Tetrahedron Vol. 36, pp. 3367 to 3375
Pergamon Press Ltd., 1980. Printed in Great Britain.

MARASMIC ACID—II

TOTAL SYNTHESIS OF (±)-MARASMIC ACID

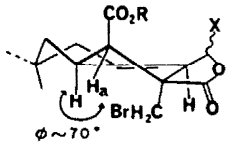
W. J. GREENLEE*[a] and R. B. WOODWARD[b]
Department of Chemistry, Harvard University, Cambridge, MA 02138, U.S.A.

(*Received in USA 22 November* 1979)

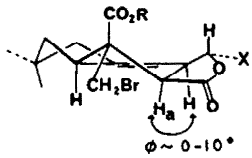
Marasmic acid (**1**), one of the many fungal metabolites isolated from the *Basidiomycetes*, has been the target of recent synthetic efforts.[1,2] Our initial synthetic approach to the natural product, which involved as a key step cyclopropanation of Diels–Alder adduct **2** via 1,3-dipolar addition of diazomethane, and photolysis of the resulting pyrazoline mixture, led instead to synthesis of isomarasmic acid (**3**), which lacks the *cis* relationship of the cyclopropane ring to the adjacent hydrogen at the ring fusion present in marasmic acid.

In order to circumvent this difficulty while maintaining the basic Diels–Alder approach to the hydrindane ring skeleton, we studied additions to diene system **4**, of an alternate dienophile, bromomethylmaleic anhydride (**5**). We hoped that cyclopropanation of the expected *endo* adducts *via* intramolecular displacement of bromide would produce a single cyclopropane with the correct stereochemistry. We then intended to derive the desired lactol function by a selective reduction of the anhydride.

Although attempts to prepare adducts of bromomethylmaleic anhydride with diene acetal **7**[2] at elevated temperatures led to tarry mixtures, storage of a solution of the two components in methylene chloride for five days afforded crystalline adducts **9** and **10** (1:1 mixture) which were separated by chromatography on silica gel (58% yield). Unfortunately, the reaction proved unreproducible, and yields of 30% or less were usually obtained. Treatment of anhydrides **9** and **10** with refluxing methanol containing a catalytic amount of



	R	X	H_a	J_{obs}	J_{calc}[12]
11	$-CH_3$	$-OCH_3$	3.15 δ	2 Hz	0-2 Hz
			3.25	2	
13	-H	-H	3.32	1	
15	$-CH_3$	-H	3.30	1	
18	$-C(CH_3)_3$	-H	3.24	1	



12	$-CH_3$	$-OCH_3$	3.09 δ	6 Hz	6-15 Hz
14	-H	-H	3.13	7	
16	$-CH_3$	-H	3.10	7	
19	$-C(CH_3)_3$	-H	2.97	6	

Fig. 1. NMR spectra ($CDCl_3$).

[a]NSF Predoctoral Fellow, 1972–1975. Present Address, Merck Sharp and Dohme Research Laboratories, Merck and Co., Inc., Rahway, NJ 07065.
[b]Deceased, 8 July 1979.

sulfuric acid gave pseudoesters **11** and **12** respectively.† While cyclopropanation of **11** and **12**, followed by a selective reduction of the pseudoester moiety,‡ represented the most direct route to marasmic acid, the troublesome Diels–Alder step led to its abandonment.

A far better Diels–Alder reaction was that obtained with diene alcohol **8**,[1b] prepared by reduction of diene aldehyde **6**[2] with diisobutylaluminum hydride (85% yield). When a solution of **8** and anhydride **5** in methylene chloride was allowed to stand, a mixture of adducts **13** and **14** began to precipitate within a few hours.† These were separated by fractional recrystallization in 58% combined yield and converted to the corresponding methyl esters **15** and **16**‡ by treatment with ethereal diazomethane. Subjection of a crude mixture of the bromoesters to the action of potassium *t*-butoxide in benzene gave cyclopropane **17** in 47% overall yield (from **8**).

Having in hand an efficient synthesis of cyclopropane **17**, which possesses the carbon skeleton of marasmic acid, we sought a method for transforming its lactone ring to the dialdehyde system of the natural product. We hoped to accomplish this as shown in Fig. 2. After partial reduction of the lactone ring of I (CO_2R = hindered ester), the resulting hemiacetal II would be converted to a pseudoester III. Pseudoester formation would free the hydroxymethyl group, allowing oxidation (with concommitant migration of the double bond) to the aldehyde IV. Hydrolysis of the pseudoester moiety of IV would then furnish the natural product.

With this approach in mind, the crude mixture of bromoacids **13** and **14** (in methylene chloride) prepared as described above was treated with isobutylene in the presence of *p*-toluenesulfonic acid (4 days), affording a mixture of t-butyl esters **18** and **19**. Subjection of the bromoesters to the action of potassium t-butoxide in benzene–t-butanol gave cyclopropane **20** in 44% overall yield (from **8**). Reduction of **20** with diisobutylaluminum hydride in toluene at −78° gave hemiacetal **21**, isolable as a colorless oil in 57% yield.† Exposure of the crude hemiacetal to trifluoroacetic acid effected de-esterification and lactonization, furnishing **24** in 65% overall yield. This etiolactone was also prepared without use of a hindered ester by saponification of cyclopropane **17** (95% yield), followed by treatment of the resulting lactone acid **25** with diisobutylaluminum hydride (50% yield). However, overreduction to lactone alcohol **26** also took place (25% yield).

Obtention of **24**, an intermediate possessing the desired stereochemistry‡ and having two of three oxygenated C atoms in the correct oxidation state, was very encouraging. However, attempts to convert **24** to a pseudoester were unsuccessful. Treatment with refluxing methanol containing *p*-toluenesulfonic acid did afford a product in which methanol had been incorporated, but this proved to be acetal **27**. Subjection of **24** to sodium methoxide in methanol also failed to furnish the desired pseudoester moiety. Saponification of **24** produced acid **28** (itself unstable toward relactonization), which could be converted only to **27** (ethereal diazomethane, followed by exposure to acidic methanol; 79% yield).

Acetal **27** was readily transformed to an intermediate possessing a free hydroxymethyl group by mercaptal formation. Thus combination of **27** with 1,3-propanedithiol and boron trifluoride etherate in absolute chloroform afforded **29** in 85% yield. It was hoped that oxidation of **29** to the corresponding aldehyde (with concommitant double bond migration), followed by hydrolysis of the mercaptal by one of the recently-reported mild methods,[4] would provide an efficient route to the 1,4-dialdehyde system. Unfortunately, all attempts to perform the required oxidation failed. Several dimethylsulfoxide-based oxidations[6] were employed, but none gave a trace of aldehyde, a result which suggested interference by, or participation of the mercaptal function in these reactions.¶ We attempted to effect an intramolecular oxidation of the hydroxymethyl group by preparing sulfoxide **30** (sodium periodate; 81% yield) in the hope that the sulfoxide function might substitute for dimethylsulfoxide in a Moffatt-type oxidation. However, treatment of **30** with several reagents reported to bring about oxidations of alcohols in conjunction with dimethylsulfoxide[6] gave none of the aldehyde. Although an aldehyde was obtained in low yield upon treatment of **29** with chromium trioxide in

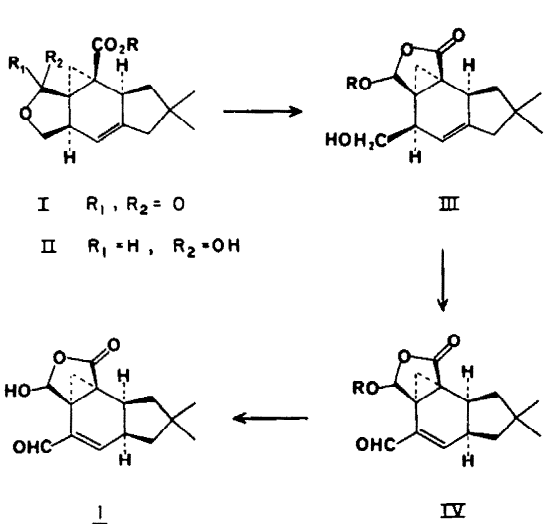


Fig. 2.

