Selective Oxidation of Phosphorus Ylides by Dimethyldioxirane. Application to the Formation of Vicinal Tricarbonyls

Harry H. Wasserman,* Carmen M. Baldino, and Steven J. Coats

Department of Chemistry, Yale University, New Haven Connecticut 06520-8107

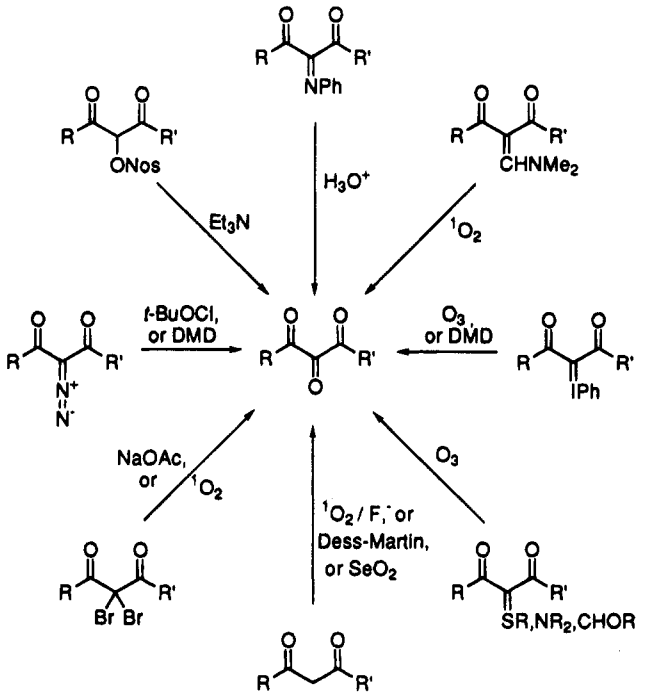
Received August 2, 1995[⊗]

Dimethyldioxirane (DMD) has proven to be an effective reagent for the selective conversion of phosphoranylidene intermediates **4** to the corresponding vicinal tricarbonyls **5**. Unlike existing oxidation protocols which employ relatively vigorous conditions, this transformation is conducted rapidly at low temperature under neutral conditions, without the necessity of an aqueous workup. Selective oxidation of the phosphorus ylides in the presence of a variety of sensitive functionality was achieved by lowering the reaction temperature and controlling the concentration of oxidant.

Introduction

The development of new methods for preparing vicinal tricarbonyls has stimulated renewed study of these reactive systems, which, as stable hydrates, take part in many reactions of value in the synthesis of organic products.[1] The recent discovery of the powerful immunosuprressants FK-506[2] and rapamycin,[3] incorporating a vicinal tricarbonyl unit in the form of a hemiacetal, has added special significance to the studies on the chemistry of this array.[4] The highly electrophilic nature of the carbonyl groups, particularly the central carbonyl, favors nucleophilic attack by donor reagents as weakly basic as amides, and the attachment of other acceptor sites to the tricarbonyl core have provided opportunities for ring-forming reactions with di- and trinucleophiles. We have demonstrated the generality and usefulness of this methodology in the preparation of pyrroles,[5] indolizidines,[6] pyrrolidines,[7] in the fusion of five- and six-membered rings to β-lactams[8,9] and in the synthesis of various natural products.[10,11] During these studies, we have developed new methods for forming tricarbonyls in which the central carbonyl group is generated by an oxidation reaction involving the cleavage of a carbon–phosphorus double bond. In this paper we describe the advantageous use of dimethyldioxirane (DMD) as an oxidant in this process.

Scheme 1



The first general method for preparing a vicinal tricarbonyl was reported almost 100 years ago by Sachs.[12] The oxidation of a 1,3-diketone was accomplished by *p*-nitroso(dimethylamino)benzene to form an imine intermediate which was then hydrolyzed by strong acid to form the central carbonyl group. Most of the methods developed since that time have similarly involved oxidation of 1,3-dicarbonyl systems as summarized in Scheme 1.

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1995.

(1) For reviews of 1,2,3-tricarbonyl chemistry see: (a) Schönberg, A. Singer, E. *Tetrahedron* **1978**, *34*, 1285. (b) Rubin, M. B. *Chem. Rev.* **1975**, *75*, 177.

(2) Tanaka, H.; Kuroda, A.; Marusawa, H.; Hatanaka, H.; Kino, T.; Goto, T.; Hashimoto, M.; Taga, T. *J. Am. Chem. Soc.* **1987**, *109*, 5031.

(3) (a) Findlay, J. A.; Radics, L. *Can. J. Chem.* **1980**, *58*, 579. (b) Swindells, D. C. N.; White, P. S.; Findlay, J. A. *Can. J. Chem.* **1978**, *56*, 2491. (c) Vézina, C.; Kudelski, A.; Sehgal, S. N. *J. Antibiot.* **1975**, *28*, 721. (d) Sehgal, S. N.; Baker, H.; Vézina, C. *J. Antibiot.* **1975**, *28*, 727.

