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THE SYNTHESIS OF (+)-MATATABIETHER AND RELATED METHYLCYCLOPENTANE MONOTERPENES

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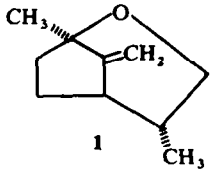
Abstract—The syntheses of (+)-matatabiether (**1**), neonepetalactone (**15**) and related alcohols **3** and **5**, and dihydropyran **2** are described. 5-Isopropenyl-2-methyl-1-cyclopentene-1-carboxaldehyde (**6**) was converted by LAH reduction and acetylation to 2-acetoxymethyl-3-isopropenyl-2-methylcyclopentene (**8**) which was hydroborated to give 3(β-hydroxyisopropyl2-acetoxymethyl-2-methylcyclopentene (**9**). Hydrolysis of **9** and cyclization with acid gave dihydropyran **2** and a small amount of matatabiether (**1**). Oxymercuration demercuration of acetate **9** gave a readily separable mixture of 1-acetoxymethyl-4,8-dimethyl-2-oxabicyclo[3.3.0]octane (**13**) and 8-acetoxymethyl-1,4-dimethyl-2-oxabicyclo[3.2.1]octane (**12**). Pyrolysis of acetate **12** afforded (+)-matatabiether (**1**), while hydrolysis of **12** gave alcohol **3**.

Oxidation and esterification of aldehyde **6** gave methyl 5-isopropenyl-2-methyl-1-cyclopentene-1-carboxylate (**18**). Hydroboration of **18** and heating the resulting hydroxyester to 200° gave neonepetalactone **15** contaminated by small amounts of dihydronepetalactone **20** and an isomeric dihydronepetalactone **21**. Catalytic hydrogenation of neonepetalactone yields isodihydronepetalactone (**22**). These conversions establish the complete stereochemistry of neonepetalactone and matatabiether.

DURING an investigation of the volatile oil from the cat-attracting plant *Actinidia polygama*, Sakan *et al.* isolated and characterized matatabiether (**1**)[1] and a number of related bicyclic ethers and hydroxy ethers including compounds **2**, **3** and **4**.[2] As part of a continuing investigation of the terpenes of *Actinidia polygama* and *Nepeta cataria*[3] we wish to report the synthesis of compounds **1**, **2**, **3** and **5** by a route which establishes their absolute configuration and permits an assignment of stereochemistry to the CH_3—CH—CH_2—O group. This work complements the degradative studies carried out in Professor Sakan's laboratory.



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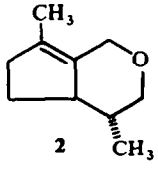

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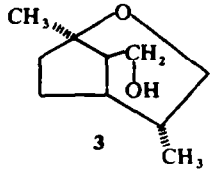

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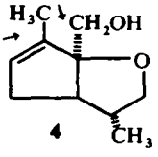

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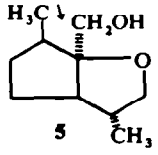

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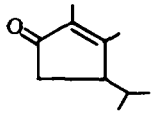
The aldehyde **6**[4] was chosen as a starting material since it incorporates the basic skeleton of methylcyclopentane terpenes. Proper modification of the aldehyde group, anti-Markownikoff hydration of the isopropenyl group and subsequent cyclization provides a pathway to the desired bicyclic ethers.

Aldehyde **6** was converted to the unsaturated alcohol **7** in high yield by reduction with LAH or sodium borohydride. The alcohol was acetylated in order to set the stage for the selective hydroboration of the isopropenyl double bond in **8**. Hydroboration was accomplished with bis(3-methyl-2-butyl)borane[5] and yielded the hydroxy acetate **9**. Hydrolysis of **9** gave diol **10** which failed to crystallize.

When **10** was heated in benzene with a trace of *p*-toluenesulfonic acid, one major product, pyran **2**, whose spectral properties (Experimental) are consistent with the assigned structure, and a small amount of matatabiether **1** was obtained, besides recovered diol **10**. The IR and NMR spectra of ether **2** are identical with those of pyran **2** kindly provided by Professor Sakan.

In one experiment a small amount of a third compound was isolated by gas phase chromatography. This substance exhibited IR maxima at 5·85 and 6·05 μ and UV absorption at 236 mμ (ε 8,900) characteristic of an α,β-unsaturated ketone. The NMR spectrum displayed an isopropyl doublet at 0·60 and 0·98 ppm, and two vinyl Me signals at 1·63 and 1·94 ppm. This information, taken together with a parent ion at *m/e* 152 in its mass spectrum, permits structure **11** to be assigned to this product. Ketone **11** most likely arises from alcohol **7**, an impurity in the sample of diol **10** used in this particular dehydration experiment, *via* a series of prototropic shifts.

