

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>

A CONVENIENT DIRECT SYNTHESIS OF α -N,N-DIALKYLAMINOPHOSPHONATES UNDER APROTIC CONDITIONS

Catherine Malhiac^a; Jean-Claude Combret^a; Kamal Boussad^a; Jean-Louis Klein^a

^a Laboratoire d'Hétérochimie Organique (IRCOF), Université de Rouen, Cedex, France

To cite this Article Malhiac, Catherine , Combret, Jean-Claude , Boussad, Kamal and Klein, Jean-Louis(1996) 'A CONVENIENT DIRECT SYNTHESIS OF α -N,N-DIALKYLAMINOPHOSPHONATES UNDER APROTIC CONDITIONS', Phosphorus, Sulfur, and Silicon and the Related Elements, 113: 1, 299 — 301

To link to this Article: DOI: 10.1080/10426509608046402

URL: <http://dx.doi.org/10.1080/10426509608046402>

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.

Communication

A CONVENIENT DIRECT SYNTHESIS OF α -N,N-DIALKYLAMINOPHOSPHONATES UNDER APROTIC CONDITIONS

CATHERINE MALHIAC, JEAN-CLAUDE COMBRET,* KAMAL BOUSSAD
and JEAN-LOUIS KLEIN

*Laboratoire d'Hétérochimie Organique (IRCOF), Université de Rouen,
F-76821 Mont Saint Aignan, Cedex, France*

(Received August 9, 1995; in final form January 9, 1996)

A general one-pot synthesis of N,N-dialkylaminophosphonates under aprotic conditions is proposed using aromatic, heteroaromatic or aliphatic aldehydes and N,N-dialkyl-aminosilanes under trimethylsilyltriflate catalysis.

Key words: α -N,N-Dialkylaminophosphonates, dialkylaminosilanes, one-pot aprotic reaction.

INTRODUCTION

Aminophosphonic acids are well-known bioactive and useful chemical compounds as well as their esters (aminophosphonates) and N-mono or dialkyl derivatives.¹ Modification of the alkyl chain is also of interest, especially in case of aromatic or heteroaromatic substituents.²

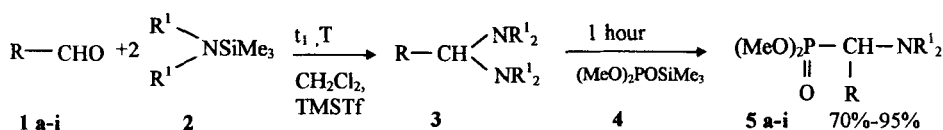
The main route to these compounds is a Mannich-type reaction first used by Fields³ and recently extended to methods using amino derivatives of carbonyl compounds and silicon reagents.⁴ Studies in this laboratory have demonstrated the utility of a new aminoalkylation system for the synthesis of β -dialkylaminoesters⁵ and we propose here a direct and efficient synthesis of α -dialkylaminophosphonates under aprotic conditions.

RESULTS AND DISCUSSION

In a previous work, we described the reaction between dialkylaminosilanes **2** and aromatic aldehydes **1** at room temperature under trimethylsilyltriflate catalysis leading to corresponding aminals **3**.⁵ Addition of trimethylsilyldimethyl phosphite to the mixture without isolation of **3** results in a smooth reaction that leads to dialkylaminophosphonates **5** (same results may be obtained after isolation, characterisation of **3** and reaction with TMS dimethylphosphite, but "direct" reaction of **1**, **2** and **4** does not give satisfactory results).

Using this procedure, even enolizable aldehydes may be reacted rapidly with good yields, under strict control of the temperature in the first step of the reaction (enamine formation increases with higher temperature).