(4) (a) Wasserman, H. H.; Ennis, D. S.; Power, P. L.; Ross, M. J.; Gomes, B *J. Org. Chem.* **1993**, *58*, 4785. (b) Henke, S. L.; Hadad, C. M.; Morgan, K. M.; Wiberg, K. B.; Wasserman, H. H. *J. Org. Chem.* **1993**, *58*, 2830. (c) Albers, M. W.; Walsh, C. T.; Schreiber, S. L. *J. Org. Chem.* **1990**, *55*, 4984. (d) Van Duyne, G. D.; Sandaert, R. F.; Karplus, P. A.; Schreiber, S. L.; Clardy, J. *Science* **1991**, *252*, 839.

(5) (a) Wasserman, H. H.; Cook, J. D.; Fukuyama, J. M.; Rotello, V. M. *Tetrahedron Lett.* **1989**, *30*, 1721. (b) Wasserman, H. H.; Frechette, R.; Oida, T.; van Duzer, J. H. *J. Org. Chem.* **1989**, *54*, 6012.

(6) (a) Wasserman, H. H.; Cook, J. D.; Vu, C. B. *J. Org. Chem.* **1990**, *55*, 1701. (b) Wasserman, H. H.; Vu, C. B.; Cook, J. D. *Tetrahedron* **1992**, *48*, 2101.

(7) (a) Wasserman, H. H.; Cook, J. D.; Vu, C. B. *Tetrahedron Lett.* **1990**, *31*, 4945.

(8) (a) Wasserman, H. H.; Han, W. T. *J. Am. Chem. Soc.* **1985**, *107*, 1444. (b) Wasserman, H. H.; Han, W. T. *Tetrahedron Lett.* **1984**, *25*, 3743.

(9) (a) Wasserman, H. H.; Han, W. T. *Tetrahedron Lett.* **1984**, *25*, 3747. (b) Wasserman, H. H.; Niu, C. *BioMed. Chem. Lett.* **1993**, *3*, 2437. (c) Wasserman, H. H.; Henke, S. L.; Luce, P.; Nakanishi, E. *J. Org. Chem.* **1990**, *55*, 5821. (d) Wasserman, H. H.; Henke, S. L.; Nakanishi, E. *J. Org. Chem.* **1992**, *57*, 2641.

(10) Wasserman, H. H. *Aldrichim. Acta* **1987**, *20*, 63 and references cited therein.

(11) (a) Wasserman, H. H.; Lombardo, L. J. *Tetrahedron Lett.* **1989**, *30*, 1725. (b) Wasserman, H. H.; Rotello, V. M.; Krause, G. B. *Tetrahedron Lett.* **1992**, *33*, 5419. (c) Wasserman, H. H.; Kuo, G. H. *Tetrahedron Lett.* **1991**, *32*, 7131. (d) Wasserman, H. H.; Kuo, G. H. *Tetrahedron* **1992**, *48*, 7071. (e) Wasserman, H. H.; Amici, R.; Frechette, R.; van Duzer, J. H. *Tetrahedron Lett.* **1989**, *30*, 869. (f) Wasserman, H. H.; Kuo, G. H. *Tetrahedron Lett.* **1989**, *30*, 873. (g) Wasserman, H. H.; Amici, R. M. *J. Org. Chem.* **1989**, *54*, 5843. (h) Wasserman, H. H.; Kelly, T. A. *Tetrahedron Lett.* **1989**, *30*, 7117.

(12) Sachs, F.; Harold, V. *Ber.* **1907**, *40*, 2714.

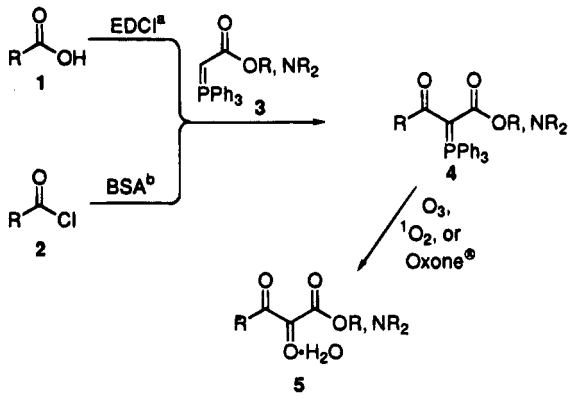
0022-3263/95/1960-8231$09.00/0

These methods along with others developed in the course of synthetic studies related to FK-506[13] have limitations with respect to the availability of starting materials, efficiency of the reaction sequences, and the functionalities which can tolerate the strong oxidizing conditions.