When diol **10** was passed through a 5 ft SE30 gas chromatographic column at 155° the two cyclic ethers were obtained in a ratio of 1·3 : 1·0. The minor product proved to



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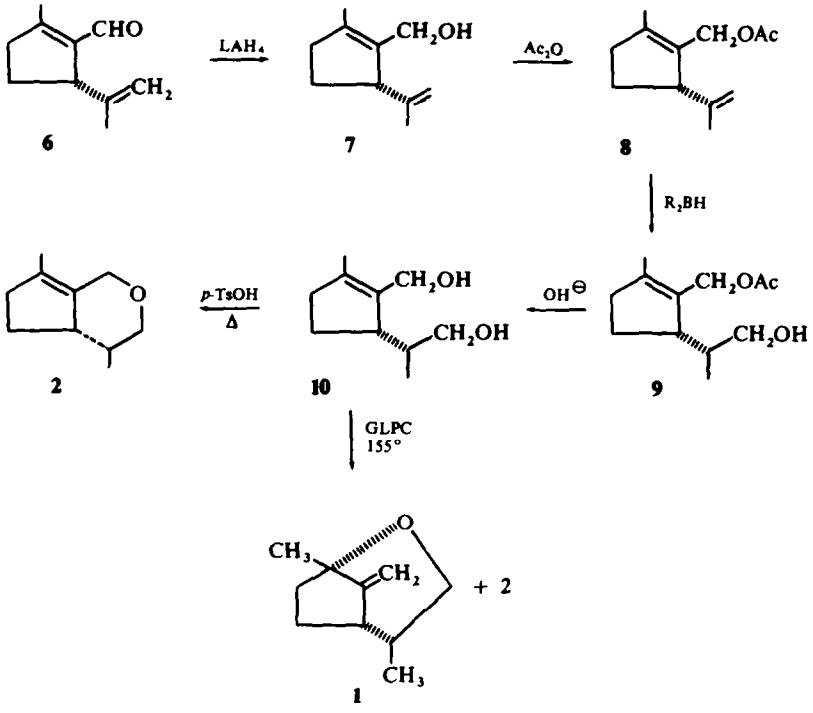
be identical with pyran **2**, whereas the major ether was identical in all respects, except sign of optical rotation, with an authentic sample of matatabiether (**1**). These observations and those made by Sakan[1] suggest that dehydration of diol **10** yields matatabiether (**1**) as a kinetically favored product which in the presence of acid isomerizes[1] to the more thermodynamically stable pyran **2**.

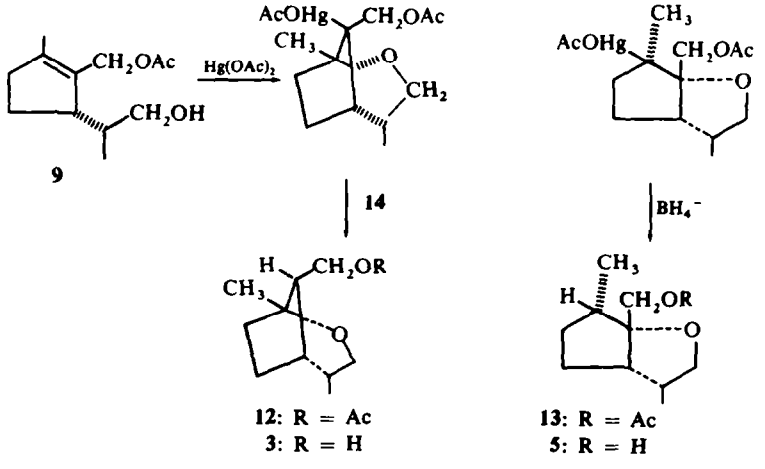
In view of the failure of the direct cyclization to produce matatabiether (**1**) free of dihydropyran **2**, attention was directed toward an alternate procedure for effecting the desired cyclization. For this purpose we visualized the use of an oxymercuration-demercuration sequence which has occasionally been employed to prepare cyclic ethers.[6]

When acetate **9** was stirred with mercuric acetate in t-butyl alcohol for 24 hr, and reduction was carried out *in situ* with sodium borohydride, a mixture of acetates **12** and **13** was obtained, contaminated by alcohols **3** and **5** presumedly arising by hydrolysis of the acetates during the reduction step. In order to facilitate separation, the mixture was reacetylated to give a mixture comprised exclusively of acetates **12**

and **13**. The acetates were separated by column chromatography (silica gel) or by GLPC. The major product, obtained in 42% yield, proved to be acetate **12**. Since oxymercuration normally results in a *trans*-addition with the mercury entering from the least hindered side of the molecule,[7] the intermediate organomercurial can be



formulated as **14**. Hydride reduction is known to occur with retention of configuration[8] and should lead to the bicyclic acetate **12** with the acetoxymethyl group *syn* to the ether O atom. By the same token, one would expect the ether oxygen and the Me group to be *cis* in the minor product, acetate **13**, which was isolated in 13% yield.



