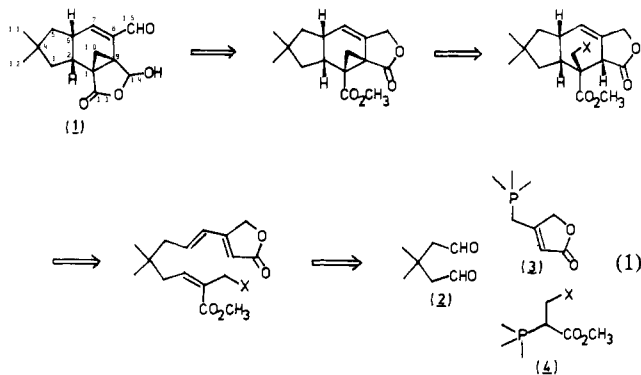


Stereocontrol in the Intramolecular Diels-Alder Reaction. 1. An Application to the Total Synthesis of (\pm) Marasmic Acid

Sir:

The development of the intramolecular Diels-Alder reaction as a basic synthetic strategy has seen rapid growth in the past few years.^{1,2} With the intention of developing a predictive model of stereocontrol and reactivity, we have undertaken basic studies of factors influencing stereocontrol^{3a} and complementary applications to various complex target molecules.

We chose marasmic acid (1), a unique sesquiterpene antibiotic,^{4,5} as a potential target, since its molecular structure seemed to lend itself to a particularly efficient test of the methodology. Retrosynthetic analysis of the molecule as in eq 1 represents a



highly convergent scheme based upon the key synthons 2-4. After our work was under way, the first total synthesis of marasmic acid was completed by Woodward and Greenlee, who employed a different bond construction sequence.⁶

In order to implement the scheme shown in eq 1, we chose monoprotected dialdehyde 5. Aldehyde 5 was readily prepared in five steps in 50-60% overall yield from 3-methyl-2-buten-1-ol by the route shown in Scheme I.^{3,7,8} Aldehyde 5 was then

(1) Reviews: (a) Oppolzer, W. *Synthesis* 1978, 793. (b) *Angew. Chem., Int. Ed. Engl.*, 1976, 16, 10. (c) Carlson, R. G. *Annu. Rep. Med. Chem.* 1974, 9, 270. (d) Brieger, G.; Bennett, J. N. *Chem. Rev.* 1980, 80, 63.

(2) (a) Rousch, W. R. *J. Org. Chem.* 1979, 44, 4008 and references therein. (b) Stork, G.; Morgans, D. J., Jr. *J. Am. Chem. Soc.* 1979, 101, 7110. (c) Stork, G.; Morgans, D. J., Jr. *Tetrahedron Lett.* 1979, 1959. (d) Yamamoto, H.; Sham, H. L. *J. Am. Chem. Soc.* 1979, 101, 1609. (e) Näf, F.; Decorzant, R.; Thommen, W. *Helv. Chim. Acta* 1979, 62, 114. (f) Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* 1978, 100, 6289. (g) Glass, R. S.; Herzog, J. D.; Sobezak, R. L. *J. Org. Chem.* 1978, 43, 3209. (h) Büchi, G.; Henson, A.; Limacher, J. *Ibid.* 1977, 42, 3323; Näf, F.; Decorzant, R.; Thommen, W. *Helv. Chim. Acta* 1977, 60, 1196. (i) Oppolzer, W.; Fehr, C.; Warneke, J. *Helv. Chim. Acta* 1977, 60, 48. For stereochemical studies see: (j) Nader, B. et al. *J. Am. Chem. Soc.* 1980, 102, 1153. (k) White, J. D.; Sheldon, B. G.; Solheim, B. A.; Clardy, J. *Tetrahedron Lett.* 1978, 5189. (l) Parker, K. A.; Adamchuk, M. R. *Ibid.* 1978, 1689. (m) Oppolzer, W.; Frostl, W. *Helv. Chim. Acta* 1975, 58, 590. (n) Oppolzer, W. *Tetrahedron Lett.* 1974, 1001. (o) Gschwend, H. W.; Lee, A. O.; Meier, H.-P. *J. Org. Chem.* 1973, 38, 2169. (p) Gschwend, H. W.; Meier, H.-P. *Angew. Chem.* 1972, 84, 281. (q) Oppolzer, W. *J. Am. Chem. Soc.* 1971, 93, 3836. (r) House, H. O.; Cronin, T. C. *J. Org. Chem.* 1965, 30, 1061.

