Synthesis of (−)-Pinidine and a Putative Biosynthetic Precursor: 5,9-Dioxodecanoic Acid

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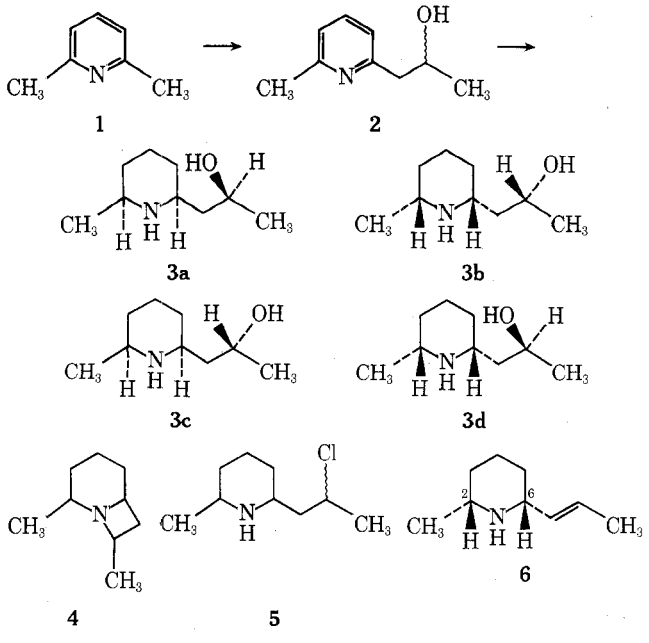
Received March 18, 1975

2-Methyl-6-(2-hydroxypropyl)pyridine (**2**) was obtained by reaction of the monolithium salt of 2,6-lutidine with acetaldehyde. Hydrogenation of the hydrochloride of **2** yielded *cis*-2-methyl-6-(2-hydroxypropyl)piperidine as a pair of diastereomers. Heating this alcohol with potassium bisulfate afforded (±)-pinidine, which was resolved with optically active 6,6′-dinitrodiphenic acid. [10-^{14}C]-5,9-Dioxodecanoic acid was prepared and fed to *Pinus jeffreyi* plants, as a potential precursor of pinidine. However, there was no significant incorporation of activity into the alkaloid, indicating that this compound is probably not an intermediate between acetate and pinidine.

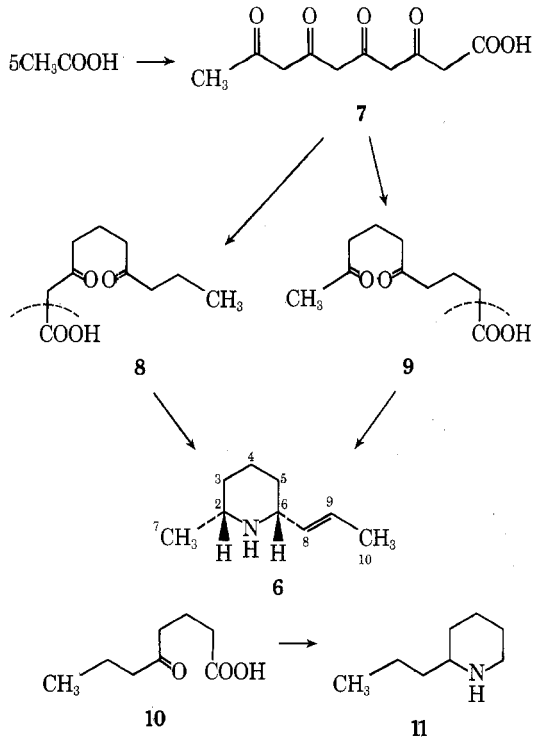
The alkaloid pinidine was isolated from various species of *Pinus* by Tallent et al.,[2] who established its structure as 2-methyl-6-(2-propenyl)piperidine.[3] Hill and coworkers deduced[4] the absolute configuration as illustrated in formula **6**: (*R*)-2-methyl-(*R*)-6-[(*E*)-2-propenyl]piperidine. This article describes the first synthesis of this simple piperidine alkaloid.

