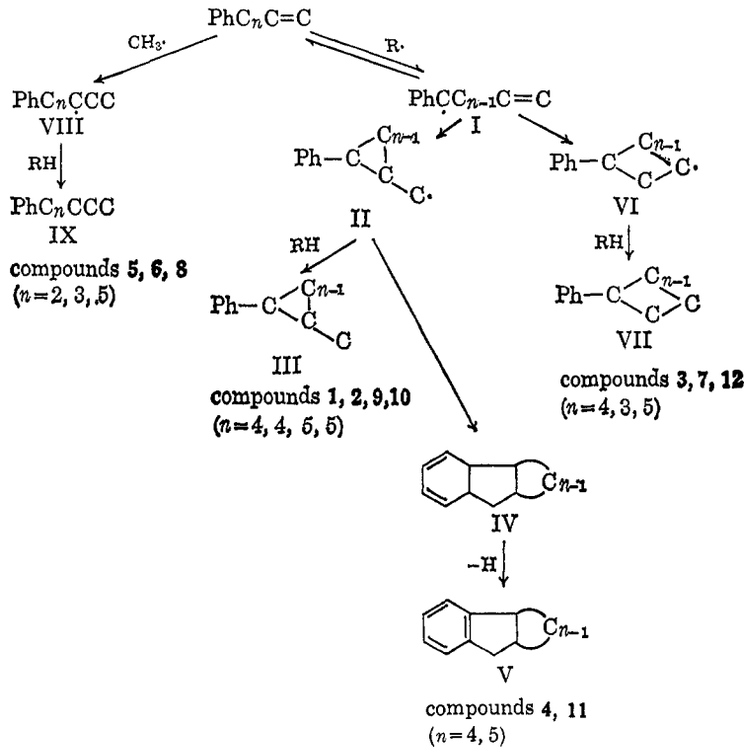
SCHEME I

FORMATION OF THE MONOMERIC PRODUCTS FROM ω-PHENYL-1-ALKENES



ture of 90°; otherwise decomposition would occur at higher temperatures. The molar area responses (over Carbowax 20M column) are as follows: (A) di-*t*-butyl peroxide, 1.0; *t*-butyl alcohol, 0.58; acetone, 0.44; (B) naphthalene, 1.0; 6-phenyl-1-hexene, 0.94: phenylcyclohexane, 0.71; 1,2,3,3a,8,8a-hexahydrocyclopent[*a*]indene, 0.78; 1-methyl-2-phenylcyclopentanes, 0.62; *n*-hexylbenzene, 1.0, and (C) 1,4-di-*t*-butylcyclohexane, 1.0; 1-methyl-2-phenylcyclohexane, 0.87; 1,2,3,-4,4a,9a-hexahydrofluorene, 0.70; *n*-heptylbenzene, 0.91. Their relative retention times were tabulated in the preceding papers.[3,4]

Resin Acids. IX. Cationic Cyclization of Pimaric Acid Derivatives. Partial Synthesis of (−)-Hibaene[1]

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The partial synthesis of (−)-hibaene and (−)-hibane from pimaric acid is described. Cationic cyclization of methyl 16-hydroxy-$\Delta^{8(14)}$- and $\Delta^{8(9)}$-dihydropimarate alkyl and arylsulfonates did not result in derivatives of hibane, but led, contrary to expectations, to compounds of type **16** with rearrangement of the carbon skeleton.

The tetracyclic diterpene (−)-hibaene (**1**) (Chart I) has been isolated in two laboratories[3,4] from different sources and its structure elucidated.[3] Its enantiomer (+)-hibaene **2a** (stachene) has also been encountered in nature.[5,6] The absolute configuration assigned to these compounds has been confirmed by correlation[7] of monogynol **2b** with isostevane **3** and conversion[8] of (+)-hibaene to (−)-kaurene (**4**). More recently, the total synthesis of the racemate has been accomplished.[9]

Our own efforts in this area were begun before the discovery of the hibaenes and their derivatives[10] and were based on the notion that cationically induced cyclization of suitably substituted derivatives of pimaradienes **5** might lead to compounds based on the carbon skeleton **6** whose eventual discovery in nature could be anticipated. Choice of starting material was originally dictated by the relative accessibility of isopimaric acid **7**. In the event this led[11] to substances which turned out to be derivatives of isohibaene **8**

(1) Supported in part by grants from the National Science Foundation (GP-1962) and the Petroleum Research Fund of the American Chemical Society. Previous paper: W. Herz, R. C. Blackstone, and M. G. Nair, *J. Org. Chem.*, **31**, 1800 (1966).

(2) On leave from the University College of South Wales and Monmouthshire, Cardiff.

(3) Y. Kitahara and A. Yoshikoshi, *Tetrahedron Letters*, 1771 (1963); *Bull. Chem. Soc., Japan*, **37**, 890 (1964); **38**, 735 (1965).

(4) L. H. Briggs, R. C. Cambie, P. S. Rutledge, and D. W. Stanton, *Tetrahedron Letters*, 2223 (1964).

(5) R. D. H. Murray and R. McCrindle, *Chem. Ind.* (London), 500 (1964).

(6) A. H. Kapadi and S. Dev, *Tetrahedron Letters*, 2751 (1964).

(7) J. R. Hanson, *Chem. Ind.* (London), 1579 (1964).

(8) A. H. Kapadi and S. Dev, *Tetrahedron Letters*, 1255 (1965).

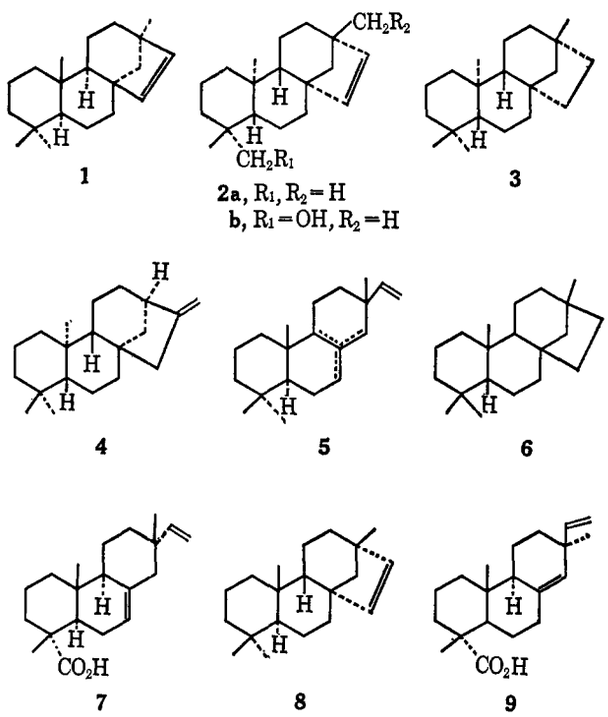
(9) R. E. Ireland and L. N. Mander, *Tetrahedron Letters*, 2627 (1965).

(10) The first such compound to be reported was beyerol: P. R. Jefferies, R. S. Rosich, D. E. White, and M. C. Wood, *Australian J. Chem.*, **15**, 521 (1962).

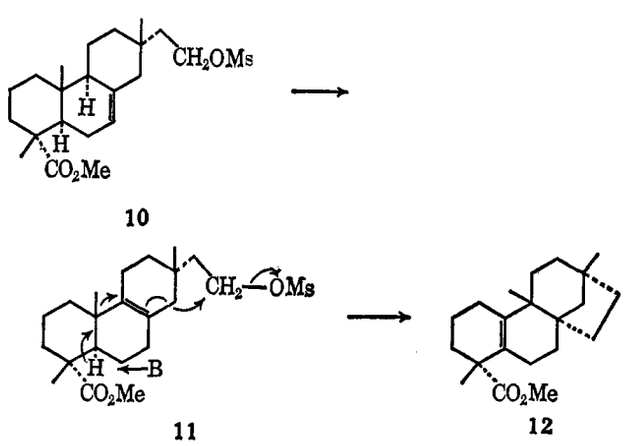
(11) W. Herz, D. Melchior, R. N. Mirrington, and P. J. S. Pauwels, *J. Org. Chem.*, **30**, 1873 (1965).

[8,13-epi-(−)-hibaene],[12] a ring system representatives of which have so far not been isolated from natural sources. With the configurational aspects clarified by the recent publications,[7,12] pimaric acid **9** became the obvious point of departure for further work. The present paper describes these studies which have culminated in a successful partial synthesis of (−)-hibaene and possess other features of interest as well.

CHART I



In the isopimaric acid series, solvolysis of **10** and **11** had resulted[11] not only in the desired cyclization of the two-carbon side chain toward C-8, but also in migration of a methyl group and formation of **12**, presumably by the indicated mechanism.