(3) (a) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* in press. (b) However, it has been observed previously in some cases that even the intermolecular cycloaddition of α -substituted acrylates do not follow the endo rule. See Berson, J. A.; Hamlet, Z.; Mueller, W. A. *J. Am. Chem. Soc.* 1962, 84, 297.

(4) Structural studies: (a) Dugan, J. J.; de Mayo, P.; Nisbet, M.; Robinson, J. R.; Anchel, M. *J. Am. Chem. Soc.* 1966, 88, 2838. (b) X-Ray: Chadwick, P. D.; Sim, G. A. *J. Chem. Soc., Chem. Commun.* 1971, 431.

(5) Previous synthetic studies: (a) Helmlinger, D.; de Mayo, P.; Nye, M.; Westfelt, L.; Yeats, R. B. *Tetrahedron Lett.* 1970, 349. (b) Wilson, S. R.; Turner, R. B. *J. Org. Chem.* 1973, 38, 2870.

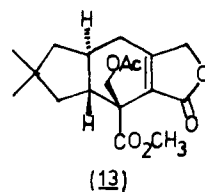
(6) Woodward, R. B.; Greenlee, W. J. *J. Am. Chem. Soc.* 1976, 98, 6075.

(7) All new compounds possessed satisfactory spectral data and correct analytical data by combustion or high resolution mass spectral analysis.

transformed to the (*Z*)-2-bromoacrylate 6 as shown in Scheme II in 90% yield by treatment with (α -bromocarboethoxy)-methyltriphenylphosphorane.^{8,9} Reduction of the ester 6 with DIBAL-H at room temperature in benzene afforded the (*Z*)-bromo alcohol 7 in 90% yield.⁸ Construction of the key *Z*-substituted dienophile unit presumed to be required for production of the cis ring junction after cycloaddition was then accomplished by carbomethoxylation of 7 with Ni(CO)₄ in anhydrous CH₃OH in the presence of NaOCH₃, providing the (*Z*)-hydroxymethyl methyl ester 8 in 95% yield.^{8,10} Ester 8 was then smoothly transformed to aldehyde 9, suitable for coupling to obtain the (*Z,E*)-diene unit, by acetylation (AcCl/Py) and hydrolysis (2 N HCl/HOAc) in 98% overall yield.⁸

The required butenolide phosphonate 10 was prepared as shown in Scheme III in three steps in good overall yield.^{11a} Wadsworth-Emmons coupling of 9 with butenolide phosphonate 10 in DMF then proceeds smoothly at -5-0 °C, affording cleanly the (*Z,E,Z*)-triene 11 in ~80% yield.^{3,8,11b}

The key cycloaddition was best conducted by heating 11 at 200 °C for 0.5 h in toluene.¹² Under these conditions a separable mixture of two cycloadducts was produced in the ratio of ~1:1 (92%).^{13,14} The structures of the adducts were assigned as *cis*-12 (mp 128-129 °C) (Scheme IV) and *trans*-13 (mp 145.5-146.5