Scheme 1



T : reaction temperature

 t_1 : reaction time (first step of reaction : NMR disappearance of 1)

TABLE I
Dialkylaminophosphonates 5

	R	R ¹	t ₁ (h)	T	Yield % ⁽¹⁾	MW(g/mole)	MS ⁽²⁾	³¹ P NMR
5a	C ₆ H ₅	CH ₃	0.5	RT	95	243	243 134 (100)	23.5 ppm
5b		CH ₃	0.5	RT	95	286	244 135(100)	24.2 ppm
5c		CH ₃	4	RT	95	233	233 124(100)	23.8 ppm
5d		CH ₃	4	RT	92	249	249 140(100)	23.4 ppm
5e	C ₆ H ₅		0.5	RT	95	285	285 176(100)	23.6 ppm
5f	CH ₃		3.5	0°C	70	223	223 114(100)	29.4 ppm
5g	(CH ₃) ₂ CH	CH ₃	0.5	0°C	90	209	209 100(100)	30.1 ppm
5h	C ₆ H ₅ CH ₂		1	-20°C	70	299	299/ 208(100) 190(70)	26.7 ppm
5i	φ-CH=CH	CH ₃	1	RT	75	269	269 160(100)	23.6 ppm

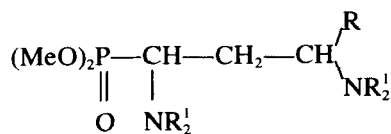
 t_1 : reaction time (first step)

(1) After purification

(2) detected M⁺ and most important fragment ions (see note 7)

Scheme 1 presents the sequence used in this new, simple and general one pot synthesis of aminophosphonates 5 and several examples are collected in Table I.⁶

Reaction with unsaturated aldehydes is more complicated and is under current investigation⁸; however expected 5i is easily isolated from cinnamaldehyde but a mixture of 5 and bis dialkylaminophosphonate 6 is obtained from aliphatic α ethylenic aldehydes.⁹



EXPERIMENTAL

^1H , ^{13}C , ^{31}P NMR spectra were recorded on a BRUKER AC 200 spectrometer in CDCl_3 as solvent. All RMN spectra were measured with SiMe_4 or H_3PO_4 as internal standard.

Mass spectra were recorded on a GC/MS HEWLETT-PACKARD HP 5890/MSD 5970 at 70 eV.

General Procedure

All reactions are achieved under inert gas atmosphere. To a mixture of aldehyde (10^{-2} mole/ 10 cm^3 CH_2Cl_2) is added a solution of **2** ($2 \cdot 10^{-2}$ mole/ 10 cm^3 CH_2Cl_2). Stirring is kept during the indicated time (Table I), and a solution of TMS dimethyl phosphite is then added. After one hour, the solvent is evaporated and 20 cm^3 of water is added to the residue. The aqueous layer is extracted with diethylether. The solution is dried, evaporated under vacuum and the residue is purified by distillation or flash-chromatography (gradient $(\text{CH}_3)_2\text{CO}-\text{CH}_2\text{Cl}_2$).

