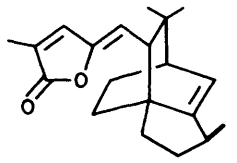
Enantioselective Synthesis of the Tricyclo[5.2.2.0^{1,5}]undecane Skeleton using Aprotic Michael-Additions; Formal Total Synthesis of (+)-Isoeremolactone

Dietrich Spitzner* and Gisela Sawitzki
Institut für Chemie, University of Hohenheim, D-7000 Stuttgart 70, Germany

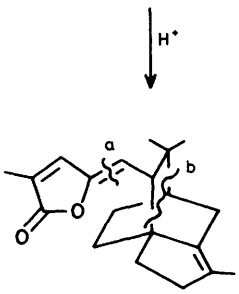
The (formal) total synthesis of the diterpene (+)-isoeremolactone (**2**) is described starting from the tricyclic ester (**15**), which was formed by an aprotic Michael-addition (AMA) sequence. The structure of the ester (**15**) was confirmed by *X*-ray analysis. The key compound (**4**) for the synthesis of (**2**) was made from (**15**) in 8 steps (25% overall yield).

The shift of the double bond in the unusual diterpene (+)-eremolactone (**1**) from *Eremophila* spp.[1] occurs very readily yielding (+)-isoeremolactone (**2**).

Retrosynthetic disconnection of (**2**) (Scheme 1) leads to the



(**1**)



(**2**)

building blocks (**3**) (five C atoms) and (**4**) (15 C atoms). The latter being formally a sesquiterpene with a tricyclo-[5.2.2.0^{1,5}]undecane framework, was made[2a] from (+)-zizanoic acid (**24**); thus its absolute stereochemistry and hence that of (**1**) and (**2**) as well, was defined. There are no sesquiterpenes yet known possessing a tricyclo[5.2.2.0^{1,5}]undecane skeleton in spite of its thermodynamic stability ('stabilomer').[3] On the basis of this relationship between (**24**) and both (**1**) and (**2**) further disconnection of (**4**) leads to (**6**) and (−)-(**7**)[4]†, and we considered reconnecting these by an aprotic Michael-addition (AMA) sequence.[5]

However, terminally disubstituted Michael-acceptors [*e.g.* (**6**)] fail to react with the dienolate (**11**), which was generated under kinetic control from (**7**). The acrylates (**8**)[6] and the crotonates (**9**) do give 1:1 adducts, (**12**) and (**13**), in high yield (90%) but subsequent introduction of the required 8-methyl groups proved to be rather lengthy and not rewarding.[7] We solved this problem by using ethyl cyclopropylideneacetate (**10**) as an equivalent (spirocyclopropanes are easily hydrogenated[9] to *geminal* dimethyls) of senecioates in the AMA (Scheme 2).

The adduct (**15**) was formed in high yield as a single product

† We thank Dr. U. Eder, Schering AG, Berlin, for a generous sample of (+)-(**7**).

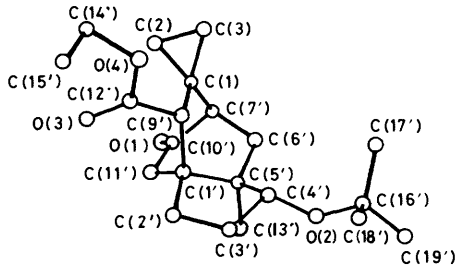
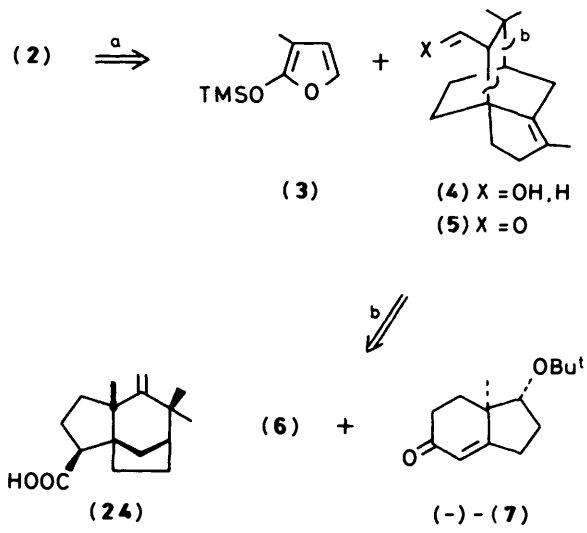


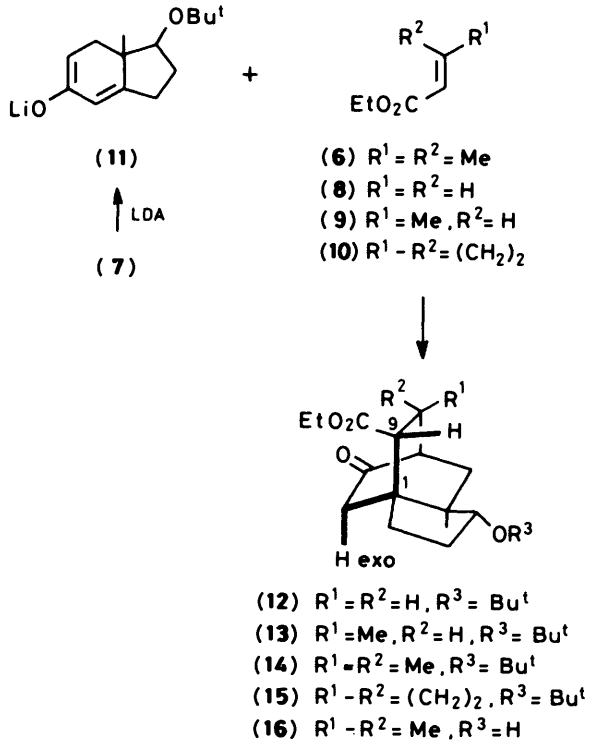
Figure. Molecular structure of compound (**15**)



