(5) Graham Johnson, Ph.D. Thesis, Heriot-Watt University, Edinburgh, Scotland, Aug 1975, p 206.
(6) To an ice-cold, stirred solution or suspension of 50 mmol of the carbamate ($ROCONH_2$) in 40 mL of reagent grade methanol was added 5.63 mL (5.4 g, 50 mmol) of *tert*-butyl hypochlorite (Frinton Laboratories). After 15 min a methanolic solution (25 mL) of sodium hydroxide (2.0 g, 50 mmol) was added dropwise over a period of several minutes. The ice bath was removed and stirring was continued for 10 min. Then the solvent was removed on a rotary evaporator (bath <45 °C) and the resulting white solid residue[7] was triturated with dry ether, isolated by filtration, and washed with dry ether to afford the *N*-chloro-*N*-sodiocarbamate (ROCONClNa). The *N*-chlorosodiocarbamates prepared and isolated in this way are quite hygroscopic and should be stored in a desiccator in a freezer (ca. −20 °C). When stored in this way at low temperature these reagents are stable for at least 2 months.
(7) This crude salt can be used directly, in which case the entire oxyamination procedure is carried out in one reaction vessel. Application of this procedure, using *tert*-butyl carbamate, to (*E*)-stilbene afforded an 83% yield of the vicinal hydroxycarbamate. This compared favorably with the 87% yield realized with the ether-washed salt (Table I, example 4). However, in the few cases so far tried the crude salt modification appears to result in slower reactions and in some cases poorer yields than the method using the ether-washed salts. To demonstrate that the reaction can be performed on a moderate scale the crude salt (**2c**) of ethyl carbamate was prepared on a 200-mmol scale and was used directly to transform 24.16 g (134 mmol) of (*E*)-stilbene to 29.4 g (77%) of the oxyaminated product (mp 122–123 °C).
(8) *Warning:* It was noted early in this work that salts **2e** and **2f** derived from menthyl and bornyl carbamates were unstable and were therefore best used directly after removal of the methanol. More recently, the stability of salts **2** from even the simpler carbamates has become a concern to us. On one occasion, when EtOCONClNa was prepared on a 250-mmol scale, it decomposed rapidly (but not explosively), turning dark and releasing heat and gases. However, we had twice earlier prepared this same chloramine salt on a 100-mmol scale without incident. There are conflicting statements in the literature[3] about the stability of these *N*-chlorosodiocarbamates. For the present, *we recommend that salts* **2** *never be prepared on greater than a 200-mmol scale.* We are now developing in situ procedures in which the entire reaction sequence is carried out in acetonitrile, obviating the need for dealing with the dry *N*-chlorocarbamate salts (**2**). These modifications will be described in a future publication.
(9) Note that this general procedure calls for use of 2 equivalents (based on salt **2**) of silver nitrate. The extra equivalent of silver nitrate was found to accelerate the reaction. However, the magnitude of this effect was very dependent on the structure of the carbamate. It was most noticeable with ethyl carbamate, which took 18 h to reach completion when only 1 equiv (1.5 mmol) of silver nitrate was used, while with 2 equiv of $AgNO_3$ present, the reaction was over in 2 h (Table I, example 3). In spite of the rate differences there was no significant difference in the final yields. The other carbamates shown in Scheme I gave rapid reactions even with only 1 equiv of $AgNO_3$. We speculate that this might be due to better solubility imparted by the larger organic moieties. Thus the extra equivalent of silver nitrate is not essential, but may in some cases give faster reactions.
(10) Recipe for OsO_4 catalyst solution: 1 g (3.94 mmol) of OsO_4, 199 mL of reagent grade *tert*-butyl alcohol, and, as a stabilizer, 1 mL of 70% or 90% *tert*-butyl hydroperoxide (Aldrich); each milliliter contains 5 mg (~0.02 mmol) of OsO_4. The resulting catalyst solution is stored in a brown bottle at room temperature.
(11) The purpose of this bisulfite treatment is to reduce, and thereby remove, the small amount of osmium that may be bound to the organic products. If a molecule were sensitive to this step, then it could be omitted. Thus far all the hydroxycarbamates we have obtained were stable to this bisulfite treatment.
(12) E. Herranz, unpublished results.
(13) The beneficial effect of nucleophiles (e.g., Et_4NOAc and Et_4NOH) on osmium catalyzed reactions of olefins has been observed previously: K. B. Sharpless and K. Akashi, *J. Am. Chem. Soc.*, **98**, 1986 (1976); K. Akashi, R. E. Palermo and K. B. Sharpless, *J. Org. Chem.*, in press.
(14) Address correspondence to this author at the Department of Chemistry, Stanford University, Stanford, Calif. 94305.

