Dess−Martin Periodinane Oxidation of Alcohols in the Presence of Stabilized Phosphorus Ylides: A Convenient Method for the Homologation of Alcohols via Unstable Aldehydes

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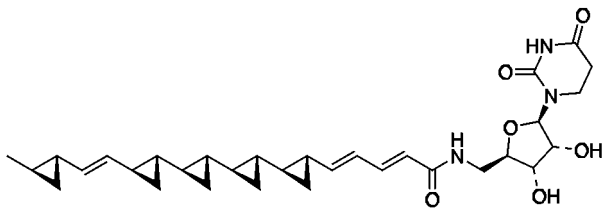
Both FR-900848 (**1**)[1] and U-106305 (**2**),[2] which are structurally remarkable polycyclopropane natural products noted for antifungal activities and the inhibition of



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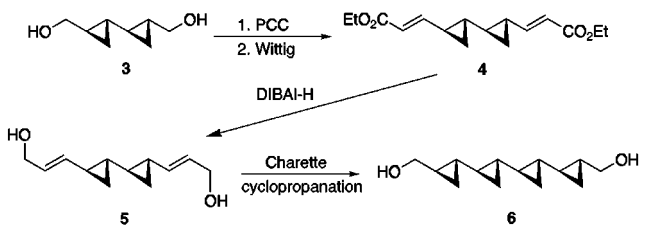
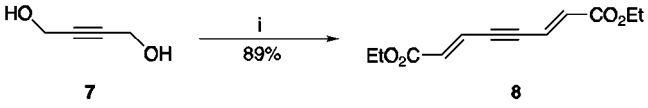
2

cholesteryl transfer proteins, respectively, have been the subject of considerable synthetic efforts recently.[3] During the course of our studies on the structural elucidation and total syntheses of these substances, we have repeatedly used a double oxidation, Wittig homologation, DIBAl-H reduction and Charette cyclopropanation[4] sequence to generate polycyclopropane arrays (Scheme 1). Several of the dialdehydes in this sequence were found to be sensitive substances and as such, the Wittig reaction was carried out directly following oxidation. During these studies we had occasion to examine the Dess−Martin periodinane oxidation[5] of diols in the presence of ester ylides. This process, which is precedented in the work of Huang on radiopharmaceuticals,[6] is especially valuable for the generation and in situ trapping of particularly unstable dialdehydes such as 2-butynedial and 2,4-hexadiynedial.

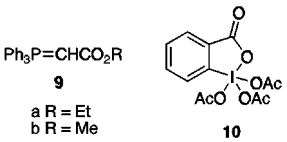
Scheme 1



Scheme 2



[a] Reagents and conditions: (1) $PhCO_2H$ (4 equiv), **9a** (4 equiv), **10** (2.4 equiv), DMSO, CH_2Cl_2; $NaHCO_3$, H_2O, Et_2O.



Dess−Martin periodinane **10** was added to a mixture of 2-butyne-1,4-diol (**7**), the ester ylide **9a**, and benzoic acid, an additive to accelerate the reaction and to enhance the *E*:*Z* selectivity of the Wittig reaction,[7] and this smoothly provided the adduct **8** (89%) as a mixture of *trans-trans* and *trans-cis* isomers (4:1) (Scheme 2). It is clear that this in situ oxidation and Wittig homologation is very convenient compared for the handling of 2-butynedial,[8] a sensitive dialdehyde prepared from the acid-mediated hydrolysis of acetal derivatives and prone to rapid decomposition. This instability is underscored by the fact that Dess−Martin oxidation of 2-butyne-1,4-diol (**7**) and subsequent addition of the ylide **9a** failed to provide any dienyne **8** whatsoever. This oxidation/Wittig homologation sequence was applied to further examples (Table 1). The formation of dienediyne diester **12** and tetraene **18** further illustrate the usefulness of the method for the preparation and direct derivatization of unstable aldehydes. Although the reaction of 1,2-ethanediol (**13**) gave the diene diester **14** in only modest yield (27%), direct reaction of commercial 40% aqueous glyoxal with ylide **9a** proceeded in better yield [89%, (*E*,*E*):(*E*,*Z*) = 2.5:1]. The preparation of diene **14** in this way represents an improvement over existing methods.[3] Oxidation/homologation of 1,3-propanediol (**15**) gave ethyl (*E*)-2,4-pentadienoate (**16**) probably via elimination of 3-hydroxypropanal or an iodine(III) derivative. An attempt to use the method to prepare and trap trifluoroacetaldehyde was unsuccessful. In this example only a trace of diethyl fumarate (3%) was formed presumably via oxidation of the ylide.