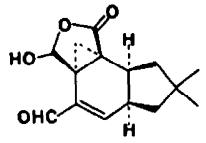
†The regioisomeric adducts were differentiated by analysis of the proton NMR spectra as shown in Fig. 1.

‡Such a reduction of a pseudoester, leading to a 1,4-dicarbonyl system, has been reported.[3]

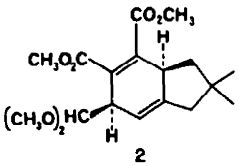
†Hemiacetal **21** was quite unstable, and purification by chromatography on silica gel was accompanied by loss of material. It was more fully characterized by conversion to acetals **22** and **23** (Experimental). Careful exclusion of traces of acid from neat **21** was necessary due to its tendency to form a mixture of two diastereomeric acetal dimers (loss of water). For preparative purposes the crude hemiacetal was used immediately in the next step.

‡Formation of etiolactone **24** confirmed the expected stereochemistry of the Diels–Alder adducts **13** and **14**. The alternative structure (that derived from *exo* adducts is impossibly strained.

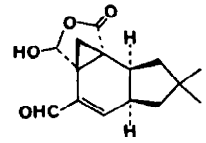
¶ Participation of the adjacent mercaptal function might lead to intramolecular displacement of dimethylsulfoxide from the oxosulfonium ion common to these oxidation procedures. Although we have no direct evidence for such participation for mercaptal **29**, displacements of this type involving external nucleophiles are known.[5]



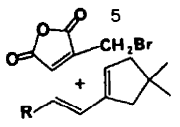
1



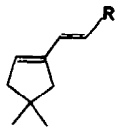
2



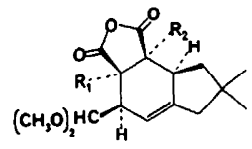
3



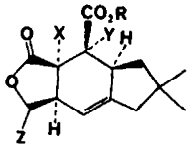
4



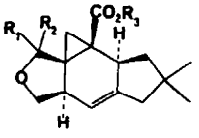
	R
6	-CHO
7	$-CH(OCH_3)_2$
8	$-CH_2OH$



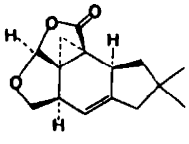
	R_1	R_2
9	$-CH_2Br$	-H
10	-H	$-CH_2Br$



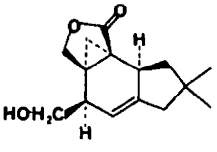
	X	Y	Z	R
11	$-CH_2Br$	-H	$-OCH_3$	$-CH_3$
12	-H	$-CH_2Br$	$-OCH_3$	$-CH_3$
13	$-CH_2Br$	-H	-H	-H
14	-H	$-CH_2Br$	-H	-H
15	$-CH_2Br$	-H	-H	$-CH_3$
16	-H	$-CH_2Br$	-H	$-CH_3$
18	$-CH_2Br$	-H	-H	$-C(CH_3)_3$
19	-H	$-CH_2Br$	-H	$-C(CH_3)_3$



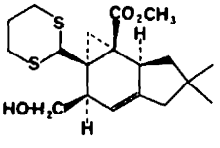
	R_1	R_2	R_3
17	R_1,R_2 = O		$-CH_3$
20	R_1,R_2 = O		$-C(CH_3)_3$
21	-H	-OH	$-C(CH_3)_3$
22	-H	$-OCH_3$	$-C(CH_3)_3$
23	$-OCH_3$	-H	$-C(CH_3)_3$
25	R_1,R_2 = O		-H
27	-H	$-OCH_3$	$-CH_3$
28	-H	-OH	-H



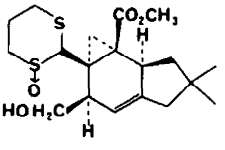
24



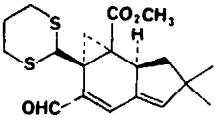
26



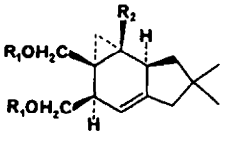
29



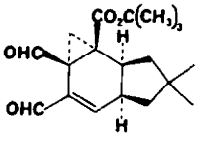
30



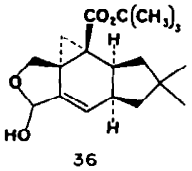
31



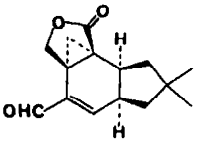
	R_1	R_2
32	-H	$-CO_2C(CH_3)_3$
33	-H	$-CH_2OH$
34	-COCl	$-CO_2C(CH_3)_3$



35



36



37

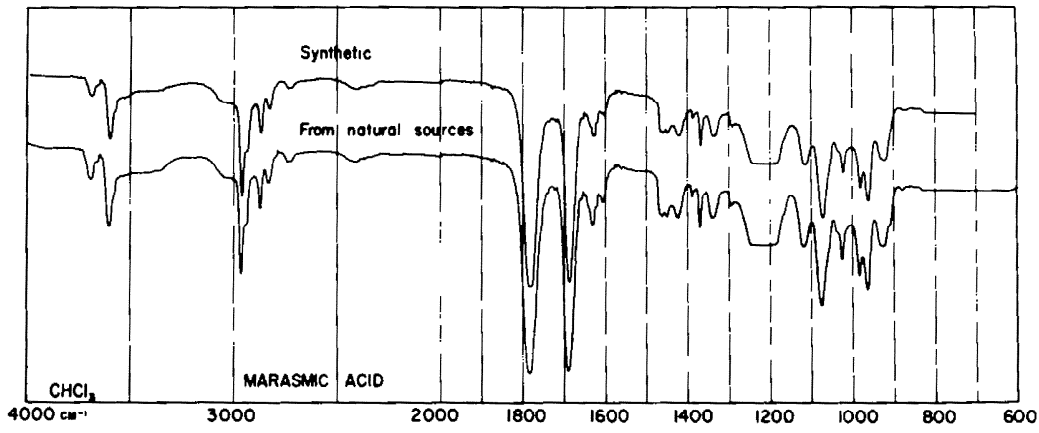


Fig. 3. IR spectrum of Marasmic acid ($CHCl_3$).

pyridine,[7] this proved to be diene aldehyde **31** (15% yield).

Faced with the difficulty of transforming the etiolactone of **24** to the desired dialdehyde system, we chose a less direct approach. This involved reduction of hemiacetal **21** to a diol and simultaneous oxidation of the two hydroxymethyl groups. Although direct oxidations of 1,4-diols usually afford lactones,[8] 1,4-butanediol itself has been converted to succindialdehyde by treatment of the corresponding dichloroformate with dimethylsulfoxide.[9] A similar procedure was applied successfully for marasmic acid. Lactone **20** was reduced with diisobutylaluminum hydride (as described above) and the crude hemiacetal **21** was reduced further with sodium borohydride in methanol, affording diol **32** (67%) and a small amount of triol **33** (6% yield). Addition of an ether solution of **32** containing two equivalents of quinoline to an excess of ethereal phosgene provided dichloroformate **34** in high yield. Treatment of crude **34** with dimethylsulfoxide and then triethylamine[9] afforded dialdehyde **35** in 25% overall yield (from **32**).† De-esterification of **35** with trifluoroacetic acid in benzene gave (±)-marasmic acid (**1**) (50% yield) identical to that derived from natural sources‡ by IR (Fig. 3), UV (Table 1), proton NMR (Fig. 4), and mass spectra (Fig. 5).

Table 1. UV spectrum of Marasmic acid (95% EtOH)

Source	λ_{max}	ϵ
Synthetic	239 nm	9220
Natural Sources		
	240	9100
lit.[10]	241	9700

†Small amounts of a mixture of **36** and **37** (15–20%), derived by incomplete oxidation of the more-hindered hydroxymethyl group of **32**, were also isolated. Attempts to improve the yield of dialdehyde **35** by use of cosolvents (HMPA or methylene chloride) at lower temperatures were unsuccessful.

