pressure. Chromatography on silica gel eluting with 12% EtOAc in hexanes afforded 119 mg (90%) of methoxymethyl ether **19a**, a colorless oil. The ^1H NMR and infrared spectra of this material were identical with those of an authentic sample provided by Professor Ireland.[3]

1β-Methyl-2α-[(*E*)- and -(*Z*)-2-butenyl]-5α-[(*tert*-butyldimethylsilyl)oxy]-1,2,4aβ,5,6,7,8,8aα-octahydronaphthalene-1α-carboxaldehydes (34 and 35). To a stirred, cooled (−45 °C) solution of 191 mg (1.0 mmol) of CuI in 2 mL of dry THF and 1 mL of dry Me_2S was added 3.6 mL (1.80 mmol) of a 0.5 M solution of a 12:88 mixture of (*E*) and (*Z*)-2-butenyllithium in Et_2O. The mixture was stirred at −45 °C for 30 min and cooled to −78 °C whereupon 146 mg (0.5 mmol) of dienal **8** in 1 mL of dry THF was added. The mixture was stirred at −78 °C for 14 h, 1.0 mL (7.9 mmol) of Me_3SiCl was added and the reaction mixture was allowed to warm to 23 °C over 2 h. The mixture of silyl enol ethers was hydrolyzed at 23 °C by stirring for 10 min with 10 mL of 10% aqueous HCl. The mixture was diluted with Et_2O and washed with 10% NH_4OH, H_2O, and brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure and chromatography on silica gel eluting with 5% EtOAc in hexanes afforded 162 mg (93%) of a mixture of four aldehydes (**32**/**33** and their C1 epimers); IR (film) ν 3000, 2940, 2900, 2690, 1720, 1460, 1440, 1375, 1255 cm^{-1}. Anal. Calcd for $C_{21}H_{36}O_2Si$: C, 72.36; H, 10.41. Found: C, 72.14; H, 10.48.

To a stirred solution of 50 mg (0.14 mmol) of the aldehyde mixture in 3 mL of dry THF at 23 °C was added 250 μL (0.16 mmol) of 1.64 M potassium hexamethyldisilazide in toluene. After stirring at 23 °C for 1 h, the solution was cooled to −78 °C and treated with 62 μL (1.0 mmol) of methyl iodide. The mixture was allowed to warm to 23 °C over 3 h, diluted with 15 mL of Et_2O, washed with saturated aqueous NH_4Cl, H_2O, and brine, and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure and chromatography on silica gel eluting with 1% EtOAc in hexanes afforded 18 mg (35%) of aldehyde **34** and 32 mg (63%) of aldehyde **35** as colorless oils.

34: IR (film) ν 3010, 2920, 2845, 2700, 1720, 1460, 1380, 1260 cm^{-1}; ^1H NMR (400 MHz) δ 1.01 (s, 3 H, C-1 CH_3), 1.45 (3H, dd, J = 1.5, 8.4 Hz, vinyl CH_3), 1.78 (3 H, bs, vinyl CH_3), 3.02 (1 H, m, H2), 4.11 (1 H, bs, H5), 5.35 (2 H, m, H3, butenyl H), 5.61 (1 H, bd, J = 10.0 Hz, H4), 9.34 (1 H, s, CHO). Anal. Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.60; H, 10.63.

35: IR (film) ν 3010, 2915, 2845, 2720, 1720, 1470, 1450, 1380, 1265 cm^{-1}; ^1H NMR (400 MHz) δ 0.98 (3 H, s, C1 CH_3), 1.57 (6 H, m, vinyl CH_3's), 3.30 (1 H, m, H_2), 4.07 (1 H, bs, H5), 5.70–5.40 (3 H, m, vinyl H's), 10.0 (1 H, s, CHO). Anal. Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.72; H, 10.60.

Acknowledgment. Financial support from the National Institutes of Health (National Cancer Institute, Grant CA34247) is gratefully acknowledged. We thank the South Carolina National Science Foundation Regional Nuclear Magnetic Resonance Center for cooperation in obtaining high field ^1H NMR spectra. We are grateful to Professor R. E. Ireland for spectra of his chlorothricin degradation product.

Registry No. (±)-**2**, 101492-67-5; **2** (lactol), 101492-68-6; (±)-**3**, 101492-69-7; (±)-**4**, 101492-70-0; (±)-**5**, 101492-71-1; (±)-**6**, 101492-72-2; (±)-**7**, 101492-73-3; (±)-**7** (piperidine enamine), 101492-74-4; (±)-**7** (phenylseleno deriv.) (isomer 1), 101492-75-5; (±)-**7** (phenylseleno deriv.) (isomer 2), 101627-02-5; (±)-**8**, 101492-76-6; (±)-**9**, 101492-77-7; (±)-**10**, 101627-03-6; (±)-**11**, 101492-78-8; (±)-**13**, 101492-79-9; (±)-**14**, 101492-80-2; (±)-**15**, 101492-81-3; (±)-**16**, 101492-82-4; (±)-**17**, 101492-83-5; (±)-**18**, 101492-84-6; (±)-**19**, 101627-04-7; **21**, 101492-91-5; **22**, 101492-92-6; **23**, 101492-93-7; **24**, 101492-94-8; (±)-**25**, 101492-95-9; **25** (lactol), 101492-96-0; (±)-**26**, 101492-97-1; (±)-**27**, 101492-98-2; (±)-**28**, 101492-99-3; (±)-**29**, 101493-00-9; (±)-**30**, 101493-01-0; (±)-**31**, 101493-02-1; (±)-**32** (isomer 1), 101492-85-7; (±)-**32** (isomer 2), 101492-87-9; (±)-**33** (isomer 1), 101492-86-8; (±)-**33** (isomer 2), 101492-88-0; (±)-**34**, 101492-89-1; (±)-**35**, 101492-90-4; $Ph_3PCHCOOEt$; 4-bromo-1,1-diethoxybutane, 78668-96-9; 2,4-pentadienal, 764-40-9; 1-lithio-4-pentene, 54313-25-6; methyl 4-(diethylphosphono)crotonate, 67629-62-3; chlorothricin, 34707-92-1.

Condensation of Long-Chain α-Phosphono Carboxylates with Aldehydes

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The condensation of several long-chain α-phosphono carboxylates with propanal was examined as a prototype route to trans and cis α-substituted conjugated esters. With the diisopropylphosphono and the dimethylphosphono bis-homogeranic esters A6 and A7, the trans product predominated by ca. 9:1. A similar trend was observed with the diisopropyl and dimethyl α-phosphono-ω-undecylenates B3 and B4. The bis(trifluoroethyl) α-phosphono-ω-undecylenate B5 afforded the cis product B11 as the major isomer with 8:1 stereoselectivity. Condensations of the α-(triphenylphosphorylidene)-ω-dodecenylate C3 with several representative aldehydes gave only trans products within the limits of detection. Thus, α-phosphorylidene esters show uniformly high trans stereoselectivity regardless of α-alkyl substitution. The phosphonates, on the other hand, show markedly diminished stereoselectivity when long-chain α-substituents are present.

Pursuant to synthetic investigations on cembranoid natural products we required both trans and cis conjugated esters such as A8 and A10 with long-chain functionalized α-substituents.[1] A simple route to both intermediates seemed possible on the basis of Nagaoka and Kishi's findings that Horner–Wadsworth–Emmons condensation of α-phenyl propionaldehyde with ethyl α-(diisopropylphosphono)propionate leads mainly to the trans conjugated ester whereas methyl or ethyl α-(dimethylphosphono)propionate afford primarily the cis isomers.[2] Ratios of 9:1 or better were reported with KO-*t*-Bu as the base in THF at −78 °C.

