Synthetic Communications

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

A Facile Synthesis of Diethyl 1-Formylalkane Phosphonates via Ozonolysis of 1-Alkyl Allylic Phosphonates

Jun Mo Gil , Jung Hwan Hah , Kwang Young Park & Dong Young Oh

To cite this article: Jun Mo Gil , Jung Hwan Hah , Kwang Young Park & Dong Young Oh (2000) A Facile Synthesis of Diethyl 1-Formylalkane Phosphonates via Ozonolysis of 1-Alkyl Allylic Phosphonates, Synthetic Communications, 30:5, 789-794, DOI: 10.1080/00397910008087090

To link to this article: http://dx.doi.org/10.1080/00397910008087090

Published online: 04 Dec 2007.

SYNTHETIC COMMUNICATIONS, 30(5), 789-794 (2000)

A FACILE SYNTHESIS OF DIETHYL 1-FORMYLALKANE PHOSPHONATES *VIA* OZONOLYSIS OF 1-ALKYL ALLYLIC PHOSPHONATES

Jun Mo Gil, Jung Hwan Hah, Kwang Young Park and Dong Young Oh*

Department of Chemistry, Korea Advanced Institute of Science and Technology, 373-1, Kusung-Dong, Yusung-Gu, Taejon, 305-701, Korea.

Abstract: The 1-formylalkanephosphonates were obtained by the ozonolysis of the corresponding 1-alkylated allylphosphonates, which had been previously prepared by treatment with *n*-BuLi, followed by addition of alkyl halides.

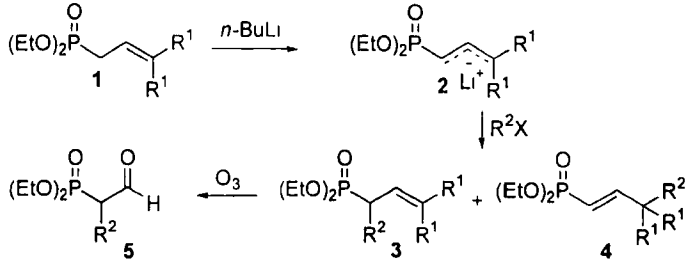
It is well known and established that 1-formylalkanephosphonates have long been of interest to the chemists. Their applications are especially interesting in the formation of carbon-carbon double bond[1] and the synthesis of 2-aminoalkanephosphonates,[2] since they display unique properties. For example, these reagents can be used to control regio- and stereoselectivity for olefin synthesis in homologations of aldehydes and ketones to α,β-unsaturated carbonyl compounds *via* the Wadsworth-Horner-Emmons condensation.

Aside from the significant progress that expanded the Wadsworth-Horner-Emmons reaction,[1] synthetic routes[3] to 1-formylphosphonates are limited in terms

of hard rigorous conditions and low yields due to the competitive reactions. The common disadvantage of the reported methods is the necessity of the extraction step, in which a lot of 1-formylphosphonates are lost since they are water-soluble.

In the continuation of our work on the development of convenient synthetic routes[4] to β-carbonylphosphonates, we have reported such routes by the ring opening reactions of epoxysulfones and the reactions of α-phosphorylated carbanions with aryl nitrile, followed by hydrolysis.[5] These methods gave efficient and facile route to β-ketophosphonates, however, it had not been easy to prepare 1-formylalkanephosphonates *via* these methods, and therefore we have been interested in the synthesis of these compounds.

In this paper, we wish to report our results on a facile synthesis of 1-formylalkanephosphonates *via* 1-alkylation with subsequent ozonolysis of allylic phosphonates which are precursors of the butadiene moieties.[6]



Scheme

Lithium derivative **2** was allowed to react with alkyl halides. Nucleophilic addition of the allylic anion **2** *via* its 1-carbon atom occurred as a main reaction in good yields with traces of 3-alkylated adducts. When the electrophiles (R^2X) were more bulky, 3-alkylated adduct increased remarkably. When R^1=Me, the

alkylated product was only **3**. The structure of the products was unambiguously determined by NMR (^1H, ^{13}C) spectroscopy, as the phosphorus coupling constants of vinylic carbons for the α- or β-position differ by $\Delta J_{C\text{-}P}$= 180 Hz. The ratios of isomeric adducts formed by the addition of allylic anion **2** *via* the 1- or 3-carbon were calculated by the ^1H NMR integration.