(8) Partial spectral data: 5: IR (cm⁻¹) 2720, 1720; NMR δ 9.77 (t, *J* = 3 Hz, 1), 4.47 (t, *J* = 5 Hz, 1), 3.27 (s, 6), 2.28 (d, *J* = 3 Hz, 2), 1.63 (d, *J* = 5 Hz, 2), 1.77 (s, 6). 6: IR (cm⁻¹) 1727, 1630; NMR δ 7.33 (t, *J* = 7 Hz, 1), 4.50 (t, *J* = 5 Hz, 1), 4.35 (q, *J* = 7 Hz, 2), 3.35 (s, 6), 2.39 (d, *J* = 7 Hz, 2), 1.62 (d, *J* = 5 Hz, 1), 1.33 (t, *J* = 7 Hz, 3), 1.02 (s, 6). 7: IR (cm⁻¹) 3450; NMR δ 6.18 (t, *J* = 8 Hz, 1), 4.57 (t, *J* = 5 Hz, 1), 4.33 (s, br, 2), 3.40 (s, 6), 2.20 (t, *J* = 8 Hz, 2), 1.62 (d, *J* = 5 Hz, 2), 0.96 (s, 6). 8: IR (cm⁻¹) 3450, 1732, 1667; NMR δ 6.37 (t, *J* = 9 Hz, 1), 4.52 (t, *J* = 5 Hz, 1), 4.37 (m, 2), 3.82 (s, 3), 3.35 (s, 6), 2.55 (m, 3), 1.6 (d, *J* = 5 Hz, 2), 1.0 (s, 6). 9: IR (cm⁻¹) 2735, 1742, 1720, 1655, 1232; NMR δ 9.76 (t, *J* = 3 Hz, 1), 6.37 (t, *J* = 8 Hz, 1), 5.10 (s, br, 2), 3.78 (s, 3), 2.7-2.0 (m, 4), 2.03 (s, 3), 1.0 (s, 6). 11: IR (cm⁻¹) 1648, 1597, 1230; NMR δ 7.15 (t, *J* = 8 Hz, 1), 6.40 (m, 2), 5.92 (s, br, 1), 5.07 (s, br, 2), 4.87 (d, *J* = 4 Hz, 2), 3.97 (s, 3), 2.7-2.08 (m, 4), 2.07 (s, 3), 1.00 (s, 6). 14: IR (cm⁻¹) 1737 (br), 1675; NMR δ 4.73 (s, 2), 4.63 (s, 2), 3.70 (s, 3), 2.6-1.0 (m, 8), 2.0 (s, 3), 1.06 (s, 3), 1.02 (s, 3). 13: IR (cm⁻¹) 1750 (br), 1667; NMR δ 4.83 (s, 2), 4.73 (s, 2), 3.77 (s, 3), 2.6-1.0 (m, 8), 2.03 (s, 3), 1.10 (s, 3), 1.05 (s, 3). 12: IR (cm⁻¹) 1770, 1730, 1220; NMR δ 5.77 (s, br, 1), 4.87 (m, 2), 4.63 (s, br, 2), 3.67 (s, 3), 2.10 (s, 3), 1.03 (s, br, 6). 15: IR (cm⁻¹) 3500, 1755, 1730, 1680; NMR δ 4.80 (s, br, 2), 4.12 (dd, *J*₁ = 10 Hz, *J*₂ = 4 Hz, 1), 3.75 (s, 3), 3.42 (dd, *J*₁ = 10 Hz, *J*₂ = 4 Hz, 1), 1.17 (s, 3), 1.07 (s, 3). 16: IR (cm⁻¹) 1755, 1738, 1685, 1370, 1180; NMR δ 4.85 (s, br, 2), 4.68 (AB, *J* = 10 Hz, 2), 3.77 (s, 3), 3.00 (s, 3), 1.17 (s, 3), 1.07 (s, 3). 17: IR (cm⁻¹) 3115, 1790, 1737, 1270, 1155; NMR δ 6.82 (d, *J* = 2 Hz, 1), 3.76 (s, 3), 2.08 (d, *J* = 5 Hz, 1), 1.75 (d, *J* = 5 Hz, 1), 1.10 (s, 3), 1.00 (s, 3).

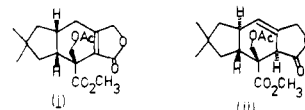
(9) Denney, D. B.; Ross, S. T. *J. Org. Chem.* 1962, 27, 998.

(10) Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc.* 1969, 91, 1233.

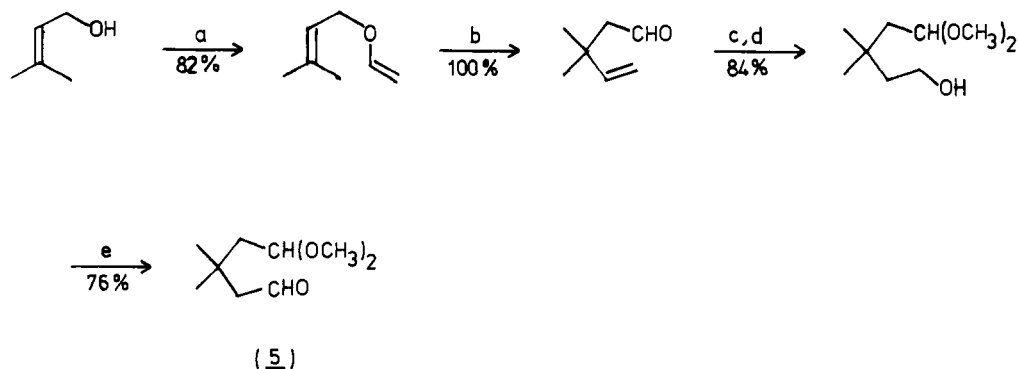
(11) (a) Another route to (bromomethyl)butenolide (Scheme III) was reported after our studies were completed; Sum, F. W.; Weiler, L. *J. Am. Chem. Soc.* 1979, 101, 4401. (b) Yields (20-70%) for this reaction were found to be erratic when DME, the commonly employed solvent for the Wadsworth-Emmons coupling, was utilized. When the reaction was conducted in DMF, the process occurred much faster and afforded pure products in reproducibly high yields.

