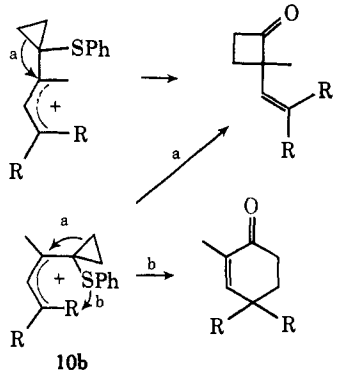
ment generated the cyclobutanones **8** and **9** demonstrating the feasibility of the spiroannelation of conjugated ketones. The cyclobutanone structures are firmly established spectroscopically by the presence of the carbonyl frequency at 1779 and 1776 cm^{-1} and the presence of the methylene group α to the carbonyl group in the nmr spectrum at approximately 2.9–3.1 as an apparent triplet ($J \sim 9$ Hz). Interestingly, in the case of **4**, rearrangement may be envisioned to give either a cyclobutanone or a cyclohexenone—the latter to the extent that a cisoid allyl cation **10b** is formed. The fact that only cyclobutanone can be seen in the infrared spectrum of a crude mixture is indicative of either the exclusive formation of the transoid allyl cation **10a** or high preference for a 1,2 shift compared



10b

to a 1,4 shift. Thus, the method nicely complements the sulfonium ylide technique and allows spiroannelation for virtually every type of carbonyl compound.[9,9a]

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(9) For related use of sulfide stabilized anions as sulfur ylide substitutes, see T. Durst, R. Viaw, R. Van Den Elzen, and C, H. Nguyen, *Chem. Commun.*, 1334 (1971); T. Durst, R. Viaw, and M. R. McCloy, *J. Amer. Chem. Soc.*, **93**, 3077 (1971); C. R. Johnson and C. W. Schroek, *ibid.*, **93**, 5303 (1971); M. Yashimini and M. J. Hatch, *ibid.*, **89**, 5831 (1967).

(9a) NOTE ADDED IN PROOF. A recent report describes the generation and rearrangement of cyclopropylallyl cations in which cyclobutyl derivatives were not found; see K. Rajeswari and T. S. Sorensen, *J. Amer. Chem. Soc.*, **95**, 1239 (1973).

(10) Camille and Henry Dreyfus Teacher–Scholar Grant Recipient.

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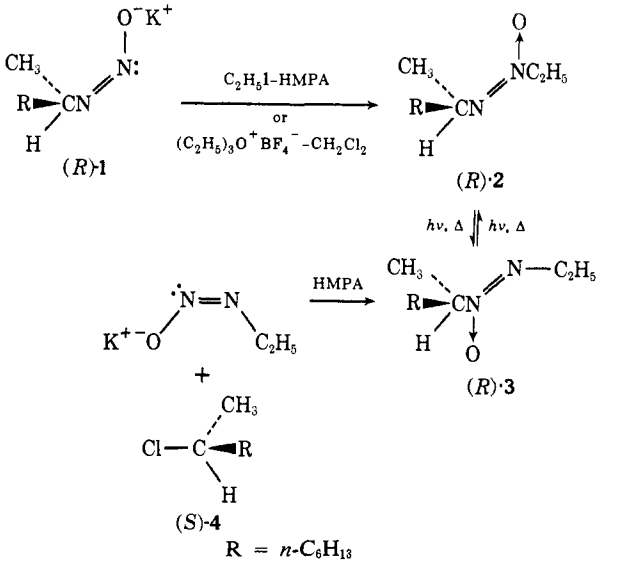
Stereospecific Synthesis of Azoxyalkanes[1]

Sir:

Successful synthesis of the naturally occurring and biologically potent chiral azoxyalkanes elaiomycin[2] and LL-BH872α[3] will probably require a novel method of construction of the azoxy functionality.[4] The alkylation of alkane diazotates[1,5] could be that method. It is flexible, or applicable to the synthesis of many unsymmetrical azoxyalkanes, directed, affording one structurally predictable azoxyalkane, and utilizes common precursors.[1]

Now we show that this method satisfies the final basic requirement for a general synthesis; it accommodates chirality at the carbon atoms α or α' to the azoxy function. We report the first *stereospecific* syntheses of such azoxyalkanes, by *two* independent, albeit related methods. The basic reactions are outlined in Scheme I, in which the key step is the "photo-

Scheme I



thermal" interconversion[6] of isomeric azoxyalkanes **2** and **3**.

