One-Pot Conversion of α,β-Unsaturated Alcohols into the Corresponding Carbon-Elongated Dienes with a Stable Phosphorus Ylide−$BaMnO_4$ System. Synthesis of 6′-Methylene Derivatives of Neplanocin A as Potential Antiviral Nucleosides. New Neplanocin Analogues. 11[1]

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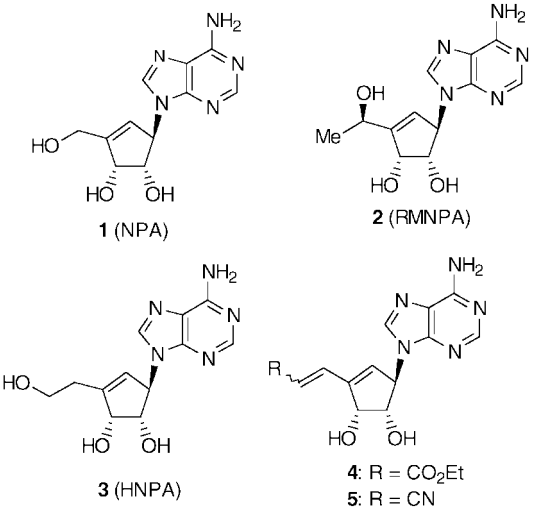
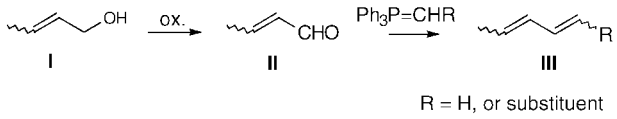
Wittig reaction is a highly versatile method for forming alkenes from carbonyl derivatives.[2] An example of utilizing Wittig reaction is shown in Scheme 1: oxidation of α,β-unsaturated alcohols (**I**),[3] in which the C−H bonds at the α-position of the hydroxyl group are "activated" by an adjacent π-bond, and subsequent Wittig reaction of the resulting α,β-unsaturated aldehydes (**II**) gives the corresponding diene derivatives (**III**). This type of procedure is often useful for constructing carbon-elongated diene structures in synthetic organic chemistry. In this paper, we describe an efficient one-pot method for converting α,β-unsaturated alcohols (**I**) into the corresponding carbon-elongated diene products (**III**) with a stabilized phosphorus ylide−$BaMnO_4$ system.

Considerable attention has recently been focused on carbocyclic nucleosides because of their biological importance.[4] We previously performed chemical modifications of neplanocin A (NPA, **1**),[5] a carbocyclic nucleoside

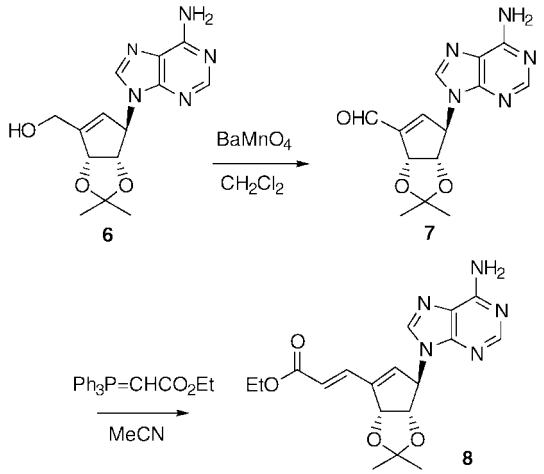


antibiotic, to develop potent antiviral agents.[6] In these studies, we found that some 6′-modified analogues of neplanocin A, e.g., (6′*R*)-6′-*C*-methylneplanocin A (RM-

Scheme 1



Scheme 2



NPA, **2**) and 6′-homoneplanocin A (HNPA, **3**), showed significant antiviral activities. During the course of the study, we further needed 6′-methylene derivatives of NPA, such as **4** and **5**. A straightforward method for preparing these compounds would be that as indicated in Scheme 1. Thus, we examined the oxidation of **6** by various methods,[7] and the 6′-formyl derivative **7** was produced only when **6** was treated with $BaMnO_4$,[8] which is known to be a useful oxidant of primary allylic alcohols to aldehydes, in CH_2Cl_2 (Scheme 2). Due to its instability, the aldehyde **7** was immediately treated with $Ph_3P{=}CHCO_2Et$ without purification to give the desired

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(1) This paper constitutes Part 169 of Nucleosides and Nucleotides; Part 168: Ueno, Y.; Kumagai, I.; Haginoya, M.; Matsuda, A. *Nucleic Acids Res.* **1997**, *25*, 3777−3782.