‡We are grateful to Dr. P. de Mayo for a sample of (+)-marasmic acid from natural sources, which we recrystallized twice from hexane-ethyl acetate, mp 172–173° [lit.[10] m.p. 173–174° (EtOAc)] in an evacuated capillary.

EXPERIMENTAL

M.ps unless otherwise stated were taken on a Kofler hot-stage apparatus and are uncorrected as are all bg pts. Mass spectra were recorded on an AEI MS-9 double-focusing instrument at 70 eV. NMR spectra were obtained using Varian HA-100 and XL-100 instruments. Chemical shifts are recorded in ppm downfield from TMS as internal standard. Coupling constants are reported in Hertz. IR spectra were measured on Perkin-Elmer 137 and 457A instruments. UV spectra were taken on a Cary model 14 spectrophotometer. Elemental analyses were performed by Scandinavian Microanalytical Laboratories, Herlev, Denmark. Silica gel used for preparative separations was Woelm grade, activity 1. Analytical tlc was performed on 0.25 mm silica gel plates containing a 254 nm indicator (Analtech). Spots were visualized by staining with iodine vapor. For preparative layer separations, 0.5 mm and 2.0 mm silica gel plates containing PF 254 indicator (Analtech) were used. Methylene chloride, dimethylsulfoxide, t-butanol, pyridine, quinoline, and triethylamine were distilled from calcium hydride and stored over 4 Å molecular sieves. MeOH (dry) was distilled from magnesium methoxide and stored over 3 Å molecular sieves. Potassium was cleaned at 70° under 4:1 toluene: t-amyl alcohol.

Bromomethylmaleic anhydride (**5**). A soln of 2-bromo-2-(bromo-methyl) succinic anhydride[11] (43.5 g, 0.160 mol) in dry benzene (550 ml) was cooled (ice bath) and 2,6-lutidine (17.4 g, 0.160 mol) was added with vigorous stirring over 30 min. The mixture was allowed to warm to room temp over 30 min, then filtered and concentrated. Distillation of the oily, black residue gave 26.5 g (0.138 mol, 87%) of **5**, b.p. 102–103° (0.4 mm) [lit.[11] b.p. 116–117° (1.2 mm)] as a light yellow liquid. IR (film) 1850, 1775 cm^{-1}. NMR ($CDCl_3$) 4.26 (2H, d, J = 1), 6.96 (1H, t, J = 1).

2-Bromomethyl-11,11-dimethyl-3,5-dioxo-4-oxatricyclo [7,3,0,$0^{2,6}$] *dodec-8-ene-7-carboxaldehyde dimethyl acetal* (**9**) and *6-bromomethyl-11,11-dimethyl-3,5-dioxo-4-oxatricyclo* [7,3,0,$0^{2,6}$] *dodec-8-ene-7-carboxaldehyde dimethyl acetal* (**10**). A soln of **7**[2] (490 mg, 2.50 mmol) and **5** (477 mg, 2.50 mmol in dry benzene (1.0 ml) was stirred under argon for 5 days. The crude product was placed onto a column (1 × 35 cm) of silica gel (30 g), slurry packed in 14:1 hexane:ether. Elution with the same solvent gave 218 mg (0.564 mmol) of **9** (white solid).

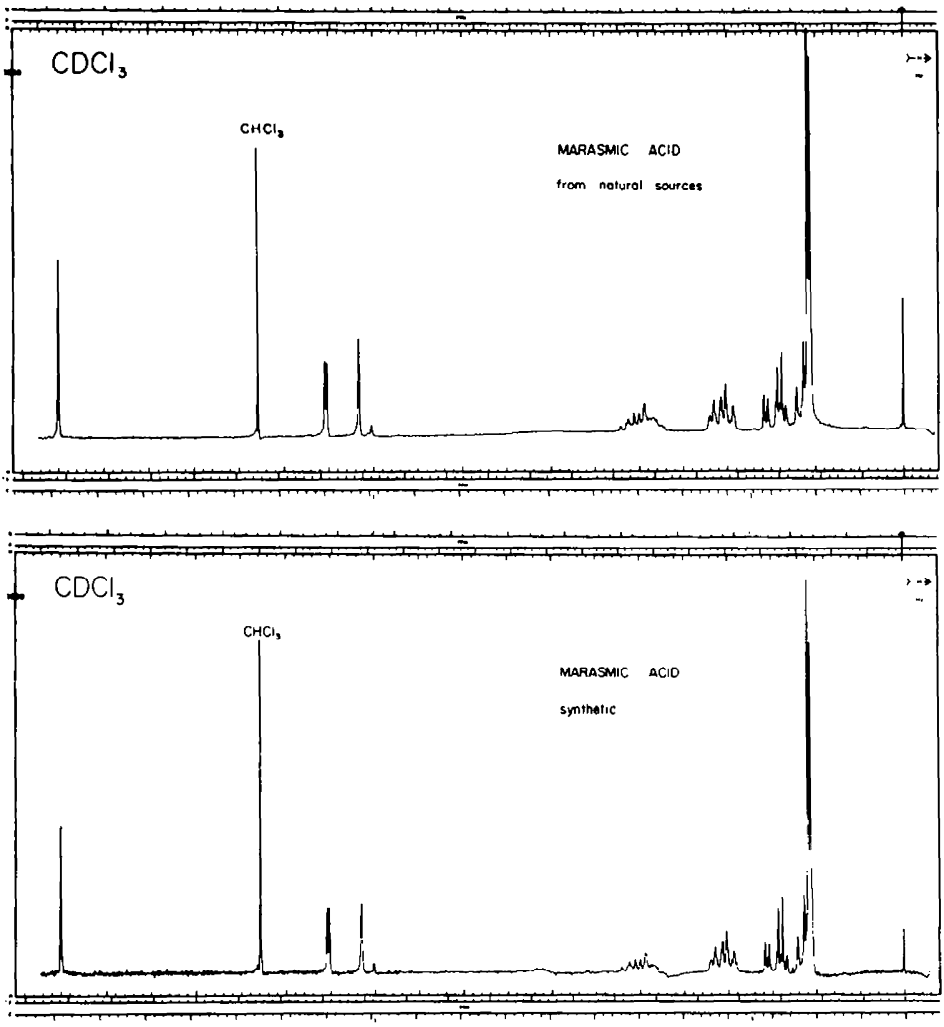


Fig. 4. NMR spectrum of Marasmic acid ($CDCl_3$).

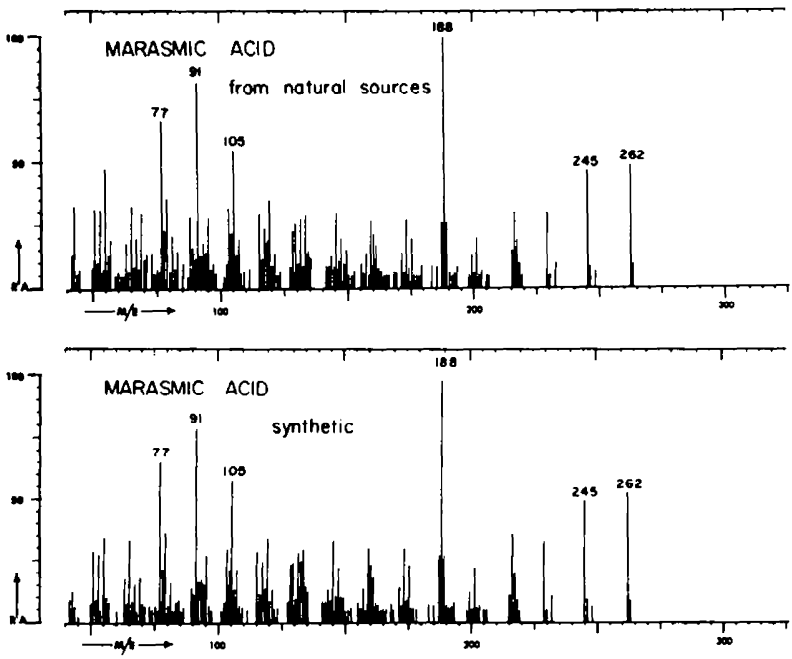


Fig. 5. Mass spectrum of Marasmic acid (70 eV).

