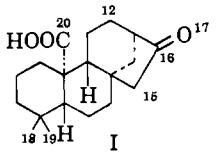
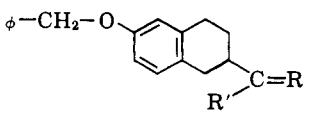
carboxy-17,20-bisnorkaurane (I)[3] which can be converted to the above two groups of natural products.

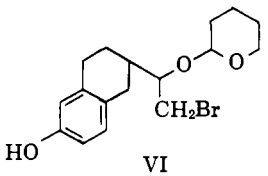
6-Benzyloxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid (II), m.p. 149–150°, prepared from the corresponding phenol,[4] was treated successively with



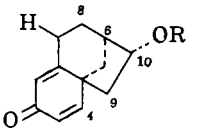
I



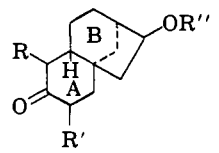
II, R = O; R′ = OH
III, R = O; R′ = CH_2Br
IV, R = OH, H; R′ = CH_2Br
V, R = OTHP, H; R′ = CH_2Br



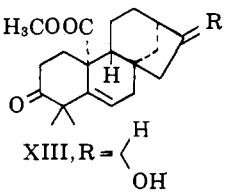
VI



VII, R = THP
VIII, R = H

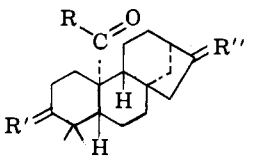


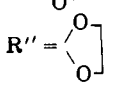
IXa, R = R′ = H; R″ = Bz
X, R = COOMe; R′ = H; R″ = Bz
XI, R = R″ = H; R′ = COOMe



XIII, R =

XIV, R = O



XV, R = OCH_3; R′ = R″ = O
XVI, R = OH; R′ = H_2; R″ = 
XVII, R = OMe; R′ = H_2; R″ = 

oxalyl chloride, diazomethane, and hydrobromic acid to afford a bromoketone (III), m.p. 64–65°. The sodium borohydride reduction of III provided a mixture of epimeric bromohydrins (IV), which was converted to the tetrahydropyranyl ethers (V). Hydrogenolysis of V with palladium on carbon gave the corresponding phenols (VI). The base treatment of VI under similar conditions to those used previously[1] effected the cyclization of only one isomer of VI to give the tetrahydropyranyl ether of a hydroxy dienone (VII). The corresponding hydroxy compound (VIII) melted at 115–116° (λ_{max}^{MeOH} 245 mμ (1.8 × 10^4), λ_{max}^{Chl} 3.0, 6.04, 6.18, 6.25 μ). The over-all yield of VIII from II is approximately 30%. The stereochemistry of the hydroxyl group of VIII is assigned as shown in VIII, based on the stereochemical course of cyclization.[5] A model shows that the ethereal oxygen atom of the *uncyclized* phenol in the transition state interacts severely with a hydrogen atom at position 8.

(3) All formulas shown in this paper are taken to represent racemates.

(4) J. Jacques and A. Horeau, *Bull. soc. chim. France*, 512 (1950). The ether cleavage of 6-methoxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid was effected with HBr–acetic acid.

(5) Attempts to cyclize 6-hydroxy-1,2,3,4-tetrahydronaphthalenes substituted in the 2 position with the following groups failed: an oxidethyl group, an α-keto-β-bromoethyl group, and the ethylene glycol ketal of α-keto-β-bromoethyl. This clearly defines the steric course of cyclization and presents excellent evidence to support the mechanism proposed for the S_N2 reaction of haloketones. See E. L. Eliel, "Steric Effects in Organic Chemistry," M. Newman, Ed., Chapman and Hall, New York, N. Y., 1956, p. 103.

Catalytic hydrogenation of the benzoate, m.p. 116–117°, of VIII with palladium–calcium carbonate afforded two isomeric tetrahydro compounds (IXa, m.p. 103–104°, and IXb), m.p. 105–106°, in a 7:3 ratio. Conversion of IXa to known *cis*-decalin-9-acetic acid[6] and further to the *cis*-decalin-9-carboxylic acid[6,7] shows that the A and B rings of IXa are *cis* fused.

Carbomethoxylation of IXa with triphenylmethyl sodium and carbon dioxide and methylation afforded a β-keto ester (X), m.p. 150–152°.[8] Alternatively, X was obtained by a similar carbomethoxylation of the benzoate of VIII (m.p. of the product, 108–109°) followed by hydrogenation. Therefore the carbomethoxy group of X must be located at position 1.

Ring A was constructed by a conventional method. Addition of ethyl vinyl ketone followed by cyclization provided a tetracyclic unsaturated ketone (XII), m.p. 126–127°. Exhaustive methylation of the tetrahydropyranyl ether of XII and then removal of the protective group afforded a dimethyl compound (XIII), m.p. 154–155°, which was oxidized with the Jones reagent to give an amorphous diketone (XIV). Catalytic hydrogenation of XIV resulted in only one saturated compound (XV), m.p. 130–131°, in approximately 60% yield. The Wolff–Kishner reduction on the monoketal of XV removed the ketone and provided an acid (XVI),[9] m.p. 205–207°, and an acid hydrazide. The corresponding ketal methyl ester (XVII) and keto acid (I) melted at 96–97.5° and 249–250°, respectively.