(2) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863−927.

(3) For examples of oxidation of allycil alcohols, see: (a) Ebenezer, W. J.; Wighy, P. In *Comprehensive Organic Functional Group Trasformations*; Katritzky, A. R., Methi-Cohn, O., Rees, C. W., Eds.; Pergamon Press: Oxford, 1995; Vol 3; pp 57 and 215. (b) Procter, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 7, pp 305−325.

(4) (a) Marquez, V. E. Carbocyclic nucleosides. In *Advances in Antiviral Drug Design;* JAI Press: Greenwich, CT, 1996; Vol 2, p 89−146. (b) Borthwick, A. D.; Biggadike, K. *Tetrahedron* **1992**, *48*, 571−623. (c) Agrofoglio, L.; Suhas, E.; Farese, A.; Condom, R.; Challand, S. R.; Earl, R. A.; Guedj, R. *Tetrahedron* **1994**, *50*, 10611−10670.

(5) (a) Yaginuma, S.; Muto, N.; Tsujino, M.; Sudate, Y.; Hayashi, M.; Otani, M. *J. Antibiot.* **1981**, *34*, 359−366. (b) Hayashi, M.; Yaginuma, S.; Yoshioka, H.; Nakatsu, K. *J. Antibiot.* **1981**, *34*, 675−680.

(6) (a) Shuto, S.; Obara, T.; Toriya, M.; Hosoya, M.; Snoeck, R.; Andrei, G.; Balzarini, J.; De Clercq, E. *J. Med. Chem.* **1992**, *35*, 324−331. (b) Shuto, S.; Obara, T.; Saito, Y.; Andrei, G.; Snoeck, R.; De Clercq, E.; Matsuda, A. *J. Med. Chem.* **1996**, *39*, 2392−2399. (c) Obara, T.; Shuto, S.; Saito, Y.; Snoeck, R.; Andrei, G.; Balzarini, J.; De Clercq, E.; Matsuda, A. *J. Med. Chem.* **1996**, *39*, 3847−3852. (d) Shuto, S.; Obara, T.; Yaginuma, S.; Matsuda, A. *Chem. Pharm. Bull.* **1997**, *45*, 138−142. (e) Shuto, S.; Obara, T.; Saito, Y.; Yamashita, K.; Tanaka, M.; Sasaki, T.; Andrei, G.; Snoeck, R.; Neyts, J.; Padalko, E.; Balzarini, J.; De Clercq, E.; Matsuda, A. *Chem. Pharm. Bull.* **1997**, *45*, 1163−1168.

(7) For example, Swern, Moffatt, Pr_4NRuO_4, and PDC oxidations of **6** were tried, but no **7** was obtained.

(8) $BaMnO_4$ is easy to handle and requires no activation, which makes it particulary useful for large-scale reactions; see: (a) Firouzabadi, H.; Ghaderi, E. *Tetrahedron Lett.* **1978**, 839−840. (b) Fatiadi, A. J. *Synthesis* **1987**, 85−127. (c) Kim, K. S.; Chung, S.; Cho, I. H.; Hahn, C. S. *Tetraherdon Lett.* **1989**, *30*, 2559−2562.

