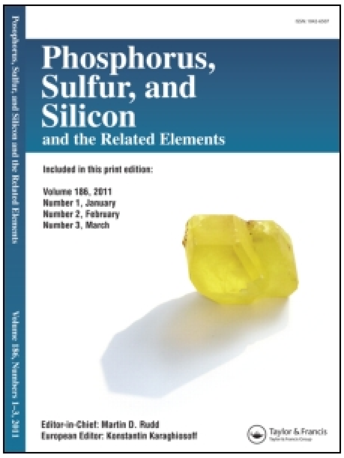


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Z-Selective Preparation of β-Monosubstituted α,β-Unsaturated Amides Using Diphenylphosphonoacetamides

Satoshi Kojima[a]; Tsugihiko Hidaka[a]; Yuko Ohba[a]; Katsuo Ohkata[a]
[a] Department of Chemistry, Graduate School of Science, Hiroshima University, Higashi-Hiroshima, Japan

To cite this Article Kojima, Satoshi , Hidaka, Tsugihiko , Ohba, Yuko and Ohkata, Katsuo(2002) 'Z-Selective Preparation of β-Monosubstituted α,β-Unsaturated Amides Using Diphenylphosphonoacetamides', Phosphorus, Sulfur, and Silicon and the Related Elements, 177: 3, 729 — 732

To link to this Article: DOI: 10.1080/10426500210268

URL: http://dx.doi.org/10.1080/10426500210268

Phosphorus, Sulfur and Silicon, 2002, Vol. 177:729–732
Copyright © 2002 Taylor & Francis
1042-6507/02 $12.00 + .00

Z-SELECTIVE PREPARATION OF β-MONOSUBSTITUTED α,β-UNSATURATED AMIDES USING DIPHENYLPHOSPHONOACETAMIDES

Satoshi Kojima, Tsugihiko Hidaka, Yuko Ohba,
and Katsuo Ohkata
Department of Chemistry, Graduate School of Science,
Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima
739-8526, Japan

(Received June 25, 2001)

*The Horner-Wadsworth-Emmons reaction of diphenylphosphonoacetamides [$(PhO)_2P(O)CH_2CONRR'$] (**2a**: R, R′ = CH_2Ph; **2b**: R = CH_2Ph, R′ = H; **2c**: R = Me, R′ = OMe) was examined. The reaction of **2a** was found to be Z-selective for benzaldehyde with selectivities up to 94:6. Reagent **2b** led to reasonable selectivity for both benzaldehyde (85:15) and 3-phenylpropionaldehyde (87:13), while **2c** was somewhat effective only for the latter aldehyde (83:17).*

Keywords: α,β-unsaturated amides; Horner-Wadsworth-Emmons reaction; *Z*-selectivity

Methods for the preparation of the thermodynamically less stable *Z*-olefins bearing electron-withdrawing groups by the Wittig or the Horner-Wadsworth-Emmons (HWE) reaction[1–5] are limited.[6–10] For α,β-unsaturated amides we have reported on the effectiveness of *N*,*N*-dibenzyl-triphenylsilylacetamide (**1**).[11] However, for mono-*N*-substituted amides, the mere generation of the enolate of the Peterson reagent lead to decomposition. In an attempt to overcome this default and seek further utility, we have carried out an examination on diphenylphosphonoacetamides, analogs of the highly successful phosphonoacetates by Ando.[10,12,13]

Examined were [$(PhO)_2P(O)CH_2CONRR'$] with three different patterns of substitution upon the amide nitrogens (**2a**: R, R′ = CH_2Ph; **2b**: R = CH_2Ph, R′ = H; **2c**: R = Me, R′ = OMe), as representatives

---

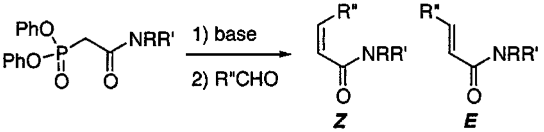
Address correspondence to Satoshi Kojima, Department of Chemistry, Graduate School of Science, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan. E-mail: skojima@sci.hiroshima-u.ac.jp

TABLE I The Reaction of **2a**

Entry	R″	Base	Z:E	Yield (%)
1	Ph	*n*-BuLi[a]	73:27	95
2	Ph	NaH	88:12	71
3	Ph	*t*-BuOK	92:8	65
4	Ph	KHMDS	94:6	96
5	$Ph(CH_2)_2$	NaH	67:33	77
6	$Ph(CH_2)_2$	*t*-BuOK	60:40	39
7	$Ph(CH_2)_2$	KHMDS	50:50	80

[a] The reaction temp was gradually raised to 0°C.

of *N*,*N*-disubstituted reagents, *N*-monosubstituted reagents, and reagents bearing the potential for further transformation to ketones, respectively.[14] The reagents were prepared by the reaction of diphenyl phosphite with the corresponding chloroacetamides in the presence of NaH in fair to good yield (**2a**, 77%; **2b**, 90%; **2c**, 61%).