Reaction of the monolithium salt of 2,6-lutidine (**1**) with acetaldehyde afforded (*RS*)-2-methyl-6-(2-hydroxypropyl)pyridine (**2**).[5] Hydrogenation of the hydrochloride of **2** in ethanol in the presence of Adams catalyst yielded a pair of diastereomers. It has been shown that the hydrogenation of 2,6-dialkylpyridines leads almost exclusively to *cis*-dialkylpiperidines.[6] The pair of diastereomers can therefore be depicted by the structures **3a,b** and **3c,d.** Attempts to separate these isomers by TLC or GLC were unsuccessful. One pair of enantiomers, mp 80–81°, separated from ethyl acetate.[7] The *O*-acetyl derivatives of the mixture of alcohols **3** could be separated by GLC, the more abundant pair of enantiomers (58%) being identical with the *O*-acetyl derivative of the alcohol, mp 80–81°. The relative stereochemistry of the *O*-acetates could not be assigned by an examination of their NMR or ir spectra. Initial attempts to obtain pinidine from the alcohols **3** were unsuccessful. On heating the *O,N*-ditosylate of the alcohol, mp 80–81°, in dimethyl sulfoxide at 100° an oil was obtained which is considered to be 2,8-dimethyl-1-azabicyclo[4.2.0]octane (**4**).[8] Treatment of this oil with concentrated hydrochloric acid resulted in opening of the azetidine ring, affording 2-methyl-6-(2-chloropropyl)piperidine (**5**), identical with material obtained by the action of thionyl chloride on the alcohol, mp 80–81°. Heating the chloro compound **5** with potassium hydroxide in triethylene glycol failed to yield any pinidine. Only starting material was recovered when the mixture of alcohols **3** was heated with 85% phosphoric acid, or with sulfuric acid (50 or 98%). No dehydration was achieved when the hydrochloride of **3** was heated with hexamethylphosphoric triamide.[9] Smooth dehydration of the alcohols **3** was finally accomplished by heating their hydrochlorides with potassium bisulfate at 170°. The resultant (±)-pinidine was resolved with optically active 6,6′-dinitrodiphenic acid.[10] (−)-Pinidine (+)-6,6′-dinitrodiphenate separated from a mixture of methanol and ethyl acetate. The (−)-pinidine recovered from this salt as its hydrochloride was identical (mixture melting point, crystalline form, optical rotation) with the natural alkaloid isolated from *Pinus jeffreyi.* (+)-Pinidine crystallized from ethyl acetate as a salt with (−)-6,6′-dinitrodiphenic acid.

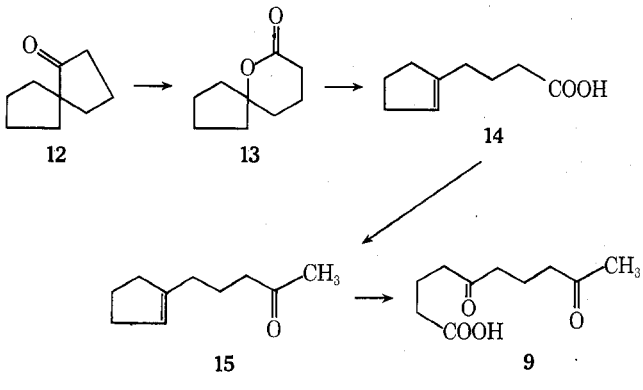


We have previously shown[11] that the administration of sodium [1-^{14}C]acetate to *Pinus jeffreyi* plants yielded radioactive pinidine which was labeled on the alternate carbons: C-2, -4, -6, and -9. This result is consistent with the hypothesis that the alkaloid is derived from the ten-carbon poly-β-keto acid **7,** with loss of the carboxyl group. Two alternate ways in which the acid **7** can be utilized for the formation of pinidine are illustrated in Scheme I. It is suggested that reduction affords either 3,7-dioxodecanoic acid (**8**) or 5,9-dioxodecanoic acid (**9**). Reaction with a nitrogen source, followed by reduction and dehydrogenation, would then afford pinidine.[12] Support for such intermediates as **8** and **9** is provided by the discovery that 5-oxooctanoic acid (**10**) is an excellent precursor of coniine (**11**) in the hemlock plant.[13] We have thus prepared [10-^{14}C]-5,9-dioxodecanoic acid by the method illustrated in Scheme II, and tested it as a precursor of pinidine. Spiro[4.4]-1-nonanone (**12**)[14] was subjected to a Baeyer–Villiger oxidation with *m*-chloroperbenzoic acid, affording the lactone **13,** which on hydrolysis and dehydration yielded 4-(1-cyclopentenyl)butanoic acid (**14**). The lithium salt of this acid was formed by reaction with 1 equiv of methyllithium. A second equivalent of [^{14}C]methyllithium then afforded [1-^{14}C]-5-(1-cyclopentenyl)-2-pentanone (**15**).[15] Oxidation of **15** with a mixture of sodium metaperiodate and potassium permanganate yielded [10-^{14}C]-5,9-dioxodecanoic acid (**9**).[16] This labeled acid was fed to 3-year-old *Pinus jeffreyi* plants by the wick method in two separate experiments (for 5 and 10 weeks). However, the resultant pinidine had very low activity, representing incorporations of only 0.0003 and 0.004%, respectively. We thus conclude that 5,9-dioxodecanoic acid is not

