Synthesis and Mass Spectra of Tricyclic C_{22}, C_{23}, and C_{24} Terpane Isomers of the *ent*-Isocopalane Series[1]

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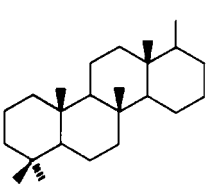
In order to develop a procedure for the synthesis of *ent*-isocopalanes for comparison with the tricyclic terpanes present in sediments and crude oils, requirements for successful cyclization of labda-8(17),13-dienes to C-15-substituted *ent*-isocopalanes were studied. The results were used for the preparation of 15-ethyl-, 15-*n*-propyl-, and 15-isobutyl-*ent*-isocopalane (18,19-bisnor-, 18,19,20-trisnor- and 19-nor-13αH,14αH-cheilanthane). The mass spectra of these substances were indistinguishable from the mass spectra of their 13βH,14αH, 13βH,14βH, and 13αH,14βH isomers, obtained in small quantity as components of mixtures; none contained the abundant m/z 261 peak ascribed to the tricyclic terpanes in sediments and crude oils.

The alkane fractions of many sediments and crude oils contain tricyclic and tetracyclic terpanes whose identity has been a matter of recent interest because of their potential utility as biological markers.[1-7] Their distribution is ordinarily studied by computerized gas chromatography–mass spectrometry (CGCMS) with the help of a base peak at m/z 191 displayed by members of both series. Among the tetracyclic terpanes, four have recently been identified as the C_{24}–C_{27} components **1** and **2a–c** (Chart I) of a series of hopane-derived 17,21-secohopanes.[8]

In work on components of the tricyclic series, which usually extends from C_{19}–C_{30}, with the C_{23} component (or components) predominant, Albrecht and co-workers have synthesized a number of tricyclic C_{19}–C_{21} compounds and reported that three of them, **3a–c**, were present in sediments and petroleums of various ages and origins.[11] These and the other members of the homologous series are thought to be derived from an as yet unknown tricyclohexaprenane **3d**, which presumably represents the C_{30} member of the series. Ekweozor and Strausz[12] isolated the most abundant tricyclic terpane in Athabasca oil sand bitumen, a C_{23} component, and proposed for it structure **3e** (18,19-bisnor-13βH,14αH-cheilanthane[12]) on the basis of its mass spectral fragmentation pattern and correlation of its NMR spectrum with the spectrum of the tricyclic sesterterpene cheilanthatriol (**5**).[13,14] Stereochemistry **4b** was ascribed to a minor C_{23} component.

As part of our work on biogenetic-type syntheses of the tetracyclic sesterterpenoid scalaranes from bicyclic precursors,[10] we have simultaneously investigated routes to tricyclic compounds of type **6** or **7** where R is a group suitable for eventual cyclization to scalaranes.[15] In view of the reports cited in the previous paragraph, it was tempting to extend our work to the preparation of compounds of type **8** for comparison with the tricyclic terpanes

Chart I



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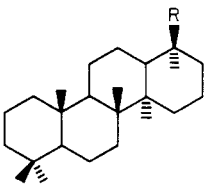
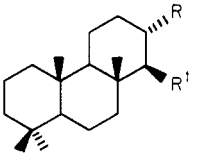
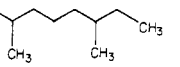
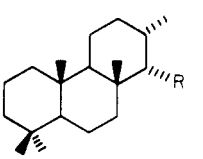


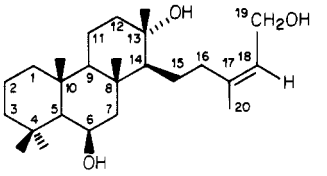
2a, R = Me
b, R = Et
c, R = *n*-Pr



3a, R = Me; R′ = H
b, R = H; R′ = Me
c, R, R′ = Me
d, R = Me; R′ = 
e, R = Me; R′ = *n*-Bu
f, R = Me; R′ = CO_2Me
g, R = Me; R′ = $CH_2CH_2CO_2Me$
h, R = Me; R′ = *n*-Pr



4a, R = *n*-Pr
b, R = *n*-Bu



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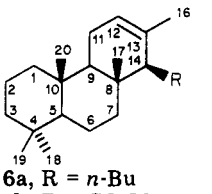
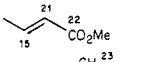
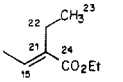
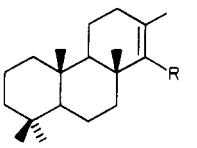


6a, R = *n*-Bu
b, R = CO_2Me
c, R = 
d, R = 



7a, R = *n*-Bu
b, R = $CH_2CH_2CO_2H$
c, R = CO_2Me
d, R =

(1) The initial phases of work at the Florida State University were supported by a grant from the National Science Foundation.
(2) Anders, D. E.; Robinson, W. E. *Geochim. Cosmochim. Acta* **1971**, *35*, 1661.
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(8) Trendel, J.-M.; Restle, A.; Connan, J.; Albrecht, P. *J. Chem. Soc. Chem. Commun.* **1982**, 304; see also ref 9 and 10.
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(11) Aquino Neto, F. R.; Restle, A.; Connan, J.; Albrecht, P.; Ourisson, G. *Tetrahedron Lett.* **1982**, *23*, 2027.
(12) Ekweozor, C. M.; Strausz, O. P. *Tetrahedron Lett.* **1982**, *23*, 2711.
(13) Khan, H., Zaman, A.; Chetty, G. L.; Gupta, A. S.; Dev, S. *Tetrahedron Lett.* **1971**, 4443.
(14) Gupta, A. S.; Dev, S.; Sangare, M.; Septe, B.; Lukacs, G. *Bull. Soc. Chim. Fr.* **1976**, 1879.
(15) Herz, W.; Prasad, J. W., unpublished experiments.

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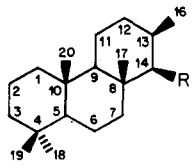
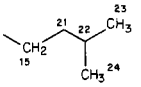
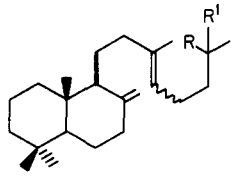
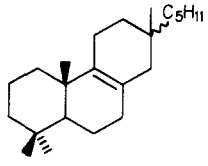
Chart II



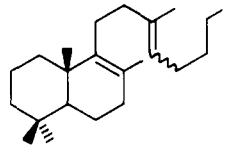
8a, R = *n*-Pr
b, R = *n*-Bu
c, R = 
d, R = $CH_2CH_2CO_2Me$
e, R = $CH_2CH_2CO_2H$
f, R = $CH_2CH_2CH_2OH$
g, R = $CH_2CH_2CH_2OTs$
h, R = $CH_2CH_2CH_2Cl$
i, R = $CH_2CH_2C(O)CH_3$
j, R = $CH_2CH_2CH(OH)CH_3$
k, R = $CH_2CH_2C(OH)(CH_3)_2$



9a, R, R′ = =O
b, R, R′ = H, OH
c, R, R′ = H, OTs
d, R, R′ = H



10a, α-C_5H_{11}
b, β-C_5H_{11}



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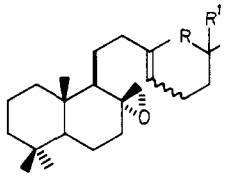
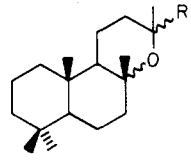
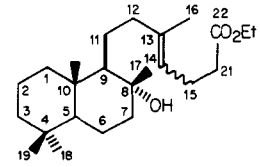


12a, R, R′ = =O
b, R, R′ = H, OH
c, R, R′ = H, OTs
d, R, R′ = H

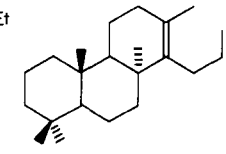


13a, R = *n*-C_5H_{11}
b, R = $CH_2CH_2CO_2H$

Chart III



14a, 13(*E*)
b, 13(*Z*)



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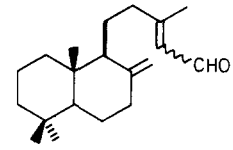
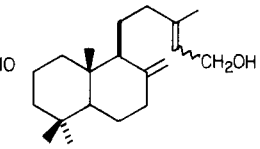
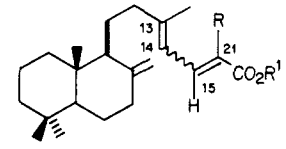


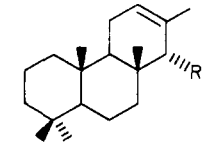
16a, 13(*E*)
b, 13(*Z*)

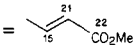
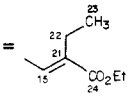


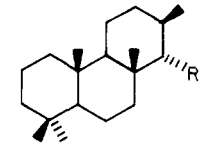
17a, 13(*E*)
b, 13(*Z*)



18a, R = H; R′ = Me; 13(*E*)
b, R = H; R′ = Me; 13(*Z*)
c, R, R′ = Et; 13(*E*)
d, R, R′ = Et; 13(*Z*)



19a, R = 
b, R = 



20a, R = *n*-Pr
b, R = *n*-Bu

in sediments and crude oils. In the present article we define the requirements for successful cyclization of labda-8(17),13-diene derivatives to compounds of type **6** and describe their use in synthesis of three tricyclic terpanes, the C_{22}, C_{23}, and C_{24} hydrocarbons **8a–c** (Chart II). The mass spectra of these substances do not exhibit the abundant m/z 261 peak ascribed[11,12] to the tricyclic terpanes in sediments and crude oils, but neither do the mass spectra of the C_{22} epimers **3h**, **4a**, and **20a** and the C_{23} epimers **3e**, **4b**, and **20b**, which were obtained, in small quantity, together with **8a** or **8b** by modification of the synthesis.