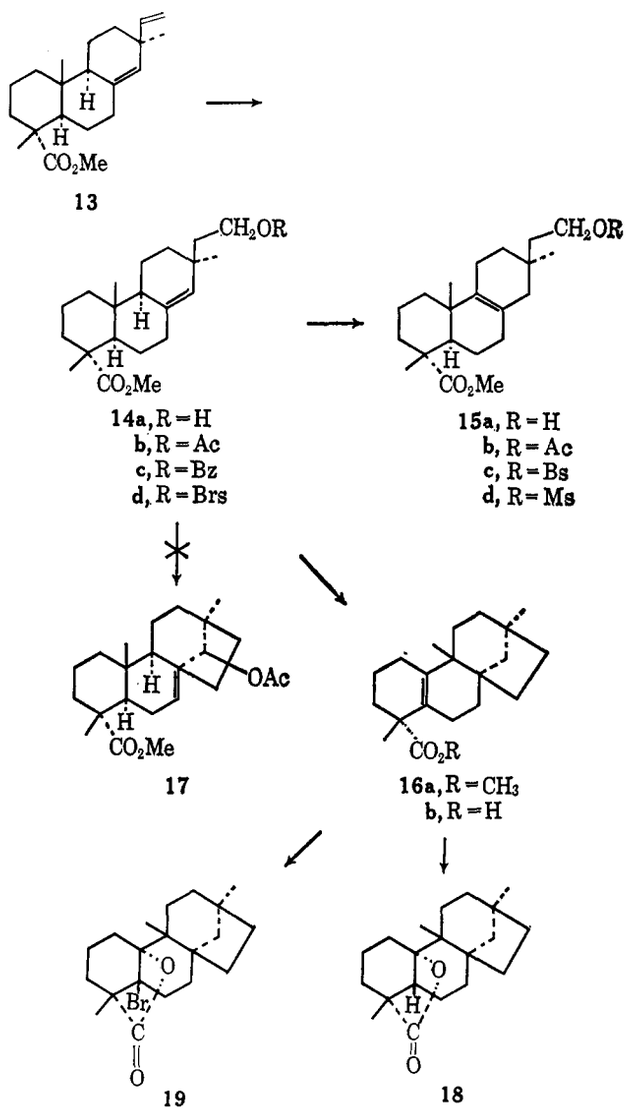


An analogous frustration of the proposed synthetic scheme in the pimaric acid series was not anticipated because the stereochemistry (C-10 methyl and two-carbon side chain *cis*) would not have permitted the concerted series of reactions adumbrated in **11**. These expectations were disappointed.

(12) The partial synthesis of isohibaene itself was accomplished by E. Wenkert, P. W. Jeffs, and J. R. Mahajan, *J. Am. Chem. Soc.*, **86**, 2218 (1964).

Selective monohydroboration of methyl pimarate **13** with diisoamylborane[13] proceeded somewhat less smoothly than that of methyl isopimarate.[11] The syrupy reaction product **14a** (80%) (Scheme I) was accompanied by small amounts of starting material and a diol (20%), evidence for whose formulation as **21** will

SCHEME I

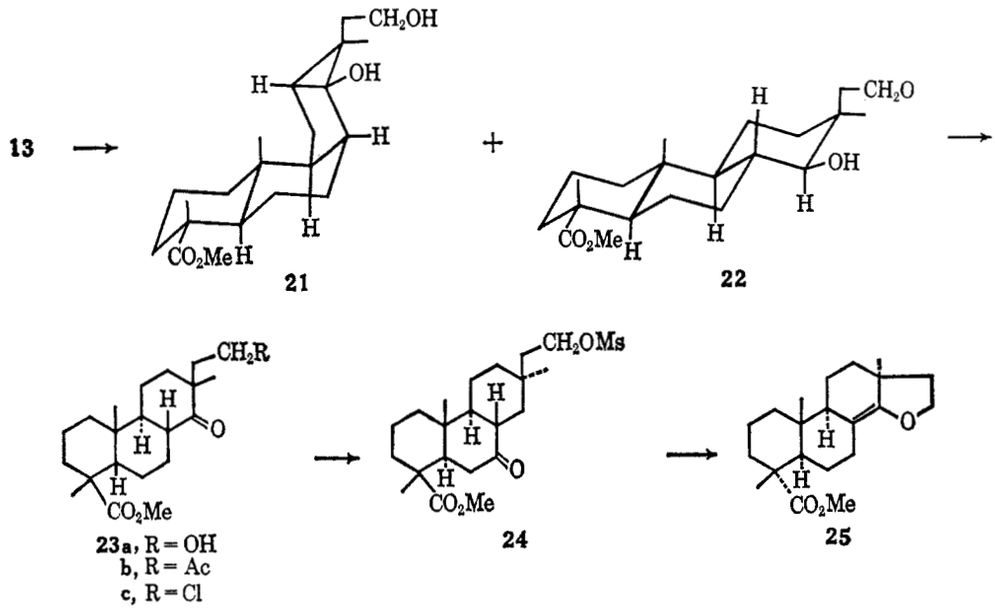


be presented subsequently. Compound **14a** was characterized as the crystalline benzoate **14c** and brosylate **14d**. The acetate **14b** was smoothly isomerized by hydrogen chloride–chloroform to the $\Delta^{8(9)}$ isomer **15b** which on mild hydrolysis gave **15a**. Some difficulty was encountered in forming sulfonate esters; the brosylates **14d** and **15c**, for example, were formed only partially after lengthy reaction periods. The mesylate **15d** could be formed to completion after 4 days of reaction, although it was not crystalline.

Acetolysis of **14d** resulted in cyclization, accompanied by rearrangement, to **16a** rather than the desired tetracyclic diester **17**. That the double bond had migrated to the $\Delta^{8(9)}$ position prior to cyclization was shown by acetolysis of **15d** which also furnished **16a**. The structure of **16a** was inferred from its nmr spec-

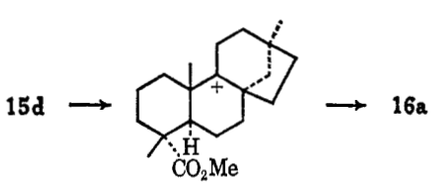
(13) H. C. Brown and G. Zweifel, *ibid.*, **82**, 3222, 3223 (1960); **83**, 1241 (1961).

SCHEME II



trum, which exhibited no low-field signals characteristic of olefinic protons, and was verified by transformations similar to those used for the analogous substance **12** in the isopimaric acid series.[11] Hydrolysis of **16a** furnished an amorphous acid **16b**, characterized as the crystalline cyclohexylamine salt, which was β,γ unsaturated (loss of CO_2 on heating)[14] and could be converted to the γ-lactone **18** (infrared band at 1760 cm^{-1}). Treatment of **16a** with bromine afforded an unstable bromo γ-lactone **19** (infrared band at 1760 cm^{-1}).

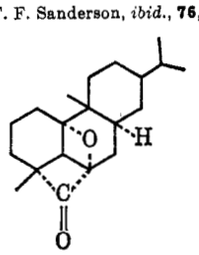
The formation of **16a** from **14** or **15d** requires a stepwise sequence of reactions involving the carbonium ion **20** since the stereoelectronics are not favorable to a concerted reaction. The transformation **20** → **16a**



20

then parallels well-known acid-catalyzed rearrangements of dihydroabietic,[14,15] isopimaric,[16] and pimaric[16] acid.

(14) For analogous reactions which were used in the structure proof of i see L. A. Subluskey and T. F. Sanderson, *ibid.*, **76**, 3512 (1954).



i

(15) D. H. R. Barton, *Chem. Ind.* (London), 638 (1948); L. Velluz, G. Muller, A. Petit, and J. Mathieu, *Bull. Soc. Chim. France*, 401 (1954); W. Herz and H. J. Wahlborg, *J. Org. Chem.*, **30**, 1881 (1965).

(16) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959); B. Green, A. Harris, and W. B. Whalley, *J. Chem. Soc.*, 4715 (1958); Le-Van-Thoi and J. Ourgaud, *Bull. Soc. Chim. France*, 202 (1956).

With the failure of this approach to the desired tetracyclic system, efforts were made to adapt the previously studied sequence of reactions[11] to the synthesis of hibane and hibaene. Dihydroboration of methyl pimarate with diborane followed by the usual oxidative work-up afforded two diols, **21**, mp 185° (50%), and **22**, 170.5° (19%), the former being identical with the diol isolated as a minor product in the monohydroboration of **13**.

On the grounds that hydroboration would be expected to occur more readily from the less hindered side, particularly when the bulky diisoamylborane is employed, the major product was formulated as **21** and the minor product, unobserved in the hydroboration with diisoamylborane, as **22**. These assignments were fully confirmed by the nmr spectra. In the spectrum of the higher melting, predominating diol, the H-14 proton gave rise to a doublet (J = 9 cps) at relatively high field (δ = 2.8 ppm), while, in the spectrum of the minor product, the H-14 signal was located under the methoxyl resonance at 3.7 ppm. Models of **21** and **22** (see Scheme II) show that, in the former (*cis* B/C ring junction), H-14 is shielded by the methyl group at C-10. No such shielding would be expected in the case of **22**, where the ring junction is *trans*.