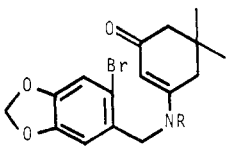
Eugenio Herranz, Scott A. Biller, K. Barry Sharpless* [14]
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received January 3, 1978

An Intramolecular Cyclization of Enaminones Involving Benzyne Intermediates and Application to the Synthesis of γ-Lycorane and Related Compounds

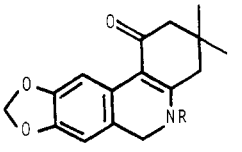
Sir:

The area of reactivity and versatility of the enaminone[1] ($>N_c-C_e=C_b-C_d=O_a$) possessing three nucleophilic sites (a, b, and c) and two electrophilic sites (d and e) is of current interest[2] particularly in heterocyclic chemistry, which shows diverse and sometimes complicated reactivity. Although many and increasing examples concerning reactions of enaminones have been reported,[2] a search of the literature indicates that no work has been done on the arylation of enaminones. The purpose of this communication is to demonstrate a new intramolecular arylation of enaminones and the use of this reaction for the synthesis of γ-lycorane and related compounds. Our procedure represents the crucial ring closure of enaminones utilizing an intramolecular reaction of benzyne intermediates which was hinted by a cyclization reaction[3] involving electrophilic attack by alkynes on enaminone systems.

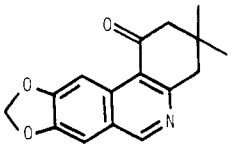
Condensation of 5,5-dimethylcyclohexa-1,3-dione with 2-bromo-4,5-methylenedioxybenzylamine, prepared by Gabriel synthesis from the corresponding benzyl chloride, gave the bromoenaminone **1** in 83% yield: mp 223–224 °C. Treatment of **1** with lithium diethylamide in THF at room temper-



1, R = H
2, R = C_2H_5



3, R = H
4, R = C_2H_5



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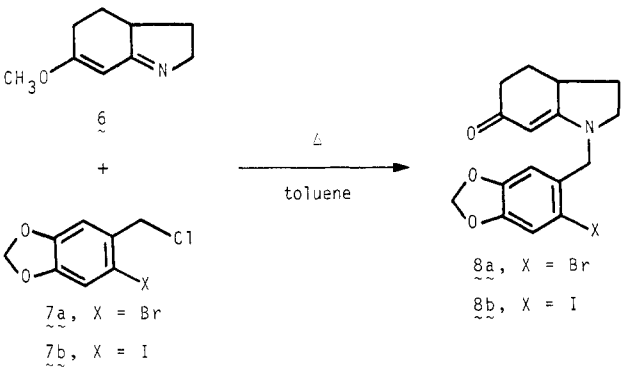
ature for 2 h gave the 3,4-dihydro-1(2*H*)-phenanthridone **5** in 26% yield: mp 175–177 °C; NMR ($CDCl_3$) δ 7.06, 8.73, and 8.86 (each s, 1 H, ArH). This compound may have arisen from initial intramolecular arylation of **1** yielding the 3,4,5,6-tetrahydro-1(2*H*)-phenanthridone **3** as an intermediate followed by oxidative aromatization.

N-Alkylation of **1** with ethyl iodide was carried out in refluxing toluene in the presence of NaH to give **2** in 80% yield: mp 167–169 °C. In a similar manner to that described for **1**, **2** was treated for 30 min to yield the 3,4,5,6-tetrahydro-1(2*H*)-phenanthridone **4** in 55% yield: mp 123–124 °C; NMR ($CDCl_3$) δ 6.40 and 8.80 (each s, 1 H, ArH).

