established methods,[13,14] to octane 2-diazotate (**1**). Alkylation with ethyl iodide in hexamethylphosphoric triamide (HMPA)[1] produced active **2**, $\alpha^{30}\mathrm{D}$ − 16.8°,[12,15] which was purified by distillation at 85–87° (2 Torr), followed by gas chromatography.[8] The distilled yield was ~50%, and the product was spectrally identical with authentic *d,l*-**2**.[1] Photothermal isomerization gave **3**, $\alpha^{30}\mathrm{D}$ −18.9°.[12,15,16] A second alkylation of **1** (from *l*-urethane of 83.5% optical purity) with Meerwein's reagent gave **2**, $\alpha^{30}\mathrm{D}$ −17.1°,[12,15,17] which was isomerized to **3**, $\alpha^{30}\mathrm{D}$ −19.4°.[12,15]

If the conversion of *l*-2-octylurethane, *via* diazotate **1** and azoxyalkane **2**, to azoxyalkane **3** were completely stereospecific, then $\alpha^{30}\mathrm{D}$ −19.15 ± 0.25° (neat, 1 dm) must represent optically pure (*R*)-**3**. Gratifyingly, (*S*)-(+)-2-chlorooctane (**4**), $\alpha^{25.5}\mathrm{D}$ +24.67°,[12] 78.2% optically pure,[18–20] reacted with ethane diazotate in HMPA (Scheme I) to give a 22% yield of (*R*)-**3**, $\alpha^{30}\mathrm{D}$ −15.09°.[12] This rotation, when corrected for the optical purity of the chloride, gives $\alpha^{30}\mathrm{D}$ −19.3°, *experimentally identical with the rotation obtained by* the **1** → **2** → **3** pathway.[22]

We conclude that the representative azoxyalkanes **2** and **3** can be prepared stereospecifically from easily available optically active precursors. Their facile photochemical interconversion makes each available by two synthetic sequences. Further, the stereochemical data prove that diazotate alkylation occurs by SN2 attack (complete inversion[20]) of the diazotate on the alkylating agent.

Synthesis of specific chiral azoxyalkanes is therefore eminently practical, and the present method is applicable to syntheses of the naturally occurring compounds.[23] Moreover, diazotate **1** affords **2** with no loss of optical activity, which demonstrates that the diazotate is configurationally stable to the conditions of its generation. This fact, which could only be assumed until now, bears importantly on mechanistic deamination chemistry related to **1**.[13,24]

Finally, the relatively high acidity of azoxymethane[25] gave concern that **2** and **3** might not be configurationally stable to the (basic) conditions of their formation. However, when either azoxyalkane was treated overnight with refluxing 3 *M* $NaOCH_3$–C_2H_5OD, only the α or α′ *methylene* protons and not the methine protons (at the chiral centers) appeared to exchange (nmr). Active **2** racemized only to the extent of ~5% after 1 hr under these vigorous conditions.

Acknowledgments. We thank the National Institutes of Health and the National Science Foundation for financial support.

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(14) R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966).

(15) Corrected for the optical purity of the urethane precursor.

(16) (a) CD data: (*R*)-**2** $[\theta]_{252}$ +2.12 × 10^3, $[\theta]_{230}$ −4.87 × 10^3; (*R*)-**3** $[\theta]_{275}$ −1.90 × 10^2, $[\theta]_{230}$ +2.69 × 10^3. Both samples were measured in ethanol; ellipticities are corrected to optical purity (see below). The data for (*R*)-**2** match those for (*R*)-*ONN*-1-cyclohexylazoxyethane.[16b] Note the "mirror image" CD behavior of (*R*)-**2** and (*R*)-**3**. (b) W. J. McGahren and M. P. Kunstmann, *J. Org. Chem.*, **37**, 902 (1972).

(17) We thank Dr. Andrew Mamantov for this experiment.

(18) Based upon $\alpha^{20}\mathrm{D}$ 31.6°: H. R. Hudson, *Synthesis*, **1**, 112 (1969), Table 5, note *c*; H. M. R. Hoffmann, *J. Chem. Soc.*, 1249 (1964).

