

This article was downloaded by:

On: 28 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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>

RAPID AND EFFICIENT ARBUZOV REACTION UNDER MICROWAVE IRRADIATION

Didier Villemin^a; Fabrice Simeon^a; Hugues Decreus^a; Paul-Alain Jaffres^b

^a Ecole Nationale Supérieure d'Ingénieurs de Caen (ISMRA) Université de Caen, Caen, Cedex, France ^b University of St Andrews, School of Chemistry, College Gate, Fife, Scotland

To cite this Article Villemin, Didier, Simeon, Fabrice, Decreus, Hugues and Jaffres, Paul-Alain (1998) 'RAPID AND EFFICIENT ARBUZOV REACTION UNDER MICROWAVE IRRADIATION', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 133: 1, 209 – 213

To link to this Article: DOI: 10.1080/10426509808032465

URL: <http://dx.doi.org/10.1080/10426509808032465>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

RAPID AND EFFICIENT ARBUZOV REACTION UNDER MICROWAVE IRRADIATION

DIDIER VILLEMEN^{a*}, FABRICE SIMEON^a, HUGUES DECREUS^a and
PAUL-ALAIN JAFFRES^b

^a*Ecole Nationale Supérieure d'Ingénieurs de Caen (ISMRA) Université de Caen,
UMR 6507, 6 Boulevard du Maréchal Juin F-14050 Caen Cedex, France and*

^b*University of St Andrews, School of Chemistry, College Gate, Fife KY16 9AJ,
Scotland*

(Received 30 September, 1997)

Diethyl alkylphosphonates are efficiently and rapidly prepared in good yields (75–99%) from trialkylphosphates and alkyl halides under short microwaves irradiations.

Keywords: microwaves irradiation; alkylphosphonates; Arbuzov reaction

INTRODUCTION

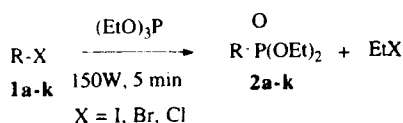
One of the methods commonly used for the synthesis of diethyl alkylphosphonates is the Michaelis-Arbuzov reaction,^{1–2}. These phosphonates are widely used as synthon for Wittig-Horner reactions³ and for the synthesis of pharmaceutical products and other physiologically active organophosphoric compounds.⁴ Over the last twenty years, phosphonates have attracted considerable attention as precursors of phosphonic acids which are used in the synthesis of new hybrid organic-inorganic supports and catalysts.⁵

* Corresponding author.

RESULTS AND DISCUSSION

Various functionalized phosphonates can easily be prepared by the Arbuzov reaction (scheme 1), which is a cheap and very efficient method. The fact that an ionic intermediate of the reaction was postulated,⁶ allowed us to think that the use of microwaves might improve the yield and the rate of the reaction.⁷ According to our previous works⁸, we employed a focused microwave with a monomode cavity. A sample has been taken out of the mixture periodically for analysis by ³¹P NMR spectroscopy. Disappearance of the NMR singlet of triethylphosphite (at 138 ppm) was proportional to the increase of the phosphonate signal (from 28 to 32 ppm). The medium time of reaction was found to be 5 minutes at 150 Watts of irradiation.

The results are summarised in Table I. Entries **a** to **e** report the phosphonation of monohalide substrates while entries **f** to **k** report the monophosphonation of polyhalide substrates.



SCHEME 1

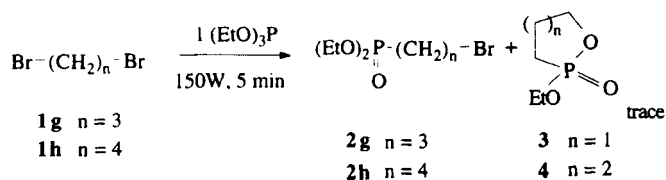
TABLE I Reaction of triethylphosphite with halogenide under focused microwave irradiation (M.W.)

N°	Substrat 1	Products(1) 2	³¹ P NMR (CDCl ₃)	M.W. Heating 5 min yield % ⁽²⁾ [lit.]
a	I-CH ₃	P-CH ₃	30.2	99 ⁽⁵⁾ [1]
b	Br-(CH ₂) ₃ Ph	P-(CH ₂) ₃ Ph	30.6	90[9]
c	Br-CH ₂ Ph	P-CH ₂ Ph	26.3	95[11]
d	Br-CH ₂ -CH=CH ₂	P-CH ₂ -CH=CH ₂	26.7	89[12]
e	Br-(CH ₂) ₃ CN	P-(CH ₂) ₃ CN	29.2	75
f	CCl ₄	P-CCl ₃	5.4	78[13]
g	Br-(CH ₂) ₃ Br ⁽³⁾	P-(CH ₂) ₃ Br	30.3	91[14]
h	Br-(CH ₂) ₄ -Br ⁽³⁾	P-(CH ₂) ₄ Br	31.1	90[14]
i	Br-(CH ₂) ₅ -Br ⁽³⁾	P-(CH ₂) ₅ -Br	31.7	94[14]
j	Br-(CH ₂) ₉ -Br ⁽³⁾	P-(CH ₂) ₉ -Br ⁽⁴⁾	32.4	91
k	Br-(CH ₂) ₁₀ -Br ⁽³⁾	P-(CH ₂) ₁₀ -Br ⁽⁴⁾	32.6	88