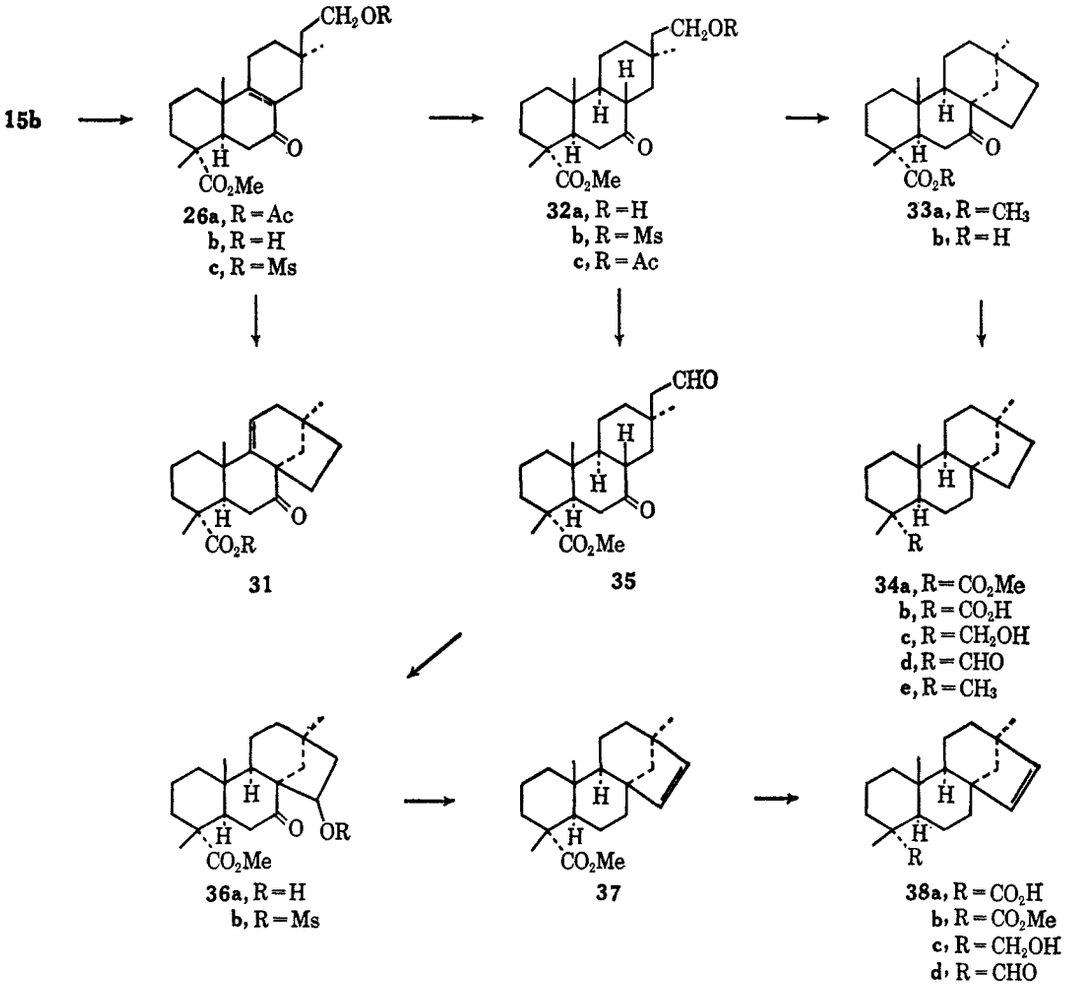
Selective oxidation of both diols with N-bromoacetamide afforded the crystalline ketone **23a**, the B/C *trans* ring junction being established by the ORD curve (strong negative Cotton effect)[17] and the nmr spectrum. The signal of the C-13 methyl group appears downfield (1.00 ppm) relative to that of the parent diols (0.90 and 0.91 ppm). Models show that these protons are in the plane of the ketonic carbonyl group and are consequently deshielded in the B/C *trans* structure. The keto group in this molecule was unreactive toward the usual reagents.[18]

When the mesylate **24** was stirred with potassium *t*-butoxide, cyclization occurred to form the crystalline enol ether **25** rather than the desired tetracyclic ketone.

(17) C. Djerassi and W. Klyne, *J. Chem. Soc.*, 4929 (1962).

(18) For analogous behavior of 14-keto all-*trans*-tetrahydroabietic acid, see A. W. Burgstahler and J. N. Marx, *Tetrahedron Letters*, 3333 (1964).

SCHEME III



Assignment of structure **25** was originally based on spectroscopic evidence; in particular, the nmr spectrum exhibited a multiplet centered at 4.1 ppm due to the OCH_2 protons and the C-10 methyl resonance had shifted upfield, from 1 ppm in **23** and **24**, to the characteristically shielded position (0.81 ppm) also typical of isopimaric acid and its derivatives.[7] Facile transformation of **25** to **23c** on treatment with methanolic hydrogen chloride established this point chemically.

The formation of **25** in an *Ausweichsreaktion* is perhaps attributable to the strong 1,3-diaxial interaction offered by C-10 methyl to axial attack by the two-carbon side chain. Since similar results were at this time recorded by Wenkert and his associates with ketones prepared from pimaradiene,[19] further exploration of this route was abandoned and attention directed to the introduction of a ketone group at C-7. In compounds such as **32** (Scheme III), because of the strain on the resulting ring system, O-alkylation is not a suitable alternative to C-alkylation at C-8. Moreover, the possibility, apparent from models, of reducing hindrance exerted by C-10 methyl to axial attack by the two-carbon side chain by utilizing a $\Delta^{8(9)}$-ketone appeared attractive.

First attempts to brominate **14a** or **b** in the allylic position or to oxidize them with selenium dioxide, chromic acid, or lead tetraacetate were discouraging. Chromic acid oxidation of **15b** (Scheme IV) furnished a crystalline diketone formulated as **28a**, by retroaldol reaction of **27** formed from the hoped for **26**, or perhaps **29a**. This result was surprising in view of the report[20] that the triacetate **30a** could be oxidized to the α,β-unsaturated ketone **30b**, but oxidation of methyl dihydropimarate similarly only yielded **28** or **29b** rather than a compound corresponding to **26**.

However, oxidation of **15b** with *t*-butyl chromate[21] under carefully defined conditions gave the α,β-unsaturated ketone **26a** (Scheme III) in about 50% yield. The gummy product was isolated as the crystalline 2,4-dinitrophenylhydrazone which was cleaved with acetone and stannous chloride.[22] This led to the ketonic alcohol **26b**, hydrolysis of the acetoxy group accompanying the cleavage. The carbonyl group was placed at C-7 by analogy with the results of similar oxidations in the triterpene field.[23] The reactivity of the keto group, *e.g.*, its ready formation of a dinitrophenyl hydrazone, indicated that it was not located at C-14, by contrast with the marked inert character of **23a**, nor at C-11 since steroidal 11-ketones are known to be unreactive.[24] Confirmation was provided by the further transformations of **26b**.

(19) E. Wenkert, A. Afonso, P. Beak, R. W. J. Carney, P. W. Jeffs, and J. D. McChesney, *J. Org. Chem.*, **30**, 713 (1965).

(20) A. Diara, C. Asselineau, P. Laszlo, and J. Pudles, *Bull. Soc. Chim. France*, 99 (1963).

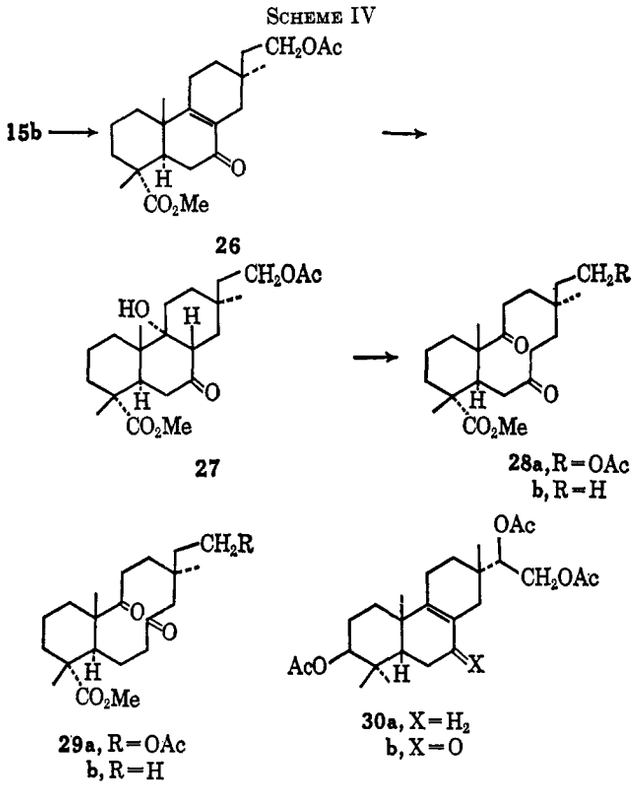
(21) E. Menini and J. K. Norymberski, *Biochem. J.*, **84**, 195 (1962).