Several fractions containing mixtures of **9** and **10** (116 mg) were collected, and then 227 mg (0.587 mmol) of pure **10** (white solid) was obtained from late fractions. The total yield was thus 561 mg (1.45 mmol, 58%). For analysis **9** was recrystallized twice from hexane, giving slender needles, m.p. 88–93°. Found: C, 52.66; H, 6.04; Br, 20.59. Calc for $C_{17}H_{23}BrO_5$: C, 52.72; H, 5.99; Br, 20.63. IR (KBr) 1850, 1780 cm^{-1}. NMR ($CDCl_3$) 0.95 (3H, s), 1.18 (3H, s), 3.36 (3H, s), 3.50 (3H, s), 3.86 (2H, AB, J_{AB} = 12, δ_{AB} = 58), 4.63 (1H, d, J = 6), 5.6 (1H, m). Two recrystallizations of **10** from hexane–acetone gave a sample, m.p. 137–138°. Found: C, 52.69; H, 5.93; Br, 20.36, IR (KBr) 1850, 1780 cm^{-1}. NMR ($CDCl_3$) 0.92 (3H, s), 1.10 (3H, s), 3.46 (3H, s), 3.56 (3H, s), 3.65 (2H, AB, J_{AB} = 10, δ_{AB} = 34), 5.07 (1H, d, J = 9), 5.7 (1H, m).

3-*Bromomethyl*-2-*carbomethoxy*-11,11-*dimethyl*-6-*methoxy*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one* (**11**). A soln of **9** (44.5 mg, 0.115 mmol) and conc H_2SO_4 (2 drops) in MeOH (5 ml) was heated at reflux for 2 hr. The mixture was diluted with brine (10 ml) and extracted with ether (3 × 15 ml). The combined ether portions were washed twice with brine, dried ($MgSO_4$) and concentrated, giving 47.7 mg of crude **11**. This was purified by preparative tlc on silica gel (1:1 hexane: ether), providing 24.8 mg (0.064 mmol, 56%) of **11** as a white solid (broad melting range). The NMR spectrum showed two epimers (1:1 mixture). IR (CCl_4) 1750 cm^{-1}. NMR ($CDCl_3$) epimer 1: 0.97 (3H, s), 1.00 (3H, s), 3.15 (1H, d, J = 2), 3.52 (3H, s), 3.76 (3H, s), 4.98 (1H, d, J = 8), 5.4 (1H, m); epimer 2: 1.08 (6H, s), 3.25 (1H, d, J = 2), 3.42 (3H, s), 3.68 (3H, s), 4.99 (1H, d, J = 10), 5.4 (1H, m).

2-*Bromomethyl*-2-*carbomethoxy*-11,11-*dimethyl*-6-*methoxy*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one* (**12**). A soln of **10** (39.7 mg, 0.102 mmol) was treated as described above for **9**, giving 37.4 mg of crude **12** as a light-brown oil. This was purified by preparative tlc on silica gel as for **11**, giving 21.7 mg (0.056 mmol, 55%) of **12** (single epimer). IR (CCl_4) 1775, 1740 cm^{-1}. NMR ($CDCl_3$) 1.00 (3H, s), 1.02 (3H, s), 3.09 (1H, d, J = 6), 3.60 (2H, AB, J_{AB} = 10, δ_{AB} = 24), 3.58 (3H, s), 3.60 (3H, s), 5.37 (1H, d, J = 6), 5.6 (1H, m).

(E)-3-(4,4-*Dimethylcyclopentenyl*)-2-*propen*-1-*ol* (**8**). A soln of **6**[2] (1.5 g, 10.0 mmol) in dry benzene (10 ml) was added to 15.6 ml (10.6 g, 15.0 mmol) of ice-cold 20% diisobutylaluminum hydride (in hexane). The mixture was stirred at room temp for 2 hr and then diluted with 10% H_2SO_4 (75 ml). The aqueous layer was extracted with ether (3 × 50 ml), and the combined organic portions were washed with brine, dried ($MgSO_4$) and concentrated. Distillation gave 1.30 g (8.52 mmol, 85%) of **8**, b.p. 57–58° (0.07 mm) [lit.[1b] b.p. 69–75° (0.2 mm)]. IR (film) 3300, 3020, 1650, 1610 cm^{-1}. UV (95% C_2H_5OH) 235 nm (13,700). NMR ($CDCl_3$) 1.10 (6H, s), 1.21 (4H, s), 4.12 (2H, d, J = 6), 5.56 (1H, d of t, J = 6, 15), 5.52 (1H, broad s), 6.34 (1H, d, J = 15). For analysis, **8** was converted to the acetate. To 1.25 g (8.25 mmol) of **8** were added Ac_2O (3.75 ml) and dry pyridine (6.50 ml) and the resulting soln was stirred for 22 hr. The mixture was concentrated, diluted with water (50 ml) and extracted with ether (3 × 35 ml). The combined ether portions were washed with 10% H_2SO_4, saturated bicarbonate, and brine, dried ($MgSO_4$) and concentrated. Distillation gave 1.38 g (7.15 mmol, 86%) of (E)-3-*acetoxy*-1-(4,4-*dimethylcyclopentenyl*)*propene*, b.p. 55.5–58.5° (0.06 mm). Found: C, 73.97; H, 9.41. Calc. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. IR (film) 3020, 1740, 1650, 1610 cm^{-1}. UV (95% C_2H_5OH) 236 nm (17,100). NMR ($CDCl_3$) 1.10 (6H, s), 2.04 (3H, s), 2.12 (4H, s), 2.56 (1H, d, J = 6), 5.45 (1H, d of t, J = 6, 15), 6.40 (1H, d, J = 15), 5.58 (1H, broad s). MS *m/e* 194 (M^+).

3-*Bromomethyl*-2-*carboxy*-11,11-*dimethyl*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one* (**13**) and 2-*Bromomethyl*-2-*carboxy*-11,11-*dimethyl*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one* (**14**). A soln of **8** (304 mg, 2.00 mmol) and **5** (382 mg, 2.00 mmol) in CH_2Cl_2 (0.6 ml) was stirred for 20 hr. Bromoacids were obtained in four crops (405 mg, 1.18 mmol, 59%). The first two crops (from CH_2Cl_2) were exclusively the less-soluble isomer **13**, m.p. 170–178° (159 mg). The last two crops consisted predominantly of the more-soluble **14** (246 mg). Four recrystallizations of **13** from hexane–ether gave the analytical sample, m.p. 172–174°. Found: C, 52.26; H, 5.76; Br, 23.23. Calc. for $C_{15}H_{19}BrO_4$: C, 52.47; H, 5.58; Br, 23.29. IR (KBr) 3500–2500, 1735, 1730 cm^{-1}. NMR ($CDCl_3$) 1.00 (3H, s), 1.12 (3H, s), 2.1–2.2 (2H, broad s), 3.32 (1H, broad s), 4.10 (1H, t, J = 8), 4.16 (2H, AB, J_{AB} = 10, δ_{AB} = 51), 4.56 (1H, d of d, J = 8, 7), 5.40 (1H, m), 6.70 (1H, broad). MS *m/e* 342, 344 (M^-). Four recrystallizations of **14** from hexane–ether gave the analytical sample, m.p. 177–177.5° (sealed capillary). Found: C, 52.45; H, 5.70; Br, 23.24. IR (KBr) 3500–2500, 1760, 1700 cm^{-1}. NMR ($CDCl_3$) 1.01 (3H, s), 1.10 (3H, s), 1.2 1.9 (2H, m), 2.1–2.3 (2H, broad), 4.18 (1H, t, J = 8), 4.54 (1H, d of d, J = 8, 10), 3.13 (1H, d, J = 6), 3.68 (2H, AB, J_{AB} = 10, δ_{AB} = 23), 5.4 (1H, m), 6.2–6.5 (1H, broad). MS *m/e* 342, 344 (M^-).