(12) This reaction was conducted at a variety of temperatures from 110-200 °C with minimal variance in the product ratio. The higher temperature was preferred owing to the short reaction time required which minimized byproduct formation.

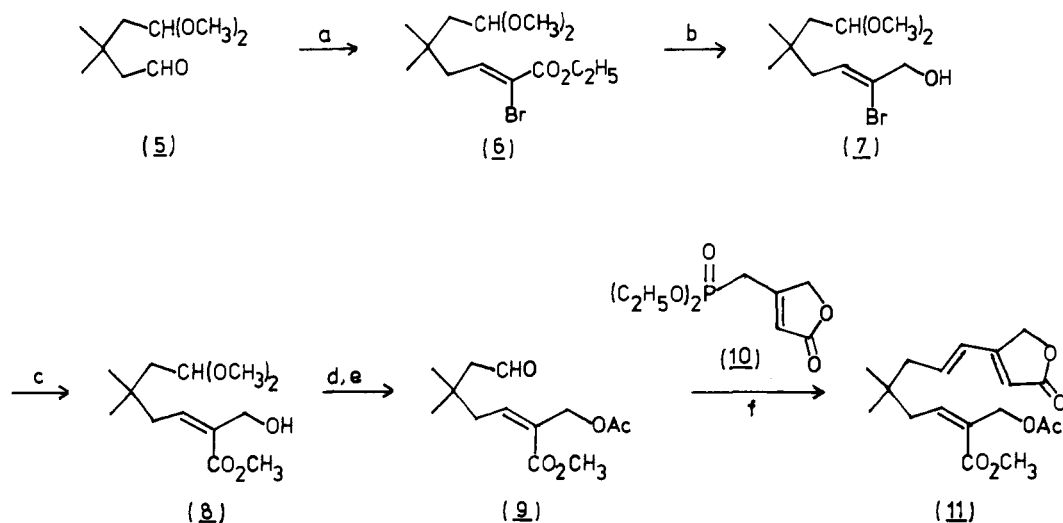
(13) Traces of the conjugated *cis* adduct i and nonconjugated *trans* adduct ii were also detected. None of adduct ii was ever isolated due to rapid isomerization into conjugation during attempted purification.



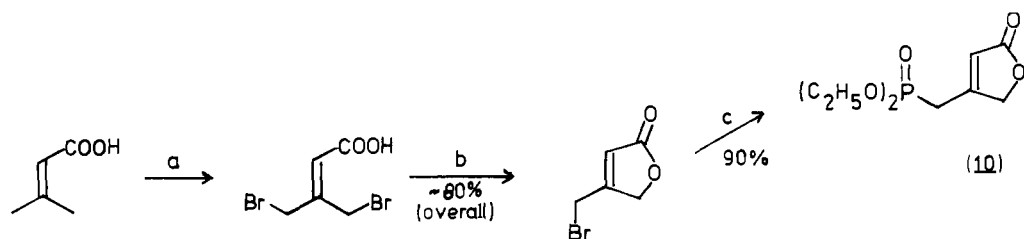
(14) The formation of 13 must occur by cyclization of 11 via the usually disfavored exo transition state due to nonbonded interactions between the allylic methylene and the H on the γ carbon of the diene segment.

Scheme I^a

^a Reagents: (a) $\text{Hg}(\text{OAc})_2/\text{CH}_2=\text{CHOC}_2\text{H}_5$ (excess), Δ , 10 h; (b) reflux (1 atm)/24 h; (c) $\text{CH}_3\text{OH}/\text{HCl}$; (d) $\text{BH}_3\cdot\text{THF}/\text{H}_2\text{O}_2/3\text{N NaOH}$; (e) $\text{CrO}_3\text{-}2\text{py}/\text{CH}_2\text{Cl}_2$, 25°C , 20 min.