(22) J. Demaecker and R. H. Martin, *Nature*, **173**, 266 (1954).

(23) C. Dorée, J. M. McGhie, and F. Kurzer, *ibid.*, **163**, 140 (1949).

(24) H. J. E. Loewenthal, *Tetrahedron*, **6**, 269 (1959).

SCHEME IV



The keto alcohol **26b** on treatment with methanesulfonyl chloride yielded a mesylate **26c** which was cyclized smoothly by potassium *t*-butoxide to the tetracyclic ketone **31**, the structure being confirmed by the appearance in the nmr spectrum of a triplet centered at 5.1 ppm due to H-11. Catalytic hydrogenation of this substance, under varying conditions, gave undoubtedly some of the desired ketone **33**, but the product was, on spectral and thin layer evidence, heterogeneous, both double bonds and keto group having been attacked.

The ketone **33** was, however, reached by catalytic reduction of the unsaturated keto alcohol **26b**. This afforded a mixture of epimerides which was successfully equilibrated by base to give the noncrystalline B/C *trans*-ketol **32a**. The assignment of configuration at C-9 follows from a study of molecular models of **26**, it being apparent that the α face is much less hindered, and the ORD curve of **32a** which exhibited a weak negative Cotton effect.[25] The configuration of C-8 is therefore H_β, although this is not relevant to the cyclization step (*vide infra*).

Treatment of **32a** with methanesulfonyl chloride gave the corresponding mesylate **32b**, though, as experienced elsewhere in this work, reaction was slow and sensitive to rise of temperature. However, after several days of reaction time, the ester was obtained in excellent yield and proved to be crystalline, which fact supported the view that **32a** was stereochemically homogeneous. The mesylate cyclized smoothly under the influence of potassium *t*-butoxide to the crystalline **33** which was converted, by desulfurization of its thioketal, to the tetracyclic **34a** and thence to **34b**. The former was transformed *via* the alcohol **34c** and the aldehyde **34d**, to (−)-hibane (**34e**), identical in all respects with an authentic sample.[27]

For the synthesis of (−)-hibaene itself, the possibility of effecting a partial oxidation of **32a** to the aldehyde **35** was envisaged since it was felt that under mildly basic conditions the aldehyde might be induced to cyclize *in situ* to the aldol **36a**. Although direct oxidation of **32a** with dimethyl sulfoxide–dicyclohexylcarbodiimide[28] was unsuccessful, oxidation of **32b** by Kornblum's procedure[29] led to a mixture of the aldehyde **35** and the aldol **36**. Treatment of the mixture with base then effected complete aldolization to the crystalline **36a** in 90% yield over-all, the depicted configuration at C-15 being based on the observation that in the model of the C-15 epimer the hydroxyl group is seriously hindered sterically by the C-10 methyl group. This may account for the stereospecificity of the aldol condensation.

The mesylate **36b**, on being subjected to the action of boiling lutidine, afforded **37** (60% over-all from ketomesylate **32b**) which gave crystalline hibaic acid **38a** after Wolff–Kishner reduction. Reduction of the ester **38b** to **c** followed by oxidation to **38d** and another Wolff–Kishner reduction gave an oil which was a 2:1 mixture of (−)-hibaene (**1**) and (−)-hibane (nmr, glpc).[30] Separation and identification was effected by column chromatography; the partially synthetic (−)-hibaene was indistinguishable from authentic material in all respects (glpc, tlc, nmr, infrared, rotation, and mixture melting point).

Experimental Section[31]

Hydroboration of Methyl Pimarate with Diisoamylborane.—Sodium borohydride, 0.60 g (100% excess), and 20 ml of dry diglyme were stirred until solution was complete. 2-Methyl-2-butene, 2.80 g (100% excess), was added and the mixture was stirred and cooled in ice during the gradual addition of 2.84 g (100% excess) of boron trifluoride etherate during 10 min. Stirring was continued at 0° for a further 2 hr, then ice–salt cooling was applied during the gradual addition of a solution of 3.16 g of methyl pimarate in 5 ml of diglyme over 10 min. The reaction mixture was stirred for 45 hr with gradual rise to room temperature. Ice cooling was applied during the cautious successive addition of 6 ml of ice–water, 20 ml of 3 *N* aqueous

(25) *Cf.* steroidal 7-ketones[26] and the 7-ketone of the isopimaric acid series.

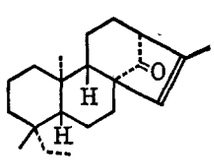
(26) P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1965, pp 36, 103.

(27) We gratefully acknowledge gifts of (−)-hibaene and (−)-hibane from Professor Kitahara which permitted us to make this comparison.

(28) K. Pfitzner and J. G. Moffat, *J. Am. Chem. Soc.*, **85**, 3027 (1963).

(29) N. Kornblum, W. J. Jones, and G. J. Anderson, *ibid.*, **81**, 4113 (1959).

(30) For a similar observation during the Wolff–Kishner reduction of ii see ref 8.



ii

(31) Melting points and boiling points are uncorrected. Small-scale distillations were carried out in a Kugelrohr apparatus; the temperature recorded is that of the bath, not the true boiling points. Analyses were by Dr. F. Pascher, Bonn, Germany. Infrared spectra were run as Nujol mulls unless otherwise specified, ultraviolet spectra in 95% ethanol, rotations in chloroform. ORD curves were run through the courtesy of Drs. Lin Tsai and Herman Ziffer in methanol on a Cary Model 60 recording spectropolarimeter. Nmr spectra were run on a Varian A-60 spectrometer in deuteriochloroform solution with tetramethylsilane as internal reference. Signals are reported in parts per million, with the multiplicity indicated in the usual[11] manner. Petroleum ether indicates the fraction of bp 60–80°. Pimaric acid used in this work was supplied by Dr. B. L. Hampton to whom we express our heartfelt thanks.

sodium hydroxide, and 20 ml of 30% hydrogen peroxide. The mixture was stirred for 1 hr, poured into a large volume of ice–water, and thoroughly extracted with ether. The combined extracts were washed with water, dried, and concentrated. This left a syrupy residue, 3.2 g, which was dissolved in petroleum ether and chromatographed on silica gel. Elution with benzene afforded 0.6 g of unchanged methyl pimarate while benzene–ether (1:1) eluted 2.15 (80%) g of alcohol **14a** which could not be induced to crystallize: bp (bath temperature) 205–210° (0.25 mm); infrared bands ($CHCl_3$) at 3600–3400 (OH), 1720 cm^{-1} (ester); nmr signals at 5.2 br (one proton, H-14, $w_{0.5}$ = 4 cps), 3.72 t (two protons, CH_2OH, J = 7 cps), 3.68 s (methoxyl), 1.20, 0.93, 0.82 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25; O, 14.35. Found: C, 75.43; H, 10.65; O, 14.06.

Elution with ether gave 0.65 g (20%) of diol **21**.

Acetylation of **14a** with acetic anhydride–pyridine gave the acetate **14b** as an oil: bp (bath temperature) 195–200° (0.25 mm); infrared bands ($CHCl_3$) at 1730 (acetate), 1720 cm^{-1} (ester), no hydroxyl; nmr signals at 5.22 br (one proton, H-14, $w_{0.5}$ = 4.5 cps), 4.13 t (two protons, CH_2OAc, J = 7 cps), 3.67 s (methoxyl), 2.03 s (acetate), 1.20, 0.94, 0.80 ppm (methyl singlets).

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64; O, 17.00. Found: C, 73.80; H, 9.66; O, 16.58.

Benzoylation of **14a** with benzoyl chloride–pyridine followed by chromatography over alumina (Alcoa F-20) with solvents of increasing polarity (petroleum ether, petroleum ether–benzene, benzene, benzene–ether) gave, in the benzene fraction, gummy material **14c** which was crystallized by dissolving in methanol and cooling to Dry Ice temperature. The colorless crystals melted at 74°: $[\alpha]^{25}D$ 23.6° (*c*. 0.973); nmr signals at 8.9 c and 7.8 c (five aromatic protons), 5.2 br (H-14), 4.3 c (two protons, CH_2OBz), 3.58 s (methoxyl), 1.17, 0.99, and 0.78 ppm (methyl singlets).

Anal. Calcd for $C_{28}H_{38}O_4$: C, 76.67; H, 8.73; O, 14.59. Found: C, 76.85; H, 8.66; O, 14.88.

The brosylate **14d** was prepared in the usual manner by allowing the mixture of **14a**, *p*-bromobenzenesulfonyl chloride, and pyridine to stand for 5 days and chromatographing the crude neutral product over silica gel. Fractions were monitored by tlc and nmr spectroscopy. Those containing brosylate were combined and recrystallized from *n*-hexane: mp 90–91°; yield 40%; nmr signals at 7.62 c (four aromatic protons), 5.0 br (H-14), 4.08 t (two protons, CH_2OBs), 3.58 s (methoxyl), 1.17, 0.85, and 0.68 ppm (methyl singlets).