Scheme I



Scheme II



an intermediate between acetate and pinidine. Work is in progress to test the diketo acid **8**, and its decarboxylation product, nona-2,6-dione, as precursors of pinidine.

Experimental Section[17]

(*RS*)-2-Methyl-6-(2-hydroxypropyl)pyridine (2). Butyllithium (0.178 mol) in hexane (90 ml) was added slowly to a solution of 2,6-lutidine (19 g, 0.178 mol) in THF (250 ml) maintained at −35°. Acetaldehyde (20 g, 0.45 mol) dissolved in THF (50 ml) was added slowly keeping at the same temperature. The reaction mixture was then allowed to warm to 0°, and water (100 ml) was added. Evaporation under reduced pressure removed the THF and the residual aqueous solution was extracted with ether. The residue obtained on evaporation of the dried ($MgSO_4$) extract was distilled (bp 65–67°, 0.5 mm) yielding **2** as a pale yellow oil (16.5 g, 61%). The hydrochloride of **2** was obtained by passing HCl gas into a solution of **2** in a mixture of ether and ethanol. Crystallization from a mixture of ethanol and ethyl acetate afforded colorless needles, mp 126–127°.

Anal. Calcd for $C_9H_{14}NOCl$: C, 57.60; H, 7.52; N, 7.46; Cl, 18.89. Found: C, 57.44; H, 7.34; N, 7.36; Cl, 19.03.

Hydrogenation of 2 to Yield a Mixture of Diastereomers of *cis*-2-Methyl-6-(2-hydroxypropyl)piperidine (3a–d). (*RS*)-2-Methyl-6-(2-hydroxypropyl)pyridine hydrochloride (4.48 g) in ethanol (200 ml) was hydrogenated in the presence of Adams catalyst (0.2 g) at 3 atm pressure for 6 hr. The filtered reaction mixture on evaporation yielded a white solid (4.56 g, 98%), mp 150–165°. This mixture of hydrochlorides was dissolved in water, made alkaline with potassium hydroxide, and extracted with ether. The dried ($MgSO_4$) extract on evaporation afforded a colorless oil (3.29 g) which was dissolved in ethyl acetate (50 ml) and cooled to −20°. Colorless prisms separated (0.36 g, 11%), mp 80–81°.

Anal. Calcd for $C_9H_{19}NO$: C, 68.74; H, 12.18; N, 8.91. Found: C, 68.48; H, 11.19; N, 8.84.

This alcohol afforded a hydrochloride, colorless plates, mp 193–194°.

Anal. Calcd for $C_9H_{20}NOCl$: C, 55.80; H, 10.41; N, 7.23. Found: C, 55.94; H, 10.73; N, 7.14.

***cis*-2-Methyl-6-(2-acetoxypropyl)piperidine.** The hydrochloride of the alcohol **3**, mp 80–81° (100 mg), was stirred with acetyl chloride (5 ml) for 4 hr at room temperature. Excess acetyl chloride was removed in vacuo, and the residue was dissolved in water, made basic with potassium carbonate, and extracted with ether. HCl gas was passed into the dried ($MgSO_4$) extract, affording the hydrochloride of 2-methyl-6-(2-acetoxypropyl)piperidine, mp 238–239° after crystallization from chloroform–ethyl acetate. It had an R_f of 0.30 by tlc on silica gel F-254 (Merck) developing with chloroform–methanol–concentrated NH_3 (85:15:1).