Irradiation of *d,l*-**2**[1] in hexane at 254 nm gave a photostationary mixture of **3** and **2** (1.28:1 by gc). The **3**:**2** distribution did not change upon extended photolysis,[7] and the same distribution was obtained by photolysis of **3**. The new azoxyalkane, **3**, was isolated by gas chromatography.[8] It showed characteristic[9] ir bands at 1490 and 1290 cm^{-1} (neat) and λ_{max} 218 nm (log ϵ 3.82) and 285 (1.89) indicative of a *trans*-azoxyalkane.[6,9] The nmr (CCl_4) revealed a quartet, δ 3.39 (J = 7 Hz, 2 H), for $=NCH_2-$, and a multiplet centered at δ 4.23 (1 H) for $=N(O)CH<$. The remaining protons appeared as a multiplet from $\sim$2.0 to 0.6. The chemical shifts of the methylene and methine protons are consistent with structure **3**,[1,10] particularly in comparison with those of *sec*-$C_4H_9N(O)=N$-*n*-C_8H_{17}.[1] A satisfactory elemental analysis was obtained.

l-2-Aminooctane[11] was converted to the *l*-urethane, $\alpha^{25}D$ −3.25°,[12] 72.6% optically pure,[13] and thence, by

(1) Alkyl Diazotates. XII. Part XI: R. A. Moss, M. J. Landon, K. M. Luchter, and A. Mamantov, *J. Amer. Chem. Soc.*, **94**, 4392 (1972).

(2) C. L. Stevens, B. T. Gillis, and T. H. Haskell, *ibid.*, **81**, 1435 (1959), and references therein.

(3) W. J. McGahren and M. P. Kunstmann, *ibid.*, **92**, 1587 (1970); **91**, 2808 (1969).

(4) Discussions of the inadequacy of older synthetic methods and of the biological properties of azoxyalkanes appear in ref 1.

(5) R. A. Moss and M. J. Landon, *Tetrahedron Lett.*, 3897 (1969).

(6) K. G. Taylor and T. Riehl, *J. Amer. Chem. Soc.*, **94**, 250 (1972); J. Swigert and K. G. Taylor, *ibid.*, **93**, 7337 (1971).

(7) However, leakage to several unidentified minor products (total $\sim$30%) did occur.

(8) 10 ft × 0.25 in., 10% TCEP on 40/60 Gas-Chrom R, at 163°.

(9) B. W. Langley, B. Lythgoe, and L. S. Rayner, *J. Chem. Soc.*, 4191 (1952).

(10) J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963); B. Korsch and N. V. Riggs, *Tetrahedron Lett.*, 523 (1964); F. D. Greene and S. S. Hecht, *J. Org. Chem.*, **35**, 2482 (1970).

(11) F. G. Mann and J. W. G. Porter, *J. Chem. Soc.*, 456 (1944).

(12) Rotations reported in this paper were determined on gc-purified samples, in a 0.1-dm cell as *neat* liquids, using a Perkin-Elmer Model 141 spectropolarimeter. Experimental and literature values are *corrected* to l = 1 dm.

(13) Based upon $\alpha^{23}D$ −4.48°: R. A. Moss and S. M. Lane, *J. Amer. Chem. Soc.*, **89**, 5655 (1967).

established methods,[13,14] to octane 2-diazotate (**1**). Alkylation with ethyl iodide in hexamethylphosphoric triamide (HMPA)[1] produced active **2**, $\alpha^{30}D$ − 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**, $\alpha^{30}D$ −18.9°.[12,15,16] A second alkylation of **1** (from *l*-urethane of 83.5% optical purity) with Meerwein's reagent gave **2**, $\alpha^{30}D$ −17.1°,[12,15,17] which was isomerized to **3**, $\alpha^{30}D$ −19.4°.[12,15]

If the conversion of *l*-2-octylurethane, *via* diazotate **1** and azoxyalkane **2**, to azoxyalkane **3** were completely stereospecific, then $\alpha^{30}D$ −19.15 ± 0.25° (neat, 1 dm) must represent optically pure (*R*)-**3**. Gratifyingly, (*S*)-(+)-2-chlorooctane (**4**), $\alpha^{25.5}D$ +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**, $\alpha^{30}D$ −15.09°.[12] This rotation, when corrected for the optical purity of the chloride, gives $\alpha^{30}D$ −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.

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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 $\alpha^{20}D$ 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, $\alpha^{25}D$ −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 $\alpha^{23}D$ +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).

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

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

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

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).

$$1 \xrightarrow[THF]{NaH} (CH_3O)_2\overset{O}{\overset{\|}{P}}CHCOCH_3 \xrightarrow{BuLi}$$
4

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

(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).