The $Pt(C_2H_4)Yb$ interaction in I is obviously a weak interaction not unlike the d-transition metal olefin–alkali metal interactions found by Jonas and Klein.[11]

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Supplementary Material Available: Tables of atomic positional parameters, thermal parameters, and bond lengths and angles (8 pages). Ordering information is given on any current masthead page.

(11) (a) Jonas, K. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 47. (b) Brauer, D. J.; Krüger, C.; Roberts, P. J.; Tsui, Y. H. *Ibid.* **1976**, *15*, 48. (c) Goddard, R.; Krüger, C.; Pörschke, K. R.; Wilke, G. *J. Organomet. Chem.* **1986**, *308*, 85–103. (d) Klein, H. F.; Gross, J.; Bassett, J. M.; Schubert, U. *Z. Naturforsch., B* **1980**, *35b*, 614–619. (e) Klein, H. F.; Witty, H.; Schubert, U. *J. Chem. Soc. Chem. Commun.* **1983**, 231–232.

Total Synthesis of (±)-3-Demethoxyerythratidinone: Demonstration of a Radical Cyclization Route to a Site Specific Enol Derivative

Samuel J. Danishefsky* and James S. Panek[1]

Department of Chemistry, Yale University
New Haven, Connecticut 06511

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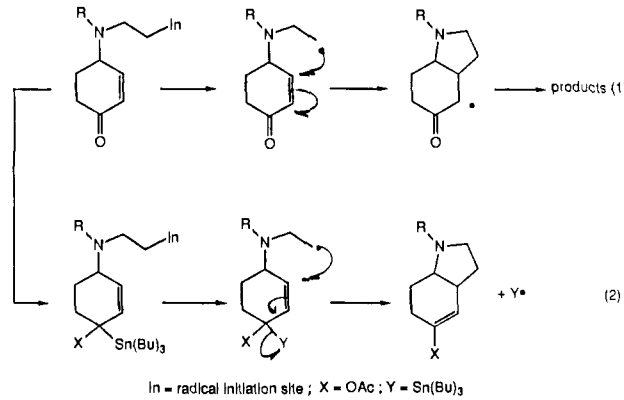
3-Demethoxyerythratidinone (**12**) was isolated from *Erythrina lithosperma* in 1971 by Barton and colleagues.[2a] Though it is structurally one of the simplest of the erythrina alkaloids,[2b] its total synthesis was not achieved until 1984 by Tsuda in several related ways.[3] One of the Tsuda intermediates en route to **12** was the dihydro compound **9**. The conversion[4] of **9** to **12** was accomplished, in ca. 30% yield.

The synthetic studies described herein arose from a convergence of several considerations. It was intended to explore the wider ramifications of a strategem which we first described in 1982[5,6] wherein a β-oxygen-substituted free radical, generated in the presence of a proximate α,β-unsaturated carbonyl system, can cyclize by an intramolecular Giese-type reaction.[7] It was hoped to extend the process to a carbon radical bearing a vicinal nitrogen atom in the connecting chain. This formulation, expressed in eq 1, was in fact realized (vide infra **8** → **9**).

Still more attractive was the possibility of establishing a site-specific enol derivative directly through a free radical cyclization dynamic. The concept is expressed in eq 2. The advantages to be gained from smooth access to regiochemically defined enolate equivalents need not be underscored at this time, since they were well perceived and demonstrated by Stork[8a] and House[8b] many years ago. Hitherto, such systems have been traditionally developed through carbanionic intermediates. In this paper we report the realization of this concept in practice via the use of an allylic geminal acyloxystannane (see sequence **8** → **10** → **11**).[9a,b] This new chemistry is the basis of a remarkably direct synthesis of the titled compound, **12**.



The starting material was the Boc derivative of dopamine dimethyl ether (**1**)[10] which upon bromination (Br_2/CH_2Cl_2–K_2CO_3, −78 °C) afforded a 94% yield of the bromo compound **2**,[11] mp 101–103 °C. The potassium salt, generated in situ by the treatment of **2** with potassium hydride in tetrahydrofuran (THF, 25 °C), was converted to its corresponding aryllithium species **2a** by metalation with *n*-BuLi in THF (−78 °C). The other building block was the interesting enone ketal **4**, mp 66–68 °C,[11] obtained (88%) by enol silylation of the commercially available **3** (Me_3SiOTf; Et_3N; CH_2Cl_2) followed by oxidation with palladium(II) acetate (MeCN, 25 °C, 12–14 h).[12]

Coupling of **2a** with **4** (THF, −78 → −30 °C, 8–10 h) afforded the tertiary alcohol **5**[11] in 80–90% yield. The latter underwent a most useful transformation through the action of trimethylsilyl triflate in methylene chloride (−78 °C, 8–10 h). While, in qualitative terms, the formation of **6**[11,13] (mp 169–171 °C) need occasion little surprise, the precise order of steps is not currently known. Treatment of **6** with DBU afforded a 95% yield of the spiro enone, mp 128–130 °C.[7,11] The goal substrate **8**[11] was obtained in 45% yield[14] by the reductive amination of **7** with phenylselenoacetaldehyde **15** (5 equiv) (via sodium cyanoborohydride, 6 equiv, in 1:1 THF–methanol). The directness of this route compensates for the modest yield of the reductive amination.

