other hand, treatment of salt **1** with lithium (*R*)-(−)-2,2,2-trifluorophenylethoxide in 1:1 (*R*)-(−)-2,2,2-trifluorophenylethanol[8]–pentane at −10° led to thioether **3** in 54% yield with $[\alpha]^{25}D$ −1.45 ± 0.12° (*c* 4.12, $CHCl_3$). Use of (*S*)-(+)-alcoholate in its corresponding alcohol under the same conditions generated thioether **2** with $[\alpha[^{25}D$ +1.12 ± 0.54° (*c* 5.56, $CHCl_3$). To evaluate the optical purity of the thioethers, use of the chiral shift reagent tris[(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium[9] [henceforth abbreviated $Eu(CFP)_3$] was made. While separation of the signals for the *S*-CH_3 groups in the enantiomers could be achieved, cleaner results were obtained by oxidizing the thioether to the sulfone **4** (mp 38.5–40°) in 99% yield with *m*-chloroperbenzoic acid in ether at 0°. By addition of 21.7 mol % of $Eu(CFP)_3$ to a $CDCl_3$ solution of the racemic thioether, the CH_3SO_2 signal shifts from δ 2.74 to two singlets of equal intensity at 3.74 and 3.82. Treatment of the thioether of $[\alpha]^{25}D$ −1.45° in this way generated the corresponding sulfone, $[\alpha]^{25}_{365}$ −3.48 ± 0.18° (*c* 1.09, $CHCl_3$), in which the nmr spectrum showed a 5 ± 1% difference in the peak heights (average of 11 values) with the methyl singlet at highest field being the larger.

The use of optically active 1,4-bis(dimethylamino)-2,3-dimethoxybutane as solvent has been shown to enhance the optical yields in organometallic additions.[10] Rearrangement of the salt **2** with lithium (*S*)-(+)-2,2,2-trifluorophenylethoxide in a 1:1 mixture of dry tetrahydrofuran and (*S,S*)-(+)-1,4-bis(dimethylamino)-2,3-dimethoxybutane under nitrogen at −20° generated thioether **3** in 48% yield with $[\alpha]^{25}_{365}$ +2.90 ± 0.30° (*c* 0.62, $CHCl_3$). Oxidation with *m*-chloroperbenzoic acid as above gave the sulfone of $[\alpha]^{20}_{365}$ +6.33 ± 0.70° (*c* 1.43, $CHCl_3$) whose nmr spectrum in the presence of $Eu(CFP)_3$ indicated an enantiomeric purity of 12 ± 2% (average of 22 values) in which the downfield CH_3SO_2 singlet was the more intense. The net optical yield observed represents the optical yields for proton abstraction and ylide rearrangement.

In a related case, the [2,3] sigmatropic rearrangement has been found to proceed with >94% optical induction.[11] This observation suggests that in the present case the optical induction observed represents the preference in the proton abstraction step. The unusually high optical yields for such a process in this simple base system would clearly support a contention that in the highly asymmetric environment of an enzyme system such a process would exhibit complete optical induction. The demonstration that a great deal of the stereochemical control is inherent in the chemistry of such systems suggests more serious attention should be given to the hypothesis of Scheme I as a possible biogenetic model.

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(11) B. M. Trost and R. F. Hammen, *J. Amer. Chem. Soc.*, **95**, 962 (1973). For related work, see J. E. Baldwin and J. E. Patrick, *ibid.*, **93**, 3556 (1971); V. Rautenstrauch, *Chem. Commun.*, 4 (1970); R. K. Hill and T. H. Chan, *J. Amer. Chem. Soc.*, **88**, 866 (1966).

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Rearrangement of Pyruvates to Malonates. β-Lactams by Ring Contraction

Summary: Periodate treatment of α-keto-γ-lactams results in rearrangement with ring contraction to β-lactams.

Sir: Numerous methods for the synthesis of β-lactams by ring closure or ring expansion have been developed,[1] but there are very few methods using ring contraction.[2] We have found that the oxidative rearrangement of α-ketoacyl derivatives with periodate, which has been reported for both acyclic and cyclic α-keto esters and amides,[3] appears to be generally extensible to the synthesis of β-lactams by oxidative ring contraction of α-keto-γ-lactams.

For example, the monocyclic α-ketolactam, 1-methyl-2,3-pyrrolidinedione (**2**), rearranges to 3-carboxy-1-methyl-2-azetidinone (**3**). The bicyclic compounds, **5a–c**, rearrange to bicyclic β-lactams, **6a–c**. When the β substituent, R_1 in **5**, is hydrogen or methyl, only one of the two possible isomers is obtained; however, when R_1 is bromine, both isomers are formed. The synthesis and rearrangement of these α-ketolactams, **2** and **5a–c**,[4] are presented below.

