Pergamon

Tetrahedron Letters, Vol. 35, No. 48, pp. 9071-9072, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01935-5

A Facile Synthesis of α-Phosphono Esters through Methoxycarbonylation of α-Phosphono Carbanions.

Jon K.F. Geirsson* and Jon T. Njardarson

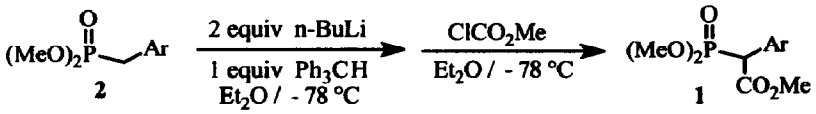
Science Institute, University of Iceland,
Dunhaga 3, IS-107 Reykjavik, Iceland

Abstract: This paper describes a concise and effective synthesis of methyl α-phosphonoaryl acetates, effected by reacting α-phosphono carbanions with methyl chloroformate. Yields are high, and the purification of the products is readily achieved with column chromatography.

α-Phosphono esters are widely employed substrates in olefin synthesis *via* the Horner-Wadsworth-Emmons (HWE) reaction.[1] A significant limitation to this reaction constitutes the preparation of the α-phosphono esters and substantial effort is currently being made towards the development of a general synthesis of β-keto phosphonates and α-phosphono esters.[2-8] In the context of recent work on the photoisomerization of methyl α-arylcinnamates, we required a series of α-phosphono esters **1** in considerable amount for use in the HWE reaction.[9]

Known synthetic procedures with either nucleophilic phosphoryl reagents like trimethyl phosphite or dimethyl phosphite anion[3] or electrophilic phosphoryl reagents like dimethyl chlorophosphate[4] or dimethyl phosphorochloridite,[5] were disappointing with regard to yields or preparative ease.

A different approach to the synthesis of **1** is to introduce the methoxycarbonyl group in the last step by reacting an α-phosphono carbanion with a suitable reagent like methyl chloroformate or dimethyl carbonate.[6] Suchlike approaches have appeared sporadically in the literature,[7] and in this report we describe an effective synthesis of **1** in a procedure which is based on such an approach (Scheme 1).



Scheme 1

As outlined in Scheme 1, methyl chloroformate was reacted with an α-phosphono carbanion, which could be generated with a variety of bases. It is essential to use 2 mol equiv of base and the optimized reaction conditions[10] make use of a base which did not react with methyl chloroformate or **1**. The best combination of yield and preparative ease was to use diethyl ether as the solvent.

As tacitly indicated above, we explored a variety of reaction conditions and conclude that in addition to the choice of base and solvent, the reaction is also very sensitive to the reaction temperature: Conducting the reaction at temperatures above -78 °C always resulted in considerably diminished yields. This is concordant with remarks on the instability of α-phosphono carbanions at temperatures above -65 °C.[8]

The results in Table 1 demonstrate that the synthetic sequence allows some structural variation with regard to activating and deactivating substituents on the aromatic ring.

Table 1. Formation of α-Phosphono Esters **1**.

Product	Ar	Yield %	^{1}H NMR δ (ppm): [α-H, d]	Product	Ar	Yield %	^{1}H NMR δ (ppm): [α-H, d]
1a	C_6H_5	80	4.28 (J_{HP}=23.5 Hz)	**1e**	4-MeC_6H_4	75	4.16 (J_{HP}=23.4 Hz)
1b	4-ClC_6H_4	61	4.19 (J_{HP}=23.8 Hz)	**1f**	2,4,6-$Me_3C_6H_2$	59	4.60 (J_{HP}=28.6 Hz)
1c	2,4-$Cl_2C_6H_3$	72	4.96 (J_{HP}=25.0 Hz)	**1g**	4-$MeOC_6H_4$	70	4.23 (J_{HP}=23.5 Hz)
1d	2,6-$Cl_2C_6H_3$	70	5.13 (J_{HP}=27.4 Hz)				

The availability of starting materials and the preparative ease of this procedure should make it attractive. Finally, it is worthy of note that the procedure has been scaled up to produce 5 - 15 g of phosphonates **1**.

