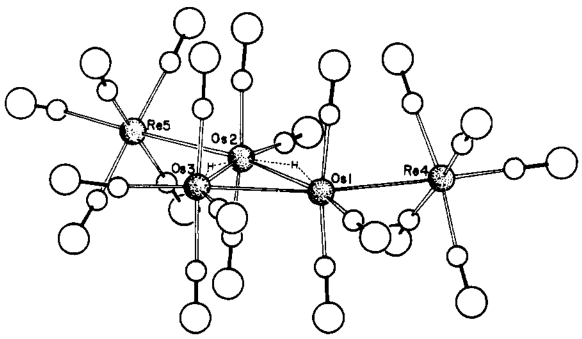

Figure 1. The $H_2Re_2Os_3(CO)_{20}$ molecule, with the probable positions of the hydride ligands indicated.

a rhenium atom bonded to equatorial sites of two of these atoms. The Os(1)-Os(3) bond lengths in the two independent molecules are 2.876 (3) and 2.876 (3) Å—i.e., closely similar to the Os-Os bond length of 2.877 (3) Å (average) found in $Os_3(CO)_{12}$.[15] In contrast to this, the remaining Os··Os distances are significantly longer, with Os(1)-Os(2) = 3.058 (3) and 3.061 (3) Å and Os(2)-Os(3) = 3.083 (3) and 3.074 (3) Å. We believe that these vectors are bridged by μ_2-hydrido ligands. (In other molecules simple μ_2-hydrido bridged osmium-osmium bond lengths are 2.989 (1) Å for $(\mu_2\text{-H})(H)Os_3(CO)_{11}$[15] and 3.019 (1) Å for $(\mu_2\text{-H})(H)Os_3(CO)_{10}PPh_3$.)[16] The osmium-rhenium bond lengths are normal, with Os(1)-Re(4) = 2.952 (4) and 2.946 (4) Å and Os(2)-Re(5) = 2.982 (3) and 2.975 (3) Å. The angles involving the equatorial rhenium atoms are as follows: ∠Os(2)-Os(1)-Re(4) = 104.1 (1) and 104.0 (1)° and ∠Os(3)-Os(2)-Re(5) = 104.2 (1) and 102.9 (1)°. Each metal atom has a regular coordination geometry, there being three carbonyl ligands associated with Os(1) and Os(2), four for Os(3), five for Re(4) and Re(5).

Treatment of $Os_3(CO)_{12}$ with $Me_3NO{\cdot}2H_2O$ (1 equiv) in acetonitrile followed by excess $HRe(CO)_5$ in benzene provided a single new product, which was isolated as a yellow solid in ~50% yield after TLC. Spectroscopic data for this material is consistent with the formula $HReOs_3(CO)_{16}$[17] and it is assigned structure I. In an attempt to prepare $H_3ReOs_3(CO)_{24}$, $Os_3(CO)_{10}(NCMe)_2$[9] was treated with 1 equiv $Me_3NO{\cdot}2H_2O/NCMe$[18] and then $HRe(CO)_5$, but the product isolated was $HReOs_3(CO)_{15}$.[19] Similar treatment of $H_2Re_2Os_3(CO)_{20}$ provided $H_2Re_2Os_3(CO)_{19}$. However, subsequent experiments showed that $H_2Re_2Os_3(CO)_{19}$ could be formed by allowing $H_2Re_2Os_3(CO)_{20}$ to react with $Me_3NO{\cdot}2H_2O/NCMe$ alone; an analogous reaction gave $HReOs_3(CO)_{15}$ from $HReOs_3(CO)_{16}$. The detailed structures of these more condensed clusters remain to be determined. Nevertheless, it is clear that the combination of $HRe(CO)_5$ coupling with Me_3NO decarbonylation provides considerable control of metal-metal bond formation in the Re-Os system. The efficacy of these techniques with other heterometallic combinations is being explored.

Acknowledgments. This research was supported by NSF grants CHE 75-14460 to J.R.S. and CHE 77-04981 to M.R.C. A loan of osmium tetroxide from Engelhard Industries is also gratefully acknowledged.