Hydrolysis of acetates **12** and **13** gave alcohols **3** and **5**, respectively. The hydroxyl IR stretching absorption of alcohol **3**, determined in carbon tetrachloride solution, was not altered by dilution suggesting the presence of an intramolecular H-bond between the OH group and the ethereal oxygen. This observation confirms the structural assignment arrived at on the basis of mechanistic considerations. The IR and NMR spectra of alcohol **3** were identical with those of the naturally occurring alcohol **3** isolated by Sakan, while the spectra of **5** were identical with those of the dihydro alcohol obtained on catalytic hydrogenation of naturally occurring **4**.[2]

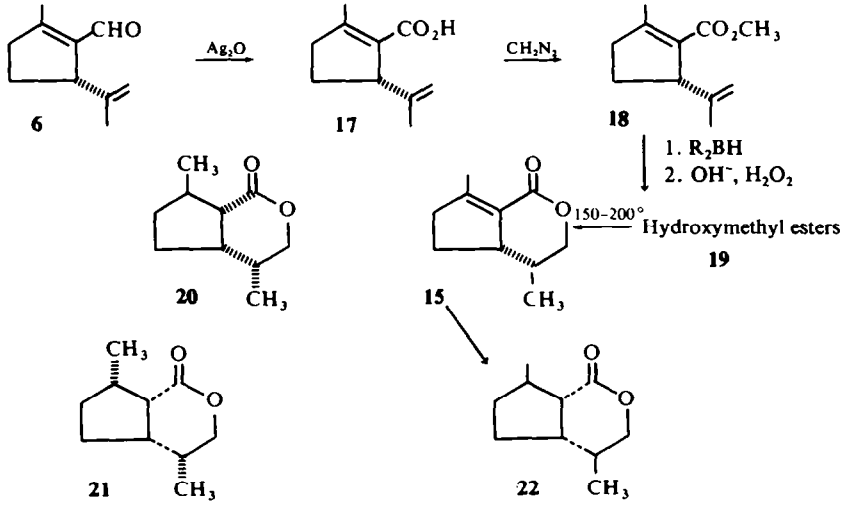
Pyrolysis of acetate **12** gave a sample of pure (+)-matatabiether whose spectral properties and VPC retention time were identical with those of an authentic sample of (−)-matatabiether.

We turn next to a description of a synthesis of neonepetalactone **15** which, in turn, has been converted to isodihydronepetalactone **22** permitting an assignment of stereochemistry to the methyl group attached to the lactone ring.

Silver oxide oxidation of aldehyde **6** gave unsaturated acid **17** which was converted to methyl ester **18** with diazomethane. Selective hydroboration of the terminal double bond was achieved with bis(3-methyl-2-butyl)borane[5] and gave what appeared to be a mixture of saturated and unsaturated hydroxy esters, with the unsaturated hydroxy ester **19** predominating.

Lactonization of the hydroxyesters was accomplished by heating the mixture at 190–200° for 1 hr or by injecting a sample into a gas chromatogram using an injector port temperature of 200° and a column temperature of 175–190°. Better than 80% of the lactone mixture which resulted was comprised of neonepetalactone whose spectra were identical with those of natural neonepetalactone isolated from *Actinidia polygama*.[1]

The remainder of the lactone mixture was comprised of 9·5–15·5% of dihydronepetalactone **20** and 2–7% of another saturated lactone, tentatively assigned structure **21**, whose GLPC retention time was very close to that of neonepetalactone **15**. The IR spectrum of lactone **21** was remarkably similar to that of dihydronepetalactone **20**. Lactone **21** exhibits a peak at 8·84 μ which is not present in **20**, while **20** shows a peak



at 9·12 μ which is not displayed by **21**; the only other distinguishing feature in their IR spectra involves differences in intensity of peaks between 11·0–12·0 μ. When a sample of pure **21** was heated with potassium carbonate in xylene no change was noticed suggesting its formulation as a *cis-cis*-dihydronepetalactone.