4-Ethoxycarbonyl-1-methyl-2,3-pyrrolidinedione (**1**),[5] heated in refluxing 2.9 *M* HCl (50 min), followed by extraction[6] and sublimation, gave 1-methyl-2,3-pyrrolidinedione (**2**, 63%, mp 89–91°). Reaction of **2** with periodate (pH 7.0, 24 hr), followed by destruction of excess periodate with bisulfite, extraction at pH 4.0, and chromatography on silica gel, gave 3-carboxy-1-methyl-2-azetidinone (**3**, 30%), ir 1745 (br) cm^{-1}.

1-Azabicyclo[4.3.0]nonane-8,9-dione (**5a**, 60%, mp 62–66°) was obtained from 7-ethoxycarbonyl-1-azabicyclo[3.2.0]nonane-8,9-dione (**4a**),[7] by an analogous

(1) Summarized in M. S. Manhas and A. K. Bose, "beta-Lactams: Natural and Synthetic," part 1, Wiley-Interscience, New York, N. Y., 1971.

(2) (a) S. N. Ege, *Chem. Commun.*, 759 (1968); (b) M. F. Chasle and A. Foucaud, *C. R. Acad. Sci., Ser. C*, **268**, 2034 (1969); (c) G. Lowe and D. D. Ridley, *Chem. Commun.*, 328 (1973).

(3) M. L. Rueppel and H. Rapoport, *J. Amer. Chem. Soc.*, **94**, 3877 (1972).

(4) All new compounds have been characterized spectrally (ir in $CHCl_3$ and nmr in $CDCl_3$). Elemental compositions were established by combustion analyses and mass spectra.

(5) P. L. Southwick, E. P. Previc, J. Casanova, Jr., and E. H. Carlson, *J. Org. Chem.*, **21**, 1087 (1956).

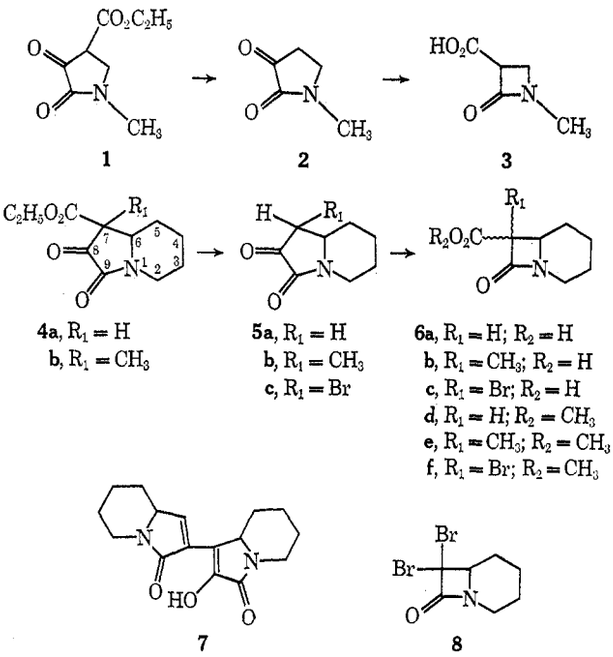
(6) Owing to high water solubility, most of the reported compounds were isolated from aqueous solution by continuous extraction with methylene chloride.

(7) R. Adams, S. Miyano, and M. D. Nair, *J. Amer. Chem. Soc.*, **83**, 3323 (1961).

procedure (reflux time 2.5 hr). Chromatographing **5a** on silica with $CHCl_3$ resulted in self-condensation to **7** [mp 219–224° dec; nmr δ 0.8–2.5 (m, 12 H), 2.6–3.2 (m, 2 H), 3.7–4.5 (m, 4 H), 6.59 (d, J = 2.2 Hz, 1 H), 12.9 (s, 1 H); uv (C_2H_5OH) 249 nm (ε 12,300), 297 (14,200)], a facile self-condensation also observed with other α-keto-γ-lactams.[5] Reaction of **5a** with excess periodate in lithium phosphate buffer (pH 6.3) was complete in 20 min, determined by the decrease in absorbance at 223 nm, and crystallization (acetone–hexane) of the extracted product gave 7-carboxy-8-oxo-1-azabicyclo[4.2.0]octane (**6a**): 70%; mp 145–146°; nmr δ 1.1–2.3 (m, 6 H), 2.5–3.1 (m, 1 H), 3.5–4.1 (m, 2 H), 3.75 (d, J = 1.8 Hz, 1 H), 9.2 (s, 1 H); ir 1753, 1722 cm^{-1}.[8] The 1.8-Hz coupling constant establishes the C-6 and C-7 protons as trans;[9] no evidence for any cis isomer was found. Esterification of **6a** with diazomethane gave **6d** and gas chromatography[10] of this ester gave a single symmetrical peak.