As exemplified in Scheme 1 (clockwise), such procedures include the following: hydrolysis of imines,[12] singlet oxygen oxidation of enamines,[8] oxidation of phenyl iodonium ylides by ozone[14] or dimethyldioxirane,[15] ozonolysis of enol ethers and other ylides containing either sulfur or nitrogen,[16] oxidation of 1,3-dicarbonyl compounds by singlet oxygen in the presence of fluoride ion,[17] Dess–Martin oxidation,[18] or selenium dioxide oxidation,[19] reaction of 2,2-dibromo 1,3-diones with singlet oxygen[20] or sodium acetate,[21] dimethyldioxirane[22] or *tert*-butylhypochlorite[23] oxidation of 2-diazo-1,3-dioxo derivatives, and elimination of the nosyl group in an α-nosyloxy 1,3-diketone.[24]

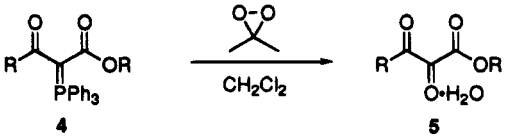
One procedure recently worked out in our laboratory generates precursors of the tricarbonyl system by a mild, generally applicable coupling reaction starting with carboxylic acids. In this convergent method, the carboxylic acid or its acid chloride undergoes reaction with the phosphorane **3** to form the ylide **4** as shown in Scheme 2.[25] This ylide **4** can be looked on as a tricarbonyl precursor or a protected tricarbonyl, since it can be readily converted to this system by oxidative cleavage of the carbon–phosphorus double bond. To date, this oxidation has been accomplished with singlet oxygen,[26]

Scheme 2



[a]EDCI = 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
[b]BSA = *N,O*-Bis(trimethylsilyl)acetamide

Scheme 3



ozone,[27] and Oxone.[28] These two-step procedures are particularly convenient and general, providing good to excellent yields of phosphorus ylides and corresponding tricarbonyls. Of the oxidants employed, Oxone has thus far proven to be the mildest oxidizing agent for the second step conversion. While Oxone has provided some degree of selectivity, certain functional groups including sulfides, enol ethers, isolated olefins, and nitrogen-containing heterocycles undergo serious competitive oxidation in the presence of this reagent.

Results and Discussion

Seeking to obtain selectivity in the oxidative generation of the tricarbonyl from the intermediate ylide, we have now investigated the use of DMD, an oxidant which has been shown to be efficient and highly selective for a variety of substrates.[29] Solutions of DMD in acetone are prepared by the reaction of Oxone with acetone according to known methods.[30] The oxygen transfer with DMD occurs rapidly at low temperature under neutral conditions.

We have now found (Scheme 3) that the phosphorus ylide intermediates **4** can be selectively oxidized to the corresponding vicinal tricarbonyl by DMD in the presence of a variety of oxidizable functional groups, as outlined in Table 1.[31] For the phosphorus ylides shown in entries 1 and 2, Table 1, DMD provides the tricarbonyls in quantitative yield. These reactions were conducted with

(13) For other methods of vicinal tricarbonyl formation see: (a) reactions of α-keto esters with lithiodithianes: Egbertson, M.; Danishefsky, S. J. *J. Org. Chem.* **1989**, *54*, 11. (b) Aldol addition of a protected α-hydroxy amide or ester to an aldehyde as applied to total synthesis of FK506: Jones, T. K.; Mills, S. G.; Reamer, R. A.; Askin, D.; Desmond, R.; Volante, R. P.; Shinkai, I. *J. Am. Chem. Soc.* **1989**, *111*, 1157. Jones, T. K.; Reamer, R. A.; Desmond, R.; Mills, S. G. *J. Am. Chem. Soc.* **1990**, *112*, 2998. Nakatsuka, M.; Ragan, J. A.; Sammakia, T.; Smith, D. B.; Uehling, D. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 5583. (c) Dess–Martin oxidation of 2-(phenylthio)-3-hydroxy amides: Linde, R. G., II; Jeroncic, L. O.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 2534. (d) From acyltriazolinedione ylides: Wilson, R. M.; Hengge, A. C. *J. Org. Chem.* **1990**, *55*, 197. (e) From 2,3-dihydroxyalkanoates: Inokuchi, T.; Liu, P.; Torii, S. *Chem. Lett.* **1994**, 1411.

(14) Schank, K.; Lick, C. *Synthesis* **1983**, 392.

(15) Wasserman, H. H.; Coats, S. J. Unpublished results; also see ref 29d.

(16) (a) For sulfur ylides see: Schank, K.; Schuhknecht, C. *Chem. Ber.* **1982**, *115*, 3032. (b) For nitrogen ylides see: Schank, K.; Lick, C. *Chem. Ber.* **1982**, *115*, 3890. (c) For enol ethers see: Schank, K.; Schuhknecht, C. *Chem. Ber.* **1982**, *115*, 2000.

(17) Wasserman, H. H.; Pickett, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 4695.

(18) Batchelor, M. J.; Gillespie, R. J.; Golec, J. M. C.; Hedgecock, C. J. R. *Tetrahedron Lett.* **1993**, *34*, 167.

(19) Williams, D. R.; Benbow, J. W. *J. Org. Chem.* **1988**, *53*, 4643. Also see ref 1.

(20) Mahran, M. R.; Abdou, W. M.; Sidky, M. M.; Wamhoff, H. *Synthesis* **1987**, 506.

(21) Bigelow, L. A.; Hanslick, R. S. In *Organic Syntheses*; Blatt, A. H.. Ed.; John Wiley and Sons Inc.: New York, **1943**; Coll. Vol. II, p 244.