Hydrogenation of a lactone mixture containing approximately 84% **15** and 15% **20**, in ethyl acetate using Adams catalyst and a trace of acid, gave a mixture comprised of 20% dihydronepetalactone **20** and 80% isodihydronepetalactone **22**. When another sample of neonepetalactone which was freed of dihydronepetalactone **20** by GLPC, but still contained lactone **21**, was hydrogenated using Adams' catalyst, only isodihydronepetalactone **22** and lactone **21** were obtained. Since the Me group attached to the lactone ring is stable to hydrogenation conditions,[1] it can be assigned a *beta* configuration in synthetic neonepetalactone **15** and an *alpha* configuration in the naturally occurring enantiomorph.

It can be discerned from these results that hydroboration of **18** proceeds with high stereoselectivity to give unsaturated hydroxy ester **19** with a *beta* Me group. Some 1,4-reduction of the conjugated double bond in **18** must precede hydroboration of the isopropenyl group to give an intermediate whose isopropenyl group is attacked to give a saturated hydroxyester whose methyl group is *alpha*. Precedent for this high degree of selectivity is found in the hydroboration of similarly constituted compounds.[4]

It seems reasonable to assume that hydroboration of unsaturated acetate **8** should follow the same course as ester **18**. As a consequence the Me group in **1**, **2**, **3**, **5**, **9**, **10**, **12** and **13** should have a *beta* configuration. The Me group in naturally occurring matatabiether (**1**) must therefore be *alpha* and matatabiether must have the absolute configuration expressed in formulation **1**.

EXPERIMENTAL

All b.ps and m.ps are uncorrected. IR spectra were measured with a Perkin–Elmer Infracord spectrometer, Model 137-B. NMR spectra were determined with a Varian Associates A-60 spectrometer. Chemical shifts are given in ppm with TMS as an internal reference. The mass spectra were measured with a Hitachi RMU-6D mass spectrometer using an all-glass inlet system heated at 180°, a source temp of 155°, an ionizing current of 52 μA, and an ionization energy of 75 eV. Microanalyses were performed by Dr. C. S. Yeh and associates.

2-Acetoxymethyl-3-isopropenyl-1-methyl-1-cyclopentene (**8**). A soln of 3·43 g (0·0715 mole) sodium borohydride in 50 ml water was added dropwise with stirring to a cooled soln of 24·2 g (0·162 mole) of **6**[4] in 90 ml MeOH. The mixture was stirred at 0° for 30 min and 50% AcOH was added until the soln was acidic. The mixture was extracted with ether, the ether soln was dried over $MgSO_4$, and the ether was removed. The residue was taken up in 50 ml Ac_2O containing 8 drops pyridine and the resulting soln was kept at room temp for 22 hr. Distillation afforded 24·2 g (77·4%) of **8**, b.p. 66–67° (0·6 mm), n_D^{20} 1·4707; IR 5·72, 6·05, and 11·20 μ; NMR (CCl_4) δ 1·62 (d, 3, J = 1Hz, CH_3—C=C), 1·78 (s, 3, CH_3—C=C), 1·95 (s, 3, CH_3—CO), 3·38 (m, 1, CH(C=C)$_2$), 4·47 (ABq, 2, C=C—CH_2—O), and 4·68 ppm (broad s, 2, C=CH_2). (Found: C, 74·21; H, 9·58. Calc. for $C_{12}H_{18}O_3$: C, 74·19; H, 9·34%).

2-Acetoxymethyl-3(β-hydroxyisopropyl)1-methylcyclopentene (**9**). A soln of 60 ml 0·78 M diborane in THF was added to a stirred and cooled soln of 15·4 g (0·193 mole) 2-methyl-2-butene in 65 ml THF under N_2. After stirring at 0° for 2 hr, 10·3 g (0·053 mole) of **8** in 25 ml THF was added. The resulting soln was stirred at room temp overnight and after cooling to 0°, 1 ml water was added. After the addition of 28 ml 3N NaOH, 28 ml 30% H_2O_2 was added dropwise at such a rate that the temp did not go above 35° (ca. 45 min). After stirring an additional hr, water and K_2CO_3 were added and the layers separated. The aqueous layer was extracted with ether and the combined organic layers were washed with saturated salt soln and then dried over $MgSO_4$. Distillation gave 9·4 g (83·6%) of a light yellow oil, 112–114° (0·5 mm) and 1·5 g residue. A VPC purified sample of **9** showed n_D^{26} 1·4817; IR 2·92, 5·76 and 8·15 μ; NMR

($CDCl_3$) 0·94 (d, 3, J = 6·6 Hz, CH_3—CH—), 1·72 (broad s, 3, CH_3—C=C), 1·98 (s, 3, CH_3—CO), 3·33 (m, 3, —CH_2—OH), and 4·54 ppm (s, 2, C=C—CH_2—OAc).

