% yield after chromatography. Simmons–Smith cyclopropanation[3] produced the 12,13-methano compound **8** in 65% yield. The stereochemistry about the cyclopropane ring should be trans as it was derived from a trans olefin;[3] however, the stereochemistry about the carbinol remains to be established.

VPC analysis (1% SE-30, 200 °C) indicated that this material contained 93% of the desired product. Careful chromatography afforded a 27% yield of 97% pure material, which was saponified with methanolic KOH in 89% yield to the acid **9**. This acid inhibited the conversion of (8Z,11Z,14Z)-8,11,14-eicosatrienoic acid to PGE_1 by the prostaglandin synthetase in bovine seminal vesicle microsomal fractions.[4]

Experimental Section

General. Reactions were carried out under an argon atmosphere. Solvents were dried or distilled before use (THF was distilled under argon from lithium aluminum hydride). Boiling points were uncorrected. Evaporative distillations were done with a Büchi Kugelrohr apparatus. Vapor-phase chromatograms were obtained with a Hewlett-Packard 5711A gas chromatograph, equipped with a flame-ionization detector. A 6-ft by 0.25-in. o.d., 1% SE-30, high-performance Chromosorb W (AW-DMCS, 80–100 mesh) glass column was used. Helium was the carrier gas. Infrared spectra were taken with a Perkin-Elmer 137 spectrophotometer, and NMR spectra were obtained with a Varian A-60A NMR spectrometer using tetramethylsilane as an internal standard (δ 0) and solvents as specified. High-resolution mass-spectral analyses were obtained by Dr. David Thomas, Department of Bio-Organic Chemistry, SRI, on a CEC 21-110B high-resolution mass spectrometer, equipped with facilities for combination VPC/MS. Thin-layer chromatograms were run on Analtech analytical silica gel plates.

7-Carboxyheptyltriphenylphosphonium Bromide. The procedure of Corey and co-workers[5] for preparing 5-carboxypentyltriphenylphosphonium bromide was modified. A solution of 157 g (0.70 mol) of commercially available 8-bromooctanoic acid and 172 g (0.70 mol) of triphenylphosphine in 1400 mL of acetonitrile (distilled from P_2O_5) was stirred at reflux for 16 h and then concentrated at reduced pressure to afford a colorless oil, which was triturated with dry benzene and washed in succession with dry benzene and ether. Each fraction was evaporated and then weighed. No material was extracted in the final wash of seven. During the washing procedure the material crystallized. Drying at reduced pressure afforded 251 g (76%) of 7-carboxyheptyltriphenylphosphonium bromide as a white microcrystalline powder: mp 116–120 °C; IR ($CHCl_3$) 3050–3450 (OH of CO_2H), 1710 (C=O of CO_2H), 1575, 1100 cm^{-1}; NMR ($CDCl_3$) δ 2.25 (m, 2 H, CH_2CO_2), 3.6 (m, 2 H, CH_2P), 7.85 (m, 15 H, ArH), 9.0 (s, 1 H, CO_2H). Anal. Calcd for $C_{26}H_{30}BrPO_2$: C, 64.33; H, 6.23; Br, 16.46; P, 6.38. Found: C, 64.54; H, 6.46; Br, 16.43; P, 6.41.

4-Benzyloxybutanal (1). To a stirred suspension of 72.8 g (0.34 mol) of pyridinium chlorochromate[6] and 300 mg of anhydrous sodium acetate in 450 mL of dichloromethane was quickly added 40.6 g (0.23 mol) of 4-benzyloxy-1-butanol.[6] This mixture, which turned from orange to deep brown, was stirred at room temperature for 1.5 h and then diluted with ether and filtered through Florisil with ether as a rinse. Fractional distillation afforded 23.1 g (58%) of **1** as a colorless oil: bp 165–172 °C (20 mm) [lit.[7] bp 143 °C (10 mm)]; IR (film) 2700, 1725, 1100, 695 cm^{-1}; NMR ($CDCl_3$) δ 2.27–2.7 (m, 2 H, CH_2CHO), 3.51 (t, J = 6 Hz, 2 H, $ArCH_2OCH_2$), 4.67 (s, 2 H, $ArCH_2$), 7.63 (s, 5 H, ArH), 8.0 (t, J = 1 Hz, 1 H, CHO).