The Dess−Martin periodinane oxidation of a mixture of a stabilized phosphorus ylide and an alcohol should find further use in the preparation and functionalization of delicate aldehydes.

Experimental Section

Diethyl Octa-2(*E*),6(*E*)-dien-4-yne-1,8-dioate (8) and Diethyl Octa-2(*E*),6(*Z*)-dien-4-yne-1,8-dioate. 2-Butyne-1,4-diol

(1) Yoshida, M.; Ezaki, M.; Hashimoto, M.; Yamashita, M.; Shigematsu, N.; Okuhara, M.; Kohsaka, M.; Horikoshi, K. *J. Antibiot.* **1990**, *43*, 748.

(2) Kuo, M. S.; Zielinski, R. J.; Cialdella, J. I.; Marschke, C. K.; Dupuis, M.; Li, G. P.; Kloosterman, D. A.; Spilman, C. H.; Marshall, V. P. *J. Am. Chem. Soc.* **1995**, *117*, 10629.

(3) For example see: (a) Barrett, A. G. M.; Doubleday, W. W.; Kasdorf, K.; Tustin, G. J. *J. Org. Chem.* **1996**, *61*, 3280. (b) Barrett, A. G. M.; Kasdorf, K. *J. Chem. Soc., Chem. Commun.* **1996**, 325. (c) Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 7863. (d) Barrett, A. G. M.; Kasdorf, K. *J. Am. Chem. Soc.* **1996**, *118*, 11030. (e) Falck, J. R.; Mekonnen, B.; Yu, J.; Lai, J.-Y. *J. Am. Chem. Soc.* **1996**, *118*, 6096. (f) Charette, A. B.; Lebel, H. *J. Am. Chem. Soc.* **1996**, *118*, 10327.

(4) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651. Charette, A. B.; Prescott, S.; Brochu, C. *J. Org. Chem.* **1995**, *60*, 1081. Charette, A. B.; Marcoux, J.-F. *Synlett* **1995**, 1197.

(5) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.

(6) Huang, C. C. *J. Labeled Compd. Radiopharm.* **1987**, *24*, 675.

(7) Vedejs, E.; Peterson, M. J. *Adv. Carbanion Chem.* **1996**, *2*, 1; *Top. Stereochem.* **1994**, *21*, 1. Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 8608.

(8) Gorgues, A.; Le Coq, A. *Tetrahedron Lett.* **1979**, 4825.

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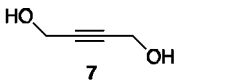
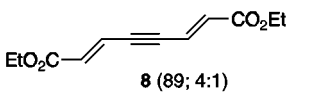
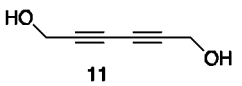
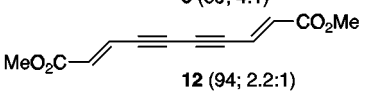
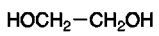
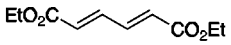
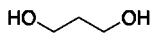
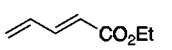
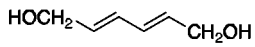
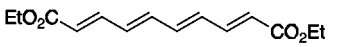
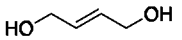
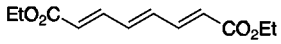
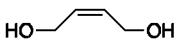
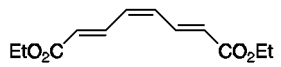
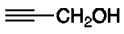
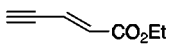
Table 1. Dess−Martin Oxidation of Diols in the Presence of Ylides

