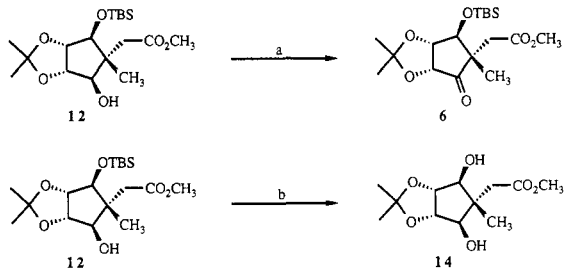
Scheme IV[a]



[a] (a) PDC, CH_2Cl_2, 3-Å sieves, HOAc; (b) *n*-Bu_4NF, THF, 23 °C.

It should be noted that a more direct means of constructing carbohydrate template **11** can be envisioned as arising from a direct Wittig with hemiketal **8**, which would apparently avoid the protection–deprotection sequence realized above. However, in our previous experience with Wittig reactions of arabinose lactols[4] with stabilized ylides, we have only observed the undesired cis isomer as the major product. Similar results with furanose lactols have been observed by Wilcox and co-workers.[13] It appears that the C_5 hydroxyl functionality in the acyclic form of the lactol plays a role in the formation or decomposition of the oxaphosphatane and leads to a predominance of the cis isomer. Blocking the C_5 hydroxyl functionality as its *tert*-butyldimethylsilyl ether and "locking" the hemiketal in its acyclic ketone form insures the trans product will predominate in the Emmons Wittig reaction.[13]

Thus, treatment of **11** with samarium diiodide in tetrahydrofuran at −78 °C in the presence of methanol as a proton donor produced the highly oxygenated cyclopentane **12** and a minor lactone product **13** in a ca. 5:1 ratio, respectively, as shown in Scheme III. The major product could be easily isolated by flash chromatography in 65% yield. A final oxidation of the sole ring hydroxyl funtionality to ketone **6** in 81% yield completed the synthesis of the protected C ring of anguidine, as shown in Scheme IV.

The stereochemistry of **12** was confirmed by deprotection of the *tert*-butyldimethylsiloxyl moiety by treatment with fluoride ion. A plane of symmetry was clearly apparent in *syn*-diol **14** as was evidenced by the simple ^1H NMR and the 10-line ^{13}C NMR spectra. Additional confirmation of the stereochemistry of this cyclization came from difference NOE experiments. Irradiation of the methylene protons on the ester appendage produced a 9.8% enhancement of the two equivalent β-disposed protons on the hydroxy-bearing ring carbons. Thus, a combination of chemical and spectroscopic methods unequivocally confirmed the stereochemistry of this polyoxygenated ring.

In conclusion, the enantioselective synthesis of the C ring of anguidine has been accomplished in eight steps from the known (L)-arabinose lactol **7**. The key transformation involved the one-electron reductant samarium diiodide in the transformation of a carbohydrate to a carbocycle. In this reaction, the stereoselective cyclization of **11**, which contains an aldehyde tethered to an activated alkene, produced the polyoxygenated cyclopentane **12**, a crucial intermediate in the synthesis. Additional efforts in the samarium diiodide mediated conversion of carbohydrates to carbocycles and their use in synthesis will be reported in due course.

Acknowledgment. Support for this work from the American Cancer Society (Grant No. IN47495), the Division of Sponsored Research, and the Department of Chemistry at the University of Florida is gratefully acknowledged.

(13) Webb, T. H.; Thomasco, L. M.; Schlachter, S. T.; Gaudino, J. J.; Wilcox C. S. *Tetrahedron Lett.* **1988**, 6823.

The Chemistry of Vicinal Tricarbonyls. A Total Synthesis of (±)-3-Demethoxyerythratidinone

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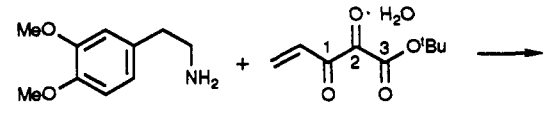
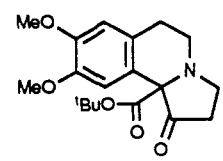
Summary: The tricyclic pyrrolidone carboxylate **3** formed from the reaction of 2-(3,4-dimethoxyphenyl)ethylamine (**1**) with the vinyl tricarbonyl reagent **2** has been converted to the erythrina alkaloid (±)-3-demethoxyerythratidinone (**12**).