SCHEME 1

In the reaction of **2a** with benzaldehyde, higher selectivity was achieved in the order of $Li^+ < Na^+ < K^+$.[†] It was also found that NaH and *t*-BuOK, which could not be used for **1** could be used here. Considering the availability of the reagent and range of usable bases in the olefin forming reaction, **2a** scores favorably with **1** toward aromatic aldehydes. For 3-phenyl propionaldehyde, an aliphatic aldehyde, the selectivity was found to be only modest, with a maximum of ca. 2:1 (Table I).

The reaction of **2b** with benzaldehyde in the presence of either 1 or 2 equiv of base was found to proceed with selectivities up to 85:15 (Table II). The use of 2 equiv was to assure full conversion in the presence of product bearing a somewhat acidic amide group. A general trend was that the use of 2 equiv of base compared to 1 equiv gave higher yield but somewhat lower selectivity, and NaH turned out to exhibit highest selectivities for both aromatic and aliphatic aldehydes. This presents

---

[†] General procedure: To the reagent (0.20 mmol) in THF was added base (0.20 mmol), followed by aldehyde (0.22 mmol) at −78°C. After stirring for 3 h, the solution was quenched with aq NH_4Cl, worked up, and subjected to PTLC purification to give the product.

TABLE II The Reaction of **2b**

Entry	R″	Base	Z : E	Yield (%)
1	Ph	NaH[b]	85:15	55
2	Ph	NaH[c]	68:32	84
3	Ph	t-BuOK[b]	78:22	91
4	Ph	KHMDS[b]	81:19	77
5	Ph	KHMDS[c]	76:24	93
6	$Ph(CH_2)_2$	n-BuLi[a,b]	84:16	82
7	$Ph(CH_2)_2$	NaH[b]	87:13	44
8	$Ph(CH_2)_2$	NaH[c]	86:14	77
9	$Ph(CH_2)_2$	KHMDS[b]	80:20	52
10	$Ph(CH_2)_2$	KHMDS[c]	74:26	52

[a] The reaction temp was gradually raised to 0°C.
[b] 1 equiv of base was used.
[c] 2 equiv of base was used.

TABLE III The Reaction of **2c**

Entry	R″	Base	Z : E	Yield (%)
1	Ph	n-BuLi[a]	67:33	49
2	Ph	NaH	71:29	79
3	Ph	t-BuOK	67:33	85
4	Ph	KHMDS	72:28	67
5	$Ph(CH_2)_2$	n-BuLi[a]	75:25	90
6	$Ph(CH_2)_2$	NaH	83:17	83
7	$Ph(CH_2)_2$	t-BuOK	65:35	85
8	$Ph(CH_2)_2$	KHMDS	67:33	92

[a] The reaction temp was gradually raised to 0°C.

the first *Z*-selective synthesis for unsaturated amides bearing an *N*-hydrogen.

The selectivity of the reaction of Weinreb type HWE reagent **2c** with benzaldehyde was found to be disappointing (Table III). However, the reaction of 3-phenylpropionaldehyde proceeded with a reasonable selectivity of 83:17 using NaH. Transformational application of the products is currently under investigation.

REFERENCES

[1] B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, **89,** 863–927 (1989).
[2] S. E. Kelly, *Comprehensive Organic Synthesis* (Pergamon Press, Oxford, 1991), vol. 1, pp. 730–817.
[3] A. W. Johnson, *Ylides and Imines of Phosphorus* (Wiley-Interscience, New York, 1993).

[4] E. Vedejs and M. J. Peterson, *Top. Stereochem.*, **21,** 1–157 (1994).
[5] O. I. Kolodiazhnyi, *Phosphorus Ylides* (Wiley-VCH: Weinheim, 1999).
[6] W. C. Still and C. Gennari, *Tetrahedron Lett.*, **24,** 4405–4408 (1983).
[7] S. Kojima, R. Takagi, and K.-y. Akiba, *J. Am. Chem. Soc.*, **119,** 5970–5971 (1997).
[8] T. Y. Zhang, J. C. O'Toole, and J. M. Dunigan, *Tetrahedron Lett.*, **39,** 1461–1464 (1998).
[9] W. Yu, M. Su, and Z. Jin, *Tetrahedron Lett.*, **40,** 6725–6728 (1999).
[10] K. Ando, *Tetrahedron Lett.*, **36,** 4105–4108 (1995).
[11] S. Kojima, H. Inai, T. Hidaka, and K. Ohkata, *Chem. Commun.*, 1795–1796 (2000).
[12] K. Ando, *J. Org. Chem.*, **65,** 4745–4749 (2000).
[13] K. Ando, *Synlett*, 1272–1274 (2001). Professor K. Ando of the University of the Ryukyus has carried out independent studies with similar amide reagents.
[14] S. Nahm and S. M. Weinreb, *Tetrahedron Lett.*, **22,** 3815–3818 (1981).