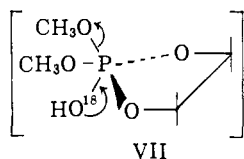


postulated in the hydrolysis of the cyclic triesters to the cyclic diesters, should also collapse with preservation of the five-membered ring.

It was shown that no oxygen from the water was incorporated into the carbonyl function of the ester I. These conclusions are based on mass spectrometry of the intact ester.



In discussing the behavior of phosphorus esters, Westheimer and co-workers³ have recently stressed the possible effect on phosphate stability of p-d double bonding between the ester oxygens and the phosphorus atom. They point out that resistance of a ring to this double bonding should result in lower stabilization for cyclic phosphates than for open chain phosphates. A difference in stability among phosphates, for this or for other reasons, may be, at least partly, responsible for the behavior of our cyclic and open-chain phosphotriesters toward water in aprotic solvents. It may be possible to hydrate the phosphoryl group of the less stable cyclic ester but not that of the more stable open chain esters.

Benzene solutions of the cyclic triesters I and III were treated with one mole equivalent of water at 20°; stirring was continued for about 5 min. in the former and 90 min. in the latter case (to disappearance of turbidity). Removal of solvent and of methanol left residues which were triturated with ether and then recrystallized.

The diketol triester I has been described.⁵ The ketal triester III had m.p. 89–90° (hexane); infrared (CCl₄, μ) PO at 7.70, POC– at 9.43 and 9.56, no OH or CO; H¹ n.m.r. (CDCl₃, τ) doublet CH₃OP at 6.16, J_{HP} 12.3 c.p.s., one singlet CH₃O–C– at 6.73, one CH₃–C– at 8.56, the other at 8.64; intensities: 1:1:4:4:4. *Anal.* Calcd. for C₁₁H₂₁O₇P: C, 44.6; H, 7.2; P, 10.5. Found: C, 44.2; H, 7.2; P, 11.1.

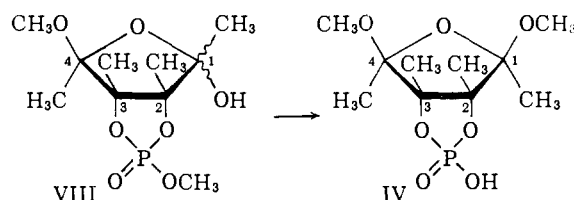
Diketol diester II had m.p. 138–140° (ethyl acetate-hexane); infrared (CHCl₃, μ) broad P(O)OH with minimum at 3.7, CO at 5.85, PO at 7.97, POC– at 9.77. *Anal.* Calcd. for C₈H₁₃O₆P: C, 40.6; H, 5.5; P, 13.2; mol. wt., 236. Found: C, 40.4; H, 5.5; P, 13.3; neut. equiv., 224.

The cyclohexylammonium salt had m.p. 179–180° (CH₂Cl₂-ether); CO at 5.85 and 5.88 μ (CH₂Cl₂). *Anal.* Calcd. for C₁₄H₂₆O₆NP: C, 50.2; H, 7.8; N, 4.2. Found: C, 50.3; H, 7.9; N, 3.9.

Ketal diester IV had m.p. 115–116° (acetonitrile); infrared (CCl₄, μ) broad P(O)OH with minimum at 3.8, PO at 8.00, POC– at 9.71, and no CO; H¹ n.m.r. (CDCl₃, τ) acidic H¹ at –2.57, one singlet CH₃OC– at 6.73, one CH₃–C– at 8.60, the other at 8.63. *Anal.* Calcd. for C₁₀H₁₆O₇P: C, 42.6; H, 6.7; P, 11.0. Found: C, 42.6; H, 6.7; P, 11.3. Cyclohexylammonium salt had m.p. 189–191° (CH₂Cl₂-ether); no CO in infrared. *Anal.* Calcd. for C₁₆H₃₂O₇NP: C, 50.4; H, 8.5; N, 3.7; P, 8.1. Found: C, 50.7; H, 9.1; N, 3.8; P, 8.3.

The preparation of the ketal phosphodiester IV is of intrinsic interest. IV was obtained when a solution of the hemiketal phosphotriester⁵ VIII in anhydrous acetonitrile was kept several hours at 20°. This is a new type of molecular rearrangement of a furanose-2,3-cyclic phosphate in which the C-1-hydroxyl group exchanges places with the methoxyl group attached to

the phosphorus. The details of this rearrangement are being investigated.



Treatment of the diester IV with diazomethane provided the triester III used in the hydrolysis experiments.

Acknowledgment.—The authors gratefully acknowledge the cooperation and advice of Professor E. Eliel (University of Notre Dame) in proton n.m.r. spectroscopy. They appreciate the opportunity of examining the manuscripts of Kaiser, Panar, and Westheimer^{2c} and of Covitz and Westheimer³ before publication.

(6) Alfred P. Sloan Fellow, 1961–1963.