Our first approach to the C_{23} hydrocarbon **8b** was based on the hope that acid-catalyzed cyclization of **9d** (mixture of *E* and *Z* isomers), easily available from **9a**[10] via **9b** and **9c**, might lead to **6a** or **7a**, although the competitive process—attack by the 8,17-double bond on the carbocation generated at C-13—was envisaged as a distinct possibility. In fact, Lewis acids such as BF_3 and $SnCl_4$ gave mixtures consisting mainly of epimers **10a** and **10b**, while use of formic acid at room temperature merely caused isomerization to **11**. Attempted cyclization of epoxide **12d** (mixture of *E* and *Z* isomers), prepared by subjecting 8α,17-epoxymanool[16] to the Carroll reaction with ethyl acetoacetate[10] and exposing the product **12a** to the sequence of reactions previously used for **9a**, produced mainly analogues **13a** of manoyl and epimanoyl oxide, whereas use of formic acid gave predominantly dehydration products and a small amount of **6a** as evidenced by a strong MS peak at m/z 192 resulting from RDA cleavage of ring C.

A tricyclic acid (**7b** or **15**), prepared by Mellor and Pinto[17] in unspecified yield from sclareol by transesterification with triethyl orthoacetate, Claisen rearrangement to mixture **14a,b**, and subsequent cyclization, seemed an attractive alternate intermediate for tricyclic terpanes. Repetition of this work, with attention to the quantity of propionic acid used in the Claisen rearrangement (see Experimental Section), gave **14a,b** in approximately 50% yield. *E* and *Z* isomers (Chart III) could be separated by HPLC and were characterized by ^{13}C NMR spectrometry (Table III). However, as cyclization of the *E,Z* mixture followed by repeated TLC afforded **7b** in only 13% yield and the major product fraction appeared to be **13b**, this route was not pursued further. The assignment of 9β-methyl configuration to **7b** is based on a comparison of its ^{13}C NMR spectrum (Table III) with that of other compounds of type **7** prepared from methyl *ent*-isocopalate (**6b**)[15] and with that of **7d** (vide infra).

As a result of these difficulties[18] it became evident that in order to effect cyclization of labda-8(17),13-dienes and their derivatives in the desired direction the 13,14-double

(16) Grant, P. K.; Liau, H. T. L. *Aust. J. Chem.* **1978**, *31*, 1777.

(17) Mellor, J. M.; Pinto, J. A. N. *J. Chem. Soc., Perkin Trans 1* **1975**, 1009.

(18) We remark in passing that attempts to apply various chain-lengthening procedures to methyl *ent*-isocopalate, its dihydro derivatives, and similar compounds for preparation of compounds of type **6**, **8**, or **3** were not successful.

Table I. Mass Spectra of 8a-c (70 eV)[a]

	m/z (relative intensity)
8a	304 (M^+, 37), 289 (20), 191 (100), 177 (6), 163 (5), 151 (5), 150 (5), 137 (15), 123 (22), 109 (19), 105 (5), 95 (27), 81 (22), 69 (27), 68 (11), 67 (16), 57 (9), 55 (29)
8b	318 (M^+, 25), 303 (13), 191 (100), 177 (6), 137 (17), 123 (18), 109 (19), 95 (28), 81 (24), 69 (30), 68 (12), 67 (17), 57 (10), 55 (29)
8c	332 (M^+, 15), 317 (11), 191 (100), 177 (7), 163 (5), 151 (6), 150 (6), 137 (20), 123 (28), 121 (11), 109 (30), 97 (11), 95 (45), 83 (19), 82 (21), 81 (40), 69 (52), 67 (24), 57 (20), 55 (40)

[a] Conditions as described in the introduction to Experimental Section.

bond must be deactivated so as to induce initial protonation predominantly at the 8,17-double bond. Following this reasoning, we undertook the preparation of **18a,b** and found that they indeed underwent cyclization to tricyclic compounds of type **6** in good yield.

$LiAlH_4$ reduction of the mixture of *E* and *Z* aldehydes **16a,b** from pyridinium chlorochromate oxidation of manool[19] and separation of the product by HPLC gave the *E* and *Z* alcohols **17a** and **17b**,[20] which were reoxidized (pyridinium dichromate)[23] as needed to **16a** and **16b**, which were unstable. The geometry assigned to the alcohols and the derived aldehydes was based on the shifts of the C-12 and C-16 signals (Table I) found in **17a** at δ 39.01 and 16.18 and in **17b** at δ 30.48 and 23.18.[24] Reaction of **16a** and **16b** with trimethyl phosphonoacetate under modified Wittig reaction conditions[25] gave pure **18a** and **18b** in 51% and 42% yield after purification by HPLC. Both of these were 15-*E* derivatives ($J_{15,21}$ = 15 Hz) but exhibited the expected differences in the ^{13}C NMR spectra for 13-*E* and -*Z* isomers (for **18a**, C-12 and C-16 at δ 38.36 and 17.43, for **18b** C-12 and C-16 at δ 31.49 and 24.29).

Cationic cyclization of **18a** and **18b** separately (BF_3·OEt_2, benzene) proceeded without complications, though somewhat sluggishly at room temperature, to give **6c** and **19a**, respectively, in about 67% yield (based on recovered starting material). The ^1H and ^{13}C NMR spectra of the products were appropriate for the structures shown, the signal of H-12 in **6c** at δ 5.48 being allylically coupled to the vinylic methyl at δ 1.49 and the signal of H-15 (dd at δ 6.83) being not only coupled to H-21 (d at δ 5.83, $J_{15,21}$ = 15 Hz) but also to H-14 (br d at δ 2.53, $J_{14,15}$ = 9 Hz). The ^1H NMR spectrum of **19a** differed from that of **6c** chiefly in the chemical shift of H-14 (br d at δ 2.07, $J_{14,15}$ = 9 Hz). More significant were differences in the ^{13}C NMR spectra (Table III); as anticipated from the differing stereochemistry at C-14, C-9 and C-17 of **19a** are shielded and deshielded by ca. 7 and 9 ppm relative to C-9 and C-17 of **6c**. That addition of the 13,14-double bond of **18a** to the cationic center of C-8 had taken place from the more accessible α-face as it does in the case of methyl (*E*)- and (*Z*)-anticopalate[26] was also shown by the ^{13}C NMR spectrum where C-17 and C-20 appear at fields higher than

Table II. GC Data of 8a-c[a]

compound	retention time, min
$C_{22}H_{40}$ (8a)	10.15
$C_{23}H_{42}$ (8b)	11.64
$C_{24}H_{44}$ (8c)	12.51

[a] Column 1 and conditions described at the beginning of the Experimental Section.

20.[40] Lastly, the mass spectra of both **6c** and **19a** exhibited strong peaks at *m/z* 192 due to RDA fragmentation of ring C.

Because the rate of cyclization of **18a** was slow at room temperature, the reaction was carried out at 70 °C. However, this produced only **7d**, presumably by isomerization of the initially formed **6c**.

Catalytic hydrogenation of **6c** (PtO_2, MeOH–EtOAc) furnished in high yield the tetrahydro derivative **8d**, which was free of isomers by ^1H and ^{13}C NMR criteria. That hydrogenation of the tricyclic system had taken place from the α-face of the molecule, as in the case of methyl *ent*-isocopalate (**6b**) under neutral conditions,[27] was shown by the chemical shift of C-16 (δ 15.23).[28] Further transformations of **8d** to the C_{22} hydrocarbon **8a** by way of **8f** and **8g** proceeded unexceptionally. The substance was essentially free of contaminants as indicated by GC; the MS data are listed in Table I, GC retention time in Table II, and the ^{13}C NMR spectrum in Table III.