(22) Saba, A. *Synth. Commun.* **1994**, *24*, 695.

(23) (a) Regitz, M.; Schwall, H.; Heck, G.; Eistert, B.; Bock, G. *Liebigs Ann. Chem.* **1965**, *690*, 125. (b) Regitz, M.; Adolph, H. G. *Chem. Ber.* **1968**, *101*, 3604. (c) Regitz, M.; Adolph, H. G. *Ann. Chem.* **1969**, *723*, 47. (d) Detering, J.; Martin, H.-D.; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 695.

(24) (a) Hoffman, R. V.; Wilson, A. L.; Kim, H.-O. *J. Org. Chem.* **1990**, *55*, 1267. (b) Hoffman, R. V.; Kim, H.-O.; Wilson, A. L. *J. Org. Chem.* **1990**, *55*, 2820. (c) Hoffman, R. V.; Huizenga, D. J. *J. Org. Chem.* **1991**, *56*, 6435.

(25) Wasserman, H. H.; Ennis, D. S.; Blum, C. A.; Rotello, V. M. *Tetrahedron Lett.* **1992**, *33*, 6003. Cooke, M. P., Jr.; Burman, D. L. *J. Org. Chem.* **1982**, *47*, 4955.

(26) Wasserman, H. H.; Rotello, V. M.; Williams, D. R.; Benbow, J. W. *J. Org. Chem.* **1989**, *54*, 2785.

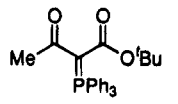
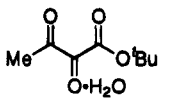
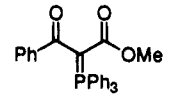
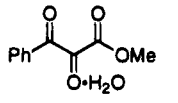
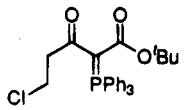
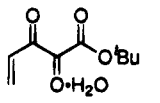
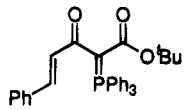
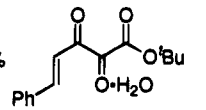
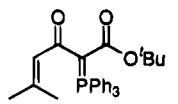
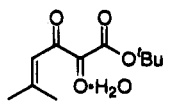
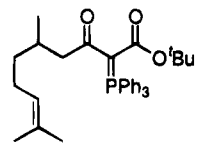
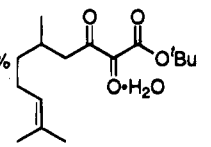
(27) Wasserman, H. H.; Fukuyama, J.; Murugesan, N.; van Duzer, J.; Lombardo, L.; Rotello, V.; McCarthy, K. *J. Am. Chem. Soc.* **1989**, *111*, 371.

(28) Wasserman, H. H.; Vu, C. B. *Tetrahedron Lett.* **1990**, *31*, 5205.

(29) For recent reviews see: (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (b) Curci, R. in *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI: Greenwich, CT, 1990; Vol. 2, Chapter 1. (c) Adam, W.; Hadjiarapoglou, L.; Curci, R.; Mello, R. In *Organic Peroxides*; Ando, W., Ed.; Wiley: New York, 1993; Chapter 4, pp 195–219. (d) Adam, W.; Hadjiarapoglou, L. In *Topic in Current Chemistry*; Herrmann, W. A., Ed.; Springer-Verlag, Berlin, 1993; Vol. 164, p 45–62.

(30) (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847. (b) Adam, W.; Chan, Y. Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800. (c) Adam, W.; Hadjiarapoglou, L.; Smerz, A. *Chem. Ber.* **1991**, *124* 227.

Table 1. Phosphorus Ylide Oxidations

entry	phosphorus ylide		tricarbonyl	DMD	other
1		76%		100%[a]	79%[e]
2		96%		100%[a]	63%[f]
3[i]		91%		82%[b]	80%[g]
4[j]		97%		85%[c]	61%[f]
5[i]		77%		100%[c]	60%[e]
6		94%		83%[d]	71%[h]

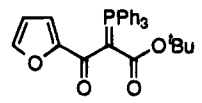
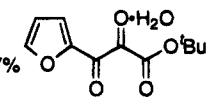
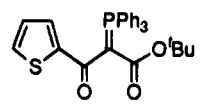
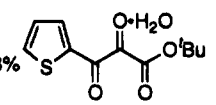
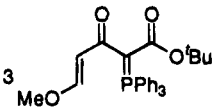
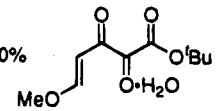
[a] 3.0 equiv DMD, 25 °C, 1 h. [b] a) 3.0 equiv DMD, 25 °C; b) THF/$NaHCO_3$ (aq). [c] 2.0 equiv DMD, -78→25 °C, 4 h. [d] 1.8 equiv DMD, -78→25 °C, 4 h. [e] 1.5 equiv Oxone, THF/H_2O, 25 °C, 12 h. [f] Sensitox, O_2, $CHCl_3$, hν. [g] a) 1.5 equiv Oxone, THF/H_2O, 25 °C; b) THF/$NaHCO_3$ (aq). [h] 3.0 equiv Oxone, 5:1 benzene/H_2O, 55 °C. [i] see ref. 28. [j] see ref. 25.