(Z)-12-Benzyloxy-8-dodecenoic Acid (2). The procedure of Grieco and Reap[8] was modified. After removal of the mineral oil by washing with pentane, 0.23 mol of sodium hydride was rapidly stirred with 200 mL of dry dimethyl sulfoxide (Me_2SO) in a 75 °C oil bath until solution was achieved. The light-brown solution was cooled to room temperature and then added dropwise to a stirred solution of 71.8 g (0.15 mol) of 7-carboxyheptyltriphenylphosphonium bromide in 300 mL of Me_2SO with ice cooling so that the internal temperature was 20–25 °C. After two-thirds of the sodium dimsylate solution had been added, the reaction mixture became bright red. After the addition was completed, stirring was continued for 20 min. Then 10.6 g (0.59 mol) of **1** in 10 mL of Me_2SO was added at such a rate that the internal temperature did not rise. After one-half of the aldehyde had been added, the red color began to fade and a precipitate formed. After the reaction mixture had been stirred at room temperature for 2.5 h, it was poured into ether and acidified to pH 3 with cold 2 M $NaHSO_4$ solution. The aqueous layer was extracted with ether. The combined ether extracts were extracted with 1 N sodium hydroxide and water. The aqueous extracts were acidified to pH 3 with 2 M $NaHSO_4$ and extracted with ether. Drying (Na_2SO_4) of the ethereal extracts and concentration at reduced pressure gave 17.1 g of a yellow oil. Chromatography (800 g of silica gel, 15% ethyl acetate in ether, R_f 0.77) afforded 15.7 g of **2**. Quantitative evaporative distillation at 165 °C (0.03 mm) afforded 15.7 g (87%) of **2** as a colorless oil: IR (film) 2700–3350 (OH of CO_2H), 1725 (C=O of CO_2H) cm^{-1}; NMR ($CHCl_3$), 3.53 (t, J = 6 Hz, 2 H, $ArCH_2OCH_2$), 4.55 (s, 2 H, $ArCH_2$), 5.43 (m, 2 H, HC=CH), 7.40 (s, 5 H, ArH). MS calcd for $C_{19}H_{28}O_3$, 304.2038; found, 304.2066.

(Z)-12-Hydroxy-8-dodecenoic Acid (3). Sodium (4.74 g, 0.21

mol) was dissolved in 1000 mL of ammonia; then 15.7 g (0.05 mol) of (*Z*)-12-benzyloxy-8-dodecenoic acid in 100 mL of THF was added. The blue solution was stirred at reflux temperature for 4 h, and then 11.2 g (0.21 mol) of ammonium chloride was added slowly to quench the reaction mixture. Ether (200 mL) was added, and the ammonia was allowed to evaporate overnight under a stream of argon. The reaction mixture was diluted with water and ether and acidified to pH 3 with 2 M $NaHSO_4$. The aqueous layer was extracted with ether. The ether extracts were washed with water and brine, dried (Na_2SO_4), and concentrated at reduced pressure to 11.3 g (11.05 g theoretical) of crude **3** as a colorless oil: IR (film) 2700–3350 (OH), 1725 (C=O), 1060, 760, 695 cm^{-1}; NMR ($CDCl_3$) δ 3.63 (t, J = 6 Hz, 2 H, OCH_2), 5.5 (m, J_{cis} = 5 Hz, 2 H, HC=CH), 6.1–6.7 (broad s, 2 H, OH and CO_2H).

Methyl (*Z*)-12-Hydroxy-8-dodecenoate (4). A solution of diazomethane in dichloromethane was added to 11 g (51 mmol) of the crude (*Z*)-12-hydroxy-8-dodecenoic acid, prepared as described above, in 50 mL of CH_2Cl_2 until the solution turned yellow. Excess diazomethane was decomposed by the dropwise addition of acetic acid. Solvent was removed at reduced pressure to afford 11.2 g of crude ester which was chromatographed (360 g of silica gel, 1:1 ether–hexane, R_f 0.31) and evaporatively distilled at 110–115 °C (0.03 mm) to afford 8.73 g (74% from **2**) of **4** as a colorless oil: IR ($CHCl_3$) 3350 (OH), 1710 (CO_2CH_3), 1155, 730 cm^{-1}; NMR ($CDCl_3$) δ 3.32 (t, J = 6 Hz, 2 H, OCH_2), 3.33 (s, 3 H, CO_2CH_3), 5.4 (m, J_{cis} = 5 Hz, 2 H, CH=CH); VPC (1% SE-30, program 120 °C, 8 °C/min), major peak (>99% peak area, t_R 14 min), minor peak (<1% peak area, t_R 21 min). MS calcd for $C_{13}H_{22}O_2$ (M − H_2O), 210.1620; (found, 210.1640); *m/e* (trimethylsilyl ether) 300 (M^+).

