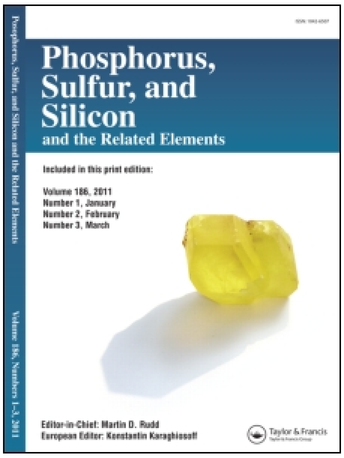


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Studies on Organophosphorus compounds 87. A Convenient Procedure for the Preparation of Diethyl 2-Oxoalkylphosphonates

Chengye Yuan[a]; Rongyuan Xie[a]
[a] Chinese Academy of Sciences, Shanghai Institute of Organic Chemistry, Shanghai, China

To cite this Article Yuan, Chengye and Xie, Rongyuan(1994) 'Studies on Organophosphorus compounds 87. A Convenient Procedure for the Preparation of Diethyl 2-Oxoalkylphosphonates', Phosphorus, Sulfur, and Silicon and the Related Elements, 90: 1, 47 — 51

To link to this Article: DOI: 10.1080/10426509408016385

URL: http://dx.doi.org/10.1080/10426509408016385

Phosphorus, Sulfur, and Silicon, 1994, Vol. 90, pp. 47-51
Reprints available directly from the publisher
Photocopying permitted by license only

STUDIES ON ORGANOPHOSPHORUS COMPOUNDS 87. A CONVENIENT PROCEDURE FOR THE PREPARATION OF DIETHYL 2-OXOALKYLPHOSPHONATES

CHENGYE YUAN and RONGYUAN XIE
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

(Received April 28, 1994; in final form June 2, 1994)

A facile one-pot procedure for the synthesis of diethyl 2-oxoalkylphosphonates is described. It involves an Arbuzov rearrangement of triethylphosphite with 1-bromoketone in which the carbonyl function was masked in the form of benzenesulfonyl hydrazone. Subsequent deprotection via oxidative cleavage affords the title compounds with fair yields.

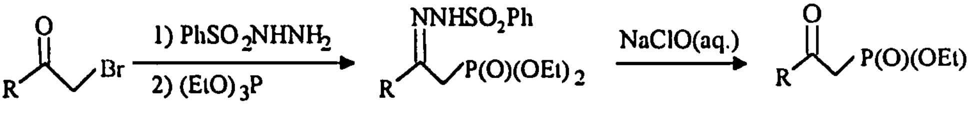
Key words: 2-Ketoalkylphosphonates, Arbuzov rearrangement, carbonyl protection.

INTRODUCTION

2-Oxoalkylphosphonates or β-ketophosphonates are useful intermediates for the synthesis of α,β-unsaturated carbonyl compounds via the Horner-Wadsworth-Emmons reaction.[1] These bifunctional phosphorus-based ligands have been successfully used for the coordination of various metal ions.[2,3] The synthesis of β-ketophosphonates has attracted the interest of organic chemists. The acylation of alkylphosphonate anions can be considered as the general approach to β-ketophosphonates,[4,5] though it suffers from the problem of low reactivity due to proton exchange between the β-ketophosphonates generated and 1-lithioalkylphosphonates, the α-proton of the former being more acidic than those of the starting alkylphosphonates. A more recent method based on the formation of the reactive α-phosphoryl nitronate is an interesting approach leading to 1-aryl-2-oxoalkylphosphonates.[6] P-Alkylation of dialkylphosphite with alkyl chloroacetate was achieved under catalytic phase transfer conditions.[7] Among the numerous methods reported for the formation of β-ketophosphonates, the Arbuzov reaction involving trialkylphosphite and α-halogenoketone seems to be the most convenient.[8] However, this method is usually in competition with the Perkow reaction which forms enolphosphonates due to insufficient reactivity of the phosphite. In order to prevent the participation of α-halogenoketone in the Perkow reaction, Corbel suggested to mask the carbonyl function of α-halogenoketone by formation of a methoxycarbonylhydrazono-derivative.[9] Consequently, all of the methods described in the literature for the preparation of β-ketophosphonates have limitations in terms of reaction conditions employed, formation of by-products and the availability of starting materials. Further careful investigation of a more convenient method for the preparation of the title compounds seems necessary.

