Reactions of 1-Oxoalkanephosphonate Tosyhydrazones with Sodium Borohydride: A New Synthesis of Dimethyl Alkanephosphonates and Dimethyl 1-Diazoalkanephosphonates

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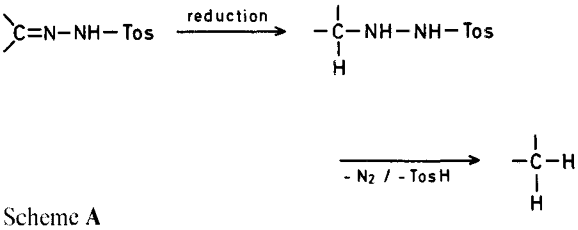
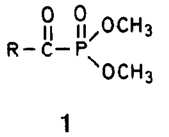
It is well known that the reduction of tosylhydrazones with alkali metal aluminium hydrides and alkali metal borohydrides gives rise to saturated hydrocarbons in high yields under mild conditions via the intermediate formation of *N*-alkyl-*N'*-tosylhydrazines[1] according to Scheme **A**.



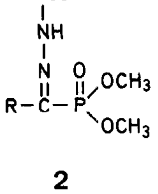
Scheme **A**

In this communication we report an extension of this reaction to tosylhydrazones in conjugation with electron-withdrawing groups, e.g. the 1-oxoalkanephosphonate tosylhydrazones **2**. These compounds are readily prepared by the reaction of tosylhydrazine with a 1-oxoalkanephosphonate **1** in methanol[2,3].



$R-C(=O)-P(=O)(OCH_3)_2$

1



$R-C(=N-NH-Tos)-P(=O)(OCH_3)_2$

2

Table 3. Dimethyl 1-Oxoalkanephosphonate Tosylhydrazones **2**

Compound **2**	M.p.	Yield (%)	Elemental Analyses				
a	105–106°	75	$C_{14}H_{23}N_2O_5PS$ (362.38)	calc. found	C 46.41 46.57	H 6.35 6.49	N 7.73 7.64
c	74–75°	77	$C_{18}H_{31}N_2O_5PS$ (418.49)	calc. found	C 51.67 51.59	H 7.41 7.47	N 6.70 6.78
e	149–150°	82	$C_{22}H_{23}N_2O_5PS$ (458.46)	calc. found	C 52.68 52.76	H 6.58 6.47	N 6.83 6.90

Table 4. Dimethyl Alkanephosphonates **3**

Compound **3**	B.p./torr	I.R. (neat) cm^{-1} $\nu_{P=O}$	ν_{POC}[a]	ν_{POC}[b]	^{1}H-N.M.R. (neat) δ ppm	Elemental Analyses			
a	67–68°/0.2	1245	1030	810	0.7–2.0 (m, 11 H), 3.7 (d, 6 H, J = 10.5 Hz)	$C_7H_{17}O_3P$ (180.18)	calc. found	C 46.67 46.73	H 9.44 9.04
b	56–57°/0.1	1240	1030	810	0.7–1.9 (m, 13 H), 3.62 (d, 6 H, J = 10.5 Hz)	$C_8H_{19}O_3P$ (194.20)	calc. found	C 49.48 49.53	H 9.79 9.88
c	115–117°/0.2	1240	1025	815	0.7–1.9 (m, 19 H), 3.65 (d, 6 H, J = 10.5 Hz)	$C_{11}H_{25}O_3P$ (236.28)	calc. found	C 55.93 56.04	H 5.99 5.90
d	110–112°/0.5	1245	1025	810	3.10 (d, 2 H, J = 21.75 Hz), 3.51 (d, 6 H, J = 10.5 Hz), 7.25 (m, 5 H)	$C_9H_{13}O_3P$ (200.16)	calc. found	C 54.00 53.82	H 6.50 6.44
e	120–121°/0.45	1245	1030	805	1.1–3.1 (m, 6 H), 3.6 (d, 6 H, J = 10.5 Hz), 7.20 (m, 5 H)	$C_{11}H_{17}O_3P$ (228.22)	calc. found	C 57.89 57.97	H 7.46 7.39

[a] Symmetrical.
[b] Asymmetrical.

