acetate **12**. Sodium ethoxide (0.01 *M*) in 1:2 ethanol–benzene at reflux effected fragmentation and *in situ* aldol cyclization to generate trimethyloctalone **13**. This regioselective annelation procedure complements the normal Robinson process (eq 1) in that the two-carbon arm is bonded to the carbonyl carbon and the one-carbon arm to the α carbon (eq 2).

The immensity of the applications of the Michael reaction foreshadows the potentiality of this new electronically reversed Michael-type alkylation.

Acknowledgment. We wish to express our appreciation to the National Science Foundation and the National Institutes of Health for their generous support of our programs.

(11) Camille and Henry Dreyfus Foundation Teacher–Scholar Grant recipient.

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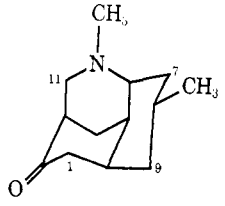
The Total Synthesis of (±)-Luciduline

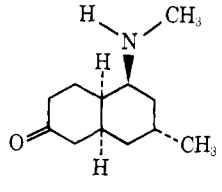
Sir:

The known *Lycopodium* alkaloids constitute a diverse class of skeletal types[1] which appear to be linked biogenetically to lysine,[2] the primary source of structural atoms in this group of naturally occurring bases. We report herein a stereoselective synthesis of (±)-luciduline (**1**)[3] which features several generally useful methods of carbocycle synthesis.[4,5]



1

Systematic analysis of the possible synthetic routes to **1** readily suggests that the tricyclic skeleton of luciduline can be established from ketoamine **2** *via* an intramolecular Mannich reaction, C-11 being derived from formaldehyde. Consequently, the stereoselective synthesis of **2** became our primary objective.



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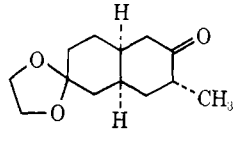
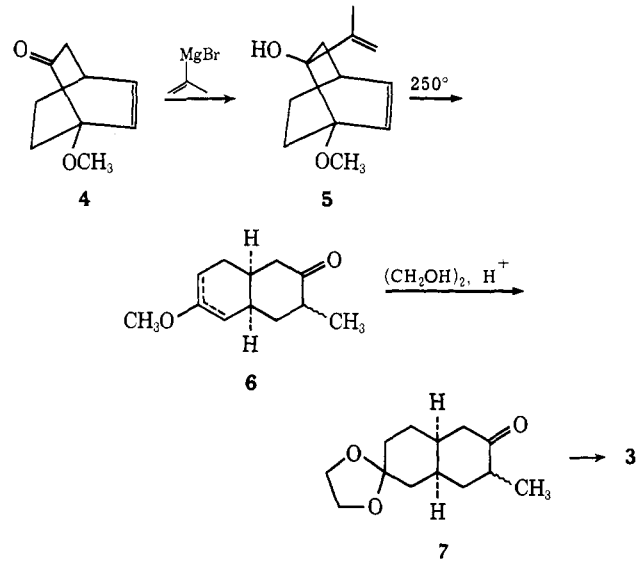


3

Although potential routes to **2** may be visualized from 5-methylcyclohexane-1,3-dione, we felt that the controlled introduction of the required sites of asymmetry in **2** could best be achieved through ketal ketone **3**, the synthesis of which may be accomplished as summarized in Scheme I.

Scheme I



4 **5** **6** **7**

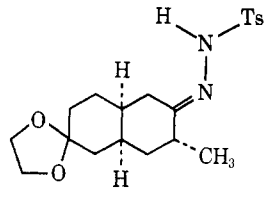
As previously reported by us, bicyclo[2.2.2]oct-5-en-2-one derivatives such as **4** may be conveniently synthesized in good yield from 2,5-dihydroanisole and the useful ketene equivalent 2-chloroacrylonitrile.[4] Furthermore, oxy-Cope rearrangement[6] of **5** followed by ketalization of **6** affords **7** in greater than 65% yield.[5] Contrary to our earlier report,[5] the ketal ketone **7** obtained on chromatography is an equilibrium 60:40 mixture of methyl epimers in which the desired α isomer **3** predominates. The lack of stereochemical definition at this stage was readily overcome by a single recrystallization of **7** (hexane) affording the desired α-methyl epimer **3**, mp 117–118°, in good yield. A simple re-equilibration–crystallization recycle of the isomer mixture **7** obtained from the filtrate yielded additional amounts of **3** with negligible losses of material.