The requisite phosphonates A6 and A7 for our intended application were easily prepared starting with alcohol A1.[3] Oxidation with MnO_2 afforded aldehyde A2 whose homologation to alcohol A4 was effected via Wittig condensation and hydroboration–oxidation. Alkylation of sodio

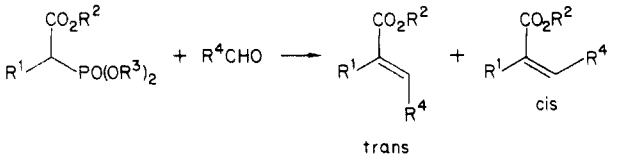
(1) Marshall, J. A.; Cleary, D. G. *J. Org. Chem.*, in press. Cleary, D. G. *The Synthesis of 7(8)-Desoxyasperdiol and Related Studies*, PhD. Thesis, University of South Carolina, August 1985, pp 62–84. For a review of cembranolide natural products, see: Weinheimer, A. J.; Chang, C. W. J.; Matson, J. A. *Fortschr. Chem. Org. Naturst.* **1979**, *36*, 286.

(2) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

(3) Corey, E. J.; Tius, M. A.; Das, J. *J. Am. Chem. Soc.* **1980**, *102*, 1742.

0022-3263/86/1951-1735$01.50/0

Table I. Horner–Wadsworth–Emmons Condensations of α-Phosphono Esters



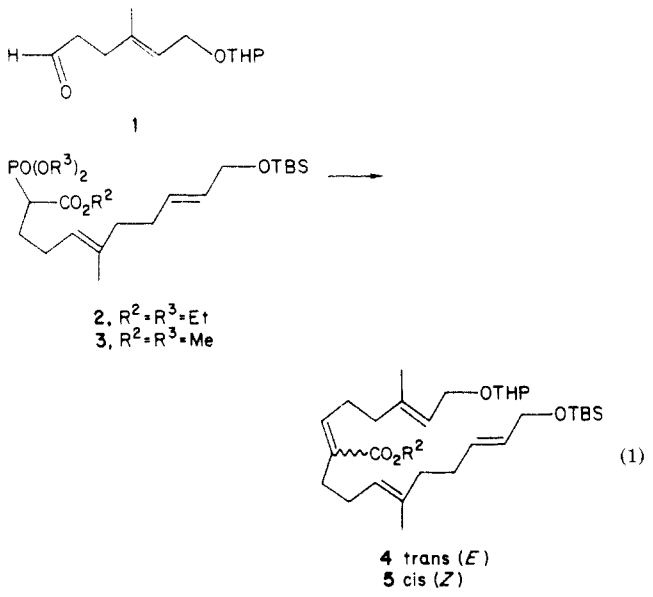
entry	R^1	R^2	R^3	R^4	conditns[a]	yield (%)	trans:cis
1	*b*	Et	*i*-Pr	Et	A[c]	59	90:10[d]
2	*b*	Me	Me	Et	A[c]	48	85:15[d]
3	*e*	Et	Et	*f*	A	66	85:15[d]
4	*e*	Et	Et	*f*	B	73	60:40[d]
5	*e*	Me	Me	*f*	B	80	55:45[d]
6	CH_2=$CH(CH_2)_9$	Me	*i*-Pr	Et	A	40	81:19[g]
7	CH_2=$CH(CH_2)_9$	Me	Me	Et	A	77	84:16[g]
8	CH_2=$CH(CH_2)_9$	Me	Me	Et	B	62	73:27[g]
9	CH_2=$CH(CH_2)_9$	Me	Me	*n*-C_8H_{17}	A[h]	99	84:16[g]
10	CH_2=$CH(CH_2)_9$	Me	Me	*n*-C_8H_{17}	A	72	85:15[g]
11	CH_2=$CH(CH_2)_9$	Me	Me	*n*-C_8H_{17}	C	96	80:20[g]
12	CH_2=$CH(CH_2)_9$	Me	Me	*n*-C_8H_{17}	B	54	72:28[g]
13	CH_2=$CH(CH_2)_9$	Me	CF_3CH_2	*n*-C_8H_{17}	B	94	13:87[g]

[a] A = KO-*t*-Bu, THF, −78 °C; B = $KN(SiMe_3)_2$, THF, 18-crown-6, −78 °C; C=KO-*t*-Bu, THF, 18-crown-6, −78 °C. [b] R^1 = CH_2CH_2C-H=$C(CH_3)CH_2CH_2CH$=$C(CH_3)CH_2OTBS$ (Scheme I). [c] The temperature was allowed to reach 23 °C. [d] Analysis by integration of the ^1H NMR spectrum. [e] R^1 = CH_2CH_2CH=$C(CH_3)CH_2CH_2CH$=$CHCH_2OTBS$ (eq 1). [f] R^4 = $CH_2CH_2C(CH_3)$=$CHCH_2OTHP$ (eq 1). [g] Analysis by glass capillary gas chromatography. [h] A fourfold excess of phosphonate was employed.

(diisopropyl- or (dimethylphosphono)acetate with the tosylate derivate A5 completed the sequence (Scheme I).

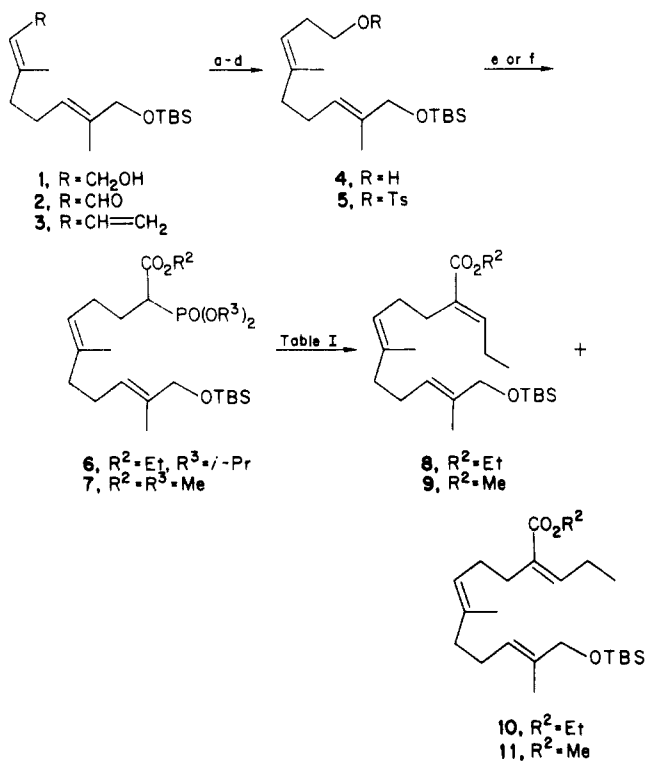
Preliminary condensations were carried out on propanal. The diisopropyl phosphonate A6 afforded a 9:1 mixture of the trans and cis conjugated esters A8 and A10, as expected. However, the dimethylphosphono ester A7 unexpectedly gave an 85:15 mixture of the trans and cis methyl esters A9 and A11 (Table I, entry 2).[4]

In some concurrent studies (eq 1) we found that the condensation of aldehyde **1** with the diethyl phosphonate **2** afforded predominantly the trans product **4** (R^2 = Et) with the KO-*t*-Bu–THF base–solvent system at −78 °C (Table I, entry 3). Still reported improved cis:trans ratios



in condensations of various aldehydes with methyl α-(dimethylphosphono)propionate when KHMDS-18-crown-6 in THF was employed as the base–solvent system.[5] Under these conditions phosphonate **2** still gave mainly the trans product **4** (R^2 = Et) but to a lesser degree (Table I, entry 4). The dimethyl phosphonate **3** gave a slightly greater amount of the cis isomer **5** (R^2 = Me) but the trans product still predominated (Table I, entry 5).[6]

Scheme I.[a,b] Series A



[a] (a) MnO_2, CH_2Cl_2, 25 °C; (b) Ph_3P=CH_2, THF, −78 °C; (c) $[Me_2CHCH(Me)]_2BH$, THF, −10 °C; H_2O_2, NaOH, 25 °C; (d) *p*-TsCl, Et_3N, 4-$(Me_2N)C_5H_4N$, 0 °C; (e) $(MeO)_2POCH_2CO_2Me$, NaH, Me_2SO, 25 °C; (f) $(i\text{-PrO})_2POCH_2CO_2Et$, NaH, THF, 25 °C. [b] TBS = *t*-$BuMe_2Si$, Ts = *p*-$CH_3C_6H_4SO_2$.