2-Hydroxymethyl-3(β-hydroxyisopropyl)1-methylcyclopentene (**10**). A mixture of 5·9 g of **9** and 30 ml 5% NaOH aq and 10 ml MeOH was warmed on a steam-cone for 3 hr, kept at room temp for 22 hr and then extracted with ether. Distillation of the ether extract gave 4·0 g (86%) of a very viscous oil, b.p. 138–140° (1 mm); IR 2·98 and weak 6·02 μ; NMR ($CDCl_3$) 0·86 (d, 3, CH_3—CH—), 1·66 (s, 3, CH_3—C=C), 3·35 (m, 2, CH—CH_2—O), 4·03 (s, 2, C=C—CH_2O), and 4·55 ppm (broad s, 2, —OH). The mass spectrum of **10** showed important ions at *m/e* 152 (44%), 137 (88%), 122 (35%), 110 (31%), 109 (43%), 107 (90%), 95 (74%), 93 (44%), 91 (73%), 81 (47%), 79 (84%), 77 (53%), 67 (51%), 65 28%), 55 (39%), 43 (97%), 41 (100%) and 39 (94%). (Found: C, 70·39; H, 10·64. Calc. for $C_{10}H_{18}O_2$: C, 70·55; H, 10·66%).

The *bis*-trimethylsilyl ether derivative of **10** was prepared by stirring with hexamethyldisilazane in pyridine for 4 hr and exhibited b.p. 65° (0·05 mm); IR 6·02, 9·2, 9·55, 10·70, 11·25 and 11·80 μ; NMR (CCl_4) −0·02 (s, 9, $(CH_3)_3Si$), 0·03 (s, 9, $(CH_3)_3Si$), 0·88 (d, 3, J = 6·6 Hz, CH_3—CH), 1·64 (s, 3, CH_3—C=C), 3·32 (M, 2, CH_2—O), and 4·09 ppm (broad s, 2, —C=C—CH_2—O). (Found: C, 61·34; H, 10·96; Si, 17·60. Calc. for $C_{16}H_{34}O_2Si_2$: C, 61·08; H, 10·89; Si, 17·85%).

Dehydration of diol **10**—*dihydropyran* **2**. A soln of 2·7 g of **10**, and 0·217 g *p*-toluenesulfonic acid in 70 ml benzene was refluxed for 12 hr using a Soxhlet extractor filled with molecular sieves. The soln was cooled, ether was added, and the resulting soln was washed with Na_2CO_3 aq and water. After drying over $MgSO_4$, the soln was evaporatively distilled to give 0·5 g of liquid at ca. 10 mm, and 60 mg of viscous **10** at 1 mm. A non-volatile residue of 0·4 g remained.

The volatile liquid was further purified using a 3m Carbowax 20M on Chromosorb column at 145°. The major component, pyran **2**, eluting after 28 min, was collected and showed $[\alpha]_D^{25}$ + 112° (CCl_4); IR 5·95, 9·06, 9·90 μ; NMR (CCl_4) 0·85 (d, 3, CH_3—CH), 1·62 (s, 3, CH_3C=C), 3·63 (m, 2, (CH—CH_2—O), 3·67 and 4·34 ppm (AB-q, 2, C=C—CH_2—). Pyran **2** displayed abundant ions in its mass spectrum at *m/e* 152 (99%), 137 (100), 110 (53), 109 (40), 107 (50), 95 (65), 94 (48), 93 (39), 91 (39), 81 (75), 79 (92), 77 (38), 67 (39), 41 (49), and 39 (37). (Found: C, 78·94; H, 10·84. Calc. for $C_{10}H_{16}O$: C, 78·90; H, 10·59%).

In one experiment a small amount of another compound with longer retention time (38 min) was isolated and displayed IR absorption at 5·85, and 6·05 μ; λ_{max} 236 mμ (ε 8,900); NMR (CCl_4) 0·60 (d, 3, CH_3—CH), 0·98 (d, 3, CH_3—CH, 1·63 (s, 3, CH_3—C=C), and 1·94 ppm (s, 3, CH_3—C=C). The compound, assigned structure **11**, showed a molecular ion at *m/e* 152 (34%) and important ions at *m/e* 110 (100%), 109 (37), 95 (43), 81 (44), 67 (18), 53 (35), 43 (53), 41 (64), and 39 (95).