Scheme 1. Retrosynthetic disconnection of (**2**)

having the ester group *syn* to the carbonyl-bearing bridge, as indicated by a long-range coupling (^4J 2.1 Hz) between 9'-H and 11'-H_{exo} (W-shaped pathway), and a single crystal *X*-ray analysis of (**15**) (Figure) confirmed the interpretation of the n.m.r. data. This stereochemistry remains unchanged during the next steps (Scheme 3).

Compound (**15**) possesses the required 15 carbon atoms already, although the 5'-methyl group has to be shifted to C-4', and C-10' de-oxygenated to a methylene group. Although we envisaged for the latter step thioketalization of (**14**) followed by Raney-nickel desulphurization, attempted thioketalization gave only the keto alcohol (**16**), and (**15**) itself rearranged under Lewis acid catalysis to a multitude of compounds, among them (**25**). We by-passed this difficulty by (i) reducing the ketone (**15**) with sodium borohydride to a 1:1 mixture of epimeric alcohols (**17**), (ii) esterifying this mixture with *p*-tolyl thiochloro-



Scheme 2. Aprotic double Michael–addition of α,β-unsaturated esters with the dienolate (**11**)

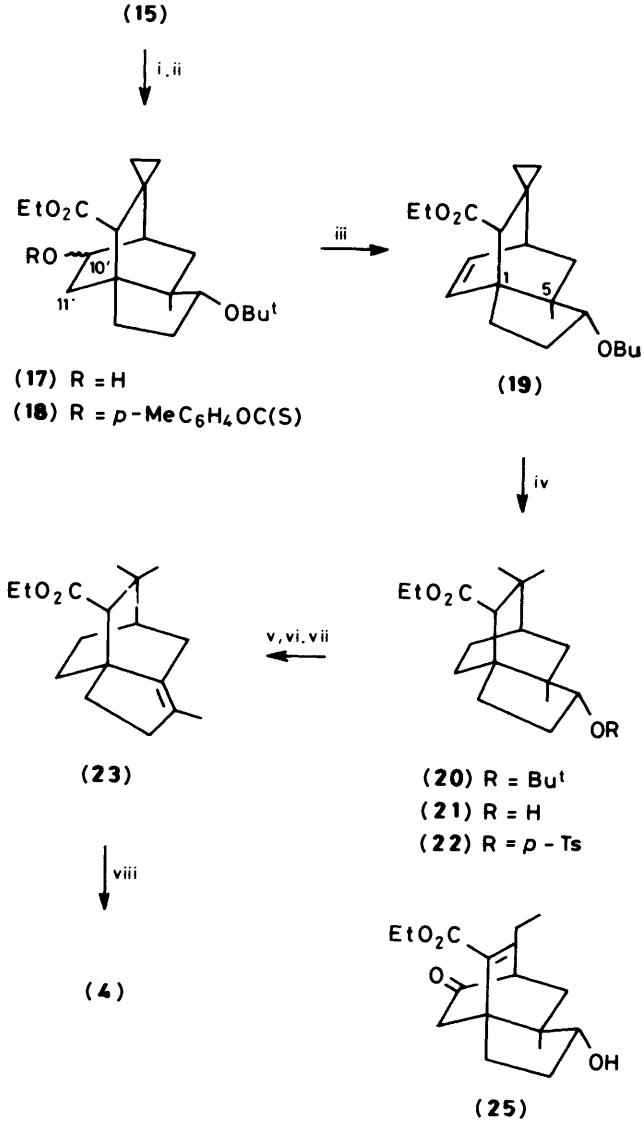
formate[10] in pyridine in the presence of DMAP[11] to give (**18**), (iii) pyrolysing the resulting *O*-thiocarbonates to the olefin (**19**), and finally hydrogenating the latter over PtO_2 to give the de-oxygenation product (**20**) in good overall yield [72% from (**15**)]. There was some danger of unwanted 1,2-alkyl migrations to form isomeric skeletons during the pyrolysis, but phase-sensitive 2D-NOESY measurements (*e.g.* 9′-H enhances both 4′-H, and 6′-H, but none of the olefinic protons) revealed an unchanged tricyclo[5.2.2.0^{1,5}]undecane system. Cleavage of the t-butyl ether, and esterification of the resulting secondary alcohol (**21**) with toluene-*p*-sulphonyl chloride in pyridine–DMAP gave the crystalline *p*-tosylate (**22**) which was solvolysed in buffered water–acetone at 100 °C to yield the ester olefin (**23**). N.m.r. data revealed the shift of the formerly angular 5-methyl group to an olefinic carbon (C-4), and the unchanged orientation of the ester group at C-9, which was essential for the final steps toward (**2**). However, prolonged exposure to base and/or heat caused some epimerization at C-9. The 1,2-methyl shift in (**22**) (from C-5 to C-4 and concomitant loss of 4-H to form an olefinic bond between C-4 and C-5) is probably a non-concerted process, due to the uncomfortable *syn* positioning of the leaving (*p*-TsO) and migrating (Me) group in (**22**). Reduction of the ester in (**23**) with lithium aluminium hydride gave the sesquiterpenoid alcohol (**4**) which was identical with a sample prepared[2a] from natural (**24**).* Oxidation gave the aldehyde (**5**). This sensitive aldehyde [it epimerizes more easily than the ester (**23**)!] has already been condensed with 2-trimethylsiloxy-3-methylfuran (**3**)[12] by both R. Ramage and H. Takei[2] to yield compound (**2**), identical with a sample from natural sources.†