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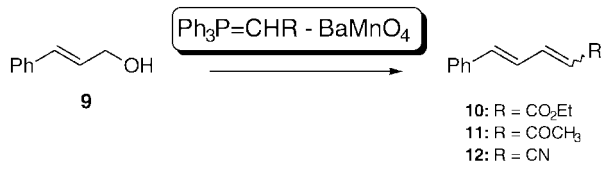
Table 1. One-Pot Synthesis of Diene Derivatives 10−12 from Cinnamyl Alcohol (9)[a]

entry	oxidant	ylide	solvent	temp	time (h)	product	% isolated yield (*E*/*Z*[b])
1	$BaMnO_4$	$Ph_3P{=}CHCO_2Et$	CH_2Cl_2	rt	24	10	99 (5.8)
2	$BaMnO_4$	$Ph_3P{=}CHCO_2Et$	CH_2Cl_2	reflux	4	10	98 (6.5)
3	$BaMnO_4$	$Ph_3P{=}CHCO_2Et$	CH_2ClCH_2Cl	reflux	1.5	10	99 (7.3)
4	$BaMnO_4$	$Ph_3P{=}CHCO_2Et$	toluene	reflux	1	10	93 (7.5)
5	$BaMnO_4$	$Ph_3P{=}CHCO_2Et$	DMF	100 °C	1.5	10	98 (7.6)
6	CMD	$Ph_3P{=}CHCO_2Et$	CH_2Cl_2	rt	24	10	38 (4.5)[c]
7	CMD	$Ph_3P{=}CHCO_2Et$	toluene	reflux	24	10	94 (5.3)
8	$BaMnO_4$	$Ph_3P{=}CHCOCH_3$	CH_2Cl_2	reflux	21	11	81 (*E* only)
2	$BaMnO_4$	$Ph_3P{=}CHCN$	toluene	reflux	0.8	12	89 (3.4)

[a] Reactions were carried out in 0.2 M substrate solution in the presence of oxidant (1.5 equiv) and ylide (1.3 equiv). [b]Determined by HPLC. [c]Starting material was recovered in 57% yield.

Scheme 3



diene **8** in low yield (37% from **6**). Therefore, we decided to develop more efficient procedures for converting allylic alcohols (**I**), including **6**, as well as similar "activated" alcohols such as benzylic alcohols into the corresponding dienes (**III**).

We tested reactions with cinnamyl alcohol (**9**) as a substrate under various reaction conditions and found that **9** is readily converted into diene **10** by treatment with $BaMnO_4$ in the presence of $Ph_3P{=}CHCO_2Et$ (Scheme 3).[9] This reaction is very convenient because isolation of the intermediary aldehyde is not necessary. The reaction of **9** as a substrate was therefore investigated in more detail, and the results are summarized in Table 1. The reactions were performed with 1.5 equiv of an oxidant and 1.3 equiv of a stable ylide. Entries 1−5 are reactions with $BaMnO_4$ and $Ph_3P{=}CHCO_2Et$. When the reaction was carried out in CH_2Cl_2 at room temperature for 24 h, the diene **10** was isolated quantitatively as a mixture of (*E*)- and (*Z*)-isomers (*E*/*Z* = 5.8, entry 1). This reaction proceeded in a variety of polar and nonpolar solvents to give **10** almost quantitatively, and the reaction rate was significantly increased at a higher temperature (entries 2−5). Activated manganese dioxide (MnO_2) is one of the mildest and most used oxidant for allylic alcohols.[3,10] While various methods for preparing activated MnO_2 have been reported,[10] Shioiri and co-workers recently reported that chemical manganese dioxide (CMD), an industrial product used in making batteries, was a more effective oxidizing reagent compared with MnO_2 activated by previous methods.[11] Therefore, we compared CMD with $BaMnO_4$ in this reaction and found that CMD also functioned as an oxidant in this reaction system. However, the reaction was slower than that with $BaMnO_4$; the reaction carried out under the same conditions as indicated in entry 1, except that $BaMnO_4$ was replaced by CMD, gave a 38% yield of diene **10** along with the recovery of **9** (57%) after 24 h (entry 6). The reaction with CMD was much faster under reflux in toluene, and it was completed after 24 h to give the diene **10** in 94% yield (*E*/*Z* = 5.3, entry 7). We then investigated the reaction with other stable phosphorus ylides. When **9** was heated with $Ph_3P{=}CHCOMe$ in the presence of $BaMnO_4$ under reflux in CH_2Cl_2, the corresponding diene **11** (*E* only) was obtained in 81% yield. Similarly, cyanomethylene diene derivative **12** was also synthesized in high yield when $Ph_3P{=}CHCN$ was used as a stable ylide. These results suggest that various stable phosphorus ylides can be used in this reaction system. It has been shown that a large excess of oxidant is usually required to complete the oxidation reactions by $BaMnO_4$ and MnO_2.[8,10,11a] Thus, it is noteworthy that only 1.5 equiv of $BaMnO_4$ was needed for this oxidation−Wittig reaction.

