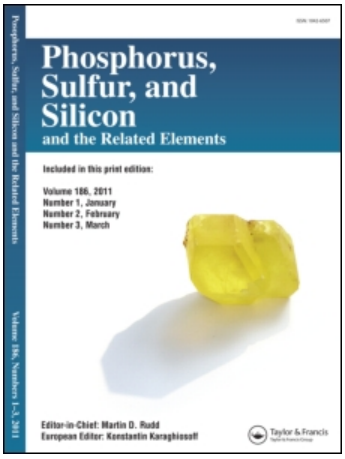
This article was downloaded by:
On: *28 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

Allenes through Horner-Wadsworth-Emmons Olefination of Alkenylphosphonates

Yasuo Nagaoka[a]; Hideki Inoue[a]; Kiyoshi Tomioka[a]
[a] Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan

Online publication date: 27 October 2010

To cite this Article Nagaoka, Yasuo , Inoue, Hideki and Tomioka, Kiyoshi(2002) 'Allenes through Horner-Wadsworth-Emmons Olefination of Alkenylphosphonates', Phosphorus, Sulfur, and Silicon and the Related Elements, 177: 6, 1843 — 1846
To link to this Article: DOI: 10.1080/10426500212268
URL: http://dx.doi.org/10.1080/10426500212268

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.

Phosphorus, Sulfur and Silicon, 2002, Vol. 177:1843–1846
Copyright © 2002 Taylor & Francis
1042-6507/02 $12.00 + .00
DOI: 10.1080/10426500290093432

Downloaded At: 11:51 28 January 2011

ALLENES THROUGH HORNER-WADSWORTH-EMMONS OLEFINATION OF ALKENYLPHOSPHONATES

Yasuo Nagaoka, Hideki Inoue, and Kiyoshi Tomioka
Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto, Japan

(Received July 29, 2001; accepted December 25, 2001)

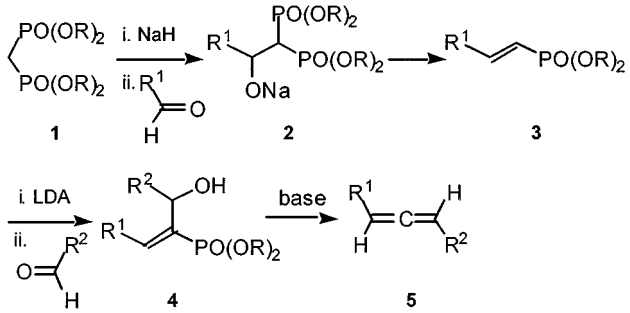
*Mono- and di-substituted allenes **5** were synthesized by successive Horner-Wadsworth-Emmons olefination starting from methylenebisphosphonate **1** and two carbonyl compounds. The key to success is KH or KH-18-crown-6 as a base for the second HWE olefination of hydroxyalkenylphosphonates **4**.*

Keywords: Allene; 18-crown-6; double olefination; Horner-Wadsworth-Emmons reaction; phosphonate

We have been engaged in the chemistry of lithium phosphonates[1] in which Baylis-Hillmann type products **4** were obtained upon LDA treatment of alkenylphosphonates **3** with aldehydes and subjected to Horner-Wadsworth-Emmons (HWE) olefination using NaH as a base, giving the corresponding allenes **5** in up to 72% yields.[2] Allenes are recent focus of versatile class of intermediates in a variety of organic synthetic processes.[3] The major allene synthesis relies on a S_N2' replacement of propargylic leaving groups[4] and others involve dehydrohalogenation of vinylic halides,[5] reductive elimination of halogenated cyclopropanes,[6] and so on.[7–10] Our synthesis is conceptually different from these and is advantageous in the retrosynthetic simplicity. Two sp^2 and one sp carbon atoms of allene functionality are constructed by sequential double HWE olefinations of the three components, methylenebisphosphonate **1** with two carbonyl compounds as shown in Scheme 1.[11] Realization of this scenario is critically dependent on the efficacy of the second HWE olefination of hydroxyalkenylphosphonate **4**, because the

We gratefully acknowledge financial support from Japan Society for Promotion of Science and the Ministry of Education, Science, Sports and Culture, Japan.