Anal. Calcd for $C_{11}H_{22}NO_2Cl$: C, 56.04; H, 9.41; N, 5.94. Found: C, 55.84; H, 9.21; N, 5.67.

The mixture of the hydrochlorides of the diastereomeric alcohols **3** was similarly acetylated and afforded a mixture which could be separated by TLC in the previously described system affording two compounds having R_f values of 0.30 and 0.36. These two compounds were also obtained by GLC (10% Carbowax 20M on 70:80 Chromosorb W at 136°). The compound with a shorter retention time (42%) afforded a hydrochloride, mp 225–226°.

Anal. Calcd for $C_{11}H_{22}NO_2Cl$: C, 56.04; H, 9.41; N, 5.94. Found: C, 56.05; H, 9.27; N, 5.85.

The more abundant (58%) pair of enantiomorphs yielded a hydrochloride, mp 238–239°, identical (ir, mixture melting point) with the hydrochloride of the acetyl derivative of the alcohol **3**, mp 80–81°.

***cis*-2-Methyl-6-(2-hydroxypropyl)piperidine *O,N*-Ditosylate.** The alcohol **3**, mp 80–81° (380 mg), was added to a rapidly stirred mixture of ether (10 ml) and water (5 ml) containing *p*-toluenesulfonyl chloride (1.93 g) and sodium hydroxide (0.5 g). After 5 hr the mixture was filtered, and the residue was dissolved in chloroform, washed with dilute sodium hydroxide, and dried over potassium carbonate. The residue obtained on evaporation was crystallized from ethanol–ether, affording colorless plates of the *O,N*-ditosylate (570 mg, 49%), mp 157–158°.

Anal. Calcd for $C_{23}H_{31}NO_5S_2$: C, 59.33; H, 6.71; N, 3.01. Found: C, 59.08; H, 7.00; N, 3.03.

Attempted Detosylation of *cis*-2-Methyl-6-(2-hydroxypropyl)piperidine *O,N*-Ditosylate. *cis*-2-Methyl-6-(2-chloropropyl)piperidine (5). The *O,N*-ditosylate (139 mg) dissolved in dimethyl sulfoxide (8 ml) was heated for 5 hr at 100°. Water (30 ml) was added to the mixture, which was then extracted with ether. Evaporation of the dried ($MgSO_4$) extract afforded an oil (23 mg), ir (neat) 1442 cm^{-1} (azetidine CH_2[19]), which was dissolved in ether and treated with HCl gas. The hydrochloride of **5** separated, mp 191–192°.

Anal. Calcd for $C_9H_{19}NCl_2$: C, 50.95; H, 9.03; N, 6.60. Found: C, 50.70; H, 9.06; N, 6.70.

This same compound was obtained by stirring the alcohol **3**, mp 80–81°, with thionyl chloride at room temperature for 18 hr.

(±)-Pinidine Hydrochloride. The hydrochlorides of the mixture of alcohols **3** (15 g) were ground with freshly fused potassium bisulfate (45 g) and heated in a round-bottomed flask for 75 min at 175°. The cooled reaction mixture was dissolved in water (300 ml), made basic with sodium hydroxide, and extracted with ether (4 × 100 ml). The residue obtained on evaporation of the dried ($MgSO_4$) extract was distilled, affording (±)-pinidine as a colorless oil (4.9 g, 45%), bp 175–177° (762 mm) [bp reported[2] for (−)-pinidine, 176–177° (751 mm)]. On passing HCl gas into an ether solution of the (±)-pinidine, its hydrochloride separated as colorless prisms: mp 192–193°; ir (KBr) 2524, 2400 (NH_2^+), 1578 (C=C), 966 cm^{-1} (C=CH trans); NMR ($CDCl_3$) δ 1.18–2.16 (12 H, m), 2.84–3.80 (2 H, m, $CHNH_2^+CH$), 5.69–6.26 (2 H, m, C=CH), 8.80–10.00 (2 H, NH_2^+); mass spectrum *m/e* 139 (M^+ − HCl).

Anal. Calcd for $C_9H_{18}NCl$: C, 61.52; H, 10.32; N, 7.97. Found: C, 61.58; H, 10.40; N, 7.93.