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(10) Solutions of $HRe(CO)_5$ are conveniently prepared in good yield on a small scale by reduction of $Re(CO)_5Br$ with zinc and acetic acid (cf. $H_2Os_3(CO)_{12}$ from $Os_3(CO)_{12}Br_2$[11]): G. A. Pearson and J. R. Shapley, unpublished results.
(11) J. R. Moss and W. A. G. Graham, *Inorg. Chem.*, **16,** 75 (1977).
(12) M^+, m/e 1512 (^{187}Re, ^{192}Os); $(M - xCO)^+$ (x = 1–13) and $(M - HRe(CO)_4 - yCO)^+$ (y = 0–11) also observed.
(13) ^{13}C NMR (CH_2Cl_2, parts per million downfield from TMS): 193.4 (2 C), 183.8 (2 C), 183.0 (1 C), 177.8 (1 C), 176.2 (2 C), 165.5 (1 C), 163.8 (1 C). No signals for carbonyls attached to rhenium were observed, either at 30 or at −50 °C, suggesting that CO exchange between osmium and rhenium is very slow.
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(17) Mass spectrum: M^+, m/e 1212 (^{187}Re, ^{192}Os); also $(M - xCO)^+$ (x = 1–16) and $(M - HRe(CO)_4 - yCO)^+$ (y = 1–10). ^1H NMR (CH_2Cl_2): τ 28.8. A compound of the same formula, identified by mass spectroscopy, was obtained in an impure state by Knight and Mays.[4]
(18) This treatment is assumed to provide mainly $Os_3(CO)_9(NCMe)_3$, since addition of $PPhMe_2$ to the solution leads to $Os_3(CO)_9(PPhMe_2)_3$. However, the triacetonitrile species has not been isolated.
(19) Mass spectrum: M^+, m/e 1184 (^{187}Re, ^{192}Os), and $(M - xCO)^+$ (x = 1–15); also series involving Os_3 and ReOs ions. ^1H NMR (CH_2Cl_2): τ 26.8 (s, 1 H vs. $HOs_3(CO)_{10}OMe$ internal standard). IR (C_6H_{12}): ν_{CO} 2114 (vw), 2084 (m), 2058 (m), 2029 (m), 2015 (sh), 2002 (s), 1991 (m), 1981 (w), 1971 (m), 1965 (sh), 1932 (w) cm^{-1}. A compound of formula $HReOs_3(CO)_{15}$ was isolated by Knight and Mays;[4] its molecular structure was recently determined to be rhomboidal (M. R. Churchill and F. J. Hollander, *Inorg. Chem.*, **16,** 2493 (1977)). However, $HReOs_3(CO)_{15}$ prepared as described here appears to differ from Knight and Mays' compound in solubility and IR spectrum. We have not yet been able to obtain crystals of our compound suitable for x-ray diffraction.
(20) Mass spectrum: M^+, m/e 1484 (^{187}Re, ^{192}Os), and $(M - xCO)^+$ (x = 1–19); also series involving $ReOs_3$, Os_3, Re_2Os, and Re_2 ions. ^1H NMR (CH_2Cl_2): τ 25.6 (d, 1 H), 26.0 (d, 1 H); J = 0.8 Hz. IR (C_6H_{12} ν_{CO}): 2107 (m), 2078 (m), 2062 (m), 2051 (m), 2015 (s), 2004 (s), 2000 (s), 1994 (s), 1986 (m), 1976 (s), 1964 (s), 1950 (vw), 1930 (w) cm^{-1}.

