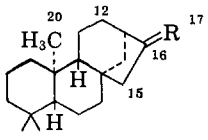
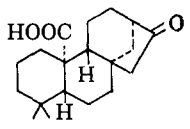
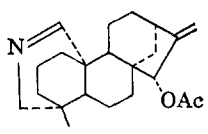
10-carboxy-17,20-bisnorkaurane (I)[1] in good yield and a new synthesis of (−)-kaurene (II) from intermediate I.



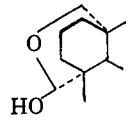
II, R = CH_2
XV, R = O



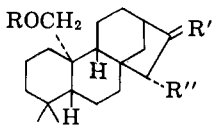
I



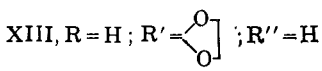
III



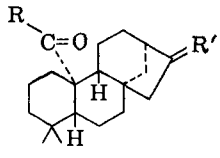
IV



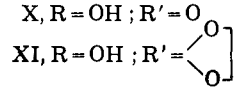
V, R = H; R′ = CH_2; R″ = OH
VI, R = Ac; R′ = O; R″ = OAc
VII, R = Ac; R′ = O; R″ = H



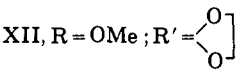
XIII, R = H; R′ = ; R″ = H



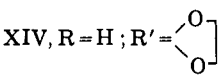
IX, R = H; R′ = O
X, R = OH; R′ = O



XI, R = OH; R′ =



XII, R = OMe; R′ =



XIV, R = H; R′ =

Veatchine azomethine acetate (III), prepared from crude Garrya alkaloids,[2] was treated with nitrous acid[3] to afford a hemiacetal (IV).[2] The Wolff-Kishner reduction of IV gave a diol (V), the diacetate, m.p. 98–99°, of which was converted to the corresponding ketone (VI), m.p. 184–185°, with the Lemieux-Johnson reagent.[4] Treatment of VI with calcium in liquid ammonia[5] removed the acetate group of ring D and afforded a keto monoacetate (VII), m.p. 139–140° (m.p. of the corresponding hydroxy ketone (VIII), 85.5–86.5°). The Jones oxidation of VIII at 0° afforded exclusively a keto aldehyde (IX), m.p. 157–160° with decomposition, which was further oxidized at room temperature with the same oxidant to give a keto acid (X), m.p. 251–252.5°. Melting points of the corresponding ketal carboxylic acid (XI),[6] ketal methyl ester (XII), and hydroxymethyl ketal (XIII), prepared from XII with lithium aluminum hydride, are 202–203°, 102–103°, and 85–86°, respectively.

Infrared spectra of X, XI, and XII are completely superimposable with those of the corresponding racemates[1] in each case. Oxidation of the hydroxyl group of XIII with chromic acid in pyridine provided a ketal aldehyde (XIV), m.p. 160–163° with decomposition, which was subjected to Wolff-Kishner reduction and acid hydrolysis to afford a ketone (XV), m.p. 116–117°. Infrared spectral comparison of XV to the corresponding racemate (XVI)[7] established their identity.

(2) H. Vorbrueggen and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 2990 (1962).
(3) J. W. ApSimon, O. E. Edwards, and R. Howe, *Can. J. Chem.*, **40**, 630 (1962).
(4) R. Pappo, D. S. Allen, R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, **21**, 478 (1956).
(5) J. H. Chapman, J. Elks, G. H. Phillipps, and L. J. Wyman, *J. Chem. Soc.*, 4344 (1956), ref. 2.
(6) XI, $[\alpha]^{27}D$ −30° (*c* 1.2, chloroform).
(7) R. A. Bell and R. E. Ireland, *Tetrahedron Letters*, **No. 4**, 269 (1963).

The synthesis of XV completes a total synthesis of kaurene, since XVI has previously been converted to kaurene.[7,8] This synthesis is also the first conversion of a diterpene alkaloid to a naturally occurring diterpene,[9] and thus the *direct* correlation of the two groups of natural products has now been accomplished.[10,11]

Acknowledgment.—The author is deeply indebted to Professor Carl Djerassi for generously providing crude alkaloids of Garrya Laurifolia without which this work would not have been completed.

The author is grateful to Professor Ireland for supplying an authentic sample of XVI. The levorotatory ketone (XV) was prepared from (−)-kaurene by Briggs, *et al.*, *J. Chem. Soc.*, 1345 (1963). However, this enantiomer was not available to the author.