(19) Chloride **4** was prepared from *l*-2-octanol, $\alpha^{25}\mathrm{D}$ −6.89°, 86% optically pure,[21] by the method of R. G. Weiss and E. I. Snyder, *Chem. Commun.*, 1358 (1968).

(20) 2-Octyl-X (X = NH_2, OH, Hal) of the same rotational sign are of the same optical series; see M. Vogel and J. D. Roberts, *J. Amer. Chem. Soc.*, **88**, 2262 (1966); J. A. Mills and W. Klyne, *Progr. Stereochem.*, 194 (1954). *Absolute* configurations drawn in this paper derive from these relations, and from absolute assignments for 2-aminobutane: A. Kjaer and S. E. Hansen, *Acta Chem. Scand.*, **11**, 898 (1957).

(21) Based upon $\alpha^{23}\mathrm{D}$ +8.04°: A. Streitwieser, Jr., and W. D. Schaeffer, *J. Amer. Chem. Soc.*, **78**, 5597 (1956).

(22) Alkylation of ethane diazotate with active **4**-Br or **4**-I gave (−)-**3** with 91 or 55%, respectively, of the maximum rotation, presumably because these 2-halooctanes are racemized by halide anions released *during* the slow diazotate alkylations: G. M. Love, unpublished.

(23) R. A. Moss and T. B. K. Lee, submitted for publication.

(24) R. A. Moss and K. M. Luchter, *J. Org. Chem.*, **37**, 1155 (1972); R. A. Moss, A. W. Fritz, and E. M. Emery, *ibid.*, **36**, 3881 (1971); R. A. Moss, D. W. Reger, and E. M. Emery, *J. Amer. Chem. Soc.*, **92**, 1366 (1970).

(25) M. H. Benn and P. Kazmaier, *J. Chem. Soc., Chem. Commun.*, 887 (1972).

(26) Fellow of the Alfred P. Sloan Foundation.

Robert A. Moss,*[26] George M. Love
Wright Laboratory, School of Chemistry
Rutgers University, The State University of New Jersey
New Brunswick, New Jersey 08903

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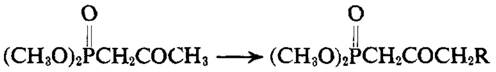
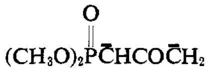
Alkylation of the Dianion of β-Keto Phosphonates. A Versatile Synthesis of Dimethyl (2-Oxoalkyl)phosphonates

Sir:

Recently we required a method to substitute a β-keto phosphonate ester at the γ carbon (eq 1). One method

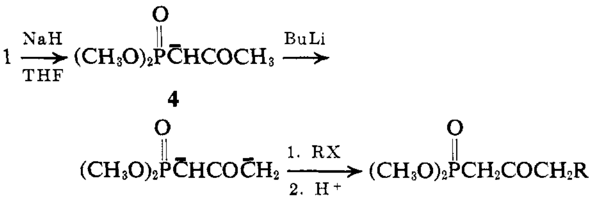


$$\underset{\mathbf{1}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2COCH_3} \longrightarrow \underset{\mathbf{2}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2COCH_2R} \qquad (1)$$



$$\underset{\mathbf{3}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}\bar{C}HCO\bar{C}H_2}$$

to bring about this transformation is to alkylate the γ carbon of the 1,3-dianion **3**. Monoanions derived from phosphonate esters which possess charge-stabilizing electron-withdrawing substituents (*e.g.*, carbonyl) have been extremely useful in the synthesis of certain olefins from aldehydes and ketones.[1] However, dianions of type **3** have not previously been generated.[2] We now report that such dianions can be generated and undergo specific alkylation at the γ carbon (eq 2).



$$1 \xrightarrow[\text{THF}]{\text{NaH}} \underset{\mathbf{4}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}\bar{C}HCOCH_3} \xrightarrow{\text{BuLi}}$$

$$\underset{\mathbf{3}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}\bar{C}HCO\bar{C}H_2} \xrightarrow[\text{2. } H^+]{\text{1. RX}} \underset{\mathbf{2}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2COCH_2R} \qquad (2)$$

Treatment of dimethyl 2-oxopropylphosphonate[3] (**1**) with sodium hydride in THF produced the insoluble monoanion **4**, and subsequent metalation of **4** with *n*-butyllithium generated the dianion **3**. When a solution of **3** in THF was treated with a variety of alkylating

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(1) L. Horner, H. Hoffmann, and H. G. Wippel, *Ber.*, **91**, 61 (1958); W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, **93**, 1733 (1961).

