

Tandem Wittig Reactions of 1,1-Diphenylphosphorinanium Salt

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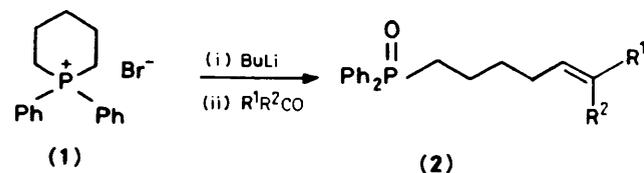
The title cyclic phosphonium salt (1) reacted with various aldehydes to give the phosphine oxides (2a—d) in good yield; these when treated with aldehydes in the presence of BuLi gave the alcohols (4a, b). The alcohol (4a) was easily converted into the 1,6-diene (5) by treatment of NaH in DMF. The stereoselectivities of these reactions are also described.

Although the Wittig reaction is one of the most versatile methods for the synthesis of alkenes, reorganization of bonding in the intermediate results in loss of the phosphorus group. If, however, the latter is retained in the product as a phosphine oxide, it is then available for Horner-Wittig reactions. Although Lednicer^{1,2} solved this problem in part by using phospholenes, his yields of products were low. Here we develop Muchowski's³ method which employs a five-membered phosphonium salt, to provide a powerful way of linking three separate carbon units.

Results and Discussion

The title compound, 1,1-diphenylphosphorinanium bromide⁴ (1) was prepared in 89% overall yield from the reaction of 1,5-dibromopentane with tetraphenyldiphosphine,⁵ the latter being generated *in situ* from diphenylphosphine and chloro(diphenyl)phosphine.

The Wittig reaction of (1) with benzaldehyde in the presence of butyl-lithium in tetrahydrofuran (THF) at room temperature gave 6-phenylhex-5-enyl(diphenyl)phosphine oxide (2a) (63%) as an *E,Z* mixture (*E:Z* = 68:32).



- a; R¹ = Ph, R² = H
 b; R¹ = C₆H₄NMe₂-*p*, R² = H
 c; R¹ = CH=CHPh, R² = H
 d; R¹ = Me, R² = H
 e; R¹ = R² = Me

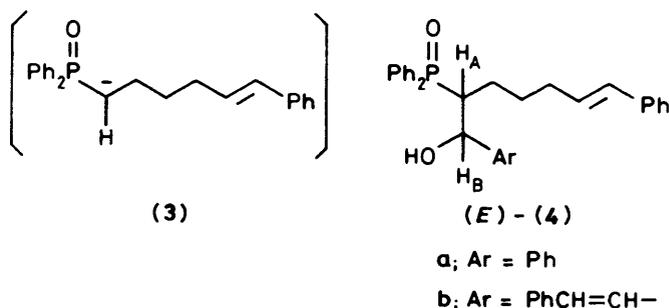
The ratio of the isomers was estimated by the peak areas of the vinylic protons in the n.m.r. spectrum of crude product (2a) which appeared at δ 5.55 (dt, *J* 11.6 and 7.2 Hz, for *Z*), 6.37 (d, *J* 11.6 Hz, *Z*), 6.10 (dt, *J* 15.8 and 6.8 Hz, *E*), and 6.31 (d, *J* 15.8 Hz, *E*) p.p.m. The (*E*)-hexene, (*E*)-(2a), was purified by recrystallization of the crude mixture of isomers from chloroform-hexane. The n.m.r. spectrum of the product (2b) [formed from reaction of (1) with *p*-dimethylaminobenzaldehyde] showed only *E* vinylic protons at δ 5.93 (dt, *J* 15.8 and 6.9 Hz) and 6.26 (d, *J* 15.8 Hz) p.p.m. The *E:Z* ratio of (2d) could not be determined because the vinylic protons of (2d) overlapped in the n.m.r. spectrum at 5.25–5.45 p.p.m.

Treatment of (*E*)-(2a) with butyl-lithium at –78 °C gave a reddish orange solution which reacted readily with benzaldehyde to give exclusively the *erythro*-alcohol (*E*)-(4a) in 82% yield (*J*_{AB} < 1 Hz).