Scheme II^a

^a (a) $\text{Ph}_3\text{P}=\text{CBrCO}_2\text{C}_2\text{H}_5/\text{PhH}$, Δ ; (b) DIBAL-H (2.5 equiv)/ PhH , 25°C , 2 h; (c) $\text{Ni}(\text{CO})_4$ (4 equiv)/ NaOCH_3 (1.5 equiv)/anhyd CH_3OH , 50°C , 2.5 h; (d) $\text{CH}_3\text{COCl}/\text{pyridine}$, $0^\circ\text{C}/1\text{ h}$; (e) $2\text{N-H}_2\text{SO}_4/\text{HOAc}$, 0°C , $\sim 2\text{ h}$; (f) NaH/DMF , $-5\text{--}0^\circ\text{C}$, 0.5 h.

Scheme III^a

^a (a) *N*-Bromosuccinimide (2.2 equiv)/ CCl_4 ; (b) $\text{NaOH}/\text{H}_2\text{O}$, room temperature; (c) $(\text{CH}_3\text{CH}_2\text{O})_3\text{P}$, Δ .

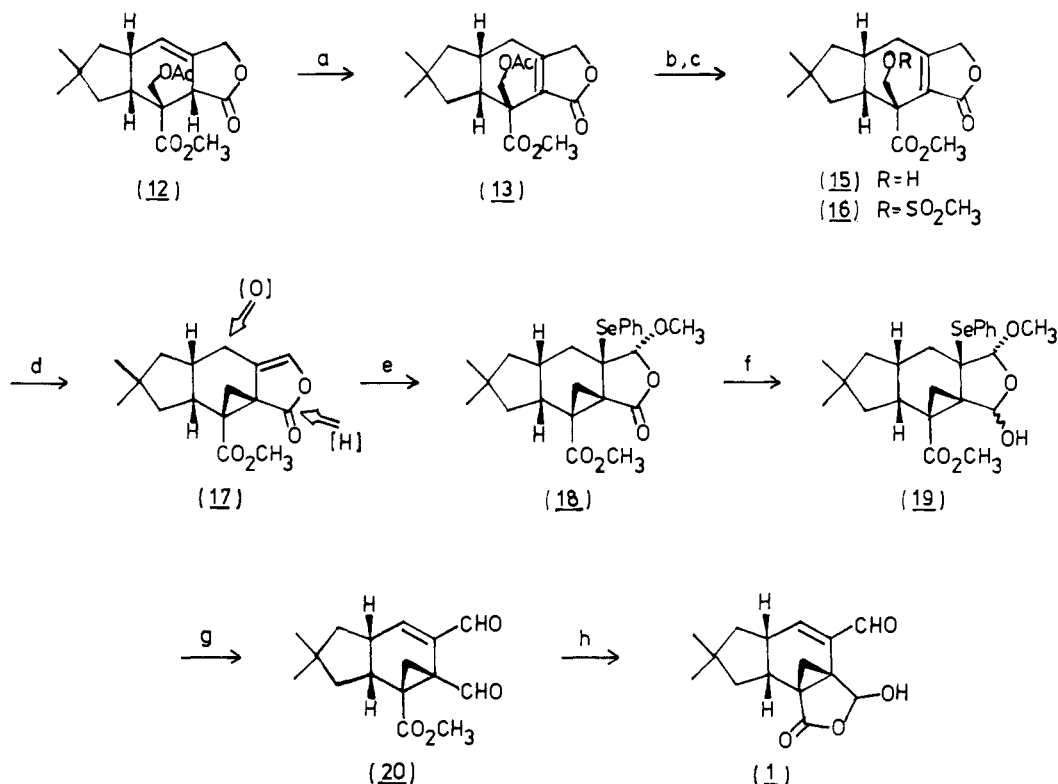
$^\circ\text{C}$) on the basis of NMR spectral data and further confirmed by conversion to (\pm)-marasmic acid⁶ (vide infra). The presence of traces of acid was found to increase the proportion of the trans isomer **13** to $\sim 3:1$. These results suggest that the endo rule, which is not even generally applicable for prediction of the stereochemical outcome for highly substituted dienophiles in intermolecular reactions, is also not the primary determinant in intramolecular reactions, and an alternate model must be developed.^{3b}