(2) (a) A recent report has demonstrated that β-keto phosphonium salts (*e.g.*, acetonyltriphenylphosphonium chloride) undergo a sequential twofold ionization with generation of a "1,3-dianion": J. D. Taylor and J. F. Wolf, *J. Chem. Soc., Chem. Commun.*, 876 (1972). (b) For a review on dianions of β-dicarbonyl compounds, see T. M. Harris and C. M. Harris, "Organic Reactions," Vol. 17, Wiley, 1969, p 155; also see, L. Weiler, *J. Amer. Chem. Soc.*, **92**, 6702 (1970).

(3) F. A. Cotton and R. A. Schunn, *ibid.*, **85**, 2394 (1963).

agents, including isopropyl iodide, a facile reaction occurred. The monoalkylated products were isolated in good yield (Table I). Yields have not been optimized.

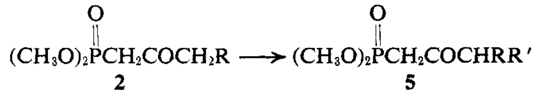
Table I. Alkylation of Dianion from $(CH_3O)_2P(=O)CH_2COCH_3$

R-X	Yield of 2,[a,b] %	Bp of 2, °C (P, mm)
CH_3I	71	68-70 (0.1)
$CH_3CH_2CH_2CH_2I$	70	88-89 (0.1)
$CH_3CH_2CH_2CH_2Br$	70	87-89 (0.1)
$(CH_3)_2CHI$	65	74-76 (0.07)
$CH_2{=}CHCH_2Br$	75	84-85 (0.1)
$C_6H_5CH_2Cl$	70	120-122 (0.5)

[a] All substances exhibited nmr, ir, and analytical data in accord with the assigned structures and were further identified by comparison with authentic samples prepared by alternate routes. [b] Yields refer to distilled products. Crude yields were on the order of 90%.

It was evident from the nmr spectra that alkylation occurred exclusively at the γ carbon. Furthermore, spectral analysis of the crude reaction mixture failed to give any evidence of alkylation at the α carbon, dialkylation, or O-alkylation. The nmr spectra of **2**[4] have a two proton doublet (J_{HP} = 23 Hz) at δ 3.13 due to the α-methylene protons. The absence of a three proton singlet at *ca.* δ 2.30 further indicated that alkylation occurred only on the γ carbon.

We have also alkylated γ-substituted β-keto alkylphosphonates (eq 3). Starting with dimethyl 2-oxopropylphosphonate (**1**), it is possible to generate the dianion **3**, alkylate with RX, generate the dianion of this alkylated product with an additional equivalent of *n*-butyllithium, and add a second alkylating agent (R′X) to yield **5**; for example, phosphonate **5** (R = *n*-Bu, R′ = benzyl) could be obtained in low yield from **1** in this manner. One can, however, obtain high yields of **5** if the monoalkylated product **2** was isolated and purified before proceeding with the second alkylation (Table II).



$$\underset{\mathbf{2}}{\mathrm{(CH_3O)_2\overset{\underset{\|}{O}}{P}CH_2COCH_2R}} \longrightarrow \underset{\mathbf{5}}{\mathrm{(CH_3O)_2\overset{\underset{\|}{O}}{P}CH_2COCHRR'}} \qquad (3)$$

Table II. Alkylation of Dianion from Dimethyl 2-Oxoheptylphosphonate

R-X	Yield of 5,[a,b] %
CH_3I	71
$CH_3CH_2CH_2CH_2I$	73
$CH_2{=}CHCH_2Br$	70
$C_6H_5CH_2Cl$	67

[a] Yields refer to pure product after purification on silica gel. [b] All substances exhibited nmr, ir, and analytical data in accord with the assigned structures.