Diol	Product (%; *E,E*:*E,Z*)[a]
 **7**	 **8** (89; 4:1)
 **11**	 **12** (94; 2.2:1)
 **13**	 **14** (27; 5:1)
 **15**	 **16** (47, *E* only)
 **17**	 **18** (50; 4.7:1)
 **19**	 **20** (82; 4:1)
 **21**	 **22** (24; 7:2)
 **23**	 **24** (85; 10:1)
CF_3CH_2OH **25**	-

(a) The ratio refers to the diene formed in the reaction as determined by ^{1}H NMR spectroscopy.

(177 mg, 2.0 mmol), $PhCO_2H$ (977 mg, 8.0 mmol), and $EtO_2CCH{=}PPh_3$ (**9a**) (2.79 g, 8.0 mmol) were dissolved in dry CH_2Cl_2 (15 mL) and dry DMSO (2.5 mL). Dess−Martin periodinane (**10**) (2.04 g, 4.8 mmol) was added, and the mixture turned orange-red brown within seconds and started to boil. After 30 min at room temperature, saturated aqueous $NaHCO_3$ solution, Et_2O, and some solid $NaHCO_3$ were added. After stirring for 10 min, the mixture was filtered, the organic layer was separated and concentrated in vacuo. The residue was chromatographed on silica (hexanes:Et_2O 6:1) to give **8** (318 mg, 72%) and (*E,Z*)-**8** (79 mg, 18%) as colorless oils. **8**: TLC R_f 0.41 (hexanes:Et_2O 6:1); IR (film) 1716, 1626, 1312, 1265, 1175, 1164, 1036, 960 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (2H, d, J = 15.2 Hz), 6.32 (2H, d, J = 15.2 Hz), 4.25 (4H, q, J = 7.1 Hz), 1.32 (6H, t, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 132.1, 123.8, 93.9, 61.0, 14.2; MS (CI, NH_3) *m/e* 240 (M + NH_4)$^+$, 223 (M + H)$^+$, 193; exact mass (CI, NH_3) calcd for $C_{12}H_{15}O_4$ (M + H)$^+$, 223.0970, found (M + H)$^+$ 223.0972. (*E,Z*)-**8**: TLC R_f 0.34 (hexanes:Et_2O 6:1); IR (film) 1715, 1621, 1304, 1178, 1031, 960 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (1H, dd, J = 2.7, 15.9 Hz), 6.25 (1H, d, J = 15.9 Hz), 6.22 (1H, dd, J = 2.7, 11.5 Hz), 6.11 (1H, d, J = 11.5 Hz), 4.18 (2H, q, J = 7.2 Hz), 4.15 (2H, q, J = 7.2 Hz), 1.25 (3H, t, J = 7.2 Hz), 1.23 (3H, t, J = 7.2 Hz); MS (CI, NH_3) *m/e* 240 (M + NH_4)$^+$, 223 (M + H)$^+$, 193; exact mass (CI, NH_3) calcd for $C_{12}H_{15}O_4$ (M + H)$^+$, 223.0970, found (M + H)$^+$ 223.0962.

The following compounds were prepared according to the procedure described for compounds **8** and (*E,Z*)-**8**.