Next, the reaction was examined with a variety of α,β-unsaturated alcohols as substrates, and the results are summarized in Table 2. The reactions were carried out with $BaMnO_4$ (1.5 equiv) as the oxidant and $Ph_3P{=}CHCO_2Et$ (1.3 equiv) as the stable phosphorus ylide. The reaction of geraniol was performed under reflux in toluene to give the desired Wittig reaction product in 55% yield (entry 1). When $CHCl_3$ was used as solvent, the yield was significantly improved and the product was obtained in 92% yield without epimerization of the C−C bond (entry 2). Similar results were obtained with nerol as a substrate, giving the Wittig product without epimerization (entries 3 and 4). $BaMnO_4$ is an effective oxidant not only for allylic alcohols but also for other α,β-unsaturated alcohols such as benzyl alcohols. Accordingly, treatment of benzyl alcohol under conditions similar to those in entry 1 gave ethyl *trans*-cinnamate quantitatively, as expected (entry 5). Although 2-pyridinemethanol has been shown to be oxidized by activated MnO_2[10c] or CMD[11c] to give 2-pyridinecarbaldehyde, the yields were moderate. The corresponding Wittig product of 2-pyridinecarbaldehyde was readily obtained in high yield from 2-pyridinemethanol in this reaction system (entry 6). Thiophene- and furanemethanols were also good substrates to give the desired products (entries 7 and 8). Thus, thienyl and pyridinyl groups, which are sensitive to a variety of oxidating agents, survived under

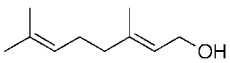
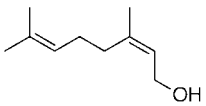
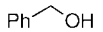
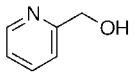
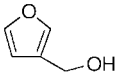
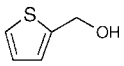
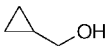
(9) Although we investigated other oxidating agents in this reaction system, these were unsuccessful. For example, when **9** was treated with Dess−Martin reagent or PDC in the presence of $Ph_3P{=}CHCO_2Et$, no **10** was obtained.

(10) (a) Cahiez, G.; Alami, M. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; 1995; Vol 5 (L−M), pp 3229−3235. (b) Papadopoulos, E. P.; Jarrar, A.; Issidorides, C. H. *J. Org. Chem*. **1966**, *31*, 615−616. (c) Goldman, I. M. *J. Org. Chem*. **1969**, *34*, 1979−1981.

(11) The yields of MnO_2 oxidation sometimes vary, since the reactivity of activated MnO_2 depends on the method of preparation, and commercially available activated MnO_2 is not efficient for all of the desired oxidation reactions (see ref 8a). Shioiri reported that CMD has a constant efficiency as an oxidant: (a) Hamada, Y.; Shibata, M.; Sugiura, T.; Kato, S.; Shioiri, T. *J. Org. Chem*. **1987**, *52*, 1252−1255. (b) Matsubara, J.; Nakao, K.; Hamada, Y.; Shioiri, T. *Tetrahedron Lett*. **1992**, *33*, 4187−4190. (c) Shioiri, T.; Aoyama, T.; Hamada, Y. *Wako Junyaku Jihou* **1997**, *65*, 12−14.