3-*Bromomethyl*-2-*carbomethoxy*-11,11-*dimethyl*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one* (**15**). A soln of **13** (81.7 mg, 0.238 mmol) in ether (2 ml) was treated with an excess of ethereal diazomethane. After 2 min, solvent was removed under reduced pressure, giving 84.3 mg (0.236 mmol, 99%) of **15**, m.p. 73–73.5°. Three recrystallizations from hexane gave the analytical sample, m.p. 76–77.5°. Found: C, 53.84; H, 6.06; Br, 22.48. Calc. for $C_{16}H_{21}BrO_4$: C, 53.79; H, 5.92; Br, 22.37. IR (KBr) 1750, 1730 cm^{-1}. NMR ($CDCl_3$) 1.01 (3H, s), 1.10 (3H, s), 1.4–1.9 (2H, m), 2.14 (2H, broad s), 3.30 (1H, broad s), 4.08 (1H, t, J = 10), 4.56 (1H, t, J = 10), 3.70 (3H, s), 4.17 (2H, AB, J_{AB} = 12, δ_{AB} = 34), 5.4 (1H, m). MS *m/e* 356, 358 (M^+).

2-*Bromomethyl*-2-*carbomethoxy*-11,11-*dimethyl*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one* (**16**). Bromoacid **14** (42.4 mg, 0.124 mmol) was treated with an excess of ethereal diazomethane, giving 44.2 mg of **16** as a colorless oil. Preparative tlc on silica gel (ether) gave 41.0 mg (0.115 mmol, 93%) of pure ester. IR (film) 1760, 1730 cm^{-1}. NMR ($CDCl_3$) 1.00 (3H, s), 1.03 (3H, s), 4.19 (1H, t, J = 8), 4.50 (1H, d of d, J = 8, 10), 3.10 (1H, d, J = 7), 3.61 (3H, s), 3.64 (2H, AB, J_{AB} = 10, δ_{AB} = 21), 5.4 (1H, m). MS *m/e* 356, 358 (M^+).

12-*Carbomethoxy*-9,9-*dimethyl*-3-*oxatetracyclo* [10,1,0,$0^{1,5}$,$0^{7,11}$] *tridec*-6-*en*-2-*one* (**17**). A soln of **8** (1.00 g, 6.57 mmol) and bromomethylmaleic anhydride (1.25 g, 6.57 mmol) in anhyd ether (2 ml) was stirred for 22 hr. The crude mixture of **13** and **14** was then treated with excess ethereal diazomethane, giving **15** and **16** as a thick, brown oil. This was dissolved in dry benzene (50 ml) and added to freshly prepared t-BuOK (11.8 mmol) under N_2. After 5 min, tlc on silica gel (1:1 hexane: ether) showed complete consumption of bromoesters. The mixture was diluted with 10% H_2SO_4 (100 ml), the layers were separated, and the aqueous layer was extracted with ether (3 × 50 ml). The combined organic portions were washed with brine, dried ($MgSO_4$) and concentrated, giving a thick, brown oil. This was dissolved in CH_2Cl_2 (10 ml) and treated with excess ethereal diazomethane. Removal of solvent gave 1.43 g of crude **17**, which was placed onto a column (2 × 60 cm) of silica gel (75 g), slurry-packed in 7:3 hexane: ether. Elution with the same solvent gave 0.863 g (3.12 mmol) of **17**, m.p. 88–90° (47% overall yield from **8**). Three recrystallizations from ether gave the analytical sample, m.p. 90–91°. Found: C, 69.48; H, 7.38. Calc. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. IR (KBr) 1770, 1730 cm^{-1}. NMR ($CDCl_3$) 1.00 (3H, s), 1.08 (3H, s), 3.62 (3H, s), 4.01 (1H, d of d, J = 8, 7), 4.64 (1H, t, J = 8), 5.3 (1H, m). MS *m/e* 276 (M^+).

t-*Butyl* 3-*bromomethyl*-11,11-*dimethyl*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one*-2-*carboxylate* (**18**) and t-*Butyl* 2-*bromomethyl*-11,11-*dimethyl*-5-*oxatricyclo* [7,3,0,$0^{3,7}$] *dodec*-8-*en*-4-*one*-2-*carboxylate* (**19**). A soln of **8** (3.04 g, 20.0 mmol) and bromomethylmaleic anhydride (3.82 g, 20.0 mmol) in CH_2Cl (6 ml) was stirred for 36 hr. The mixture was then diluted with CH_2Cl_2 to a volume of 120 ml and transferred to a Paar bottle. Isobutylene was condensed into the chilled soln (Dry ice) until the total volume was 195 ml, *p*-toluenesulfonic acid (1.0 g) was added, and the bottle was sealed with a rubber stopper and allowed to stand at room temp for 4 days. The bottle was cooled and opened, and the mixture was poured into a well-stirred, two-phase mixture of ether (250 ml) and $NaHCO_3$ aq (150 ml). The layers were separated and the

aqueous layer was extracted with ether (3 × 50 ml). The combined ether portions were passed through a column of neutral alumina (Woelm, activity 2, 100 g). Removal of solvent under reduced pressure gave 6.51 g of **18** and **19** (1:1 mixture) as a red oil. Tlc on silica gel (1:1 hexane:ether) showed overlapping spots, R_f 0.7. The crude mixture of esters was used in the next step (see below). In one experiment crude bromoester (0.571 g) was placed onto a column (2 × 50 cm) of silica gel (65 g), slurry-packed in 9:1 hexane:ether. Elution was begun with the same solvent. Initial fractions contained pure **19** (66.9 mg, white solid). Late fractions gave pure **18** (60.7 mg, colorless oil). Intermediate fractions contained the bulk of the material as mixtures of the bromoesters (346 mg). Three recrystallizations of **19** from hexane–ether gave the analytical sample, m.p. 139–140.5°. Found: C, 57.19; H, 6.92; Br, 20.25 Calc. for $C_{19}H_{27}BrO_4$: C, 57.15; H, 6.82; Br, 20.01. IR (KBr) 1770, 1720 cm^{-1}, NMR ($CDCl_3$) 1.00 (3H, s), 1.10 (3H, s), 1.43 (9H, s), 1.4–1.8 (2H, m), 2.1–2.3 (2H, m), 2.97 (1H, d, J = 6), 3.67 (2H, AB, J_{AB} = 10, δ_{AB} = 24), 4.18 (1H, t, J = 8), 4.53 (1H, d of d, J = 8, 10), 5.5 (1H, m). Compound **18**: IR (film) 1770, 1730 cm^{-1}. NMR ($CDCl_3$) 0.97 (3H, s), 1.10 (3H, s), 1.40 (9H, s), 3.24 (1H, broad s), 4.08 (2H, AB, J_{AB} = 11, δ_{AB} = 46), 4.07 (1H, t, J = 8), 4.51 (1H, t, J = 8), 5.3 (1H, m).

t-Butyl 9,9-dimethyl-3-oxatetracyclo [10,1,0,0^{1,5},0^{7,11}] *tridec-6-en-2-one-12-carboxylate* (**20**). The crude mixture of **18** and **19** (6.51 g) prepared as described above, was dissolved in benzene (90 ml) and a soln of t-BuOK (27.8 mmol, 1.7 equiv.) in t-BuOH (40 ml) was added. After 10 min, tlc on silica gel (1:1 hexane:ether) showed a single spot (R_f 0.5). The mixture was acidified by addition of 2N HCl (7 ml), and the organic layer was decanted from the supersaturated salt soln, which was rinsed twice with ether. The combined organic portions were concentrated and then diluted with ether (500 ml). The soln was passed through a column of neutral alumina (Woelm, activity 2, 60 g). Removal of solvent gave 4.43 g of crude **20** as a red-colored oil. Purification on a column (2.5 × 62 cm) of silica gel (140 g) with 4:1 hexane:ether gave 2.80 g (8.77 mmol) of **20**, m.p. 76–82° (44% yield overall from **8**). Recrystallization from hexane gave 2.27 g of material, m.p. 81–83.5°. Found: C, 71.62; H, 8.22. Calc. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. IR (KBr) 1760, 1720 cm^{-1}. NMR ($CDCl_3$) 1.02 (3H, s), 1.08 (3H, s), 1.38 (9H, s), 1.42 (2H, AB, J_{AB} = 5, δ_{AB} = 100), 3.85 (1H, t, J = 8), 4.52 (1H, t, J = 8), 5.2 (1H, m).