Methyl (*Z*)-11-Formyl-8-undecenoate (5). A mixture of 2.63 g (26 mmol) of chromic anhydride and 2.1 mL (26 mol) of pyridine in 50 mL of dichloromethane was stirred at ambient temperature for 20 min;[2] then 1.0 g (4.4 mmol) of **4** in 5 mL of dichloromethane was added and stirring was continued for 20 min. The mixture was filtered through two 25-g portions of Florisil with three 20-mL portions of dichloromethane as a rinse. Concentration at reduced pressure afforded 0.77 g of a yellow oil: TLC (15% EtOAc in hexane) R_f 0.43, 0.76 (**5**). Chromatography (30 g of Florisil, 15% EtOAc in hexane) followed by evaporative distillation at 100 °C (0.05 mm) afforded 0.68 g (69%) of **5** as a colorless oil: IR (film) 2800 (CHO), 1740 (CO_2CH_3), 1725 (CHO) cm^{-1}; NMR ($CDCl_3$) δ 3.67 (s, 3 H, CO_2CH_3), 5.3–5.7 (m, 2 H, HC=CH), 8.0 (broad s, 1 H, CHO). MS calcd for $C_{13}H_{22}O_3$, 226.1569 found, 226.1596; calcd for $C_{12}H_{19}O_2$ (M − OCH_3), 195.1385; found, 195.1387.

Methyl (8*Z*,12*E*)-14-Oxo-8,12-nonadecadienoate (6). Dimethyl (2-oxoheptyl)phosphonate (0.68 mL, 3.3 mmol) was added to a stirred suspension of 144 mg of 50% sodium hydride–mineral oil dispersion (3.0 mmol of sodium hydride) in 4 mL of dry hexamethylphosphoric triamide. After solution had been achieved (20 min), the reaction mixture was diluted with 4 mL of dimethoxyethane (DME) and cooled in an ice bath, while 0.60 g (2.7 mmol) of **5** in 4 mL of DME was added over a period of 0.5 h by a syringe drive apparatus. The addition syringe was rinsed with 1 mL of DME. Stirring was continued for 0.5 h more, at which time TLC (20% EtOAc in hexane) indicated maximization of product [R_f 0.91 (mineral oil), 0.75 (12*E* isomer), 0.65 (12*Z* isomer), and 0.50 (**5**)]. The reaction mixture was acidified with acetic acid, diluted with water, and extracted with ether. The ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated at reduced pressure to 1.2 g of a yellow oil, which was chromatographed (50 g of silica gel, 20% ethyl acetate in hexane) to afford 0.15 g (18%) of **6** and its 12*Z* isomer in a ratio of 2:1, and 0.74 g (69%) of **6** as a colorless oil: IR (film) 1740 (CO_2CH_3), 1710 (s cis HC=CHC=O), 1680 (s trans HC=CHC=O), 1630 (HC=CH), 970, 875, 725 cm^{-1}; NMR ($CDCl_3$) δ 3.65 (s, 3 H, CO_2CH_3), 5.4 (m, J_{cis} = 5 Hz, 2 H, HC=CH), 6.1 (m, J_{AB} = 16 Hz, 1 H, (*E*)-HC=CHC=O), 6.8 (m, J_{AB} = 16 Hz, J_{BX} = 6 Hz, 1 H, (*E*)-CH_2HC=CHC=O); MS calcd for $C_{20}H_{34}O_3$: 322.2508; found: 322.2520. In another experiment, the 12*Z* isomer was isolated by chromatography as a colorless oil: IR (film) 1740 (CO_2CH_3), 1700 and 1675 (HC=CHC=O), 1625 (HC=CH), 1160, 1070 cm^{-1}; NMR ($CDCl_3$) δ 3.63 (s, 3 H, CO_2CH_3), 5.37 (m, J_{cis} = 5 Hz, 2 H, HC=CH), 6.2 (m, 2 H, HC=CHC=O).