Table 1. Reactions of (1) with aldehydes

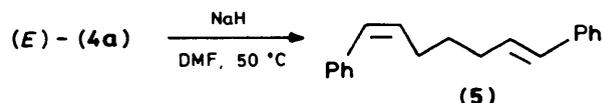
Products	Yield (%) ^a	<i>E:Z</i> ^b	<i>M</i> ⁺
(2a)	63 ^c	68:32	360
(2a) ^d	58	38:62	—
(2b)	96	100:0	403
(2c)	95	65:35	386
(2d)	40 ^e	—	298
(2e)	64 ^e	—	312

^a Based on (1). ^b Estimated by ¹H n.m.r. ^c Compound (4) was obtained in 5% yield together with the alkene (2a). ^d At –78 °C. ^e Yields isolated by Kugelrohr distillation.



The *threo* isomer⁶ was not detected by n.m.r. spectroscopy. Approach of the aldehyde to the carbanion (3) from the less hindered site,⁷ *i.e.* *Re-Re* or *Si-Si* faces, may explain the stereoselectivity of these reactions. In sequential Wittig and Horner-Wittig reactions in one reaction vessel, the phosphonium salt (1) was treated with benzaldehyde in the presence of BuLi in THF at room temperature and the resulting mixture then cooled, and treated with BuLi and benzaldehyde; the *erythro* alcohol (4a) was obtained in 87% yield.

Conversion of the *erythro*-(*E*)-(4a) into the 1,6-diene (5) in good yield preceded elimination of the diphenylphosphinate ion by treatment of NaH in DMF.⁶ The isomer ratio of the product was estimated by g.l.c. and ¹H n.m.r. (*E,Z:E, E* < 92:8).



Experimental

M.p.s were taken with a Yanagimoto micro-melting point apparatus. I.r. spectra were obtained using a JASCO IR-A spectrometer. ¹H and ¹³C N.m.r. spectra were recorded with a Bruker AC-250 spectrometer using tetramethylsilane as internal reference. Mass spectra were obtained with a JEOL JMS-01SG-2 spectrometer on-line to a JEOL JEC-6 spectrum

Table 2. ^{13}C N.m.r. chemical shifts (p.p.m.) and P-C coupling constants (J_{PC} , Hz): primed numbers refer to the carbons of the aromatic ring

Compounds	C-1	C-2	C-3	C-4	C-5	C-6	C-1'	C-2'	C-3'	C-4'
(<i>E</i>)-(2a)	29.58	21.07	30.52	32.37	130.04	130.32	133.19	130.76	128.62	131.64
	(72.3)	(3.8)	(14.5)	—	or 130.32	or 130.04	(97.5)	(9.4)	(12.0)	(1.9)
(<i>E</i>)-(2b)	29.60	21.07	30.85	32.41	125.94	130.02	133.28	130.77	128.60	131.59
	(71.1)	(4.4)	(14.5)	—	—	—	(97.5)	(9.4)	(12.0)	(1.9)
(<i>E</i>)-(2c)	29.58	21.06	30.51	32.23	134.67	131.01	133.19	130.76	128.63	131.64
	(71.1)	(3.8)	(14.5)	—	—	—	(97.5)	(8.8)	(10.7)	(2.5)
(<i>E</i>)-(2d)	29.69	21.15	30.82	31.94	129.86	125.32	133.18	130.77	128.62	131.66
	(72.3)	(3.8)	(13.8)	—	—	—	(98.1)	(9.4)	(11.3)	—
(<i>Z</i>)-(2d)	29.58	20.90	30.76	26.35	130.62	124.29	—	—	—	—
	(72.3)	(3.8)	(14.5)	—	—	—	—	—	—	—
(2e)	29.76	21.15	31.16	27.49	123.98	131.81	133.35	130.83	128.65	131.63
	(71.7)	(3.8)	(13.8)	—	—	—	(97.5)	(8.8)	(12.0)	(3.1)

^a P-C coupling constants are indicated in parentheses.

computer. High-resolution mass spectra were obtained with JEOL JMS-DX300 and JMS-DX303 spectrometers.