Table 2. Reaction of "Activated" Alcohols with $Ph_3P{=}CHCO_2Et{-}BaMnO_4$ System[a]

RH−OH $\xrightarrow{Ph_3P=CHCO_2Et - BaMnO_4}$ R=$CHCO_2Et$

entry	substrate (RH-OH)	conditions	R=$CHCO_2Et$ yield (%)	R=$CHCO_2Et$ *E/Z*
1		toluene, 8 h	55	*E* only
2		$CHCl_3$, 21 h	92	11
3		toluene, 6 h	55	13
4		$CHCl_3$, 21 h	90	9
5		benzene, 2 h	99	23
6		CH_2Cl_2, 24 h	94	9
7		$CHCl_3$, 4 h	93	12
8		$CHCl_3$, 1 h	100	13
9		benzene, 6 h	100	22
10		toluene, 66 h	17[b]	1.2

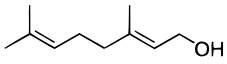
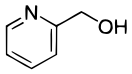
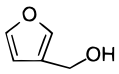
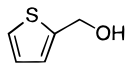
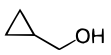
[a] Substrate was heated under reflux in the indicated solvent in the presence of 1.5 equiv of $BaMnO_4$ and 1.3 equiv of $Ph_3P{=}CHCO_2Et$ until both substrate alcohol and its intermediary aldehyde disappeared on TLC, except for entry 10. [b] After 66 h, obtained as a mixture with phenyl methyl ketone, and the yield was determined from the ^1H NMR spectrum.

these reaction conditions. This reaction system also converted cyclopropanemethanol[12] into the cyclopropyl alkene derivative quantitatively (entry 9). Thus, all of the primary "activated" alcohols tested were effective substrates in this reaction system, and the corresponding C2-elongated products were obtained in very high yields (entries 5−9). However, this reaction system was not effective for a secondary benzylic alcohol (entry 10), which could be predicted from the known insufficient reactivity of stable phosphorus ylides to ketones.[13]

We next investigated the reactions by a stepwise oxidation−Wittig reaction procedure with several substrates and compared the results with those of the above one-pot method. The reactions were carried out with $BaMnO_4$ (1.5 equiv) and $Ph_3P{=}CHCO_2Et$ (1.3 equiv), and the results are summarized in Table 3. Substrates were heated with BaMnO4 under reflux in $CHCl_3$, and the resulting aldehyde, which was not isolated, was then treated with $Ph_3P{=}CHCO_2Et$ in the same solvent. As a result, the yields were lower than those of the corresponding one-pot reactions. Thus, the effectiveness of the one-pot method was clearly demonstrated.

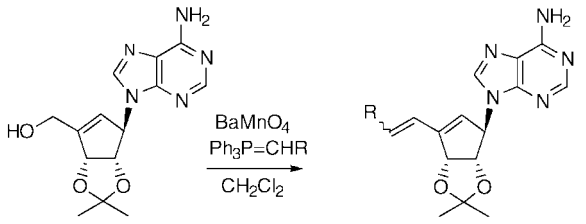
Table 3. Stepwise Reaction with $BaMn_4O$ and $Ph_3P{=}CHCO_2Et$[a]

RH-OH $\xrightarrow{\text{1) } BaMnO_4 \text{ 2) } Ph_3P=CHCO_2Et}$ R=$CHCO_2Et$

entry	substrate (RH-OH)	conditions	R=$CHCO_2Et$ yield (%)	R=$CHCO_2Et$ *E/Z*[b]
1		1) reflux, 21 h 2) rt, 24 h	76	13
2		1) reflux, 24 h 2) rt, 15 min	73	5
3		1) reflux, 4 h 2) rt, 15 h	53	21
4		1) reflux, 4 h 2) reflux, 30 min	80	15
5		1) reflux, 72 h[c] 2) rt, 48 h	0	–

[a] Substrate was heated under reflux in $CHCl_3$ in the presence of 1.5 equiv of $BaMnO_4$ for the same time as the corresponding entry in Table 2 or until the substrate disappeared on TLC, and then insoluble oxidant was filtered off. The filtrate was evaporated, and the residual aldehyde was treated with 1.3 equiv of $Ph_3P{=}CHCO_2Et$ in $CHCl_3$ until it disappeared on TLC. [b] Determined from the ^1H NMR spectrum. [c] The corresponding Wittig reaction product was also not obtained at all when CH_2Cl_2 was used as a solvent for the oxidation reaction.