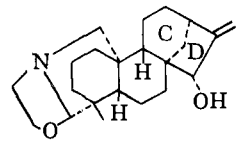
(8) The first synthesis of kaurene has recently been reported by R. A. Bell, R. E. Ireland, and R. A. Pastyka, *J. Org. Chem.*, **27**, 3741 (1962).
(9) Conversions of diterpene alkaloids into degradation products of diterpenes have been reported: W. A. Ayer, C. E. McDonald, and G. G. Iverach, *Tetrahedron Letters*, **No. 17**, 1095 (1963); L. H. Zalkow and N. N. Girotra, *J. Org. Chem.*, **28**, 2037 (1963), ref. 2.
(10) Satisfactory analyses and spectra (infrared, n.m.r.) were obtained for all new compounds described herein.
(11) This investigation was supported by a grant (GM 10369) from the National Institutes of Health, Public Health Service.

MELLON INSTITUTE SATORU MASAMUNE
PITTSBURGH, PENNSYLVANIA
RECEIVED OCTOBER 9, 1963

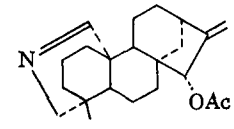
Total Syntheses of Diterpenes and Diterpene Alkaloids. IV.[1] Garryine

Sir:

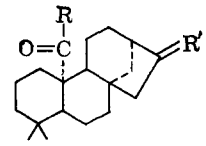
Relatively uncomplicated diterpene alkaloids may be conveniently divided into two categories, the Garrya series and Atisine-type alkaloids.[2] The former alkaloids possess a [3.2.1]bicyclooctane C,D ring structure, whereas a [2.2.2]bicyclooctane system is present in compounds of the latter series. We now wish to report the first synthesis of garryine (I), a representative alkaloid of the Garrya alkaloids.



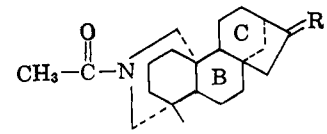
I



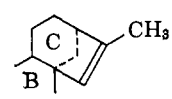
VIII



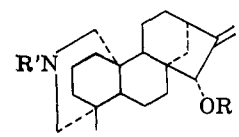
III, R = OH; R′ = O
IV, R = NH·NH_2; R′ =
V, R = N_3; R′ =



VI, R =
VII, R = O
IX, R = CH_2



X



XI, R = H; R′ = C_2H_5
XII, R = Ac; R′ = C_2H_5
XIII, R = Ac; R′ = CN
XIV, R = R′ = H

(1) Part II: S. Masamune, *J. Am. Chem. Soc.*, **86**, 288 (1964); part III: S. Masamune, *ibid.*, **86**, 289 (1964).
(2) For review, see ref. 2 of part II.

We have also completed the conversion of this alkaloid to atisine (II), which will be described separately.

The synthesis of 16-keto-10-carboxy-17,20-bisnorkaurane (III) has already been described.[1] Treatment of the acid chloride of III, (−)-isomer, with anhydrous hydrazine afforded a crude acid hydrazide, m.p. 265–270°, which was further converted to an acid hydrazide ketal (IV), m.p. 256–258°, with ethylene glycol and three equivalents of *p*-toluenesulfonic acid. Compound IV exhibited an infrared spectrum identical with that of its *dl* compound described previously.[1] Reaction of IV with nitrous acid gave an unstable azide (V) (λ_{max} (methylcyclohexane) 4.69, 5.80 μ) which was irradiated at $-10 \sim -15°$ with a Hanovia 450-w. mercury lamp.[3] Careful column chromatography separated a lactam fraction of the photolysis product, which was reduced with lithium aluminum hydride and then acetylated to give an acetamide ketal (VI), m.p. 185–186°, in approximately 5% yield in addition to other compounds. The acid hydrolysis of VI afforded a keto amide (VII), m.p. 164–165°, which proved to be identical with the compound prepared from veatchine azomethine acetate (VIII).[4] Reaction of VII with methylene triphenylphosphorane in dimethyl sulfoxide[5] led to an exocyclic methylene compound (IX), m.p. 147–148° (λ_{max}^{Chl} 11.36 μ; n.m.r. signal of two olefinic protons, 5.20 τ), which was isomerized to an endocyclic isomer (X),[6] m.p. 148–149°, (λ_{max}^{Chl} 12.24 μ, n.m.r. signal of one olefinic proton, 4.93 τ) with dry hydrogen chloride in cold acetic acid.[7] The n.m.r. spectral analysis of an equilibrated mixture showed that it consisted of 75% of X and 20% of IX. The photosensitized (hematoporphorin) oxygenation[8] of X followed by the lithium aluminum hydride reduction of the resulting hydroperoxide (λ_{max}^{Chl} 3.1, 11.0 μ) in diethyl ether[8] gave an oily alcohol (XI) (λ_{max}^{Chl} 2.8, 11.05 μ). The corresponding acetate (XII) melted at 85–86°.[9] The von Braun reaction on XII proceeded smoothly to afford an N-cyano compound (XIII), m.p. 220–221° (λ_{max}^{Chl} 4.51, 5.8, 11.0 μ). The lithium aluminum hydride reduction[10] of XIII gave a cyclic secondary amine (XIV), m.p. 166–167°, which was identical in every respect with the compound obtained by the lithium aluminum hydride reduction[4] of VIII.

