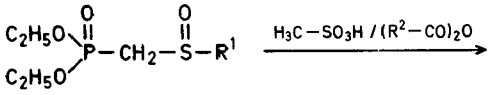
The Pummerer Rearrangement of Alkyl or Aryl Diethoxyphosphinylmethyl Sulfoxides

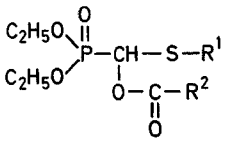
Stephen E. DINIZO, David S. WATT*

Department of Chemistry, University of Colorado, Boulder, Colorado 80309, U.S.A.

In connection with our interest in the synthesis of highly substituted phosphonate reagents[1], we sought to prepare diethyl methanephosphonates bearing an oxygen and a sulfur substituent. We investigated the acid-catalyzed Pummerer rearrangement[2] of the diethoxyphosphinylmethyl sulfoxides **1** in the presence of various carboxylic acid anhydrides and obtained the desired methanephosphonates **2** in good yield. A recent publication of Mikołajczyk[3] reported the synthesis of the alkoxy analogs of **2** in low yield and prompted us to communicate our results.



1



2

The diethoxyphosphinylmethyl sulfoxides **1** were prepared by the Arbusov reaction[4,5] of chloromethyl thioethers ($ClCH_2$—S—R) with triethyl phosphite followed by the sodium periodate oxidation[5] of the α-diethoxyphosphinylmethyl sulfides to furnish **1**. The Pummerer rearrangements of **1** catalyzed by methanesulfonic acid[6] (0.25 equivalents) in the presence of acetic, propanoic, butanoic, 2,2-dimethylpropanoic, or benzoic anhydride led to the α-acyloxy-α-(diethoxyphosphinyl)-methyl sulfides **2** in good yield (Table 1). The rearrangements were performed in neat solutions of the carboxylic acid anhydride[7] (with the exception of benzoic anhydride) at 25° but were best conducted using 2.0 equivalents of the carboxylic acid anhydride in a refluxing dichloromethane solution to facilitate the isolation of **2** from excess carboxylic acid anhydride at the end of the reaction. The methylthio compounds **2** ($R^1 = CH_3$) were unstable to chromatography[8] on silica gel or alumina and, consequently,

were isolated by distillation. In contrast, the phenylthio compounds **2** ($R^1 = C_6H_5$) were conveniently purified by silica gel chromatography.

Preparation of α-Acyloxy-α-(diethoxyphosphinyl)-methyl Sulfides (2); General Procedure:

To the sulfoxide **1** (1.0 mmol) and the carboxylic acid anhydride (2.0 mmol) in dry dichloromethane (2 ml) was added methanesulfonic acid (24 mg, 0.25 mmol). The solution was refluxed for 3 h with exclusion of moisture, cooled, diluted with 5% sodium carbonate solution (25 ml) and extracted with three 20 ml portions of ether. The combined ether solutions were dried over anhydrous magnesium sulfate and concentrated. The product was isolated by (procedure A) preparative thick layer (2 mm) chromatography on a 20 × 20 cm Merck silica gel F 254 plate using ether as the eluent or (procedure B) evaporative distillation at ~125° (0.5 torr).

Received: September 27, 1976

We wish to thank the National Institutes of Health (GM-22978-01) for their generous financial support.

Table 1. Preparation of Alkyl or Aryl α-Acyloxy-α-(diethoxyphosphinyl)-methyl Sulfides **2**

Product	R^1	R^2	Purification procedure[a]	Yield[b] [%]	n_D (temp.)
2a	CH_3	CH_3	B	81	1.4611 (20°)
2b	CH_3	C_2H_5	B	73	1.4551 (22°)
2c	CH_3	n-C_3H_7	B	74	1.4585 (21°)
2d	CH_3	t-C_4H_9	B	66	1.4547 (22°)
2e	C_6H_5	CH_3	A	72	1.5103 (21°)
2f	C_6H_5	C_2H_5	A	58	1.5076 (22°)
2g	C_6H_5	n-C_3H_7	A	55	1.5053 (21°)
2h	C_6H_5	t-C_4H_9	A	62	1.4984 (22°)
2i	C_6H_5	C_6H_5	A	38[c]	1.5490 (22°)