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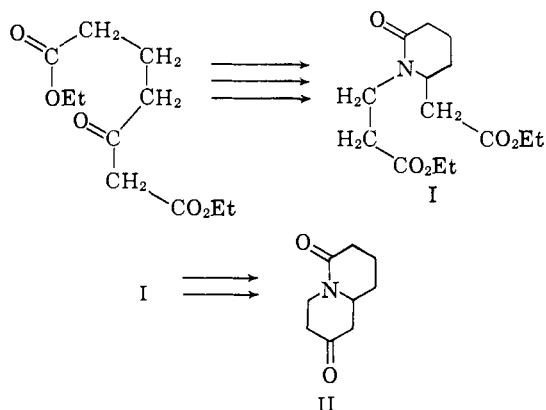
RECEIVED JUNE 14, 1963

Total Synthesis of *d,l*-Matrine

Sir:

We wish to report the application of our quinolizidine synthesis^{1,2} to the total synthesis of *d,l*-matrine (IV) the principal alkaloid of *Sophora flavescens* Ait. The stereochemistry and structure of matrine have been put forth by several groups of workers.^{3–5}

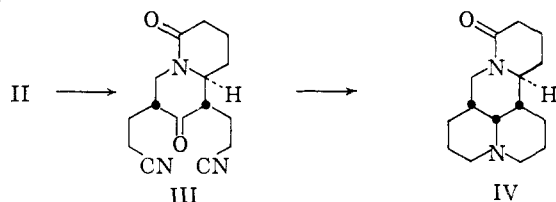
Diethyl-3-oxo-pimalate⁶ was condensed with the ethyl ester of β -alanine by refluxing a mixture of the two (0.27 mole of diester to 0.29 mole of β -alanine ester) in benzene and removing the water formed *via* azeotropic distillation. The solvent was removed *in vacuo* and



the crude product was reduced with Adams catalyst at 2000 p.s.i. in ethanol solution containing several drops of acetic acid. The crude reduction product obtained after removing the solvent was heated *in vacuo* at steam-bath temperature for 6 hr. to effect lactamization. Distillation afforded I (65% over-all yield), b.p.

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- (3) F. Bohlman, W. Weise, D. Raktze, and C. Arndt, *Ber.*, **91**, 2167, 2177 (1958).
- (4) K. Tsuda, *et al.*, *ibid.*, **69**, 429 (1936); *J. Org. Chem.*, **21**, 1481 (1956).
- (5) E. Ochai, S. Okuda, and H. Minato, *J. Pharm. Soc. Japan*, **72**, 1481 (1956).
- (6) Prepared *via* a modification of the procedures of B. Riegel and W. M. Lillienfeld, *J. Am. Chem. Soc.*, **67**, 1273 (1945), and J. H. Hunter and J. A. Hogg, *ibid.*, **71**, 1924 (1949).

162–165° (0.05 mm.), infrared maxima at 5.78 and 6.13 μ (C, 58.35; H, 8.20; N, 5.02). Diekmann cyclization with sodium hydride in refluxing benzene gave a crystalline keto ester which was decarboxylated by refluxing 6 hr. in glacial acetic acid to the ketone II (55% over-all yield), b.p. 122°–124° (0.1 mm.), m.p. 34–35°, infrared maxima at 5.78 and 6.02 μ , DNP m.p. 215–215.5° (C, 51.45; H, 5.27; N, 20.55).



8-Oxo-2-quinolizidone II was biscyanoethylated *via* a modification of the Stork⁷ enamine procedure with acrylonitrile to give the impure dinitrile III.⁸ Reduction of III with 5% palladium on charcoal in acetic acid solution at room temperature and 50 p.s.i. gave a product which yielded *d,l*-matrine (0.5 g. from 1.5 g. of impure III) upon chromatography over alumina. The *d,l*-matrine had an infrared spectrum identical with that of natural *d*-matrine, but resisted attempts at crystallization. It gave a crystalline picrate (92% yield), m.p. 167–169°, which analyzed correctly for the picrate of matrine (C, 52.67; H, 5.61; N, 14.62). Attempts to regenerate crystalline *d,l*-matrine from the picrate failed.

Acknowledgment.—We wish to acknowledge the support of this research by the National Institutes of Health through Research Grant RG-7902.

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(8) This material was a mixture of mono- and dinitriles and resisted purification. It was converted to a product suitable for catalytic hydrogenation by molecular distillation.

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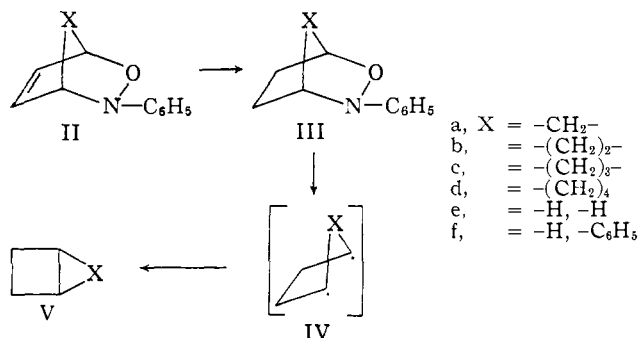
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RECEIVED JUNE 3, 1963

The Pyrolysis of 2-Phenyltetrahydro-1,2-oxazines as a Simple Preparative Entry to Cyclobutanes

Sir:

The dienophilic activity of nitrosobenzene (I) has been demonstrated¹ and the products from I and simple dienes have been shown to possess typical Diels–Alder adduct structures II^{2,3}; in a number of instances, the adducts have been shown to be thermally unstable, re-



(1) R. L. McKee in "The Chemistry of Heterocyclic Compounds," R. H. Wiley, Ed., Interscience Publishers, Inc., New York, N. Y., 1962, p. 332.