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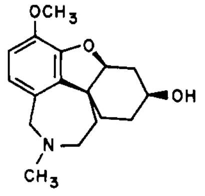
Total Synthesis of *dl*-Lycoramine

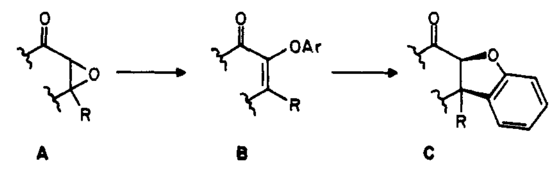
Sir:

Lycoramine (1) is one of the galanthamine-type alkaloids found in plants of the *Amaryllidaceae.*[1] We now report a total synthesis of *dl*-lycoramine.[2]



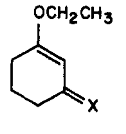
I

The synthesis of 1 features a new benzodihydrofuran ring construction (e.g., A → B → C). In the sequence, heteroatom-directed photoarylation[3] (B → C) establishes the crucial carbon-carbon bond[4] joining an aromatic ring to a quaternary carbon atom located at a ring junction. The photoreaction **5a** → **6** → **7** to be described here is representative of a general

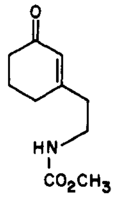


method for synthesis of complex aryl annelated dihydrofurans.[5] We especially note the varied functionality compatible with this method of aromatic ring substitution.

Reaction of the enol ethyl ether **2a** of 1,3-cyclohexanedione with the sodium salt of diethyl cyanomethylphosphonate in refluxing tetrahydrofuran (THF) solution gave the vinyl nitrile **2b** as a 60:40 mixture of two double-bond isomers in 98% yield. Without separation of isomers, **2b** was converted to enone **3** (bp 150 °C at 0.1 mmHg; IR 2.93, 5.83, 5.93, 6.12 μ), by lithium aluminum hydride reduction in ether to give primary amine **2c**; reaction of **2c** with methyl chloroformate (benzene-aqueous sodium bicarbonate) to give urethane **2d**; and finally hydrolysis-rearrangement of **2d** with 10% H_2SO_4 in methanol-THF solution at room temperature (76% overall yield of **3** from **2a**). Epoxidation of **3** with alkaline hydrogen peroxide in aqueous methanolic solution at room temperature afforded epoxy ketone **4** in 70% yield (IR 2.92, 5.83 μ).



2a, X=O
b, X=CHCN
c, $X=CHCH_2NH_2$
d, $X=CHCH_2NHCO_2CH_3$



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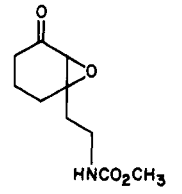
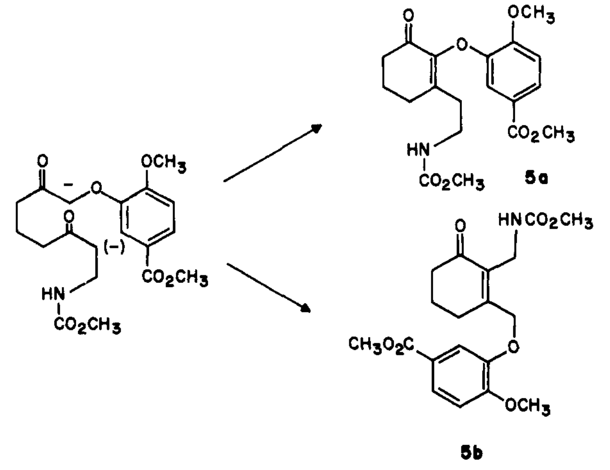
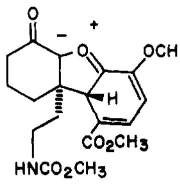


4

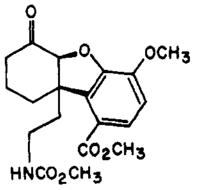
We were now ready to combine epoxy ketone **4** with the second half of the lycoramine ring system. Reaction of 5-carbomethoxy-2-methoxyphenol[6] with 1 equiv of potassium hydride in 18-crown-6 (1 equiv)-THF solution followed by addition of **4** (1 equiv) and heating to reflux for 8 h gave aryloxenone **5a** in 50% isolated yield (mp 120-121 °C; IR 2.89, 5.78, 5.83, 5.91 μ) and an isomeric enone **5b** (mp 90-93 °C, 15% yield). The formation of both **5a** and **5b** is explained by consideration of an intermediate diketone enolate, from which cyclization-dehydration may occur to give either **5a** or **5b** as shown.[7]