* Dr. E.-J. Bruncke, DRAGOCO, Holzminden, Germany, is thanked for natural zizanoic acid (**24**).

† Compound (**1**), kindly provided by Dr. E. L. Ghisalberti, University of Western Australia, Nedlands, Australia, was rearranged to give compound (**2**).

Experimental

M.p.s were determined with a Büchi SMP-20 apparatus and are uncorrected. Kieselgel 60 (silica gel, 70—230 mesh ASTM) was used for column chromatography, Kieselgel 60 GF_{254} for preparative LC, and Kieselgel 60 PF_{254} (silica gel plates No. 5562, 0.2 mm layer) for t.l.c. These materials were purchased from Merck, Darmstadt, Germany. ^1H N.m.r. (250 MHz) and ^{13}C n.m.r. (62.88 MHz) spectra were measured for solutions in $CDCl_3$ ($SiMe_4$ as internal standard) on a Bruker WM 250 instrument. I.r. spectra were recorded on a Zeiss IMR 25 and mass spectra were taken on a Varian MAT 311 A (low and high resolution). Chiroptical measurements were performed with a Perkin-Elmer 241 polarimeter. Microanalyses were carried out by the microanalytical laboratory of the Institut für Organische Chemie und Biochemie, University of Stuttgart, Germany.



Scheme 3. Reagents, conditions, and yields for the sequence (**15**) ⟶ (**4**): i, $NaBH_4$–EtOH, (**17**), 99%; ii, *p*-tolyl thiochloroformate–pyridine–DMAP (**18**); iii, 240 °C/12 Torr, (**19**), 73% from (**17**); iv, H_2–PtO_2–AcOH at 2 atm and room temp., (**20**), 91%; v, *p*-TsOH–benzene–reflux, (**21**), 96%; vi, *p*-TsCl-pyridine–DMAP, (**22**), 79%; vii, water–acetone (1:1) at 100 °C for 2 d, (**23**), 61%; vii, $LiAlH_4$–ether, (**4**), 85%

Table 1. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
O(1)	4 680(4)	972(3)	10 301(1)
C(1)	4 535(4)	−1 312(4)	9 333(1)
C(1′)	3 061(4)	1 037(3)	9 068(1)
O(2)	6 045(3)	2 746(2)	8 168(1)
C(2)	5 360(5)	−2 790(4)	9 250(1)
C(2′)	1 712(4)	1 787(4)	8 727(1)
O(3)	185(3)	−1 175(3)	9 224(1)
C(3)	4 040(4)	−2 596(4)	9 653(1)
C(3′)	2 798(4)	2 264(4)	8 276(1)
O(4)	1 562(3)	−2 663(3)	8 690(1)
C(4′)	4 736(4)	1 801(3)	8 370(1)
C(5′)	4 875(4)	1 752(3)	8 925(1)
C(6′)	6 419(4)	852(4)	9 141(1)
C(7′)	5 690(4)	−103(4)	9 554(1)
C(9′)	3 219(4)	−641(3)	8 965(1)
C(10′)	4 435(5)	748(4)	9 877(1)
C(11′)	2 755(4)	1 228(4)	9 611(1)
C(12′)	1 459(4)	−1 456(4)	8 982(1)
C(13′)	5 006(5)	3 353(4)	9 115(1)
C(14′)	45(5)	−3 721(4)	8 712(1)
C(15′)	−1 391(5)	−3 179(4)	8 388(1)
C(16′)	6 847(4)	2 318(3)	7 714(1)
C(17′)	7 914(4)	898(4)	7 767(1)
C(18′)	5 458(5)	2 148(4)	7 321(1)
C(19′)	8 108(5)	3 574(4)	7 602(1)

Table 2. Bond lengths (Å) with estimated standard deviations in parentheses

O(1)–C(10′)	1.215(4)	C(1)–C(2)	1.506(5)
C(1)–C(3)	1.520(5)	C(1)–C(7′)	1.537(4)
C(1)–C(9′)	1.556(4)	C(1′)–C(2′)	1.555(4)
C(1′)–C(5′)	1.571(4)	C(1′)–C(9′)	1.565(4)
C(1′)–C(11′)	1.542(4)	O(2)–C(4′)	1.429(4)
O(2)–C(16′)	1.457(4)	C(2)–C(3)	1.513(5)
C(2′)–C(3′)	1.564(4)	O(3)–C(12′)	1.203(4)
C(3′)–C(4′)	1.548(5)	O(4)–C(12′)	1.374(4)
O(4)–C(14′)	1.502(4)	C(4′)–C(5′)	1.552(4)
C(5′)–C(6′)	1.549(4)	C(5′)–C(13′)	1.560(4)
C(6′)–C(7′)	1.546(4)	C(7′)–C(10′)	1.523(5)
C(9′)–C(12′)	1.526(4)	C(10′)–C(11′)	1.535(5)
C(14′)–C(15′)	1.497(5)	C(16′)–C(17′)	1.535(5)
C(16′)–C(18′)	1.526(4)	C(16′)–C(19′)	1.525(5)