[a] Procedure A: preparative thick layer chromatography; procedure B: evaporative distillation.
[b] Yield of isolated product based on sulfoxide **1**.
[c] Solvent: 1,2-dichloroethane instead of dichloromethane.

[1] S. E. Dinizo, R. W. Freerksen, W. E. Pabst, D. S. Watt, *J. Org. Chem.* **41**, 2846 (1976).
[2] For a review, see T. Durst, *Adv. Org. Chem.*, **6**, 356 (1969).
[3] M. Mikołajczyk, B. Costisella, S. Grzejszczek, A. Zatorski, *Tetrahedron Lett.* **1976**, 477.
[4] M. Green, *J. Chem. Soc.* **1963**, 1324.
[5] M. Mikołajczyk, A. Zatorski, *Synthesis* **1973**, 699.
[6] H. J. Monteiro, and A. L. Gemal, *Synthesis* **1975**, 437.
[7] For example, **1** ($R^1 = CH_3$) afforded **2a** in 81% yield following the procedure in the Experimental Section and in 74% yield using 2 ml Ac_2O/mmol of **1** and 0.25 equiv of methanesulfonic acid for 3 h at 25°.
[8] For example, the % recovery of **2a** following chromatography on Merck silica gel F 254, pH = 7 buffered Merck silica gel F 254 and Merck alumina F 254 was 11%, 16%, and 13%, respectively.

Table 2. Analytical and Spectral Data for Phosphonates **2**.