6-Phenylhex-5-enyl(diphenyl)phosphine Oxide (2a).—(a) *At room temperature.* A solution of butyl-lithium (15% in hexane; 18.5 ml, 28.9 mmol) was added dropwise to a suspension of the phosphonium salt (1) (8.83 g, 26.3 mmol) in dry THF (200 ml) at room temperature under nitrogen. After 30 min, a solution of benzaldehyde (3.07 g, 28.9 mmol) in dry THF (20 ml) was added to the wine coloured solution, and the resultant mixture was stirred for 1 h at this temperature (the colour disappeared). Water was added, and the mixture extracted with ether (80 ml \times 3). The organic extracts were combined, washed with water and brine, dried (Na_2SO_4), and concentrated under reduced pressure to give creamy solids which were chromatographed on silica gel using ethyl acetate as eluant to give the *title compound* (2a) (5.97 g, 63%) and 1-hydroxy-1,7-diphenylhept-6-en-2-yl(diphenyl)phosphine oxide (4a) (0.66 g, 5%). Recrystallization of crude (2a) from CHCl_3 -hexane gave pure (*E*)-(2a) m.p. 91.4–92.5 °C; ν_{max} 1590 cm^{-1} (C=C); m/z (75 eV) 360 (M^+); δ_{H} (CDCl_3) 1.57–1.77 (4 H, m, CH_2), 2.17–2.36 (4 H, m, CH_2), 6.10 (1 H, dt, J 15.8 and 6.8 Hz, $\text{CH}_2\text{CH}=\text{CHPh}$), 6.31 (1 H, d, J 15.8 Hz, $\text{CH}_2\text{CH}=\text{CHPh}$), 7.17–7.35 (5 H, m, C=CPh), 7.41–7.51, (6 H, m, *m*- and *p*-H), and 7.71–7.79 (4 H, m, *o*-H) (Found: C, 80.3; H, 7.0. $\text{C}_{24}\text{H}_{25}\text{OP}$ requires C, 80.0; H, 7.0%). ^{13}C N.m.r. data are summarized in Table 2.

The *E*:*Z* ratio of crude (2a) was estimated from the peak area of the vinylic protons at δ 6.10 (dt, J 15.8 and 6.8 Hz, *E*), 6.31 (dt, J 15.8 Hz, *E*), 5.55 (dt, J 11.6 and 7.2 Hz, *Z*), and 6.37 p.p.m. (d, J 11.6 Hz, *Z*).

(b) *At -78 °C.* A solution of BuLi (15% in hexane; 4.23 ml, 6.60 mmol) was added to a suspension of phosphonium salt (1) (2.01 g, 6.0 mmol) in THF (60 ml) at room temperature. After 30 min, the deep red solution was cooled to -78°C , a solution of benzaldehyde (0.70 g, 6.6 mmol) in THF (10 ml) was added, and the mixture was stirred for 1 h. The mixture was then extracted with ether, and the ether extract was dried (Na_2SO_4), and concentrated to give (2a) (1.26 g, 58%). The ratio of *E*:*Z* isomers was 38:62.

Similarly, 6-(*p*-dimethylaminophenyl)hex-5-enyl(diphenyl)phosphine oxide (2b) was obtained (3.09 g, 96%) from compound (1) (2.68 g, 8.0 mmol), butyl-lithium (15% in hexane; 6.4 ml, 10 mmol) and *p*-dimethylaminobenzaldehyde (1.5 g, 10.1 mmol) at room temperature. Compound (2b) had m.p. 113.4–113.5 °C; ν_{max} 1598 cm^{-1} (C=C); m/z (75 eV) 403 (M^+); δ_{H} (CDCl_3) 1.52–1.74 (4 H, m, CH_2), 2.12–2.34 (4 H, m, CH_2), 2.92 (6 H, s, NMe_2), 5.93 (1 H, dt, J 15.7 and 6.9 Hz, $\text{CH}_2\text{CH}=\text{CHC}_6\text{H}_4$), 6.25 (1 H, d, J 15.7 Hz, $\text{CH}_2\text{CH}=\text{CHC}_6\text{H}_4$), 6.67 (2 H, d, C_6H_4),

7.19 (2 H, d, C_6H_4), 7.39–7.52 (4 H, m, *m*- and *p*-H), and 7.67–7.77 (4 H, m, *o*-H) (Found: C, 77.7; H, 7.5; N, 3.2. $\text{C}_{26}\text{H}_{30}\text{NOP}$ requires C, 77.4; H, 7.5; N, 3.5%).