The following procedure for the preparation of dimethyl 2-oxoheptylphosphonate (**2**) (R = *n*-Bu) is representative. A dry 100-ml flask equipped with septum inlet and magnetic stirrer containing 0.44 g of sodium hydride (57%, washed with hexane to remove mineral oil) was flushed with nitrogen and maintained under a positive pressure of nitrogen. Approximately 25 ml of freshly distilled anhydrous THF was added followed by the dropwise addition (*via* syringe) of dimethyl 2-oxopropylphosphonate (10 mmol, 1.7 g). The reaction mixture was stirred at room temperature for 1.5 hr to allow for formation of the monoanion (white precipitate). Then, 11 mmol (6.6 ml of 1.66 *M*) of *n*-butyllithium in hexane was added dropwise (0°) and the resultant solution was stirred for 20 min. The white precipitate of the monoanion disappeared immediately upon addition of the *n*-butyllithium. Butyl iodide (12 mmol, 2.2 g) was added (0°) and the reaction mixture was stirred at room temperature for 30 min. The reaction was quenched by the addition of 5% aqueous HCl and the product was isolated by extraction with chloroform. After drying the combined organic extracts, the solvents were removed under reduced pressure and the crude product was distilled to yield 1.6 g (70%) of dimethyl 2-oxoheptylphosphonate which was identical (nmr, ir, ms, glc) with an authentic sample.

The specific alkylation at γ carbon of **1** *via* dianion **3** makes dimethyl 2-oxopropylphosphonate a useful reagent in organic synthesis and provides a general high-yield synthesis of β-keto phosphonates for use in the Horner–Emmons modification of the Wittig olefin synthesis. The preparation of dimethyl 2-oxoheptylphosphonate (**2**)[5] (R = *n*-Bu) as illustrated above provides a new route to a key prostaglandin reagent.[6] Furthermore the reaction sequence allows for eventual modification of the alkyl portion of the C_8 side chain found in prostaglandins.

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(4) The nmr spectrum of dimethyl 2-oxopropylphosphonate has the following signals: δ ($CDCl_3$) 2.30 (s, 3 H, COMe), 3.00 (d, 2 H, J_{HP} = 23 Hz, PCH_2), 3.72 [d, 6 H, J_{HP} = 11 Hz, $(MeO)_2PO$].

(5) Previously prepared from ethyl hexanoate and dimethyl α-lithiomethanephosphonate: E. J. Corey and G. T. Kwiatkowski, *J. Amer. Chem. Soc.*, **88**, 5654 (1966). The preparation of **2** (R = *n*-Bu) and similar keto phosphonates is usually impractical by the Michaelis–Arbusov reaction: B. A. Arbusov, *Pure Appl. Chem.*, **9**, 307 (1964).

(6) For some recent uses of **2** (R = *n*-Bu) in prostaglandin synthesis, see E. J. Corey, S. M. Albonico, U. Koelliker, T. K. Schaaf, and R. K. Varma, *J. Amer. Chem. Soc.*, **93**, 1491 (1971); E. J. Corey and P. A. Grieco, *Tetrahedron Lett.*, 107 (1972); P. Crabbé and A. Guzmán, *ibid.*, 115 (1972); H. L. Slates, Z. S. Zelowski, D. Taub, and N. L. Wendler, *J. Chem. Soc., Chem. Commun.*, 304 (1972).

Paul A. Grieco,* C. S. Pogonowski
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15213

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Photochemical Formation of Oxazolidines from Aryl Ketones and Aliphatic Imines

Sir:

As part of a broadly based study of the interaction between electronically excited reagents and nitrogen-containing systems,[1] we have investigated the photochemical reaction of aryl ketones with aliphatic Schiff bases. Here we report the novel, synthetically useful formation of substituted oxazolidines from irradiation

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(1) A. A. Baum, L. A. Karnischky, D. McLeod, Jr., and P. H. Kasai, *J. Amer. Chem. Soc.*, **95**, 617 (1973).