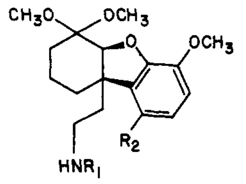
Pyrex-filtered irradiation of **5a** (0.05 M) in benzene-methanol solution (1:1, argon saturated) for 1.5 h gave the cis-fused dihydrofuran **7** (glass; IR 5.79, 6.20 μ); ketalization of **7** with methanol-trimethyl orthoformate-sulfuric acid gave crystalline **8a** (mp 140-143 °C) in 86% overall yield from **5a.** On the basis of analogy between the conversion **5a** → **7** and previous work,[5] we suggest that the photoreaction occurs by conrotatory cyclization of **5a** to give an intermediate carbonyl ylide **6**, from which protonation-deprotonation in methanol gives the cis-fused dihydrofuran **7**.



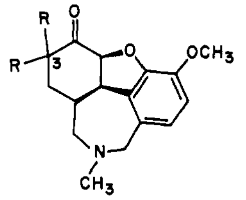
6



7



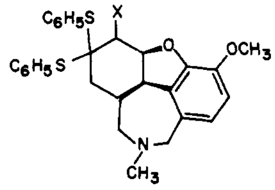
8a, $R_1=R_2=CO_2CH_3$
b, $R_1=CH_3$; $R_2=CH_2OH$



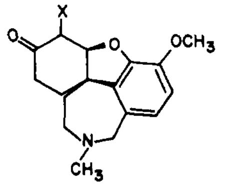
9a, R=H
b, $R=SC_6H_5$

With ketal **8a**, the azacycloheptane ring in lycoramine could now be established. Lithium aluminum hydride reduction of **8a** afforded the amino alcohol **8b** in 99% yield. Cyclization of **8b** with thionyl chloride-triethylamine (2 equiv) in chloroform solution at −20 °C and deketalization with 1 M H_2SO_4 at room temperature gave amino ketone **9a** in 76% yield: IR 5.81 μ; *m/e* 287.

The last stage of our synthesis plan, a 1,2-carbonyl transposition in **9a** to give lycoraminone (**11b**),[8] required transformation of C(3) to the oxidation state of a ketone.[9] Thus, generation of the lithium enolate of **9a** with lithium tetramethylpiperidide (2.1 equiv) in THF-hexamethylphosphoramide at −78 °C, followed by addition of phenyl phenylthiosulfonate[10] (2.5 equiv) in THF at 0 °C and warming to room temperature gave thioketal ketone **9b** (IR 5.85 μ). Reduction of **9b** with lithium aluminum hydride in ether at room temperature gave the alcohol **10a,** which was converted to the mesylate **10b** in 70% overall yield from **9a.**[11] Thioketal hydrolysis in **10b** was carried out with mercuric chloride-mercuric oxide (2 equiv) in aqueous acetonitrile at 50 °C[12] to give keto mesylate **11a.**



10a, X=OH
b, X=OMs



11a, X=OMs
b, X=H

Treatment of **11a** with chromous chloride[13] in aqueous acetone gave *dl*-lycoraminone (**11b**, mp 99-100 °C, lit.[2] mp 99-100 °C, IR 5.83 μ) in 85% yield from **10b.**

Stereoselective lithium aluminum hydride reduction of **11b** in refluxing THF, as described by Uyeo and co-workers[2] gave *dl*-lycoramine (**1**, mp 94-97 °C, lit.[2] mp 98-99 °C). The VPC and TLC properties and 90-MHz proton nuclear magnetic resonance and low resolution mass spectra of synthetic lycoramine, *m/e* (calcd for $C_{17}H_{23}NO_3$, 289.1676) 289.1672, were identical with those of the natural material.[14,15,16]

Acknowledgment. This work was supported by the National Institutes of Health (Grant No. GM 21159-02 and DA 01552-01).