When **10** was injected into a gas chromatogram using a 5 ft SE-30 column at 155° a mixture of ethers eluted within 1–2 min. The mixture was rechromatographed using a 3m Carbowax-20M column at 145° and three peaks with retention times of 13, 16 and 28 min were collected, and were present in a ratio of 1·7:9·7:7·2, respectively. The second and third peaks were identified by spectral analysis as matatabiether (**1**), and pyran **2**. Too little of the first peak was obtained for proper identification.

Oxymercuration of hydroxy acetate **9**—*acetates* **12** *and* **13**. A mixture of 16·0 g (0·0756 mole) of **9**, 24·09 g (0·0756 mole) mercuric acetate, and 80 ml t-BuOH was stirred at room temp for 25 hr. The resulting mixture was cooled to 0° and 75 ml of 3N NaOH was added, followed by 75 ml of 0·5 M $NaBH_4$. The soln was extracted with ether, and the ether was dried over $MgSO_4$. The ether was removed leaving a product shown to be a mixture of acetates and alcohols by IR spectroscopy and GLPC analysis. The residue was dissolved in 20 ml Ac_2O containing 6 drops pyridine. After standing 24 hr the soln was distilled affording 11·2 g, b.p. 98–110° (2·5 mm) and 2·45 g of recovered diacetate, b.p. 126–130° (2·3 mm).

A 8·5 g sample of the first fraction was chromatographed on a silica gel column. Elution with 7·5–50% ether in benzene gave 1·50 g of **13**, 0·80 g of a mixture of **12** and **13**, and 4·93 of **12**.

A sample of **13** purified by GLPC showed $[\alpha]_D^{25}$ −18° (2·2, CCl_4), IR 5·75, 8·20 and 9·65 μ; NMR (CCl_4) 0·97 (d, 6, 2 CH_3—CH), 1·97 (s, 3, CH_3—CO), and 3·90 ppm (s, 2, —O—CH_2). The mass spectrum displayed a molecular ion at *m/e* 212 (1·0%) and major fragment ions at *m/e* 152 (16%), 139 (100), 69 (91), 55 (26), 43 (76), and 41 (33). (Found: C, 68·05; H, 9·43. Calc. for $C_{12}H_{20}O_3$: C, 67·89; H, 9·50%).

A sample of **12** purified by GLPC showed $[\alpha]_D^{25}$ −3·2° (3·2, CCl_4), IR 5·75, 8·17, 9·50, and broad peaks at 9·55 and 9·70 μ; NMR (CCl_4) 0·73 (d, 3, CH_3—CH), 1·13 (s, 3, CH_3—C—O), 1·94 (s, 3, CH_3—CO), 3·08 (m, 2, CH—CH_2—O), and 4·28 ppm (d, 2, —CH—CH_2—OAc). The mass spectrum

exhibited a molecular ion at *m/e* 212 (2%) and important ions at *m/e* 183 (11%), 153 (41), 95 (24), 81 (17), and 43 (100). Found: C, 67·81; H, 9·56. Calc. for $C_{12}H_{20}O_3$: C, 67·89; H, 9·50%).

1-Hydroxymethyl-4,8-dimethyl-2-oxabicyclo[3.3.0]*octane* (**5**). A 1·5 g sample of **13** was hydrolyzed by stirring with 10 ml 10% NaOH aq for 8 hr at room temp. The mixture was extracted with ether, the ether soln was dried and the ether removed. The resulting **5** was purified using a 5 ft SF-96 column and showed $[\alpha]_D^{25}$ −17° (7·8, CCl_4); IR (CCl_4) 2·88 and 9·63 μ; NMR (CCl_4) 0·95 (d, 3, CH_3—CH), 3·10 (s, 1, OH), 3·29 and 3·56 (ABq, 2, J_{AB} = 11·5 Hz, —CH_2—O), and 3·97 (t, 2, CH—CH_2—O). The mass spectrum of **5** exhibited a molecular ion at 170 (0·3%) and important ions at *m/e* 139 (81%), 69 (100), 55 (31), and 41 (43). (Found: C, 70·54; H, 10·88. Calc. for $C_{10}H_{18}O_2$: C, 70·55; H, 10·66%).

