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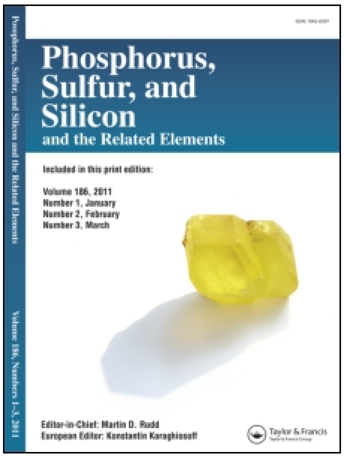

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To cite this Article Lentsch, Loriann M. and Wiemer, David F.(1999) 'Nucleophilic Additions to β-Keto Phosphonates', Phosphorus, Sulfur, and Silicon and the Related Elements, 144: 1, 573 — 576

To link to this Article: DOI: 10.1080/10426509908546309

URL: http://dx.doi.org/10.1080/10426509908546309

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Phosphorus, Sulfur and Silicon, 1999, Vol. 144-146, pp. 573-576
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Nucleophilic Additions to β-Keto Phosphonates

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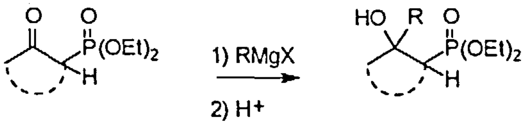
Nucleophilic addition to the carbonyl group of β-keto phosphonates has been studied with several Grignard reagents. Allyl magnesium halides have proven particularly effective.

Keywords: β-keto phosphonate; Grignard reaction

INTRODUCTION

β-Keto phosphonates have proven to be versatile reagents in organic synthesis[1] and new strategies for phosphonate synthesis are of general interest.[2] While most classical methods are based on phosphorus nucleophiles, including strategies such as the Arbuzov[3] reaction and phosphonate acylation,[4] a number of more recent methods have relied upon electrophilic phosphorus reagents.[5] As an extension of our studies in this vein, we examined the reaction of representative β-keto phosphonates with organometallic reagents (Eq. 1). Because additions to the carbonyl group would extend the carbon skeleton and may incorporate additional functionality, such reactions would significantly expand the range of accessible phosphonates.[6]

Eq. 1



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RESULTS AND DISCUSSION

Reaction of an organometallic reagent with a β-keto phosphonate might be expected to involve a proton transfer reaction or possibly addition to the phosphorus itself. Previous examples of Grignard additions made it appear unlikely that reaction at phosphorus would prove competitive to addition to the carbonyl group, but did not include the possibility of proton transfer because the α-carbon was fully substituted.[6] We chose to focus on addition of allyl Grignard reagents to representative β-keto phosphonates, in part because the allyl group of an adduct could be readily converted to a variety of other functional groups.[7] As shown in Table 1, these additions were generally successful with each of the substrates examined.

Addition of phosphonate 1 to a slight excess of allyl magnesium chloride in THF gave the desired adduct in low yield, but reaction with excess Grignard reagent significantly improved the yield. Higher reaction temperatures resulted only in decomposition, and addition of cerium chloride did not result in improved yield at either 0 °C or at -78 °C, even though $CeCl_3$ is reported to improve the reaction of Grignard reagents with other enolizable ketones.[8] In the presence of boron trifluoride etherate, addition of the allyl Grignard reagent was markedly improved, with only a single product observed by ^{31}P NMR and an isolated yield of 78% attained.

Reasonable yields of the allyl adducts also were obtained with each of the other three β-keto phosphonates examined. In each of these cases, the reactions were conducted in the presence and absence

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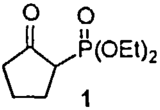
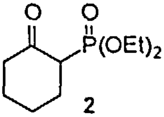
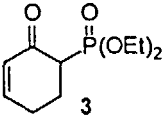
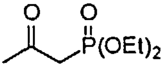
TABLE 1. Reaction of β-Keto Phosphonates with Allyl Magnesium Chloride

Phosphonate	Grignard	Eq.	Temp.(°C)	Yield
 **1**		1.5	0 to rt	18%
1		5	0 to rt	61%
1		5	reflux	--
1	 $CeCl_3$	3	-78	42%
1	 $BF_3 \cdot OEt_2$	5	0	78%
 **2**		5	0 to rt	36%
2	 $BF_3 \cdot OEt_2$	5	0	51%
 **3**		5	0 to rt	29%
3	 $BF_3 \cdot OEt_2$	5	0	62%
 **4**		5	0 to rt	22%
4	 $CeCl_3$	5	-78	48%
4	 $BF_3 \cdot OEt_2$	5	0	80%

of BF_3OEt_2. Significantly improved yields were obtained in the presence of this Lewis acid in all three cases.

These studies have shown that allylation of β-keto phosphonates is viable through addition of allyl Grignard reagents to the carbonyl group. Further transformation of the allyl functionality should extend the range of structures available through this process.

Acknowledgments

We thank Mr. Chad Schwitters for his experimental assistance, the University of Iowa Center for Biocatalysis and Bioprocessing for support in the form of a fellowship for LML, and the University of Iowa Graduate College for partial support of this research.

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References

[1] Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989,** *89,* 863–927.
[2] Wiemer, D. F. *Tetrahedron* **1997,** *53,* 16609–16644.
[3] Arbuzov, B. A. *Pure Appl. Chem.* **1964,** *9,* 307–335.
[4] a) Corey, E. J.; Kwiatkowski, G.T. *J. Am. Chem. Soc.* **1966,** *88,* 5654–5656. b) Mathey, F.; Savignac, P. *Tetrahedron* **1978,** *34,* 649–654. c) Aboujaoude, E. E.; Collignon, N.; Savignac, P. *J. Organomet. Chem.* **1984,** *264,* 9–17.
[5] Baker, T. J.; Wiemer. D. F. *J. Org. Chem.* **1998,** *63,* 2613–2618, and references cited therein. b) Lee, K.; Wiemer, D. F. *J. Org. Chem.* **1991,** *56,* 5556–5560.
[6] Previous examples of Grignard additions to β-keto phosphonates include: a) Berkowitz, D. B.; Eggen. M.; Shen, Q.; Shoemaker, R. K. *J. Org. Chem.* **1996,** *61,* 4666–4675 b) Tsai, H. J.; Thenappan. A.; Burton, D. J. *J. Org. Chem.* **1994,** *59,* 7085–7091.
[7] Yamamoto, Y.; Asao, N. *Chem. Rev* **1993,** *93,* 2207–2293.
[8] Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989,** *111,* 4392–4398.