

## A New Synthesis of Cyclic $\beta$ -Keto Phosphonates from $\alpha$ -Nitro Epoxides and a Dialkyl Phosphite

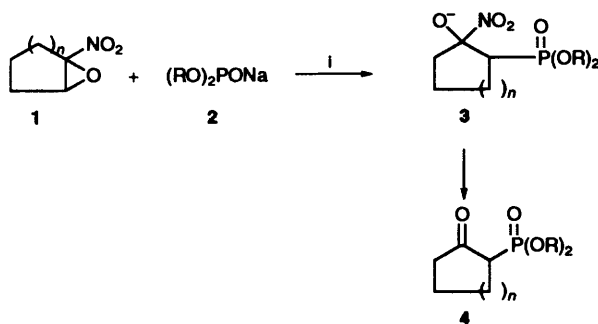
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Cyclic  $\beta$ -keto phosphonates are readily prepared in good yields by the reaction of a dialkyl phosphite anion and  $\alpha$ -nitro epoxides.

Both acyclic and cyclic  $\beta$ -keto phosphonates are commonly employed in the Wadsworth–Horner–Emmons condensation to prepare  $\alpha,\beta$ -unsaturated carbonyl compounds.<sup>1</sup> As a result of several syntheses,<sup>2</sup> the former were, until recently, more readily available from the latter. In preparing such compounds the Arbuzov reaction is limited to the use of highly reactive  $\alpha$ -halogeno ketones with trialkyl phosphites because of the poor nucleophilicity of the latter together with their tendency to undergo a Perkow reaction to give enol phosphates. Cyclic  $\beta$ -keto phosphonates have also been prepared by the reaction of  $\alpha$ -halogeno epoxides with triethyl phosphite in a lengthy and somewhat tedious procedure, by the reaction of ketone enolates with dialkyl phosphorochloridite, followed by aerial oxidation,<sup>4</sup> and *via* base-mediated rearrangement of the enol phosphates.<sup>5</sup>

In connection with our work on the additions of nitroalkenes, we recently reported a synthesis of 1-aryl-1-cyanomethylphosphonates<sup>6</sup> and 1-aryl-2-oxoalkylphosphonates.<sup>7</sup> Here, we report a new convenient synthesis of cyclic  $\beta$ -keto phosphonates **4** from the reaction of dialkyl phosphite anion **2**



Scheme 1 i, THF, room temp.

with  $\alpha$ -nitro epoxides **1** which function as a ketone equivalent with  $\alpha$ -cation reactivity. It is assumed that the dialkyl phosphite anion **2** attacks the carbon  $\beta$  to the nitro group regio-specifically and that this is followed by epoxide ring opening and elimination of nitrite. By this procedure, 2-(dialkoxyphosphinoyl)cycloalkanones **4** were prepared in good yields. The results are summarized in Table 1. The starting  $\alpha$ -nitro epoxides<sup>8</sup> **1** were easily prepared from alkenes *via* nitro alkenes.<sup>9</sup> This new route to cyclic  $\beta$ -keto phosphonates **4** has the advantages of good yields, mild reaction conditions and ready availability of  $\alpha$ -nitro epoxides as starting materials.

### Experimental

Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use. NMR spectra were recorded on a Bruker FT 80 spectrometer. Mass spectra were recorded with Hewlett Packard 5985A instrument operating at 70 eV. The  $\alpha$ -nitro epoxides **1** were prepared as reported previously.

Table 1 Preparation of the cyclic  $\beta$ -keto phosphonates **4**

Compd. <b>4</b>	<i>n</i>	R	Time (h)	Yield (%) <sup>a</sup>
<b>a</b>	1	Et	5	60
<b>b</b>	1	Bu	10	56
<b>c</b>	2	Me	2	80
<b>d</b>	2	Et	1.5	80
<b>e</b>	2	Bu	3	96
<b>f</b>	3	Bu	15	85

<sup>a</sup> Isolated yields are based on  $\alpha$ -nitro epoxides.