Address correspondence to Yasuo Nagaoka, Faculty of Engineering, Kansai University, Suita, Osaka 564-8680, Japan. E-mail: ynagaoka@ipcku.kansai-u.ac.jp



SCHEME 1

first olefination of methylenebisphosphonate **1** to **3** through **2** is a well-established high yield process.[12] We describe herein the high yield HWE olefination of alkenylphosphonate **3** with a wide range of carbonyl compounds. The accurate selection of a base for HWE olefination of **4** was the key for success.

It readily comes to an answer that olefination of **4** requires formation of an unfavorable phosphooxetane that involves one sp^2 carbon in the four-membered ring. Furthermore, the 120 degree bond angle by the sp^2 carbon is a significantly unfavorable factor in intramolecular nucleophilic attack of an alcoholic oxygen nucleophile to P=O phosphorous electrophile to form the four-membered ring. The analysis leads to suggestion that olefination of **4** requires efficient activation of a nucleophilic alcoholic oxygen. However, strong base is likely to deprotonate allene protons to result in isomerization into alkyne and diene. We began our studies to find an appropriate base for olefination of **4**.

We set **4a** (R^1 = Ph, R^2 = *t*-Bu, R = Et or *i*-Pr) as an olefination testing hydroxyphosphonate to allene **5a** (R^1 = Ph, R^2 = *t*-Bu), because **4a** and **5a** are the most simple alcohol and allene with regard to abstractable protons (Table I). The lithium alkoxide, generated by treating **4a** (R = Et) with 1 equiv of BuLi in THF, was the least reactive alkoxide to afford **5a** in 30% yield along with concomitant formation of inseparable complex mixture after 5 h under reflux (Entry 1 in Table I). The excellent conversion was achieved by treating the potassium alkoxide, formed with KH, in THF at 60°C for 5 min to give **5a** in 92% yield (Entry 3 in Table I). The reaction of **4a** (R = Et, *i*-Pr) can be performed at much lower temperature (0°C) for 0.5 h by further addition of 0.1 equiv of 18-crown-6 to give **5a** in the same 92% yield (Entry 6 in Table I). At the higher reaction temperature (60°C) for 5 min and in the presence of 1 equiv of 18-crown-6, the major product was the isomerized alkyne in 75% yield (Entry 4 in Table I). Isomerization of **5a** could be prevented by lowering reaction temperature to 0°C affording **5a** in 89% yield (Entry 5

Downloaded At: 11:51 28 January 2011

TABLE I Base Dependency of Olefination Efficacy of **4a**

Entry	R	Base	18-crown-6 (equiv)	Temp (°C)	Time (min)	Yield (%) 5
1	Et	BuLi		Reflux	300	30
2	Et	NaH		50	30	72
3	Et	KH		60	5	92
4	*i*-Pr	KH	1.0	60	5	25
5	*i*-Pr	KH	1.0	0	15	89
6	*i*-Pr	KH	0.1	0	30	92
7	Et	KDA		60	60	41
8	Et	KHMDS		25	15	88
9	Et	KOH[a]		150	80	55
10	Et	*t*-BuOK[b]		40	15	62
11	Et	*t*-BuOCs		60	10	70

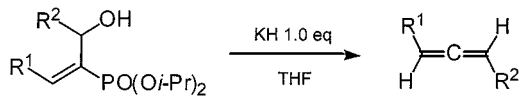
[a]DMSO was used as a solvent.
[b]1.5 equiv.

Downloaded At: 11:51 28 January 2011

in Table I). The effects of 18-crown-6 are apparent and favorable for the olefination through nucleophilic activation of the potassium alkoxide. Other potassium bases were less effective than KH (Entries 7–10 in Table I). The softer base, *t*-BuOCs was less effective than KH (Entry 11 in Table I). Thus we could find KH and KH-18-crown-6 as suitable olefination bases for **4a**.

The conditions found above were successfully applicable to olefination of other hydroxyphosphonates **4** as summarized in Table II.