(4) Control experiments with (dimethylphosphono)- and (diisopropylphosphono)propionates confirmed the literature results within a few percent of the reported ratios for condensations with α-phenylpropionaldehyde.[2] To obtain high cis:trans ratios it was necessary to employ an excess (fourfold is recommended)[2] of the phosphonate relative to base and aldehyde. Lower cis:trans ratios also resulted from higher reaction temperatures.

(5) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

Since phosphonates A7, **2**, and **3** all possess long α-alkyl chains whereas both Kishi and Still employed *α-methyl* phosphonates, these findings suggest that the α-substituent of the phosphonate plays an important stereochemical role in Horner–Wadsworth–Emmons condensations.[7] In order to further probe this phenomenon we conducted a brief study of condensations between α-phosphono-ω-undecylenates B3, B4, and B5 and the representative aldehydes propanal and nonanal under several different reaction conditions. The use of phosphonate B5 was prompted by Still's work on the corresponding propionate.[5]

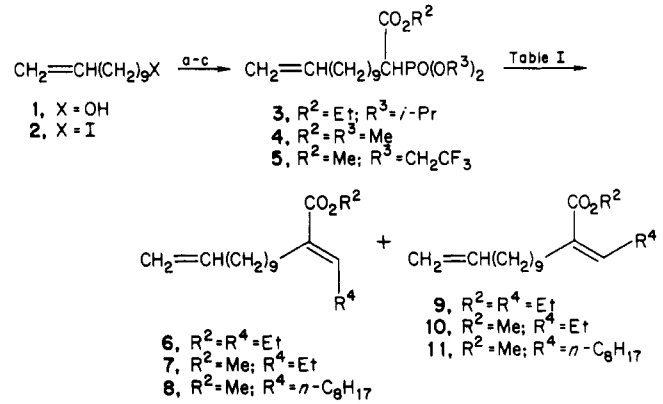
The highest cis:trans ratio was obtained with bis(2,2,2-trifluoroethyl)phosphonate B5 and nonanal (Table I, entry 13). Under comparable conditions, the dimethyl phosphono ester B4 gave a predominance of the trans conjugated esters B7 and B8 with both propanal and nonanal (Table I, entries 8 and 12). Condensations employing propanal with the KO-*t*-Bu-THF base–solvent system gave mainly the trans conjugated ester in ratios that were little affected by the nature of the phosphono alkoxy grouping (Table I, entries 6 and 7). In both the isopropyl and methyl cases, B3 and B4, a 4:1 mixture of trans and cis products was obtained, with the methyl derivative B4 actually showing a slightly higher preference for the trans product.

In repeating Kishi's condensations of methyl α-(dimethylphosphono)propionate with α-phenylpropionaldehyde, we found that a large excess of phosphonate reagent was required for optimum cis:trans product ratios.[2,4] Under identical conditions phosphonate B4 afforded no detectable product with α-phenylpropionaldehyde, even after 10 h at −78 °C. Furthermore, the condensation of B4 with octanal under these conditions was unaffected by stoichiometry (Table I, entries 9 and 10). We also found that 18-crown-6 significantly enhanced the cis:trans product ratios in condensations of methyl α-(dimethylphosphono)propionate with α-phenylpropionaldehyde. No such enhancement could be detected for phosphonate B4 in condensations with nonanal (Table I, entry 11). Again, we were unable to detect any product from B4 and α-phenylpropionaldehyde after 16 h at −78 °C.

Even the KHMDS–18-crown-6 modification[5] failed to give a predominance of the cis isomer with phosphonate B4 (Table I, entry 8). In contrast, the analogous methyl α-(dimethylphosphono)*propionate* condenses with octanal to give a 91:9 mixture of cis- and trans-conjugated esters.[5,6] Thus an α-alkyl substituent can significantly alter the stereoselectivity of the Horner–Wadsworth–Emmons condensation.

The observed predominance of trans products in the foregoing condensations suggests that α-substitution may sterically retard the elimination step of the reaction, thereby allowing equilibration of the intermediate oxaphosphetane.[8] Support for this explanation was secured by carrying out parallel condensations of phosphono ester B4 with nonanal at −78 °C with KO-*t*-Bu as the base. Each

Scheme II.[a] Series B



[a] (a) $(i\text{-PrO})_2POCH_2CO_2Et$, NaH, DME, 25 °C; (b) $(MeO)_2POCH_2CO_2Me$, NaH, Me_2SO, 25 °C; (c) $(CF_3CH_2O)_2POCH_2CO_2Me$, NaH, Me_2SO, 25 °C.

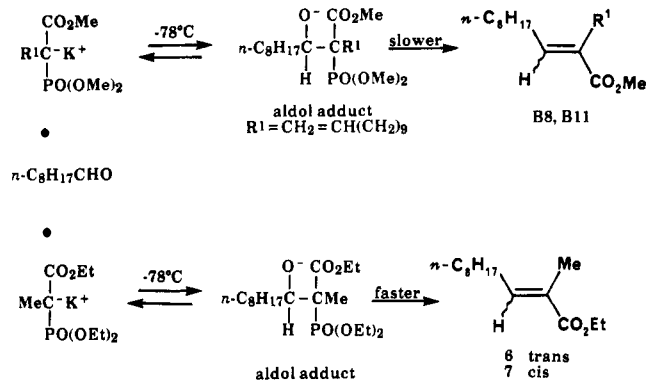


Figure 1. Perturbation of Horner–Emmons aldol equilibrium through addition of a more reactive phosphonate to a reaction in progress.

of the identical reaction mixtures contained a weighed amount of decalin as an internal standard to allow analysis by gas chromatography. After 30 min, one of the two was quenched with aqueous acid and the other was treated with the more reactive Horner–Emmons reagent derived from ethyl α-(diethylphosphono)propionate and then allowed to stir for an additional 45 min.[9] The control experiment showed peaks corresponding to 32% decalin, 5% nonanal, and 63% of the conjugated ester products B8 and B11 as an 85:15 trans:cis mixture. The reaction quenched with the phosphonopropionate showed 28% decalin, 1% nonanal, 51% of B8 and B11 (85:15 mixture), and 16% of the α-methylundecylenates **6** and **7** as a 65:35 mixture (Figure 1). Since the α-methylundecylenates are formed in amounts appreciably higher than the amount of aldehyde found to be present in the control experiment, reversal of the ω-tridecylenate aldol addition step (Figure 1) seems likely.

Equilibration of the conjugated esters **8**,**9** and B8,B11 was effected with sodium isopropylthiolate in DMF at elevated temperatures.[7b] The α-methylundecylenates **8** and **9** afforded a 90:10 mixture after 0.5 h at 90 °C and a 93:7 mixture after 16 h at 140 °C. The α-undecenylundecylenates B8 and B11 were slow to equlibrate under these conditions. At 140 °C a starting 93:7 mixture of cis and trans isomers gave rise to a 63:37 mixture in favor of the trans isomer B8 after 18 h while a 99:1 starting mixture of trans and cis isomers was converted to a 93:7 mixture

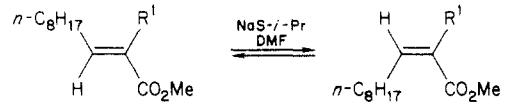
(6) A control experiment with methyl α-(dimethylphosphono)-propionate and nonanal confirmed the ratio of cis and trans condensation products within a few percent of the reported values for the KHMDS–18-crown-6 base–solvent system.[5]

(7) Only a few studies of α-phosphono ester condensations other than propionates have been reported. In these cases, relatively poor stereoselectivity has been observed: (a) Kinstle, T.; Mandanas, B. *J. Chem. Soc., Chem. Commun.* **1968**, 1699. (b) Semmelhack, M. F.; Tomesch, J. C.; Czarny, M.; Boettger, S. *J. Org. Chem.* **1978**, *43*, 1259. (c) Sasaki, K. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1252; **1967**, *40*, 2968.