(2) G. Kresze and G. Schulz, *Tetrahedron*, **12**, 7 (1961); G. Kresze, G. Schulz, and F. Firl, *Angew. Chem. Intern. Ed. Engl.*, **2**, 263 (1963).

(3) N. F. Hepfinger, Ph.D. Thesis, University of Pittsburgh, 1963; C. E. Griffin, N. F. Hepfinger, and B. L. Shapiro, unpublished results.

generating starting materials.^{2,3} We now wish to report that the reduced forms of these adducts, 2-phenyltetrahydro-1,2-oxazines (III), undergo a pseudo Diels–Alder reversal with the formation of I and the cyclobutane V derived from the original diene. The conversion of dienes to the corresponding cyclobutanes has been achieved previously by the thermal and catalytic decomposition of tetrahydropyridazines^{4–8}; the decomposition of III is analogous and probably proceeds through a similar diradical intermediate IV.^{4,6} The ease of the over-all reaction (diene \rightarrow V) and the ready availability of starting materials indicate that the process constitutes a useful entry into simple and fused cyclobutane systems. Additionally, fragmentation and rearrangement of the diradical IV to olefinic products appear to be less prevalent than in tetrahydropyridazine decompositions.^{7,8}

The formation of bicyclo[2.1.0]pentane (Va) is typical of the process. The adduct IIa^{2,3} of cyclopentadiene and I was reduced in ethanol at 0° according to the method of Brown and Brown.⁹ IIIa was isolated by elution from Florisil with hexane and further purified by Celite chromatography and recrystallization (-70°) from pentane; IIIa [Found: C, 75.67; H, 7.82; N, 7.80] melted at 40–41° and the absence of unsaturation was confirmed by its infrared spectrum. The pyrolytic behavior of IIIa was determined by g.l.c.¹⁰ Use of an inlet temperature of 225° led to the detection and identification of a trace amount of cyclopentadiene, I and products arising from its decomposition at 225°, and a major peak (*ca.* 70%) identified as Va. The identity of Va was established by infrared and p.m.r. and g.l.c. behavior comparisons with an authentic sample.⁵ At higher injection port temperatures, a mixture of Va and its isomer, cyclopentene, were formed; at temperatures in excess of 300°, only the olefin could be detected.¹¹ Larger scale pyrolyses¹² of IIIa also resulted in the formation of Va. In a typical run, 1.2 g. of IIIa led to the isolation of Va (55%), cyclopentene (30%), and cyclopentadiene (trace). Over-all yields of 10–18% of Va from cyclopentadiene have been obtained routinely.

In like manner, bicyclo[2.2.0]hexane¹³ (Vb), bicyclo[3.2.0]heptane¹⁴ (Vc), bicyclo[4.2.0]octane¹⁴ (Vd), cyclobutane¹⁵ (Ve), and phenylcyclobutane¹⁶ (Vf) have been prepared from the adducts II of I and cyclohexadiene, cycloheptatriene, cyclooctadiene-1,3, butadiene, and 1-phenylcyclobutadiene, respectively. Because of their limited stability, the tetrahydrooxazines III were pyrolyzed without extensive purification; isolations were achieved by column chromatography. Gas-

(4) G. C. Overberger, N. R. Byrd, and R. B. Mesrobian, *J. Am. Chem. Soc.*, **78**, 1961 (1956).

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(6) S. G. Cohen, S. Hsiao, E. Saklad, and C. H. Wang, *J. Am. Chem. Soc.*, **79**, 4400 (1957).

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(10) All g.l.c. analyses were carried out with an F & M Model 720 gas chromatograph using a coupled column of 15 in. of 30% silver nitrate-ethylene glycol on firebrick and 4.5 ft. of silicone oil on firebrick with a helium flow rate of 40 ml./min. Column temperatures of 25–100° were employed. We are indebted to M. L. Halberstadt for supplying the details of this chromatographic separation procedure.

(11) The thermal isomerization of Va to cyclopentene has been extensively studied, *cf.* M. L. Halberstadt and J. P. Chesick, *J. Am. Chem. Soc.*, **84**, 2688 (1962), and *ref. 5*.

(12) Pyrolyses have been carried out by the use of a free flame with the sample contained in a tube of large surface area attached to a vacuum system; pyrolysis products were collected in liquid nitrogen traps.

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(16) F. H. Case, *J. Am. Chem. Soc.*, **56**, 715 (1934).