TABLE II Effects of Substituents R^1 and R^2 on the Reaction of **4**



4 **5**

Entry	4	R^1	R^2	18-crown-6 (equiv)	Temp (°C)	Time (min)	Yield (%) 5
1	a	Ph	*t*-Bu	0.1	0	30	92
2	b	Ph	c-Hex		60	10	61
3	c	Ph	$Ph(CH_2)_2$		60	20	71
4	d	Ph	Me		60	20	40
5	d	Ph	Me	0.1	0	60	73
6	e	Ph	Ph		60	40	17
7	f	*t*-Bu	$Ph(CH_2)_2$		60	20	79
8	g	c-Hex	$Ph(CH_2)_2$	0.1	60	60	77
9	h	H	$Ph(CH_2)_2$	1.0	60	10	42
10	i	*t*-Bu	Ph		60	60	55

The olefination proceeded smoothly to give the corresponding allenes **5b–d** in good yields even when methine, methylene, and methyl groups (R^2) are adjacent to the allene function (Entries 2–5 in Table II). Especially, KH-crown base improved the reaction yield to 73% from 40% even when R^2 is a methyl group that is readily deprotonated (Entry 5 in Table II). When methylene is at one end of the allene such as **5f–h** ($R^2 = Ph(CH_2)_2$), the reaction proceeded smoothly to afford the allenes in relatively high yields (Entries 7–9 in Table II).

In conclusion, mono- and di-substituted allenes were efficiently synthesized by successive Horner-Wadsworth-Emmons olefinations starting from methylenebisphosphonate **1** and two carbonyl compounds.

REFERENCES

Downloaded At: 11:51 28 January 2011

[1] (a) M. Mizuno, K. Fujii, and K. Tomioka, *Angew. Chem. Int. Ed. Engl.*, **37,** 515 (1998); (b) Y. Nagaoka and K. Tomioka, *Organic Letters*, **1,** 1467 (1999); (c) Y. Nagaoka, H. Inoue, E. Nawal, and K. Tomioka, *Chem. Commun.*, 122 (2002); (d) H. Inoue, H. Tsubouchi, Y. Nagaoka, and K. Tomioka, *Tetrahedron*, **58,** 83 (2002).

[2] Y. Nagaoka and K. Tomioka, *J. Org. Chem.*, **63,** 6428 (1998).

[3] (a) S. Patai (ed.), *The Chemistry of Ketenes, Allenes, and Related Compounds* (John Wiley and Sons, Inc., Chichester, 1980) Parts 1 and 2; (b) H. Schuster and G. Coppola, *Allenes in Organic Synthesis* (John Wiley and Sons, Inc., New York, 1984).

[4] For a recent variation: A. G. Myers and B. Zheng, *J. Am. Chem. Soc.*, **118,** 4492 (1996).

[5] (a) K. M. Brummond, E. A. Dingess, and J. L. Kent, *J. Org. Chem.*, **61,** 6096 (1996); (b) K. Tanaka, K. Otsubo, and K. Fuji, *Synlett.*, 933 (1995).

[6] W. E. Doering and P. M. LaFlamme, *Tetrahedron*, **2,** 75 (1958).

[7] K. M. Brummond, E. A. Dingess, and J. L. Kent, *J. Org. Chem.*, **61,** 6096 (1996).

[8] K. A. Raynolds, P. G. Dopico, M. S. Brody, and M. G. Finn, *J. Org. Chem.*, **62,** 2564 (1997).

[9] B. Delouvrie, E. Lacote, L. Fensterbank, and M. Malacria, *Tetrahedron Lett.*, **40,** 3565 (1999).

[10] M. Ogasawara, H. Ikeda, and T. Hayashi, *Angew. Chem. Int. Ed. Engl.*, **39,** 1042 (2000).

[11] R. L. Danheiser, Y. M. Choi, M. Menichincheri, and E. J. Stoner, *J. Org. Chem.*, **58,** 322 (1993).

[12] M.-P. Teulade, P. Savignac, E. E. Aboujaoude, S. Lietge, and N. Collignon, *J. Organomet. Chem.*, **304,** 283 (1986).