8d also served as an intermediate for the synthesis of the C_{23} and C_{24} hydrocarbons **8b** and **8c**. Hydrolysis to **8e** followed by reaction with MeLi at −20 °C gave **8i** and **8k** in 14% and 48% yield; respectively. $NaBH_4$ reduction of **8i** gave a mixture of diastereomers **8j** whose tosylation (TsCl, DMA, Et_3N) did not proceed smoothly. Following chromatography, $LiAlH_4$ reduction of the crude product gave **8b** in 31% yield based on **8i**. A considerable improvement in the overall yield of **8b**, essentially free of contaminants by NMR and GC criteria, was effected by coupling **8g** with CH_3MgCl in the presence of Li_2CuCl_4.[29] This gave **8b** in 77% yield accompanied by a small amount (14%) of **8h**. An alternative approach involving condensation of **16a** and **16b** separately with triethyl phosphonobutyrate to **18c** and **18d** followed by cyclization to **6d** (50%) and **19b** (37%) failed when the conditions required for hydrogenation of the relatively hindered 15,21-double bond (with a view to eventual decarboxylaltion) resulted in loss of stereochemical integrity at C-13 and C-14. Lastly, dehydration of **8k** ($POCl_3$, pyridine) followed by catalytic hydrogenation of the olefin mixture afforded the C_{24} hydrocarbon **8c**, which was pure by NMR and GC criteria.

Significant peaks in the low-resolution mass spectra (70 eV) of **8a–c** are listed in Table I. We note the lack of an abundant ion at *m/z* 261, which according to Albrecht and co-workers[11] is a prominent feature in the mass spectra of the higher tricyclic terpanes from sediments and crude oils[30] and which they ascribed to the loss of a side chain of variable length attached to a basic C_{19} skeleton. On this basis, **8a–c** and their higher homologues would not be components of the tricyclic terpane fraction. Ekweozor and Strausz[12] also reported such an ion for the major (their peak 5b) and minor (their peak 5a) tricyclic C_{23} terpane in Athabascia oil sand bitumen and attributed the dif-

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(29) Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.
(30) Under our conditions the relative abundance of the *m/z* 261 peak in the mass spectra of **8a–c** is 1% or less.

Table III. ^{13}C NMR Spectra[a] (δ)

carbon	6c	6d	7b	7d	8a	8b	8c	8d	8e	8f	8k
1	39.92	39.96	39.67	39.65	40.13	40.13	40.08	40.05	40.02	40.05	40.07
2	18.57	18.54	18.64	18.63	18.80	18.79	18.76	18.74	18.17	18.71	18.74
3	41.96	42.06	42.12	42.10	41.68	42.27	42.25	41.52	42.17	41.64	42.66
4	33.18	33.21	33.25	33.24	33.34	33.34	33.32	33.21	33.28	33.29	33.31
5	56.54	56.74	56.56	56.39	56.69	56.69	56.66	56.53	56.50	56.60	56.65
6	18.53	18.62	17.81	18.63	18.31	18.30	18.27	18.22	18.71	18.22	18.25
7	41.96	41.98	34.74	39.87	42.28	41.67	41.64	42.19	41.48	42.19	42.22
8	37.48	37.51	39.41	38.41	38.66	38.75	38.80	37.65	37.62	37.64	38.93
9	54.48	54.43	56.56	55.73	51.59	61.59	61.57	61.35	61.29	61.46	61.51
10	36.72	37.56	37.45	37.58	37.70	37.70	37.67	38.76	38.73	38.71	37.67
11	22.72	22.75	18.64	17.50	16.35	16.34	16.38	16.25	16.23	16.32	16.34
12	123.62	122.43	33.97	34.33	35.08	35.08	35.06	34.79	34.73	34.92	34.97
13	131.25	121.98	127.20	131.75	29.37	29.34	29.25	29.12	29.09	29.31	29.31
14	59.75	54.70	138.64	139.41	53.68	53.91	54.15	53.34	53.18	53.75	54.62
15	149.94*	141.82	22.64	144.39	27.92	30.41	37.53	21.29	21.05	21.57	19.96
16	22.34	22.26	19.27*	21.23	15.36*	15.34*	15.36	15.23	15.17	15.23	15.26
17	15.74	15.86	20.97	16.34	17.60*	17.59*	17.60	17.51	17.48	17.49	17.65
18	33.42	33.45	33.75	33.24	33.34	33.34	33 32	33.31	33.29	33.29	33.31
19	21.71	21.74	21.34	21.34	21.44	21.43	21.40	21.38	21.38	21.38	21.41
20	15.69	15.30	16.47	16.34	16.39*	16.49*	16.33	16.31	16.32	16.31	16.31
21	122.73*	135.58	38.48	122.53	27.14	25.14	23.03	32.77	32.66	31.38	41.66
22	166.53	20.26	179.24	166.50	14.57	23.15	28.36	174.65	180.32	63.55	72.32
23		13.86				14.17	23.17				29.42
24		167.76					22.35				29.06
misc	51.38[b]	60.23[c]		51.38[b]				51.43[b]			
		14.38									

carbon	14a	14b	17a	17b	18a	18b	18c	18d	19a	19b
1	39.86	39.72	38.41	38.82	39.15	38.22	39.45	39.01	39.17	39.69
2	18.49	18.52	19.34	19.29	19.42	19.42	19.42	19.43	18.63	18.54
3	42.04	42.04	42.14	42.03	42.19	42.17	42.17	42.19	41.84	41.86
4	33.27	33.26	33.43	33.37	33.61	33.59	33.59	33.61	33.21	33.21
5	56.20	56.18	55.49	55.38	55.60	55.58	55.57	56.60	56.47	56.59
6	20.62	20.56	24.41	24.36	24.51	24.49	24.49	24.49	18.52	18.63
7	44.59	44.32	38.30	38.20	39.15	39.01	38.36	38.30	39.66	38.95
8	74.04	73.99	148.25	148.22	148.41	148.36	148.47	148.41	37.18	37.20
9	61.33	62.06	56.33	55.80	56.23	55.95	56.01	56.04	47.21	47.18
10	39.28	39.12	39.53	39.39	39.72	39.61	39.66	39.60	36.64	36.72
11	23.59	23.62	21.63	21.38	21.74	22.03	20.05	20.00	23.18	22.93
12	43.07	35.71	39.01	30.48	38.36	31.49	39.09	31.56	123.16	122.51
13	137.74	138.11	139.43	138.99	150.76	150.76	148.77	138.77	130.76	132.02
14	122.40	122.67	123.30	124.85	123.03	124.36	140.24	121.36	59.39	54.75
15	23.81	23.97	58.88	58.52	141.25	141.04	133.92	133.70	149.89	142.72
16	16.15	23.50	16.18	23.18	17.43	24.29	17.21	24.76	22.53	22.85
17	23.75	24.13	106.22	106.22	106.30	106.43	106.30	106.32	22.53	20.29
18	33.42	33.42	33.57	33.45	33.61	33.59	33.59	33.61	33.34	33.38
19	21.52	21.50	21.79	21.60	21.74	21.74	21.73	21.71	21.79	21.79
20	15.49	15.49	14.41	14.38	14.52	14.59	14.37	14.37	15.60	15.68
21	34.54	34.76			118.31	118.31	131.01	130.92	121.62	134.18
22	173.60	173.56					21.73	22.09	166.70	20.04
23							14.52	14.57		13.92
24							168.63	168.49		168.12
misc	60.22[c]	60.26[c]			51.26[b]	51.26[b]	60.23[c]	60.12[c]	51.35[b]	60.31[c]
	14.28	14.27					14.16	14.19		14.32

[a] Assignments of signals marked by asterisks were established by selective decoupling. [b] OMe. [c] OEt.

ference in relative abundance, given as 58% in peak 5a and 20% in peak 5b, to axial (in peak 5a) vs. equatorial (in peak 5b) attachment of the C_4H_9 side chain to C-14 of the tricyclic nucleus. However, from the bar graph mass spectrum of peak 5b reproduced in a later publication,[31] a spectrum essentially identical with that of **8b**, the relative abundance of the m/z 261 ion is less than 3%[32] as is the case for **8a–c**. On this basis, **8a–c** could not necessarily be excluded as components of the tricyclic terpane series.

To resolve the discrepancy relating to the ion at m/z 261, synthesis of authentic type **3** hydrocarbons containing a three- or four-carbon side chain at C-14 was attempted. We hoped to utilize the discovery of Fêtizon and coworkers[27] that catalytic hydrogenation of methyl *ent*-isocopalate (**6b**) in acetic acid solution produces some **3f**, although **3f** itself proved to be an unsuitable starting material.[18] Hydrogenation of **6c** with PtO_2–acetic acid gave a mixture of **3g** and **8d** containing a disappointingly small percentage of **3g** (ca. 15% as estimated from the slightly different OMe signals in the ^1H NMR spectrum), but the amount of **3g** could not be increased and other solvent–catalyst combinations were ineffective. Consequently the mixture was carried through the reactions previously used for the syntheses of **8a** and **8b**.

(31) Payzant, J. D.; Montgomery, D. S.; Strausz, O. P. *Tetrahedron Lett.* **1983**, *24*, 651.