References and Notes

(1) For an excellent review of the chemistry of *Amaryllidaceae* alkaloids, see W. C. Wildman in "The Alkaloids", Vol. XI, R. H. F. Manske, Ed., Academic Press, New York, N.Y., 1968, p 307 and references cited therein.

(2) For previous total synthetic efforts with lycoramine and dehydrolycoramine (galanthamine), see D. H. R. Baton and G. W. Kirby, *J. Chem. Soc.*, 806 (1962); R. A. Abramovitch and S. Takahashi, *Chem. Ind. (London)*, 1039 (1963); B. Franck, J. Lubs, and G. Dunkelmann, *Angew. Chem.*, **79**, 989 (1967); N. Hazama, H. Irie, T. Mizutani, T. Shingu, M. Takada, S. Uyeo, and A. Yoshitake, *J. Chem. Soc. C*, 2947 (1968); Y. Misaka, T. Mizutani, M. Sekido, and S. Uyeo, *ibid.*, 2954 (1968); T. Kametani, K. Yamaki, H. Yagi, and K. Fukomuto, *Chem. Commun.*, 425 (1969); T. Kametani, *Symp. Pap. Symp. Chem. Nat. Prod., 15th*, 123 (1971); and T. Kametani and K. Fukomoto, *Acc. Chem. Res.*, **5**, 219 (1972).

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(4) The biogenesis of this bond in lycoramine seems to involve phenolic oxidative coupling. Early total synthetic approaches followed this biogenetic route; see ref 1 and 2.

(5) The synthetic potential of heteroatom-directed photoarylation has been noted in recent reports from this laboratory; for example, see A. G. Schultz and R. D. Lucci, *J. Chem. Soc., Chem. Commun.*, 925 (1976). The synthesis of *dl*-lycoramine represents our first application of the methodology to natural products total synthesis.

(6) Prepared in 60% overall yield from isovanillin by a modification of the procedure described by C. Schuerch, *J. Am. Chem. Soc.*, **70**, 2293 (1948).

(7) The isomeric mixture **5a** and **5b** is easily separated by silica gel chromatography. See P. M. McCurry and R. K. Singh, *J. Org. Chem.*, **39**, 2316 (1974), and S. Danishefsky and A. Zimmer, *ibid.*, **41**, 4059 (1976), for recent studies of the factors controlling the direction of base-catalyzed aldol cyclizations of 1,4 and 1,5 diketones, respectively.

(8) The rationale for designing a synthetic intermediate to **1** with a ketone carbonyl positioned as shown in **5a** will be considered in a full paper dealing with heteroatom-directed photoarylation in aryl vinyl ethers.

(9) A detailed study of 1,2-carbonyl transposition in a related keto dihydrofuran has been performed: Y. K. Yee and A. G. Schultz, submitted for publication.

(10) D. Barnard, *J. Chem. Soc.*, 4673 (1957). Bissulfenylation of ester enolates has been developed by B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, **98**, 4887 (1976). However, it has been reported that bissulfenylations "are not easily achieved in ketones compared to esters and are somewhat capricious" (B. M. Trost and Georges Massiot, *J. Am. Chem. Soc.*, **99**, 4405 (1977)). We find that bissulfenylation of ketone **9a** may be consistently performed in 80% isolated yield.

(11) The carbonyl transposition described here is similar to that used by J. A. Marshall and H. Roebke, *J. Org. Chem.*, **34**, 4188 (1969). An essential modification is the incorporation of keto mesylate **11a** (rather than an α-acetoxy ketone) into the sequence. With the ring system considered here, α-acetoxy ketones failed to undergo reductive cleavage under a variety of conditions and chromous chloride was found to be required for reductive cleavage of **11a**; see ref 9.

(12) D. Seebach and D. Steinmüller, *Angew. Chem., Int. Ed. Engl.*, **7**, 619 (1968).

(13) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **36**, 2324 (1969).

(14) We wish to thank Professor William C. Wildman for a generous sample of authentic (−)-lycoramine.