Ethyl (1S,4S,5S,7S,8R,9S)-5,8-*Dimethyl*-10-*oxo*-4-*t*-*butoxytricyclo*[5.2.2.0^{1,5}]*undecane*-9-*carboxylate* (**13**).—A solution of (+)-(**7**) (11.10 g, 50 mmol) in dry THF (100 ml) was added with a syringe to a solution of LDA (54 mmol) in THF (200 ml) under an argon atmosphere; the ester (**9**) (12.0 g, 105 mmol, neat) was then added dropwise with a syringe. Cooling was discontinued and the reaction mixture allowed to warm to room temperature; it was then acidified with crushed ice (300 ml) conc. HCl (25 ml), and extracted with dichloromethane (3 × 200 ml). The organic layer was filtered through silica gel (200 g), concentrated, and the oily residue distilled in the kugelrohr (170 °C/0.05 Torr) to give the title compound (**13**) (14.7 g, 87.5%), which crystallized with time, m.p. 93—94 °C; the crude product contained *ca.* 5% of an isomeric ester; $[\alpha]_D^{23}$ +130° (*c* 0.6 in ethanol); $\nu_{max.}$(film) 1 725 and 1 175 cm^{-1}; *m*/*z* 336 (*M*$^+$, 15%), 280 (25), 236 (70), 166 (50), 147 (40), 122 (50), and 57 (100); δ_H 4.19 (2 H, q, *J* 7 Hz, ester), 4.02 (1 H, dd, *J* 19 and 5 Hz, 4-H), 3.03 (1 H, d, *J* 19 Hz, 11-H$_{exo}$), 2.4—1.4 (10 H, m), 1.30 (3 H, t, *J* 7 Hz, ester), 1.17 (9 H, s, Bu^t), 1.08 (3 H, d, *J* 6.4, 8-Me), and 0.86 (3 H, s, 5-Me); δ_C 216.2(s), 174.6(s), 78.3(d), 72.6(s), 60.5(t), 51.0(d), 50.1(d), 48.9(s), 45.9(s), 42.0(q), 32.7(t), 32.1(t), 28.9(s), 28.7 (3 × q, Bu^t), 17.9(d), 17.1(q), and 14.4(q).

Ethyl (1′R,4′R,5′R,7′R,9′R)-5′-*Methyl*-10′-*oxo*-4′-*t*-*butoxyspiro*(*cyclopropane*-1,8′-*tricyclo*[5.2.2.0$^{1',5'}$]*undecane*-9′-*carboxylate* (**15**).—A solution of the ester (**10**) (0.500 g, 3.96 mmol) in dry THF (5 ml) was added to a solution of the dienolate (**11**), prepared from compound (−)-(**7**) (0.700 g, 3.15 mmol) and LDA (4 mmol) in dry THF (50 ml) at −78 °C under an argon atmosphere. The reaction mixture was allowed to warm to 0 °C overnight, and then acidified with 1M HCl and extracted with methylene dichloride. The organic phase was dried, filtered through silica gel, concentrated, and the remaining oil distilled in a kugelrohr apparatus (150 °C/0.03 Torr) to give the title compound (**15**) (1.005 g, 91.7%), which crystallised with time, m.p. 85—86 °C; $[\alpha]_D^{20}$ − 103.3° (*c* 0.58 in hexane) (Found: C, 72.25; H, 9.3; *M*, 348.2298 $C_{21}H_{32}O_4$ requires C, 72.38; H, 9.26%; *M*, 348.2301); $\nu_{max.}$(CH_2Cl_2) 1 725 cm^{-1}; *m*/*z* 348 (*M*$^+$, 20%), 292 (50), 246 (60), and 57 (100); δ_H 4.16—4.04 (3 H, m, ester CH_2 and 4′-H), 3.41 (1 H, d, *J* 18.8 Hz, 11′-H$_{endo}$), 3.08 (1 H, d, *J* 2.1 Hz, 9′-H), 2.23 (1 H, dd, *J* 18.8 and 2.1 Hz, 11′-H$_{exo}$), 2.2—1.4 (7 H, m), 1.26 (3 H, t, *J* 7 Hz, ester Me), 1.21 (9 H, s), 0.89 (3 H, s, 5-Me), and 0.64—0.4 (4 H, m, cyclopropyl); δ_C: 215.8(s), 172.6(s), 78.2(d), 72.6(s), 60.2(t), 54.4(d), 49.1(s and d), 45.3(s), 43.0(t), 37.3(t), 32.6(t), 29.3(t), 28.7(q), 21.1(s), 17.7(q), 14.2(q), 12.0(t), and 10.2(t).

