vary from a typical double bond distance to longer than a normal single bond (1.89 (2) – 2.52 (3) Å). The structure and bonding in **5** are clearly quite unusual, but in one resonance form **5** can be viewed as containing a rhenium(III) center with a terminal oxo ligand, Re(O)(μ-O-)(EtC$\equiv$CEt)$_2$, similar to **2**, and a rhenium(I) center, Re(μ-O-)(EtC$\equiv$CEt)$_3$, related to ReI(EtC$\equiv$CEt)$_3$[17] and isoelectronic W(CO)(PhC$\equiv$CPh)$_3$.[18]

The ^{1}H and ^{13}C NMR spectra of **5** at −40 °C show eight nonequivalent ethyl groups and eight acetylenic carbon resonances,[11] but on warming four of the sets of ethyl groups coalesce to two sets; the nature of this fluxional process will be described in detail in a future publication. On heating to 100 °C, **5** stoichiometrically converts to **4** in 1 h (Scheme I). Our inability to observe a 2-butyne analogue of **5** starting from **1** may be due to its more facile conversion to **3**. The fact that the isomer with two terminal oxo groups bound to rhenium(II) centers (**4**) is thermodynamically more stable than the isomer with a bridging oxo ligand (**5**) indicates that rhenium–oxygen multiple bonding is favorable in this case despite the low formal oxidation state.

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Supplementary Material Available: Listing of spectroscopic and analytical data for **3**–**5** and tables of atomic coordinates, bond distances and angles, anisotropic temperature factors, and hydrogen atom coordinates for **3** and **5** (12 pages); tables of observed and calculated structure factors for **3** and **5** (27 pages). Ordering information is given on any current masthead page.

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A Convergent Strategy for Synthesis of *Erythrina* Alkaloids

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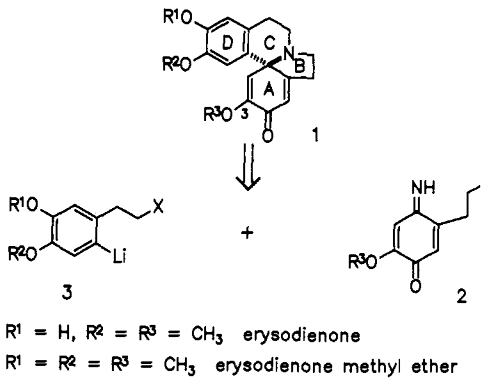
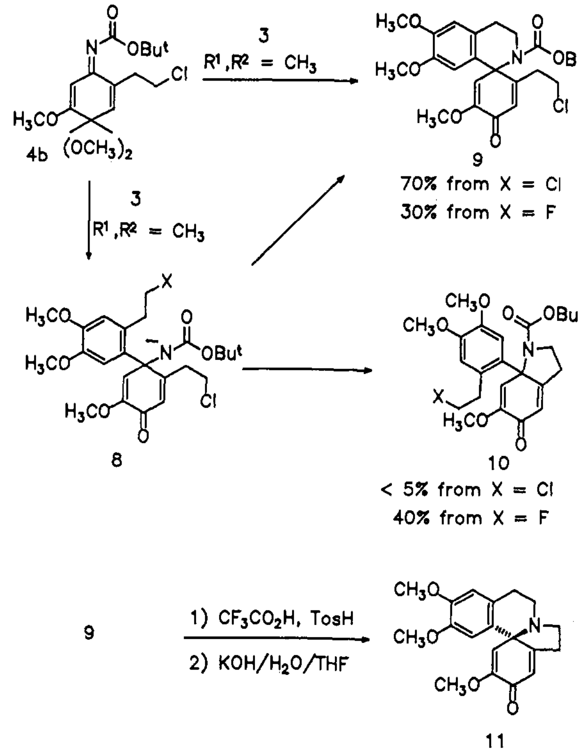
The synthesis of *Erythrina* alkaloids and homoerythrinans has been of interest for over 25 years,[1,2] and a variety of synthetic strategies have been employed in preparing the tetracyclic ring system of these compounds.[1,3] The addition of a functionalized organolithium reagent, e.g., **3**, to a quinone imine such as **2** would comprise a new, convergent strategy to the ring system of these biologically and synthetically interesting compounds (Scheme I). Quinone imide ketals are available in one step by anodic oxidation of the corresponding *p*-alkoxyanilides[4] and could serve as regiospecific equivalents of quinone imine such as **2**. Since the dienone moiety of the A ring has been converted to the various oxygenation patterns present in the naturally occurring compounds,[1,5] an intermediate such as **1** would be especially useful synthetically. We report herein the successful execution of the general strategy outlined in Scheme I to afford the methyl ether of erysodienone.