8-Phenylhept-5,7-dienyl(diphenyl)phosphine oxide (2c) was similarly obtained (2.21 g, 95%) (*E,E*:*E,Z* = 65:35) from compound (1) (2.01 g, 6.0 mmol), BuLi (15% in hexane; 4.23 ml, 6.6 mmol), and *E*-cinnamaldehyde (0.89 g, 6.66 mmol). Recrystallization of crude (2c) from benzene-hexane gave pure (*E,E*)-(2c) m.p. 126.9–127.1 °C; ν_{max} 1588 cm^{-1} (conjugate diene); m/z (75 eV) 386 (M^+); δ_{H} (CDCl_3) 1.50–1.69 (4 H, m, CH_2), 2.09–2.33 (4 H, m, CH_2), 5.73 (1 H, dt, J 15.1 and 7.0 Hz, $\text{CH}_2\text{CH}=\text{CH}$), 6.15 (1 H, dd, J 15.1 and 10.3 Hz, $\text{CH}_2\text{CH}=\text{CH}$), 6.41 (1 H, d, J 15.7 Hz, $\text{CH}=\text{CHPh}$), 6.70 (1 H, dd, J 10.3 and 15.7 Hz, $\text{CH}=\text{CHPh}$), 7.15–7.78 (15 H, m, Ph) (Found: C, 80.7; H, 7.0. $\text{C}_{26}\text{H}_{27}\text{OP}$ requires C, 80.8; H, 7.0%).

Hept-5-enyl(diphenyl)phosphine oxide (2d) was obtained (0.72 g, 40%) as an oil (purified by Kugelrohr distillation oven temp. 200 °C/0.5 mmHg) from treatment of compound (1) (2.01 g, 6 mmol) with BuLi (15% in hexane; 4.23 ml, 6.6 mmol) and freshly distilled acetaldehyde (0.53 g, 12 mmol). Compound (2d): ν_{max} 1586 cm^{-1} (C=C); m/z (75 eV) 298 (M^+); δ_{H} (CDCl_3) 1.40–1.68 (7 H, m, Me and CH_2), 1.92–2.07 (2 H, m, CH_2), 2.16–2.33 (2 H, m, CH_2), 5.25–5.45 (2 H, m, vinylic protons), 7.43–7.54 (6 H, m, *m*- and *p*-H), 7.70–7.78 (4 H, m, *o*-H) (Found: M^+ , m/z 298.1497. $\text{C}_{19}\text{H}_{23}\text{OP}$ requires 298.1487).

6-Methylhept-5-enyl(diphenyl)phosphine oxide (2e) was obtained (1.20 g, 64%) as a yellow oil (purified by Kugelrohr distillation oven temp. 215 °C/5 mmHg) from compound (1) (2.01 g, 6.0 mmol), BuLi (15% in hexane; 4.23 ml, 6.6 mmol) and absolute acetone (0.46 g, 7.92 mmol). Compound (2e): ν_{max} 1590 cm^{-1} (C=C); m/z (75 eV) 312 (M^+); δ_{H} (CDCl_3) 1.43 (2 H, quintet, P-C-C- CH_2), 1.55–1.71 (8 H, m, P-C- CH_2 and = CMe_2), 1.96 (2 H, q, J 7.2 Hz, $\text{CH}_2\text{C}=\text{C}$), 2.27 (2 H, m, J_{PH} 11.3 Hz, PCH_2), 5.04 (1 H, t, J 7.2 Hz, $\text{CH}=\text{C}$), 7.43–7.55 (6 H, m, *m*- and *p*-H), 7.70–7.78 (4 H, m, *o*-H) (Found: M^+ , m/z 312.1687. $\text{C}_{20}\text{H}_{25}\text{OP}$ requires M , 312.1643).

erythro-1-Hydroxy-1,7-diphenylhept-6-en-2-yl(diphenyl)phosphine Oxide (4a).—(a) *From (E)-(2a).* A solution of BuLi (15% in hexane; 3.5 ml, 5.46 mmol) was added to a solution of (*E*)-(2a) (1.80 g, 4.99 mmol) in THF (60 ml) at -78°C under nitrogen and the mixture was stirred for 20 min at this temperature. The colour of the reaction mixture changed to dark red at this point. A solution of benzaldehyde (0.58 g, 5.46 mmol) in THF (20 ml) was then added dropwise at -78°C and the mixture was stirred for an additional h (the dark red colour disappeared). After aqueous work-up at room temperature, the mixture was extracted with ether, dried