3 equiv of DMD at room temperature and were generally complete within 1 h as revealed by TLC analysis or the disappearance of the yellow reaction color. In addition, these reactions required no special precautions for the exclusion of water or atmospheric oxygen. The analogous oxidations with either Oxone or singlet oxygen are also presented for comparison.

Our first examples of selective oxidation involved variously substituted conjugated olefins (Table 1, entries 3–5). Despite the oxidizability of carbonyl-conjugated olefins by DMD,[31a] they remained intact under the comparatively mild conditions used in the conversion of the phosphorus ylides to the corresponding tricarbonyls. In reactions where oxidation selectivity was required, DMD was added at −78 °C and the resulting solution was then warmed slowly to room temperature. With a trisubstituted isolated olefin (Table 1, entry 6), more care was required in that a deficiency of DMD (1.8 equiv) was employed in order to avoid overoxidation to the epoxide. This series of examples shows that DMD can oxidize the carbon–phosphorus double bond in the presence of

(31) Functional group oxidation by DMD: (a) α,β-unsaturated carbonyls: Adam, W.; Hadjiarapoglou, L.; Nestler, B. *Tetrahedron Lett.* **1990**, *31*, 331. Baumstark, A. L.; Harden, D. B. *J. Org. Chem.* **1993**, *58*, 7615. (b) Furans: Adger, B. J.; Barrett, C.; Brennan, J.; McGuigan, P.; McKervey, M. A.; Tarbit, B. *J. Chem. Soc., Chem. Commun.* **1993**, 1220. (c) thiophenes: Miyahara, Y.; Inazu, T. *Tetrahedron Lett.* **1990**, *31*, 5955. (d) β-Oxo enol ethers: Adam, W.; Hadjiarapoglou, L. *Chem. Ber.* **1990**, *123*, 2077.

Table 2. Hetero-Substituted Phosphorus Ylide Oxidations

entry	phosphorus ylide		tricarbonyl	DMD	other
1		97%		97%[a]	60%[b]
2		88%		97%[a]	88%[b]
3		80%		70%[a]	0%[b]

[a] 2.0 equiv DMD, -78→25 °C, 4 h. [b] 1.5 equiv Oxone, THF/H_2O, 25 °C, 12 h..

unsaturation and that the conversions to the tricarbonyl are improved relative to known methods.

The preparation of tricarbonyls with substituents containing heteroatoms and heteroaromatics is of special interest in the synthesis of biologically interesting agents. Furan-[31b] and thiophene-substituted[31c] ylides (Table 2, entries 1, and 2) were oxidized selectively by DMD to the tricarbonyl in much improved conversion relative to the Oxone procedure. Another sensitive functional group, the β-oxo enol ether (Table 2, entry 3), was readily converted to the tricarbonyl using DMD while the Oxone procedure resulted in oxidative degradation. However, like other oxidizing agents previously studied, DMD was not selective in oxidizing phosphorus ylides in the presence of nitrogen heterocycles including pyrroles, indoles, and pyridines.[32]

Conclusion

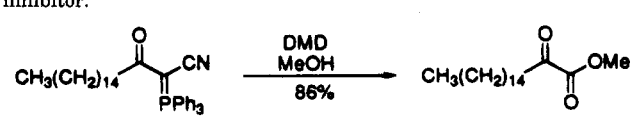
Dimethyldioxirane has proven to be an effective reagent for the selective conversion of phosphorus ylide intermediates **4** to the corresponding vicinal tricarbonyls **5**.[33] Unlike existing oxidation protocols which employ relatively vigorous conditions, this transformation is conducted rapidly at low temperature under neutral conditions, without the necessity of an aqueous workup. The DMD conversions take place much more rapidly than the corresponding Oxone reactions. Selective oxidation of the phosphorus ylides in the presence of a variety of sensitive functionality was achieved by lowering the reaction temperature and controlling the amount of reagent. Use of DMD under these conditions should provide easier access to more complex and biologically interesting vicinal tricarbonyl systems.

Experimental Section

General Procedure A. Preparation of 3-Oxo-2-(triphenylphosphoranylidene)alkanoates. A dry 15 mL round-

(32) We have recently found that Davis reagent (2-(phenylsulfonyl)-3-phenyl oxaziridine) also provides selective oxidation of phosphorus ylides in excellent yields after 6–24 h at rt. Unfortunately nitrogen heterocycles are oxidized competitively.

(33) In work to be published elsewhere, we have used DMD for the preparation of an α-keto ester, which has been evaluated as an enzyme inhibitor.



bottomed flask was charged with *tert*-butyl (triphenylphosphoranylidene)acetate (1.0 mmol) and BSA (1.2 mmol) in dry CH_2Cl_2 or benzene (5 mL). The stirred solution was cooled to 5 °C, and the appropriate acid chloride (1.0 mmol) was added via syringe. The resulting slurry was stirred as it warmed to room temperature for 2–16 h under N_2. The reaction was quenched by the addition of H_2O (2 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 1 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated.