Dimethyl deca-2(*E*),8(*E*)-diene-4,6-diyne-1,10-dioate (12): yellow crystals, mp 104−106 °C (lit.[9] 105−107 °C); TLC R_f 0.38 (hexanes:Et_2O 6:1); IR (film) 2135, 1715, 1610, 1441, 1307, 1273, 1178, 963 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.84 (2H, d, J = 15.5 Hz), 6.40 (2H, d, J = 15.5 Hz), 3.79 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 133.5, 123.3, 81.2, 81.1, 52.1; MS (CI, NH_3) *m/e* 236 (M + NH_4)$^+$, 218 (M$^{+\bullet}$); exact mass (CI, NH_3) calcd for $C_{12}H_{10}O_4{\cdot}NH_4$ (M + NH_4)$^+$, 236.0923, found (M + NH_4)$^+$ 236.0926. (*E,Z*)-**12**: yellow solid, mp 72−73 °C (lit.[9] 76−78 °C); TLC R_f 0.28 (hexanes:Et_2O 6:1); IR (film) 2131, 1733, 1716, 1612, 1440, 1328, 1258, 1226, 1192, 1173, 953 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (1H, d, J = 15.9 Hz), 6.39 (1H, d, J = 15.9 Hz), 6.33 (1H, d, J = 11.5 Hz), 6.26 (1H, d, J = 11.5 Hz), 3.81 (3H, s), 3.80 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 164.5, 133.1, 132.2, 123.6, 121.4, 84.2, 82.1, 81.6, 80.7, 52.1, 51.8; MS (CI, NH_3) *m/e* 236 (M + NH_4)$^+$, 219 (M + H)$^+$; exact mass (CI, NH_3) calcd for $C_{12}H_{10}O_4{\cdot}NH_4$ (M + NH_4)$^+$, 236.0923, found (M + NH_4)$^+$ 236.0923.

Diethyl hexa-2(*E*),4(*E*)-diene-1,6-dioate (14): white crystals, mp 57−59 °C (pentane−Et_2O) (lit.[10] 63−64 °C); TLC R_f 0.28 (hexanes:Et_2O 3:1); IR (film) 1699, 1613, 1253, 1172, 1026, 863 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.34 (2H, m), 6.14−6.22 (2H, m), 4.23 (4H, q, J = 7.1 Hz), 1.30 (6H, t, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 140.8, 128.4, 60.9, 14.2; MS (CI, NH_3) *m/e* 216 (M + NH_4)$^+$, 199 (M + H)$^+$; exact mass (CI, NH_3) calcd for $C_{10}H_{14}O_4{\cdot}NH_4$ (M + NH_4)$^+$, 216.1236, found (M + NH_4)$^+$ 216.1235.

Ethyl (*E*)-2,4-pentadienoate (16):[11] colorless oil; TLC R_f 0.47 (hexanes:Et_2O 6:1); IR (film) 1723, 1299, 1260, 1155, 1036, 979 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (1H, dd, J = 11.0, 15.4 Hz), 6.48 (1H, ddd, J = 10.4, 11.0, 16.9 Hz), 5.93 (1H, d, J = 15.4 Hz), 5.63 (1H, d, J = 16.9 Hz), 5.50 (1H, d, J = 10.4 Hz), 4.23 (2H, q, J = 7.1 Hz), 1.32 (3H, t, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 144.6, 134.7, 125.4, 122.2, 60.4, 14.2; MS (CI, NH_3) *m/e* 144 (M + NH_4)$^+$, 127 (M + H)$^+$; exact mass (CI, NH_3) calcd for $C_7H_{11}O_2$ (M + H)$^+$, 127.0759, found (M + H)$^+$ 127.0761.

Diethyl deca-2(*E*),4(*E*),6(*E*),8(*E*)-tetraene-1,10-dioate (18): pale yellow crystals, mp 132−136 °C (from hexanes−Et_2O) (lit.[12] 131−132 °C); TLC R_f 0.46 (hexanes:Et_2O 3:1); IR (film) 1704, 1628, 1012, 878 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (2H, dd, J = 10.9, 15.3 Hz), 6.48−6.65 (4H, m), 5.97 (2H, d, J = 15.3 Hz), 4.23 (4H, q, J = 7.1 Hz), 1.31 (6H, t, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 143.4, 138.9, 133.6, 123.0, 60.5, 14.3; MS (CI, NH_3) *m/e* 268 (M + NH_4)$^+$, 251 (M + H)$^+$; exact mass (CI, NH_3) calcd for $C_{14}H_{19}O_4$ (M + H)$^+$, 251.1283, found (M + H)$^+$ 251.1288.