(Na_2SO_4), and concentrated to give a mixture (2.22 g) of (*E*)-(4a) and (*E*)-(2a) (87:13). Pure (*E*)-(4a) was obtained by recrystallization from CHCl_3 -hexane; it had m.p. 145.4–145.6 °C; ν_{max} . 3360 (OH) and 1585 cm^{-1} (C=C); $\delta_{\text{H}}(\text{CDCl}_3)$ 0.70–0.93 (2 H, m, CH_2), 1.57–1.93 (4 H, m, CH_2), 2.47 (2 H, m, PCH_A), 4.86 (1 H, s, OH), 5.28 (1 H, d, $^3J_{\text{PH}}$ 9.3 Hz, $J_{\text{AB}} < 1$ Hz, HOCH_BPh) 5.67 (1 H, dt, J_{CD} 15.8 Hz, J_{CF} 6.9 Hz, $\text{CH}_2\text{CH}_C=\text{CH}_D\text{Ph}$), 6.03 (1 H, d, J_{CD} 15.8 Hz, $\text{CH}_2\text{CH}_C=\text{CH}_D\text{Ph}$), and 7.15–8.01 (20 H, m, Ph). These signals were assigned from a H–H correlation spectrum (COZY); $\delta_{\text{C}}(\text{CDCl}_3)$ 20.61 (C-3) 29.39 (C-4, $^3J_{\text{PC}}$ 6.3 Hz), 32.48 (C-5), 44.60 (C-2, $^1J_{\text{PC}}$ 67.3 Hz), 70.76 (C-1, $^2J_{\text{PC}}$ 1.9 Hz), 129.85, 130.05 (C-6 and C-7), and 131.77 (C-s, $^1J_{\text{PC}}$ 94.3 Hz). These signals were assigned from a C–H two-dimensional correlation spectrum (NOEZY) of (*E*)-(4a). (Found: C, 79.7; H, 6.7. $\text{C}_{31}\text{H}_{31}\text{O}_2\text{P}$ requires C, 79.6; H, 6.9%).

(b) *From compound (1) (one pot reaction)*. A solution of BuLi (15% in hexane; 4.7 ml, 7.4 mmol), was added dropwise to a solution of compound (1) (2.3 g, 6.7 mmol) in dry THF (70 ml) at room temperature under nitrogen. After 10 min, a solution of benzaldehyde (0.79 g, 7.4 mmol) in THF (10 ml) was added dropwise to the mixture and the resultant mixture was stirred at room temperature for 1 h. The mixture was then cooled to -78 °C and a solution of BuLi (4.7 ml, 7.4 mmol) was added dropwise, followed by a solution of benzaldehyde (0.79 g, 7.4 mmol) in dry THF (10 ml) at the same temperature. After 1 h at -78 °C the mixture was subjected to aqueous work-up at room temperature and extracted with ether. The organic extract was washed with water and brine, dried (Na_2SO_4), and concentrated to give (4a) (2.7 g, 87%) as an *E:Z* mixture (*E:Z* = 76:24); the ratio of *E:Z* was estimated by the peak areas of the ^1H n.m.r. spectrum at δ 6.03 (*E*) and 6.19 (*Z*).

Similarly, 3-hydroxy-1,9-diphenylnona-1,8-dien-4-yl(diphenyl)phosphine oxide (4b) was obtained (2.40 g, 98%) from (*E*)-(2a) (1.80 g, 5.0 mmol), BuLi (3.5 ml, 5.5 mmol), and cinnamaldehyde (0.73 g, 5.5 mmol) at -78 °C. Compound (4b) had m.p. 130–130.5 °C; ν_{max} . 3320 (OH), 1586 cm^{-1} (C=C); m/z (75 eV) 493 (M^+); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.20–2.13 [6H, m, $\text{P}(\text{CH}_A\text{CH}_B\text{CH}_C\text{CH}_D\text{CH}_E=\text{CH}_F)\text{COH}_G\text{CH}_H\text{CH}_I=\text{CH}_J$], 2.46 (1 H, ddt, $J_{\text{AP}} = J_{\text{AB}}$ 6.2, J_{AH} 1.5 Hz, H_A), 4.76–4.90 (2 H, m, H_G and H_H), 5.87 (1 H, dt, J_{DE} 6.8, J_{EF} 15.8 Hz, H_E), 6.14 (dd, J_{HI} 5.1, J_{IJ} 15.8 Hz, H_I), 6.18 (d, J_{EF} 15.8 Hz, H_F) (peaks at 6.14 and 6.18 overlapped and show two protons), and 6.67 (1 H, dd, J_{HI} 1.4, J_{IJ} 15.8 Hz, H_J). [Small peaks were observed downfield from H_A (2.46 p.p.m.), but we could not assign whether the peaks were