General Procedure B. Preparation of 3-Oxo-2-(triphenylphosphoranylidene)alkanoates. A dry 15 mL round-bottomed flask was charged with *tert*-butyl (triphenylphosphoranylidene)acetate (1.2 mmol) and the appropriate carboxylic acid (1.0 mmol) in dry CH_2Cl_2 (5 mL). The stirred solution was cooled to 5 °C, and EDCI (1.1 mmol) was added in one portion. The resulting slurry was stirred as it warmed to room temperature for 16 h under N_2. The reaction was quenched by the addition of H_2O (2 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 1 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated.

***tert*-Butyl 3-Oxo-2-(triphenylphosphoranylidene)butanoate** (Table 1, entry 1a). Procedure A: Chromatography (SiO_2, 60% EtOAc/hexane) afforded 4.0 g (98%) as a white solid: IR (neat) ν max 3054, 3009, 2965, 2930, 1667, 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 9H), 2.34 (s, 3H), 7.7–7.3 (m, 15H).

Methyl 3-Phenyl-3-oxo-2-(triphenylphosphoranylidene)propionate (Table 1, entry 2a). Procedure A: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 300 mg (95%) as a pale yellow foam: ^1H NMR ($CDCl_3$) δ 3.14 (s, 3H), 7.33–7.35 (m, 4H), 7.45–7.52 (m, 8H), 7.69–7.79 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 49.4, 69.9, 124.8, 126.0, 126.9, 127.7, 127.8, 128.1, 128.3, 129.2, 129.3, 130.3, 131.5, 131.7, 132.2, 132.9, 142.4, 142.5, 167.7, 192.92; IR (KBr) ν max 3060, 2940, 1720, 1670, 1590, 1500, 1480, 1440, 1340, 1290, 1190, 1100, 1080, 1030, 910, 730 cm^{-1}; HRMS calcd for $C_{28}H_{23}O_3P$ $[M + H]^+$ 439.1462, found 439.1463.

***tert*-Butyl 5-Methyl-3-Oxo-2-(triphenylphosphoranylidene)-4-hexenoate** (Table 1, entry 5a). Procedure A: Chromatography (SiO_2, 50% Et_2O/hexane) afforded 0.5 g (77%) as a white solid: IR (neat) ν max 3060, 2974, 2931, 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (s, 9H), 1.85 (s, 3H), 1.89 (s, 3H), 6.93 (brs, 1H), 7.35–7.50 (m, 10H), 7.60–7.73 (m, 5H); HRMS calcd for $C_{29}H_{31}O_3P$ $[M + H]^+$ 459.2089, found 459.2084.

***tert*-Butyl 5,9-Dimethyl-3-oxo-2-(triphenylphosphoranylidene)-8-decenoate** (Table 1, entry 6a). Procedure A: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 2.7 g (94%), or procedure B afforded 2.4 g (84%): IR (neat) ν max 3080, 2980, 2890, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 9H), 1.18–1.38 (m, 6H), 1.56 (brs, 3H), 1.68 (brs, 3H), 1.85–2.05 (m, 2H), 2.75–2.82 (m, 2H), 5.00–5.12 (m, 1H), 7.32–7.75 (m, 15H). Anal. Calcd for $C_{28}H_{41}O_3P$: C, 77.24; H, 7.82. Found: C, 77.17; H, 7.85.

***tert*-Butyl 3-(2-Furanyl)-3-oxo-2-(triphenylphosphoranylidene)propionate** (Table 2, entry 1a). Procedure A: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 700 mg (97%) as a pale yellow solid: H NMR ($CDCl_3$) δ 1.06 (s, 9H), 6.42 (dd, 1H, J = 1.63 Hz), 7.15 (d, 1H, J = 3.27 Hz), 7.42–7.54 (m, 10H), 7.72–7.79 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 28.0, 82.1, 110.9, 114.1, 128.4, 131.6, 133.2, 133.2, 142.7, 154.2, 166.5, 199.9; IR (KBr) ν max 3040, 2980, 1670, 1570, 1510, 1460, 1170, 1100, 1060, 750, 690 cm^{-1}; HRMS calcd for $C_{29}H_{27}O_4P$ $[M + H]^+$ 471.1725, found 471.1723. Anal. Calcd for $C_{29}H_{27}O_4P$: C, 74.03; H, 5.78. Found: C, 74.11; H, 5.78.