**General Experimental Procedure.**—2-(Diethoxyphosphinoyl)-cyclohexanone **4d**. To a stirred solution of the dialkyl phosphite (4.0 mmol) in THF (5 cm<sup>3</sup>) was added NaH (50%; 193 mg, 4.0 mmol) at room temperature. After 30 min, the  $\alpha$ -nitro epoxide **1** (2.0 mmol) in THF (5 cm<sup>3</sup>) was added to the reaction mixture which was then stirred at room temperature for 1.5 h. The resulting mixture was quenched with saturated aqueous NH<sub>4</sub>Cl and partitioned with diethyl ether (2 × 20 cm<sup>3</sup>). The organic layer was separated, dried (MgSO<sub>4</sub>) and evaporated to leave a crude oil. This was purified by flash chromatography (silica gel, 230–400 mesh) using ethyl acetate as eluent. Compound **4d** *R*<sub>F</sub> 0.45;  $\nu_{\max}/\text{cm}^{-1}$  2920, 1680, 1630, 1240 (P=O), 1010–1050 (P–O) and 950;  $\delta_{\text{H}}(\text{CDCl}_3, 80 \text{ MHz})$  1.32 (dt, 6 H, *J* 7.1, 1.0), 1.51–2.64 (m, 8 H), 2.97 (dt, 1 H, *J*<sub>PH</sub> 23.5, *J*<sub>HH</sub> 5.6) and 3.96–4.33 (m, 4 H); *m/z* (70 eV) 234 (*M*<sup>+</sup>, 7.2%), 138 (25), 111 (26) and 84 (100).

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### References

- (a) W. S. Wadsworth Jr. and W. D. Emmons, *J. Am. Chem. Soc.*, 1961, **83**, 1733; (b) H. Horner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano, *Chem. Ber.*, 1962, **95**, 581; (c) W. S. Wadsworth Jr., *Org. React. (N.Y.)*, 1977, **25**, 73; (d) W. C. Still and C. Gennari, *Tetrahedron Lett.*, 1983, **24**, 4405; (e) M. A. Blanchette, W. Choi, J. T. Davis, A. P. Essensfeld, S. Masamune, W. R. Roush and T. Sakai, *Tetrahedron Lett.*, 1984, **25**, 2183; (f) J. A. Mashall, B. S. DeHoff and D. G. Cleary, *J. Org. Chem.*, 1986, **51**, 1735.
- (a) P. Coutrot, P. Savignac and F. Mathay, *Synthesis*, 1978, 36; (b) M. Honda, T. Katsuki and M. Yamaguchi, *Tetrahedron Lett.*, 1984, **25**, 3857; (c) S. Hong, K. Chang, B. Ku and D. Y. Oh, *Tetrahedron Lett.*, 1989, **30**, 3307; (d) R. K. Bockman Jr., M. A. Walter and H. Koyano, *Tetrahedron Lett.*, 1989, **30**, 4787; (e) M. M. Kobat, *Tetrahedron Lett.*, 1993, **34**, 8543; (f) S. M. Ruder and V. R. Kulkarni, *Synthesis*, 1993, 945; (g) D. Y. Kim, J. Y. Mang and D. Y. Oh, *Synth. Commun.*, 1994, **24**, 629.
- C. Herzig and J. Gasteiger, *Chem. Ber.*, 1982, **115**, 601.
- K. Lee and D. F. Wiemer, *J. Org. Chem.*, 1991, **56**, 5556.
- (a) T. Calogeropoulou, G. B. Hammond and D. F. Wiemer, *J. Org. Chem.*, 1987, **52**, 4185; (b) K. B. Gloer, T. Calogeropoulou, J. A. Jackson and D. W. Wiemer, *J. Org. Chem.*, 1990, **55**, 2842.

6 D. Y. Kim and D. Y. Oh, *Synth. Commun.*, 1987, **17**, 953.

7 D. Y. Kim, K. Lee and D. Y. Oh, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2451.

8 H. Newman and R. B. Anger, *Tetrahedron*, 1970, **26**, 825.

9 (a) E. J. Corey and H. Estreicher, *J. Am. Chem. Soc.*, 1978, **100**, 6294; (b) E. J. Corey, H. Estreicher, *Tetrahedron Lett.*, 1980, **21**, 1113; (c) P. Dampawan and W. W. Jajac, Jr., *Tetrahedron Lett.*, 1982, **23**, 135; (d) T. Hayma, S. Tomata, Y. Yakeuchi and Y. Nomura, *Tetrahedron Lett.*, 1982, **23**, 4733; (e) A. G. M. Barrett

and G. Graboski, *Chem. Rev.*, 1986, **86**, 751; (f) J. R. Hwu, K. L. Chen and S. Ananthan, *J. Chem. Soc., Chem. Commun.*, 1994, 1425.

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