Anal. Calcd for $C_{27}H_{37}BrO_6S$: C, 58.59; H, 6.70; Br, 14.46. Found: C, 58.59; H, 6.82; Br, 14.56.

Isomerization of Acetate 14b.—A solution of 1.0 g of **14b** in 50 ml of dry chloroform was cooled in ice–salt and saturated with dry hydrogen chloride, passage being continued for 4 hr. The solution was washed with ice–water, aqueous sodium bicarbonate, and water, dried, and evaporated to give 0.95 g of acetate **15b**: bp (bath temperature) 200° (0.2 mm); nmr signals at 4.17 t (two protons, CH_2OAc, J = 7 cps), 3.68 s (methoxyl), 2.03 s (acetate), 1.20, 1.00, 0.87 ppm (methyl singlets), no olefinic resonances.

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64; O, 17.00. Found: C, 73.66; H, 9.84; O, 16.65.

Alcohol 15a.—A solution of 0.83 g of **15b** in 15 ml of methanol was allowed to stand with 5 ml of 1.5 *N* aqueous potassium carbonate at room temperature overnight. The mixture was diluted with water, saturated with salt, extracted with ether, and worked up as usual to give 0.73 g of **15a**: bp (bath temperature) 210° (0.2 mm); infrared bands ($CHCl_3$) at 3650, 3500 (nonbonded and bonded hydroxyl), 1720 cm^{-1} (ester); nmr signals at 3.68 t (two protons, CH_2OH, J = 7.5 cps), 3.63 s (methoxyl), 1.19, 0.98, 0.84 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25; O, 14.35. Found: C, 75.51; H, 10.13; O, 14.45.

The mesylate **15d** of the above alcohol was obtained in the usual manner, after 4 days at 0°, as an oil: infrared bands ($CHCl_3$) at 1715 (ester), 975–930 cm^{-1} (mesylate), no hydroxyl; nmr signals at 4.28 t (two protons, CH_2OSO_2Me, J = 7.5 cps), 3.63 s (methoxyl), 2.98 s (mesylate), 1.20, 1.00, 0.90 ppm (methyl singlets).

Acetolysis of Mesylate 15d.—A solution of 0.75 g of **15d** in 50 ml of glacial acetic acid was refluxed for 2 hr, poured into ice–water, and extracted with ether. The extract was washed with aqueous sodium bicarbonate and water, dried, and evaporated to yield 0.6 g of tetracyclic ester **16a** as an oil: bp (bath temperature) 160° (0.15 mm); infrared bands (neat) at 1730, 1225 (ester), 1645 cm^{-1} weak (olefin), no hydroxyl; nmr signals at 3.62 s (methoxyl), no other resonances downfield from 2.3, 1.27, 0.99, 0.99 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19; O, 10.11. Found: C, 79.14; H, 10.64; O, 10.16.

The same material was obtained in approximately the same yield by acetolysis of **14d**.

Tetracyclic Acid 16b.—The foregoing ester, 0.57 g, was mixed with 25 ml of a 1 *N* solution of potassium *t*-butoxide in dimethyl sulfoxide and kept at room temperature for 40 hr.[32] Dilution with ice water afforded a clear solution which was acidified with 30 ml of 2 *N* hydrochloric acid. The white precipitate of **16b** was collected, washed well with water, and dried under reduced pressure: yield, 0.52 g. It was amorphous and could not be induced to crystallize; it collapsed at about 80° and lost CO_2 at 250–260°. The cyclohexylamine salt, obtained by mixing cold etheral solutions of 0.15 g of acid and 0.1 g of cyclohexylamine and keeping at room temperature overnight, crystallized from ether as elongated prisms: mp 181–182°; $[\alpha]D$ −4° (*c* 0.55).

Anal. Calcd for $C_{26}H_{43}NO_2$: C, 77.75; H, 10.79; N, 3.49. Found: C, 77.74; H, 10.25; N, 3.15.

Lactonization of Acid 16b.—Acid **16b**, 0.2 g, was added slowly with stirring to 3 ml of concentrated sulfuric acid at −10° and stirring continued for 1 hr at that temperature. The clear, dark solution was poured onto ice and the product was isolated in the usual manner by ether extraction. The neutral residue of γ-lactone **18**, 0.2 g, was purified by distillation: bp (bath temperature) 195–200° (0.2 mm); infrared band ($CHCl_3$) at 1760 cm^{-1} (γ-lactone); nmr signals at 1.05, 0.95, 0.95 ppm (methyl singlets), no resonances downfield from 2.5 ppm.

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00; O, 10.58. Found: C, 79.30; H, 9.90; O, 10.53.

Bromolactonization of Acid 16b.—To a solution of 0.03 g of **16b** in 1.5 ml of methanol–carbon tetrachloride (2:1) was added a dilute solution of bromine in carbon tetrachloride until an orange color persisted. The mixture was diluted with ether, washed with water and aqueous sodium bicarbonate, dried, and evaporated to give an oily bromo lactone which decomposed on attempted distillation and could not be purified adequately for analysis, infrared band ($CHCl_3$) at 1760 cm^{-1} (γ-lactone).

Hydroboration of Methyl Pimarate with Diborane.—To a mechanically stirred solution of 6.32 g of methyl pimarate and 1.3 g of sodium borohydride in 50 ml of dry diglyme was added gradually during 1.5 hr 6.3 g of boron trifluoride etherate in 10 ml of dry diglyme at room temperature. Stirring was continued for 3.5 hr after addition was complete. With stirring and ice cooling, 3 ml of ice–water was added cautiously, followed by 15 ml of 3 *N* aqueous sodium hydroxide, and 15 ml of 30% hydrogen peroxide. After stirring for 1 hr, the mixture was kept at room temperature overnight, poured into 250 ml of ice–water, and kept several days at 0°. The precipitate was collected, washed thoroughly with water, and dried under reduced pressure: yield of crude product, 8.7 g. It was stirred thrice with 50-ml portions of ether and filtered. The insoluble residue, wt 3.5 g (50%), crystallized from 50% aqueous ethanol as rhombic prisms of diol **21**: mp 185°; $[\alpha]^{25}D$ −36° (*c* 0.73); infrared bands ($CHCl_3$) at 3400 (OH), 1720 cm^{-1} (ester); nmr signals at 3.64 s (methoxyl) superimposed on CH_2OH triplet, 2.82 d (one proton, H-14, J = 9.5 cps), 1.17, 1.00, 0.90 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{36}O_4$: C, 71.55; H, 10.30; O, 18.15. Found: C, 71.76; H, 10.38; O, 17.82.

Acetylation of **21** with acetic anhydride–pyridine at 25° for 16 hr gave the diacetate which crystallized from ethanol as colorless needles: mp 115–116°; infrared bands at 1735 (acetates), 1720 cm^{-1} (ester), no hydroxyl absorption; nmr signals at 4.52 d (one proton, H-14, J = 9.5 cps), 4.18 t (two protons, CH_2OAc, J = 8 cps), 3.67 s (methoxyl), 2.07 s (two acetates), 1.18, 0.91, 0.89 ppm (methyl singlets).

Anal. Calcd for $C_{25}H_{40}O_6$: C, 68.77; H, 9.24. Found: C, 68.93; H, 9.14.

The three ethereal filtrates from the separation of **21** were used to extract the aqueous filtrate; they were combined, washed with water, dried, and evaporated, leaving a syrup which solidified on trituration with ether. The solid, wt 1.35 g (19%), crystallized from 50° aqueous ethanol as matted needles of diol **22**: mp 170.5°; $[\alpha]^{25}D$ +9° (*c* 0.9) infrared bands ($CHCl_3$) at 3400 (OH), 1715 cm^{-1} (ester); nmr signals at 3.66 s (methoxyl) super-

(32) F. C. Chang and N. F. Wood, *Tetrahedron Letters*, 2969 (1964).

imposed on CH_2OH triplet and CHOH doublet, 1.20, 1.06, 0.91 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{36}O_4$: C, 71.55; H, 10.30; O, 18.15. Found: C, 71.73; H, 10.01; O, 18.01.