Crystal data. $C_{21}H_{32}O_4$, *M* = 348.5. Orthorhombic, space group $P2_12_12_1$ (No. 19), *a* = 7.561(3), *b* = 9.140(4), *c* = 27.895(14) Å, *V* = 1 927.8 Å^3, *Z* = 4, λ = 0.710 69 Å, *T* = 160 K, D_c = 1.20 g cm^{-3}, crystal dimensions *ca.* 0.3 × 0.35 × 0.5 mm, μ(Mo-K_α) = 0.86 cm^{-1}.

Data collection. SYNTEX P2$_1$ diffractometer, ω scan (2.0—29.3° min^{-1}), graphite-monochromated Mo-K_α-radiation. 2 558 Unique reflections measured ($2\theta < 55°$, $+hkl$) giving 2 109 with $I > 3\sigma(I)$.

Structure analysis and refinement. Direct methods followed by full matrix least-square refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions with unrefined isotropic temperature factors. The refinement converged to $R = 0.058$ and $R_w = 0.046$ [$w = 1/\sigma^2$ (*F*)]. All calculations were performed with the SHELXTL package of crystallographic programs.* A labelled drawing of the molecule is given in the Figure, the atomic co-ordinates, bond lengths, and bond angles of the non-hydrogen atoms are listed in Tables 1, 2, and 3.

Tables of the isotropic and anisotropic temperature factors and the hydrogen atom co-ordinates are available on request from the Cambridge Crystallographic Data Centre.†

Ethyl (1′R,4′R,5′R,7′S,9′R)-5′-*Methyl*-4′-*t*-*butoxyspiro*(*cyclopropane*-1,8′-*tricyclo*[5.2.2.0$^{1',5'}$]*undec*-10′-*ene*)-9′-*carboxylate* (**19**).—The ketone (**15**) (0.900 g, 2.6 mmol) was treated with $NaBH_4$ (0.150 g, 4 mmol) to give the alcohol (**17**) (0.90 g, 99.4%) as a mixture of epimers (kugelrohr, b.p. 150 °C/0.02 Torr), which were not separated. This mixture was dissolved in dry methylene dichloride (20 ml) and pyridine (3 ml) and treated with *p*-tolyl thiochloroformate (1.1 equiv.) in the presence of a catalytic amount of DMAP to yield the corresponding *O*-thiocarbonates (**18**). The pyrolysis of crude (**18**) was carried out in a kugelrohr oven at 240 °C and 12 Torr, and the distillate was purified by chromatography on silica gel using pentane–ether (9:1, v/v) as eluant to give the olefin (**19**)

* G. M. Sheldrick, SHELXTL, Revision 5.1 (Eclipse 32 K), December 1985, unpublished

† See Instructions for Authors (1988), *J. Chem. Soc., Perkin Trans. 1*, 1988, Issue 1.

Table 3. Bond angles (°) with estimated standard deviations in parentheses

C(2)–C(1)–C(3)	60.0(2)	C(2)–C(1)–C(7′)	118.1(3)
C(3)–C(1)–C(7′)	117.4(3)	C(2)–C(1)–C(9′)	121.1(3)
C(3)–C(1)–C(9′)	122.3(3)	C(7′)–C(1)–C(9′)	110.1(3)
C(2′)–C(1′)–C(5′)	103.5(2)	C(2′)–C(1′)–C(9′)	111.7(2)
C(5′)–C(1′)–C(9′)	107.1(2)	C(2′)–C(1′)–C(11′)	116.9(3)
C(5′)–C(1′)–C(11′)	109.5(2)	C(9′)–C(1′)–C(11′)	107.6(2)
C(4′)–O(2)–C(16′)	117.9(2)	C(1)–C(2)–C(3)	60.5(2)
C(1′)–C(2′)–C(3′)	105.7(2)	C(1)–C(3)–C(2)	59.5(2)
C(2′)–C(3′)–C(4′)	106.5(2)	C(12′)–O(4)–C(14′)	116.7(2)
O(2)–C(4′)–C(3′)	115.0(2)	O(2)–C(4′)–C(5′)	111.3(2)
C(3′)–C(4′)–C(5′)	104.0(2)	C(1′)–C(5′)–C(4′)	101.9(2)
C(1′)–C(5′)–C(6′)	109.8(2)	C(4′)–C(5′)–C(6′)	117.0(2)
C(1′)–C(5′)–C(13′)	111.1(2)	C(4′)–C(5′)–C(13′)	108.4(2)
C(6′)–C(5′)–C(13′)	108.6(2)	C(5′)–C(6′)–C(7′)	108.7(2)
C(1)–C(7′)–C(6′)	108.1(2)	C(1)–C(7′)–C(10′)	104.5(3)
C(6′)–C(7′)–C(10′)	112.0(3)	C(1)–C(9′)–C(1′)	108.3(2)
C(1)–C(9′)–C(12′)	110.1(2)	C(1′)–C(9′)–C(12′)	114.0(2)
O(1)–C(10′)–C(7′)	124.6(3)	O(1)–C(10′)–C(11′)	123.2(3)
C(7′)–C(10′)–C(11′)	112.0(3)	C(1′)–C(11′)–C(10′)	108.5(3)
O(3)–C(12′)–C(4)	123.3(3)	O(3)–C(12′)–C(9′)	127.7(3)
O(4)–C(12′)–C(9′)	108.9(2)	O(4)–C(14′)–C(15′)	108.4(3)
O(2)–C(16′)–C(17′)	111.3(2)	O(2)–C(16′)–C(18′)	111.4(2)
C(17′)–C(16′)–C(18′)	110.1(3)	O(2)–C(16′)–C(19′)	103.7(2)
C(17′)–C(16′)–C(19′)	109.1(3)	C(18′)–C(16′)–C(19′)	111.0(3)