(8) (a) Redjal, A.; Seyden-Penne, J. *Tetrahedron Lett.* **1974**, 1733 and references therein. (b) Deschamps, B.; Lampin, J. P.; Mathey, F.; Seyden-Penne, J. *Tetrahedron Lett.* **1977**, 1137. (c) Breuer, E.; Bannet, D. M. *Tetrahedron Lett.* **1977**, 1141. (d) Etemad-Moghadam, G.; Seyden-Penne, J. *Tetrahedron* **1984**, *40*, 5153.

(9) In a competition experiment between phosphonate B4 and ethyl α-(diethylphosphono)propionate (KO-*t*-Bu, THF, −78 °C) for nonanal, the phosphonopropionate was found to be 4 times as reactive as B4 according to GC analysis of the products.

Table II. Equilibration of Conjugated Esters



8, R^1 = Me
B8, R^1 = CH_2=CH$(CH_2)_9$

9, R^1 = Me
B11, R^1 = CH_2=CH$(CH_2)_9$

R^1	trans:cis[a] initial	trans:cis[a] final	time (h)	temp (°C)
Me	4/96	90/10	0.5	90
Me	60/40	93/7	16 h	140
CH_2=CH$(CH_2)_9$	7/93	63/37	18 h	140
CH_2=CH$(CH_2)_9$	99/1	93/7	15 h	140

[a] Analysis by glass capillary gas chromatography.

of the same after 15 h (Table II). Although equilibrium has not been reached in these latter examples, it seems clear that the trans isomers **8** and B8 are more stable than their cis counterparts **9** and B11.[10]

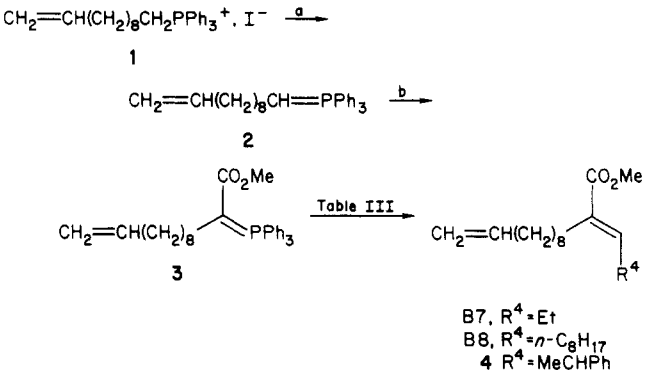
The observed predominance of trans conjugated esters in the foregoing Horner–Wadsworth–Emmons condensations may thus be attributed to a reversible addition (aldol) step followed by a slow elimination step with a productlike transition state. Factors that accelerate the elimination step tend to diminish the reversibility of the aldol step thereby favoring cis products.[8]

In view of the relatively modest trans:cis ratios obtained in the foregoing phosphonate condensations, we were interested in exploring alternative routes to the trans esters. The α-phosphorylidene esters offered an attractive alternative.[2] Indeed, in recent work on cembranoid synthesis, the triphenylphosphorylidene analogue of phosphonate A7 was found to give high trans:cis product ratios in its condensation with a base-senstive α-benzyloxy aldehyde (Table III, entry 1).[1] Accordingly, we decided to examine this methodology in the dodecylenic series C3 to determine its applicability for the synthesis of trans-conjugated esters with long-chain α-substituents.

Phosphorylidene ester C3 (Scheme III) was prepared from the phosphonium salt C1 via deprotonation with 2 equiv of KHMDS followed by in situ reaction of the ylide C2 with methyl chloroformate.[1,11] By using KHMDS in excess it is possible to fully utilize the strongly basic ylide C2.[12] Otherwise, the initially formed phosphonium salt consumes a full equivalent of C2 through proton transfer. As neither the excess KHMDS nor the product ylide C3 appear to compete with ylide C2 for methyl chloroformate, these conditions permit efficient acylation with only 1 equiv of valuable phosphonium reagent.[11]

Condensation of C3 with the afore-mentioned α-benzyloxy aldehyde gave the trans ester in 53% yield as the only strereoisomer detected by integration of the high field ^{1}H NMR spectrum (Table III, entry 2).[1] Condensation with propanal, nonanal, and 2-phenylpropanal likewise proceeded with excellent stereoselectivity affording the trans esters B7, B8, and C4 as the only products detected by glass capillary gas chromatography (Table III, entries 3, 4, and 5). The reaction with 2-phenylpropanal was significantly slower than the rest.

Scheme III.[a] Series C



[a] (a) Ph_3P, C_6H_6, Δ; $KN(SiMe_3)_2$; THF, −78 °C to 25 °C; (b) MeOCOCl, 0 °C to 25 °C.

In summary, we have found the cis stereoselectivity of Horner–Wadsworth–Emmons condensations to be seriously compromised by long-chain α-alkyl substituents on the phosphonate moiety. Dimethyl, diethyl, and diisopropylphosphonates all give trans conjugated esters as the predominant products. Bis(trifluoroethyl)phosphonates favor cis products, but here too a long-chain α-alkyl substituent diminishes the stereoselectivity. On the other hand, condensations of α-triphenylphosphorylidene esters seem unaffected by α-substitution. High trans:cis ratios are observed, even with long-chain α-alkyl substituents. This method is also preferred for condensations with base-sensitive aldehydes.

Experimental Section

The apparatus and methods described by G. W. Kramer, M. M. Midland, and A. B. Levy[13] were used to maintain an argon or nitrogen atmosphere in the reaction flask. Anhydrous solvents were obtained by distillation from sodium benzophenone ketyl (diethyl ether, tetrahydrofuran, 1,2-dimethoxyethane), calcium hydride (dichloromethane), or sodium (benzene and toluene). Infrared absorption maxima are reported in wavenumbers (cm^{-1}) and are standardized by reference to the 1601-cm^{-1} peak of polystyrene. Proton magnetic resonance spectra were recorded on Varian EM-390 and Bruker WH-400 spectrometers. All samples were prepared as dilute solutions in deuteriochloroform ($CDCl_3$). Chemical shifts (δ) are reported downfield from tetramethylsilane (Me_4Si), in parts per million (ppm) of the applied field. Peak multiplicities are abbreviated: singlet, s; doublet, d; triplet, t; quartet, q; pentuplet, p; envelope, e; multiplet, m. Coupling constants (*J*) are reported in hertz (Hz). Glass capillary GC was carried out on Hewlett-Packard 5890A instrument with a 25M Alltech Superox 4 column. Combustion microanalyses were performed by Atlantic Laboratories, Atlanta, GA. Column chromatography was performed by using E. Merck silica gel 60 (20–400 mesh ASTM) according to the procedure of W. C. Still, M. Kahn, and A. Mitra.[14]

(2*E*,6*E*)-3,7-Dimethyl-8-[(*tert*-butyldimethylsilyl)oxy]-2,6-octenal (A2). To a stirred slurry of 10.85 g (125 mmol) of freshly prepared MnO_2 in 30 mL of CH_2Cl_2 was added 9.7 g (34 mmol) of alcohol A1.[3] The resulting slurry was stirred for 48 h, diluted with 50 mL of CH_2Cl_2, filtered through Florisil, and concentrated under reduced pressure to afford 7.95 g (83%) of aldehyde A2 as a fragrant yellow oil which was used without further purification: ^{1}H NMR (90 MHz) δ 0.06 (s, $Si(CH_3)_2$), 0.90 (s, $SiC(CH_3)_3$), 1.58 (s, C-7 vinyl CH_3), 2.16 (s, C-3 vinyl CH_3), 2.25 (m, C-4 and C-5 allylic H), 3.97 (s, C-8 H), 5.33 (m, C-6 H), 5.84 (d, *J* = 8.8 Hz, C-2 vinyl H), 9.98 (d, *J* = 8.7 Hz, CHO).