Oxidation of Diol 21.—A mixture of 0.70 g of **21**, 20 ml of *t*-butyl alcohol, 3 ml of water, and 0.30 g (1.1 moles) of N-bromoacetamide was kept at ambient temperature for 24 hr, then poured onto ice–water. The product was extracted thrice with ether and the combined extracts were washed with aqueous sodium thiosulfate, aqueous sodium bicarbonate, and water, dried, and concentrated. The residual gum was taken up in a small amount of petroleum ether and kept at 0° for several hours. Unchanged diol, wt 0.13 g, was removed. The filtrate was evaporated to dryness and the residue was dissolved in benzene–petroleum ether (1:1) and chromatographed over 50 g of silica gel. Elution with benzene–ether (2:1) afforded 0.4 g of ketone **23a** which crystallized from petroleum in large rhombic prisms: mp 98.5°; $[\alpha]^{25}D$ −50° (*c* 0.5); infrared bands (CH_3CN) at 1715 (ester), 1700 cm^{-1} (ketone); nmr signals at 3.66 s (methoxyl) superimposed on CH_2OH triplet, 1.18, 1.03, 1.00 ppm (methyl singlets); ORD curve (*c* 0.04), $[\alpha]_{589}$ −20°, $[\alpha]_{308}$ −2000°, $[\alpha]_{269}$ +2270°, $[\alpha]_{240}$° +1850° (last reading). The ketone did not react with 2,4-dinitrophenylhydrazine.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 72.15; H, 9.45; O, 18.23.

Oxidation of Diol 22.—A cognate oxidation of 0.05 g of **22** in 3 ml of *t*-butyl alcohol with 0.03 g of N-bromoacetamide in 1 ml of water afforded 0.03 g of the same crystalline ketone, mp and mmp 98.5°.

Acetylation of **23a** with acetic anhydride-pyridine gave **23b** as an oil: bp (bath temperature) 215–220° (0.2 mm); infrared bands (CH_3CN) at 1730 (ester, acetate), 1700 cm^{-1} (ketone); nmr signals at 4.05 t (two protons, CH_2OAc, J = 7 cps), 3.67 s (methoxyl), 2.0 s (acetate), 1.20, 1.03, 1.03 ppm (methyl singlets).

Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24; O, 20.38. Found: C, 70.36; H, 8.87; O, 20.51.

Mesylate 24.—A solution of 0.25 g of **23a** in 2 ml of dry pyridine was cooled to 0° and treated with 0.5 ml of methanesulfonyl chloride. After 18 hr at 0°, the mixture was cooled during the addition of a slight excess of N,N-dimethyltrimethylenediamine, shaken at 0° for 15 min, then poured into 30 ml of ice–2 *N* hydrochloric acid. The oily product was taken up in ether; the extract was washed with water and sodium bicarbonate solution, dried, and evaporated to give 0.15 g of **24** which crystallized from petroleum as feathery needles: mp 144.5° dec; infrared band ($CHCl_3$) at 1700 cm^{-1} (ketone), no hydroxyl; nmr signals at 4.15 m (two protons, CH_2OSO_2Me), 3.66 s (methoxyl), 2.95 s (mesylate), 1.18, 1.05, 1.01 ppm (methyl singlets).

Anal. Calcd for $C_{22}H_{36}O_6S$: C, 61.66; H, 8.47; S, 7.45. Found: C, 61.33; H, 8.96; S, 7.43.

Enol Ether 25.—To a chilled solution of potassium *t*-butoxide prepared from 0.5 g of potassium and 35 ml of dry *t*-butyl alcohol was added a solution of 0.55 g of **24** in 25 ml of *t*-butyl alcohol. The mixture was stirred for 2 hr under nitrogen at room temperature, poured into ice water, and the product was isolated with ether. Evaporation of the washed and dried ether extract yielded 0.45 g of **25** which crystallized from methanol as colorless needles: mp 119°; $[\alpha]^{25}D$ −123° (*c* 0.61); infrared bands (CH_3CN) at 1720 cm^{-1} (ester); nmr signals at 4.10 m (two protons, CH_2O—C=C—), 3.67 s (methoxyl), 1.17, 1.04, 0.81 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70; O, 14.44. Found: C, 76.29; H, 9.35; O, 14.83.

Chloro Ketone 23c.—A solution of 0.1 g of **25** in 10 ml of methanol and 1 ml of concentrated hydrochloric acid was refluxed for 1 hr, diluted with water, and extracted with ether. The product obtained after the usual work-up crystallized from petroleum as colorless needles of **23c**: mp 106.5°; infrared bands (CH_3CN) at 1720 (ester), 1700 cm^{-1} (ketone); nmr signals at 3.67 s (methoxyl), 3.3 m (two protons, CH_2Cl), 1.18, 1.02, 1.02 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{33}ClO_3$: C, 68.38; H, 8.95; Cl, 9.63. Found: C, 68.62; H, 8.71; Cl, 9.03.

Oxidation of 15b with Chromic Acid.—To a solution of 0.52 g of **15b** in 6 ml of glacial acetic acid was added a solution of 0.55 g of chromic acid in 15 ml of glacial acetic acid and 0.5 ml of water and the mixture kept at room temperature for 24 hr. Ice–water was added and the product was extracted into ether. Evaporation of the washed and dried extract afforded 0.45 g of diketone **28** or **29a** which crystallized from methanol as colorless needles: mp 137°; infrared bands at 1730 (acetate), 1720 (sh, ester), 1700 cm^{-1} (ketones); nmr signals at 4.1 m (two protons, CH_2OAc), 3.67 s (methoxyl), 3.1–2.1 (complex series of bands of intensity six protons, CH_2CO), 2.03 s (acetate), 1.21, 1.01, 0.93 ppm (methyl singlets).

Anal. Calcd for $C_{23}H_{36}O_6$: C, 67.62; H, 8.82; O, 23.50. Found: C, 67.87; H, 8.82; O, 23.73.

A cognate oxidation of methyl $\Delta^{8(9)}$-dihydropimarate gave the analogous diketone **28** or **29b** which crystallized from methanol as needles, mp 130°.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 72.41; H, 9.61; O, 18.09.

Oxidation of Acetate 15b with *t*-Butyl Chromate.—*t*-Butyl chromate solution was prepared by adding cautiously 20 ml of *t*-butyl alcohol to 6.8 g of chromic acid, with ice cooling. Carbon tetrachloride, 60 ml, was added and the solution was washed well with water, dried, filtered, and mixed with 10 ml of glacial acetic acid and 2.6 ml of acetic anhydride (total volume 90 ml).

A solution of 1.75 g of **15b** in 30 ml of carbon tetrachloride was mixed with 25 ml of *t*-butyl chromate solution and refluxed on a steam bath for 26.5 hr. Ice–water was added and the layers were separated with the aid of chloroform. The aqueous layer was extracted once with chloroform and the combined organic layers were washed with aqueous sodium bicarbonate, water, dried, and concentrated. The brown oily residue, 1.95 g, was distilled under reduced pressure, bp (bath temperature) 230–235° (0.2 mm); the pale yellow oil was dissolved in 5 ml of methanol and mixed with a solution of 0.7 g of 2,4-dinitrophenylhydrazine in 10 ml of methanol containing 2 ml of concentrated sulfuric acid. After several hours at 0°, the red precipitate was collected and washed with a little cold methanol: yield, 0.95 g. A sample crystallized from ethanol as red plates, mp 146°, λ_{max} 392 mμ (ε 22,100).

Anal. Calcd for $C_{29}H_{38}N_4O_8$: C, 61.05; H, 6.67; N, 9.83. Found: C, 61.02; H, 6.92; N, 9.55.

On two occasions, this derivative separated from methanol as red prisms, mp 209–210°, ultraviolet spectrum identical with the above, mmp 146°.

Anal. Found: C, 60.66; H, 6.59; N, 10.03.

A solution of 0.8 g of the above dinitrophenylhydrazone (mp 146° or 210°) in 160 ml of acetone and 4 ml of concentrated hydrochloric acid was refluxed for 0.75 hr, cooled, and treated with a solution of 4.0 g of stannous chloride dihydrate in 16 ml of concentrated hydrochloric acid. After addition of 24 ml of water, the mixture was refluxed for 0.75 hr under nitrogen. The acetone was removed under reduced pressure and the residue was diluted with water and twice extracted with ether. The combined extracts were washed until colorless with 1 *N* hydrochloric acid, then with aqueous sodium bicarbonate and water, dried, and concentrated to give 0.4 g of keto alcohol **26b**: bp (bath temperature) 225–230° (0.2 mm); λ_{max} 250 mμ (ε 10,800); infrared bands ($CHCl_3$) at 3650, 3450 (nonbonded and bonded hydroxyl), 1715 (ester), 1650, 1600 cm^{-1} (α,β-unsaturated ketone); nmr signals at 3.72 t (two protons, CH_2OH, J = 7 cps), 3.67 s (methoxyl), 1.27, 1.13, 0.88 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26; O, 18.37. Found: C, 71.80; H, 8.97; O, 18.13.

The 2,4-dinitrophenylhydrazone separated from ethanol as deep orange-red prisms, mp 214–215°, λ_{max} 392 mμ (ε 23,700).

Anal. Calcd for $C_{27}H_{36}N_4O_7$: C, 61.35; H, 6.87; N, 10.60. Found: C, 60.77; H, 6.76; N, 10.47.

The oily mesylate **26c** was prepared by treatment of **26b** with methane–sulfonyl chloride–pyridine at 0° for 5 days: nmr signals at 4.36 t (two protons, CH_2OSO_2Me, J = 7 cps), 3.68 s (methoxyl), 3.03 s (mesylate), 12.8, 1.14, 0.91 ppm (methyl singlets).