Treatment of compound **8** with $(n\text{-}Bu)_3SnH$[16] (2–4 equiv, benzene reflux) in the presence of catalytic AIBN (5–10 mol %) led to an 88% yield of **9**.[3] Thus the conjecture embodied in eq 1 has been demonstrated in practice. The internal "Michael-like" free radical cyclization has been demonstrated with a nitrogen

(1) Present address: Department of Chemistry, Boston University, Boston, MA 02215.

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(9) For recent reports which serve as precedents, see: (a) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *Tetrahedron Lett.* **1985**, *26*, 957. (b) Keck, G. E.; Enholm, E. J. *Tetrahedron Lett.* **1985**, *26*, 3311.

(10) Tsuda has reported the carbomethoxy version of **10**, see: Tsuda, Y.; Isobe, K.; Toda, J.; Taga, *J. Heterocycl.* **1976**, *5*, 157.

(11) This compound displayed satisfactory ^1H NMR (250 or 500 MHz), infrared, MS, and high-resolution mass spectrum.

(12) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.

(13) Though the stereochemistry of the C5–C6 ring junction (erythrina numbering) of cyclic carbonate **6** was not rigorously proven, ^1H NMR (500 MHz) and proton-decoupling experiments fully support the stereochemistry of the ring junction to be cis, as expected.

(14) For reasons that we do not yet understand, the reaction does not go to completion, even with excess reagents. Substantial amounts of pure enone **7**, ca. 20–25%, are recovered. These are not included in the yield.

(15) Toshimitsa, A.; Aoai, S.; Uemura, S.; Okano, M. *J. Org. Chem.* **1980**, *45*, 1953. Toshimitsu, A.; Aoai, T.; Owada, H.; Uemara, S.; Okano, M. *Tetrahedron* **1985**, *41*, 5301.

(16) Cf.: Burke, S. D.; Fobare, W. F.; Armistead, D. M. *J. Org. Chem.* **1982**, *47*, 3348.

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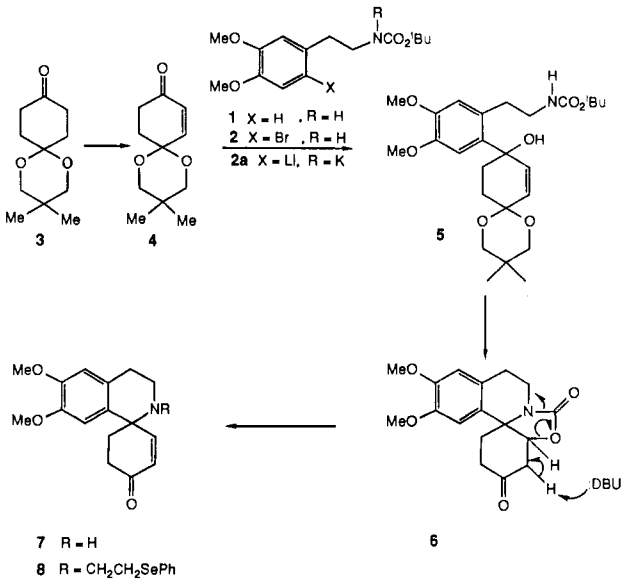
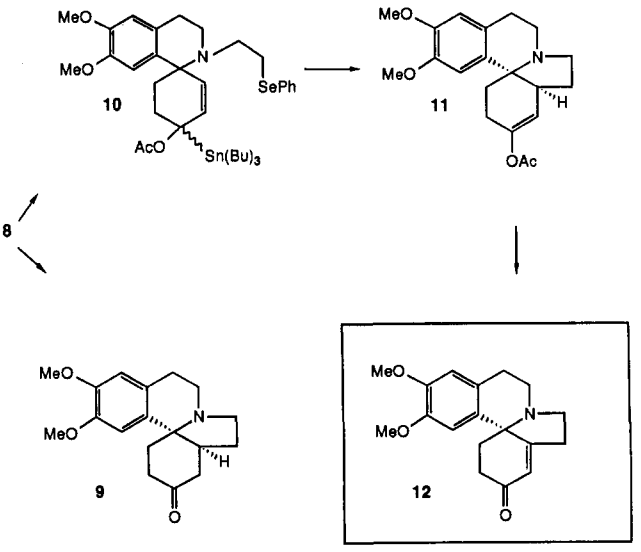