(2*E*,6*E*)-2,6-Dimethyl-2,6,8-nonatrienyl *tert*-Butyldimethylsilyl Ether (A3). To a stirred, cooled (−78 °C) suspension

(10) A problem encountered in prolonged equilibration experiments was eventual cleavage of the methyl ester by the mercaptide to afford the carboxylic acid salt. Equilibration was not effected by the less nucleophilic benzenethiolate.

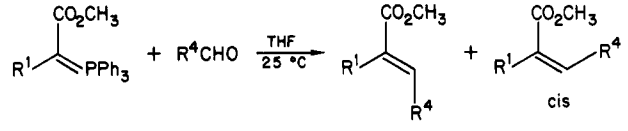
(11) Bestmann, H. J. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 645. Schlessinger, R. H.; Poss, M. A.; Richardson, S.; Lin, P. *Tetrahedron Lett.* **1985**, *26*, 2391.

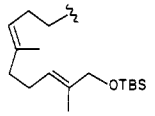
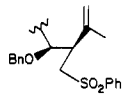
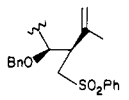
(12) For the use of silazides as bases for ylide formation, see: Bestmann, H. J.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694. Sreekumar, C.; Darst, K. P.; Still, W. C. *J. Org. Chem.* **1980**, *45*, 4260.

(13) Brown, H. C. *Organic Syntheses via Boranes*; Wiley: New York, 1975; pp 191–202.

(14) Still, W. C.; Kahn, M.; Mitra A. *J. Org. Chem.* **1978**, *43*, 2923.

Table III. Wittig Condensations of α-Phosphorylidene Esters



entry	R^1	R^4	time (h)	yield (%)	trans/cis
1			48	42	>95:5[a,b]
2	$CH_2{=}CH(CH_2)_8$		48	53	>95:5[a,b]
3	$CH_2{=}CH(CH_2)_8$	CH_3CH_2	36	38	>99:1[b,c]
4	$CH_2{=}CH(CH_2)_8$	n-C_8H_{17}	60	48	>99:1[c,c]
5	$CH_2{=}CH(CH_2)_8$	CH_3CHPh	84	21	>99:1[b,c]

[a] Analysis by integration of the 400-MHz ^1H NMR spectrum. [b] None of the cis isomer could be detected. [c] Analysis by glass capillary gas chromatography.

of 10.8 g (30 mmol) of methyltriphenylphosphonium bromide in 140 mL of THF was added dropwise 13.8 mL of 2.2 M *n*-butyllithium in hexane. The resulting yellow-orange suspension was stirred for 2 h and 6.4 g (22.6 mmol) of crude aldehyde A2 in 4 mL of THF was added over 25 min via syringe pump. The mixture was stirred for 4 h and the resulting red-black solution was allowed to warm to room temperature whereupon it was partitioned between hexane and water. The organic layer was washed 4 times with water, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel (hexane) to afford 5.15 g (81%) of triene A3 as an unstable yellow oil: ^1H NMR (90 MHz) δ 0.05 (s, $Si(CH_3)_2$), 0.89 (s, $SiC(CH_3)_3$), 1.56 (s, C-6 CH_3), 1.69 (s, C-2 CH_3), 2.06 (br s, C-4 and C-5 allylic H), 3.95 (s, C-1 H), 4.98 (br m, C-3 and C-8 vinyl H), 5.31 (m, C-7 H), 6.54 (br m, C-8 vinyl H).

(3*E*,7*E*)-4,8-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-3,7-nonadien-1-ol (A4). The procedure of Brown[15] was modified. To a stirred, cooled (−10 °C) freshly prepared solution of 12.6 mL of 1.75 M disiamylborane in THF was slowly added 2.80 g (10 mmol) of triene A3 in 3 mL of THF. The resulting solution was stirred for 5 h and carefully quenched by the sequential addition of 7.4 mL of water, 7.4 mL of 3 M aqueous NaOH, and 7.2 mL of 30% aqueous H_2O_2. The biphasic solution was vigorously stirred for 13 h, diluted with ether, washed twice with water, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel (5:95 ether–hexane) affording 2.4 g (81%) of alcohol A4 as a clear oil: ^1H NMR (90 MHz) δ 0.04 (s, $Si(CH_3)_2$), 0.89 (s, $SiC(CH_3)_3$), 1.56, 1.59 (s, vinyl CH_3), 2.04 (br s, C-4 and C-5 allylic H), 2.49 (q, J = 7.6 Hz, C-2 H), 3.48 (t, J = 7.6 Hz, C-1 H), 3.97 (s, C-9 H), 5.11 (t, J = 7.4 Hz, C-3 H), 5.31 (m, C-7 H); IR (film) ν 3340, 2940, 2905, 2850, 1480, 1465, 1260, 1120, 1070, 840, 775 cm^{-1}.

(3*E*,7*E*)-4,8-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-3,7-nonadienyl *p*-Toluenesulfonate (A5). To a stirred, cooled (0 °C) solution of 3.0 g (10 mmol) of alcohol A4, 300 mg of 4-(dimethylamino)pyridine, and 1.6 mL (11 mmol) of triethylamine in 10 mL of CH_2Cl_2 was added 2.0 g (10.5 mmol) of *p*-toluenesulfonyl chloride. The resulting solution was stirred for 4.5 h, quenched with 350 μL of methanol, and partitioned between ether and water. The organic layer was sequentially washed with water, saturated aqueous $CuSO_4$, and saturated aqueous NaCl, dried briefly over $MgSO_4$, filtered, and concentrated under reduced pressure affording 4.45 g (98%) of tosylate A5 as a pale yellow oil which was used immediately without further purification: ^1H NMR (90 MHz) δ 0.04 (s, $Si(CH_3)_2$), 0.88 (s, $SiC(CH_3)_3$), 1.51 (s, vinyl CH_3), 2.06 (br s, allylic H), 2.36 (s, aryl CH_3), 3.97 (s, C-9 H), 5.03 (t, J = 7.6 Hz, C-3 vinyl H), 5.28 (m, C-7 vinyl H), 7.57 (AB q, Δν = 10.46 Hz, J_{AB} = 9.0 Hz, Ar H).

Ethyl (5*E*,9*E*)-2-(Diisopropylphosphono)-6,10-dimethyl-11-[(*tert*-butyldimethylsilyl)oxy]-5,9-undecadienoate (A6). To a stirred suspension of 250 mg (10 mmol) of NaH in 18 mL of THF was added 2.55 g (10 mmol) of ethyl (diisopropylphosphono)acetate. The solution was stirred for 1 h and 2.0 g (4.5 mmol) of crude tosylate A5 in 1 mL of THF was added. The resulting solution was stirred for 30 h and partitioned between ether and water. The organic layer was washed with water, dried briefly over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by column chromatography on silica gel (1:1 ether–hexane) to afford 1.6 g (69%) of phosphonate A6 as a viscous pale yellow oil: ^1H NMR (90 MHz) δ 0.04 (s, $Si(CH_3)_2$), 0.89 (s, $SiC(CH_3)_3$), 1.23, 1.29 (s, isopropyl CH_3s), 1.87 (s, vinyl CH_3), 2.00 (br s, allylic H), 2.61–3.08 (br m, C-2 H), 3.93 (s, C-11 H), 4.14 (q, J = 6.6 Hz, CO_2CH_3), 4.67 (m, $HC(CH_3)_2$), 5.03, 5.29 (m, vinyl H).