(32) On the assumption that the C-13 methyl of peak **5a** was equatorial and α as in **4**, formula **3e** was suggested[12] for peak 5b, a proposal seemingly supoprted by a comparison of the ring methyl resonances of peak 5b (singlets at δ 0.76, 0.80, 0.80, and 0.84, doublet at δ 0.83) with shifts estimated from models.[12] The ring methyl shifts in the NMR spectra of **8a–c** are, however, not greatly different; for **8b** singlets are found at δ 0.80, 0.81, 0.83, and 0.84, the doublet at δ 0.87 For obvious reasons a ^{13}C NMR spectrum of peak 5b was not available for comparison with the values listed in Table II. However, see footnote 33.

GC and CGC–MS analyses of the C_{22} product from the **3g–8d** mixture revealed the presence of four $C_{22}H_{40}$ hydrocarbons in the ratio 1:4:17:77, with the retention time increasing in this order. The retention time of the major product was identical with that of **8a**, and we assume, from prior work on the hydrogenation of **6b**,[27] that the substance constituting 17% of the mixture was **3h**. By exclusion the two minor products must be the 13βH,14βH-isomer **4a** and the 13αH,14βH-isomer **20a**. Mass spectra (70 eV) of the four components were indistinguishable and essentially identical with that of pure **8a** (Table I). The peaks at m/z 261 were insignificant (<1%).[33]

GC and CGC–MS analyses of the C_{23} product from the **3g–8d** mixture also showed the presence of four components in ratio less than 0.5:approximately 1:13:85, with the retention time increasing in this order. The retention time of the major product was identical with that of **8b**; the substance constituting approximately 13% of the mixture is presumed to be **3e** and the two minor products, **4b** and **20b**. Again, mass spectra (70 eV) of the four components were indistinguishable and essentially identical with that of pure **8b**, the peaks at m/z 261 being insignificant.

Our results indicate that mass spectral data alone are not sufficient to distinguish tricyclic isocopalane isomers of type **3** from isomers of type **4**, **8**, or **20** and that if an abundant peak of m/z 261 is indeed associated with the tricyclic terpanes in sediments and crude oils, they cannot have the carbon skeleton attributed to them.[35]

Experimental Section

Melting points are uncorrected and carried out on a Meltemp or Hacker melting point apparatus. IR spectra were recorded on neat samples for liquids and gums and as KBr pellets for solids on a Perkin-Elmer Model 257 spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ at 270 MHz and ^{13}C NMR spectra at 67.89 MHz on a Bruker HX-270 spectrometer with Me_4Si as internal standard. Low-resolution mass spectra were determined on a Finnigan 4510 GC/MS instrument at 70 eV, high-resolution mass spectra on an AEI MS-902 instrument. HPLC separations were carried out on a Waters Prep LC/system 500 liquid chromatograph by using two Prepak-500/silica cartridges (5.7 × 30 cm). Flow rate and relative response were varied from experiment to experiment. Precoated silica gel sheets (60F-254, 0.2-mm thick, EM reagent) were used for analytical TLC. Preparative TLC was carried out on glass plates coated with silica gel (60PF-254+366, EM reagent) with a layer thickness of 1.5 mm. Silica gel (70–230 mesh, particle size 0.063–0.2 mm, EM reagent) was used for column chromatography. All solvents and reagents were distilled and dried according to literature procedures. GC analyses at Florida State University were carried out either on an HP 5880A instrument equipped with FID detector and 12-m OV1D1 glass capillary column using hydrogen as carrier gas with an oven temperature of 150–300 °C programmed at 5 °C/min (column 1) or on a Varian Model 2700 equipped with FID detector and 50-m OV-1 glass capillary column using nitrogen as carrier gas with oven and temperature of 100–250 °C programmed at 6 °C/min (column 2).

(*E*)- and (*Z*)-15-*n*-Propyl-8(17),13-labdadiene (9d). A solution of 0.5 g of **9a**[10] in 25 mL of MeOH was reduced with 0.1 g of $NaBH_4$ at room temperature. After 1 h the mixture was diluted with H_2O, acidified, diluted with water, and extracted with ether. Evaporation of the washed and dried ether extract furnished 0.45 g (90%) of crude alcohol mixture **9b**, which was further purified by chromatography over silica gel: IR 3350, 890 cm^{-1}; ^{1}H NMR δ 5.08 (br, superimposed triplets, H-14 of *E* and *Z* isomers), 4.84, 4.56 and 4.81, 4.52 (br, H-17a,b of *E* and *Z* isomers), 3.79 (m, H-22), 1.67m and 1.58 (br, H-16 of *E* and *Z* isomers), 1.18 (m, two d, H-23), 0.87, 0.77, and 0.76 (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{40}O$ 332.3077, found 332.3075.

A mixture of 1.2 g of **9b**, 5 mL of pyridine, 0.80 g of *p*-toluenesulfonyl chloride and 0.05 g of DMAP was left overnight at room temperature, quenched with cold dilute HCl, and extracted with ether. Evaporation of the washed and dried ether extract gave 1.2 g (68%) of tosylate mixture **9c**, which was dissolved in 15 mL of dry tetrahydrofuran and reduced with excess $LiAlH_4$ by refluxing for 1 h. Excess reagent was destroyed by addition of moist ether, and the emulsion was cleared by adjusting the pH to 2 with dilute HCl. Ether extraction followed by the usual workup, chromatography over silica gel, and elution with hexane furnished 0.6 g (79%) of *E,Z* mixture **9d**: IR 3070, 1640, 895 cm^{-1}; ^{1}H NMR δ 5.07 (two superimposed triplets, J = 7 Hz, H-14 or *E* and *Z* isomers), 4.84, 4.56 and 4.81, 4.52 (br, H-17a,b), 1.67 and 1.58 (br, H-16), 0.87, 0.80, and 0.67 (br, H-18, H-19, and H-20); M_r calcd for $C_{23}H_{40}$ 316.3128, found 316.3126.

Attempted Cyclizations of 9d. (**a**) To a solution of 0.1 g of **9d** in 20 mL of dry benzene was added dropwise 0.05 mL of anhydrous $SnCl_4$ with stirring. After 2 h at room temperature, addition of aqueous $NaHCO_3$ and extraction with ether followed by the usual workup and preparative TLC of the crude product gave 0.06 g of **10a,b**; IR 2920, 1460, 1380, which exhibited the requisite number of methyl signals in the δ 0.78–1.00 region, but no signals indicating the presence of vinyl methyls or vinylic protons; M_r calcd for $C_{23}H_{40}$ 316.3128, found 316.3120. Other significant peaks were at m/z (relative intensity) 301 (39), 259 (39), 245 (9), 231 (10), 219 (6), 205 (15), 175 (16), 163 (25), 149 (32), 135 (29), 123 (29), 121 (36), 95 (58), and 55 (100). Reaction of **9d** with $SnCl_4$ or BF_3·OEt_2 in CH_2Cl_2 at −78 °C also produced **10a,b** as the only product.

(**b**) A mixture of 0.05 g of **9d** and 3 mL of 98% formic acid was stirred at room temperature for 24 h, neutralized with 25% aqueous NaOH, diluted with H_2O, and extracted with ether. Evaporation of the washed and dried extract, column chromatography over silica gel, and elution with hexane furnished 0.022 g of **11**: ^{1}H NMR δ 5.10 (br, H-14), 1.60 and 1.55 (br, H-16 of *E* and *Z* isomers), 0.94, 0.84, and 0.83 (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{40}$ 316.3128, found 316.3149.

(*E*)- and (*Z*)-15-Acetonyl-8α,17-epoxylabd-13-ene (12a). 8α,17-Epoxymanool, prepared by the literature procedure,[16] had NMR signals as follows: δ 5.85 (dd, J = 16, 10 Hz, H-14), 5.15 (dd, J = 16, 1.5 Hz, H-15a), 4.99 (dd, J = 10, 1.5 Hz, H-15b), 2.74 (m, H-17a), 2.47 (d, J = 4 Hz, H-17b), 1.22 (H-16), 0.89, 0.83, and 0.80 (H-18, H-19, and H-20). A mixture of 0.5 g of this substance and 1.2 g of freshly distilled ethyl acetoacetate was heated at 180 °C under argon for 3 h. Excess ester was removed by distillation in vacuo. Chromatography of the residue over silica gel and elution with hexane–ether (17:3) gave 0.35 g (67%) of **12a**: ^{1}H NMR δ 5.04 (two superimposed triplets, J = 7 Hz, H-14 of *E* and *Z* isomers), 2.73 and 2.44 (m, H-17a,b), 2.21 (methyl ketone), 1.63 and 1.57 (br, H-16 of *E* and *Z* isomers), 0.89, 0.83 and 0.79 (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{38}O_2$ 346.2870, found 346.2860. Other significant peaks were at (relative intensity) m/z 275 (9), 262 (9), 207 (9), 177 (19), 163 (7), 161 (8), 159 (6), 151 (5), 149 (12), 147 (13), 135 (14), 133 (22), 123 (36), 121 (25), 119 (23), 109 (39), 95 (100), 81 (70), 69 (72), and 55 (76).