Sir: In an earlier report on the chemistry of tricarbonyl systems we described the reaction of 2-(3,4-dimethoxyphenyl)ethylamine (**1**) with the vinyl tricarbonyl ester **2** followed by treatment with a Lewis acid ($POCl_3$) to yield the tricyclic product **3**.[1] The ready formation of **3** is a consequence of the enhanced reactivity of the central carbonyl at C-2 in **2** which, together with the adjacent α,β-unsaturated carbonyl grouping, provides a trielectrophilic receptor for the donor sites in **1**. This reaction is of special interest in that the two carbonyl groups at C-1 and C-3 in **2**, which play an activating role in the reaction of **1** with **2**, remain favorably disposed for further elaboration of the tricyclic product **3** to the tetracyclic system found in the erythrina family of alkaloids.



1 **2**



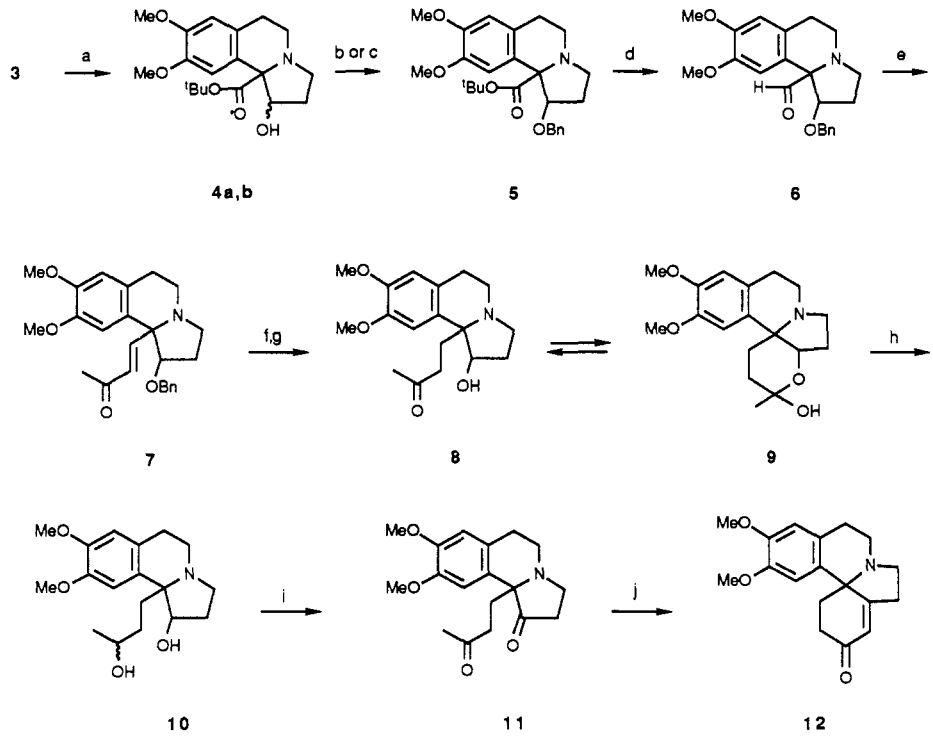
3

We now describe the use of compound **3** for the formation of (±)-3-demethoxyerythratidinone (**12**). This alkaloid, first isolated from *Erythrina lithosperma* by Barton,[2,3] has been synthesized in a number of recent in-

(1) Wasserman, H. H.; Fukuyama, J.; Murugesan, N.; van Duzer, J.; Lombardo, L.; Rotello, V.; McCarthy, K. *J. Am. Chem. Soc.* **1989**, *111*, 371.

