Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

for

Angew. Chem. Int. Ed. Z50270

69451 Weinheim, Germany

Lewis Acid-Catalyzed Room Temperature Michaelis-Arbuzov Rearrangement.

Pierre-Yves Renard[*], Philippe Vayron, Eric Leclerc, Alain Valleix
and Charles Mioskowski[*]

Experimental procedure :

Reagents were from Aldrich co. All solvents were distilled before use, and reactions were performed under N_2 atmosphere. All chromatography (flash) was performed with Merck Silicagel 60 (0.02-0.04 mm). TLC was performed with fluorescent Merck F254 glass plates. NMR spectra were recorded on a Brucker AC-300 (300.15 MHz for ^1H, 75.4 MHz for ^{13}C and 121.5 MHz for ^{31}P) in $CDCl_3$ unless stated. Chemical shifts (δ are given in ppm and the coupling constant J is expressed in Hertz. MS were obtained with a Finnigan-Mat 4600 quadrupole system (Chemical ionization with NH_3). Flash column chromatography was performed on Merk silicagel (60Å, 230-400 mesh). Elemental analyses were recorded at the « institut de chimie des substances naturelles », Gif sur Yvette.

Phosphites were either purchased when commercially available (Aldrich or STREM) or directly prepared from the corresponding phosphorus (III) chloride using conventional methodologies (reaction performed in dried diethyl ether using 1.0 equivalent of alcohol and 1.5 equivalents of dried triethyl amine; careful triethylammonium chloride filtration under an N_2 atmosphere, and excess reactant removal yielded phosphites which were used without further purification).

A typical reaction process could be summarized as follows: In a flame-dried reaction vessel, topped with a reflux condenser and under nitrogen atmosphere, 5 molar% trimethylsilyl trifluoromethane sulfonate was added to a 1.0 M phosphinite (respectively phosphonite or phosphite) solution in degassed and freshly-distilled chloroform. After three days at room temperature (or one hour at 60°C), the excess solvents were removed under vacuum, and the crude material was directly submitted to silicagel column chromatography (using a 1/9 acetone/dichloromethane mixture as the eluting solution), yielding pure phosphine oxide (respectively phosphinate or phosphonate).

Methyl diphenylphosphine oxide (**2**) : ^{1}H NMR (300.15 MHz, $CDCl_3$) δ : 7.73-7.66 (m, 4H), 7.49-7.40 (m, 6H), 1.98 (d, *J(H,P)* = 13 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ : 134.1, 133.0 (d, J(C,P) = 98Hz),132.7 (d, *J(C,P)* = 5Hz, 2C), 131.4 (d *J(C,P)* = 12Hz, 2C), 16.2 (d, *J(C,P)* = 75Hz) ; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 30.4; MS (CI, NH_3) *m/z* : 217 $[M+H]^+$, 234 $[M + NH_4]^+$.

Ethyl diphenylphosphine oxide (table 1 entry 5) : ^{1}H NMR (300.15 MHz, $CDCl_3$) δ : 7.78-7.71 (m, 4H), 7.53-7.45 (m, 6H), 2.30 (d of q, *J(H,P)* = 11.5 Hz, *J(H,H)* = 7.5 Hz, 2H), 1.20 (d of t, *J(H,P)* = 17.5 Hz, *J(H,H)* = 7.5 Hz, 3H) ; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ : 133.2 (d, J(C,P) = 102 Hz),131.8, 131.0 (d, *J(C,P)* = 5Hz, 2C), 128.8 (d *J(C,P)* = 11.5Hz, 2C), 22.7 (d, *J(C,P)* = 73Hz), 18.9 ; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 34.6 ; MS (CI, NH_3) *m/z* : 231 $[M+H]^+$, 248 $[M + NH_4]^+$.

Benzyl diphenylphosphine oxide (table 1, entries 6 and 7) : ^{1}H NMR (300.15 MHz, $CDCl_3$) δ : 7.74-7.67 (m, 4H), 7.55-7.42 (m, 6H), 7.22-7.20 (m, 2H), 7.19-7.09 (m, 3H), 3.65 (d, *J(H,P)* = 14 Hz, 2H) ; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 29.7 ; MS (CI, NH_3) *m/z* : 293 $[M+H]^+$, 310 $[M + NH_4]^+$.