REFERENCES AND NOTES

- (a) E. K. Baylis, C. D. Campbell and J. G. Dingwall, *J. Chem. Soc., Perkin Trans I*, 2845 (1984) and including references; (b) P. Kafarski and P. Mastalerz, "Aminophosphonates": "Natural Occurrence Biochemistry and Biological Properties," *Beiträge der Wirkstoffforschung, Ak. Ind. Kompl. DDR*, Vol. 21, 1984, pp. 32–83; (c) L. Maier and P. J. Diel, *Phosphorus, Sulfur and Silicon*, **57**, 57 (1991).
- For a recent report on synthesis of various thiophenic derivatives see C. Hubert, B. Oussaid, G. Etamad-Moghadam, M. Koenig and B. Garrigues, *Synthesis*, 51 (1994) and references therein.
- E. K. Fields, *J. Amer. Chem. Soc.*, **74**, 1528 (1952).
- T. Morimoto, M. Aono and M. Sekiya, *J. Chem. Soc., Chem. Commun.*, 1055 (1984); T. Morimoto, T. Takahashi and M. Sekiya, *J. Chem. Soc., Chem. Commun.*, 794 (1984); A. A. Prishchenko, M. V. Livantsov, N. V. Boganova and I. F. Lutsenko, *Zh. Obshch. Khim.*, **59**, 2383 (1989); G. Courtois and L. Miginiac, *Synth. Commun.*, **21**, 201 (1991).
- P. Aube, I. Christot, J.-C. Combret and J.-L. Klein, *Bull. Soc. Chim. Fr.*, 1009 (1988).
- Satisfactory microanalysis ($\text{C} \pm 0.28$, $\text{H} \pm 0.25$, $\text{N} \pm 0.30$) as well as spectroscopic data in good agreement with assigned structures obtained for all new products **5**. Data ^1H NMR (in ppm): **5a**: 2.25 (s, 6H), 3.30 (d, 3H, $J = 10\text{ Hz}$), 3.70 (d, 3H, $J = 10\text{ Hz}$), 3.75 (d, 1H, $J = 24\text{ Hz}$), 7.25 (m, 5H); **5b**: 2.40 (s, 6H), 3.50 (d, 3H, $J = 10\text{ Hz}$), 3.90 (d, 3H, $J = 10\text{ Hz}$), 3.95 (d, 1H, $J = 24\text{ Hz}$), 7.50 (m, 2H), 8.70 (m, 2H); **5c**: 2.30 (s, 6H), 3.55 (d, 3H, $J = 10\text{ Hz}$), 3.80 (d, 3H, $J = 10\text{ Hz}$), 3.95 (d, 1H, $J = 24\text{ Hz}$), 6.40 (m, 2H), 7.40 (m, 1H); **5d**: 2.35 (s, 6H), 3.50 (d, 3H, $J = 10\text{ Hz}$), 3.85 (d, 3H, $J = 10\text{ Hz}$), 4.10 (d, 1H, $J = 24\text{ Hz}$), 7.25 (m, 3H); **5e**: 2.70 (m, 4H), 3.40 (d, 3H, $J = 10\text{ Hz}$), 3.80 (d, 3H, $J = 10\text{ Hz}$), 3.65 (m, 5H), 7.30 (m, 5H); **5f**: 1.20 (dd, 3H, $J = 7\text{ Hz}$, 18 Hz), 2.75 (m, 5H), 3.60 (m, 4H), 3.70 (d, 3H, $J = 11\text{ Hz}$), 3.80 (d, 3H, $J = 11\text{ Hz}$); **5g**: 0.95 (d, 3H), 1.00 (d, 3H), 2.40 (d, 6H), 2.60 (dd, 1H, $J = 7\text{ Hz}$, 15 Hz), 3.60 (d, 3H, $J = 11\text{ Hz}$), 3.70 (d, 3H, $J = 10\text{ Hz}$); **5h**: 2.75 (m, 5H), 3.65 (m, 4H), 3.80 (d, 3H, $J = 11\text{ Hz}$), 3.90 (d, 3H, $J = 11\text{ Hz}$), 4.10 (d, 2H), 7.2 (m, 5H); **5i**: 2.50 (s, 6H), 3.75 (d, 3H, $J = 11\text{ Hz}$), 3.85 (d, 3H, $J = 11\text{ Hz}$), 3.80 (m, 1H), 6.35 (ddd, 1H, $J = 15\text{ Hz}$, 10 Hz, 7 Hz), 6.65 (dd, 1H, $J = 16\text{ Hz}$, 3 Hz), 7.40 (m, 5H).
- All compounds exhibit analogous characteristic MS data with a major fragmentation path of molecular ion (loss of phosphorous group) leading to a iminium moiety (an easy loss of the benzyl group also occurs for **5h**); all other fragments are very weak with however molecular ion being always noticeable.
- C. Malhiac, J. C. Combret and A. Atmani, to be published.
- C. Malhiac, Doctorat de Chimie, Rouen, France, 1993.