Table 5. *Dimethyl 1-Diazoalkanephosphonates 4*

Compound **4**	M.p.	B.p./torr	I.R. (neat) cm^{-1} ν_{N_2}	$\nu_{P=O}$	ν_{POC}[a]	ν_{POC}[b]	^{1}H-N.M.R. (CCl$_4$) δ ppm	Elemental Analyses				
a	—	77–78°/0.44	2080	1245	1030	835	0.7–1.1, 1.1–1.6, 1.9–2.5, (m, 9 H), 3.75 (d, 6 H, J = 12 Hz)	$C_7H_{15}N_2O_3P$ (206.18)	calc. found	C 40.78 40.90	H 7.28 7.33	N 13.59 13.74
b	—	92–93°/0.6[c]										
c	—	103–104°/0.6	2070	1240	1025	815	0.7–1.1, 1.1–1.7, 1.85–2.5 (m, 17 H), 3.68 (d, 6 H, J = 12 Hz)	$C_{11}H_{23}N_2O_3P$ (262.28)	calc. found	C 53.24 53.36	H 9.27 9.81	N 11.29 11.32
d	44°[d]	—										
e	—	—[e]	2080	1245	1030	805	—					

[a] Symmetrical.
[b] Asymmetrical.
[c] Lit.[2]: b.p. 82°/0.44 torr
[d] Lit.[6]: m.p. 44–44.5°.
[e] Underwent decomposition during distillation.

dimethyl 1-diazoalkanephosphonates[2] and to dimethyl alkanephosphonates which are otherwise obtained under more vigorous conditions[5].

Melting and boiling points are uncorrected. I.R. and N.M.R. spectra were recorded on Perkin Elmer 257 and Jeol 60 HL spectrometers, respectively.

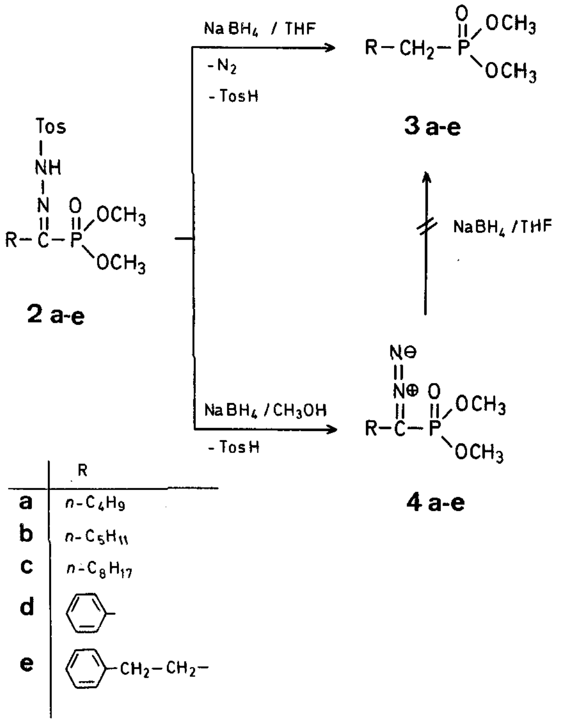
Dimethyl 1-Oxoalkanephosphonates 1 and Dimethyl 1-Oxoalkanephosphonate Tosylhydrazones 2:

Compounds **1** and their tosylhydrazones **2** were obtained according to the general procedure reported by Marmor and Seyferth[2] (see Tables 2 and 3).

Dimethyl Alkanephosphonates 3; General Procedure:

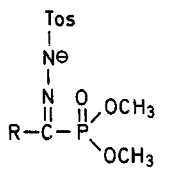
A solution of dimethyl 1-oxoalkanephosphonate tosylhydrazone (35 mmol) in dry tetrahydrofuran (200 ml) was stirred under nitrogen in a three-necked flask fitted with a reflux condenser. Sodium borohydride (0.2 mol) was added over 10–15 min. The reaction mixture was stirred for 1 h and then heated under reflux for 6–8 h. The suspension was quenched with water and allowed

According to the general behaviour of tosylhydrazones with sodium borohydride, when the reaction is carried out in anhydrous tetrahydrofuran under reflux for 6–8 h, the normal reduction of the carbon-nitrogen double bond occurs[1] and the dimethyl alkanephosphonates **3** are isolated in 65–75% yield. However, if the reaction is carried out in methanol (alcohols are widely used in sodium borohydride reductions[4]) under reflux for 1–2 h, an α-elimination of *p*-toluenesulfinic acid (TosH) occurs and the dimethyl 1-diazoalkanephosphonates **4** are isolated in 80–95% yield (Scheme **B**).



Scheme **B**

Under these conditions, the composition of the reaction mixture is essentially controlled by resonance stabilisation of the anion **5** and of the diazo compound **4** – resulting from expulsion of the tosyl anion – thus preventing the reduction of the carbon-nitrogen double bond.



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The results are listed in Table 1.