1-phenylethyl diphenylphosphine oxide (table 1 entry 8) : ^{1}H NMR (300.15 MHz, $CDCl_3$) δ : 7.95-7.88 (m, 4H), 7.56-7.53 (m, 2H), 7.49-7.43 (m, 4H), 7.28-7.17 (m, 5H), 3.61 (quint *J(H,P) = J(H,H)* = 7.5 Hz, 1H), 1.60 (dd, *J(H,P)* = 7.5 Hz, *J(H,P)* = 16 Hz, 3H) ; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ : 138.2, 132.0 (d, J(C,P) = 125 Hz), 131.8, 131.5, 131.4, 131.3, 131.2, 129.3, 129.2, 128.8, 128.7, 128.3, 128.2, 128.0, 127.0, 41.0 (d, *J(C,P)* = 43Hz), 15.55 ; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 34.0 ; MS (CI, NH_3) *m/z* : 307 $[M+H]^+$.

2-methoxybenzyl diphenylphosphine oxide (table 1, entry 9) : ^{1}H NMR (300.15 MHz, $CDCl_3$) δ : 7.72-7.65 (m, 4H), 7.46-7.33 (m, 7H), 7.11 (t, *J(H,H)* = 7.5 Hz, 1H), 6.83 (t, *J(H,H)* = 7.5 Hz, 1H), 6.62 (d, *J(H,H)* = 7.5 Hz, 1H), 3.73 (d of d, *J(H,P)* = 35 Hz, *J(H,H)* = 14 Hz, 2H), 3.41 (s, 3H) ; ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 156.85, 132.9 (d, J(C,P) = 92Hz),131.8 (d, *J(C,P)* = 5Hz), 131.7, 1328.2(d *J(C,P)* = 12Hz), 128.1, 120.6, 119.9 (d, *J(C,P)* = 7.5 Hz), 110.3, 54.9, 31.2 (*J(C,P)* = 68 Hz) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 30.55. MS (CI, NH$_3$) *m/z* : 323 [M+H]$^+$; elemental analysis calcd (%) for $C_{20}H_{19}O_2P$: C 74.52, H 5.94; found C 74.52, H 5.99.

Diethyl Benzyl phosphine oxide (table 1, entry 10) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.22-7.11 (m, 5H), 3.00 (d, *J(H,H)* = 14.5 Hz, 2H), 1.53 (d of q *J(H,H)* = 7.5 Hz, *J(H,P)* = 11.5 Hz, 4H), 1.03 (d of t, *J(H,H)* = 7.5 Hz, *J(H,P)* = 15 Hz, 6H) ; ^{13}C NMR (75.4 MHz, CDCl$_3$) δ :132.2 (d, *J(C,P)* = 7.5 Hz), 129.5 (d, *J(C,P)* = 4 Hz, 2C), 128.8 (2C), 126.8, 35.2 (d, *J(C,P)* = 59 Hz), 29.3, 19.6 (d, *J(C,P)* = 66 Hz), 5.6 (d, *J(C,P)* = 4 Hz) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 50.29. MS (CI, NH$_3$) *m/z* : 197 [M+H]$^+$, 214 [M + NH$_4$]$^+$.

Dimethyl phenyl phosphine oxide (table 1 entry 11) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.76-7.69 (m, 2H), 7.54-7.46 (m, 3H), 1.73 (d, *J(H,P)* = 13 Hz, 6H) ; ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 132.0 (d, *J(C,P)* = 84 Hz), 131.7, 129.7 (d, *J(C,P)* = 6 Hz), 128.75 (d, *J(C,P)* = 14 Hz), 18.1 (d, *J(C,P)* = 71 Hz) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 45.4.

Phenyl ethyl methylphosphine oxide (table 1, entry 12) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.76-7.58 (m, 2H), 7.48-7.42 (m, 3H), 3.27 (d of q, *J(H,P)* = 14Hz, *J(H,H)* = 7 Hz, 1H, first isomer), 2.00-1.80 (m, 2H), 1.64 (d, *J(H,P)* = 13 Hz, 3H), 1.06 (d of t, *J(H,P)* = 18Hz, *J(H,H)* = 7.5 Hz, 3H).) ; ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 133.8 (d, *J(C,P)* = 94 Hz), 131.7, 130.4 (d, *J(C,P)* = 8 Hz), 128.8 (d, *J(C,P)* = 12 Hz), 24.4 (d, *J(C,P)* = 73 Hz), 15.1 (d, *J(C,P)* = 77 Hz), 5.8 (d, *J(C,P)* = 5Hz) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 38.0.