8-Hydroxymethyl-1,4-dimethyl-2-oxabicyclo[3.2.1]*octane* (**3**). A 100 mg sample of VPC pure **12** stirred with 1 ml 10% NaOH aq at room temp for 6 hr. The mixture was worked up as described above to give a liquid **3** which was purified by GLPC and showed $[\alpha]_D^{25}$ + 4·6° (5·24, CCl_4); IR (CCl_4) 2·83 and 9·21 μ; NMR (CCl_4) 0·68 (d, 3, CH_3—CH), 1·14 (s, 3, CH_3—C—O), 3·10 (m, 2, CH—CH_2—O), and 3·82 ppm (d, 2, CH—CH_2—OH). The alcohol **3** displayed a molecular ion at *m/e* 170 (8%) and important fragmentation ions at *m/e* 141 (62%), 43 (100), and 41 (36). (Found: C, 70·45; H, 10·70. Calc. for $C_{10}H_{18}O_2$: C, 70·55; H, 10·66%).

(+)-Matatabiether (**1**). The acetate **12** (4·93 g) was dropped under N_2 press through a helix packed glass column heated by a furnace to 560 ± 10°. The column was washed with pentane and the pentane soln containing the pyrolysate was washed with water and 10% Na_2CO_3 aq. The soln was dried over $MgSO_4$ and distilled at 0·8 mm until the vapor temp reached 60° to give 1·4 g of liquid which was collected at −78°. The distilland, 2·0 g, was mostly unreacted **12** as indicated by IR analysis. This material was pyrolysed a second time to yield another 0·4 g of volatile product and 1·0 g of unreacted acetate.

The volatile product proved to be essentially pure **1** by GLPC analysis. A sample of **1** purified by GLPC showed $[\alpha]_D^{25}$ +158° (5·21, CCl_4); IR 5·99, 9·20 and 11·14 μ; NMR (CCl_4) 0·76 (d, 3, J = 6·5 Hz, CH_3—CH), 1·23 (s, 3, CH_3—C—O), 3·27 and 3·60 (m, 2, J_{AB} 12·0 Hz, J_{BX} 10·1, J_{AX} 6·0 Hz, CH—CH_2—O), 4·68 ppm (s, 2, C=CH_2). The mass spectrum of **1** displayed a molecular ion at *m/e* 152 (32%) and other important ions at *m/e* 137 (59%), 110 (32), 109 (36), 107 (30), 105 (24), 95 (63), 77 (29), 67 (33), 43 (100), 41 (47), and 39 (44). (Found: C, 79·05; H, 10·59. Calc. for $C_{10}H_{16}O$: C, 78·90; H, 10·59%).

The IR and NMR spectra, and GLPC retention time (24 min on a 20% Carbowax 20M on Chromosorb column at 148°) of synthetic **1** were identical to those of naturally occurring matatabiether, $[\alpha]_D^{27}$ −153° ($CHCl_3$).

Methyl 5-isopropenyl-2-methyl-1-cyclopentene-1-carboxylate (**18**). 10% NaOH aq was added dropwise under N_2 to a soln of 40 g (0·265 mole) of **6** and 135·9 g (0·795 mole) $AgNO_3$ in 400 ml EtOH and 200 ml water until the pH of the mixture reached 12. After stirring overnight, the basic soln was extracted with ether, and the EtOH was then removed from the aqueous soln by distillation under reduced press. The resulting aqueous soln was acidified with conc HCl and extracted with CH_2Cl_2. The CH_2Cl_2 was removed and the residue was taken up in pentane and a small amount of insoluble solid was removed. The pentane was removed leaving 39·0 g (88·5%) crude acid. A 10 g sample of the acid was taken up in MeOH and treated with an excess of diazomethane. Distillation gave 10·2 g of **18**, b.p. 68–70° (0·9 mm); IR 5·89, 6·10, and 11·25 μ; λ_{max} 230 mμ (ε 7,900); NMR (CCl_4) 1·67 (m, 3, CH_3—C=CH_2), 2·11 (m, 3, CH_3—C=C—C—), 4·62 (s, 3, —OCH_3), and 4·56 ppm (m, 2, C=CH_2). (Found: C, 72·94; H, 9·43. Calc. for $C_{11}H_{16}O_2$: C, 73·30; H, 8·95%).

Hydroboration of methyl 5-isopropenyl-2-methyl-1-cyclopentene-1-carboxylate neonepetalactone (**15**). A soln of 90 ml 0·743 M (0·0646 mole) diborane in THF was added under N_2 to a cooled and stirred soln of 19·1 g (0·273 mole) 2-methyl-2-butene in 50 ml THF. The mixture was stirred at 0° under N_2 for 2 hr and then 12·9 g (0·0718 mole) of **18** in 25 ml THF was added. The mixture was kept at 0° for 2 hr and at room temp for 14 hr. After cooling to 0°, 39 ml of 3M NaOH was added, followed by dropwise addition of 39 ml 30% H_2O_2 at such a rate that the temp did not rise above 30°. The mixture was then worked up in the usual manner and on distillation afforded 0·6 g of a forerun, b.p. 43–93° (0·4 mm), and 7·9 g hydroxy methyl ester, b.p. 93–110° (0·4 mm).