Cyclization of Mesylate 26c.—A solution of 0.55 g of **26c** in 25 ml of dry *t*-butyl alcohol was added in one lot to a stirred solution of 0.9 g of potassium in 70 ml of dry *t*-butyl alcohol under nitrogen, the mixture was stirred for 3.5 hr and poured into ice–water, and the product was isolated with ether. Concentration of the washed and dried extract gave 0.35 g of the tetracyclic ketone **31** as an oil: bp (bath temperature) 185° (0.2 mm); infrared bands (CH_3CN) at 1725 (ester), 1700 cm^{-1} (ketone); nmr signals at 5.27 t (one proton, H-11, J = 3 cps), 3.66 s (methoxyl), 1.26, 1.22, 1.10 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.62; H, 9.63.

The 2,4-dinitrophenylhydrazone crystallized from a large volume of ethanol as yellow matted needles, mp 231°.

Anal. Calcd for $C_{27}H_{34}N_4O_6$: C, 63.51; H, 6.71; N, 10.97. Found: C, 63.45; H, 6.76; N, 10.99.

Saturated Keto Alcohol 32a.—A solution of 0.2 g of **26a** in 20 ml of absolute ethanol was shaken under hydrogen in the presence of 0.2 g of 5% palladized charcoal for 22 hr. The suspension was filtered and the filtrate was poured into water, the product being isolated with ether in the usual way. The crude product, 0.2 g, was dissolved in 5 ml of ethanol and treated with 0.3 g of potassium hydroxide in 2 ml of water. After 0.5 hr at ambient temperature, the solution was diluted and the product was isolated with ether. Purification by distillation gave 0.2 g of **32a** as an oil: bp 225–230° (0.15 mm); infrared bands (CH_3CN) at 1720 (ester), 1700 cm^{-1} (ketone); nmr signals at 3.65 s (methoxyl), 3.64 t (two protons, CH_2OH, J = 7.5 cps) (center arm of triplet superimposed on methoxyl signal), 1.23, 1.10, 0.93 ppm (methyl singlets); ORD curve (c 0.227) $[\alpha]_{400}$ +9°, $[\alpha]_{313}$ −140°, $[\alpha]_{270}$ +423°, $[\alpha]_{253}$ +397° (last reading).

The 2,4-dinitrophenylhydrazone crystallized from methanol as yellow prisms: mp 129–130°; nmr signals at 3.72 s (methoxyl), 3.71 t (two protons, CH_2OH, J = 7.5 cps), 1.31, 1.10, 1.02 ppm (methyl singlets), usual aromatic resonances.

Anal. Calcd for $C_{27}H_{38}N_4O_7$: N, 10.56. Found: N, 10.32.

The mesylate **32b**, obtained after 4 days treatment with methanesulfonyl chloride–pyridine at 0°, crystallized from ether as prisms: mp 125°; infrared bands at 1720 (ester), 1700 (ketone), 990–950 cm^{-1} (mesylate); nmr signals at 4.25 t (two protons, CH_2OSO_2Me, J = 7.5 cps), 3.67 s (methoxyl), 3.00 s (mesylate), 1.23, 1.11, 0.97 ppm (methyl singlets).

Anal. Calcd for $C_{22}H_{36}O_6S$: S, 7.47. Found: S, 7.24.

Alternative Route to 32b.—The crude oil, obtained from the oxidation of 8.75 g. of **15b** with *t*-butyl chromate, was taken up in hexane and chromatographed on 200 g of alumina. Elution with benzene–ether (9:1 and 4:1) afforded 4.29 g of unsaturated keto acetate **26a** as a pale yellow oil: infrared bands (CCl_4) at 1730 (ester, acetate), 1660, 1600 cm^{-1} (α,β-unsaturated ketone).

Hydrogenation of 9 g of **26a** in 200 ml of ethanol containing 4 g of 5% palladized charcoal for 3 hr gave, after filtration and evaporation of the filtrate, keto acetate **32c**: infrared bands ($CHCl_3$) at 1730 (ester, acetate), 1705 cm^{-1} (sh, ketone). A solution of this material in 250 ml of 2 *N* aqueous methanolic sodium hydroxide was kept at room temperature for 3 hr, poured into water, saturated with salt, and extracted with ether. Evaporation of the washed and dried extract gave 7.5 g of oil (mainly **32a** as indicated by infrared and nmr) which was used directly to prepare **32b** as described above.

Cyclization of Mesylate 32b.—A solution of 0.43 g of **32b** in 25 ml of dry *t*-butyl alcohol was added to a solution of 0.4 g of potassium in 100 ml of *t*-butyl alcohol, the mixture was stirred under nitrogen for 4 hr and diluted with water, and the product was isolated with ether. Spectral measurements indicated the presence of some tetracyclic acid **33b**; so the whole was treated with a slight excess of ethereal diazomethane. Evaporation of the ether after 15 min gave 0.3 g of tetracyclic keto ester **33a** which crystallized from aqueous methanol as glistening plates: mp 93°; $[\alpha]^{25}D$ −3° (c 0.55); infrared bands at 1735 (ester), 1700 cm^{-1} (ketone); nmr signals at 3.67 s (methoxyl), 1.21, 1.10, 1.03 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70; O, 14.44. Found: C, 76.41; H, 9.39; O, 14.25.

A solution of 0.04 g of **33a** in 0.15 ml of ethanedithiol was treated with 0.1 ml of boron trifluoride etherate to give the thioketal which crystallized from methanol–chloroform as matted colorless needles, mp 230°.

Anal. Calcd for $C_{23}H_{36}O_2S_2$: S, 15.68. Found: S, 15.92.

Methyl Dihydrohibaate (34a).—A solution of 0.1 g of thioketal in 50 ml of absolute ethanol was refluxed for 24 hr with 1 teaspoonful of Raney nickel. The nickel was removed from the cool mixture by filtration through Celite and the filtrate was evaporated to afford 0.07 g of **34a** which crystallized from methanol as colorless prisms: mp 99.5°; infrared bands at 1730, 1225 cm^{-1} (ester); nmr signals at 3.67 s (methoxyl), 1.17, 0.96, 0.96 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; O, 10.05. Found: C, 79.38; H, 10.27; O, 10.24.

Dihydrohibaic Acid (34b).—A solution of 0.6 g of **34a** in 20 ml of anhydrous ether was added to a suspension of 0.4 g lithium aluminum hydride in 150 ml of anhydrous ether and the mixture was refluxed for 2 hr. The excess reagent was destroyed by successive addition of wet ether, water, and 1 *N* aqueous hydrochloric acid; the product was isolated in the usual way. The crude solid **34c**, 0.42 g, showed infrared bands at 3400, 1050–1005 cm^{-1} (multiplet) (OH), no carbonyl absorption; nmr signals at 3.43, 3.09 (AB quartet, two protons, CH_2OH, J_{AB} = 11 cps), 2.02 s (one proton, O*H*), 0.96, 0.95, 0.76 ppm (methyl singlets). The crude material was used directly in the following experiments. A solution of 0.2 g of crude **34c** in 10 ml of acetic acid was treated with excess Jones reagent for 20 min and diluted with water, and the product was collected and washed well with water. Crystallization from methanol afforded colorless needles of **34b**: mp 219–220°; $[\alpha]D$ +8° (c 0.52); infrared bands at 1695, 1280 cm^{-1} (COOH); nmr signals at 10.0 br (one proton, COO*H*), 1.18, 0.97, 0.97 ppm (methyl singlets).

Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59; O, 10.51. Found: C, 78.82; H, 10.60; O, 10.68.

(−)-Hibane (34e).—A stirred solution of 0.2 g of crude **34c** in 25 ml of pure acetone at −5° under nitrogen was treated dropwise with deaerated Jones reagent until an excess of reagent persisted for 2 min. The mixture was diluted and the crude aldehyde **34d** was isolated by ether extraction: infrared bands (CCl_4) at 2700, 1735 cm^{-1} (aldehyde). This material was refluxed with 20 ml of diethylene glycol and 1 ml of 95% hydrazine hydrate for 20 min, concentrated to bp 200° (vapor), and allowed to cool for 30 min. Potassium hydroxide, 1.9 g, 5.0 ml of diethylene glycol, and 0.5 ml of hydrazine hydrate were added, the mixture was refluxed for 4 hr, then cooled, and diluted with water, and the product was isolated with ether. The residue was distilled at 180° (bath temperature, 1 mm) to give 0.12 g of (−)-hibane (**34e**): mp and mmp 41–42°; nmr signals at 0.93, 0.93, 0.85, 0.82 ppm (methyl singlets); infrared and nmr spectra identical with those of authentic material, mp 42°. Identity was also confirmed by vpc.

Anal. Calcd for $C_{20}H_{34}$: C, 87.51; H, 12.49. Found: C, 87.61; H, 12.63.