Phenyl (1-phenyl-ethyl) methyl phosphine oxide (table 1 entry 13) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.75-7.60 (m, 2+2H), 7.51-7.44 (m, 3+3H), 7.21-7.15 (m, 2+2H), 6.95-6.90 (m, 3+3H), 3.27 (d of q, *J(H,P)* = 14Hz, *J(H,H)* = 7 Hz, 1H, first isomer), 3.05 (d of q, *J(H,P)* = 12Hz, *J(H,H)* = 7 Hz, 1H, second isomer), 1.67 (d, *J(H,P)* = 13 Hz, 3H, first isomer), 1.64 (d, *J(H,P)* = 13 Hz, 3H, second isomer) 1.52 (d of d, *J(H,P)* = 14 Hz, *J(H,H)* = 7 Hz, 3H, first isomer), 1.42 (t, *J(H,P)* = *J(H,H)* = 7 Hz, 1H, second isomer) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 42.7.

2-methoxybenzyl phenyl methyl phosphine oxide (table 1 entry 14) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.62-7.54 (m, 2H), 7.48-7.40 (m, 3H), 7.20 (broad t, *J(H,H)* = 7.0 Hz, 1H), 7.09 (broad d(*J(H,H)* = 7.0 Hz, 1H), 6.85 (broad t, *J(H,H)* = 7.0 Hz, 1H), 6.77 (d, *J(H,H)* = 6.0 Hz, 1H), 3.63 (s, 3H), 3.42 (dd, *J(H,H)* = 7.0 Hz, *J(H,P)* = 14 Hz, 2H), 1.63 (d, *J(H,P)* = 15 Hz, 3H).) ; ^{13}C NMR (75.4 MHz, CDCl$_3$) δ :156.88, 132.5, 132.0 (d, *J(C,P)* = 114 Hz),131.5, 130.4 (d, *J(C,P)* = 7.5 Hz), 128.4, 128.3 (d, *J(C,P)* = 4 Hz), 120.8, 120.5, 110.4, 55.1, 33.9 (d, *J(C,P)* = 65 Hz), 29.3, 14.6 (d, *J(C,P)* = 70 Hz) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 36.85 ; MS (CI, NH$_3$) *m/z* : 261 [M+H]$^+$; elemental analysis calcld (%) for $C_{15}H_{17}O_2P$: C 69.22, H 6.61; found C 69.26, H 6.58.

2-(methyl phenyl phosphinoylmethyl) 1-benzyloxy-4-(2-nitroethyl)-benzene (table 1 entry 15) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.56-7.46 (m, 3H), 7.43-7.37 (m, 7H), 7.03 (broad d, *J(H,H)* = 8.5 Hz, 1H), 6.99 (broad s, 1H), 6.84 (d, *J(H,H)* = 8.5 Hz, 1H), 4.93 (s, 2H), 4.52 (t, *J(H,H)* = 7.5, 2H), 3.42 (dd, *J(H,H)* = 6.5 Hz, *J(H,P)* = 14.5Hz, 2H), 3.18 (d, *J(H,H)* = 7.5 Hz, 2H), 1.60 (d, *J(H,P)* = 13 Hz, 3H); ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 43.2.

tert-butyl benzyl phenyl phosphine oxide (table 1 entry 16) ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.78-7.71 (m, 2 H), 7.48-7.33 (m, 3 H), 7.30-7.25 (m, 2H), 7.19-7.10 (m, 3H), 3.33-3.49 (m, 2H), 1.12 (d, *J(H,P)* = 15 Hz, 9H); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 132.1 (d, *J(C,P)* = 7.5 Hz), 131.5, 131.4, 130.2 (d, *J(C,P)* = 93 Hz), 130.2, 130.1, 129.4, 128.3 (d, *J(C,P)* = 12 Hz), 128.0, 126.5, 33.4 (d, *J(C,P)* = 65 Hz), 31.3 (d, *J(C,P)* = 61 Hz), 24.8; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 44.8; MS (CI, NH$_3$) *m/z* : 273 [M+H]$^+$, 290 [M + NH$_4$]$^+$.