t-Butyl 9,9-dimethyl-2-hydroxy-3-oxatetracyclo [10,1,0,0^{1,5},0^{7,11}] *tridec-6-ene-12-carboxylate* (**21**). To a cooled (−78°) soln of **20** (0.500 g, 1.57 mmol) in toluene (15 ml) was added with vigorous stirring, 2.65 mmol (1.68 equiv) of 20% diisobutylaluminum hydride (in hexane). The mixture was stirred for 4 hr (Dry-ice cooling), and then excess hydride was destroyed by slow addition of a soln of MeOH (2 molar) in hexane. The mixture was diluted with 10% H_2SO_4 (25 ml), the layers were separated, and the aqueous layer was extracted with ether (3 × 25 ml). The combined organic portions were washed with brine, dried (Na_2SO_4) and concentrated, giving 0.504 g of crude **21** as a light yellow oil. This was placed onto a column (1 × 35 cm) of silica gel (15 g), slurry-packed in 7:3 hexane:ether. Elution with the same solvent gave 288 mg (0.897 mmol, 57%) of pure **21** as a colorless oil. IR (film) 3400, 1720 cm^{-1}. NMR ($CDCl_3$) 0.94 (3H, s), 1.08 (3H, s), 1.41 (9H, s), 3.61 (1H, d of d, J = 5, 8), 3.8–4.3 (1H, broad), 4.33 (1H, t, J = 8), 4.88 (1H, broad s), 5.3 (1H, m).

t-Butyl-9,9-dimethyl-2-methoxy-3-oxatetracyclo [10,1,0,0^{1,5},0^{7,11}] *tridec-6-ene-12-carboxylates* (**22** and **23**). The crude hemiacetal (0.746 g) prepared as described above by treatment of **20** (0.744 g, 2.44 mmol) in toluene (25 ml) with 4.10 mmol of diisobutylaluminum hydride (20% in hexane), was dissolved in benzene (20 ml) and MeOH (20 ml), and 2 drops of 2N HCl were added. The mixture was allowed to stand for 15 min, then was concentrated under reduced pressure, giving 0.790 g of crude acetals as a light yellow oil. This mixture was placed onto a column (1.5 × 40 cm) of silica gel (35 g), slurry-packed in 9:1 hexane:ether. Elution with the same solvent gave in early fractions 51.3 mg of pure **22** (white solid). After collection of intermediate fractions containing 225 mg of mixtures of the acetals, 260 mg of pure **23** (colorless oil) was obtained. The total yield of acetals was thus 536 mg (1.60 mmol; 66%). For analysis **22** was recrystallized three times from hexane, m.p. 69–70°. Found: C, 71.83; H, 9.17. Calc. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.02. IR (KBr) 1720 cm^{-1}. NMR ($CDCl_3$) 0.73 (1H, 1/2 of AB, J_{AB} = 5), 0.88 (3H, s), 1.14 (3H, s), 1.44 (9H, s), 3.17 (3H, s), 3.80 (1H, t, J = 8), 4.36 (1H, t, J = 8), 4.60 (1H, s), 5.4 (1H, m). Acetal **23** was purified by careful preparative tlc on silica gel (1:1 hexane:ether). The resulting colorless oil was dried to constant weight at room temp (0.05 mm). Found: C, 71.54; H, 8.99. IR (neat) 1720 cm^{-1}. NMR ($CDCl_3$) 0.90 (3H, s), 1.08 (3H, s), 1.40 (9H, s), 3.28 (3H, s), 3.75 (1H, d of d, J = 8, 3), 4.29 (1H, d of d, J = 8, 6), 4.48 (1H, s), 5.35 (1H, m).

4,4-Dimethyl-10,15-dioxapentacyclo [9,2,2,0^{1,12},0^{2,6},0^{8,12}] *pentadec-6-en-14-one* (**24**). The crude hemiacetal (1.02 g) prepared as described above by treatment of **20** (1.00 g, 3.14 mmol) with diisobutylaluminum hydride in toluene soln was dissolved in cold (−15°) trifluoroacetic acid (25 ml). After 5 min, trifluoroacetic acid was removed under reduced pressure, leaving a dark brown residue. This was placed onto a column (1 × 35 cm) of silica gel (35 g), slurry-packed in 4:1 hexane:ether. Elution with the same solvent gave 493 mg (2.00 mmol, 65%) of **24**, m.p. 78–84°. Two recrystallizations from hexane–ether gave the analytical sample, m.p. 87–88°. Found: C, 73.15; H, 7.39. Calc. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37). IR (KBr) 3050, 1775 cm^{-1}. NMR ($CDCl_3$) 1.01 (3H, s), 1.12 (3H, s), 1.41 (2H, AB, J_{AB} = 5, δ_{AB} = 32), 3.55 (1H, d of d, J = 8, 6), 4.24 (1H, t, J = 8), 5.1 (1H, m), 5.35 (1H, s). MS *m/e* 246 (M+).

12-Carboxy-9,9-dimethyl-3-oxatetracyclo [10,1,0,0^{1,5},0^{7,11}] *tridec-6-en-2-one* (**25**). A soln of **17** (4.28 g, 15.5 mmol) in MeOH (60 ml) and 1.25 N NaOH (62 ml; 5 equiv.) was heated at 90–95° for 6.5 hr under N_2. The cooled mixture (ice bath) was diluted with MeOH (60 ml) and acidified by addition of 1N H_2SO_4 (75 ml). The soln was warmed at 50–55° for 3 hr, cooled and extracted with ether (3 × 60 ml). The combined ether portions were washed with brine, dried ($MgSO_4$) and concentrated, giving 3.88 g (14.8 mmol, 95.5%) of **25**, m.p. 185–187.5°. Two recrystallizations from ether gave the analytical sample, which was dried at 110° (0.1 mm) for 24 hr. Found: C, 68.71; H, 7.14. Calc. for $C_{16}H_{18}O_4$: C, 68.68; H, 6.92. IR (KBr) 3500–2500, 1770, 1710 cm^{-1}. NMR ($CDCl_3$) 1.00 (3H, s), 1.10 (3H, s), 4.01 (1H, d of d, J = 8, 9), 4.64 (1H, t, J = 8), 5.3 (1H, m), 8.4–8.6 (1H, broad). MS *m/e* 262 (M^-).

Etiolactone **24** and *4,4-dimethyl-8-hydroxymethyl-11-oxatetracyclo* [7,3,1,0,0^{2,6}] *tridec-6-en-12-one* (**26**). To a cold (−78°) soln of **25** (3.81 g, 14.5 mmol) in CH_2Cl_2 (800 ml) was added by syringe 42 ml (2.8 equiv.) of diisobutylaluminum hydride soln (20% in hexane). After 3 hr a soln of MeOH (2 molar) in hexane (20 ml; 40 mmol) was added over 20 min. The mixture was allowed to warm to room temp and was diluted with 10% H_2SO_4 (200 ml). The layers were separated and the organic layer was extracted with CH_2Cl_2 (3 × 100 ml). The combined organic portions were washed with brine and dried ($MgSO_4$). Removal of solvent gave 3.47 g of a light yellow oil. This was placed onto a column (2.5 × 60 cm) of silica gel (140 g), slurry-packed in 4:1 hexane:ether. Elution with the same solvent gave 1.13 g (4.60 mmol, 32%) of **24**, m.p. 67.5–70°, identical to that prepared previously. Further elution with ether gave 0.916 g (3.69 mmol, 25%) of **26**. For analysis, **26** was recrystallized four times from hexane–acetone, giving a sample, m.p. 117–118.5°. Found: C, 72.60; H, 8.23. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. IR (KBr) 3350, 1740 cm^{-1}. NMR ($CDCl_3$) 1.02 (3H, s), 1.14 (3H, s), 1.29 (2H, AB, J_{AB} = 4, δ_{AB} = 8), 3.08 (2H, ABX, J_{AB} = 11, δ_{AB} = 20, J_{AX} = 4, J_{BX} = 7), 4.39 (2H, AB, J_{AB} = 10, δ_{AB} = 12), 5.0 (1H, m). MS *m/e* Calc. for $C_{15}H_{20}O_3$: 248.1412. Found: 248.1425.