***tert*-Butyl 3-Oxo-3-(2-thiophene-yl)-2-(triphenylphosphoranylidene)propionate** (Table 2, entry 2a). Procedure A: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 580 mg (88%) as a yellow solid: ^1H NMR ($CDCl_3$) δ 1.05 (s, 9H), 7.01 (d, 1H, J =3.99 Hz), 7.32 (t, 1H, J =4.91 Hz), 7.40–7.49 (m, 9H), 7.74–7.81 (m, 6H), 7.94 (d, 1H, J = 3.55 Hz); ^{13}C NMR ($CDCl_3$) δ 27.7, 69.8, 78.3, 125.8, 126.2, 127.0, 128.1, 128.3, 128.4, 130.2, 131.3, 132.7, 132.8, 146.6, 166.2, 182.6; IR (KBr) ν max 3030, 2990, 1670, 1480, 1310, 1250, 1170, 900, 700 cm^{-1}; HRMS calcd for $C_{29}H_{27}O_3PS$ $[M + H]^+$ 487.1497, found 487.1488.

***tert*-Butyl 5-Methoxy-3-oxo-2-(triphenylphosphoranylidene)-4-*trans*-pentenoate** (Table 2, entry 3a). Procedure B: Chromatography (SiO_2, EtOAc) afforded 490 mg (75%) as a yellow foam: ^1H NMR ($CDCl_3$) δ 1.00 (s, 9H), 3.18 (d, 1H, J = 4.42 Hz), 3.26 (s, 3H), 5.02 (d, 1H, J = 4.42 Hz), 7.31–7.37 (m, 9H), 7.60–7.66 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 27.8, 43.0, 52.4, 72.7, 78.2, 102.4, 126.1, 127.4, 128.1, 128.3, 128.4, 131.1, 132.5, 132.7, 166.7, 192.5; IR (KBr) ν max 3060, 2980, 1660, 1550, 1440, 1360, 1170, 1070, 700 cm^{-1}; HRMS calcd for $C_{28}H_{29}O_4P$ $[M + H]^+$ 461.1882, found 461.1881.

General Procedure C. Oxidation of 3-Oxo-2-(triphenylphosphoranylidene)alkanoates with Dimethyldioxirane. A round-bottomed flask was charged with a solution of the appropriate 3-oxo-2-(triphenylphosphoranylidene)alkanoate (0.5 mmol) in CH_2Cl_2 (2.0 mL), and to this was added a solution of dimethyldioxirane in acetone (0.1 M, 3.0 equiv). The reaction mixture was stirred at 25 °C. After 1 h, the starting material had been consumed. The crude mixture was concentrated and purified on silica gel.

General Procedure D. Oxidation of 3-Oxo-2-(triphenylphosphoranylidene)alkanoates with Dimethyldioxirane. A round-bottomed flask was charged with a solution of the appropriate 3-oxo-2-(triphenylphosphoranylidene)alkanoate (0.5 mmol) in CH_2Cl_2 (2.0 mL) and then cooled to −78 °C. The reaction mixture was then treated with a solution of dimethyldioxirane in acetone (0.1 M, 2.0 equiv) and gradually warmed to 25 °C over a 4 h period. The crude mixture was concentrated and purified on silica gel.

***tert*-Butyl 2,3-Dioxobutanoate Hydrate** (Table 1, entry 1b). Procedure C: Chromatography (SiO_2, 20% EtOAc/hexane) afforded 100 mg (100%) as a white solid: IR (neat) ν max 3406, 2985, 2938, 1745, 1722 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (s, 9H), 2.27 (s, 3H), 4.92 (brs, 2H); ^{13}C NMR ($CDCl_3$) δ 23.1, 27.7, 85.0, 92.7, 168.0, 201.3; HRMS calcd for $C_{16}H_{28}O_5$ $[M + H]^+$ 301.2016, found 301.2020.

Methyl 3-Phenyl-2,3-dioxopropionate Hydrate (Table 1, entry 2b). Procedure C: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 105 mg (100%) yellow oil: ^1H NMR ($CDCl_3$) δ 3.66 (s, 3H), 5.81 (bs, 2H), 7.38–7.44 (m, 2H), 7.54–7.58 (m, 1H), 8.05–8.08 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 53.4, 91.9, 128.6, 129.0, 129.8, 131.1, 170.1, 191.4; IR (neat) ν max 3600–3300, 3060, 2940, 1760, 1750, 1690, 1600, 1450, 1440, 1230, 1130, 1100, 1010 cm^{-1}; HRMS calcd for $C_{10}H_{10}O_5$ $[M + H]^+$ 211.0603, found 211.0606.

***tert*-Butyl 5-Phenyl-2,3-dioxo-4-*trans*-pentenoate Hydrate** (Table 1, entry 4b). Procedure D: Chromatography (SiO_2, 25% EtOAc/hexane) afforded 14 mg (85%) as a white solid: ^1H NMR ($CDCl_3$) δ 1.47 (s, 9H), 5.25 (s, 2H), 6.92 (d, 1H, J = 16.25 Hz) 7.31–7.68 (m, 5H), 7.91 (d, 1H, J = 16.25 Hz); IR ($CHCl_3$) ν max 3450, 3025, 3010, 2980, 1735, 1695, 1395, 1370, 1120, 1070 cm^{-1}; HRMS calcd for $C_{15}H_{18}O_5$ $[M + H]^+$ 279.1232, found 279.1220. Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.12; H, 6.48.