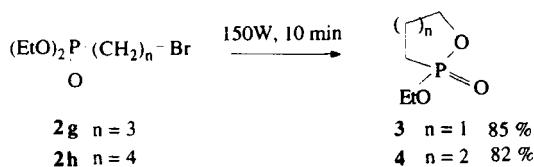
(1) P = P(O)(OEt)₂; (2) Purified by distillation; (3) 3 equivalents; (4) for characterisation see ref. [15] (5) heating for 3 min.

In all these examples after 5 minutes under microwave irradiation all the triethylphosphite reacts and no trace of it was detected by ^{31}P NMR. The times required are shorter by microwave irradiation than by thermal activation. The yields are equivalent or better than those obtained under classical conditions. In order to compare microwave activation to thermal heating we monitored by ^{31}P NMR the phosphonation of 3-phenylethylbromide **1b** during a thermal heating reaction. We showed that at least 35 minutes were required in order to have a total disappearance of triethylphosphite in the solution. When the substrate is iodomethane (**1a**) only 3 minutes of microwave irradiation is required. By a thermal heating⁹ the same reaction is polluted with diethylethylphosphonate which is difficult to separate from the main product. In this case microwave heating, because of the shorter reaction time, allows to avoid the formation of by-products.

With dibromoalkane (**1g** to **1k**) an excess of substrate was employed in order to avoid a double Arbuzov reaction which formed diphosphonate. With compounds **1g** and **1h** as substrate traces of oxaphospholane **3** or oxaphosphane **4** were observed (scheme 2). These compounds result from cyclisation which required a thermal heating at 180°C for 2 hours.¹⁰ Under microwave activation, compounds **3** and **4** have been isolated in very good yield by 10 min. irradiation of a pure sample of 3-bromopropylphosphonate **2g** or 4-bromobutylphosphonate **2h** (scheme 3).



SCHEME 2



SCHEME 3

The conclusion of this work is that microwave activation decreases hugely the time of the Arbuzov reactions. Such process can be used for large scale synthesis of alkylphosphonates (see experimental section). This work was realised with triethylphosphite as starting substrate but we can expect to have a similar activation by microwave with other alkyl phosphites.

EXPERIMENTAL

Focused microwaves : cavity TE₀₁ at 2450 MHz with a universal generator MES 73–800.⁸ ¹H and ¹³C NMR spectra were recorded on a BRUKER AC 250 spectrometer in CDCl₃ as solvent. These spectra were measured with SiMe₄ as internal standard. ³¹P NMR was recorded on a BRUKER WP 80 SY with H₃PO₄ as external standard. Mass spectra were recorded on Nermag R10.10H spectrometer.

General Procedure

Example : iodomethane **1a** (3.55 g ; 0.025 mol) and triethylphosphite (4.15 g ; 0.025 mol) are placed in a quartz tube. The solution is irradiated at 150 W for 3 minutes. NMR analyses (³¹P and ¹H) show that methyl diethylphosphonate is obtained with a good purity.

In the case of polyhalide substrates (**1f–1k**) 3 equivalents of substrate (**1f–1k**) are used. At the end of the heating (5 min.) the phosphonates are purified by distillation under vacuum and the excess of dibromide substrate is recovered. This methodology is suitable for scale up to 0.2 mole of monohalide substrate or 0.12 mole of polyhalide substrate.

References

- [1] A. Michaelis, R. Kaehne, *Ber.*, **31**, 1048 (1898).
- [2] For a review of the Arbuzov reaction see A.B. Arbuzov, *Pure Appl. Chem.*, **9**, 307 (1964).
- [3] W.S. Wadsworth, *Org. React.*, **25**, 73 (1977) and R.D. Clarck, L.G. Kozar, C.H. Heatcock, *Synth. Commun.*, **5**, 1(1975).
- [4] See for exemples A.J. Kirby, S.G. Warren, *The Organic Chemistry of Phosphorus*, (Amsterdam, 1967) pp.37–40 ; G.M. Kosolapoff, *Organophosphorus Compounds* (John Wiley & sons, New York, 1950). H.J. Bestmann and R. Zimmermann in "Organic Phosphorus Compounds", eds. G.H. Kosolapoff and L. Maier, John Wiley & Sons, New York, 1972. Vol. 3, 1–183.