Methyl (5*E*,9*E*)-2-(Dimethylphosphono)-6,10-dimethyl-11-[(*tert*-butyldimethylsilyl)oxy]-5,9-undecadienoate (A7). In the manner described above for phosphonate A6 the dimethyl phosphonate A7 was prepared from 225 mg (9.0 mmol) of NaH, 2.3 g (9.0 mmol) of trimethyl phosphonoacetate, and 2.0 g (4.5 mmol) of tosylate A5 in a combined volume of 12 mL of Me_2SO. The product (1.45 g, 69% yield) was purified by chromatography on silica gel (1:1 ether–hexane): ^1H NMR (90 MHz) δ 0.04 (s, $Si(CH_3)_2$), 0.88 (s, $SiC(CH_3)_3$), 1.24, 1.51 (s, vinyl CH_3s), 2.01 (br s, allylic H), 2.71–3.19 (br m, C-2 H), 3.68 (d, J = 3.0 Hz, $PO(OCH_3)_2$), 3.81 (s, OCH_3), 3.96 (s, C-11 H), 5.07, 5.31 (m, vinyl Hs). Anal. Calcd for $C_{22}H_{43}O_6PSi$: C, 57.12; H, 9.37. Found: C, 57.25; H, 9.39.

(2*E*,6*E*,10*E*)-2,6-Dimethyl-10-carbethoxy-2,6,10-tridecatrienyl *tert*-Butyldimethylsilyl Ether (A8). To a stirred, cooled (0 °C) suspension of 57 mg (0.5 mmol) of freshly sublimed KO-*t*-Bu in 1.8 mL of THF was added 270 mg (0.5 mmol) of phosphonate A6 in 0.2 mL of THF. The resulting solution was allowed to stir and warm to room temperature whereupon it was cooled (−78 °C) and 60 μL (0.8 mmol) of freshly distilled propanal was slowly added. The mixture was stirred for 5 h, allowed to warm to room temperature, quenched with saturated aqueous NH_4Cl, and partitioned between ether and water. The organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified via column chromatography on silica gel (1:15 ether–hexane) to afford 120 mg (59%) of ester A8 as a clear oil: ^1H NMR (90 MHz) δ 0.06 (s, $Si(CH_3)_2$), 0.89 (s, $SiC(CH_3)_3$), 1.01 (t, J = 7.6 Hz, C-13 H), 1.26 (t, J = 7.8 Hz, OCH_2CH_3), 1.56 (s, vinyl CH_3), 1.83–2.39 (br m, allylic H), 3.93 (s, C-1 H), 4.17 (q, J = 7.8 Hz, OCH_2CH_3), 5.11 (t, J = 7.4 Hz, vinyl H), 5.31 (m, vinyl H), 5.78 (t, J = 8.2 Hz, (*Z*)-C-11 H), 6.68 (t, J = 8.1 Hz, (*E*)-C-11 H). Integration of the foregoing spectrum indicated a 90:10 ratio of *E* and *Z* isomers A8 and A10. Anal. Calcd for $C_{18}H_{36}O_2Si$: C, 69.17; H,

(15) Brown, H. C.; Moerikofer, A. W. *J. Am. Chem. Soc.* **1961**, *83*, 3417.

11.63. Found: C, 69.26; H, 11.69.

(2*E*,6*E*,10*E*)-2,6-Dimethyl-10-carbomethoxy-2,6,10-tridecatrienyl *tert*-Butyldimethylsilyl Ether (A9). The above procedure was employed with 287 mg (0.5 mmol) of phosphonate A7 in 0.3 mL of THF to afford 107 mg (48%) of ester A9 as a clear oil: ^{1}H NMR (90 MHz) δ 0.05 (s, $Si(CH_3)_2$), 0.90 (s, $SiC(CH_3)_3$), 1.03 (t, J = 7.8 Hz, C-13 H), 1.54 (s, vinyl CH_3), 1.81–2.41 (m, allylic H), 3.95 (s, C-1 H), 5.13, 5.29 (m, vinyl H), 5.75 (t, J = 8.0 Hz, (*Z*)-C-11 H), 6.64 (t, J = 8.0 Hz, (*E*)-C-11 H). Integration of the foregoing spectrum indicated an 85:15 mixture of *E* and *Z* isomers A9 and A11.

Ethyl 2-(Diisopropylphosphono)-12-tridecenoate (B3). To a slurry of 432 mg (18 mmol) of NaH in 15 mL of dry DME at room temperature was added 4.05 g (16.05 mmol) of ethyl α-(diisopropylphosphono)acetate. The resulting solution was treated with 1.5 g (5.35 mmol) of 11-iodo-1-undecene and the reaction mixture was stirred overnight. Following workup and chromatography (40% ethyl acetate-hexanes) as described for A7, 1.4 g (65%) of phosphonate B3 was isolated as an oil: IR (film) ν 3040 2955, 2905, 2835, 1730, 1635, 1470, 1260, 990 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 (e, CH_2s), 1.33 (d, J = 7 Hz, CH_3s), 1.80–2.20 (m, allylic CH_2), 2.87 (ddd, J = 5, 5, and 23 Hz, CH), 4.20 (q, J = 7 Hz, CH_2CH_3), 4.52–5.16 (m, vinyl Hs, OCHs), 5.56–6.04 (m, vinyl H). Anal. Calcd for $C_{21}H_{41}O_5P$: C, 62.35; H, 10.22. Found: C, 62.45; H, 10.25.

Methyl 2-(Dimethylphosphono)-12-tridecenoate (B4). To a slurry of 480 mg (20 mmol) of NaH in 16 mL of dry Me_2SO at room temperature was added 2.9 mL (18 mmol) of trimethyl α-phosphonoacetate dropwise. The resulting solution was treated with 4.02 g (14.3 mmol) of 11-iodo-1-undecene and the mixture was stirred overnight. Following workup and chromatography (50% ethyl acetate–hexanes) as described above, there was obtained 3.3 g (69%) of phosphonate B4 as a pale yellow oil: IR (film) ν 3050, 2900, 2830, 1735, 1635, 1260, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (e, CH_2s), 1.70–2.17 (m, allylic CH_2), 2.98 (ddd, J = 5, 5, and 23 Hz, CH), 3.74 (d, J = 3 Hz, OMe), 3.83 (d, J = 1 Hz, CO_2Me), 4.80–5.10 (m, vinyl Hs), 5.56–6.01 (m, vinyl H). Anal. Calcd for $C_{16}H_{31}O_5P$: C, 57.47; H, 9.34. Found: C, 57.28; H, 9.40.

Methyl 2-[Bis(2,2,2-trifluoroethyl)phosphono]-12-tridecenoate (B5). To a slurry of 245 mg (10.2 mmol) of NaH in 8 mL of dry Me_2SO was added 2.5 g (7.86 mmol) of methyl α-[bis(trifluoroethyl)phosphono]acetate slowly to curtail excessive foaming. After the addition was complete, 2.2 g (7.86 mmol) of 11-iodo-1-undecene was added. The solution was allowed to stir overnight followed by workup and chromatography (25% ethyl acetate–hexanes) as described for A7 affording 1.8 g (49%) of phosphonate B5 as an oil: IR (film) ν 3060, 2920, 2845, 1735, 1640, 1300, 1270, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (e, CH_2s), 1.8–2.2 (m, allylic CH_2, $CHCH_2$), 3.10 (ddd, J = 6, 6, and 22 Hz, CH), 3.78 (s, CO_2Me), 4.40 (dp, J = 3 and 9 Hz, CF_3CH_2O), 4.80–5.12 (m, vinyl CH_2), 5.57–6.02 (m, vinyl H). Anal. Calcd for $C_{18}H_{29}O_4PF_6$: C, 45.96; H, 6.21. Found: C, 46.09; H, 6.26.

