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.

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

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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 conversion⁴ 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 $8 \rightarrow 9$).

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 ad-

(4) The precise regioselectivity of the sulfenylation reaction which was the first step of the dehydrogenation sequence is not clearly revealed from Tsuda's data

(5) Danishefsky, S. J.; Chacalamannil, S.; Uang, B.-J. J. Org. Chem. 1982, 47, 2231. Danishefsy, S.; Taniyama, E.; Webb, R. R. Tetrahedron Lett. 1983, 24, 11. Danishefsy, S.; Taniyama, E., Ibid. 1983, 24, 15.

(6) For recent reviews concerning the use of free radical cyclizations in organic synthesis, see: Giese, B., Ed.; Tetrahedron Symposia-in-Print; *Tetrahedron*, 1985, 41 (19), 3887–4289. Hart, D. Science (Washington, D.C.) 1984, 223, 883.

(7) Giese, B.; Horler, H.; Zwick, W. Tetrahedron Lett. 1982, 23, 531.



vantages 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 $8 \rightarrow 10$ \rightarrow 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 silvlation of the commercially available 3 (Me₃SiOTf; Et₃N; CH₂Cl₂) followed by oxidation with palladium(II) acetate (MeCN, 25 °C, 12-14 h).12

Coupling of 2a with 4 (THF, $-78 \rightarrow -30$ °C, 8-10 h) afforded the tertiary alcohol 5¹¹ 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% yield¹⁴ 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 $(n-Bu)_3SnH^{16}$ (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

(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), (11) The solution 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)

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^{(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.

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^{(2) (}a) 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. (b) For recent reviews on erythrina alkaloids, see: Chawla, A. S.; Jackson, A. H. Nat. Prod. Rep. 1984, 371. Dyke, S. F.; Quessy, S. N. In The Alkaloids: Chemistry and Physiology; Vol XVIII, chapt. 1, eds. Manske, R. H. F., Rodrigo, R. G. A., Eds.; Academic: New York, 1981; Vol. XVIII, Chapter

⁽³⁾ Tsuda, Y.; Nakai, A.; Kazo, I.; Suzuki, F.; Haruna, M. Heterocycles **1984**, *22*, 1817.

^{(8) (}a) Stork, G.; Darling, S. D. J. Am. Chem. Soc. 1964, 86, 1761. (b) For a compilation of early studies in this area, see: House, H. O. Rec. Chem. Prog. 1967, 28, 99.

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

⁽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) G.; Bucke, S. D.; Echera, W. E. Armierard, D. M. J. Org. Chem.



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-butyllithiostannane¹⁷ (Et₂O, -78 °C). Following extractive isolation, the resultant hydroxystannane was immediately acetylated with acetic anhydride (DMAP, CH₂Cl₂, Et₃N) to afford an 83% yield of ca. a 1:1 mixture of stereoisomers 10. Happily, treatment of mixture 10 with (n-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) NaIO₄, 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.

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(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

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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 phenylseleno¹¹ 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

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

⁽¹⁸⁾ The stereochemistry of the C5-C6 ring junction (erythrina number-ing) 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.

⁽¹⁾ Arigoni, D.; Barton, D. H. R.; Caglioti, L.; Corey, E. J.; Sukh Dev; Ferrini, P. G.; Glazier, E. R.; Jeger, O.; Melera, A.; Pradhan, S. K.; Schaffner, K.; Sternhell, S.; Templeton, J. F.; Tobinaga, S. *Experentia* 1960, 16, 41.

⁽²⁾ For a recent review, see: Taylor, D. A. H. Prog. Chem. Org. Nat. Prod.

^{1984, 45, 1.} (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.