12-Carbomethoxy-9,9-dimethyl-2-methoxy-3-oxatetracyclo [10,1,0,0^{1,5},0^{7,11}] *tridec-6-ene* (**27**). A soln of **24** (0.500 g, 2.03 mmol) in MeOH (22 ml) and 1.25 N NaOH (6.5 ml, 8.1 mmol) was stirred under N_2 for 2 hr. The mixture was neutralized by addition of 2N HCl and the soln (pH ~ 6) was extracted with CH_2Cl_2 (4 × 25 ml). The combined

organic portions were washed with brine and concentrated. The residue was dissolved in ether (10 ml) and treated with an excess of ethereal diazomethane. Solvent was removed under reduced pressure and the residue was dissolved in MeOH (30 ml) containing 3 drops of conc HCl. The solution was allowed to stand for 5 min, and solvent was again removed, giving 0.577 g of a light yellow oil. Tlc on silica gel (1:1 hexane:ether) showed **27** (R_f 0.6) and starting material (R_f 0.45). The crude product was purified on a column (1 × 40 cm) of silica gel (30 g), with 6:1 hexane:ether, giving 0.469 g (1.61 mmol, 79%) of **27**, m.p. 52–53°. Three recrystallizations from hexane gave the analytical sample, m.p. 51–53°. Found: C, 69.78; H, 8.31. Calc. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. IR (KBr) 1730 cm^{-1}, NMR ($CDCl_3$) 0.82 (1H, $\frac{1}{2}$ of AB, J_{AB} = 5), 0.97 (3H, s), 1.10 (3H, s), 3.20 (3H, s), 3.58 (3H, s), 3.60 (1H, d of d, J = 7, 3), 4.16 (1H, t, J = 7), 4.24 (1H, s), 5.2 (1H, m). MS *m/e* 292 (M^+).

1-*Carbomethoxy*-4,4-*dimethyl*-9-(2,6-*dithiacyclohexyl*)-8-*hydroxymethyltricyclo* [7,1,0,$0^{2,6}$] *dec*-6-*ene* (**29**). Acetal **27** (238 mg, 0.815 mmol) was combined with 2.0 ml of a soln of 1,3-propanedithiol (0.4 molar) in abs $CHCl_3$. To the cooled mixture (ice bath) was added 1.35 ml (2.15 equiv.) of a soln of BF_3 etherate (1.29 molar) in $CHCl_3$. After 30 min the mixture was diluted with 5% $NaHCO_3$ aq (10 ml) and extracted with CH_2Cl_2 (4 × 10 ml). The combined organic portions were washed with 1.25 N NaOH (10 ml) and brine, dried (K_2CO_3) and concentrated, giving 0.310 g of crude mercaptal as a light yellow solid. Recrystallization from hexane–CH_2Cl_2 gave 228 mg or mercaptal, m.p. 104–110°. Preparative tlc on alumina (1:1 hexane:ether) provided an additional 28.5 mg of **29**, giving a total of 257 mg (7.00 mmol, 86%). Four recrystallizations from hexane–acetone gave the analytical sample, m.p. 108.5–110.5°. Found: C, 61.70; H, 7.53; S, 17.45. Calc. for $C_{19}H_{28}O_3S_2$: C, 61.92; H, 7.66; S, 17.40. IR (KBr) 3500, 1700 cm^{-1}. NMR ($CDCl_3$) 0.99 (3H, s), 1.07 (3H, s), 1.45 (2H, AB, J_{AB} = 5, δ_{AB} = 50), 3.6–4.0 (4H, m), 3.71 (3H, s), 4.00 (1H, s), 4.1–4.3 (2H, m), 5.3 (1H, m). MS *m/e* 368 (M^+).

1-*Carbomethoxy*-4,4-*dimethyl*-9-(2,6-*dithiacyclohexyl*-S-*oxide*)-8-*hydroxymethyltricyclo* [7,1,1.$0^{2,6}$] *dec*-6-*ene* (**30**). To a soln of **29** (40.9 mg, 0.11 mmol) in methanol (3 ml) was added a soln of sodium periodate (23.8 mg, 0.11 mmol) in water (1.5 ml). A white ppt of sodium iodate appeared immediately. After 1 hr, the mixture was filtered and concentrated. The solid residue was extracted several times with ether. The combined ether portions were filtered and the solvent was removed, giving 34.2 mg (0.89 mmol, 81%) of **30**, m.p. 196–201°. Recrystallization from hexane–CH_2Cl_2 gave 23.0 mg of crystals, m.p. 202–206.5°. NMR ($CDCl_3$) showed two sulfoxide epimers (1:1 mixture). Tlc on silica gel (8% CH_3OH in CH_2Cl_2) showed two overlapping spots (R_f 0.3). For analysis a sample was recrystallized once from acetone and once from hexane–acetone, giving crystals, m.p. 202–205.5°. Found: C, 58.20; H, 7.22; S, 16.41. Calc. for $C_{19}H_{28}O_4S_2 \cdot 1/2\ H_2O$: C, 57.98; H, 7.42; S, 16.29. IR (KBr) 3350, 1725 cm^{-1}. NMR ($CDCl_3$) 1.02 (3H, s), 1.06 (9H, s), 3.69 (3H, s), 3.73 (3H, s), 3.80 (1H, s), 3.98 (1H, s), 5.3 (1H, m), 5.35 (1H, m).

1-*Carbomethoxy*-4,4-*dimethyl*-9-(2,6-*dithiacyclohexyl*)*tricyclo* [7,1,0,$0^{2,6}$] *deca*-5,7-*diene*-8-*carboxaldehyde* (**31**). CrO_3 (100 mg, 1.00 mmol) was added all at once to dry pyridine (1 ml). Stirring was continued under N_2 for 5 hr, during which time most of the precipitated complex dissolved. A soln of **29** (48.3 mg, 0.136 mmol) in dry pyridine (0.5 ml) was added. After 10 hr, tlc on silica gel (1:1 hexane:ether) showed no further change: starting material (R_f 0.4), a major product (R_f 0.5), and a minor product (R_f 0.3) were seen. Pyridine was removed under reduced pressure, and the red residue was extracted several times with ether. The combined ether portions were filtered through a short column of Celite, and solvent was removed, giving 34 mg of a light yellow oil. This was purified by preparative tlc on silica gel (7:3 hexane:ether—2 developments). The major band (R_f 0.31–0.35) gave 7.2 mg (0.019 mmol, 15%) of **31** as a white solid. Recrystallization from hexane–MeOAc gave a sample, m.p. 165–172°. IR (KBr) 1710, 1670, 1620 cm^{-1}. NMR ($CDCl_3$) 1.10 (3H, s), 1.12 (3H, s), 2.7–3.0 (4H, m), 3.84 (3H, s), 3.5–3.9 (1H, m), 4.46 (1H, s), 5.91 (1H, d, J = 3), 7.14 (1H, s), 10.70 (1H, s). UV (95% C_2H_5OH) 315 nm (10,600). MS *m/e* Calc. for $C_{19}H_{24}O_3S_2$: 364.1167. Found: 364.1164.