RESULTS AND DISCUSSION

In this paper we wish to report a convenient procedure for the preparation of diethyl 2-oxoalkylphosphonates by the Arbuzov rearrangement of triethylphosphite with 2-benzenesulfonylhydrazono-1-bromoketones. Compared with the methoxycarbonylhydrazono group the benzenesulfonylhydrazino moiety has several advantages: it is commercially available and inexpensive, and the resulting hydrazone group can be easily converted to the corresponding carbonyl compounds by oxidative cleavage in good yield. Beside these, our suggested method can be performed by a one pot procedure and provides a high purity product with satisfactory yield.



1 **2** **3**

R=Me(a),Et(b),cycPr(c),Ph(d),p-Me-C_6H_4(e),p-MeO-C_6H_4(f),p-MeO,m-Br-C_6H_3(g), p-$NO_2C_6H_4$(h), p-F-C_6H_4(i),p-Cl-C_6H_4(j), p-Br-C_6H_4(k).

The formation of the intermediate **2** by the Arbuzov reaction has been verified by the successful isolation of β-benzenesulfonylhydrazono-alkylphosphonates (**2**). The present procedure has significant advantages over others. These include convenience in operation, ease of preparation of starting material and fair yield product in addition to widespread applicability of the reaction, since both bromoacetone and phenacylbromide with various substituents gave similar yields.

EXPERIMENTAL

Infrared spectra were obtained on a Shimadzu IR-440 infrered spectrometer. ^{1}H-NMR spectra were recorded on a 60 MHz Varian EM 360 spectrometer using CCl_4 as solvent and TMS as the internal reference. ^{31}P-NMR spectra were taken with a 90 MHz FX-90Q spectrometer using CCl_4 as solvent and 85% phosphoric acid as the external standard.

Diethyl 2-methyl-2-oxo-ethylphosphonate (**3a**): To a solution of monobromoacetone (2.74 g, 0.02 mol) in tetrahydrofuran (20 mL) was added benzenesulfonohydrazide (3.44 g, 0.02 mol) with stirring at 30–40°C for 10 min to facilitate solution. After additional 0.5–1 h stirring at r.t., triethylphosphite (3.98 g or 4.1 mL, 0.024 mol) was added dropwise within 10–20 min to the resultant solution; during that time a vigorous reaction occurred. Upon another 1.5–2 h stirring, tetrahydrofuran and other volatile components were removed under reduced pressure. To the resulting residue was added chloroform (50 mL) and an aqueous sodium hypochlorite solution (20 mL). The mixture was stirred at room temperature for 10–30 min to complete the reaction as monitored by TLC. Then the organic layer was separated and the aqueous solution was extracted with chloroform (3 × 10 mL). The combined organic solutions were consequently washed with water and saturated brine then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure gave a crude product which was then purified by fractional distillation. **3a** was collected at 95–97°C (0.4 torr), yield 82%. Literature[10] bp 114°C (0.3 torr). IR (ν, cm^{-1}) 1756 (C=O), 1250 (P=O), 1030, 960 (P—O—C); ^{1}H-NMR (ppm): 4.10 (m, 4H, 2XOCH$_2$), 2.96 (d, 2H, $^2J_{PH}$ = 22.8 Hz, P—CH$_2$), 2.10 (s, 3H, COCH$_3$), 1.30 (m, 6H, 2XOCH$_2$C$\underline{H}_3$); ^{31}P-NMR: 19.8 ppm.