Scheme 4



Finally, this one-pot method was applied to the synthesis of 6′-methylene derivatives of NPA. When 2′,3′-*O*-isopropylideneneplanocin A (**6**) was heated in the presence of $BaMnO_4$ and $Ph_3{=}CHCO_2Et$ in CH_2Cl_2, the desired (*E*)-6′-ethoxycarbonylmethylene derivative **8** was isolated in 85% yield (Scheme 4). Similarly, 6′-cyanomethylene derivative **13** was readily obtained in good yield as a mixture of *E*/*Z* isomers in a ratio of 3.6:1.

We studied the reaction with various alcohols and all of the reactions gave (*E*)-alkenes selectively, which is

(12) Cyclopropylmethanols have been reported to have allylic alcohol-like reactivity: Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C. *Chem. Rev.* **1989**, *89*, 165−198.

(13) (a) Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266−1272. (b) Sakai, T.; Seko, K.; Tsuji, A.; Utaka, M.; Takeda, A. *J. Org. Chem.* **1982**, *47*, 1101−1106.

consistent with known stereoselectively of the Wittig reaction with stable ylides.[14]

As described above, the overall yields of the stepwise oxidation and Wittig reaction were lower than those of the one-pot system. This may be, at least in some cases, due to instability of the α,β-unsaturated aldehyde (**II**), which would decrease the isolate yield, especially in the oxidation step.[15] Although this one-pot reaction also occurs via unstable α,β-unsaturated aldehydes (**II**), these would be quickly converted into the corresponding Wittig reaction products (**III**), which are generally stable compared to the corresponding aldehydes (**II**). In addition, in previous $BaMnO_4$ and MnO_2 oxidations, a large excess of the oxidant is often required to complete the reaction,[8a,10] and the absorption of compounds to polar sites of the surface of the oxidation reagent has been presumed.[10a] This may also decrease the yield of the $BaMnO_4$ and MnO_2 oxidations. Accordingly, the excellent yields in this reaction system may also be due to the reactions to be completed using only a slight excess of $BaMnO_4$.

In conclusion, we developed an efficient one-pot method for elongating the carbon skeleton of α,β-unsaturated primary alcohols. This method can be effectively used in synthetic organic chemistry.

Experimental Section

Melting points are uncorrected. NMR spectra were recorded at 270 or 500 MHz (^{1}H) and at 125 MHz (^{13}C) and are reported in ppm downfield from TMS. Mass spectra were obtained by electron ionization (EI) or fast atom bombardment (FAB) method. Thin-layer chromatography was done on Merck coated plate $60F_{254}$. Silica gel chromatography was done with Merck silica gel 5715.

Reaction with a Stable Phosphorus Ylide−$BaMnO_4$ System (General Procedure). A mixture of a substrate (1.00 mmol), a stable phosphorus ylide (1.30 mmol), and $BaMnO_4$ (384 mg, 1.5 mmol) in the corresponding solvent (5 mL) was stirred under the conditions indicated in Table 1 or 2. The insoluble material was filtered off on Celite, and the filtrate was evaporated in vacuo. The resulting residue was purified by silica gel column chromatography (EtOAc/hexane). All of the products were obtained as an oil, and the ratio of (*E*)- and (*Z*)-isomer was determined by HPLC (YMC R-ODS-5-A, 75% aqueous MeOH, 1.0 mL/min, 254 nm) for Table 1 or from the ^{1}H NMR spectrum for Tables 2 and 3.

Ethyl 5-Phenyl-2,4-pentadienoate (10). (2*E*,4*E*)-Isomer:[16] EI-MS *m*/*z* 202 (M^+). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.94; H, 7.08. **(2*Z*,4*E*)-Isomer**:[17] EI-MS *m*/*z* 202 (M^+). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.82; H, 7.05.

(*E*,*E*)-6-Phenyl-3,5-hexadien-2-one (11):[18] EI-MS *m*/*z* 172 (M^+). Anal. Calcd for $C_{12}H_{12}O\cdot0.2H_2O$: C, 81.97; H, 7.11. Found: C, 82.08; H, 7.03.