(0.63 g, 73%); $[\alpha]_D^{25}$ −348° (*c* 0.24 in ethanol); *m/z* 332 (M^+, 8%), 276 (15), 230 (20), and 57 (100) (Found: *M*, 332.2352. Calc. for $C_{21}H_{32}O_3$: *M*, 332.2351); $\nu_{max.}$(neat) 3 070, 3 040, and 1 740 cm^{-1}; δ_C 173.4 (s, ester CO), 137.6 (d, C-11′), 130.0 (d, C-10′), 77.8 (d, C-4′), 72.3 (s, Bu^t), 59.7 (t, ester CH_2), 53.0 (d, C-9′), 51.4 (s, C-1′), 48.4 (s, C-5′), 42.5 (d, C-7′), 37.0 (t, C-6′), 32.3 (t, C-3′), 28.7 (q, Bu^t), 28.4 (s, C-1,8′), 28.2 (t, C-2′), 20.5 (q, 5′-Me), 14.2 (q, ester Me), 13 (t, C-3), and 11.0 (t, C-2); δ_H 6.35—6.19 (2 H, m, 10′-H and 11′-H), 4.15—3.98 (3 H, m, ester CH_2, 4′-H), 2.78 (1 H, s, 9′-H), 2.2—1.95 (2 H, m, 3′-H and 2′-H), 1.8 (1 H, d, *J* 12.5 Hz, 6′-H_{endo}), 1.72—1.4 (3 H, m, 2′-H, 3′-H and 7′-H), 1.22 (3 H, t, *J* 7 Hz, ester Me), 1.18 (9 H, s, Bu^t), 1.07 (1 H, dd, *J* 12.5 and 4.3 Hz, 6′-H_{exo}), 0.77 (3 H, s, 5′-Me), and 0.60—0.25 (4 H, m, cyclopropyl H's).

Ethyl (1S,4R,5R,7R,9R)-5,8,8-*Trimethyl*-4-*t*-*butoxytricyclo*-[5.2.2.0^{1,5}]*undecane*-9-*carboxylate* (**20**).—The cyclopropane (**19**) (0.520 g, 1.6 mmol) in glacial acetic acid (10 ml) was hydrogenated (2 atm, room temperature) for 1 d in the presence of PtO_2 catalyst (0.20 g, pre-hydrogenated in 20 ml glacial acetic acid at 2 atm, room temperature, 24 h). The catalyst was filtered off, the filtrate concentrated under reduced pressure, and the remaining colourless oil distilled (kugelrohr: 130 °C/ 0.02 Torr) to give the title compound (**20**) (0.520 g, 91%) as waxy crystals; $[\alpha]_D^{25}$ − 345° (*c* 0.5 in hexane); $\nu_{max.}$ 1 730 cm^{-1}; *m/z* 336 (M^+, 20%), 280 (30), 234 (60), 129 (70), and 57 (100) (Found: *M*, 336.2666. Calc. for $C_{21}H_{36}O_3$: *M*, 336.2664); δ_c 173.7(s), 79.2(d), 72.2(s), 59.3(t), 53.4(d), 44.9(s), 44.5(s), 39.2(d), 35.9(t), 34.3(s), 32.0(t), 30.8(t), 30.3(q), 28.9 (3 q superimposed), 25.8(q), 21.8(t), 21.7(t), 19.8(q), and 14.5(q).

Ethyl (1R,4R,5R,7R,9R)-4-*Hydroxy*-5,8,8-*trimethyl*-11-*oxo*-*tricyclo*[5.2.2.0^{1,5}]*undecane*-9-*carboxylate* (**16**).—In an attempt to thioketalize it, compound (**14**) (0.35 g) was dissolved in ethane-1,2-dithiol (1 ml) and BF_3·Et_2O (0.4 ml) added dropwise to the solution. The latter was set aside overnight at room temperature after which the reaction was stopped by the addition of saturated aqueous $NaHCO_3$. Chromatography (silica gel, pentane–ethyl acetate, 3:2 v/v) of the concentrated organic layer gave no thioketal but the alcohol (**16**) (0.150 g, 51%); $\nu_{max.}$(neat) 3 450m and 1 730s cm^{-1}; *m/z* 294 (M^+, 10%), 276 (5), 166 (50), and 41 (100); δ_C 217.4(s), 172.9(s), 79.2(d), 60.1(t), 7.0(d), 52.6(d), 48.7(s), 45.2(s), 42.4(t), 34.4(s), 33.5(t), 317.(t), 29.1(t), 28.3(q), 26.8(q), 17.4(q), and 14.2(q).