Diethyl 2-ethyl-2-oxo-ethylphosphonate (**3b**): Analogous to the preparation of **3a**, using 2-bromomethylethylketone (3.03 g, 0.02 mol), benzenesulfonohydrazide (3.44 g, 0.02 mol) and triethylphosphite (4.1 mL, 0.024 mol) for the reaction and followed by subsequent treatment with aqueous 5% sodium hypochlorite solution (20 mL). **3b** was obtained by column chromatography on silica, bp 116–119°C (0.4 torr), yield 78%. Lit.[10] bp 114°C (0.3 torr). IR (ν, cm^{-1}) 1740 (C=O), 1255 (P=O), 1040, 965 (P—O—C); ^{1}H-NMR (ppm): 4.10 (m, 4H, $2XOCH_2$), 2.99 (d, 2H, $^2J_{PH}$ = 23.2 Hz, P—CH_2), 1.29 (t, 3H, $^3J_{HH}$ = 7.0 Hz, $C\underline{H}_3CH_2$), 2.50 (m, 2H, $^3J_{HH}$ = 7.0 Hz, $CH_3C\underline{H}_2$), 1.32 (m, 6H, $2XOCH_2C\underline{H}_3$); ^{31}P-NMR: 20.0 ppm.

Diethyl 2-cyclopropyl-2-oxo-ethylphosphonate (**3c**): Analogous to the preparation of **3a**, using 2-bromomethyl cyclopropylketone (3.27 g, 0.02 mol), benzenesulfonohydrazide (3.44 g, 0.02 mol) and triethylphosphite (4.1 mL, 0.024 mol) for the reaction and followed by subsequent treatment with aqueous 5% sodium hypochlorite solution (20 mL). **3c** was obtained by column chromatography on silica a as colorless liquid bp 120–124°C (0.15 torr). Literature bp 125–128°C (0.3 torr)[11]; IR (ν, cm^{-1}) 1700 (C=O), 1255 (P=O), 1030, 965 (P—O—C); ^{1}H-NMR (CCl_4): 0.90 (m, 4H, CH_2CH_2) 1.30 (m, 6H, $2XOCH_2C\underline{H}_3$), 2.00 (m, 1H, CH), 3.24 (d, 2H, $^2J_{PH}$ = 23.1 Hz, P—CH_2), 4.18 (m, 4H, $2XOC\underline{H}_2CH_3$) ppm.; ^{31}P-NMR ($CDCl_3$): 21.1 ppm.

Diethyl-2-phenyl-2-oxo-ethylphosphonate (**3d**): To a solution prepared from 2-bromoacetophenone (3.98 g, 0.02 mol) and tetrahydrofuran (20 mL) was added benzenesulfonohydrazide (3.44 g, 0.02 mol) with stirring at 30–40°C for 10 min to facilitate solution. After additional 0.5–1 h stirring at r.t., triethylphosphite (3.98 g or 4.1 mL, 0.024 mol) was added dropwise within 10–20 min to the resultant solution. An exothermic reaction occurred. Upon another 1.5–2 h stirring, the solvent and other volatile components were removed under reduced pressure. To the residue was added chloroform (50 mL) and an aqueous 5% sodium hypochlorite solution (20 mL). The mixture was stirred at r.t. for 10–30 min to complete the reaction as monitored by TLC. The reaction mixture was worked up as described for **3a**. **3d** was obtained after purification by column chromatography on silica, bp 142–146°C (0.7 torr), yield 83%. Lit.[12] bp 150–155°C (0.9 torr). IR (ν, cm^{-1}) 1675 (C=O), 1250 (P=O), 1030, 970 (P—O—C); ^{1}H-NMR (ppm) 8.05–7.53 (m, $5H_{arom}$), 4.05 (m, 4H, $2XOCH_2$), 3.59 (d, 2H, $^2J_{PH}$ = 22.8 Hz, P—CH_2), 1.20 (t, 6H, $2XCH_3$); ^{31}P-NMR: 19.8 ppm.