Preparation of Aldol 36a.—A mixture of 12 ml of dimethyl sulfoxide and 0.25 g of sodium bicarbonate was heated gradually to 150° under nitrogen. Mesylate **32b**, 0.5 g, was added in one portion; the reaction mixture was kept at 160° (bath temperature) for 5 min. The odor of dimethyl sulfide was apparent almost immediately after addition. The cooled solution was diluted and extracted with ether. Evaporation of the washed and dried extract gave a semisolid residue whose nmr spectrum indicated a mixture of aldehyde **35** and aldol **36a**. The total product was treated with 15 ml of methanolic sodium methoxide (from 0.5 g of sodium) under nitrogen for 16 hr at room temperature. Dilution with water and extraction with ether gave 0.35 g of **36a** which crystallized from petroleum as colorless prisms: mp 146°; $[\alpha]^{25}D$ −26° (c 0.54); infrared bands ($CHCl_3$) at 3600–3400 (OH), 1720 (ester), 1700 cm^{-1} (sh, ketone); nmr signals at 4.5 m (one proton, H-16), 3.68 s (methoxyl), 1.21, 1.19, 1.06 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26; O, 18.37. Found: C, 72.37; H, 9.02; O, 17.89.

Preparation of 37.—A solution of 2.0 g of **36a** in 100 ml of pyridine at 0° was mixed with 4 ml of methanesulfonyl chloride and the mixture kept at 0° for 72 hr. The usual work-up afforded the corresponding mesylate **36b** as a yellow oil: infrared bands (CCl_4) at 1735 (ester), 1710 cm^{-1} (ketone), no hydroxyl absorption, complex absorption at 950–870 cm^{-1} (mesylate). The total product, 2.5 g, was refluxed in 50 ml of 2,6-lutidine under nitrogen for 21 hr. The cool mixture was poured onto ice–hydrochloric acid and the product was isolated with ether. The residual oil was chromatographed on a column of 50 g of silica gel prepared in hexane. Elution with 5% ether–benzene gave **37** as a colorless oil which slowly crystallized on standing, yield 1.1 g (60% from **32b**). Crystallization from aqueous methanol at 0° gave colorless silky needles: mp 69–70°; $[\alpha]D$ +19° (c 0.72); infrared bands at 1730 (ester), 1700 (ketone), 750 cm^{-1} (*cis* disubstituted double bond); λ_{max} 275 mμ (ϵ 75); nmr signals at 5.68 s (two protons, H-15, H-16), 3.71 s (methoxyl), 1.23, 1.10, 0.98 ppm (methyl singlets). The carbon analysis was consistently somewhat low.

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32, H, 9.15. Found: C, 75.78; H, 8.96.

Hibaic Acid (38a).—A solution of 0.3 g. of **37**, 5 g of potassium hydroxide, and 1 ml of 95% hydrazine hydrate in 30 ml of diethylene glycol was refluxed for 1 hr, concentrated to bp 200° (vapor), and heated under reflux for 4 hr during which time the mixture darkened. The cooled solution was diluted (no precipitate), extracted with ether to remove any neutral material, and acidified with 5 *N* aqueous hydrochloric acid; the precipitate

was isolated with ether. The brown oily product was chromatographed on deactivated alumina. Elution with benzene–ether (1:1) gave 0.2 g of **38a**, which crystallized from aqueous methanol as colorless plates: mp 173–174°; infrared bands at 1695 (acid), 755 cm^{-1} (olefin), nmr signals at 10.0 br (COO*H*), 5.73, 5.51 (AB quartet, two protons, H-15, H-16, J_{AB} = 5.5 cps), 1.19, 1.00, 0.78 ppm (methyl singlets).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.55; H, 10.08.

Methyl Hibaate (38b).—The above experiment was repeated by refluxing 0.8 g. of **37**, 6 g of potassium hydroxide, and 2 ml of 95% hydrazine hydrate in 70 ml of diethylene glycol for 2.3 hr then concentrating to 200° (vapor) and refluxing for a further 3.5 hr under nitrogen. The product was methylated with excess ethereal diazomethane to give a brown oil which was chromatographed on a column of 30 g of alumina prepared in hexane. Elution with hexane–benzene (4:1 and 3:1) gave 0.65 g of **38b**, which crystallized from methanol as colorless needles: mp 85–86°; $[\alpha]D$ −25° (*c* 0.75); infrared bands at 1735, 1230 (ester), 755 cm^{-1} (olefin); nmr signals at 5.74, 5.49 (AB quartet, two protons, H-15, H-16, J_{AB} = 5.5 cps), 3.68 s (methoxyl), 1.18, 1.01, 0.78 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 80.04; H, 10.29.

Hibaene (1).—Methyl hibaate, 0.6 g, was reduced with lithium aluminum hydride in refluxing anhydrous ether as described for methyl dihydrohibaate (**34a**) and the crude alcohol **38c** (0.6 g, infrared bands at 3400, 1060–1010, 750 cm^{-1}, no carbonyl) was oxidized to the corresponding aldehyde **38d** [infrared bands (CCl_4) at 2700, 1735 cm^{-1}, no hydroxyl] with Jones reagent in acetone at 0° as described for **34c** above. A mixture of the aldehyde, 6 g of potassium hydroxide, and 2 ml of 95% hydrazine hydrate in 70 ml of diethylene glycol was heated under reflux for 5 hr, cooled, and diluted with water; the product was isolated with ether. The pale yellow oil was taken up in hexane and filtered through a small column of alumina. The colorless oil thus obtained, $[\alpha]D$ −30°, showed two bands on vpc in the ratio of 2:1 approximately. The major and minor bands were found to represent hibaene and hibane, respectively, by enhancement of the corresponding peaks on addition of authentic material. Separation was effected by chromatography over silicic acid–silver nitrate.[33] Elution with hexane gave firstly (−)-hibane, identical with the previously prepared sample. Later fractions, monitored by vpc, contained (−)-hibaene: $[\alpha]D$ −47° (*c* 1.01); infrared bands (neat) at 1385, 1365 (*gem*-dimethyl), 755 cm^{-1} (olefin); nmr signals at 5.70 d, 5.44 d (AB quartet, two protons, H-15, H-16, J_{AB} = 6 cps), 0.99, 0.86, 0.83, 0.75 ppm (methyl singlets). The analytical sample, prepared by distillation at 200° (bath temperature, 2.0 mm), had mp and mmp 29°, and nmr and infrared spectra superimposable on the nmr and infrared spectra of authentic (−)-hibaene.

Anal. Calcd for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 88.05; H, 11.91.

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The Isolation of Rupicoline and Montanine, Two Pseudoindoxyl Alkaloids of *Tabernaemontana Rupicola* Benth.[1a]

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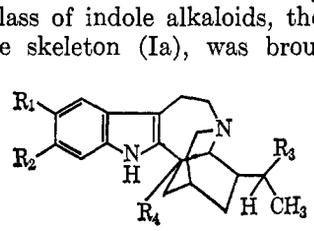
Two pseudoindoxyl alkaloids have been isolated from the South American shrub *Tabernaemontana rupicola* and, on the basis of spectral data, structures IVa and IVb were proposed for them. The structure of one of these alkaloids, called rupicoline (IVa), is confirmed by its partial synthesis from voacangine (Ib).

The investigation of alkaloids in plants of the tribe *Tabernaemontaneae*, family *Apocynaceae*, received a considerable stimulus from the structural elucidation of several alkaloids of *Tabernanthe iboga*.[3] At that time a new class of indole alkaloids, those possessing the ibogamine skeleton (Ia), was brought to light.



Ia, $R_1 = R_2 = R_3 = R_4 = H$
b, $R_1 = CH_3O$; $R_2 = R_3 = H$; $R_4 = CH_3OCO$
c, $R_1 = CH_3O$; $R_2 = H$; $R_3 = HO$; $R_4 = CH_3OCO$
d, $R_1 = R_2 = H$; $R_3 = HO$; $R_4 = CH_3OCO$

Subsequently the structures of several other alkaloids of this type have been deduced.[4] These have been isolated from species of several genera within the tribe *Tabernaemontaneae*.

Within the genus *Tabernaemontana*, alkaloids have been isolated from *Ervatamia coronaria* syn. *Tabernaemontana coronaria*,[5] *T. spharocarpa*,[6] *T. dichotoma*,[7] *T. undulata*,[5a] *T. oppositifolia*,[5a] *T. australis*,[5a] *T. crispa*,[8] *T. alba*,[9] *T. pachysiphon* var. *cumminsi*,[10] *T. affinis*,[11] *T. pandacaqui*,[12] and *T. mucronata*.[13]

T. rupicola, described by Bentham,[14] is a woody shrub 4–5 ft in height bearing white flowers. It is indiginous to the area of the Amazon and its subsidiaries in Brazil.

Two collections of this plant were studied. These varied greatly, both qualitatively and quantitatively, with respect to alkaloid content. The first, collected in October 1959 on the Rio Negro, contained 0.28% organic bases. Paper chromatography of the crude bases revealed a number of components. The second col-

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