Ethyl (1S,4R,5R,7R,9R)-4-*Hydroxy*-5,8,8-*trimethyltricyclo*-[5.2.2.0^{1,5}]*undecane*-9-*carboxylate* (**21**).—Compound (**20**) (0.460 g, 1.4 mmol) and toluene-*p*-sulphonic acid monohydrate (0.06 g) in benzene (30 ml) were refluxed for 3 h (reaction was monitored by t.l.c.: silica gel, pentane–ether, 9:1, v/v). Saturated aqueous, $NaHCO_3$ (3 ml) was added to the reaction mixture. The organic layer was separated, concentrated under reduced pressure, and the oily residue distilled in the kugelrohr (150 °C/0.03 Torr) to give the title compound (**21**) (0.367 g, 95.7%); $[\alpha]_D^{25}$ −347° (*c* 0.36 in EtOH); $\nu_{max.}$(neat) 3 440 and 1 740 cm^{-1}; *m/z* 280 (M^+, 10%), 262 (5), 234 (5), and 129 (100); (Found: *M*, 280.2030. Calc. for: $C_{17}H_{28}O_3$: *M*, 280.2038); δ_C 173.6(s), 80.6(d), 59.3(t), 53.0(d), 45.1(s), 44.8(s), 38.9(d), 36.0(t), 34.2(s), 31.3(t), 30.3(t), 30.0(q), 25.8(q), 21.9(t), 21.6(t), 18.9(q), and 14.4(q); δ_H 4.25—4.07 (3 H, m), 2.5—2.35 (1 H, m), 2.33 (1 H, d, *J* 2.3 Hz), 2.15—1.2 (11 H, m), 1.28 (3 H, t, *J* 7 Hz), 1.12 (3 H, s), 1.01 (3 H, s), and 0.98 (3 H, s).

Ethyl (1S,4R,5R,7R,9R)-5,8,8-*Trimethyl*-4-*p*-*tosyloxytri*-*cyclo*[5.2.2.0^{1,5}]*undecane*-9-*carboxylate* (**22**).—The alcohol (**21**) (0.090 g, 0.3 mmol) in dry pyridine (1 ml) was treated with toluene-*p*-sulphonyl chloride (0.10 g, 0.5 mmol) in the presence of a catalytic amount of DMAP at room temperature overnight. The pyridine was stripped off under reduced pressure and the remaining semisolid residue chromatographed on silica gel (p.l.c., pentane–ethyl acetate, 9:1, as eluant) to give the title compound (**22**) (0.112 g, 78.5%) as white crystals, m.p.. 66 °C (pentane) (Found: C, 66.15; H, 7.8; S, 7.4. $C_{24}H_{34}O_5S$ requires C, 66.17; H, 8.10; S, 7.36%); $[\alpha]_D^{20}$ −231° (*c* 0.23 in hexane); *m/z* 434 (M^+, 5%), 262 (20), and 129 (100) (Found: *M*, 434.2125. Calc. for $C_{24}H_{34}O_5S$: *M*, 434.2127); δ_C 172.8(s), 144.4(s), 134.2(s), 129.6(d), 127.6(d), 90.1(d), 59.4(t), 52.9(d), 44.9(s), 44.6(s), 38.5(d), 35.1(t), 34.1(s), 29.9(t), 29.8(q), 28.3(t), 25.5(q), 21.5(q), 21.3(t), 21.2(t), 19.7(q), and 14.3(q); δ_H 7.81 (2 H, d, *J* 8 Hz), 7.34 (2 H, d, *J* 8 Hz), 4.81 (1 H, dd, *J* 9 and 6 Hz), 4.2—4.0 (2 H, m), 2.45 (3 H, s), 2.45—2.35 (1 H, m), 2.12 (1 H, d, *J* 2 Hz), 2.1—1.95 (1 H, m), 1.8—1.3 (7 H, m), 1.28 (3 H, t, *J* 7 Hz), 1.22—1.05 (2 H, m), 1.01 (6 H, s, superimp. Me), and 0.93 (3 H, s, 3 H).

Solvolysis of the Ester (**22**): *Ethyl* (1S,7R,9R)-4,8,8-*Trimethy*-*tricyclo*[5.2.2.0^{1,5}]*undec*-4-*ene*-9-*carboxylate* (**23**).—The *p*-tosylate (**22**) (0.112 g, 0.25 mmol) dissolved in acetone (1 ml) was added to acetone–water (10 ml; 1:1, v/v) containing $CaCO_3$ (0.2 g) and the mixture, in a sealed tube, was held at 100 °C for 48 h. The acetone was distilled off and the aqueous layer extracted with ether. Concentration gave an oil, which was distilled (kugelrohr, b.p. 110 °C/0.01 Torr) to give the olefin (**23**) (0.040 g, 60.5%) (Found: C, 78.0; H, 9.95. $C_{17}H_{26}O_2$ requires C, 77.82; H, 9.92%); $\nu_{max.}$(neat) 1 735 cm^{-1}; $[\alpha]_D^{25}$ −384° (*c* 0.35 in hexane); *m/z* 262 (M^+, 50%), 247 (10), 133 (90), 130 (100), 115 (30), 105 (20), and 91 (70). (Found: 262.1928. Calc. for: *M*, $C_{17}H_{26}O_2$: 262.1933); δ_C 173.6 (s, ester CO), 138.4 (s, C-5), 126.4 (s, C-4), 59.2 (t, ester CH_2), 58.6 (d, C-9), 49.0 (s, C-1), 39.5 (d, C-7), 36.5 (t, C-3), 34.6 (s, C-8), 32.5 (t, C-2), 30.5 (q, 8-Me), 27.3 (t, C-6), 25.3 (q, 8-Me), 25.2 (t, C-10), 23.8 (t, C-11), 14.4 (q, ester Me), and 13.4 (q, C-4 Me); δ_H 4.18—4.05 (2 H, m, diastereotopic ester CH_2), 2.55—2.0 (5 H, m, 6-H, 10-H_{endo}, 3-H), 2.21 (1 H, d, *J* 2.5 Hz, 9-H), 1.95—1.8 (1 H, m, 11-H_{endo}), 1.8—1.63 (1 H, m, 2-H), 1.57 (3 H, br s, olefinic Me), 1.47—1.32 (2 H, m, 2-H, 7-H), 1.32—1.22 (2 H, m, 10-H_{exo}, 11-H_{exo}), 1.26 (3 H, t, *J* 7 Hz, ester Me), 1.13 (s, Me), and 1.01 (3 H, s, Me).