All spectra were identical with those of natural (−)-pinidine hydrochloride isolated from *Pinus jeffreyi*.[11] Hydrogenation of the

(±)-pinidine hydrochloride (0.3 g) in ethanol (45 ml) in the presence of Adams catalyst (0.15 g) for 4 hr afforded (±)-dihydropinidine hydrochloride (0.27 g), mp 218–220° (lit.[3] mp 219–220°), identical with an authentic specimen.

Resolution to Afford (−)-Pinidine (6) and (+)-Pinidine. (±)-Pinidine (2.92 g, 21 mmol) dissolved in methanol (50 ml) was mixed with a solution of (−)-6,6′-dinitrodiphenic acid[10] (3.49 g, 10.5 mmol) in methanol (50 ml), and the solution was allowed to evaporate slowly for 1 week. Ethyl acetate (50 ml) was then added, and after 2 more weeks the separated solid was removed. Crystallization of this solid from methanol afforded the (−)-6,6′-dinitrodiphenate salt of (+)-pinidine (1.32 g), mp 250–260° dec.

Anal. Calcd for $C_9H_{17}N{\cdot}C_{14}H_8N_2O_8$: C, 58.59; H, 5.34; N, 8.91. Found: C, 58.62; H, 5.52; N, 8.46.

This salt (1.3 g) was shaken with 10% HCl (200 ml) and ether (200 ml). The acid layer was made basic with potassium hydroxide and extracted with ether. HCl gas was passed into the dried ($MgSO_4$) extract, affording (+)-pinidine hydrochloride which was obtained as fine long needles (quite different from the racemic salt) from ethanol–ether (0.34 g), mp 243–244° (mixture melting point with natural pinidine 198–202°), $[\alpha]^{23}D$ (absolute EtOH, *c* 6.0) +10.2°.

(−)-Pinidine hydrochloride, mp 242–243°, $[\alpha]^{23}D$ (absolute EtOH, *c* 5.3) −9.5° (lit.[2] −11.1°), was similarly obtained from the racemic pinidine utilizing (+)-6,6′-dinitrodiphenic acid as the resolving agent.

4-(1-Cyclopentenyl)butanoic Acid (14). Spiro[4.4]-1-nonanone[13] [bp 75–79° (8 mm)] (15 g) and *m*-chloroperbenzoic acid (23.1 g, 85%) were dissolved in 1,2-dichloroethane (150 ml) and the mixture was refluxed for 6 hr. The reaction mixture was allowed to cool overnight and the separated *m*-chlorobenzoic acid was filtered off. The filtrate was extracted with 5% aqueous sodium bicarbonate. The residue obtained on evaporation of the dichloroethane was refluxed with 25% sodium hydroxide (150 ml) for 3 hr. This solution was extracted with chloroform and then acidified with concentrated hydrochloric acid. This solution was then extracted with chloroform (5 × 50 ml), dried ($MgSO_4$), and evaporated. The residue was refluxed with 20% hydrochloric acid (45 ml) for 3 hr, cooled, and extracted with chloroform. The liquid obtained on evaporation of the dried ($MgSO_4$) extract was distilled (bp 94–98°, 0.5 mm), affording 4-(1-cyclopentenyl)butanoic acid (13.6 g, 81%). This acid yielded an amide, mp 94–95° (lit.[20] mp 93°). Oxidation with potassium permanganate yielded 5-oxo-1,9-nonanedioic acid, mp 107–108° (lit.[20] mp 109°).

5-(1-Cyclopentenyl)-2-pentanone (15). In a nitrogen atmosphere a solution of methyllithium in ether (0.3 mol in 150 ml) was added slowly to a solution of 4-(1-cyclopentenyl)butanoic acid (19.2 g, 0.124 mol) in ether (200 ml) at room temperature. The mixture was then refluxed for 20 min. Water (100 ml) was then added to the cooled reaction mixture. The ether layer was dried ($MgSO_4$), evaporated, and distilled (bp 54–56°, 0.5 mm). Dry column chromatography on Woehm alumina (activity III), eluting with benzene, afforded the ketone **15** as a colorless oil (7.6 g, 40%): ir (neat) 1723 (C=O), 1655 cm^{-1} (C=C). This ketone afforded a 2,4-dinitrophenylhydrazone, mp 88–89° (lit.[15] mp 87°).