Methyl (8*Z*,12*E*)-14-Hydroxy-8,12-nonadecadienoate (7). To a stirred solution of 0.49 g (1.5 mmol) of **6** in 22 mL of THF, which was cooled in a dry ice–acetone bath, was added 2.5 mL of 0 °C 0.6 M $LiBEt_3H$ (1.5 mmol) in THF. After 10 min, monitoring by TLC [18% EtOAc in hexane, R_f 0.60 (**6**), 0.51, 0.48 (**7**), 0.29, 0.16] indicated the presence of **6**; therefore, another 0.5 mL of 0.6 M $LiBEt_3H$ (0.3 mmol) was added, and stirring was continued for 15 min. The reaction mixture was quenched at −78 °C by the addition of 0.1 mL of cold methanol–0.1 N hydrochloric acid (2:1) and 0.2 mL of methanol. After 10 min of stirring, the mixture was diluted with ether and chloroform and concentrated at reduced pressure to afford a white semisolid, which was extracted with ether. Concentration of the extracts afforded 0.42 g of a colorless oil. The organic fractions were combined and chromatographed (40 g of silica gel, 18% EtOAc in hexane) to afford 0.39 g (80%) of **7** as a colorless oil: IR (film) 3350 (OH), 1740 (CO_2CH_3), 1020, 970 cm^{-1}; NMR ($CDCl_3$) δ 3.67 (s, 3 H, CO_2CH_3), 4.07 (m, 1 H, CHOH), 5.37 (m, J_{cis} = 5 Hz, 2 H, (*Z*)-HC=CH), 5.50 (m, 2 H, (*E*)-HC=CH). MS calcd for $C_{20}H_{34}O_2$ (M − H_2O), 306.2559; found, 306.2542; *m/e* (trimethylsilyl ether), 396 (M^+).

Methyl (*Z*)-14-Hydroxy-12,13-methano-8-nonadecenoate (8). To 0.674 g (10.3 mmol) of zinc–copper Simmons–Smith couple, prepared by the procedure of LeGoff,[3] and layered with 4 mL of dry ether, were added 276 μL (3.4 mmol) of CH_2I_2 and a small crystal of iodine. The reaction was initiated by heating in a 40 °C oil bath. Heating was continued for 1 h, and then 1 mL of ether and 140 mg (0.43 mmol) of **7** in 1 mL of ether, followed by 1 mL of ether rinse, were added. Heating at reflux was continued. The progress of the reaction was determined by VPC (1% SE-30, 200 °C) of the ether fraction obtained by quenching small aliquots with 10% NaOH–ether.

When the peak corresponding to the product was maximized (1 h), the reaction mixture was worked up by dilution with 10% NaOH and water and extraction with ether. The ether extracts were washed, dried ($MgSO_4$), and concentrated in the cold and dark to afford 0.36 g of a white semisolid. The semisolid was partially dissolved in 3 mL of hexane, and the hexane-soluble portion was quickly chromatographed on 10 g of ICN neutral alumina, activity III. Elution with hexane afforded unreacted diiodomethane and elimination products. Elution with 10 mL of ether afforded 24.5 mg of an oil, the VPC (1% SE-30, 200 °C) of which showed six peaks. The third (t_R 3.1 min) and fourth peaks (t_R 3.8 min) comprised 6.4 and 74%, respectively, of the total peak area. Elution with another 20 mL of ether afforded 94.6 mg (65%) of a colorless oil, the VPC of which had the third and fourth peaks with 4 and 93%, respectively, of the total peak area. The TLC (15% ethyl acetate in hexane) of this oil showed a very small spot with an R_f value of 0.41 (elimination products), a small spot with an R_f value of 0.19 (third VPC peak), and the major spot with an R_f value of 0.14 (fourth VPC peak). This second ether fraction was very carefully chromatographed (15 g of neutral alumina, activity III, 1:1 ether–hexane) to afford 11 mg of a colorless oil (R_f 0.19, VPC t_R 3.1 min), the NMR spectrum of which had two cis vinylic protons, four cyclopropyl protons, and three methyl ester protons. This ester (6% yield) may either be an isomer of the major product or arise from cyclopropanation of the reduction product of the (12*E*)-enone, which may not have been completely removed during chromatography of the (12*Z*)-enone: *m/e* (trimethylsilyl ether) 410 (M^+). Further chromatography gave 30.7 mg of a mixture, followed by 39.5 mg (27%) of **8** as a colorless oil (R_f 0.14): VPC (1% SE-30, 200 °C) t_R 2.0 (0.6%), 2.1 (1.2%), 2.5 (0.6%), 2.8 (0.6%), and 3.8 min (97%); IR (CCl_4) 3450 (OH), 1760 (CO_2CH_3), 1030 (cyclopropyl (c-Pr) C–H) cm^{-1}; NMR (CCl_4) δ 0.07–0.77 (m, 4 H, c-Pr H), 0.8–1.1 (t, 3 H, CH_2CH_3), 1.9–2.5 (m, 8 H, CH_2C=CCH_2, CH_2-c-Pr, CH_2CO_2), 2.90 (broad s, 1 H, OH), 3.27–3.80 (m, 1 H, CHOH), 3.66 (s, 3 H, CO_2CH_3), and 5.37 (m, J_{cis} = 6 Hz, 2 H, (*Z*)-HC=CH). MS calcd for $C_{21}H_{36}O_2$ for M − H_2O, 320.2715; found, 320.2742; calcd for $C_{20}H_{35}O_2$ for M − OCH_3, 307.2637; found, 307.2667. A VPC/MS study (3% OV-25, 180 °C) of this colorless oil after trimethylsilylation showed that the peak (t_R 10 min) corresponding to the major product was homogeneous, *m/e* 410 (M^+).