Ozonolysis did not effected on phosphoryl group, but just converted olefin to corresponding carbonyl group. Moreover, this procedure required no extraction and therefore gave high yields.

Table Alkylation of allyl anionic phosphonates & Ozonolysis of 1-alkylated allylic phosphonates

Entry	R^1	R^2X	**3/4**[a]	yield (%) of **3/4**[b]	yield (%) of **5**[c]
a[d]	H	-	-	-	90
b	H	MeI	95/5	95	87
c	H	n-C_9H_{19}I	91/9	92	80
d	H		58/42	82	44
e	Me	$PhCH_2Br$	only A	93	90

[a] Determined on mixtures by ^1H NMR integration
[b] Total yields of **3** and **4** (**3** and **4** could not be separated by silica gel chromatography)
[c] Isolated yields of products from the mixture of **3** and **4**
[d] Allyl phosphonate

In conclusion, we have developed a facile synthesis of 1-formylalkanephosphonates *via* the ozonolysis of 1-alkylated allylphosphonates.

General Experimental Procedure

Alkylations of allylphosphonate: 1.35cc of 1.6M solution of *n*-Butyllithium in

hexane(2.2mmol) was added to a of 356mg of **1b**(2mmol) in THF at -78℃ under a positive pressure of nitrogen and the solution was stirred at this temperature for 1h. 0.14cc of methyl iodide bromide(2.2mmol) was added to the solution via syringe. After stirring for an additional 30 min at -78℃, the reaction mixture was allowed to warm to room temperature. After stirring for 2 h at room temperature, the reaction was quenched by the addition of 5ml saturated aqueous NH_4Cl and 365mg of the product (**3b**+**4b**) was obtained after extraction with diethyl ether (30 ml × 3), drying ($MgSO_4$), evaporation, and silica gel chromatography (using a mixture of ethyl acetate and hexane (4: 1) as an eluent).

Ozonolysis of 1-alkylated allylphosphonates: A stream of ozone was passed through a cold (-78℃), dichloromethane (8 ml) solution dissolving 192mg of the mixture of **3** and **4** until the distinctive blue color of ozone was observed. Ozone bubbling was then terminated. and the excess ozone was displaced by passing a stream of oxygen through the dichloromethane solution for 10 min. the solution was allowed to warm to room temperature, neat dimethyl sulfide (0.15cc,2 mmol) was added, and the solution was allowed to stir at refluxing dichloromethane. Concentration of the crude product, followed by silica gel column chromatography (using ethyl acetate as an eluent) provided 169mg of the 1-methyl-1-formyl-phosphonates (**5**).

1-Methylallylphosphonates(3a, 95%) **and 3-methylvinylphosphonates(4a,** 5%) : **^{1}H NMR** (300 MHz, $CDCl_3$) **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.66–6.84(m, 1H*5/100), 5.80-5.75(m, 1H*95/100), 5.70-5.51(m, 1H*5/100), 5.13-5.06(m, 2H*95/100), 4.06-

3.96(m, 4H), 2.57(dq, *J*=30.92, 7.37), 2.22-2.10(m, 2H*5/100), 1.27-1.17(m, 9H), 1.02-0.96(m, 3H*5/100) **^{13}C NMR** (75MHz, $CDCl_3$. Since the extent of **4a** was to small to show distinctive peaks on ^{13}C NMR spectra of the mixture of **3a** and **4a**, we could observe only the peaks of **3a**) δ 134.35(d, *J*=9.45), 116.86(d, *J*=28.20), 61.85(t, *J*=7.28), 36.32(d, *J*=138.3), 16.31(*J*=5.93), 13.09(d, *J*=6.00). **HRMS** cacld 192.0915 found 192.0915.

1-Formylphosphonates(5a) : **^{1}H NMR** (300 MHz, $CDCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.58-9.55(dt, 1H, *J*=3.22.1.08), 4.18-4.02(m, 4H), 3.00(dd, 2H, *J*=21, 3.28), 1.15-1.10(m, 6H) **^{13}C NMR** (75MHz, $CDCl_3$) δ 192.81(d, *J*=6.08), 62.53(d, *J*=6.45), 42.94(d, *J*=127.20), 16.16(d, *J*=6.00). **HRMS** cacld 180.0551 found 180.0546.