***tert*-Butyl 5-Methyl-2,3-dioxo-4-hexenoate Hydrate** (Table 1, entry 5b). Procedure D: Chromatography (SiO_2, 15% EtOAc/hexane) afforded 100 mg (100%): IR (neat) ν max 3410, 1750, 1724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (s, 9H), 2.00 (s, 3H), 2.26 (s, 3H), 5.11 (s, 2H), 6.16 (brs, 1H); ^{13}C NMR ($CDCl_3$) δ 21.7, 27.7, 28.2, 84.5, 92.2, 117.1, 168.9, 191.1; HRMS calcd for $C_{11}H_{18}O_5$ $[M - H_2O + H]^+$ 213.1127, found 213.1128.

***tert*-Butyl 5,9-Dimethyl-2,3-dioxo-8-decenoate Hydrate** (Table 1, entry 6b). Procedure D (1.8 equiv of DMD): Chromatography (SiO_2, 30% EtOAc/hexane) afforded 80 mg (83%): IR (neat) ν max 3470, 2990, 2940, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3H, J = 6.6 Hz), 1.18–1.45 (m, 2H), 1.50 (s, 9H), 1.60 (brs, 3H), 1.69 (brs, 3H), 1.93-2.04 (m, 2H), 2.05–2.20 (m, 1H), 2.39 (dd, 1H, J = 17.90 Hz), 2.61 (dd, 1H, J = 17.90 Hz), 4.95 (s, 1H), 4.98 (s, 1H), 5.04–5.13 (m, 1H); HRMS calcd for $C_{16}H_{28}O_5$ $[M + H]^+$ 301.2016, found 301.2020.

***tert*-Butyl 3-(2-Furanyl)-2,3-dioxopropionate Hydrate** (Table 2, entry 1b). Procedure D: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 60 mg (97%) as a yellow oil: ^1H NMR ($CDCl_3$) δ 1.32 (s, 9H), 5.21 (s, 2H), 6.53 (dd, 1H, J = 1.33 Hz), 7.37 (d, 1H, J = 3.65 Hz), 7.62 (d, 1H, J = 0.97 Hz); ^{13}C NMR ($CDCl_3$) δ 27.4, 84.8, 91.1, 112.8, 122.2, 148.2, 168.2, 180.6; IR (neat) ν max 3420, 3380, 3120, 2970, 1740, 1670,

1270, 1130, 1110, 1040, 890, 780 cm^{-1}; HRMS calcd for $C_{11}H_{14}O_6$ $[M + H]^+$ 243.0869, found 243.0870. Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.66; H, 5.87.

***tert*-Butyl 2,3-Dioxo-3-(2-thiophene-yl)propionate Hydrate** (Table 2, entry 2b). Procedure D: Chromatography (SiO_2, 25% EtOAc/hexane) afforded 66 mg (97%) as a yellow oil: ^1H NMR ($CDCl_3$) δ 1.35 (s, 9H), 5.37 (s, 2H), 7.18 (d, 1H, J = 4.80 Hz), 7.78 (t, 1H, J = 3.99 Hz), 7.93 (d, 1H, J = 3.45 Hz); ^{13}C NMR ($CDCl_3$) δ 27.4, 84.9, 92.0, 128.5, 135.9, 136.1, 137.0, 168.6, 185.3; IR (neat) ν max 3420, 3100, 2980, 1740, 1660, 1250, 1130, 720 cm^{-1}; HRMS calcd for $C_{11}H_{14}O_5S$ $[M + H]^+$ 259.0640, found 259.0638. Anal. Calcd for $C_{11}H_{14}O_5S$: C, 51.15; H, 5.46; S, 12.41. Found: C, 51.14; H, 5.47; S, 12.50.

***tert*-Butyl 5-Methoxy-2,3-dioxo-4-*trans*-pentenoate Hydrate** (Table 2, entry 3b). Procedure D: Chromatography (SiO_2, 50% EtOAc/hexane) afforded 53 mg (70%) as a yellow residue: ^1H NMR ($CDCl_3$) δ 1.50 (s, 9H), 2.94 (d, 1H, J = 5.54 Hz), 3.37 (s, 3H), 4.94 (d, 1H, J = 5.54 Hz), 5.10 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 27.5, 40.2, 53.8, 85.0, 92.7, 100.7, 167.7, 200.3; IR (KBr) ν max 3420, 2980, 1740, 1700, 1170, 1100, 1050 cm^{-1}; HRMS calcd for $C_{10}H_{16}O_6$ $[M + H]^+$ 233.1025, found 233.1017.

Acknowledgment. This research was supported by grants from the NIH and the NSF. We thank Dr. Michael R. Hale for help in other aspects of our DMD study,[33] Dr. Ji Uk Yoo for Table 1, entry 3, and Ms. Jan D. Cook for the preparation of phosphorus ylides, Table 1, entries 4 and 5.

Supporting Information Available: ^{13}C-NMR spectra for entries 2a and 2b of Table 1, and entries 2a, 3a, and 3b of Table 2. ^1H-NMR spectra for entries 5a and 5b of Table 1 (7 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.

JO9514230