Diethyl 2-(p-methylphenyl)-2-oxo-ethylphosphonate (**3e**): Similar to the preparation of **3d**, reacting bromomethyl *p*-methylphenylketone with benzene sulfonohydrazide and triethylphosphite followed by treatment with aqueous sodium hypochlorite and then purification by column chromatography on silica. **3e** was obtained in 82% yield, bp 149–153°C (0.8 torr); Lit.[12] bp 150–155°C (0.85 torr). IR (ν, cm^{-1}) 1670 (C=O), 1240 (P=O), 1030, 965 (P—O—C); ^{1}H-NMR 7.55–7.20 (m, $4H_{arom}$), 4.11 (m, 4H, 2XO—CH_2), 3.36 (d, 2H, $^2J_{PH}$ = 22.8 Hz P—CH_2), 2.36 (s, 3H, Ph—$C\underline{H}_3$), 1.30 (m, 6H, $2XCH_2C\underline{H}_3$). ^{31}P-NMR: 20.2 ppm.

Diethyl 2-(p-methoxyphenyl)-2-oxoethylphosphonate (**3f**): Similar to the preparation of **3d** using bromomethyl *p*-methoxyphenylketone, benzene sulfonohydrazide and triethylphosphite in one pot reaction followed by treatment with aqueous 5% NaClO and then purification by column chromatography on silica. **3f** was obtained in 62%, bp 152–155 (0.7 torr) Lit.[11] bp 155–156°C (0.8 torr). IR (ν, cm^{-1}) 1675 (C=O), 1245 (P=O), 1025, 965 (P—O—C); ^{1}H-NMR (ppm) 7.58–7.22 (m, $4H_{arom}$), 4.21 (m, 4H, 2XO—CH_2), 4.01 (s, 3H, OCH_3), 3.62 (d, 2H, $^2J_{PH}$ = 22.8 Hz, P—CH_2), 1.30 (m, 6H, $2XCH_2C\underline{H}_3$). ^{31}P-NMR: 20.2 ppm.

Diethyl 2-(p-methoxy-m-bromophenyl)-2-oxoethylphosphonate (**3g**): Similar to the preparation of **3d** using bromomethyl *p*-methoxy-*m*-bromophenyl ketone, benzene sulfonohydrazide and triethylphosphite in one pot reaction followed by treatment with aqueous 5% NaClO and then purification by column chromatography on silica. **3g** was obtained in 73% yield, bp 167–171°C (1.0 torr). Analysis C 42.37; H 4.58; Br 21.66; P 8.18%. Calculated for $C_{13}H_{18}BrO_5P$ (365.2), C 42.75, H 4.98, Br 21.88, P 8.48%. IR (ν, cm^{-1}) 1670 (C=O), 1250 (P=O), 1020, 960 (P—O—C), ^{1}H-NMR (ppm): 8.28–7.03 (m, $3H_{arom}$), 4.18 (m, 4H, 2XO—CH_2), 4.00 (s, 3H, OCH_3) 3.62 (d, 2H, $^2J_{PH}$ = 22.8 Hz, P—CH_2), 1.29 (m, 6H, $2XOCH_2C\underline{H}_3$); ^{31}P-NMR: 19.9 ppm.

Diethyl 2-(p-nitrophenyl)-2-oxo-ethylphosphonate (**3h**): Similar to the preparation of **3d** using bromomethyl *p*-nitrophenylketone, benzene sulfonohydrazide and triethylphosphite in one pot procedure followed by treatment with aqueous sodium hypochlorite and then purification by column chromatography on silica. **3h** was obtained in 68% yield, bp 166–172°C (1.0 torr). Lit.[12] bp 164–169°C (0.9 torr). IR (ν, cm^{-1}) 1685 (C=O), 1245 (P=O), 1035, 980 (P—O—C); ^{1}H-NMR (ppm): 7.48–7.13 (m, $4H_{arom}$), 4.15 (m, 4H, $2XOCH_2$), 3.52 (d, 2H, $^2J_{PH}$ = 22.9 Hz, P—CH_2), 1.25 (m, 6H, $2XCH_3$); ^{31}P-NMR: 18.4 ppm.