With lactone **12** readily available, its conversion to **1** was investigated. This process was initiated by exposure of lactone **12** to $\text{KO-}t\text{-Bu}$ in ether at 0°C , resulting in quantitative isomerization of **12** to the conjugated lactone **14** (Scheme IV).¹⁵ Closure of the cyclopropane ring was then accomplished by initial trans-

formation of lactone **14** to crystalline alcohol **15** (mp $186\text{--}187.5^\circ\text{C}$) in quantitative yield by treatment with *p*-TsOH in methanol at reflux, followed by conversion to the foamy mesylate **16** ($\text{CH}_3\text{SO}_2\text{Cl}/\text{NEt}_3$).⁸ The mesylate without further purification was exposed to DBU (1.5 equiv) at 65°C in THF for 8 h, providing the oily cyclopropane lactone **17** (NMR δ 6.82 (d, $J = 2\text{ Hz}$, 1), 2.08 (AB d, $J = 5\text{ Hz}$, $\Delta\nu = 15\text{ Hz}$), 1.75 (AB d, $J = 5\text{ Hz}$, $\Delta\nu = 15\text{ Hz}$)) in $>90\%$ yield.⁸ The magnitude of the separation of the cyclopropane AB quartet provided further evidence for assignment of **17** to the marasmate family.¹⁶ Lactone **17** is the sole product of kinetic control even under conditions conducive to enolate equilibration ($\text{KO-}t\text{-Bu}/t\text{-BuOH}$). The kinetic acidity of the allylic hydrogens adjacent to oxygen is highest, and cyclization ensues rapidly apparently precluding equilibration.¹⁷

(15) Since a more facile separation of **13** and **14** was possible, this isomerization typically was conducted on the mixture of **12** and **13**, and then separation of conjugated isomers **13** and **14** was effected by column chromatography or on a larger scale using the Waters Prep 500 high-performance LC system (SiO_2).

(16) The values for separation (δ AB) of the cyclopropane protons in the marasmate series are typically much smaller (15–25 Hz) than those in the isomarasmate series (30–70 Hz); see ref 4a and 5a.

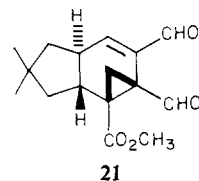
Scheme IV^a

^a (a) KOtBu/ether, 0 °C, 0.5 h; (b) *p*-TsOH (cat)/CH₃OH, 65 °C, 12 h; (c) CH₃SO₂Cl (1.1 equiv)/N(CH₂CH₃)₃ (1.5 equiv)/CH₂Cl₂, -5 °C, 0.5 h; (d) DBU (1.5 equiv)/THF, 65 °C, 8 h; (e) PhSeBr (1 equiv)/CH₃OH, room temperature, 2 h; (f) DIBAL-H (5 equiv)/PhCH₃-THF (1:1), -78 °C, 12 h; (g) MCPBA (1 equiv)/CH₂Cl₂, -78°-room temperature, then room temperature 4.5 h; (h) BBr₃/CH₂Cl₂, -20 °C, 4.5 h.

With key cyclopropane lactone (17) in hand, conversion to marasmic acid (1) only requires adjustment of the oxidation state at C-7 (oxidation) and at C-14 (reduction). This transformation involves creation of the sensitive ene-dial system, and we therefore sought to develop methodology which would permit creation of this system under mild and nearly neutral conditions. Treatment of the enol lactone 17 with phenylselenium bromide in methanol affords the regioselective trans addition of the elements of PhSeOCH₃ from the least hindered face of the molecule, providing lactone methyl ether 18 (mp 103 °C) (NMR: δ 5.78 (s, 1), 3.72 (s, 3), 3.50 (s, 3), 1.10, (s, 3), 1.03 (s, 3)) in 92% yield.¹⁸ Selective reduction of the γ -butyrolactone of 18 was then accomplished by treatment with DIBAL-H at -78 °C in PhCH₃-THF, affording the lactol ether 19 (95%) which was converted directly to (\pm)-methyl marasmate (20) (mp 62-63 °C) by exposure to MCPBA at -78 °C followed by warming to room temperature for 4.5 h (~77% yield overall from 18).^{19,20} The (\pm)-methyl marasmate

was identical with natural (+)-methyl marasmate by TLC, IR, NMR (60 and 300 MHz), and mass spectral criteria.²¹ (\pm)-Methyl marasmate was then converted to (\pm)-marasmic acid (1) (mp 171-171.5 °C) in 50% yield upon treatment with BBr₃ in CH₂Cl₂ at -20-0 °C for 4.5 h.⁶