t-Butyl-8,9-*di*(*hydroxymethyl*)-4,4-*dimethyltricyclo* [7,1,0,$0^{2,6}$] *dec*-6-*ene*-1-*carboxylate* (**32**) and 4,4-*dimethyl*-1,8,9-*tri*(*hydroxymethyl*)-*tricyclo* [7,1,0,$0^{2,6}$] *dec*-6-*ene* (**33**). Lactone **20** (2.09 g, 6.57 mmol) was treated in toluene soln (as previously described) with diisobutylaluminum hydride, giving 2.17 g of crude **21** as a light yellow oil. This was dissolved in MeOH (10 ml) and $NaBH_4$ (200 mg, 5.35 mmol) was added in small portions with stirring over 5 min. After an additional 10 min, the mixture was diluted with 5% HCl (150 ml) and extracted with ether (4 × 50 ml). The combined organic portions were washed with 5% $NaHCO_3$ aq and brine, dried (Na_2CO_3) and concentrated, giving 2.15 g of a light yellow oil. This was placed onto a column (2 × 50 cm) of silica gel (60 g), slurry-packed in 3:1 hexane:ether. Elution with the same solvent gave 1.40 g (4.35 mmol, 65%) of pure **32** as a colorless oil. Further elution with ether gave 98.5 mg (0.390 mmol, 6.0%) of pure triol **33** as a colorless oil. Both compounds were unstable and satisfactory combustion analyses could not be obtained. **32**: IR (film) 3300, 1725 cm^{-1}. NMR ($CDCl_3$) 0.98 (2H, AB, J_{AB} = 5, δ_{AB} = 29), 1.03 (3H, s), 1.06 3H, s), 1.48 (9H, s), 3.26 (1H, $\frac{1}{2}$ of AB, J_{AB} = 12), 3.6–4.2 (5H, m), 5.3 (1H, m). **33**: IR (film) 3300, 1700 cm^{-1}. NMR ($CDCl_3$) 0.62 (2H, AB, J_{AB} = 4, δ_{AB} = 9), 1.04 (3H, s), 1.05 (3H, s), 3.2–5.0 (9H, m), 5.3 (1H, m).

t-Butyl-8,9-*di*(*chloroformyloxymethyl*)-4,4-*dimethyltricyclo* [7,1,0,$0^{2,6}$] *dec*-6-*ene*-1-*carboxylate* (**34**). Phosgene was condensed into an ice-cold solution of ether (45 ml) until the total volume was 60 ml. Then a soln of **32** (0.970 g, 3.05 mmol) in ether (35 ml) containing quinoline (0.71 ml, 6.10 mmol) was added over 30 min. A white ppt began to form almost immediately. The mixture was stirred for 15 min at 0°, and for 15 min at room temp, and then solvent was removed under reduced pressure. To the white solid residue were added ether (125 ml) and 5% HCl (125 ml), the layers were separated, and the aqueous layer was extracted with ether (3 × 50 ml). The combined ether portions were washed with 5% HCl, 5% $NaHCO_3$ aq and brine, dried (Na_2SO_4) and concenrated, giving 1.24 g (2.78 mmol, 91%) of crude **34** as a light-yellow oil. IR (film) 1775, 1720 cm^{-1}. NMR ($CDCl_3$) 0.97 (1H, $\frac{1}{2}$ of AB, J_{AB} = 6), 1.04 (3H, s), 1.06 (3H, s), 1.46 (9H, s), 4.31 (2H, AB, J_{AB} = 12, δ_{AB} = 27), 4.54 (2H, d, J = 4), 5.1 (1H, m).

t-Butyl marasmate (**35**). Dichloroformate **34** (1.24 g, 2.78 mmol) was dried at room temp (0.3 mm) for 36 hr. Dry dimethylsulfoxide (8 ml) was added by syringe under N_2. Stirring was begun at 15° (water bath) and vigorous evolution of CO_2 was observed. Stirring was continued for 25 min, and then Et_3N (0.88 ml, 6.33 mmol) was added. After 20 min, the mixture was diluted with ice-cold 5% HCl (100 ml) and extracted with ether (3 × 75 ml). The combined organic portions were washed with 5% HCl, 5% and brine, dried (Na_2SO_4), and concentrated, giving 0.915 g of a light yellow oil. The crude product was placed onto a column (2 × 60 ml) of silica gel (65 g), slurry-packed in 6:1 hexane:ether. Elution with the same solvent gave 225 mg (0.708 mmol, 25%) of pure **35**, m.p. 104–107°. Further elution with 5:1 hexane:ether gave 101 mg of **36** and **37** (4:1 mixture). Two recrystallizations of **35** from hexane–EtOAc gave the analytical sample, m.p. 111–115° (evacuated capillary). Found: C, 71.06; H, 8.17. Calc. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. IR (KBr) 1730, 1700, 1675, 1620 cm^{-1}. UV (95% C_2H_5OH) 243 nm (7740). NMR ($CDCl_3$) 1.05 (6H, s), 1.40 (9H, s), 2.26 (1H, $\frac{1}{2}$ of AB, J_{AB} = 5), 6.47 (1H, d, J = 2), 9.45 (1H, s), 9.82 (1H, s).

(±)-*Marasmic acid*. A soln of **35** (85.8 mg, 0.270 mmol) in benzene (5 ml) and trifluoroacetic acid (0.15 ml) was allowed to stand for 30 min. Solvent was removed under reduced pressure, giving 80.2 mg of crude **1**. This was purified by preparative tlc on silica gel (ether), giving 35.2 mg (0.134 mmol, 50%) of marasmic acid. For analysis the acid was recrystalized three times from hexane–EtOAc, giving slender needles, m.p. 171–171.5° (evacuated capillary). Found: C, 68.62; H,

6.99. Calc. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. IR (KBr) 3300, 1770, 1675, 1630 cm^{-1}. UV (95% C_2H_5OH) 239 nm (9220). NMR ($CDCl_3$) 1.04 (3H, s), 1.07 (3H, s), 1.41 (2H, AB, J_{AB} = 5, δ_{AB} − 17), 6.13 (1H, s), 6.50 (1H, d, J − 2), 9.43 (1H, s). MS *m/e* 262 (M^+).

Acknowledgement This work was generously supported by the National Institutes of Health through grant GR01 GM 04229-22.

REFERENCES

[1a]D. Helmlinger, P. de Mayo, M. Nye, L. Westfelt and R. B. Yeats, *Tetrahedron Letters* 349 (1970). [b]S. R. Wilson and R. B. Turner, *J. Org. Chem.* **38**, 2870 (1973).

[2]W. J. Greenlee and R. B. Woodward, preceding paper; for a preliminary account of the present work, see W. J. Greenlee and R. B. Woodward, *J. Am. Chem. Soc.* **98**, 6075 (1976).

[3]R. E. Ireland and R. H. Mueller, *Ibid.* **94**, 5897 (1972).

[4]M. Fetizon and M. Jurion, *Chem. Commun.* 382 (1972); B. M. Trost, M. Preckel and L. M. Leichter, *J. Am. Chem. Soc.* **97**, 2224 (1975); H. W. Chang, *Tetrahedron Letters* 1989 (1972).

[5]T. M. Santosusso and D. Swern, *J. Org. Chem.* **40**, 2764 (1975); L. Skattebol, B. Boulette and S. Solomon, *Ibid.* **32**, 3111 (1967).

[6]K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.* **87**, 5661, 5670 (1965); J. R. Parikh and W. von E. Doering, *Ibid.* **89**, 5505 (1967); J. D. Albright and L. Goldman, *Ibid.* **87**, 4214 (1965); E. J. Corey and C. U. Kim, *Ibid.* **94**, 7586 (1972); D. H. R. Barton, B. J. Garner and R. H. Wightman, *J. Chem. Soc.* 1855 (1964); J. D. Albright, *J. Org. Chem.* **39**, 1977 (1974).

[7]G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Am. Chem. Soc.* **75**, 422 (1953).

[8]V. I. Stenberg and R. J. Perkins, *J. Org. Chem.* **28**, 323 (1963); M. Fetizon, M. Golfier and J.-M. Louis, *Tetrahedron* **31**, 171 (1975).

[9]D. H. R. Barton, B. J. Garner and R. H. Wightman, *J. Chem. Soc.* 1855 (1964).

[10]J. J. Dugan, P. de Mayo, M. Nisbet, J. R. Robinson and M. Anchel, *J. Am. Chem. Soc.* **88**, 2838 (1966).

[11]R. A. Laursen, W.-C. Shen and K. G. Zahka, *J. Med. Chem.* **14**, 619 (1971).

[12]Coupling constants listed are those expected based on the Karplus equation; L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Spectroscopy in Organic Chemistry* (2nd Ed.) p.280. Pergamon Press, Elmsford, N. Y. (1969).