Compound	Molecular Formula[a]	I.R. (liquid film) ν_{max} [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]	M.S.: *m/e* (relative intensity)
2a	$C_8H_{17}O_5PS$ (256.3)	1751	6.05 (d, 1H, J_{P-H} = 12 Hz, P(O)CH), 3.95–4.55 (m, 4H, OCH_2CH_3), 2.35 (d, 3H, J = 1.5 Hz, SCH_3), 2.16 (s, 3H, $OC(O)CH_3$), 1.35 (t, 6H, J = 7 Hz, OCH_2CH_3)	256 ($M^{\oplus}$, 20), 167 (36), 138 (44), 111 (57), 47 (14), 43 (100)
2b	$C_9H_{19}O_5PS$ (270.3)	1751	6.10 (d, 1H, J_{P-H} = 12 Hz, P(O)CH), 3.97–4.57 (m, 4H, OCH_2CH_3), 2.24–2.75 (m, 2H, $OC(O)CH_2CH_3$), 2.35 (d, 3H, J = 1.5 Hz, SCH_3), 0.95–1.54 (m, 9H, OCH_2CH_3 and $OC(O)CH_2CH_3$)	270 ($M^{\oplus}$, 36), 167 (69), 138 (76), 111 (62), 57 (100), 47 (20)
2c	$C_{10}H_{21}O_5PS$ (284.3)	1751	6.11 (d, 1H, J_{P-H} = 2 Hz, P(O)CH), 3.97–4.55 (m, 4H, OCH_2CH_3), 2.24–2.60 (m, 2H, $OC(O)CH_2CH_2CH_3$), 2.35 (d, 3H, J = 1.5 Hz, SCH_3), 1.50–2.07 (m, 2H, $OC(O)CH_2CH_2CH_3$), 1.35 (t, 6H, J = 7 Hz, OCH_2CH_3), 0.98 (broad t, 3H, J = 7 Hz, $OC(O)CH_2CH_2CH_3$)	284 ($M^{\oplus}$, 16), 167 (40), 138 (42), 111 (31), 71 (63), 60 (100), 47 (18)
2d	$C_{11}H_{23}O_5PS$ (298.3)	1742	6.07 (d, 1H, J_{P-H} = 12 Hz, P(O)CH), 3.92–4.52 (m, 4H, OCH_2CH_3), 2.35 (d, 3H, J = 1.5 Hz, SCH_3), 1.35 (broad t, 6H, J = 7 Hz, OCH_2CH_3), 1.27 (s, 9H, $OC(O)C(CH_3)_3$)	298 ($M^{\oplus}$, 12), 167 (39), 138 (36), 111 (29), 85 (14), 57 (100), 47 (8)
2e	$C_{13}H_{19}O_5PS$ (318.3)	1756, 1589	7.15–7.68 (m, 5H_{arom}), 6.39 (d, 1H, J_{P-H} = 11 Hz, P(O)CH), 3.90–4.50 (m, 4H, OCH_2CH_3), 2.10 (s, 3H, $OC(O(CH_3)$), 1.33 (t, 6H, J = 7 Hz, OCH_2CH_3)	318 ($M^{\oplus}$, 23), 167 (100), 138 (17), 111 (47), 109 (22), 77 (11), 43 (72)
2f	$C_{14}H_{21}O_5PS$ (332.4)	1744, 1578	7.21–7.59 (m, 5H_{arom}), 6.44 (d, 1H, J_{P-H} = 11 Hz, P(O)CH), 3.93–4.53 (m, 4H, OCH_2CH_3), 2.41 (broad q, 2H, J = 7 Hz, $OC(O)CH_2CH_3$), 1.32 (t, 6H, J = 7 Hz, OCH_2CH_3), 1.13 (t, 3H, J = 7 Hz, $OC(O)CH_2CH_3$)	332 ($M^{\oplus}$, 24), 167 (100), 138 (15), 111 (25), 109 (12), 77 (6), 57 (61)
2g	$C_{15}H_{23}O_5PS$ (346.4)	1749, 1582	7.22–7.70 (m, 5H_{arom}), 6.46 (d, 1H, J_{P-H} = 11 Hz, P(O)CH), 3.93–4.53 (m, 4H, OCH_2CH_3), 2.13–2.57 (m, 2H, $OC(O)CH_2CH_2CH_3$), 1.43–1.98 (m, 2H, $OC(O)CH_2CH_2CH_3$), 1.33 (t, 6H, J = 7 Hz, OCH_2CH_3), 0.92 (broad t, 3H, $OC(O)CH_2CH_2CH_3$)	346 ($M^{\oplus}$, 15), 167 (100), 138 (10), 111 (23), 109 (17), 77 (6), 71 (38)
2h	$C_{16}H_{25}O_5PS$ (360.4)	1745, 1582	7.13–7.67 (m, 5H_{arom}), 6.44 (d, 1H, J_{P-H} = 11 Hz, P(O)CH), 3.88–4.50 (m, 4H, OCH_2CH_3), 1.33 (t, 6H, J = 7 Hz, OCH_2CH_3), 1.11 (s, 9H, $OC(O)C(CH_3)_3$)	360 ($M^{\oplus}$, 10), 167 (67), 138 (35), 111 (37), 109 (45), 85 (27), 57 (100)
2i	$C_{18}H_{21}O_5PS$ (380.4)	1734, 1600, 1585	7.04–8.28 (m, 10H_{arom}), 6.69 (d, 1H, J_{P-H} = 10.5 Hz, P(O)CH), 3.88–4.64 (m, 4H, OCH_2CH_3), 1.33 and 1.30 (two t, 6H, J = 7 Hz, OCH_2CH_3)	380 ($M^{\oplus}$, 1), 138 (5), 137 (11), 111 (8), 109 (23), 105 (100), 81 (17), 77 (26)

[a] All products gave satisfactory microanalyses (C ± 0.28 ±, H ± 0.07%).