1-Methyl-1-formylphosphonates(5b) : **^{1}H NMR** (300MHz, $CDCl_3$) δ 9.70(dd, 1H, *J*=1.7, 0.7), 4.10-4.04(m, 4H), 3.03(dq, 1H, *J*=27.66, 7.00), 1.30(m, 6H), 1.30(t, 3H) **^{13}C NMR** (75MHz, $CDCl_3$) δ 196.38(d, *J*=3.9), 62.64(t, *J*=6.83), 47.44(d, *J*=128.33), 16.35(d, *J*=5.79), 7.67(d, *J*=5.33).

1-Nonyl-1-formylphosphonates(5c) : **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.61(d, 1H, *J*=3.07), 4.20-4.02(m, 4H), 3.01-2.83(m, 1H), 2.30-1.64(m, 4H), 1.39-1.20(m, 18H), 0.88-0.81(m, 3H) **^{13}C NMR** (75MHz, $CDCl_3$) δ 196.75(d, *J*=4.5), 62.62(dd, *J*=6.9, 2.63), 53.35(d, *J*=125.18), 31.83, 29.43, 29.25(d, *J*=3.68), 28.426, 28.248, 23.63(d, *J*=4.73), 22.631, 16.38(d, *J*=5.85), 16.36(d, *J*=5.85), 14.06. **HRMS** cacld 306.1960 found 306.1989.

1-Benzyl-1-formylphosphonates(5e) : **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.63(d, 1H, *J*= 1.85), 7.24-7.13(m, 5H), 4.16-4.04(m, 4H), 3.37-3.27(m, 1H), 3.10-3.00(m, 1H), 1.33-

1.21(m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.23(d, *J*= 4.7), 138.08(d, *J*= 13.88), 128.37, 128.29, 126.38, 62.63(dd, *J*= 6.67, 2.55), 54.78(d, *J*= 123.15), 29.17(d, *J*= 3.9), 16.22(d, *J*= 5.85) **^{13}C NMR** (75MHz, $CDCl_3$) δ 195.24(d, *J*=4.65), 138.10(d, *J*=13.88), 128.38, 128.29, 126.39, 62.64(dd, *J*=6.68, 2.55), 54.78(d, *J*=123.15), 29.17(d, *J*=3.90), 16.22(d, *J*=5.85). **HRMS** cacld 270.1021 found 270.0988.

REFERENCES

1. (a) Martin, S. F. *Synthesis*, **1979**, 633. (b) Nagata, W.; Hayase, Y. *J. Chem. Soc.* [C] **1969**, 460.
2. (a) Isbell, A. F.; Englert, L. F.; Rosenberg, H. *J. Org. Chem.*, **1969**, *34*, 755. (b) Fabre, G.; Collignon, N.; Savignac, P. *Can. J. Chem.*, **1981**, *59*, 2864. (c) Collignon, N.; Fabre, G.; Varlet, J. M.; Savignac, P. *Phosphorus Sulfur*, **1981**, 81.
3. (a) Aboujaoude, E. E.; Collignon, N.; Savignac, P. *Synthesis*, **1983**, 634. (b) Olah, G. A.; Ohannesian, L.; Arvanaghi, M. *J. Org. Chem.*, **1984**, *49*, 3856. (c) Coppola, G. M. *Synthesis*, **1984**, 1021. (d) Varlet, J. M.; Fabre, G.; Sauveur, F.; Collignon, N.; Savignac, P. *Tetrahedron*, **1981**, *37*, 1377.
4. (a) Hong, S.; Chang, K.; Ku, B.; Oh, D. Y. *Tetrahedron Lett.*, **1989**, *30*, 3307. (b) Lee, K.; Oh, D. Y. *Synthesis*, **1991**. 213.
5. Lee, K.; Oh, D. Y. *Synlett*, **1991**. 213.
   Lee, K.; Oh, D. Y. *Synth. Commun.*, **1991**, *21*, 279.
   Ko, Y. J.; Oh, D. Y. *Tetrahedron Lett.*, **1993**, *34*, 2147.
6. Kondo, K.; Negishi, A.; Tunemoto, D. *Angew. Chem.*, **1974**, *13*, 407.

Received 8 March 1999; revised 5 July 1999; accepted in Exeter 5 July 1999