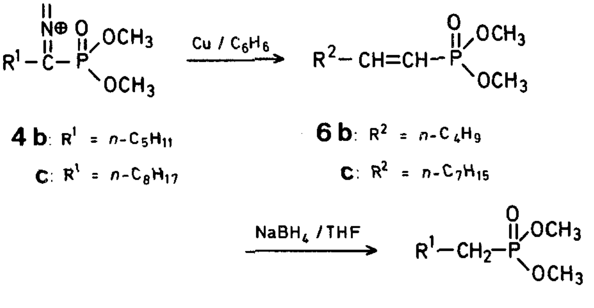
Table 1. Preparation of Dimethyl Alkanephosphonates **3** (Sodium Borohydride/Tetrahydrofuran) and Dimethyl 1-Diazoalkanephosphonates **4** (Sodium Borohydride/Methanol) from Dimethyl 1-Oxoalkanephosphonate Tosylhydrazones **2**

Compound	R	Yield (%) of **3**	Yield (%) of **4**
a	*n*-C_4H_9	72	93
b	*n*-C_5H_{11}	70	95
c	*n*-C_8H_{17}	75	89
d	C_6H_5	73	82
e	C_6H_5-CH_2—CH_2	65	85[a]

[a] Crude product

The dimethyl 1-diazoalkane phosphonates **4** are particularly stable and do not give dimethyl alkanephosphonates on treatment with sodium borohydride in refluxing tetrahydrofuran and subsequent decomposition with water (Scheme **B**).

Furthermore, the dimethyl 1-alkenephosphonates **6** – obtained from dimethyl 1-diazoalkanephosphonates by decomposition in refluxing benzene in the presence of copper powder[2] – give the corresponding dimethyl alkanephosphonates on treatment with sodium borohydride in refluxing tetrahydrofuran and subsequent decomposition with water (Scheme **C**).



Scheme **C**

These observations exclude the possibility that the diazophosphonates **4** are intermediates in the reduction of the tosylhydrazones of 1-oxoalkanephosphonates **2** to dimethyl alkanephosphonates **3**. The ease of the reaction, the high yields, and the short reaction times suggest that these reactions may be useful as an alternative synthetic route to

Table 2. Dimethyl 1-Oxoalkanephosphonates **1**

Compound **1**	Yield (%)	B.p./torr	I.R. (neat) cm⁻¹ $\nu_{C=O}$	$\nu_{P=O}$	ν_{POC}[a]	ν_{POC}[b]	¹H-N.M.R. (CDCl₃) δ ppm	Elemental Analyses			
a	82	72–74°/0.2	1695	1250	1030	830	0.7–1.9 (m, 7 H), 2.85 (t, 2 H, *J* = 7 Hz), 3.85 (d, 6 H, *J* = 10.5 Hz).	$C_7H_{15}O_4P$ (194.16)	calc. found	C 43.29 43.38	H 7.73 7.79
c	73	114–115°/0.4	1680	1255	1035	835	0.7–1.8 (m, 15 H), 2.80 (t, 2 H, *J* = 7 Hz), 3.80 (d, 6 H, *J* = 10.5 Hz).	$C_{11}H_{23}O_4P$ (250.26)	calc. found	C 52.80 52.91	H 9.20 9.29
e	84	132–135°/0.5	1655	1255	1030	835	2.7–3.3 (m, 4 H), 3.75 (d, 6 H, *J* = 10.5 Hz), 7.2 (m, 5 H).	$C_{11}H_{15}O_4P$ (242.20)	calc. found	C 54.54 54.60	H 6.20 6.34

[a] Symmetrical.

[b] Asymmetrical.

to stand for 2 h. The mixture was extracted with ether and the extract dried with sodium sulfate. The solvent was removed under reduced pressure and the crude product obtained was purified by distillation (see Table 4).

Dimethyl 1-Diazoalkanephosphonates 4; General Procedure:

A solution of dimethyl 1-oxoalkanephosphonate tosylhydrazone (25 mmol) in methanol (150 ml) was stirred under nitrogen in a three necked flask fitted with a condenser. Sodium borohydride (0.12 mol) was added over 10–20 min. The mixture became yellow in colour. The mixture was heated under reflux for 1 h, cooled, and methanol evaporated off under reduced pressure. The mixture was shaken with water, extracted with ether, the ether extracts dried with sodium sulfate, and concentrated using a rotary evaporator. The crude product was eluted through a short column containing neutral alumina, concentrated, and distilled (see Table 5).

Copper-catalysed Decomposition of Dimethyl 1-Diazoalkanephosphonates:

The copper-catalysed decomposition of compounds **4b** and **4c** was carried out according to the previously reported procedure[2].

Dimethyl 1-Hexenephosphonate **6b**: b.p. 75–76°/0.25 torr (lit.[2] b.p. 63°/0.11 torr).

Dimethyl 1-Nonenephosphonate **6c**: b.p. 102–103°/0.25 torr; yield: 63%.

$C_{11}H_{23}O_3P$	calc.	C 56.11	H 9.83
(234.26)	found	56.53	10.05

I.R. (neat): ν_{max} = 1630 (C=C), 1250 (P=O), 1025 (P—O—C, sym), 830 cm^{-1} (P—O—C, asym.).

^{1}H-N.M.R. (CCl$_4$): δ = 0.75–2.4 (m, 15 H), 3.65 (d, 6 H, J = 11 Hz), 5.3–6.1, 6.3–7.2 ppm (m, 2 H).

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