7-Ethoxycarbonyl-7-methyl-1-azabicyclo[4.3.0]nonane-8,9-dione (**4b**, mp 92–93°), obtained[11] in 30% yield by refluxing for 18 hr a benzene solution of diethyl 3-methyl-2-oxosuccinate[12] with an ether–ethanol solution of 2 molar equiv of 1-piperidiene,[13] was hydrolyzed and decarboxylated as described for the synthesis of **2** (reflux time 1.5 hr), resulting in 7-methyl-1-azabicyclo[4.3.0]nonane-8,9-dione (**5b**, 74%, mp 191–193°). Reaction of **5b** with periodate gave 7-carboxyl-7-methyl-8-oxo-1-azabicyclo[4.2.0]octane (**6b**): 50%; mp 179–181°; ir 1743, 1713 cm^{-1}; nmr δ 1.2–2.1 (m, 6 H), 1.52 (s, 3 H), 2.5–3.0 (m, 1 H), 3.6–4.0 (m, 2 H), 10.6 (s, 1 H). Gas chromatography of **6e** methyl ester (ir 1756, 1725 cm^{-1}), obtained from **6b** with diazomethane, gave a singly symmetrical peak.[10]

The bromo analog, 7-bromo-1-azabicyclo[4.3.0]-nonane-8,9-dione (**5c**, mp 121–122° from chloroform–hexane), obtained in 80% yield from **5a** by reaction with cupric bromide in methylene chloride and treated with periodate as previously described, gave a 40% yield of 7-bromo-7-carboxy-8-oxo-1-azabicyclo[4.2.0]-octane (**6c**) as a mixture of stereoisomers. Gas chromatography[10] of **6f** methyl esters (obtained from **6c** with diazomethane) indicated the presence of two isomers in the ratio of 1:9. Also present were products subsequently shown to arise from decomposition of the minor isomer of **6f** during gas chromatography; no decomposition of the major isomer took place. Column chromatography on kieselgel with 3:1 ether–petroleum ether (bp 30–60°) permitted establishing the structures of the two major decomposition products as 7,7-dibromo-8-oxo-1-azabicyclo[4.2.0]octane (**8**) [mp 73–74°; nmr δ 1.2–2.3 (m, 6 H), 2.5–3.1 (m, 1 H), 3.5–4.0 (m, 2 H); ir 1782 cm^{-1}] and **6d**. The two isomers



of **6f**, separated by column chromatography on kieselgel with 3:1 ether–petroleum ether, were hydrolyzed to the respective acids **6c** with 1 equiv of potassium hydroxide in 50% aqueous dioxane (room temperature, overnight). The major isomer had double mp 97 and 119–120°; nmr δ 1.2–2.2 (m, 6 H), 2.6–3.1 (m, 1 H), 3.6–4.1 (m, 2 H); ir 1772, 1724 cm^{-1}. The minor isomer had mp 180–182°; nmr δ 1.1–2.3 (m, 6 H), 2.6–3.1 (m, 1 H), 3.6–4.1 (m, 2 H); ir 1777, 1719 cm^{-1}.

Formation of β-lactams by this oxidative ring contraction reaction thus proceeds under mild conditions and appears to be generally applicable. The method provides a route for introduction of difunctionality at the α position of the β-lactam and is compatible with the presence of a number of substituents. Its scope is being further investigated.

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(8) Both the cis and trans isomers of the ethyl and *tert*-butyl esters of **6a** have been synthesized by a different method: G. Lowe and J. Parker, *Chem. Commun.*, 577 (1971).

(9) H. B. Kagan, J. J. Basselier, and J. L. Luche, *Tetrahedron Lett.*, 941 (1964); K. D. Barrow and T. M. Spotswood, *ibid.*, 3325 (1965).

(10) Chromatography was carried out on a 5 ft × 0.25 in. column of 5% QF-1 on Chromosorb W (80–100), AW-DMCS, at 175° and a He flow rate of 132 ml/min: T_R of **6e** = 3.9 min; T_R of **6d** = 4.3 min; T_R of **6f** (major) = 7.1 min; T_R of **6f** (minor) = 8.1 min.

(11) Based on the method used for the synthesis of 6-ethoxycarbonyl-1-azabicyclo[3.3.0]octane-7,8-dione: B. M. Goldschmidt, *J. Org. Chem.*, **27**, 4057 (1962).

(12) C. Clerc-Bory and C. Mentzer, *Bull. Soc. Chim. Fr.*, 436 (1958).

(13) Prepared by following the procedure used for the synthesis of 1-pyrroline: D. W. Fuhlhage and C. A. Van der Werf, *J. Amer. Chem. Soc.*, **80**, 6249 (1958).

A Versatile Prostaglandin Synthesis. Use of a Carboxy-Inversion Reaction

Summary: Ring contraction of the dione **5** gave the cyclopentenone **6** which was readily elaborated to the mixed peranhydride **17**; the latter then is transformed *via* a carboxy inversion reaction to **18**, a known precursor leading to the racemic prostaglandins E_2 and $F_{2\alpha}$.

Sir: By elimination of the hydroxyl group at the C-11 position in PGE_1 or PGE_2 to give either the PGA or 11-deoxy derivatives, the effects associated with the PGE compounds, *e.g.*, smooth muscle and antilipolytic properties, have been lost whereas the effect on blood