Diethyl 2-(p-fluorophenyl)-2-oxo-ethylphosphonate (**3i**): Similar to the preparation of **3d** using boromethyl *p*-fluorophenylketone, benzene sulfonohydrazide and triethylphosphite in one pot procedure followed by treatment with aqueous sodium hypochlorite and then purification by column chromatography on silica. **3i** was obtained in 73% yield, bp 156–160°C (0.7 torr), Lit.[11] bp 147–150°C (0.4 torr), IR (ν, cm^{-1}) 1680 (C=O), 1250 (P=O), 1030, 965 (P—O—C); ^{1}H-NMR (ppm) 8.22–7.00 (m, 4H$_{arom}$), 4.20 (m, 4H, 2XO—CH$_2$), 3.60 (d, 2H, $^2J_{PH}$ = 23.0 Hz, P—CH$_2$), 1.33 (m, 6H2XCH$_3$); ^{31}P-NMR: 19.5 ppm.

Diethyl 2-(p-chlorophenyl)-2-oxo-ethylphosphonate (**3j**): Similar to the preparation of **3d** using boromethyl *p*-chlorophenylketone, benzene sulfonohydrazide and triethylphosphite in one pot procedure followed by treatment with aqueous sodium hypochlorite and then purification by column chromatography on silica gel. **3j** was obtained in 72% yield, bp 162–168°C (0.9 torr), Lit.[11] bp 165–170°C (1.0 torr), IR (ν, cm^{-1}) 1690 (C=O), 1260 (P=O), 1030, 980 (P—O—C); ^{1}H-NMR (ppm): 7.46–7.10 (m, 4H$_{arom}$), 4.05 (m, 4H, 2XO—CH$_2$), 3.59 (d, 2H, $^2J_{PH}$ = 22.8 Hz, P—CH$_2$), 1.20 (m, 6H, 2XCH$_3$); ^{31}P-NMR: 20.0 ppm.

Diethyl 2-(p-bromophenyl)-2-oxo-ethylphosphonate (**3k**): Similar to the preparation of **3d** using bromomethyl *p*-bromophenylketone, benzene sulfonohydrazide and triethylphosphite in one pot procedure followed by treatment with aqueous sodium hypochlorite and then purification by column chromatography on silica. **3k** was obtained in 78% yield, bp 160–165°C (1.0 torr), Lit.[11] bp 150–155°C (0.7 torr). IR (ν, cm^{-1}) 1680 (C=O), 1245 (P=O), 1030, 970 (P—O—C); ^{1}H-NMR (ppm): 7.42–7.01 (m, 4H$_{arom}$), 4.10 (m, 4H, 2XO—CH$_2$), 3.53 (d, 2H, $^2J_{PH}$ = 22.9 Hz, P—CH$_2$), 1.24 (m, 6H, 2XCH$_3$); ^{31}P-NMR: 19.9 ppm.