(*E*)- and (*Z*)-15-*n*-Propyllabd-13-en-8α-ol (12d). Reduction of 0.3 g of **12a** with 0.1 g of $NaBH_4$ in the manner described for **9a** and preparative TLC of the crude product (hexane–ether, 1:1) furnished 0.25 g (83%) of **12b** as a gum: IR 3350, 1125, 1080 cm^{-1}; ^{1}H NMR δ 5.11 (br t, J = 7 Hz, H-14), 3.75 (m, H-22), 2.77 and 2.47 (m, H-17a,b), 1.67 and 1.59 (br, H-16 of *E* and *Z* isomers), 1.27–1.17 (doublets, H-23 of *E* and *Z* isomers), 0.89, 0.83, and 0.80 (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{46}O_2$, 348.3026, found 348.3044. Tosylation of 0.5 g of **12b** in 5 mL of pyridine with 0.3 g of *p*-toluenesulfonyl chloride and 0.05 g of DMAP in the manner described for **9b**, and purification of the crude product of chromatography over silica gel, and elution with hexane–ether (17:3) gave 0.5 g (69%) of **12c** as a gum, which was reduced with $LiAlH_4$ as described for **9c**. Reduction of 0.5 g of **12c** followed by chromatography of the crude product gave 0.3 g (90%) of **12d** as a liquid: IR 3350, 1130, 1090, 950 cm^{-1}; ^{1}H NMR δ 5.13 (two superimposed triplets, J = 7 Hz, H-14 of *E* and *Z* isomers), 1.71

(33) Although the ^{1}H NMR spectra of the C_{22} and C_{23} mixtures were essentially those of the major components **8a** and **8b**, respectively, each spectrum contained what appeared to be a new weak high-field methyl singlet at δ 0.76, which must be ascribed to **3h** in the case of the C_{22} mixture and to **3e** in the case of the case of the C_{23} mixture. As the NMR spectrum of peak 5b of Ekweozor and Strausz[12] exhibits a methyl singlet at δ 0.76, it is tempting to speculate that peak 5b indeed corresponds to **3e**.

and 1.61 (br, H-16 of two isomers), 1.13 (br, H-17), 0.90 (br t, J = 7 Hz, H-23), 0.88, 0.79, and 0.79 (H-18, H-19, and H-20). The MS did not exhibit the molecular ion; the peak of highest mass number was at m/z 316 ($M^+ - H_2O$); calcd for $C_{23}H_{40}$ 316.3128, found 316.3141. Other significant peaks were at m/z (relative intensity) 192 (51), 191 (30), 177 (64), 163 (8), 149 (18), 124 (100), 109 (33), 107 (29), 95 (54), 81 (60), and 69 (72).

Attempted Cyclizations of 12d. (a) Dropwise addition of 0.02 mL of anhydrous $SnCl_4$ to 0.05 g of **1d** in 10 mL of dry benzene with stirring for 1 h, decomposition with aqueous $NaHCO_3$, extraction with ether, and the usual workup followed by multiple preparative TLC (hexane–ether, 49:1) gave 0.03 g (60%) of a mixture, probably **13a,b**, whose NMR spectrum exhibited no signals characteristic of vinyl protons or vinyl methyls. The same mixture was obtained on exposure of **12d** to anhydrous $SnCl_4$ or BF_3·OEt_2 at −78 °C.

(b) Reaction of 0.05 g of **12d** with 4 mL of 98% formic acid for 3 h at room temperature with stirring and workup as described for **9d** followed by preparative TLC (hexane, multiple development) gave two bands. Band 1 (5 mg) was identified as a mixture of **6a** and **7a**: ^{1}H NMR δ 5.18 (m, H-12), 1.53 (br, H-16), and methyl singlets in the range 0.80–0.92; low-resolution mass spectrum, m/z (relative intensity) 316 (M^+, 35), 301 (22), 259 (85), 245 (10), 205 (15), 192 (70), 191 (94), 177 (60), 163 (72), 149 (38), 137 (58), 124 (72), 121 (70), 109 (100). Band 2, 0.022 g, was identified as a mixture as a mixture of (*E*)- and (*Z*)-15-*n*-propyl-7,13-labdadiene and (*E*)- and (*Z*)-15-*n*-propyl-8,13-labdadiene: ^{1}H NMR δ 5.37 (m, H-7), 5.11 (br q, J = 7 Hz, H-14), 1.70, 1.61, and 1.57 (br, vinyl Me of two isomers), methyl singlets in the range 0.83–0.94; M_r calcd for $C_{23}H_{40}$ 316.3128, found 316.3126; low-resolution mass spectrum, at m/z (relative intensity) 316 (5), 301 (4), 259 (9), 205 (31), 204 (34), 191 (29), 177 (17), 163 (33), 149 (45), 137 (29), 135 (44), 123 (44), 121 (51), 109 (82), 95 (73), 81 (59), 77 (15), 69 (100), 55 (95).

(*E*)- and (*Z*)-15-(2-Carbethoxymethyl)-labd-13-en-8α-ol (14a,b) and Its Cyclization. A mixture of 1 g of sclareol, 3.5 g of freshly distilled triethyl orthoacetate, 10 mL of xylene, and 0.014 g of propionic acid (more than 0.06 equiv of propionic acid decreases the yield) was heated at 145 °C (bath temperature) for 20 h under nitrogen. Removal of solvent at reduced pressure, chromatography of the residue over silica gel, and elution with hexane-ether (4:1) gave 0.5 g of **14** as a mixture of *E* and *Z* isomers. Separation of the isomers was achieved by HPLC (solvent system hexane–EtOAc, 88:12, recycle procedure). *E* isomer (**14a**): IR 3500, 1735, 1180, 945 cm^{-1}; ^{1}H NMR δ 5.00 (t, J = 7 Hz, H-14), 4911 (2p, q, J = 7 Hz, OCH_2CH_3e, 1.62 (br, H-16), 1.25 (t, J = 7 Hz, $-CO_2CH_2CH_3$), 1.11 (H-17), 0.86, 0.79, and 0.79 (H-18, H-19, and H-20). *Z* isomer (**14b**): IR 3500, 1735, 1170, 950 cm^{-1}; ^{1}H NMR δ 5.04 (t, J = 7 Hz, H-14), 4.11 (2 p, 9, J = 7 Hz, OCH_2CH_3e, 1.68 (br, H-16), 1.23 (t, J = 7 Hz, OCH_2CH_3), 1.25 (H-17), 0.87, 0.78, and 0.7, (H-18, H-19, and H-20); ^{13}C NMR spectra of **14a** and **14b** are lisited in Table III.

A solution of 0.3 g of **14a,b** and 90 μL of anhydrous $SnCl_4$ in 20 mL of anhydrous benzene was stirred in an argon atmosphere at room temperature for 1 h and worked up as described for the cyclization of **9d**. Purification by chromatography over silica gel and elution with hexane–ether (19:1) gave an ester fraction which was refluxed with 20 mL of alcoholic KOH for 2 h, diluted with water, extracted with ether, acidified, and again extracted with ether. After the usual workup the acid extract was purified by preparative TLC (hexane–ether, 17:3, multiple development) to give 0.04 g (12%) of **15**: mp 130–132 °C (lit.[17] mp 136 °C); ^{1}H NMR δ 1.55 (br, H-16), 0.94, 0.84, 0.83, and 0.81 (H-17, H-18, H-19, and H-20); mass spectrum, m/z (relative intensity) 332 (M^+), 317 (35), 259 (54), 191 (75), 179 (32), 163 (9), 149 (30), 137 (35), 133 (27), 123 (32), 121 (45), 109 (33), 95 (49), 91 (36), 85 (46), 83 (100), 79 (39), 69 (56), 55 (73). The major portion of the product, 0.15 g (49%), was a mixture of acids whose NMR spectrum exhibited no signals characteristic of vinyl protons or vinylic methyls.

8(17),13(*E*)-Labdadien-15-ol and 8(17),13(*Z*)-Labdadien-15-ol (17a,b). A solution of 20 g of manool in 100 mL of dry CH_2Cl_2 was added quickly with stirring to a suspension of 40 g of pyridinium chlorochromate in 200 mL of CH_2Cl_2. Stirring was continued overnight at room temperature. After complete disappearance of starting material (TLC) the organic layer was decanted, combined with the CH_2Cl_2 washings of the gummy precipitate, and washed with 10% aqueous NaOH, 10% HCl, H_2O, and brine. Removal of solvent furnished 17 g of gummy aldehydes **16a,b**, which were reduced without further purification as follows. A solution of 16 g of crude **16a,b** inn100 mL of anhydrous ether was added to a suspension of $LiAlH_4$ in ether with stirring and refluxed under nitrogen for 1 h. Decomposiiton of excess reagent with moist ether, acidification to pH 3, and extraction with ether followed by the usual workup gave 15 g of a crude alcohol mixture, which was chromatographed over silica gel. Elution with hexane–ether gave 12 g of **17a,b**, which was separated by HPLC using the solvent system hexane–EtOAc (89:11, flow rate 0.25 L/min) by using the peak shaving–recycling technique. This afforded 5.0 g of pure **17a** and 3.5 g of pure **17b**. ^{1}H NMR of **17a**: δ 5.34 (t, J = 7 Hz, H-14), 4.81 and 4.50 (br, H-17a,b), 4.10 (2p, d, J = 7 Hz, H-15), 1.63 (br, H-16), 0.86, 0.78, and 0.66 (H-18, H-19, and H-20). ^{1}H NMR of **17b**: δ 5.40 (t, J = 7 Hz, H-14), 4.8j and 4.54 (br, H-17a,b), 4.04 (2p, d, J = 7 Hz, H-15), 1.72 (br, H-16), 0.86, 0.78, and 0.66 (H-18, H-19, and H-20). ^{13}C NMR spectra are listed in Table III.