Diethyl octa-2(*E*),4(*E*),6(*E*)-triene-1,8-dioate (20): white crystals, mp 86−89 °C (pentane−Et_2O) (lit.[13] 88−89 °C); TLC R_f 0.32 (hexanes:AcOEt 6:1); IR (film) 1712, 1627, 1370, 1343, 1300, 1235, 1133, 1026, 866 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (2H, ddd, J = 3.2, 7.5, 15.3 Hz), 6.64 (2H, dd, J = 3.2, 7.5 Hz), 6.03 (2H, d, J = 15.3 Hz), 4.23 (4H, q, J = 7.2 Hz), 1.31 (6H, t, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 142.7, 136.9, 124.7, 60.6, 14.3; MS (CI, NH_3) *m/e* 242 (M + NH_4)$^+$, 225 (M + H)$^+$, 195; exact mass (CI, NH_3) calcd for $C_{12}H_{17}O_4$ (M + H)$^+$, 225.1127, found (M + H)$^+$ 225.1128.

Diethyl octa-2(*E*),4(*Z*),6(*E*)-triene-1,8-dicarboxylate (22):[13] white crystals, mp 57−61 °C (pentane−Et_2O); TLC R_f 0.32 (hexanes:AcOEt 6:1); IR (film) 1706, 1621, 1367, 1318, 1270, 1212, 1145, 1041, 982, 887 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78−7.87 (2H, m), 6.39−6.46 (2H, m), 6.03 (2H, d, J = 15.1 Hz), 4.26 (4H, q, J = 7.1 Hz), 1.34 (6H, t, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 137.6, 133.5, 125.1, 60.7, 14.3; MS (CI, NH_3) *m/e* 242 (M + NH_4)$^+$, 225 (M + H)$^+$; exact mass (CI, NH_3) calcd for $C_{12}H_{16}O_4{\cdot}NH_4$ (M + NH_4)$^+$, 242.1392, found (M + NH_4)$^+$ 242.1390.

Ethyl 2(*E*)-penten-4-ynoate (24):[14] colorless oil; TLC R_f 0.57 (hexanes:Et_2O 6:1); IR (film) 3293, 3263, 2105, 1719, 1306, 1270, 1181, 1039, 963 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.73 (1H, dd, J = 2.3, 15.9 Hz), 6.32 (1H, d, J = 15.9 Hz), 4.23 (2H, q, J = 7.2 Hz), 3.35 (1H, d, J = 2.3 Hz), 1.31 (3H, t, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 132.5, 123.9, 85.8, 80.2, 60.9,

(9) Farrell, I. W.; Thaller, V.; Turner, J. L. *J. Chem. Soc., Perkin Trans.* **1977**, 1886. Marvell, E. N.; Seubert, J.; Vogt, G.; Zimmer, G.; Moy, G.; Siegmann, J. R. *Tetrahedron* **1978**, *34*, 1323.

(10) Moffett, L. R., Jr.; Hill, W. E. *J. Org. Chem.* **1962**, *27*, 1454.

(11) Rodriguez, J.; Waegell, B. *Synthesis* **1988**, 534.

(12) Yanovskaya, L. A.; Stepanova, R. N.; Kogan, G. A.; Kucherov, V. F. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1963**, 774.

(13) Adger, B. J.; Barrett, C.; Brennan, J.; McGuigan, P.; McKervey, M. A.; Tarbit, B. *J. Chem. Soc., Chem. Commun.* **1993**, 1220. Kasahara, A.; Izumi, T.; Kudou, N. *Synthesis* **1988**, 704.

14.2; MS (FAB) *m/e* 123 $(M - H)^-$, 95. ***Z*-(24)**:[14] colorless oil; TLC R_f 0.34 (hexanes:Et_2O 6:1); IR (film) 2097, 1725, 1299, 1261, 1181, 1035, 979 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.22 (1H, d, J = 11.6 Hz), 6.14 (1H, dd, J = 2.4, 11.6 Hz), 4.26 (2H, q, J = 7.2 Hz), 3.63 (1H, d, J = 2.4 Hz), 1.33 (3H, t, J = 7.2 Hz).

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(14) Kovalev, B. G.; Yanovskaya, L. A.; Kucherov, V. F.; Kogan, G. A. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1963**, 127.