Scheme I. Strategy for a Convergent Approach to the *Erythrina* Alkaloid Skeleton



Scheme II. The Quinone Imide Ketal Route to *Erythrina* Alkaloids



Since many *Erythrina* alkaloids possess a methoxyl group at C-3 and since this group would be expected to deactivate the imide linkage toward organolithium addition to the imide carbon, the viability of the strategy was examined by studying the reaction of aryllithium reagents with the quinone imides **4a** and **6**. The required compounds for this study were either commercially available or prepared via standard methods from commercially

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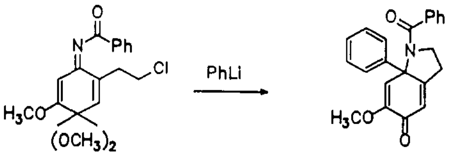
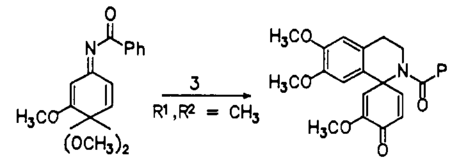
available compounds. Thus, 4,5-dimethoxy-2-(2-chloroethyl)-aniline, the key intermediate for the preparation of **4a,b**, was prepared by nitration of 3,4-dimethoxyphenylacetic acid, followed by diborane reduction of the acid to the alcohol (99%) and conversion of the alcohol to the chloride (triphenylphosphine, carbon tetrachloride, 95%). Hydrogenation of this nitro compound afforded the above aniline, which was immediately reacted with benzoyl chloride (77% over two steps). Anodic oxidation[4] of the benzanilide furnished **4a** (90%).

The addition reactions of phenyllithium with **4a** and also **3** (R^1, R^2 = CH_3, X = Cl)[6,7] with **6** were conducted at -78 °C for 0.5 h. The reaction mixtures were then warmed to room temperature and heated to reflux for 1 h to effect the intramolecular cyclization. The resulting ketals were purified by chromatography on activity III neutral alumina and hydrolyzed with 5% aqueous acetic acid to give **5** (65% overall) and **7** (67% overall) after recrystallization. This chemistry demonstrated that both the B and C rings of the *Erythrina* skeleton could be formed via intramolecular cyclization. However, all attempts to hydrolyze the amide linkages of **5** and **7** led either to no hydrolysis or to destruction of the dienone unit.



4a

5 (65%)



6

7 (67%)

The most direct method for effecting the final ring closure to the *Erythrina* tetracyclic skeleton would be hydrolysis of the amide group and intramolecular ring closure of the resulting amine with a side-chain having a leaving group. The *tert*-butoxycarbonyl group was chosen as the protecting group for the imide nitrogen in the hope that the subsequent deprotection of the amine could be effected without competing dienone-phenol rearrangement. The required precursor to **4b** was prepared by reaction of 4,5-dimethoxy-2-(2-chloroethyl)aniline with phosgene to form the isocyanate (70%), followed by reaction with *tert*-butyl alcohol to give the respective urethane (90%). Anodic oxidation of this urethane gave the quinone imide ketal **4b** in 90% yield.