For the purpose of the production of marasmic acid (1), it should be noted that trans adduct 13 also possesses the correct stereorelationship between C-1 and C-2 for conversion to the natural product. We have indeed established that the same series of transformations outlined in Scheme IV, when applied to 13, affords the trans analogue of methyl marasmate (21, viscous oil)



in comparable overall yield. The stereochemistry of the ring junction of 21 is then adjusted to cis after treatment with BBr₃ in CH₂Cl₂ by conversion to the enol acetate (CH₂=C(CH₃)-OAc/H⁺) and hydrolysis also providing (\pm)-marasmic acid (1).⁴ Thus, with the conversion of both adducts 12 and 13 to 1, this process represents an efficient synthetic route to marasmic acid and related substances.

The implications of the cyclization of triene 11 are clear. Secondary orbital interactions are energetically insufficient to overcome unfavorable nonbonded interactions in the transition state leading to the cis isomer.²² The general preference for production of trans-hydrindenes is becoming well established,^{2a}

(21) We thank Professor de Mayo for providing an authentic sample of (+)-marasmic acid for comparison.

(22) The difference in the ΔG^\ddagger leading to the two diastereomeric transition states (cis vs. trans) must be about 0 in the case of 11. This implies that secondary orbital effects are ≥ 1.25 kcal/mol and equal to the nonbonded interactions in this case.

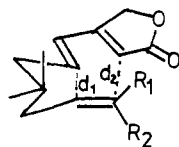
(17) This may be due to two factors: (a) better alignment of the C-H bond with the π system; (b) reflection of the stability of the alkoxyfuran enolate structure making the transition state more productlike. The former is more likely since proton transfers are generally considered to have an early transition state, reflecting a more reactantlike structure. We believe cyclization is faster than enolate equilibration, under all conditions, and deuterium incorporation studies are under way to verify this.

(18) Sharpless, K. B.; Lauer, R. F. *J. Org. Chem.* 1974, 39, 429.

(19) This conversion requires the presence of *m*-chlorobenzoic acid as catalyst to occur smoothly at room temperature.

(20) The conditions for conversion of 19 to 20 via the selenoxide bear further comment. Thermolysis of the crude selenoxide (obtained by oxidation of 19 with *m*-ClC₆H₄CO₃H at -78 °C) in refluxing hexane, after previously quenching the acids present by addition of triethylamine, resulted in recovery of ~80% of the selenoxide unchanged, accompanied by small amounts of dialdehyde 20. It was subsequently found that elimination, in this case, was catalyzed by the *m*-chlorobenzoic acid present which induced opening of the lactol ring with expulsion of methanol. Rapid thermal syn elimination of the resulting α -phenylselenoxy aldehyde then results. The alignment of the bonds for syn elimination in 19 is not particularly favorable (dihedral angle ~30°); however, upon opening the lactol ring, a substantial increase in flexibility occurs as well as more favorable electronics due to the generation of an adjacent carbonyl group.

and the data here and others from our laboratories^{3a} have established that relatively small changes in this tendency occur upon manipulation of the steric bulk or electronic characteristics of the activating groups. Nonbonded interactions and conformational preferences within the connecting chain appear dominant.^{2a} One possible explanation for this effect is that cycloaddition reactions of this type proceed through rather unsymmetrical transition states.²³ In the case of **11**, this would result in enhancement of any nonbonded interactions in the connecting chain at the expense of other nonbonded and electronic (secondary orbital) interactions in other regions of the molecule due to a significantly shorter distance d_1 vs. d_2 in the transition state (**22**).



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The implications of this analysis remain to be fully tested, and additional efforts are in progress to attempt to further influence the stereochemical outcome of the key intramolecular Diels-Alder cyclization and to develop a good predictive model for stereocontrol in these processes. Results of these investigations will be reported in due course.

Acknowledgment. This investigation was supported by research grants from the National Institutes of Health (GM 25982) and the National Science Foundation (CHE-78-07525), to whom we are extremely grateful.