The synthetic utility of this cyclization reaction was demonstrated by the synthesis of γ-lycorane and related compounds. The requisite haloenaminones were conveniently available by a one-step synthesis as follows. Upon heating the iminoenol ether **6**,[4] prepared by Birch reduction of 6-methoxyindoline in quantitative yield, with 2-bromo-4,5-methylenedioxybenzyl chloride (**7a**) in refluxing toluene, N-benzylation occurred predominantly to give the desired



6

7a, X = Br
7b, X = I

8a, X = Br
8b, X = I

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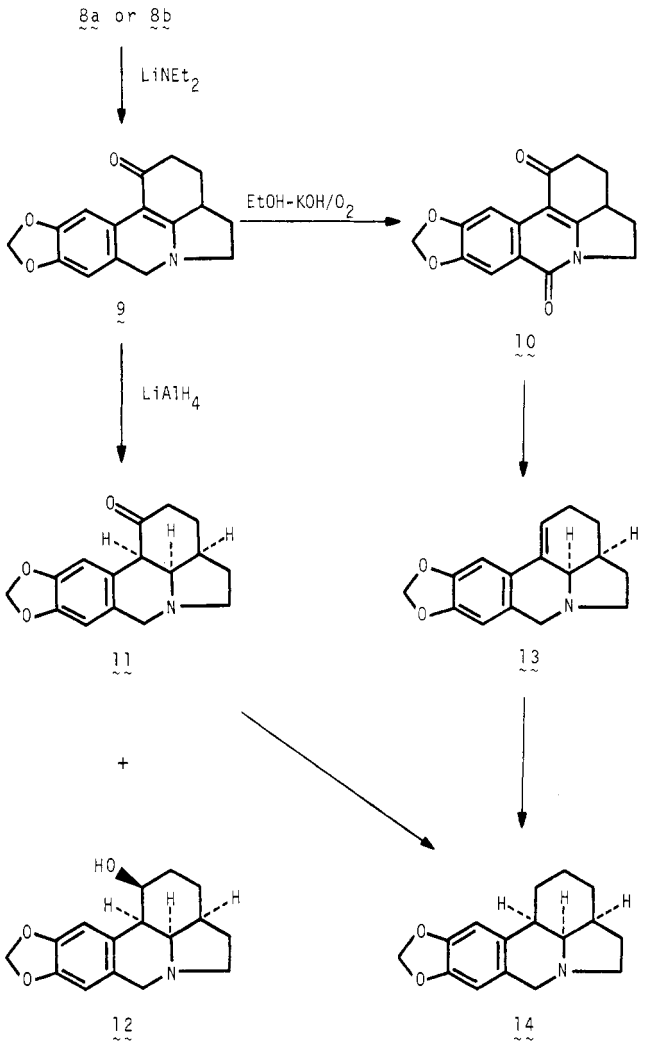
enaminone **8a** in 51% yield: mp 157–158 °C; IR ($CHCl_3$) 1605 (C=O),[5] 1580 cm^{-1} (C=C);[5] NMR ($CDCl_3$) δ 5.10[5] (s, 1 H). Similar treatment of **6** with **7b** yielded the corresponding iodoenaminone **8b** in 50% yield: mp 173–174 °C; IR ($CHCl_3$) 1605, 1580 cm^{-1}; NMR ($CDCl_3$) δ 5.09 (s, 1 H).

The ring closure of the bromoenaminone **8a** was successfully carried out in a similar manner to that described above. The reaction proceeded to completion in 30 min at room temperature, giving the pyrrolophenanthridone **9** in 49% yield: IR ($CHCl_3$) 1610, 1560 cm^{-1}; NMR ($CDCl_3$) δ 4.53 (s, 2 H, CH_2Ph), 5.87 (s, 2 H, OCH_2O), 6.34 (s, 1 H, 8-H), 8.52 (s, 1 H, 12-H). In the same manner the cyclization of the iodoenaminone **8b** afforded **9** in 35% yield. This product began to



melt at 145 °C and completely liquefied at 252 °C coinciding with the melting point reported for the keto lactam **10**,[4,6,7] which suggested that **9** would be susceptible to air oxidation to **10**. Accordingly, **9** was treated with oxygen in ethanol containing aqueous KOH to give the keto lactam **10**, mp 252–253 °C, directly identical in all respect with an authentic sample.[4] Compound **10** can be readily converted into (±)-γ-lycorane (**14**) via (±)-α-anhydrodihydrocaranine (**13**) according to a procedure previously reported.[4]