1-Cyano-4-phenyl-1,3-butadiene (12)[19] was obtained as a mixture of (1*E*,3*E*)- and (1*Z*,3*E*)-isomers: EI-MS *m*/*z* 155 (M^+). Anal. Calcd for $C_{11}H_9N$: C, 85.13; H, 5.85; N, 9.03. Found C, 85.00; H, 6.11; N, 8.91.

Ethyl 5,9-Dimethyl-2,4,8-decatrienoate (Table 2, Entries 1, 2). (2*E*,4*E*)-Isomer:[16] EI-MS *m*/*z* 222 (M^+). Anal. Calcd for $C_{14}H_{22}O_2\cdot0.1H_2O$: C, 75.03; H, 9.98. Found: C, 75.17; H, 10.08. **(2*Z*,4*E*)-Isomer**:[16] EI-MS *m*/*z* 222 (M^+). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.29; H, 10.01.

Ethyl 5,9-dimethyl-2,4,8-decatrienoate (Table 2, entries 3 and 4)[16] was obtained as a mixture of (2*E*,4*Z*)- and (2*Z*,4*Z*)-isomers: EI-MS *m*/*z* 222 (M^+). Anal. Calcd for $C_{14}H_{22}O_2\cdot0.4H_2O$: C, 73.26; H, 10.01. Found: C, 73.17; H, 9.70.

Ethyl cinnamate (Table 2, entry 5)[20] was obtained as an *E*/*Z* mixture: EI-MS *m*/*z* 176 (M^+). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.80; H, 6.97.

Ethyl 3-(2-pyridyl)-2-propenoate (Table 2, entry 6)[21,22] was obtained as an *E*/*Z* mixture: EI-MS *m*/*z* 177 (M^+). Anal. Calcd for $C_{10}H_{11}NO_2\cdot0.1H_2O$: C, 67.10; H, 6.31; N, 7.82. Found: C, 67.17; H, 6.41; N, 7.67.

Ethyl 3-(3-Furanyl)-2-propenoate (Table 2, entry 7). (*E*)-Isomer:[23] EI-MS *m*/*z* 166 (M^+). Anal. Calcd for $C_9H_{10}O_3\cdot0.2H_2O$: C, 63.67; H, 6.17. Found: C, 63.72; H, 5.98. **(*Z*)-Isomer**: ^{1}H NMR ($CDCl_3$) δ 8.13 (s, 1 H), 7.41 (d, 1 H, J = 1.8 Hz), 6.94 (d, 1 H, J = 1.8 Hz), 6.71 (d, 1 H, J = 12.5 Hz), 5.80 (d, 1 H, J = 12.5 Hz), 4.22 (q, 2 H, J = 7.0 Hz), 1.31 (t, 3 H, J = 0.70 Hz); HRMS (EI) calcd for $C_9H_{10}O_3$ 166.0630, found 166.0625.

Ethyl 3-(2-thienyl)propenoate (Table 2, entry 8)[24] was obtained as an *E*/*Z* mixture: EI-MS *m*/*z* 182 (M^+). Anal. Calcd for $C_9H_{10}O_2S$: C, 53.92; H, 5.53. Found: C, 59.25; H, 5.58.

Ethyl 3-cyclopropyl-2-propenoate (Table 2, entry 9)[25] was obtained as an *E*/*Z* mixture: EI-MS *m*/*z* 140 (M^+). Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.38; H, 8.62.

Ethyl 3-phenyl-2-butenoate (Table 2, entry 10)[26,27] was obtained as an *E*/*Z* mixture: EI-MS *m*/*z* 140 (M^+). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.64; H, 7.58.

General Procedure for Stepwise Oxidation−Wittig Reaction. A mixture of a substrate (1.00 mmol) and $BaMnO_4$ (384 mg, 1.5 mmol) in $CHCl_3$ (5 mL) was heated under the conditions indicated in Table 3. The insoluble material was filtered off on Celite, and the filtrate was evaporated in vacuo. A mixture of the resulting residue and $Ph_3P{=}CHCO_2Et$ (1.3 mmol) in $CHCl_3$ (5 mL) was stirred under the conditions indicated in Table 3. The solvent was evaporated in vacuo, and and the residue was purified by silica gel column chromatography (EtOAc/hexane). The ratio of (*E*)- and (*Z*)-isomer was determined from the ^{1}H NMR spectrum.