Wiesner, *et al.*, have alkylated XIV with ethylene bromohydrin to give dihydroveatchine, which in turn was converted quantitatively into garryine by a unique oxidation reaction with osmium tetroxide.[11] Therefore, the work described herein completes the total synthesis of a Garrya alkaloid, garryine.[12,13]

(3) Photolyses of model compounds have been performed in several places including this Laboratory. Some of the results have already been published: J. W. ApSimon and O. E. Edwards, *Can. J. Chem.*, **40**, 896 (1962); W. L. Meyer and A. S. Levinson, *Proc. Chem. Soc.*, 15 (1963).

(4) H. Vorbrueggen and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 2990 (1962).

(5) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

(6) X appears to be the same compound as that prepared from VIII by a different route, see ref. 4.

(7) L. H. Briggs and P. W. Cawley, *J. Chem. Soc.*, 1888 (1948). Although kaurene was converted to its hydrochloride under these conditions, IX rearranged directly to X.

(8) G. O. Schenk, *Angew. Chem.*, **69**, 579 (1957). For application to steroids and terpenes, see A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **83**, 1498 (1961); R. A. Bell and R. E. Ireland, *Tetrahedron Letters*, **No. 4**, 269 (1963).

(9) The over-all yield of XII from X was routinely more than 65%, and a by-product (less than 5%) appeared to be the epimeric acetate (garryfoline series).

(10) A. C. Curie, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 4693 (1961).

(11) K. Wiesner, W. I. Tayler, S. K. Figdor, M. F. Bartlett, J. R. Armstrong, and J. A. Edwards, *Chem. Ber.*, **86**, 800 (1953).

(12) Satisfactory analyses and spectra (infrared, n.m.r.) were obtained for all new compounds described herein.

(13) This investigation was supported by a grant (GM 10369) from the National Institutes of Health, Public Health Service.

Acknowledgment.—The author is grateful to Professor C. Djerassi for providing him with an abundant amount of crude alkaloids of Garrya Laurifolia.

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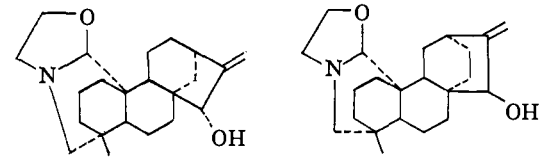
RECEIVED OCTOBER 9, 1963

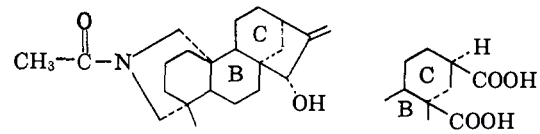
Total Syntheses of Diterpenes and Diterpene Alkaloids. V.[1] Atisine

Sir:

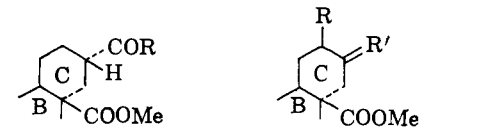
In 1954 Wiesner first proposed the correct gross structures for dihydro derivatives of veatchine (I) and atisine (II), basing his argument on a limited amount of experimental data then available.[2] Since that time unsuccessful attempts[3] apparently have been made to convert the former alkaloid to the latter. We have now accomplished such a conversion and report it herein.



I II

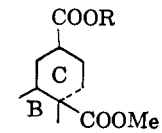


III IV



V, R = OMe
VI, R = OH
VII, R = Me

VIII, R = H; R′ = H,OAc
IX, R = H; R′ = H,OH
X, R = H; R′ = O
XI, R = COOMe; R′ = O



XII, R = Me
XIII, R = H

Compound III, prepared from veatchine azomethine acetate,[4] was oxidized with the Lemieux and Rudloff reagent[5] to afford a dicarboxylic acid, m.p. 252–254° (IV).[6] Treatment of the dimethyl ester of IV with sodium methoxide effected the epimerization of a carbomethoxy group and afforded a *trans* dimethyl ester (V), which was subsequently hydrolyzed to give

(1) Part IV: S. Masamune, *J. Am. Chem. Soc.*, **86**, 290 (1964).

(2) K. Wiesner, R. Armstrong, M. F. Bartlett, and J. A. Edwards, *Chem. Ind.* (London), 132 (1954).

(3) K. Wiesner and Z. Valenta, "Progress in the Chemistry of Organic Natural Products," Vol. XVI, Springer-Verlag, Vienna, 1958, p. 52.

(4) H. Vorbrueggen and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 2990 (1962); K. Wiesner, J. R. Armstrong, M. F. Wartlett, and J. A. Edwards, *ibid.*, **76**, 6068 (1954).

(5) R. W. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955); E. von Rudloff, *ibid.*, **33**, 1714 (1955).

(6) S. W. Pelletier, *J. Am. Chem. Soc.*, **82**, 2398 (1960).