Anal. Calcd for $C_{16}H_{26}N_4O_4$: C, 57.82. H, 6.07; N, 16.86. Found: C, 58.17; H, 6.24; N, 17.12.

5,9-Dioxodecanoic Acid (9). The ketone **15** (0.5 g) was added to stirred solution of sodium metaperiodate (2.5 g), potassium permanganate (92 mg), and *tert*-butyl alcohol (75 ml) in water (200 ml). The solution was adjusted to pH 8 by the addition of potassium carbonate, stirred for 17 hr, and then acidified with concentrated hydrochloric acid. Addition of sodium metabisulfite resulted in the formation of a clear solution which was made basic by the addition of sodium bicarbonate. The *tert*-butyl alcohol was removed by evaporation under reduced pressure. The residual aqueous solution was acidified (HCl) and extracted continuously with ether for 12 hr. The residue obtained on evaporation of the dried (Na_2SO_4) extract was crystallized from benzene–petroleum ether to yield small, white prisms of 5,9-dioxodecanoic acid (0.28 g, 43%): mp 77–78° (lit.[16] mp 78–79°), R_f 0.52 by TLC on silica gel F-254, developing with ethyl acetate; ir (KBr) 1725, 1712, 1696 cm^{-1} (C=O); uv (95% EtOH) λ_{max} 274 nm (ϵ 64); mass spectrum *m/e* 201 ($M^+ + 1$), 200 (M^+), 182 ($M^+ - H_2O$).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.02; H, 7.91.

Its methyl ester, colorless plates, mp 39–40°, was obtained by stirring in methanol with 2,2-dimethoxypropane and a trace of HCl.

Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.89; H, 8.77.

[10-^{14}C]-5,9-Dioxodecanoic Acid. [^{14}C]Methyl iodide (0.43 g, 3 mmol, nominal activity 1 mCi, Amersham-Searle) in ether was added to lithium wire (87 mg, 12.4 mmol) suspended in ether (30 ml) under argon. After stirring for 35 min the mixture was added to a slurry of lithium 4-(1-cyclopentenyl)butanoate in ether [made by the addition of 4.0 mmol of methyllithium to 0.54 g (3.5 mmol) of **14** in 50 ml of ether]. The resultant ketone **15** was isolated as described before and oxidized with periodate–permanganate to yield [10-^{14}C]-5,9-dioxodecanoic acid (135 mg, 3.92×10^8 dpm/mmol).

Administration of [10-^{14}C]-5,9-Decanoic Acid to *Pinus jeffreyi* and Isolation of the Pinidine. In our previous feeding experiments with [1-^{14}C]acetate[11] optimum incorporations were obtained by feeding for a prolonged time in July and August. Similar conditions were used in the present work. [10-^{14}C]-5,9-Dioxodecanoic acid (76 mg, 1.49×10^8 dpm) dissolved in water was fed by the wick method to *Pinus jeffreyi* plants (3 year old) growing in soil in a greenhouse. The green needles and associated small twigs (fresh wt 903 g) were harvested 10 weeks later and extracted as previously described,[11] affording pinidine hydrochloride (485 mg), 12 dpm/mg. Another feed with 56 mg of the labeled acid was carried in May and June (for 5 weeks) and yielded pinidine hydrochloride (60 mg), 5 dpm/mg.

Registry No.—**1,** 108-48-5; **2,** 55267-89-5; **2** HCl, 55267-90-8; **3,** 55267-91-9; **3** HCl, 55267-92-0; **3** acetyl derivative HCl, 55267-93-1; **3** *O,N*-ditosylate, 55267-94-2; **3a,b,** 55331-42-5; **3a,b** HCl, 55399-20-7; **3a,b** acetyl derivative HCl, 55331-43-6; **3c,d,** 55331-44-7; **3c,d** HCl, 55399-21-8; **3c,d** acetyl derivative HCl, 55331-45-8; **5** HCl, 55267-95-3; **6** HCl, 55399-22-9; (±)-**6,** 55399-23-0; (±)-**6** HCl, 55448-41-4; (±)-**6** (−)-6,6′-dinitrodiphenate salt, 55448-43-6; (+)-**6** HCl, 55399-24-1; **9,** 34862-10-7; **9** Me ester, 55267-96-4; **12,** 14727-58-3; **14,** 20126-98-1; **15,** 55267-97-5; butyllithium, 109-72-8; acetaldehyde, 75-07-0; acetyl chloride, 75-36-5; *p*-toluenesulfonyl chloride, 98-59-9; (−)-6,6′-dinitrodiphenic acid, 50573-79-0; (+)-6,6′-dinitrodiphenic acid, 50573-78-9; *m*-chloroperbenzoic acid, 937-14-4; [10-^{14}C]-5,9-dioxodecanoic acid, 55267-98-6; [^{14}C]methyl iodide, 16170-82-4.