We have succeeded in converting veatchine azomethine acetate to the corresponding levorotatory enantiomers of XVI, XVII, and I. Infrared spectra of these compounds were completely superimposable, respectively. These results confirm that the assignments of structures and stereochemistry of all synthetic intermediates are correct. The conversion of veatchine into the synthetic intermediate (I) and the syntheses of a diterpene and diterpene alkaloids are described in accompanying papers.[10,11]

Acknowledgment.—The author is very grateful to Mr. N. T. Castellucci for preparing synthetic intermediates used in this investigation.

(6) R. D. Haworth and A. F. Turner, *J. Chem. Soc.*, 1240 (1958).

(7) The Wolff–Kishner reduction converted IXa to 10-hydroxy-4a,6-ethanodecalin, m.p. 45–46° (for numbering, see VIII), which was oxidized to the corresponding ketone. The Baeyer–Villeger reaction on this ketone gave a liquid lactone, which after alkaline hydrolysis, methylation, and oxidation afforded methyl 2-keto-decalin-9-acetate. The Clemensen reduction on this keto ester proceeded smoothly to afford *cis*-decalin-9-acetic acid, m.p. 117° (m.p. of its anilide, 158°). Application of the Barbier–Wieland degradation to this 9-acetic acid led to *cis*-decalin-9-carboxylic acid as reported.[6]

(8) Carbomethoxylation of IXa with dimethyl carbonate took a different course. The product (XI), m.p. 135–137°, is highly enolic, in contrast to X, and is represented by XI. Although the C-1 enolate anion is more stable than the C-3 anion due to the *cis* fusion of the rings, a bulky dimethyl carbonate molecular prefers the less hindered site: G. Stork and R. H. Hill, *J. Am. Chem. Soc.*, **79**, 495 (1957).

(9) The resolution of this acid was only partially successful due to the limited amount of material available. The highest rotation observed was $[\alpha]^{20}D = -16$. The pure (−) enantiomer had $[\alpha]^{27}D = -30$; see paper III of this series.

(10) Satisfactory analyses and spectra (infrared, ultraviolet, 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

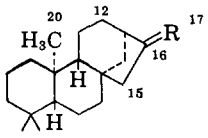
Total Syntheses of Diterpenes and Diterpene Alkaloids. III.[1] Kaurene

Sir:

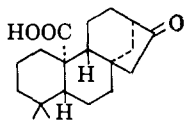
We wish to report the degradation of veatchine, a major alkaloid of Garrya Lauriforia, to (−)-16-keto-

(1) Part II: S. Masamune, *J. Am. Chem. Soc.*, **86**, 288 (1964).

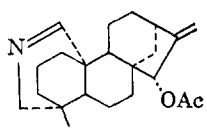
10-carboxy-17,20-bisnorkaurane (I)[1] in good yield and a new synthesis of (−)-kaurene (II) from intermediate I.



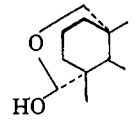
II, R = CH_2
XV, R = O



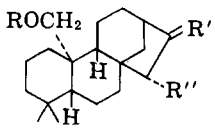
I



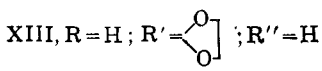
III



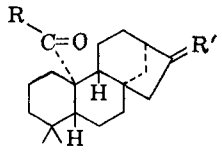
IV



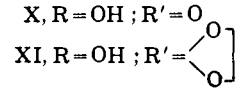
V, R = H; R′ = CH_2; R″ = OH
VI, R = Ac; R′ = O; R″ = OAc
VII, R = Ac; R′ = O; R″ = H



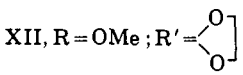
XIII, R = H; R′ = ; R″ = H



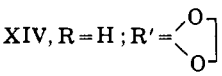
IX, R = H; R′ = O
X, R = OH; R′ = O



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.

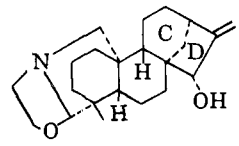
(8) The first synthesis of kaurene has recently been reported by R. A. Bell, R. E. Ireland, and R. A. Pastyka, *J. Org. Chem.*, **27**, 3741 (1962).
(9) Conversions of diterpene alkaloids into degradation products of diterpenes have been reported: W. A. Ayer, C. E. McDonald, and G. G. Iverach, *Tetrahedron 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

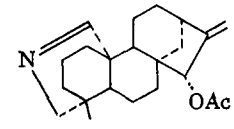
Total Syntheses of Diterpenes and Diterpene Alkaloids. IV.[1] Garryine

Sir:

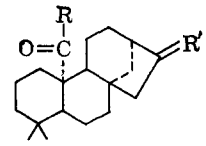
Relatively uncomplicated diterpene alkaloids may be conveniently divided into two categories, the Garrya series and Atisine-type alkaloids.[2] The former alkaloids possess a [3.2.1]bicyclooctane C,D ring structure, whereas a [2.2.2]bicyclooctane system is present in compounds of the latter series. We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



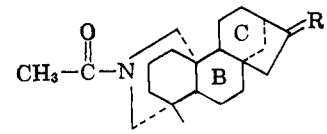
I



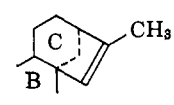
VIII



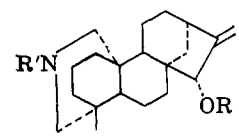
III, R = OH; R′ = O
IV, R = NH·NH_2; R′ =
V, R = N_3; R′ =



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.