Ethyl (*E*)-2-(10-Undecenyl)-2-pentenoate (B6). The procedure described above for A8 was followed using 1.11 g (2.7 mmol) of phosphonate B3 in 5 mL of THF at 0 °C and 1.57 g (2.8 mmol) of 20 wt % KO-*t*-Bu in THF. After 1 h at 0 °C, the reaction mixture was cooled to −78 °C and 216 μL (3.0 mmol) of propanal was added. The solution was stirred for 1 h at −78 °C then quenched with saturated aqueous NH_4Cl. Following workup and chromatography (3% ether–hexanes) on silica gel there was obtained 304 mg (40%) of ester as an 81:19 mixture of *E* and *Z* isomers B6 and B9 according to glass capillary GC analysis: IR (film) ν 3055, 2955, 2910, 2840, 1710, 1640, 1465, 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.99 (t, J = 7 Hz, CH_3 *Z* isomer), 1.03 (t, J = 7 Hz, CH_3 *E* isomer), 1.27 (e, CH_2s, $CO_2CH_2CH_3$), 1.90–2.43 (m, allylic Hs), 4.18 (q, J = 7 Hz, $CO_2CH_2CH_3$), 4.83–5.11 (m, terminal vinyl Hs), 5.60–6.04 (m, terminal vinyl H), 6.71 (t, J = 7 Hz, H-3). Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 77.18; H, 11.51.

Methyl (*E*)-2-(10-Undecenyl)-2-pentenoate (B7). A. From Phosphonate B4. The procedure described for ester A8 was followed using 534 mg (1.6 mmol) of phosphonate B4 and 954 mg (1.7 mmol) of a 20 wt % solution of KO-*t*-Bu in THF in 3 mL of THF. The solution was cooled to −78 °C and 144 μL (2.0 mmol) of propanal was added. After 1 h water was added, the mixture was extracted with ether, and the product was purified by chromatography (3% ether–hexanes) affording 329 mg (77%) of ester as a 84:16 mixture of *E* and *Z* isomers B7 and B10 according to glass capillary gc analysis: IR (film) ν 3055, 2910, 2840, 1720, 1640, 1470, 1435, 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.98 (t, J = 7 Hz, CH_3 *Z* isomer), 1.02 (t, J = 7 Hz, CH_3 *E* isomer), 1.27 (e, CH_2s), 1.87–2.40 (m, allylic Hs), 3.70 (s, CO_2Me), 4.80–5.10 (m, terminal vinyl CH_2), 5.55–6.00 (m, terminal vinyl H), 6.68 (t, J = 7 Hz, H-3). Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.54; H, 11.39.

B. From Phosphonium Ylide C3. A solution of 1.21 g (4.3 mmol) of 11-iodo-1-undecene and 1.13 g (4.3 mmol) of triphenylphosphine in 6 mL of benzene was heated at reflux overnight. The benzene was removed under reduced pressure and the crude product was triturated twice with ether. The ether was decanted and the oil was stored under vacuum at 0.1 mm for 12 h, giving 2.2 g (95%) of phosphonium salt C1 as a viscous oil which was used directly.

To a solution of 1.4 g (2.6 mmol) of the foregoing phosphonium salt C1 in 7 mL of THF at −78 °C was slowly added 8.5 mL of 0.62 M potassium hexamethyldisilazide (KHMDS) in toluene. The resulting red-orange ylide C2 was stirred at −78 °C for 1 h and then 200 μL (2.6 mmol) of methyl chloroformate was added. The slurry was stirred at −78 °C for 30 min and then warmed quickly to room temperature and stirred for 1 h. To this yellow-orange ylide C3 was added 194 μL (2.7 mmol) of propanal. The mixture was stirred for 38 h at room temperature and then quenched with saturated aqueous NH_4Cl. The mixture was poured into H_2O and extracted twice with ether. The ether extracts were dried over $MgSO_4$ and concentrated to an oil which was purified by silica gel chromatography (3% ether–hexanes) affording 280 mg (38%) of ester B7 as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.04 (t, J = 7 Hz, CH_3), 1.30 (e, CH_2s), 1.91–2.40 (m, allylic CH_2s), 3.73 (s, CO_2Me), 4.83–5.10 (m, terminal vinyl CH_2), 5.55–6.03 (m, terminal vinyl H), 6.71 (t, J = 7 Hz, H-3).

Methyl (*E*)-2-(10-Undecenyl)-2-undecenoate (B8). A. From Phosphonate B4. The procedure described above for ester A8 was followed using 924 mg (2.76 mmol) of phosphonate B4, 4.6 mL of 0.6 M KHMDS in toluene, and 2.9 g (11.05 mmol) of 18-crown-6 in 40 mL of THF at −78 °C to which 0.52 mL (3.0 mmol) of nonanal was added. The reaction mixture was stirred 1 h at −78 °C and then quenched with saturated aqueous NH_4Cl. Workup and chromatography (2% ether–hexanes) provided 521 mg (54%) of ester as a 72:28 mixture of *E* and *Z* isomers B8 and B11 according to glass capillary gc analysis: IR (film) ν 3050, 2910, 2840, 1715, 1640, 1460, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84 (br t, J = 5 Hz, CH_3), 1.29 (e, CH_2s), 1.83–2.48 (m, allylic CH_2s), 3.71 (s, CO_2Me), 4.83–5.10 (m, terminal vinyl CH_2), 5.58–6.03 (m, terminal vinyl H), 6.73 (t, J = 8 Hz, H-3). Anal. Calcd for $C_{23}H_{42}O_2$: C, 78.80; H, 12.08. Found: C, 78.66; H, 12.11.

B. From Phosphonium Ylide C3. Procedure B described above for ester B7 was followed using the same quantities of reagents and solvent. To the yellow-orange ylide C3 at room temperature was added 0.45 mL (2.6 mmol) of nonanal. The resulting mixture was stirred for 60 h. Following workup and chromatography there was obtained 441 mg (48%) of ester B8 as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.87 (br t, J = 5 Hz, CH_3), 1.27 (e, CH_2s), 1.87–2.35 (m, allylic CH_2s), 3.70 (s, CO_2Me 4.80–5.06 (m, terminal vinyl CH_2), 5.55–6.02 (m, terminal vinyl H), 6.70 (t, J = 8 Hz, H-3).

Methyl (*Z*)-2-(10-Undecenyl)-2-undecenoate (B11). The procedure described above for ester A8 was followed using 292 mg (0.62 mmol) of phosphonate B5, 1 mL of 0.64 M KHMDS in toluene, and 820 mg (3.1 mmol) of 18-crown-6 in 12 mL of THF at −78 °C to which was added 112 μL (0.65 mmol) of nonanal. The resulting mixture was stirred at −78 °C for 18 h and then warmed slowly to room temperature and stirred for 2 h. The product was isolated by ether extraction and purified by silica gel chromatography (2% ether–hexanes), giving 205 mg (94%) of ester as a 13:87 mixture of *E* and *Z* isomers B8 and B11 according to glass capillary GC analysis: ^{1}H NMR ($CDCl_3$) δ 0.87 (br t, J = 5 Hz, CH_3), 1.31 (e, CH_2s), 1.93–2.48 (m, allylic CH_2s), 3.72 (s, CO_2Me), 4.80–5.15 (m, terminal vinyl CH_2), 5.61–6.08 (m, terminal vinyl H, H-3).