function[9a] in a vicinal relationship to the radical species. In light of the Tsuda work,[3] the synthesis of compound **9** constituted a formal total synthesis of **12**. The reduction to practice of the synthetic logic implied in eq 2 started with treatment of compound **8** with tri-*n*-butyllithiostannane[17] (Et_2O, −78 °C). Following extractive isolation, the resultant hydroxystannane was immediately acetylated with acetic anhydride (DMAP, CH_2Cl_2, Et_3N) to afford an 83% yield of ca. a 1:1 mixture of stereoisomers **10**. Happily, treatment of mixture **10** with $(n\text{-Bu})_3SnH$ in the presence of catalytic AIBN (5–10 mol %) afforded a 65% yield of a single stereoisomer formulated as **11**.[11,18] Advantage was now taken of the site-specific enol acetate. A three-step sequence [(i) MeLi–THF; (ii) PhSeCl, −78 °C; (iii) $NaIO_4$, aqueous THF) afforded a 64% yield of crystalline **12**, mp 105–108 °C, lit.[3] mp 101–102 °C. The NMR (500 MHz) and infrared spectra of synthetic **12**, as well as its chromatographic mobility, are identical with those of a reference sample provided by Professor Tsuda.



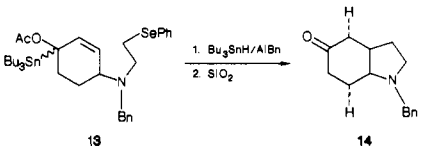
The work described herein suggests a high susceptibility for α-oxygenated, α-stannylated allylic systems to undergo free radical attack at the γ-carbon. In the case shown above, the radical source was tethered to the allylic residue by a nitrogen atom attached to the δ-carbon.[19] Other permutations for the tethering, as well as other variations in the nature of the attacking radical, might find extension to both heterocyclic and alicyclic synthesis. Such possibilities will be receiving continuing attention in our laboratories.

Acknowledgment. This work was supported by PHS Grant HL 25848. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE 7916210. A PHS Postdoctoral Fellowship (Grant 5 F32 CA07752) to J.S.P. is gratefully acknowledged. We thank Professor Yoshisuke Tsuda of Kanazawa University for providing reference materials.

(17) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

(18) The stereochemistry of the C5–C6 ring junction (erythrina numbering) of enol acetate **11** was based on ^1H NMR (500 MHz) experiments. The *J* value for the C1 vinyl proton equals 3.6 Hz. Thus, the C6 proton is equatorial and th C5–C6 ring junction is cis.

(19) That the additional rigidity imposed by the spiro tethering and the benzo linkage is not a sine qua non for the success of the reaction is suggested by the smooth transformation of the mixture cyclohexenyl epimers **13** to *cis*-*N*-benzyloctahydro-6-oxoindole (**14**).



Simple Synthetic Route to the Limonoid System

E. J. Corey,* J. Gregory Reid, Andrew G. Myers, and Robert W. Hahl

Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
Received September 26, 1986

Since the elucidation of the structure of limonin in 1960,[1] a large number of naturally occurring substances in this family, the limonoids,[2] have been isolated and characterized structurally. Despite the widespread occurrence of the limonoids (and further metabolic products such as the quassins) in nature and their interesting biological properties, the total synthesis of these compounds has remained an unsolved problem. We now report the first synthesis of the limonoid system by a simple route which is nonetheless sufficiently versatile to provide access to many limonoids.

The enol phosphate **1** was prepared in one flask in 80% yield by reaction of farnesyl bromide at 0 °C in tetrahydrofuran (THF) with the sodio and lithio derivative of methyl acetoacetate (1.2 equiv, 2 h), cooling to −78 °C, and further reaction with diethyl chlorophosphate (−78 °C for 20 min, −20 °C for 2 h).[3,4a] Slow addition of **1** (over 1.5 h) in dry nitromethane solution (0.1 M) to a solution of mercuric trifluoroacetate (0.08 M in nitromethane) at −22 °C and further reaction for 1 h at −22 °C afforded, after stirring with aqueous sodium chloride and isolation,[4a] tricyclic keto ester **2** (27–30% yield) as a crystalline solid, mp 201–202 °C.[5] Replacement of mercury by phenylseleno[11] was accomplished by treatment with diphenyl diselenide in methylene chloride solution at 23 °C with irradiation by a sunlamp (20 min), and the resulting selenide[4b] was converted to olefin **3**[4b] (70% overall) by oxidation with *m*-chloroperbenzoic acid at −78 °C in methylene chloride and then warming (in the presence of dimethyl sulfide and triethylamine) at 45 °C for 20 h. Keto ester **3** was transformed into the enol ester **4** (sodium hydride in THF at 23 °C for 3 h followed

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(3) All reactions involving air-sensitive reactants or products were conducted under dry argon.

(4) Purification by silica gel chromatography using (a) hexane–ethyl acetate and (b) hexane–ether.

(5) See: Corey, E. J.; Tius, M. A.; Das, J. *J. Am. Chem. Soc.* **1980**, *102*, 1742, 7612.

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