- [5] P.M. DiGiacomo, K.P. Callahan, P.C. Griffith, R.H. Lane, R.E. Cooksey, A.C.S. *Symp. Ser.*, **192**, 223 (1982); D.A. Burwell, M.E. Thompson, *Chem. Mater.*, 1991, **3**, 14 and 730; C.Y. Ortiz-Avila, A. Clearfield, *Inorg. Chem.*, 1985, **24**, 1773 ; P.A. Jaffrès, Ph.D. Thesis, Caen.
- [6] A.Y. Garner, E.C. Chapin, P.M. Scanlon, *J. Org. Chem.*, **24**, 532 (1959).
- [7] S. Caddick, *Tetrahedron*, **51**, 10403 (1995). We have found only one precedent, in the literature for the synthesis of phosphorus compounds under microwave irradiation: R.J. Giguere, B. Herberich, *Synth. Commun.*, **21**, 2197 (1991).
- [8] D. Villemin, B. Martin, *Synth. Commun.*, **25**, 2319 (1995) ; D. Villemin, F. Sauvaget, *Synlett.*, 435 (1994).
- [9] A.H. Ford-Moore, B.J. Perry, *Org. Synth.*, **31**, 33 (1951).
- [10] K. Bergesen, *Acta. Chem. Scand.*, **21**, 578, (1967).
- [11] F. Kagan, R.D. Birkenmeyer, R.E. Strube, *J. Am. Chem. Soc.*, **81**, 3026 (1959).
- [12] R.G. Gillis, J.F. Horwood, G.L. White, *J. Am. Chem. Soc.*, **80**, 2999, (1958).
- [13] G.M. Kosolapoff, *J. Am. Chem. Soc.*, **69**, 1002 (1947).
- [14] L. Germanaud, S. Brunel, Y. Chevalier, P. Le Perchec, *Bull. Soc. Chim. Fr.*, **4**, 699 (1988).
- [15] NMR spectra of new products :
2j: ^1H NMR 1.32 (t, $^3J_{\text{HH}} = 7.0$ Hz, $\text{CH}_3\text{CH}_2\text{O}$, 6H) 1.39 (m, 8H), 1.51–1.65 (m, 4 H), 1.77–1.88 (m, 4H) ; 3.40 (t, $J = 6.8$ Hz , $-\text{CH}_2-\text{Br}$, 2H), 4.09 (dq, $J = 7.2$ Hz, $J = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{O}$, 4H); ^{13}C NMR 16.55 (d, $^3J_{\text{CP}} = 6.1$ Hz, $\text{CH}_3\text{CH}_2\text{O}$), 22.47 (d, $^3J_{\text{CP}} = 4.5$ Hz, $-\text{CH}_2-(\text{CH}_2)_2-\text{P}$), 22.68 (C), 26.91 (C), 28.19 (C), 28.71 (C), 28.75 (C), 29.05 (C), 30.61 (d, $^2J_{\text{CP}} = 16.2$ Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{P}$), 33.43 (d, $^1J_{\text{CP}} = 70.9$ Hz, CH_2-P), 61.45 (d, $^2J_{\text{CP}} = 6.4$ Hz, $\text{CH}_3\text{CH}_2\text{O}$).
2k : ^1H NMR 1.32 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{O}$, 6H), 1.33–1.42 (m, 6H), 1.60–1.90 (m, 12H), 3.40 (t, $J = 6.8$ Hz, $-\text{CH}_2-\text{Br}$, 2H), 4.08 (dq, $^3J_{\text{HP}} = 7.2$ Hz , $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{O}$, 4H) ^{13}C NMR 16.55 (d, $^3J_{\text{CP}} = 6.02$ Hz, $\text{CH}_3\text{CH}_2\text{O}$), 22.46 (d, $^3J_{\text{CP}} = 5.35$ Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{P}$), 24.66 (C), 26.90 (C), 28.22 (C), 28.78 (C), 29.12 (C), 29.37 (C), 29.42 (C), 30.64 (d, $^2J_{\text{CP}} = 17.0$ Hz, $\text{CH}_2-\text{CH}_2-\text{P}$), 33.46 (d, $^1J_{\text{CP}} = 71.7$ Hz, $-\text{CH}_2-\text{P}$), 61.49 (d, $^2J_{\text{CP}} = 6.54$ Hz, $\text{CH}_3\text{CH}_2\text{O}$).