Methyl (*E*,*Z*)-2-(10-Undecenyl)-4-phenyl-2-pentenoate (C4). Procedure B described above for ester B7 was followed using

the same quantities of reagents and solvent. To the yellow-orange ylide C3 at room temperature was added 0.34 mL (2.6 mmol) of 2-phenylpropanal. After 84 h, workup and chromatography (5% ether–hexanes) afforded 185 mg (21%) of ester C4 as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.29 (e, CH_2s), 1.39 (d, J = 6 Hz, CH_3), 1.86–2.48 (m, allylic CH_2), 3.72 (s, CO_2Me), 3.55–3.83 (m, allylic CH), 4.82–5.13 (m, terminal vinyl CH_2), 5.56–6.04 (m, terminal vinyl H), 6.85 (d, J = 9 Hz, H-3), 7.28 (s, aryl H). Anal. Calcd for $C_{23}H_{34}O_2$: C, 80.65; H, 10.01. Found: C, 80.75; H, 10.04.

Equilibration of Conjugated Esters. A. Methyl (*E*)-2-(10-Undecenyl)-2-undecenoate (B8). A solution of 172 mg (0.49 mmol) of an 87:13 mixture of *Z* and *E* esters B11 and B8 and 1 mL (0.5 mmol) of 0.5 M sodium isopropylthiolate in 1 mL of DMF was heated at 130 °C for 3 h.[7b] The reaction mixture was cooled, diluted with water, and extracted with ether. These extracts were essentially devoid of material related to esters B8 or B11, a consequence of ester cleavage by the thiolate. The aqueous layer was acidified with 10% aqueous HCl and extracted with ether. The ether extracts were dried over $MgSO_4$ and concentrated under reduced pressure to an oil. The oil was dissolved in 3 mL of ether and treated with a ca. 3-fold excess of ethereal diazomethane at 0 °C for 30 min. The solvent was removed and the oil was purified by silica gel chromatography (3% ether–hexanes) to afford 164 mg (95%) of material consisting of 56% B8, 24% B11, and 20% of an impurity (possibly the β,γ-unsaturated isomer) according to glass capillary GC.

B. Methyl (*E*)-2-Methyl-2-undecenoate (8). A solution of 119 mg (0.56 mmol) of a 96:4 mixture of *Z* and *E* esters **9** and **8** and 140 μL (0.056 mmol) of 0.4 M sodium isopropylthiolate in DMF in 1 mL of DMF was heated at 90 °C for 30 min. Analysis of the reaction solution by capillary GC showed a 90:10 mixture of *E* and *Z* isomers.

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Registry No. **2**, 101419-98-1; **3**, 101419-99-2; **4** (R^2 = Et), 101420-04-6; **5** (R^2 = Et), 101420-05-7; **6**, 99699-33-9; **7**, 99699-34-0; **8**, 101420-17-1; **9**, 101420-16-0; **A1**, 90460-86-9; **A2**, 101419-88-9; **A3**, 101419-89-0; **A4**, 101419-90-3; **A5**, 101419-91-4; **A6**, 101419-92-5; **A7**, 101419-93-6; **A8**, 101419-94-7; **a9**, 101419-95-8; **A10**, 101419-96-9; **A11**, 101419-97-0; **B2**, 7766-49-6; **B3**, 101420-00-2; **B4**, 101420-01-3; **b5**, 101420-02-4; **b6**, 101420-08-0; **B7**, 101420-10-4; **B8**, 101420-11-5; **B9**, 101420-09-1; **B10**, 101470-97-7; **B11**, 101420-12-6; **C3**, 101420-14-8; **C4**, 101420-15-9; KHMDS, 40949-94-8; $(i\text{-PrO})_2POCH_2CO_2Et$, 24074-26-8; $(MeO)_2POCH_2CO_2Me$, 5927-18-4; EtCHO, 123-38-6; $OHCCH_2CH_2CH{=}C(CH_3)CH_2CH_2CH{=}CHCH_2OTBS$, 101420-03-5; $n\text{-}C_8H_{17}CHO$, 124-19-6; *trans*-$THPOCH_2CH{=}C(CH_3)CH_2CH_2CH{=}C(CO_2Me)CH_2CH_2CH{=}C(CH_3)CH_2CH_2CH{=}CHCH_2OTBS$, 101420-06-8; *cis*-$THPOCH_2CH{=}C(CH_3)CH_2CH_2CH{=}C(CO_2Me)CH_2CH_2CH{=}C(CH_3)CH_2CH_2CH{=}CHCH_2OTBS$, 101420-07-9; $(CF_3CH_2O)_2POCH_2CO_2Me$, 88738-78-7; $CH_2{=}CH(CH_2)_8CH_2PPh_3{}^+Cl^-$, 101420-13-7; $CH_3CH(Ph)CHO$, 93-53-8; $OHCCH(OBn)CH(CH_2SO_2Ph)C(CH_3){=}CH_2$, 101420-18-2; *trans*-$H_2C{=}C(CH_3)CH(CH_2SO_2Ph)CH(OBn)CH{=}C(CO_2CH_3)CH_2CH_2CH{=}C(CH_3)CH_2CH_2CH{=}C(CH_3)CH_2OTBS$, 101540-29-8; $Ph_3P{=}C(CO_2CH_3)CH_2CH_2CH{=}C(CH_3)CH_2CH_2CH{=}eC(CH_3)CH_2OTBS$, 100572-54-1; *trans*-$CH_2{=}CH(CH_2)_8C(CO_2CH_3){=}CHCH(OBn)CH(CH_2SO_2Ph)C(CH_3){=}CH_2$, 101420-19-3; *trans*-$CH_2{=}CH(CH_2)_8C(CO_2CH_3){=}CHCH_2CH_3$, 101420-20-6; *trans*-$n\text{-}C_8H_{17}CH{=}C(CO_2CH_3)(CH_2)_8CH{=}CH_2$, 101420-21-7; $MePPh_3{}^+Br^-$, 1779-49-3.

Microbial Transformations in Organic Synthesis. 4. Stereoselective Fungal Metabolism of 7-Methylglaucine

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The time courses for the fungal metabolism of racemic *cis*- and *trans*-7-methylglaucine (**4**/**5**, **6**/**7**, respectively) by *Fusarium solani* (ATCC 12823) and *Aspergillus flavipes* (ATCC 1030) are described. Only *cis*-7-methylglaucine (**4**/**5**) was biotransformed to 7-methyldehydroglaucine (**8**) with either culture, indicating that the reaction involves an overall cis elimination of hydrogen. The destructive resolution of **4**/**5** by the fungi was undertaken, and the enantiomeric purities and absolute configurations of residual substrates from microbiological incubations were determined by ^{1}H NMR by using the chiral shift reagent Eu(tfc)$_3$, by optical rotation (OR), and by optical rotary dispersion (ORD). A 10% enantiomeric excess of (6a*R*,7*R*)-7-methylglaucine (**5**) was isolated from *F. solani* incubations, indicative of a stereoselective oxidation of the 6a*S*,7*S* stereoisomer, while the residual substrate from *A. flavipes* was shown to be the enantiomerically pure (6a*S*,7*S*)-7-methylglaucine (**4**), indicative of a stereoselective oxidation of the 6a*R*,7*R* stereoisomer.

A potentially useful application of microorganisms in organic synthesis is the oxidation of the aporphine alkaloid (*S*)-(+)-glaucine (**1**) and the unnatural enantiomer (*R*)-(−)-glaucine (**2**) to dehydroglaucine **3** by the fungi *Fusarium solani* (ATCC 12823) and *Aspergillus flavipes* (ATCC 1030), respectively (Figure 1). The stereospecific and quantitative nature of these reactions, which allows for the destructive resolution of a racemic mixture of **1**/**2**, has been fully described.[1,2] In order to extend this reaction to the resolution of other aporphines and related alkaloids, a study was initiated to determine the mechanism of the microbial oxidation, i.e., whether an overall a cis or trans elimination of hydrogen is operative. The first approach was to study the metabolism of "methyl-blocked" analogues of glaucine, a strategy successfully employed in the steroid field to show that microbial 1,2-dehydrogenation follows a trans-1,2-diaxial course.[3,4] A previous report described the synthesis and characterization of *cis*- and

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