(1S,7R,9R)-9-*Hydroxymethyl*-4,8,8-*trimethyltricyclo*-[5.2.2.0^{1,5}]*undec*-4-*ene* (**4**).—The ester (**23**) (0.300 g, 1.1 mmol)

in dry ether (20 ml) was treated with lithium aluminium hydride (0.050 g, 1.3 mmol). The reduction was stopped by careful addition of ethyl acetate and 1M HCl. The ethereal extract was filtered through silica gel (20 g), concentrated, and the remaining colourless oil distilled in a kugelrohr at 110—120 °C/0.03 Torr to give the alcohol (**4**) (0.215 g, 85.3%), m.p. 79—80 °C (pentane); $[\alpha]_D^{23}$ −104° (*c* 1.5 in hexane) (Found: C, 82.1; H, 10.9. $C_{15}H_{24}O$ requires C, 81.76; H, 10.98%); $\nu_{max.}$(KBr) 3 375 cm^{-1}; *m/z* 220 (M^+, 50%), 205 (25), 202 (20), 187 (27), 175 (27), 133 (100), 91 (90) (Found: *M*, 220.1824. Calc. for: $C_{15}H_{24}O$. *M*, 220.1824); δ_H ($CDCl_3$—D_2O) 3.82—3.69 (2 H, m), 2.45 (1 H, br d, *J* 17 Hz), 2.22 (2 H, br s), 2.0 (1 H, br d, *J* 17 Hz), 1.9—1.6 (2 H, m), 1.57 (3 H, m), 1.5—1.1 (6 H, m), 1.14 (3 H, s), and 1.05 (3 H, s); δ_C 139.8(s), 125.8(s), 62.4(t), 54.6(d), 49.1(s), 39.9(d), 36.3(d), 34.2(s), 32.1(t and q), 27.1(t), 25.7(t), 23.9(t), 23.8(q), and 13.2(q).

Acknowledgements

This work was supported by the Fonds der Chemischen Industrie which is gratefully acknowledged. We thank Mrs. E. M. Peters, MPI für Festkörperforschung, Stuttgart, for calculations.

References

1. P. R. Jefferies, J. R. Knox, and E. J. Middleton, *Aust. J. Chem.*, 1962, **15**, 532; A. J. Birch, J. Grimshaw, and J. P. Turnbull, *J. Chem. Soc.*, 1963, 2412; A. J. Birch, G. S. R. Subba Rao, and J. P. Turnbull, *Tetrahedron Lett.*, 1966, 4749; Y.-L. Oh, and E. N. Maslen, *ibid.*, p. 3291.
2. (a) R. Ramage, O. J. R. Owen, and I. A. Southwell, *Tetrahedron Lett.*, 1983, 4487; (b) M. Asoaka, K. Ishibashi, N. Yanagida, and H. Takei, *ibid.*, p. 5127.
3. E. Osawa, K. Aigami, N. Takaishi, Y. Inamoto, Y. Fujikura, Z. Majerski, P. von R. Schleyer, E. M. Engler, and M. Farcasiu, *J. Am. Chem. Soc.*, 1977, **99**, 5361.
4. U. Eder, G. Sauer, and R. Wiechert, *Angew. Chem.*, 1971. **85**, 492; *Angew. Chem., Int. Ed. Engl.*, 1971, **10**, 496; Z. G. Hajos and D. R. Parrish, *J. Org. Chem.*, 1974, **39**, 1615.
5. R. A. Lee, *Tetrahedron Lett.*, 1973, 3333.
6. W. Weber, D. Spitzner, and W. Kraus, *J. Chem. Soc., Chem. Commun.*, 1980, 1212.
7. H. Hagiwara and H. Uda, *J. Chem. Soc., Perkin Trans. 1*, 1986, 629; W. Weber and D. Spitzner, unpublished.
8. J. Salaün, F. Bennani, J.-C. Compain, A. Fadel, and J. Ollivier, *J. Org. Chem.*, 1980, **45**, 4129; D. Spitzner and H. Swoboda, *Tetrahedron Lett.*, 1986, 1281.
9. C. Gröger, H. Musso, *Angew. Chem.*, 1976, **88**, 415; *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 373.
10. H. Gerlach and W. Müller, *Helv. Chim. Acta*, 1972, **55**, 2277.
11. G. Höfle, W. Steglich, and H. Vorbrüggen, *Angew. Chem.*, 1978, **90**, 602; *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 596.
12. E. Yoshii, T. Kaizumi, E. Kitatsuji, T. Kawazoe, and T. Kaneko, *Heterocycles*, 1976, **4**, 1663.

Received 16*th February* 1987; *Paper* 7/276