Diethyl 2-(p-methylphenyl)-2-benzenesulfonylhydrazono-ethylphosphonate (**2e**): To a solution of monobromomethyl *p*-methylphenylketone (0.02 mol) in tetrahydrafuran (20 mL) was added benzenesulfonohydrazide (0.02 mol) with stirring at 30–40°C for 10 min to facilitate solution. After additional 0.5–1 h stirring at r.t., triethylphosphite (4.1 mL, 0.024 mol) was added dropwise within 10–20 min. An exothermic reaction occurred. Upon another 1.5–2 h stirring, the solvent and other volatile components were removed in a rotatory evaporator under reduced pressure. The residue after recrystalization from ethanol gave **2e** as a colorless crystalline solid, mp 129–130°C. Analyses: C 53.59, H 5.69, N 6.77, P 7.00, S 7.21% $C_{19}H_{25}N_2O_5PS$ (424.4) required C 53.77; H 5.94; N, 6.60; P, 7.30; S, 7.55% IR (ν, KCl, cm^{-1}) 3400 (s, N—H), 1620 (m, C=N), 1250 (vs, P=O), 1040, 990 (vs, P—O—C); ^{1}H-NMR (CDCl$_3$, ppm): 1.37 (m, 6H, 2XO—CH$_2$C$\underline{H}_3$), 2.38 (s, 3H, C$\underline{H}_3$Ph), 3.89 (d, 2H, $^2J_{PH}$ = 22.6 Hz, P—CH$_2$), 4.28 (m, 4H, 2XO—CH$_2$), 7.00–7.98 (m, 9H$_{arom}$), 10.52 (s, 1H, N$\underline{H}$) ppm; ^{31}P-NMR (CDCl$_3$): 24.1 ppm.; EI (m/z) = 424 (M$^+$).

Diethyl 2-(p-chlorophenyl)-2-benzenesulfonylhydrazono-ethylphosphonate (**2j**): Similar to the preparation of **2e** starting from monobromomethyl *p*-chlorophenylketone, benzenesulfonohydrazide and triethylphosphite and then the crude product was recrystallized from ethanol. **2j** was obtained as colorless crystals, mp 134–135°C. Analyses: C 48.75, H 4.87, N 6.49, P 7.08, S 7.43. $C_{18}H_{22}ClN_2O_5PS$ (444.9) required C 48.59, H 4.98, N 6.30, P 6.96, S 7.21%. IR (ν, KCl, cm^{-1}) 3300 (s, NH), 1615 (w, C=N), 1240 (vs, P=O), 1030, 960 (vs, P—O—C), 710 (m, C—Cl); ^{1}H-NMR (CDCl$_3$, ppm): 1.30 (m, 6H, 2X—OCH$_2$C$\underline{H}_3$), 3.37 (d, 2H, $^2J_{PH}$ = 22.8 Hz, P—CH$_2$), 4.12 (m, 4H, 2XO—CH$_2$), 7.21–8.16 (m, 9H$_{arom}$), 10.39 (s, 1H, NH); ^{31}P-NMR (CDCl$_3$): 23.9 ppm; EI (m/z) = 445 (M$^+$, ^{35}Cl), 447 (M$^+$, ^{37}Cl).

ACKNOWLEDGEMENT

The project was supported by National Natural Science Foundation of China.

REFERENCES

1. W. S. Wadsworth, Jr., *Organic Reactions (N.Y.)*, **25**, 73 (1977).
2. J. L. Martin and M. Leroy, *J. Chem. Res. (s)*, 88 (1978).
3. E. X. Ma, G. L. Wang, X. M. Yan and C. Y. Yuan, *Solv. Extr. Ion Exch.*, **4**, 725 (1986).
4. E. E. Aboujaoude, N. Colligan and P. Savignac, *J. Organomet. Chem.*, **264**, 9 (1984).
5. K. Kojima and S. Saito, *Synthesis*, 949 (1992).
6. D. Y. Kim, K. Lee and D. Y. Oh, *J. Chem. Soc. Perkin Trans.*, **1**, 2451 (1992).
7. W. Z. Ye and X. G. Liao, *Synthesis*, 986 (1985).

8. F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961).
9. B. Corbel, L. Medinger, J. P. Haelters and G. Sturtz, *Synthesis*, 1048 (1985).
10. N. D. Dawson and A. Burger, *J. Am. Chem. Soc.*, **74**, 5312 (1952).
11. F. W. Lichtenthaler, *Chem. Rev.*, **61**, 507 (1961).
12. D. J. Burton and L. G. Sprague, *J. Org. Chem.*, **53**, 1523 (1988).
13. M. G. Imier and A. M. Shakirova, *Zh. Obshch Khim.*, **34**, 3950 (1964).