Wittig Reactions of 8(17),13(*E*)- and -(*Z*)-Labdadienal. Preparation of 18a–d. (a) A solution of 5 g of **17a** in 15 mL of DMF was added dropwise with stirring at 0 °C to a suspension of 10 g of pyridinium dichromate in the minimum amount of DMF. After 3 h the mixture was diluted with H_2O, dried, and evaporated in vacuo at low temperature. The resulting aldehyde **16a** (4 g, 82%) was used without further purification in the following reaction. A solution of 0.35 g of NaH in 25 mL of Me_2SO was stirred (argon atmosphere) at 60 °C until hydrogen evolution had ceased (ca. 45 min). After cooling to 10 °C, 3.2 g of trimethyl phosphonoacetate was added dropwise. Stirring was continued for 30 min at which time aldehyde **17a** (4 g) dissolved in the minimum amount of Me_2SO was added. After being stirred for 15 min, the mixture was quenched with ice-cold water and extracted with ether. The usual workup gave a gum, which was purified by column chromatography over silica gel and then by HPLC (solvent hexane–EtOAc, 98:2) to give 2.5 g (51%) of gummy **18a**: IR 3080, 1720, 1640, 1615, 1315, 1280, 1220, 1172, 1148, 1050, 990, 900 cm^{-1}; ^{1}H NMR δ 7.58 (dd, J = 15, 12 Hz, H-15), 5.96 (br d, J = 11 Hz, H-14), 5.78 (d, J = 15 Hz, H-21), 4.84 and 4.50 (br, H-17a,b), 3.75 (OMe), 1.89 (br, H-16), 0.87, 0.81, and 0.69 (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{36}O_2$ 344.2714, found (MS) 344.2679. Other significant peaks in the MS were at m/z (relative intensity, composition) 329 (40, $C_{22}H_{32}O_2$), 245 (20, $C_{18}H_{29}$), 137 (45, $C_{10}H_{17}$), and 125 (28, $C_7H_9O_2$). The ^{13}C NMR spectrum is listed in Table III.

(b) Oxidation of 3g of **17b** to **16b** followed by Wittig condensation as described in the previous paragraph and final purification by HPLC (hexane–EtOAc, 98.5:1.5) gave 1.5 g (42%) of **18b** as a thick liquid: IR 3080, 1720, 1635, 1270, 1152, 985, 890 cm^{-1}; ^{1}H NMR δ 7.51 (dd, J = 15, 12 Hz, H-15), 5.98 (br d, J = 12 Hz, H-14), 5.73 (d, J = 16 Hz, H-21), 4.92 and 4.59 (br, H-17a,b), 3.71 (OMe), 1.88 (br, H-16), 0.89, 0.87, and 0.6. (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{36}O_2$ 344.2714, found 344.2699; ^{13}C NMR spectrum is listed in Table III.

(c) Oxidation of 1.5 g of **17a** followed by condensation of the resulting aldehyde **18a** with 1.5 g of triethyl phosphono-2-butyrate in the presence of dimethyl sulfinyl carbanion generated from 0.13 g of NaH and 10 mL of Me_2SO yielded 0.50 g of gummy **18c** after a final purification by HPLC (hexane–EtOAc, 98.5:1.5, peak shaving–recycle technique); IR 3065, 1710, 1630, 1282, 1235, 1110, 1050, 900, 770 cm^{-1}; ^{1}H NMR δ 7.43 (d, J = 12 Hz, H-15), 6.09 (br d, J = 12 Hz, H-14), 4.8l and 4.53 (br, H-17a,b), 4.22 (2 p, 9, J = 7 Hz, OCH_2CH_3e, 2.41 (2 p, q, J = 7 Hz, H-22), 1.88 (br, H-16), 1.30 (t, J = 7 Hz, OCH_2CH_3), 1.03 (t, J = 7 Hz, H-23), 0.87, 0.80, and 0.68 (H-18, H-19, and H-20); M_r calcd for $C_{26}H_{42}O_2$ 386.3185, found 386.3184; ^{13}C NMR spectrum is listed in Table III.

(d) Oxidation of 1.0 g of **17b** followed by condensation of **16b** with triethyl 2-phosphonobutyrate and final purification by HPLC (hexane–EtOac, 98.5:1.5) gave 0.3 g of **18d** as a colorless liquid: IR 3080, 1710, 1640, 1240, 1120, 895, 730 cm^{-1}; ^{1}H NMR δ 7.36 (d, J = 12 Hz, H-15), 6.13 (br d, J = 12 Hz, H-14); 4.8. and 4.61 (br, H-17a,b), 4.19 (2 p, q, J = 7 Hz, OCH_2CH_3e, 2.40 (2 p, q, J = 7 Hz, H-22), 1.8. (br, H-17), 1.30 (t, J = 7 Hz, OCH_2CH_3), 1.03 (t, J = 7 Hz, H-23), 0.86. 0.80, and 0.6m (H-18, H-19, and H-20); M_r calcd for $C_{26}H_{42}O_2$ 386.3185, found 386.3213; ^{13}C NMR spectrum is listed in Table III.

Cyclizations of 18a–d. Preparation of 6c,d, 7d, and 19a,b. (a) To a solution of 4.0 g of **18a** in 30 mL of anhydrous benzene cooled to 10 °C was added dropwise with stirring (argon atmosphere) 8 mL of boron trifluoride etherate. Stirring was continued at room temperature for 72 h at which time the mixture was quenched with ice-cold water and diluted with ether. Evaporation of the washed and dried ether layer and purification of the crude product by column chromatograph (silica gel) and HPLC (hexane–EtOAc, 98.7:1.3, peak shaving–recycle technique) gave 2.0 g of **6c** as a low-melting solid: IR 1728, 1650, 1390, 1330, 1275, 1245, 1170, 1130, 1050, 1010, 800 cm^{-1}; ^1H NMR δ 6.83 (dd, J = 15, 9 Hz, H-15), 5.83 (d, J = 1k Hz, H-21), 5.48 (br, $W_{1/2}$ = 8 Hz, H-12), 3.72 (OMe), 2.53 (br d, j = 9 Hz, H-14), 1.49 (br, H-16), 0.90, 0.86, 0.84, and 0.51 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{23}H_{36}O_2$ 344.2713, found 344.2716. Other significant ions in the mass spectrum were at m/z (relative intensity, compositon) 329 (18, $C_{22}H_{33}O_2$), 192 (95, $C_{14}H_{24}$), 177 (45, $C_{13}H_{21}$), 153 (35, $C_9H_{12}O_2$), and 137 (20, $C_{10}H_{17}$). The ^{13}C NMR spectrum is listed in Table III.

Reaction of 0.5 g of 1,a with 1 mL of BF_3·OEt_2 in benzene at 70 °C for 6 h and purification by HPLc (hexane–EtOAc, 98.8:1.2, peak shaving–recycling technique) yielded 0.2 g (40%) of **7d** as a crystalline solid; mp 100–101 °C; IR 1720, 1640, 1310, 1270, 1170, 1010, 995, 870 cm^{-1}; ^1H NMR δ 7.31 (br d, J = 16 Hz, H-15), 5.7k (d, J = 16 Hz, H-21), 3.75 (OMe), 1.67 (br, H-16), 1.05 (H-17), 0.86, 0.83, and 0.81 (H-18, H-19, and H-20); M_r calcd for $C_{23}H_{36}O_2$ (344.2713, found 344.2714; ^{13}C NMR spectrum is listed in Table III.

(b) Cyclization of 0.5 g of **18b** with 1 mL of BF_3·OEt_2 at room temperature for 3 days and purification in the same manner afforded 0.25 g of **19a** as a semisolid: IR 1720, 1640, 1260, 1195, 1170, 1150, 1105, 1050, 1020, 1000, 880, 830, 732 cm^{-1}; ^1H NMR δ 6.86 (dd, J = 15, 8.5 Hz, H-15), 5.7k (br d, J = 15 Hz, H-21), 5.45 (br, H-12), 3.73 (OMe, 2.07 (br d, J = 9 Hz, H-14), 1.54 (br, H-16), 0.91, 0.88, 0.85, and 0.81 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{23}H_{36}O_2$ 344.2713, found 344.2701; ^{13}C NMR spectrum is listed in Table III.