(*Z*)-14-Hydroxy-12,13-methano-8-nonadecenoic Acid (9). To 14.4 mg (0.044 mmol) of **8** dissolved in 0.25 mL of methanol was added 0.25 mL of a 10% solution of KOH in methanol and 0.05 mL of water. The solution was stirred at room temperature for 22 h, at which time TLC (15% EtOAc in hexane) indicated the disappearance of starting material (R_f 0.14). The reaction mixture was cooled in an ice bath, while 0.1 mL of acetic acid in 0.9 mL of methanol was added. After dilution with water, the mixture was extracted with ether. The extracts were washed with water, dried (Na_2SO_4), and concentrated at reduced pressure to afford 12.8 mg (89%) of **9** as an off-white oil; IR (CCl_4) 3100–3550, 2455–2700 (CO_2H and OH), 1710 (C=O of CO_2H), and 1050 (c-Pr C–H) cm^{-1}; NMR (CCl_4) δ 0.3–0.8 (m, 4 H, c-Pr H), 0.8–1.1 (m, 3 H, CH_3), 1.8–2.5 (m, 8 H, CH_2C=CCH_2, CH_2-c-Pr, CH_2CO_2), 2.9 (m, 1 H, CHOH), 5.33 (m, J_{cis} = 5 Hz, 2 H, (*Z*)-HC=CH), and 6.4 (broad s, 2 H, OH and CO_2H). MS calcd for $C_{26}H_{52}O_3Si_2$ for bistrimethylsilyl derivative, 468.3455; found; 468.3457.

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Registry No.—1, 5470-84-8; 2, 62509-45-9; 3, 62509-46-0; 4, 62509-47-1; 5, 62509-48-2; 6, 62509-49-3; (12Z)-6, 62509-50-6; 7, 62509-51-7; 8, 62509-52-8; 9, 62509-53-9; 9 bistrimethylsilyl derivative, 62509-54-0; 8-bromooctanoic acid, 17696-11-6; triphenylphosphine, 603-35-0; 7-carboxyheptyltriphenylphosphonium bromide, 52956-93-1; 4-benzyloxy-1-butanol, 4541-14-4; dimethyl (2-oxoheptyl) phosphonate, 62509-55-1.

References and Notes

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Structure Analysis by Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Pleiocraline, a New Bisindole Alkaloid from *Alstonia deplanchei* van Heurck et Muell. Arg.[1,2]

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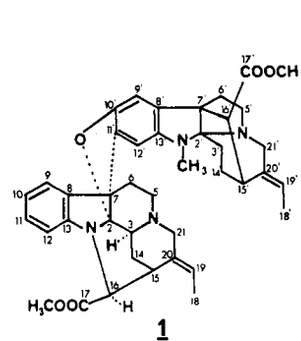
Previously, we reported[3] the ^{13}C NMR structural analysis of pleiocorine (1), a bisindole alkaloid isolated from the stems and leaves of the New Caledonian plant *Alstonia deplanchei* van Heurck et Muell. Arg. (Apocynaceae). We now wish to describe a new isomeric congener bisindole alkaloid, namely, pleiocraline (2), whose structure has also been elucidated principally from an analysis of its ^{13}C NMR spectrum.