due to those of *threo*-configuration]; $\delta_{\text{C}}(\text{CDCl}_3)$ 21.96 (C-5), 29.60 (C-6, J_{PC} 7.6 Hz), 32.64 (C-7), 43.09 (C-4, J_{PC} 67.9 Hz), 70.47 (C-3, J_{PC} 2.5 Hz), and 130.27 (C-1) p.p.m. (Found: C, 80.3; H, 6.8. $\text{C}_{33}\text{H}_{33}\text{O}_2\text{P}$ requires C, 80.5; H, 6.8%).

1,7-Diphenylhepta-1,6-diene (5).—A solution of the alcohol (*E*)-(4a) (2.00 g, 4.29 mmol) in dry dimethylformamide (DMF) (50 ml) was added dropwise to a suspension of sodium hydride (60% in oil, washed with dry hexane; 0.26 g, 6.50 mmol) and the mixture was heated at 50 °C for 3 h. After aqueous work-up, the mixture was extracted with ether and the ether extract washed with water and brine, dried (Na_2SO_4), and concentrated to give the hepta-1,6-diene (5) (0.93 g, 87%) as an *E,Z* and *E,E* mixture [*E,Z:E,E* = 92:8, estimated by the peak areas of vinylic protons in the n.m.r. spectrum of crude (5)]. Compound (5) ν_{max} . 1600 cm^{-1} (C=C); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.63 (2 H, m, $\text{PhCH}_A=\text{CH}_B\text{CH}_C\text{CH}_D\text{CH}_E\text{CH}_F=\text{CH}_G$), 2.24 (2 H, m, H_E), 2.39 (2 H, ddt, $J_{\text{BC}} = J_{\text{CD}}$ 7.5, J_{AC} 1.7 Hz, H_C), 5.68 (1 H, dt, J_{BC} 7.4, J_{AB} 11.7 Hz, H_B), 6.18 (1 H, dt, J_{EF} 6.7, J_{FG} 15.8 Hz, H_F), 6.35 (1 H, d, J_{FG} 15.8 Hz, H_G), 6.45 (1 H, dd, J_{AB} 11.7, J_{AC} 1.7 Hz, H_A), and 7.15–7.37 (10 H, m, Ph); $\delta_{\text{C}}(\text{CDCl}_3)$ 28.0 (C-3), 29.61 (C-4), 32.51 (C-5), 125.9–128.7 (Ph), 129.18 (C-1, *Z*), 130.18 (C-7, *E*), 130.47 (C-6, *E*), and 132.61 (C-2, *Z*). ^1H - and ^{13}C N.m.r. spectra were assigned by H–H and C–H two-dimensional correlation spectra (COSY) (Found: M^+ , m/z 248.1546. $\text{C}_{19}\text{H}_{20}$ requires M , 248.1565).

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References

- 1 D. Lednicer, *J. Org. Chem.*, 1970, **35**, 2307.
- 2 D. Lednicer, *J. Org. Chem.*, 1971, **36**, 3473.
- 3 J. M. Muchowski and M. C. Venuti, *J. Org. Chem.*, 1981, **46**, 459.
- 4 G. Märkl, *Angew. Chem., Int. Ed. Engl.*, 1963, **2**, 620.
- 5 W. Kuchen and H. Buchwald, *Chem. Ber.*, 1958, **91**, 2871.
- 6 A. D. Buss, W. B. Cruse, O. Kennard, and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1984, 243.
- 7 M. Schlosser and B. Schanb, *J. Am. Chem. Soc.*, 1982, **104**, 5822.

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