(c) Cyclization of 0.3 g of **18c** with 0.6 mL of BF_3·OEt_2 at room temperature for 3 days and purification by HPLC (hexane–EtOAc, 98.5:1.5) resulted in 0.15 g of **6d** as a thick liquid: IR 1710, 1295, 1230, 1110, 1050 cm^{-1}; ^1H NMR δ 6.62 (d, J = 12 Hz, H-15), 5.51 (br, H-12), 4.19 (2 p, q, J = 7 Hz, OCH_2CH_3), 2.83 (br d, J = 11 Hz, H-14), 2.3m (2 p, q, J = 7 Hz, H-22), 1.47 (br, H-16), 1.29 (t, J = 7 Hz, OCH_2CH_3), 1.04 (t, J = 7 Hz, H-23), 0.90, 0.87, 0.86, and 0.80 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{2H4i}O_2$ 386.3182, found 386.3197. Other significant ions in the mass spectrum were at m/z (relative intensity, composition) 194 (100, $C_{12}H_{18}O_2$), 191 (30, $C_{14}H_{23}$), and 121 (62, C_9H_{13}). The ^{13}C NMR spectrum is listed in Table III.

(d) Cyclization of 0.2 g of **18d** with 0.4 mL of BF_3·OEt_2 for 2 days and workup as described for **6c** gave 0.075 g of **19b** (37%) as a semisolid. Purification by HPLC (hexane–EtOAc, 98:2) afforded crystalline material: mp 104–105 °C; IR 1712, 1630, 1295, 1240, 1110, 1045, 1022, 820 cm^{-1}; ^1H NMR δ 6.57 (d, J = 12 Hz, H-15), 5.41 (br, H-12), 4.20 (2 p, q, OCH_2CH_3), 2.36 (3 p, m, H-22 and H-14), 1.54 (br, H-16), 1.32 (t, J = 7 Hz, OCH_2CH_3), 1.03 (t, J = 7 Hz, H-23), 0.95, 0.89, 0.84, and 0.81 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{26}H_{42}O_2$ 386.3182, found 386.3193; ^{13}C NMR spectrum is listed in Table III.

15-(Carbomethoxymethyl)-*ent*-isocopalane (8d).[34] A solution of 0.5 g of **6c** in 20 mL of MeOH–EtOAc (4:1) was hydrogenated in Parr apparatus in the presence of PtO_2 for 1 h, filtered, and evaporated. Purification by chromatography over silica gel afforded 0.43 g of **8d** as a crystalline solid: mp 58–59 °C; IR 1738, 1325, 1290, 1250, 1205, 1160, 1140, 1115, 1050, 1010 cm^{-1}; ^1H NMR δ 3.67 (OMe), 2.25 (m, 2 p, H-21), 0.88 (d, J = 7 Hz, H-16), 0.85, 0.84, 0.81, and 0.80 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{23}H_{40}O_2$ 348.3028, found 348.3037; ^{13}C NMR spectrum is listed in Table III. Hydrolysis of 1.0 g of **8d** by refluxing with 15 mL of 10% ethanolic KOH for 2 h, dilution with H_2O, and acidification followed by the usual workup chromatography over silica gel and elution with hexane–ether (3:1) gave 0.85 g of 15-carboxymethyl-*ent*-isocopalane (**8e**) as a crystalline solid: mp 165–167 °C; IR 3500–3100, 1700, 1290, 950 cm^{-1}; ^1H NMR δ 0.89 (d, J = 7.5 Hz, H-16), 0.84, 0.83, 0.82, and 0.79 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{22}H_{38}O_2$ 334.2872, found 334.2869; ^{13}C NMR spectrum is listed in Table III.

Catalytic reduction of 0.015 g of **6d** in 10 mL of MeOH–EtOAc (4:1) with PtO_2 for 4 h and preparative TLC of the crude product (hexane–ether) gave a thick liquid whose NMR spectrum showed to be a 1:1 mixture of **6d** and 12,13-dihydro-**6d**. Signals of the latter substance appeared at δ 6.96 (br d, J = 10 Hz, H-15), 4.17 (q, J = 7 Hz, $-OCH_2CH_3$), 1.26 (t, J = 7 Hz, OCH_2CH_3), 1.04 (t, J = 7 Hz, H-23), 0.98 (d, J = 7 Hz, H-16), 0.90, 0.87, 0.86, and 0.80 (H-17, H-18, H-19, and H-20).

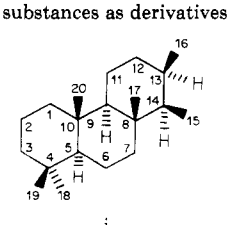
15-Ethyl-*ent*-isocopalane (8a). A solution of 0.4 g of **8d** in 5 mL of dry ether was added dropwise to 0.05 g of $LiAlH_4$ in 20 mL of ether. After 1 h at reflux, the mixture was worked up in the usual manner. Chromatography of the crude product over silica gel and elution with hexane–ether (4:1) yielded 0.33 g (89%) of **8f**: mp 124–125 °C; IR 3320, 1070, 1045 cm^{-1}; ^1H NMR δ 3.63 (2 p, br t, J = 7 Hz, H-22), 0.89 (d, J = 7 Hz, H-16), 0.84, 0.84, 0.82, and 0.80 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{22}H_{40}O$ 320.3079, found 320.3088; ^{13}C NMR spectrum is listed in Table III.

A mixture of 0.05 g of **8f**, 1 mL of triethylamine, 0.035 g of *p*-toluenesulfonyl chloride, and 0.015 g of DMAP was allowed to stand overnight, diluted with cold H_2O, stirred for 30 min, and extracted with ether. Evaporation of the washed and dried ether extract followed by rapid chromatography over silica gel gave 0.045 g of semisolid tosylate **8g**, which was pure by NMR criteria. Reduction of 0.04 g of **8g** with excess $LiAlH_4$, workup in the usual way, column chromatography over silica gel, and elution with hexane provided 0.022 g of **8a** as a white amorphous solid, mp 65–67 °C, which was pure by ^{13}C NMR (Table III) and GC criteria; ^1H NMR δ 0.88 (t, J = 7 Hz, H-22), 0.86 (d, J = 7 Hz, H-16), 0.84, 0.83, 0.82, and 0.80 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{22}H_{40}$ 304.3123, found 304.3126.

15-*n*-Propyl-*ent*-isocopalane (8b). To 0.04 g of tosylate **8g** in dry tetrahydrofuran was added at −20 °C a slight excess of methylmagnesium chloride followed by 3 drops of a THF solution of Li_2CuCl_4 prepared by mixing 0.2 mol of anhydrous LiCl and 0.1 mol of anhydrous $CuCl_2$ in 1000 mL of THF. The mixture was stirred at −20 °C for 2 h and at room temperature, diluted with H_2O, acidified witth dilute HCl, and extracted with ether. The usual workup and preparative TLC (hexane) yielded 0.02 g (77%) of **8b** as a low melting solid pure by GC and ^{13}C NMR criteria (see Table III); ^1H NMR δ 0.89 (t, J = 7 Hz, H-23), 0.87 (d, J = 7 Hz, H-16), 0.83, 0.83, 0.82, and 0.80 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{23}H_{42}$ 318.3286, found 318.3285. A more polar fraction, 5 mg (25%) of **8h**, was eluted as a gummy solid: IR 1450, 1390, 1050, 925, 730 cm^{-1}; ^1H NMR δ 3.53 (2 p, t, J = 7.5 Hz, H-22), 0.89 (d, J = 7 Hz, H-16), 0.83, 0.83, 0.82, and 0.80 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{22}H_{39}Cl$ 338.273, and 340.2700, found 338.2705 and 340.2698.

C_{23} hydrocarbon **8b** was also prepared from ketone **8i**, whose synthesis is described in the next section, as follows: A solution of 0.035 g of **8i** in 10 mL of MeOH was reduced by stirring with 0.025 g of $NaBH_4$ at room temperature for 1 h, after which time reduction was complete. Dilution with water, acidification to pH 3, extraction with ether followed by the usual workup, and purification by preparative TLC (hexane–ether, 1:1) furnished 0.025 g (71%) of diasteromeric alcohol mixture **8j**: IR 3320, 1130, 1050, 1005, 970 cm^{-1}; ^1H NMR δ 3.77 (m, H-23 of both diasteromers), 1.19 (br d, J = 7 Hz, H-24), 0.8, and 0.87 (d, J = 7 Hz, H-16 of both diasteromers), 0.86, 0.84, 0.82, and 0.80 (br, H-17, H-18, H-19,

(34) We name these substances as derivatives of *ent*-isocopalane (i).



i

(35) **Note Added in Proof**: After acceptance of this manuscript we were informed by Dr. P. Sundararaman, Chevron Oil Field Research, Richmond, CA, that coinjection of our synthetic **3e** and the major tricyclic C_{23} terpene component of sediments and crude oils showed them to be identical.

and H-20). Tosylation of 0.02 g of **8j** in 0.5 mL of pyridine by stirring with 0.012 g of tosyl chloride and 0.01 g of DMAP at room temperature for 48 h (the solution became dense and dark red), dilution with water, acidification, extraction with ether, and chromatography of the washed and dried ether extract over silica gel gave a pale yellow semisolid which was immediately reduced with excess $LiAlH_4$ in dry ether by refluxing for 1 h. The usual workup followed by chromatography over silica gel gave in the hexane eluates, 6 mg (31%) of **8b**.