Treatment of ketal ketone **3** with 1 equiv of *p*-toluenesulfonylhydrazine in anhydrous methanol for 3 hr at 25° afforded a quantitative yield of tosylhydrazone **8**, mp 137–139°, without epimerization of the methyl group. Tosylhydrazone **8** was converted to the single ketal olefin **9** with 2 equiv of methyllithium in anhydrous ether. The high regioselectivity of this reaction has been previously demonstrated.[7] Crude **9** was stereoselectively oxidized to epoxide **10**, mp 51–53°, in 80% overall yield from **3**, with *m*-chloroperbenzoic acid in chloroform.

Cleavage of **10** with sodium thiophenoxide in refluxing methanol (12 hr) proceeded regioselectively to **11**, mp 95–96° (85% yield), which was cleanly desulfurized to ketal alcohol **12**, mp 95–97° (82% yield), with Raney nickel[8] in refluxing ethanol. The entire sequence **3**–**12**

(1) D. B. McLean in "The Chemistry of the Alkaloids," S. W. Pelletier, Ed., Van Nostrand Reinhold Co., New York, N. Y., 1970, Chapter 16.
(2) R. N. Gupta, M. Castillo, D. B. MacLean, I. D. Spenser, and J. T. Wrobel, *J. Amer. Chem. Soc.*, **90**, 1360 (1968); see ref 3 for a proposed biosynthesis of luciduline.
(3) W. A. Ayer, N. Masaki, and D. S. Nkunika, *Can. J. Chem.*, **46**, 3631 (1968).
(4) D. A. Evans, W. L. Scott, and L. K. Truesdale, *Tetrahedron Lett.*, 121 (1972).
(5) D. A. Evans, W. L. Scott, and L. K. Truesdale, *ibid.*, 137 (1972).
(6) (a) J. A. Berson and M. Jones, Jr., *J. Amer. Chem. Soc.*, **86**, 5017, 5019 (1964); (b) J. A. Berson and E. J. Walsh, Jr., *ibid.*, **90**, 4729, 4730, 4732 (1968).
(7) W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *ibid.*, **90**, 4762 (1968).
(8) A. W. Burgstahler in "Reagents for Organic Synthesis," Vol. 1, Wiley, New York, N. Y., 1968, p 729.

may be carried out in 65% yield without purification of the intermediates.



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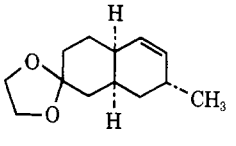

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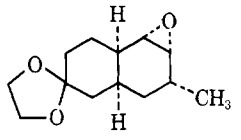

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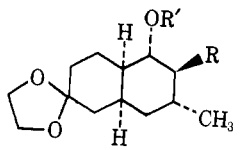
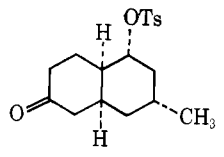


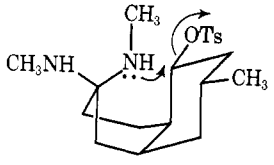
11, R = SC_6H_5; R′ = H
12, R = H; R′ = H
13, R = H; R′ = Ts

Treatment of **12** with *p*-TsCl in pyridine at 50° for 10 hr followed by acid hydrolysis of the ketal tosylate **13** (acetone, HCl, 50° for 45 min) afforded keto tosylate **14**, mp 99–100°, in 89% yield.

Introduction of the *N*-methylamine moiety into the bicyclic ketal tosylate **13** formally constitutes a simple transformation. However, both the sterically conjested concave face of the cis decalyl system and the observed tendency of cyclohexyl tosylates to undergo elimination in addition to substitution[9,10] with amine nucleophiles suggested that the elimination pathway would predominate in any attempted direct displacement process on **13**. As anticipated, treatment of **13** with either methylamine or azide ion under a variety of conditions afforded olefin as well as minor amounts of substitution products. In an attempt to circumvent this problem, the ketal function was removed in anticipation that tosylate displacement could be effected by an intra- rather than intermolecular pathway (*cf.* **15**).