Acknowledgement: Support of this work from the University of Iceland Research Fund is gratefully acknowledged. The authors wish to thank Dr. S. Jónsdóttir for performing the NMR measurement.

References and Notes:

1. Wadsworth, W. S., Jr. *Org. React.* **1977**, *25*, 73-253. Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863-927.
2. Mikolajczyk, M.; Balczewski, P. *Synthesis* **1984**, 691-694. Corbel, B.; Medinger, L.; Haelters, J. P.; Sturtz, G. *Synthesis* **1985**, 1048-1051. Teulade, M. P.; Savignac, P.; About-Jadet, E.; Collignon, N. *Synth. Commun.* **1989**, *19*, 71-81. Kim, D. Y.; Lee, K.; Oh, D. Y. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2451-2452.
3. Britelli, D. R. *J. Org. Chem.* **1981**, *46*, 2514-2520. Page, P.; Mazières, M. R.; Bellan, J.; Sanchez, M. Phosphorus Sulfur Silicon, **1992**, *70*, 205-210.
4. Kandil, A. A.; Porter, T. M.; Slessor, K. N. *Synthesis* **1987**, 411-413.
5. Lee, K.; Wiemer, D. F. *J. Org. Chem.* **1991**, *56*, 5556-5560. Boeckman, R. K., Jr.; Kamenecka, T. M.; Nelson, S. G.; Pruitt, J. R.; Barta, T. E. *Tetrahedron Lett.* **1991**, *32*, 2581-2584.
6. Tay, M. K.; About-Jadet, E.; Collignon, N.; Teulade, M. P.; Savignac, P. *Synth. Commun.* **1988**, *18*, 1349-1362.
7. Teulade, M. P.; Savignac, P. *Synth. Commun.* **1987**, *17*,125-136. Patois, C.; Savignac, P.; About-Jadet, E.; Collignon, N. *Synth. Commun.* **1991**, *21*,2391-2396. Tsai,H.J.;Thenappan,A.;Burton, D.J.*Tetrahedron Lett.* **1992**, *33*,6579-6582.
8. Teulade, M. P.; Savignac, P. *Synth. Commun.* **1987**, *17*, 125-136. Patois, C.; Savignac, P.; About-Jadet, E.; Collignon, N. *Synth. Commun.* **1991**, *21*, 2391-2396.
9. Evans, C. H.; Sigurdardottir, R.S.; Geirsson, J. K. F.; Kvaran, Á. *J. Photochem. Photobiol. A: Chem.* **1993**, *73*, 179-185. Geirsson, J. K. F.; Gudmundsson, B. Ö.; Sigurdardottir, R.S. *Acta Chem. Scand.* **1993**, *47*, 1112-1116.
10. Typical experimental procedure: 2.05 mol equiv of n-BuLi (2.5 M in hexane) were added *via* syringe to a solution of 1 mol equiv of triphenylmethane in dry ether, previously cooled to -78°C. After stirring this mixture at -78°C for 10 min, an etheral solution of **2** was added dropwise and the resulting mixture stirred for 1 hr before the methyl chloroformate was added dropwise and stirring continued for further 3-4 hrs at -78°C. The reaction was quenched at -78°C with aqueous HCl, and the dried ether phase concentrated *in vacuo*. The residue was purified by column chromatography on silica gel using CH_2Cl_2 to elude triphenylmethane. Subsequent elusion with methanol afforded **1** in high yields. If the product was contaminated with **2**, the two phosphonates were easily separated on a preparative HPLC instrument with ethyl acetate as the mobile phase.

(*Received in UK* 15 *August* 1994; *revised* 23 *September* 1994; *accepted* 30 *September* 1994)