0022-3263/89/1954-5843$01.50/0

Scheme I[a]



[a] (a) $NaCNBH_3$, HOAc, 0 °C to 20 °C, 1.5 h; (b) NaH, BnBr, THF, 3 h; (c) NaH, BnBr, NaI, THF, 7 h; (d) $LiAlH_4$, Et_2O, 0 °C, 45 min; (e) NaH, toluene, $(MeO)_2P(O)CH_2COCH_3$, reflux, 36 h; (f) H_2, 5% Pd/C, 55 psi, acetone, 4 h; (g) H_2, 10% Pd/C, acetone, cat. concentrated HCl, 16 h; (h) $NaBH_4$, MeOH, 0 °C, 30 min; (i) DMSO, $(ClCO)_2$, CH_2Cl_2, −78 °C, 1 h; Et_3N, room temperature, 10 min; (j) NaOH, MeOH, reflux, 24 h.

vestigations.[4a-d] Our synthetic plan focused on the addition of a three-carbon fragment to **3**, which would permit the formation of the required cyclohexenone ring as illustrated in Scheme I.

Compound **3** was reduced with sodium cyanoborohydride in acetic acid to give the diastereomeric alcohols **4a,b** (83%) (ca. 1:1 ratio). We found that treatment of each isomer of **4** under benzylation conditions (NaH, $PhCH_2Br$) resulted in the formation of a single diastereomer of the benzyl ether **5** (85% and 70%).[5] This protected ester was then reduced with excess lithium aluminum hydride to give the aldehyde **6** (89%).[6] Compound **6** was then converted to the *trans*-enone **7** by a Horner–Emmons reaction with the anion of 2-oxopropyl dimethyl phosphonate (73%). Hydrogenation in two stages resulted first in the reduction of the enone functionality (96%) and then in the removal of the benzyl ether protecting group (95%), forming the keto alcohol **8**. The latter existed predominantly in the hemiketal form **9** as shown by the ^1H NMR data (1:4 ratio of **8**/**9**). Reduction of this species with sodium borohydride in methanol[7] gave the diol **10**, which was then oxidized with excess Swern reagent to yield the desired diketone **11** (79%).[8] In the final step, treatment of **11** with sodium hydroxide in refluxing methanol resulted in an intramolecular aldol condensation along with dehydration to give (±)-3-demethoxyerythratidinone (**12**) (41%). The synthetic material was indistinguishable (^1H NMR, IR, mass spectrum) from a sample of the natural material.[9]

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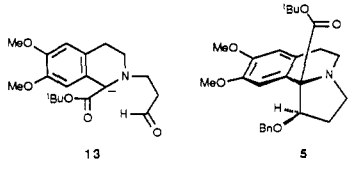
Supplementary Material Available: Spectroscopic data for all new compounds (4 pages). Ordering information is given on any current masthead page.

(2) Barton, D. H. R.; Gunatilaka, A. A. L.; Letcher, R. M.; Lobo, A. M. F. T.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1971**, 874.

(3) For a recent review on erythrina alkaloids, see: (a) Chawla, A. S.; Jackson, A. H. *Nat. Prod. Rep.* **1984**, 371. (b) Dyke, S. F.; Quessy, S. N. *The Alkaloids: Chemistry and Physiology*; Manske, R. H. F., Rodrigo, R. G. A., Eds.; Academic Press: New York, 1981; Vol. XVIII, Chapter 1.

(4) (a) Tsuda, Y.; Nakai, A.; Kazo, I.; Suzuki, F.; Haruna, M. *Heterocycles* **1984**, *22*, 1817. (b) Danishefsky, S. J.; Panek, J. S. *J. Am. Chem. Soc.* **1987**, *109*, 917. (c) Ishibashi, H.; Sato, T.; Takahashi, M.; Hayashi, M.; Ikeda, M. *Heterocycles* **1988**, *27*, 2787. (d) Irie, H.; Shibata, K.; Matsuno, K.; Zhang, Y. *Heterocycles* **1989**, *29*, 1033.

(5) We assume that the individual isomers (**4a** and **4b**) undergo equilibration in base through **13** to form the more stable benzyl ether **5**.



(6) For a recent report on the reduction of esters with $LiAlH_4$ to give aldehydes, see: Cha, J. S.; Kwon, S. S. *J. Org. Chem.* **1987**, *52*, 5486.

(7) Poss, A. J.; Belter, R. K. *J. Org. Chem.* **1988**, *53*, 1535.

(8) Attempts were made to oxidize the mixture containing **8** and **9** directly to **11**. However, only very low yields of **11** were obtained under Jones, Collins, or Swern oxidation conditions.

(9) Kindly provided by Prof. S. J. Danishefsky.