14



15

Indeed, when **14** was treated with excess monomethylamine in benzene (sealed tube, 75°, 24 hr) the desired ketoamine **2** was obtained in 94% yield uncontaminated by olefin. Although the existence of **15** is only postulated, the facility with which substitution occurs in this system renders intramolecular delivery of nitrogen through aminal **15** a distinct possibility.

With our key intermediate, **2**, now in hand the final step was accomplished by heating **2** with paraformaldehyde in 3-methylbutan-1-ol (reflux, 20 hr) to afford (±)-luciduline (**1**) (mp of HCl salt, 179–181°), identical by ir (liquid film), nmr, mass spectrum, and vpc with an authentic sample of **1**.[11]

(9) J. L. Pinkus, G. Pinkus, and T. Cohen, *J. Org. Chem.*, 27, 4356 (1962).

(10) (a) A. K. Bose, J. T. Kistner, and L. Farber, *ibid.*, 27, 2925 (1962); (b) E. J. Corey and R. L. Dawson, *J. Amer. Chem. Soc.*, 85, 1782 (1963).

(11) Satisfactory combustion analyses where obtained on all synthetic intermediates with the exception of **9**.

Acknowledgment. We are grateful to Professor W. A. Ayer for an authentic sample of luciduline and to the National Institutes of Health for generous support of this research.

(12) Camille and Henry Dreyfus Teacher-Scholar Recipient, 1971–1976; Alfred P. Sloan Fellow, 1972–1974.

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Irradiation of Triaryl Phosphate Esters. A New Photochemical Coupling Reaction[1]

Sir:

While searching for new reactions analogous to those observed when aryl *carboxylate* esters are irradiated,[2] we examined the photochemistry of various *phosphate* esters and discovered a new photochemical coupling process whose novelty and potential utility prompts this preliminary communication. The major characteristic of this new reaction, as illustrated in eq 1, is the

$$(ArO)_3PO \xrightarrow{h\nu} Ar\text{-}Ar + ArOPO_3H_2 \quad (1)$$

formation of a new carbon–carbon bond between two of the aryl groups in the ester, resulting in the production of a biphenyl derivative along with the corresponding monoaryl phosphate. Some of our results are collected in Table I.

In contrast to the photodecarboxylation reaction of aryl carboxylates,[3] in which the coupling step is accompanied by the expulsion of a stable molecule (eq 2), the

$$RCO_2Ar \xrightarrow{h\nu} RAr + CO_2 \quad (2)$$
$$R = \text{alkyl or aryl}$$

phosphate coupling reaction (eq 1) involves an oxidation–reduction sequence at some stage. The solvent ethanol most likely serves as reductant and, indeed, we have isolated acetaldehyde as its 2,4-dinitrophenylhydrazone derivative. Another contrasting feature is that neither photo-Fries products (*i.e.*, hydroxyaryl phosphonates) nor solvolysis products (*i.e.*, diaryl ethyl, aryl diethyl, or triethyl phosphate) were detected in any of the experiments listed in Table I.[4]

The lack of, *e.g.*, toluene from tri-*p*-cresyl phosphate, anisole from trianisyl phosphate, etc., or any of the corresponding ethyl ethers, strongly diminishes the possibility that free aryl radicals, carbanions, or carbonium ions are produced during the reaction. When an equimolar mixture of triphenyl and tri-*p*-cresyl phosphates in ethanol solution was irradiated for 4.5 hr, there was obtained only biphenyl (21% yield, 4% conversion) and 4,4′-dimethylbiphenyl (53% yield, 48% conversion) in the biaryl fraction. Likewise, when a similar mixture of tri-*p*-cresyl phosphate and tri-*p*-

(1) (a) Photochemical Studies. VIII. For part VII in this series, see ref 2. (b) Financial support for this work was generously provided by the National Science Foundation (GP 5785) and the National Institutes of Health (GM 11412).

(2) R. A. Finnegan and D. Knutson, *Tetrahedron Lett.*, 3429 (1968).

(3) Reference 2 and earlier articles in this series cited therein.

(4) Although the corresponding phenols were usually observed, they were shown to arise during the analysis (vpc) by thermal decomposition of the monoaryl phosphate. They could not be isolated by silica gel column chromatography.