15-Isobutyl-*ent*-isocopalane (8c). To a solution of 0.3 g of **8e** in 10 mL of THF was added at −20 °C with stirring 1.4 mL of a 1.5 M solution of methyllithium in ether. After 30 min the temperature was allowed to rise to 0 °C and maintained there for 2 h. The mixture was decomposed with ice-cold H_2O and extracted with ether. The usual workup and purification by preparative TLC (hexane–ether, 3:2) furnished as the less polar product 0.04 g (14%) of **8i** as a pale yellow solid: mp 67–68 °C; IR 1705 cm^{-1}; ^1H NMR δ 2.13 ($-COCH_3$), 0.87 (d, J = 7 Hz, H-16), 0.84, 0.83, 0.81, and 0.79 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{23}H_{40}O$ 332.3077, found 332.3065. The more polar product was 0.15 g (48%) of **8k**: mp 95–96 °C; IR 3300, 1220, 1150, 1005, 975, 955, 925 cm^{-1}; ^1H NMR δ 1.22 (H-23 and H-24), 0.88 (d, J = 7 Hz, H-16), 0.86, 0.83, 0.82, and 0.81 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{24}H_{44}O$ 34,.3390, found 348.3370; ^{13}C NMR spectrum is listed in Table III.

Dehydration of 0.1 g of **8h** with 0.2 mL of $POCl_3$ in 2 mL of pyridine by stirring for 6 h at −5 °C, decomposition with crushed ice, extraction with ether, and purification by preparative TLC (hexane–ether, 19:1) after the usual workup gave 0.085 g (90%) of an olefin mixture whose ^1H NMR spectrum indicated that it contained approximately equal amounts of the Δ^{21} and the Δ^{22} isomer; M_r calcd for $C_{24}H_{42}$ 330.3287, found 330.3293. Hydrogenation of 0.075 g of this material (PtO_2, MeOH–EtOAc, 4.1) in a Parr hydrogenator at room temperature and purification of the product by preparative TLC gave 0.06k g (85%) of **8c** as a waxy solid: mp 58–59 °C; IR 2950, 1465, 1390, 1370, 1050, 1025, 980 cm^{-1}; ^1H NMR 0.88, 0.87, and 0.86 (all d, J = 7.5 Hz, H-16, H-23, and H-24), 0.83, 0.83, 0.81, and 0.79 (H-17, H-18, H-19, and H-20); M_r calcd for $C_{24}H_{44}$ 332.3443, found 332.3423.

Preparation of the C_{22} and C_{23} Hydrocarbon Mixtures. A solution of 0.2 g of **6c** in 20 mL of glacial acetic acid was reduced in a Parr hydrogenator using PtO_2 as catalyst. After 6 h the product was worked up as described earlier for the synthesis of **8d** from **6c**. The ^1H NMR spelctrum of the gummy material (0.12 g) exhibited two $-CO_2Me$ signals at δ 3.67 (**8d**) and 3.64 (**3g**) in ca. 10:1 ratio but was otherwise identical with that of pure **8d**. $LiAlH_4$ reduction of the mixture and purification as described for pure **8d** yielded 0.10 g of a mixture containing **8f** and its stereoisomers, which was converted to a tosylate mixture, purified in the same manner as pure **8g** in 0.085-g yield. A 0.025-g portion of this material on reduction with excess $LiAlH_4$ followed by chromatography gave 0.01 g of the mixture of C_{22} hydrocarbons. GLC analysis on column 2 indicated the presence of four components, **8a** (R_f 27.58 min, 78%), **3h** (R_f 26.64 min, 17%), **4a** and **20a** (R_f 25.95 and 25.54 min, 4% and 1%). CGCMS analysis at the Chevron Oil Research Laboratory on a 7070H VG micromass mass spectrometer at 70 eV using a 60-m DB1 capillary column, temperature programmed at 150–300 °C at 2 °C/min, indicated the presence of four isomeric components with retention times of 52:57 (**8a**), 51:09 (**3h**), and 49:27 and 48:27 min, (**4a** and **20a**), respectively, whose mass spectra were indistinguishable and essentially identical with that given for **8a** in Table I.

Coupling of 0.02 g of the tosylate mixture with CH_3MgCl in the presence of Li_2CuCl_4 as described for pure tosylate **8g** and chromatography of the crude product gave 0.012 g of the mixture of C_{23} hydrocarbons. GLC analysis on column 2 indicated the presence of mainly two components, **8b** (R_f 32.96 min, 85%) and **3e** (R_f 32.04 min, 13%); the two minor constituents were represented by very weak peaks only. CGCMS analysis at the Chevron Oil Research Laboratory at 70 eV using a 60-m DB1 capillary column, a Finnigan mass spectrometer, and the INCOS data handling system revealed the presence of four isomeric components with retention times of 63:30 (**8b**), 61:57 (**3e**), and 60:00 and 58:24 min (**4b** and **20b**). Isomer 3 represented about 1.5% of the total mixture, isomer 4 less than 0.5%. The mass spectra of all four components were indistinguishable and essentially identical with that of pure **8b**.

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Registry No. **3g**, 87953-79-5; **3h**, 87953-80-8; **4b**, 87953-78-4; **6a**, 87953-40-0; **6b**, 59909-34-1; **6c**, 87953-41-1; **6d**, 87953-42-2; **3d** (12,13-dihydro derivatives), 87953-77-3; **7a**, 87953-43-3; **7b**, 88034-05-3; **7d**, 87953-44-4; **8a**, 87953-45-5; **8b**, 87953-46-6; **8c**, 87953-47-7; **8d**, 87953-48-8; **8e**, 87953-49-9; **8f**, 87953-50-2; **8g**, 87953-51-3; **8h**, 87953-52-4; **8i**, 87953-53-5; **8j** (*R* alcohol), 87953-54-6; **8j** (*S* alcohol), 87953-81-9; **8k**, 87953-55-7; **9a**, 88034-06-4; **9b**, 87953-56-8; **9c**, 87953-57-9; (*E*)-**9d**, 87969-50-4; (*Z*)-**9d**, 87953-82-0; **10a**, 87953-58-0; **10b**, 87953-59-1; (*E*)-**11**, 87953-60-4; (*E*)-**12a**, 87953-61-5; (*Z*)-**12a**, 88034-07-5; **12b**, 87953-62-6; **12c**, 87953-63-7; (*E*)-**12d**, 87953-64-8; (*Z*)-**12d**, 87953-65-9; **13a** (α-C_5H_{11}), 87953-66-0; **13a** (β-C_5H_{11}), 88034-11-1; **13b**, 87953-67-1; **14a**, 57672-83-0; **14b**, 57672-84-1; **15**, 88034-08-6; **16a**, 17633-79-3; **16b**, 38237-44-4; **17a**, 10395-43-4; **17b**, 10395-38-7; **18a**, 87953-68-2; **18b**, 88034-09-7; **18c**, 87953-69-3; **18d**, 88034-10-0; **19a**, 87953-70-6; **19b**, 87953-71-7; **20a**, 87953-72-8; **20b**, 87953-73-9; (*E*)-7,13-labdadiene, 87953-74-0; (*Z*)-7,13-labdadiene, 87953-75-1; (*Z*)-8,13-labdadiene, 87953-76-2; sclareol, 515-03-7; manool, 596-85-0; trimethyl phosphonoacetate, 5927-18-4; triethyl phosphono-2-butyrate, 17145-91-4.

Stereochemistry of Fluorination and Halofluorination of 1-Phenyl-4-*tert*-butylcyclohexene

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Acid-catalyzed liquid-phase fluorine addition with xenon difluoride to 1-phenyl-4-*tert*-butylcyclohexene (1) resulted in equal amounts of cis and trans adducts, while introduction of a methoxy group into the phenyl ring had no effect on the stereochemistry of addition. Bromofluorination and chlorofluorination of 1 with *N*-bromosuccinimide or *N*-chlorosuccinimide in the presence of a mixture of hydrogen fluoride–pyridine followed Markovnikov-type regioselectivity and proceeded stereospecifically anti, thus forming two pairs of vicinal halofluorides.

It is known that the stereochemistry of halogen addition to alkenes depends on the reagent, the structure of the alkene, and the reaction conditions.[1] Stereochemical information on the addition pathway is important for further

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