(23) Cycloaddition by a concerted but nonsynchronous mechanism involving an unsymmetrical transition state has been suggested previously: Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4092. Bond formation leads at the termini having the largest coefficient, which in our case results in a smaller distance between the reacting centers linked by the connecting chain at the transition state, magnifying any nonbonded interactions arising from atoms in the chain.

(24) (a) Fellow of the Alfred P. Sloan Foundation (1976-1980). (b) Recipient of a Research Career Development Award (CA-00273) from the National Cancer Institute of the National Institutes of Health.

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Received April 21, 1980

Structures of the Bacteriochlorophyll *c* Homologues: Solution to a Longstanding Problem

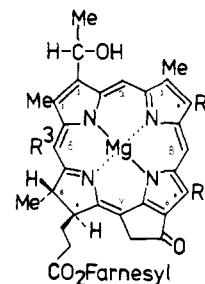
Sir:

The bacteriochlorophylls *c* and *d* are major photosynthetic pigments found in certain strains of green sulfur bacteria. There is general agreement about the structures assigned to the homologous group of six pigments in the bacteriochlorophyll *d* series,^{1,2} but despite a large amount of skilled work, the structures postulated for the fractions (or bands) which constitute the bacteriochlorophylls *c* have been the subject of continual dispute and controversy since 1965. These bacteriochlorophylls were isolated by Purdie and Holt³ and then separated as the pheophorbides into six homologous chromatographic bands. Structures

(1) Holt, A. S. In "The Chemistry and Biochemistry of Plant Pigments"; Goodwin, T. W., Ed.; Academic Press: New York, 1965; pp 3-28.

(2) Archibald, J. L.; Walker, D. M.; Shaw, K. B.; Markovac, A.; MacDonald, S. F. *Can. J. Chem.* **1966**, *44*, 345-362.

(3) Purdie, J. W.; Holt, A. S. *Can. J. Chem.* **1965**, *43*, 3347-3353.



A	BAND	R ¹	R ²	R ³	%AGE
	1	i-Bu	Et	Et	0.5%
	2	i-Bu	Et	Me	0.5%
	3	n-Pr	Et	Et	2.0%
	4	n-Pr	Et	Me	16.0%
	5	Et	Et	Me	71.0%
	6	Et	Me	Me	10.0%

B	BAND	R ¹	R ²	R ³	CONFIG. AT POSN. 2	%AGE
	1	i-Bu	Et	Me	S	4.5%
	2	i-Bu	Et	Me	R	0.1%
	3	n-Pr	Et	Me	S	5.3%
	4	n-Pr	Et	Me	R	18.3%
	5	Et	Et	Me	R	71.7%
	6	Et	Me	Me	R	0.2%

Figure 1. Structural proposals and percentage compositions for the bacteriochlorophylls *c*: (A) due to Holt, Purdie, and Wasley;³ (B) from the work described in the present paper. Percentage compositions here were obtained from high-performance LC separations,¹³ assuming equal extinction coefficients for all the bands at 405 nm.

were assigned³ after extensive degradative work, but following mass spectrometric determinations,⁴ the assignments for bands 1 and 2 and for bands 3 and 4 were interchanged to give those shown in Figure 1A.⁵ Bands 1 and 2 and bands 3 and 4 were clearly chromatographically different, so meso ethyl substituents were proposed⁶ for bands 1 and 3; since samples of these materials were no longer available, it was not possible to check these proposals by mass spectrometry. However, on the basis of synthetic⁷ and biosynthetic^{8,9} work, the presence of meso ethyl groups in the bacteriochlorophylls *c* has never been acceptable to us. There is, however, no doubt that the meso alkyl substituent is located^{2,5,8,10-12} at the δ position.

As a result of achieving excellent reverse-phase high-performance LC separations of the methyl bacteriopheophorbide *c* mixture^{13,14} and a synthesis of optically pure methyl bacteriopheo-

(4) Smith, K. M. Ph.D. Thesis, University of Liverpool, 1967.

(5) Holt, A. S.; Purdie, J. W.; Wasley, J. W. F. *Can. J. Chem.* **1966**, *44*, 88-93.

(6) Structural assignments were made⁵ on the basis of degradation to maleimides, but the pairs of bands 1 and 2 and 3 and 4 gave the same maleimides. It was therefore deduced that the differences between bands 1 and 2 and 3 and 4 must be at the meso positions which were lost as CO₂ in the CrO₃/HOAc degradation. Hence, meso ethyl groups were deduced for bands 1 and 3.

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