(*E*)-6′-Ethoxycarbonylmethylene-2′,3′-*O*-isopropylideneneplanocin A (8). A. Stepwise Method. A mixture of **6** (307 mg, 1.0 mmol) and $BaMnO_4$ (4.5 g, 17.6 mmol) in CH_2Cl_2 (50 mL) was heated under reflux for 40 h. After MeOH (40 mL) was added, the mixture was cooled to room temperature, and the insoluble material was filtered off. the filtrate was evaporated to dryness in vacuo to give crude **7** as a foam. To the foam was added MeCN (10 mL) and $Ph_3P{=}CHCO_2Et$ (383 mg, 1.1 mmol) and the mixture was stirred at room temperature for 1 h. The solution was evaporated in vacuo, and the residue was partitioned between $CHCl_3$ and saturated aqueous NaCl. The organic layer was evaporated in vacuo and the residue was purified by silica gel column chromatography (MeOH/$CHCl_3$ 1:100, then 1:40) to give **8** (138 mg, 37%) as a white form: ^{1}H NMR (DMSO-d_6) δ 8.11 and 8.04 (each s, each 1 H), 7.45 (d, 1

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H, J = 16.0 Hz), 7.25 (br s, 2 H), 6.39 (d, 1 H, J = 2.1 Hz), 6.21 (d, 1 H, J = 16.0 Hz), 5.64 (d, 1 H, J = 5.9 Hz), 5.60 (d, 1 H, J = 2.1 Hz), 4.81 (d, 1 H, J = 5.9 Hz), 4.17 (q, 2 H, J = 7.0 Hz), 1.36 and 1.32 (each s, each 3 H), 1.24 (t, 3 H, J = 7.0 Hz); EI-MS m/z 371 (M^+). Anal. Calcd for $C_{18}H_{21}N_5O_4 \cdot 0.7H_2O$: C, 57.03; H, 6.09; N, 17.78. Found: C, 57.43; H, 5.92; N, 17.58.

B. One-Pot Method. A mixture of **6** (92 m g, 0.3 mmol), $Ph_3P{=}CHCO_2Et$ (115 mg, 0.33 mmol), and $BaMnO_4$ (769 mg, 3.00 mmol) in CH_2Cl_2 (6 mL) was stirred at reflux for 24 h. The insoluble material was filtered off on Celite, and the filtrate was evaporated in vacuo. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH 1:50) to give **8** (95 mg, 85%) as a white form.

6′-Cyanomethylene-2′,3′-*O*-isopropylideneneplanocin A (13). Compound **13** was prepared as described for **8,** with $Ph_3P{=}CHCN$ instead of $Ph_3P{=}CHCO_2Et$. After purification by silica gel column chromatography, **13** was obtained as an *E*/*Z* mixture (white foam, 85 mg, 87%). The ratio of (*E*)- and (*Z*)-isomer was determined from the ^{1}H NMR spectrum: EI-MS m/z 324 (M^+); HRMS calcd for $C_{16}H_{16}N_6O_2$ 324.1335, found 324.1322. ^{1}H NMR ($CDCl_3$) δ (*E*)-isomer, 8.33 (s, 1 H), 7.68 (s, 1 H), 7.21 (d, 1 H, J = 16.5 Hz), 6.09 (d, 1 H, J = 2.6 Hz), 5.94 (d, 1 H, J = 16.5 Hz), 5.67−5.56 (m, 4 H), 4.88−4.85 (m, 1 H), 1.46 (s, 3 H), 1.38 (s, 3 H); (*Z*)-isomer, 8.36 (s, 1 H), 7.73 (s, 1 H), 6.88 (d, 1 H, J = 12.5 Hz), 6.45 (d, 1 H, J = 2.6 Hz), 5.82 (d, 1 H, J = 5.3 Hz), 5.67−5.56 (m, 4 H), 4.88−4.85 (m, 1 H), 1.50 (s, 3 H), 1.41 (s, 3 H).

Supporting Information Available: ^{1}H NMR spectra of **8** and **13** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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