On the other hand, reduction of **9** with $LiAlH_4$ in THF at room temperature stereoselectively provided (±)-α-dihydrocaranone (**11**) in 33% yield (mp 147–149 °C (lit.[8] mp 147.5–149.5 °C); IR ($CHCl_3$) 1705 cm^{-1}; NMR ($CDCl_3$) δ 3.29 and 4.00 (AB q, J = 14 Hz, CH_2Ph), 3.47 (d, J = 4 Hz, 1 H, 12b-H), 5.89 (s, 2 H, OCH_2O), 6.49 (s, 1 H, 8-H), 6.59 (s, 1 H, 12-H)) and (±)-1-epi-γ-dihydrocaranine (**12**) in 10% yield (mp 134–135 °C (lit.[8] mp 135.5–136.5 °C); IR ($CHCl_3$) 3250 cm^{-1}; NMR ($CDCl_3$) δ 3.28 and 4.04 (AB q, J = 14 Hz, CH_2Ph), 5.09 (s, 2 H, OCH_2O), 6.48 (s, 1 H, 8-H), 6.64 (s, 1 H, 12-H)). The IR and NMR spectra of these products were superimposable on those of authentic materials.[9] Conversion of α-dihydrocaranone (**11**) into γ-lycorane (**14**) has been achieved.[8,10]

References and Notes

(1) For designation, enaminone has been recommended[2b] instead of enamino ketone or β-amino-α,β-unsaturated ketone since the compounds rarely show the physical or chemical properties normally associated with ketones.
(2) For reviews see (a) T. Nishino, C. Kajima, and Y. Omote, *J. Synth. Org. Chem. Jpn.*, **34**, 526 (1976); (b) J. V. Greenhill, *Chem. Soc. Rev.*, **16**, 277 (1977).
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(4) H. Iida, S. Aoyagi, and C. Kibayashi, *J. Chem. Soc., Perkin Trans. 1*, 2502 (1975).
(5) Spectral analysis by IR, UV, and NMR has been proven to be effective for the determination of the enaminone structure: C. A. Grob, and H. J. Willkens, *Helv. Chim. Acta*, **50**, 725 (1967).
(6) K. Takeda and K. Kotera, *Chem. Pharm. Bull. (Tokyo)*, **5**, 234 (1957).
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(8) N. Ueda, T. Tokuyama, and T. Sakan, *Bull. Chem. Soc. Jpn.*, **39**, 2021 (1966).
(9) We thank Drs. T. Sakan and N. Ueda for the IR and NMR spectra of (±)-α-dihydrocaranone and (±)-1-epi-γ-dihydrocaranine.
(10) K. Kotera, *Tetrahedron*, **12**, 248 (1961).

Hideo Iida, Yoshifumi Yuasa, Chihiro Kibayashi*
Tokyo College of Pharmacy, 1432-1 Horinouchi Hachioji, Tokyo 192-03, Japan

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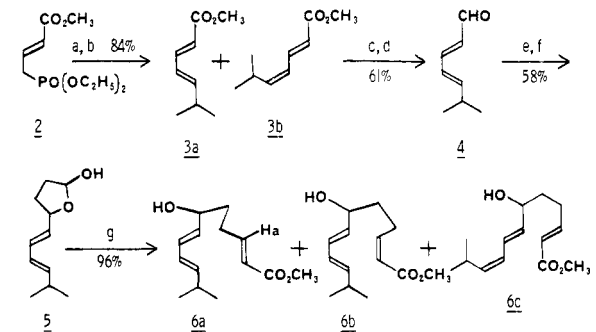
Total Synthesis of (±)-Dendrobine[1]

Sir:

Dendrobine (**1**), the major component of the Chinese drug "Chin-Shih-Hu", has been the subject of recent synthetic investigations, in part as a consequence of its structural and pharmacological similarities to picrotoxinin.[2] Herein we describe a total synthesis[3] of this alkaloid by a highly stereoselective route which utilizes an intramolecular Diels–Alder reaction[4] as the key skeleton-forming transformation.[5]

The synthesis of the Diels–Alder substrate **6a** was achieved as described in Scheme I. The mixture of dienes **3** obtained from condensation of the stabilized anion of **2** with isobutyraldehyde[7] contained 93% **3a**.[6a,8] The trans,trans stereochemistries of **3a** and **4**[6a,b] were assigned on the basis of their characteristic NMR and UV spectra, which were similar to those of methyl sorbate and sorbaldehyde, respectively.[9] Careful chromatography of the triene mixture (96% crude) obtained

Scheme I



[a] TMS_2NLi, THF, −78 °C. [b] Isobutyraldehyde, −40 °C. [c] Dibah, Et_2O. [d] CrO_3-py. [e] $BrMgCH_2CH_2CHOCH_2CH_2O-$, THF. [f] THF, aqueous HCl. [g] Carbomethoxymethylenetriphenylphosphorane, CH_2Cl_2.

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