tert-butyl methyl phenyl phosphine oxide (table 1 entry 17) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.72-7.62 (m, 2 H), 7.45-7.35 (m, 3 H), 1.62 (d, *J(H,P)* = 13Hz, 3H), 1.05 (d, *J(H,P)* = 15 Hz, 9H). ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 131.9 (d, *J(C,P)* = 7.5 Hz), 131.3, 129.6 (d, *J(C,P)* = 90 Hz), 128.1 (d, *J(C,P)* = 12 Hz), 32.5 (d, *J(C,P)* = 75 Hz), 24.4, 15.6 (d, *J(C,P)* = 72 Hz) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 50.2 ; MS (CI, NH$_3$) *m/z* : 197 [M+H]$^+$.

***tert*-butyl phenyl (1-phenyl ethyl) phosphine oxide** (table 1 entry 18) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.65-7.52 (m, 2 + 2 H), 7.45-7.20 (m, 8 + 8 H), 3.64-3.52 (m, 1H, first isomer), 3.11-3.02 (m, 1H second isomer), 1.48 (d of d, *J(H,H)* = 6.5 *J(H,P)* = 11 Hz, 3 H first isomer), 1.42 (d of d, *J(H,P)* = 7.0 *J(H,H)* = 12 Hz, 3 H second isomer), 1.1 (d, J = 10 Hz, 9 + 9 H) ; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 50.9 and 49.9 (2 isomers).

***O*-methyl methylphenylphosphinate** (table 2 entry 1) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.80-7.73 (m, 2H), 7.55-7.45 (m, 3H), 3.59 (d, *J(H,P)* = 11.5 Hz, 3H), 1.65 (d, *J(H,P)* = 14.5 Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 132.4, 131.4 (d, *J(C,P)* = 10 Hz), 131.0 (d, *J(C,P)* = 94 Hz), 128.6 (d, *J(C,P)* = 12.5 Hz), 51.1 (d, *J(C,P)* = 6 Hz), 15.7 (*J(C,P)* = 102 Hz), 5.9; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 45.2.

***O*-Ethyl ethylphenylphosphinate** (table 2, entry 2) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.75-7.68 (m, 2H), 7.52-7.39 (m, 3H), 4.09-3.99 (m, 1H), 3.87-3.74 (m, 1H), 1.95-1.74 (m, 2H), 1.23 (t, *J(H,H)* = 7.5 Hz, 3H), 1.04 (d of t, *J(H,H)* = 7.5 Hz, *J(H,P)* = 19 Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 133.0 (d, *J(C,P)* = 93 Hz), 132.2, 131.6 (d, *J(C,P)* = 16.0 Hz), 128.6 (d, *J(C,P)* = 12 Hz), 60.6 (d, *J(C,P)* = 5 Hz), 22.8 (d, *J(C,P)* = 102 Hz), 16.5 (*J(C,P)* = 7.0 Hz), 5.9; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 46.85; MS (CI, NH$_3$) *m/z* : 199 [M+H]$^+$, 216 [M + NH$_4$]$^+$.

***O*-(1-phenylethyl) (1-phenylethyl)phenyl phosphinate** (table 2, entry 3) : complex mixture of isomers, ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.80-7.65 (m, 2H), 7.52-7.10 (m, 8H), 5.30-5.10 (m, 2H) ; 3.45-3.37 and 3.25-3.10 (m, 1H), 1.35-1.50 (m, 6H); ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 43.8, 43.6, 42.8 and 42.5.

***O-O*-Diethyl methylphosphonate** (table 2, entries 5 and 6) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 4.05-3.92 (m, 4H), 1.35 (d *J(H,P)* = 17.5 Hz, 3H), 1.22 (t, *J(H,H)* = 7.0 Hz, 6H); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 61.45 (d, *J(C,P)* = 5 Hz), 16.4 (d, *J(C,P)* = 6 Hz), 11.05 (*J(C,P)* = 143.5 Hz), 5.9; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ : 31.10.