References and Notes

(1) Contribution No. 135 from this laboratory. This investigation was supported by Research Grant GM-13246 from the National Institutes of Health, U.S. Public Health Service.
(2) W. H. Tallent, V. L. Stromberg, and E. C. Horning, *J. Am. Chem. Soc.*, **77,** 6361 (1955).
(3) W. H. Tallent and E. C. Horning, *J. Am. Chem. Soc.*, **78,** 4467 (1956).
(4) R. K. Hill, T. H. Chan, and J. A. Joule, *Tetrahedron*, **21,** 147 (1965).
(5) The reported[3] yield of this compound was considerably improved by carrying out the reaction in THF at −35°.
(6) (a) J. Plimi, E. Knobloch, and M. Protiva, *Chem. Listy*, **46,** 758 (1952); (b) H. Booth, J. H. Little, and J. Feeney, *Tetrahedron*, **24,** 279 (1968); (c) J. E. Oliver and P. E. Sonnet, *J. Org. Chem.*, **39,** 2662 (1974).
(7) This compound and its derivatives were first prepared by Kathleen N. Juneau, M.S. Thesis, University of Minnesota, 1967.
(8) This cyclization to yield an azetidine is analogous to the formation of ϵ-coniceine (8-methyl-1-azabicyclo[4.2.0]octane) by heating the *O*-mesylate of 2-(2-hydroxypropyl)piperidine at 90°: G. Fodor and G. A. Cooke, *Tetrahedron, Suppl.*, **8,** 113 (1966).
(9) R. S. Monson, *Tetrahedron Lett.*, 567 (1971).
(10) E. Späth and F. Kesztler, *Ber.*, **69,** 2725 (1936).
(11) E. Leete and K. N. Juneau, *J. Am. Chem. Soc.*, **91,** 5614 (1969).
(12) The order in which these steps occur is unknown, and our failure to obtain incorporation of 5,9-dioxodecanoic acid into pinidine may indicate that a double bond at C_4–C_5 is required for formation of the alkaloid.
(13) E. Leete and J. O. Olson, *J. Am. Chem. Soc.*, **94,** 5472 (1972).
(14) R. Mayer, G. Wenschuh, and W. Töpelmann, *Chem. Ber.*, **91,** 1616 (1958).
(15) This ketone was previously obtained by the addition of the Grignard reagent formed from 5-chloro-2,2-ethylenedioxypentane to cyclopentanone, followed by an acidic work-up: C. Feugeas, *Bull. Soc. Chim. Fr.*, 2568 (1963).
(16) Previously described only in the patent literature: M. Rosenberger, German Offen. 2,129,652; *Chem. Abstr.*, **76,** 139935 (1972).
(17) Melting points are corrected. Elementary analyses were performed by M-H-W Laboratories, Garden City, Mich., or Clark Microanalytical Laboratory, Urbana, Ill. Mass spectra were determined by Dr. Roger Upham and his assistants at the University of Minnesota on an AEI-MS-30 instrument. NMR spectra were obtained on Varian T-60 or XL-100 instruments. Radioactivity measurements were carried out in a Nuclear Chicago liquid scintillation counter, Mark II, using as a solvent dioxane–ethanol with the usual scintillators.[18]
(18) A. R. Friedman and E. Leete, *J. Am. Chem. Soc.*, **85,** 2141 (1963).
(19) O. E. Edwards, G. Fodor, and L. Marion, *Can. J. Chem.*, **44,** 13 (1966).
(20) H. Christol, F. Plénat, and C. Reliaud, *Bull. Soc. Chim. Fr.*, 1566 (1968).