A sample of the hydroxy methyl ester (0·64 g) was heated to 200° at atm press for 45 min and the resulting lactone mixture was separated by chromatography on a 20% Carbowax 20M on firebrick column at 195°. Three fractions, present in a ratio of 1·2 : 1·0 : 10·8, with retention times of 57, 68, and 75 min were collected, and were identified as **20**, **21**, and **15**, respectively.

Dihydronepetalactone **20** was identified by comparison of its IR spectrum with that of an authentic sample.

Dihydronepetalactone **21** displayed an IR spectrum very similar to that of **20**. The most distinguishing feature is a peak at 8·84 μ which is not present in the spectrum of **20**. The NMR spectrum of **21** displayed 0·93 (d, 6, CH_3—CH), and 3·98 (broad m, 2, CH—CH_2—O). Insufficient material was obtained to characterize it completely.

Neonepetalactone **15** displayed m.p. 21–23°, n_D^{25} 1·5062; $[\alpha]_D^{32}$ +51·9° (CCl_4), IR 5·80 and 6·07 μ; NMR (CCl_4) 0·9 (d, 3, J = 7 Hz, CH_3CH), 2·15 (m, 3, J = 1 Hz, CH_3—C≡C—CH), 3·20 (m, 1, CH—C≡C), 4·04 and 4·32 (m, 2, J_{AB} = 12 Hz, J_{AX} = 3·0 Hz, J_{BX} = 2·5 Hz, CH—CH_2—O). The mass spectrum displayed a molecular at *m/e* 166 (6%) and important ions at *m/e* 153 (39%), 151 (61), 103 (63), 101 (100), 95 (85), 85 (45), and 67 (23). (Found: C, 72·06; H, 8·61. Calc. for $C_{10}H_{14}O_2$: C, 72·25; H, 8·49%).

(+)-Dihydronepetalactone **20** *and (+)-isodihydronepetalactone* (**22**). A 100 mg sample of GLPC pure nepetalactone was hydrogenated in EtOAc containing a small amount of AcOH, using PtO_2 as catalyst. The catalyst and solvent were removed and the residue was separated using a Carbowax 20M column at 190°. The minor component (ca. 5%), **22**, displayed $[\alpha]_D^{29}$ +6·9° (CCl_4); IR 5·73, 8·42, 9·02 and 9·40 μ. The mass spectrum showed important ions at *m/e* 168 (20%), 153 (53), 126 (20), 113 (100), 111 (20), 95 (34), 81 (95), 69 (38), and 67 (65).

The major product (ca. 95%) proved to be **20** and showed $[\alpha]_D^{29}$ +66·2° (CCl_4); IR 5·73, 8·03, 8·27, 8·50, 8·90, 9·12, and 9·38 μ; NMR (CCl_4) 0·89 (d, 3, J = 7 Hz, CH_3—CH), 1·16 (d, 3, J = 6·5 Hz, CH_3—CH), and 3·99 ppm (d and s, 2, —CH_2—O). The mass spectrum exhibited important ions at *m/e* 168 (22%), 153 (30), 126 (25), 113 (68), 95 (38), 81 (100), 69 (35), 67 (61), 55 (30), and 41 (55). (Found: C, 71·05; H, 10·03. Calc. for $C_{10}H_{16}O_2$: C, 71·39; H, 9·58%).

Hydrogenation of neonepetalactone. Neonepetalactone **15**, (0·52 g), containing ca. 15% of **20**, was hydrogenated in EtOAc containing 2 drops AcOH using PtO_2 as a catalyst. After removal of the catalyst and solvent, the residue was analysed and separated by GLPC using a 20% DEGS column at 170° indicating the presence of ca. 80% of **22**, 19% of **20**, and a trace of **15**. (−)-Isodihydronepetalactone (**22**) exhibited $[\alpha]_D^{28}$ −4·2° (3·5, CCl_4); IR 5·73, 8·42, 9·02, and 9·40 μ; NMR (CCl_4) 1·00 (d, 3, J = 6·0 Hz, CH_3—CH), 1·17 (d, 3, J = 6·5 Hz, CH_3—CH), and 3·79 and 4·07 (m, 2, J_{AB} = 11 Hz, J_{AX} = 9·5 Hz, J_{BX} = 4·04 Hz, —CH—CH_2—O). (Found: C, 71·59; H, 9·69. Calc. for $C_{10}H_{16}O_2$: C, 71·39; H, 9·58%).

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