Reaction of **3** (R^1, R^2 = CH_3, X = Cl) with **4b** essentially as outlined in the model studies afforded a crystalline product (70%) (Scheme II). However, spectroscopic data did not allow a clear choice between the two possible structures **9** and **10** (X = Cl). In simple systems, formation of a pyrrolidine is usually faster than ring closure to afford a piperidine;[8] however, it was desirable for future work to establish unequivocally the initial product from the addition. Reaction of the fluoro derivative **3** (R^1, R^2 = CH_3, X = F) with **4b** gave **9** (30%) in addition to the fluoro compound **10** (X = F, 40%).[9] This experiment established **9** as the product from reaction of **4b** with **3** (R^1, R^2 = CH_3, X = Cl). Thus, the intermediate amide anion **8** undergoes preferred closure to the six-membered ring. Reaction of **9** with trifluoroacetic acid/*p*-toluenesulfonic acid at room temperature deblocked the *tert*-butoxycarbonyl derivative to give the crude amine, which underwent cyclization to form **11** (80%), thus completing the sequence.

This chemistry comprises a new, convergent approach to the synthesis of the *Erythrina* alkaloids. The route is especially convenient since both segments of the *Erythrina* skeleton derive from 3,4-dimethoxyphenylacetic acid. In addition, this synthetic strategy could be adapted to the synthesis of the homoerythrinans and other biologically interesting nitrogen-containing spiro ring systems.

Acknowledgment. We thank the National Science Foundation for partial support of this work.

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(6) The lithium compound **3** was prepared via reaction of 2-(2-chloroethyl)-3,5-dimethoxybromobenzene with 2 equiv of *tert*-butyllithium at -78 °C. Although this reagent is known to form the corresponding benzocyclobutene on reaction at room temperature, successful annelation of this organolithium with benzonitrile has been reported.[7]

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(8) Knipe, A. C.; Stirling, C. J. M. *J. Chem. Soc. B* **1968**, 67.

(9) This product showed in the ^{1}H NMR spectrum the lowest field methylene group as a doublet of triplets with J_{HH} = 5.8 Hz and J_{HF} = 47.3 Hz and in the ^{19}F NMR spectrum the fluorine resonance at δ -218.4 as a triplet of triplets (J = 47.3 and 25.6 Hz).

(10) Part of this work was presented at the 19th Central Regional Meeting of the American Chemical Society, June 24-26, 1987, paper no. 282. The structural assignments were supported by the usual spectroscopic properties and exact mass measurements or combustion analyses. The following compounds were crystalline and had the indicated melting points: **4b**, 100 °C (dec); **5**, 223-225 °C; **5** (dimethyl ketal), 161-163 °C; **6**, 66-69 °C; **7**, 223-226 °C; **9**, 143-145 °C; **10** (X = F), 138-140 °C; **11**, 161-162 °C (dec).

NMR of Di-^{13}C-Labeled Compounds: Insights into the Effect of Alkylation, Ionization, and Micellization on Conformation†

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We have recently exploited a method[1,2] for detecting chain folding based on long-range coupling between two ^{13}C atoms spaced four carbons apart ($-{}^*CH_2-CH_2-CH_2-{}^*CH_2-$).[3] Thus, ^3J decreases from 3.5-4.0 to 1.5 Hz when a trans conformation about the central bond rotates into a gauche conformation (as was observed, for example, in the binding of an inhibitor to an enzyme).[3] The method is nondisruptive and works equally well for ordered and disordered systems. In the present communication, the power of the method is demonstrated with several dilabeled molecules whose conformations are affected by alkylation, ionization, and micellization. Information was obtained that is impossible to secure by any other means.

[1,4-$^{13}C_2$]Myristic acid, synthesized according to Scheme I, has ^3J = 3.5 ± 0.1 Hz which is independent of (a) the solvent (25 mM in chloroform, tetrahydrofuran, acetone, acetonitrile, and dimethyl sulfoxide), (b) the temperature (25-65 °C in dimethyl sulfoxide), (c) the particular doublet under scrutiny (namely that of the carbonyl or methylene carbon), and (d) the spectral mode (traced normally or with the aid of a 32-phase INADEQUATE sequence[4]). Since 3.5 Hz falls close to the value expected for a trans disposition,[5-7] myristic acid must be "linear", or nearly so, under all the above conditions (structure I). When, however,

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† Dedicated to Professor Ye Xui-Lin, Peking University, author of *Stereochemistry* (PRC, 1983).

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