Pleiocraline, $C_{41}H_{46}N_4O_5$ (by high-resolution mass spectrometry), $[\alpha]^{20}_D$ +124° (*c* 1.0, chloroform), colorless plates from methanol, decomposes above 300 °C. The mass spectrum of pleiocraline is similar to that of pleiocorine, showing an intense molecular-ion peak at *m/e* 674 but lacking any characteristic fragmentation peak except the M − 59 peak at *m/e* 615 due to the loss of a carbomethoxy group. The UV spectrum of pleiocraline showed λ_{max}^{EtOH} at 244, 295, and 344 nm (ε 29 000, 7250, and 14 150), while its infrared spectrum showed ester (1725 cm^{-1}) and dihydroindole (1605 cm^{-1}) bands but lacked NH or OH absorption. Its structural resemblance with pleiocorine was also revealed from the 240-MHz ^1H NMR spectrum[4] which showed the presence of one *N*-methyl (singlet, δ 2.65, 3 H), two carbomethoxyls (singlet, 3.70, 6 H), two ethylidene side chains (two doublets centered at 1.54 and 1.58, *J* = 7 Hz, 3 H each; two quartets centered at 5.33 and 5.42, *J* = 7 Hz, 1 H each) and six aromatic protons (between δ 6.1 and 7.2) of which two appeared as singlets (δ 6.35 and 6.6) suggesting the presence of an aromatic C(10),C(11) disubstituted indole alkaloid moiety. A one-proton doublet at δ 4.68 (*J* = 4 Hz) as well as the splitting pattern[5] of the aromatic protons suggested that pleiocraline comprises a 2,7-dihydropleiocarpamine moiety which is also known to be a constituent part of pleiocorine (1)[3] and several bisindole alkaloids such as villalstonine,[6] pycnanthine,[6] dihydropycnanthine,[7] etc.

Earlier, unambiguous carbon signal assignments of 2,7-dihydropleiocarpamine moiety of villalstonine and pleiocorine have been achieved through analysis of their ^{13}C NMR spectra.[3] Comparison of the ^{13}C NMR spectra[8] of pleiocraline (2) and pleiocorine (1) clearly indicated (see Table I) the presence



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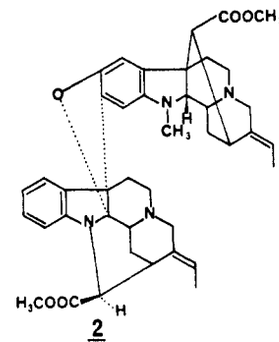

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of a 2,7-dihydropleiocarpamine unit in the new alkaloid, substituted (as in pleiocorine) at C(2) and C(7) through an oxygen and a carbon, respectively.

Table I. ^{13}C NMR Chemical Shifts of Pleiocorine (1), Pleiocraline (2), and $N_{(a)}$-Methyl Deacetyldeformyl-1,2-dihydroakuammiline (2β-H) (3)

	C(2)	C(3)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(11)	C(12)	C(13)
1	103.2	51.3	52.0[a]	24.6	54.0	134.4	121.6	119.2[b]	126.3	108.9	144.4
2	104.3	51.8	52.1[c]	24.7	54.1	134.7	122.8	118.5[d]	126.9	109.5	144.9

	C(14)	C(15)	C(16)	C(17)	C(18)	C(19)	C(20)	C(21)	$COOCH_3$
1	28.1	32.2	58.1	169.3	12.3	119.5[b]	136.1	48.2[a]	50.6
2	27.9	32.2	58.3	169.9	12.3	119.9[d]	135.2	48.2[c]	51.0

	C(2′)	C(3′)	C(5′)	C(6′)	C(7′)	C(8′)	C(9′)	C(10′)	C(11′)	C(12′)	C(13′)
1	97.5	40.6	55.0[e]	20.2[f]	56.9	134.8	106.1	151.1	127.4	100.1	143.6
2	80.3	53.0	55.0	31.5	43.2	140.3	104.8	153.4	127.8	104.3	148.2
3	79.1	52.8	54.7	31.1	43.0	*h*	120.5	119.0[g]	126.7	109.0	*h*

	C(14′)	C(15′)	C(16′)	C(17′)	C(18′)	C(19′)	C(20′)	C(21′)	$COOCH_3$	$N_{a'}$-CH_3
1	26.3[f]	34.7	50.9	173.1	13.4	122.5	138.8	58.1[e]	51.6	28.1
2	34.2	34.5	47.5	172.9	12.9	120.1	140.3	50.8	51.3	35.2
3	33.9	34.4	47.3	172.2	13.0	118.7[g]	*h*	50.6	51.3	33.9

[a-g] These assignments may be interchanged. [h] Because of high dilution these quaternary carbon signals were not observed.