(15) Compounds **5a**, **8a**, and **10a** gave satisfactory elemental analyses.

(16) NOTE ADDED IN PROOF. *dl*-Lycoramine has been obtained in 8.1% overall yield from **2a**.

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Electron Deformation Density Distribution for Cyclic Octasulfur by the SCF–Xα–SW Method

Sir:

We wish to report the first application of the self-consistent-field–Xα–scattered-wave method[1,2] to the calculation of electronic deformation density distributions, $\Delta\rho(\mathbf{r})$, i.e., the difference between a molecular electronic density distribution and the superposition of spherically averaged atomic distributions.[3] The orbital energies and wave functions calculated in the SCF–Xα–SW method have been employed successfully in a wide variety of applications;[4] however, no comparison has heretofore been made between the electron density distribution calculated with this method and experimental distributions determined by x-ray diffraction. Such comparisons provide a stringent test of the quality of the calculated wave functions.

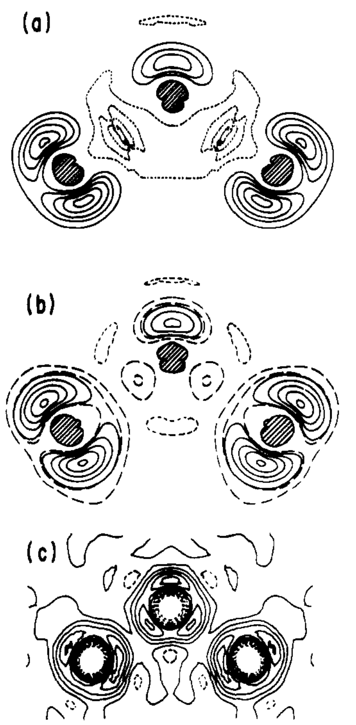

Figure 1. Deformation density for S_8 in an S–S–S face: (a) SCF–Xα–SW, s, p basis; (b) SCF–Xα–SW, extended (s, p, d, f) basis; (c) experimental, from ref 5. Contours at 0.10 e Å^{-3} (solid, positive $\Delta\rho$; short dashed, negative $\Delta\rho$). Long dashed contours in b are +0.067 and +0.007 e Å^{-3}. See ref 5 for effect of temperature parameters and differences between x-ray and neutron atomic parameters.

Coppens et al.[5] have recently reported $\Delta\rho(\mathbf{r})$ distributions for orthorhombic sulfur (S_8 molecules) derived from x-ray scattering experiments. Their results for the deformation density in a triangular S–S–S face are reproduced in Figure 1c. In Figures 1a and 1b are shown deformation densities calculated with the SCF–Xα–SW method in the muffin-tin (nonoverlapping sphere) approximation for two different basis sets. For Figure 1a, s and p waves were included in the sulfur spheres, while s, p, and d waves were used on the outer sphere; for Figure 1b, d and f waves were added to the sulfur spheres. Two intermediate cases with d waves in the sulfur spheres and waves up to $l = 2$ and $l = 4$ on the outer sphere were also examined. The results are intermediate to those shown in Figures 1a and 1b. In all cases the molecular wave functions were generated in the usual manner[6] and the electron density was calculated as the sum over contributions from all of the occupied valence levels for a mesh of 6400 points. The frozen core approximation was used throughout. A second distribution was generated by superposing the spherically averaged valence densities for s^2p^4 sulfur atoms, placed at the positions of the atoms in S_8, calculated by the Herman–Skillman method[7] (the atomic Xα method) for the same value of α (0.72475)[8] as for the molecule. A point by point subtraction was then carried out to yield the deformation density.

The comparison of Figure 1a and 1b with Figure 1c involves a number of assumptions and possible uncertainties which space restrictions do not allow us to discuss in detail. These include (i) the neglect of crystal packing effects; (ii) the neglect of molecular and crystal vibrations, i.e., temperature effects (see ref 3, 5, 9, and 10 for a discussion); (iii) possible systematic errors remaining in the experimental data (see ref 3 and 5 for