***O-O*-diethyl benzylphosphonate** (table 2, entry 7) : ^{1}H NMR (300.15 MHz, CDCl$_3$) δ : 7.31-7.28 (m, 5H), 4.05-3.95 (m, 4H), 3.15 (d, *J(H,P)* = 22 Hz, 2H), 1.23 (t, *J(H,H)* = 7.5 Hz); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ : 131.3, 129.8, 128.6, 128.4, 127.9, 126.9, 62.1 (d, *J(C,P)* = 7 Hz), 33.8 (d, *J(C,P)* = 137 Hz), 16.4 (d, *J(C,P)* = 5.5 Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 26.95.

***O-O*-dimethyl methylphosphonate** (table 2, entry 8) : ^{1}H NMR (300.15 MHz, $CDCl_3$) δ : 3.68 (d, *J(H,P)* = 11 Hz, 6H), 1.41 (d, *J(H,P)* = 17.5 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ :53.2 (d, *J(C,P)* = 5.5 Hz), 4.90 (d, *J(C,P)* = 143 Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 33.30; MS (CI, NH_3) *m/z* :125[M+H]$^+$, 142 [M + NH_4]$^+$.

***O-O*-diethyl (4-nitro 2-benzyloxy)benzylphosphonate** (table 2 entry 9) : 8.25 (t, *J(H,H)* = 3Hz, 1H), 8.14 (d of t, *J(H,H)* = 9 Hz and 3 Hz, 1H), 7.49-7.37 (m, 5H), 7.00 (d, *J(H,H)* = 9 Hz, 1H), 5.22 (s, 2H), 4.06 (quint *J(H,H)* = *J(H,P)* = 7.0 Hz, 4H), 3.34 (d, *J(H,P)* = 21.5 Hz, 2H), 1.26 (t, *J(H,H)* = 7.0 Hz, 6H) ; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ : 161.4, 141.3, 135.5, 128.8, 128.5, 127.45, 126.9 (d, *J(C,P)* = 4 Hz), 124.6, 122.4 (d, *J(C,P)* = 10 Hz), 111.5, 71.1, 62.2 (d, *J(C,P)* = 6 Hz), 27.0 (d, *J(C,P)* = 139Hz), 16.4 (d, *J(C,P)* = 5.5 Hz) ; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ : 27.50. MS (CI, NH_3) *m/z* : 380 [M+H]$^+$, 397 [M + NH_4]$^+$; elemental analysis calcd (%) for $C_{18}H_{22}NO_6P$: C 57.0, H 5.85; found. C 56.76, H 5.81.

Lewis acid screening for Arbuzov rearrangement of *O*-methyl diphenylphosphinite

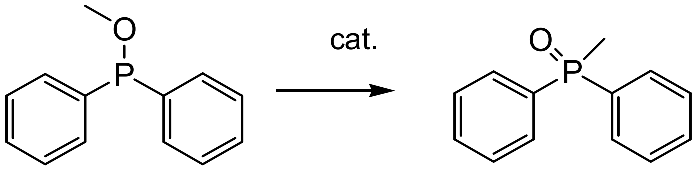

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Table 1: Lewis acid-catalyzed room temperature Arbuzov rearrangement of phosphinite (**1**) to phosphine oxide (**2**). The reaction was monitored through ^{31}P NMR, and performed at a phosphonite concentration of 3 M in $CDCl_3$ with 5 mol.% catalyst.

Lewis acid	Conversion rate (24h)	Conversion rate (48h)
Me_3Si-OTf	72%	100%
t-$BuMe_2Si$-OTf	51%	87%
BF_3OEt_2	69%	100%
$Ti(OiPr)_4$	0%	0%
$TiCl_4$[a]	0%	0%
$Cl_2C{=}N(Me)_2^+$ TfO^-	25%	41%
$Sn(OTf)_2$	7%	10%
$Cu(OTf)_2$	5%	7%
$Zn(OTf)_2$	2%	3%
$Yb(OTf)_3$	Traces	*Ca.* 2%
$ZnCl_2$	0%	0%
BBr_3[b]	0%	0%

[a]: phosphinite immediately decomposes; [b]: no further evolution after phosphonium formation.

Figure 1: Conversion rate, determined by ^{31}P NMR for the Lewis acid-catalyzed rearrangement of phosphinite (**1**) to phosphine oxide (**2**). Substrate (**1**) was used at 0.5 M in deuterated chloroform, in the presence of 5% trimethylsilyl trifluoromethane sulfonate.