and the Camille and Henry Dreyfus Foundation. Funding for the purchase of a capillary GC (NSF-RUI) and a 200-MHz NMR spectrometer (NSF-RUI, NSF-CSIP, Research Corporation, Dreyfus Foundation) are gratefully acknowledged. We would like to acknowledge the experimental assistance of Clarence Wang.

Note added in proof: The interpretation presented in this communication is consistent with the observations of Wilcox which indicate that the presence of a 1,3 diaxial-like interaction slows down the rate of [3, 3] sigmatropic rearrangement for silyl ketene acetals (Babston, R. E.; Wilcox, C. S. *Abstracts of Papers*, 191st National Meeting of the American Chemical Society, New York, April 13–18, 1986, American Chemical Society: Washington, DC; ORGN 162).

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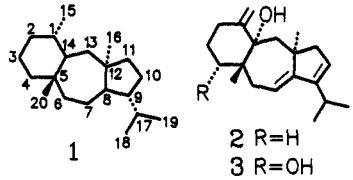
Annulations Leading to Diene Systems. Total Synthesis of the Diterpenoid (±)-(14*S*)-Dolasta-1(15),7,9-trien-14-ol

Summary: The total synthesis of (±)-**2** (the title compound) was achieved via a sequence of reactions (Scheme II) in which a newly developed annulation sequence (see **23** → **25**) played a key role.

Sir: The dolastane-type diterpenoids, which constitute a structurally and physiologically interesting family of marine natural products, possess the carbon skeleton shown in **1**.[1] The absolute stereochemistry of these substances

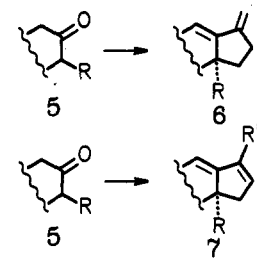


1

2 R=H
3 R=OH
4 R=OAc

is known.[1g,h] Of the various members of this class that have been reported to date, three (**2**,[1f] **3**,[1g] and **4**[1b,g]) contain a conjugated, heteroannular diene system involving carbons 7–10.

Recently, we described[2] a new annulation sequence represented in general terms by **5** → **6**. We report herein a variant of this method that produces products in which both double bonds of the diene system are endocyclic (see **5** → **7**). Furthermore, we describe a total synthesis of (±)-(14*S*)-dolasta-1(15),7,9-trien-14-ol (**2**)[1f] via a route in which the new annulation sequence plays an important role.



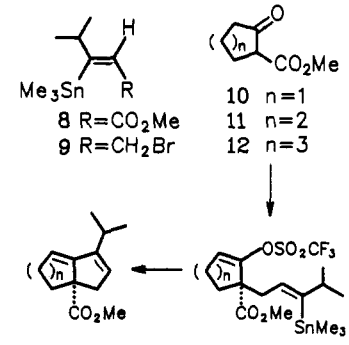
5 **6**

5 **7**

Reaction of methyl 4-methyl-2-pentynoate with $[Me_3SnCuSPh]Li$ (THF, −48 °C, 4 h; NH_4Cl)[3] produced (83%) the ester **8**[4] (Scheme I), which was conveniently converted (i-Bu_2AlH, Et_2O; Ph_3PBr_2, Et_3N, CH_2Cl_2; 80%) into the allylic bromide **9**. Alkylation (KH, THF, room temperature) of the keto esters **10**–**12** with **9** and conversion[5] of the resultant products into the enol triflates **13**–**15** was accomplished in overall yields of about 70%. Treatment of **13**–**15** with $(Ph_3P)_4Pd$ (5 mol %) in refluxing acetonitrile[6] provided cleanly and efficiently (81–84%) the bicyclic dienes **16**–**18**.

The total synthesis of (±)-**2** is outlined in Scheme II. Methylation of the commercially available keto ketal **19** was carried out via the corresponding dimethylhydrazone.[7] Cyclopropanation[8] of the enol trimethylsilyl ether of the resultant ketone **20** provided **21** (2:1 mixture of epimers). Slow addition of a DMF–pyridine (1 equiv) solution of **21** to $FeCl_3$ (3 equiv) in DMF, followed by dehydrochlorination of the β-chloro ketone thus formed,[9] gave the enone **22**. Hydrogenation of **22** afforded **23**, which was alkylated directly with the allylic bromide **9** to produce **24**.[10] Conversion of the latter substance into the corresponding enol triflate,[5] followed by direct addition of a catalytic amount of $(Ph_3P)_4Pd$ to the resultant solution, provided, after the mixture had been stirred at 30 °C for 5 min, an 81% yield of the ketal diene **25**.[11] Mild acid hydrolysis of **25** gave the ketone **26**.

Scheme I



8 R=CO_2Me
9 R=CH_2Br

10 n=1
11 n=2
12 n=3

16 n=1
17 n=2
18 n=3

13 n=1
14 n=2
15 n=3

(1) (a) Pettit, G. R.; Ode, R. H.; Herald, C. L.; Von Dreele, R. B.; Michel, C.; *J. Am. Chem. Soc.* **1976**, *98*, 4677. (b) Sun, H. H.; McConnell, O. J.; Fenical, W.; Hirotsu, K.; Clardy, J. *Tetrahedron* **1981**, *37*, 1237. (c) Ochi, M.; Watanabe, M.; Miura, I.; Taniguchi, M.; Tokoroyama, T. *Chem. Lett.* **1980**, 1229. (d) Ochi, M.; Watanabe, M.; Kido, M.; Ichikawa, Y.; Miura, I.; Tokoroyama, T. *Ibid.* **1980**, 1233. (e) Ochi, M.; Miura, I.; Tokoroyama, T. *J. Chem. Soc., Chem. Commun.* **1981**, 100. (f) Crews, P.; Klein, T. E.; Hogue, E. R.; Myers, B. L. *J. Org. Chem.* **1982**, *47*, 811. (g) Gonzales, A. G.; Norte, J. D. M. M.; Rivera, P.; Perales, A.; Fayos, J. *Tetrahedron* **1983**, *39*, 3355. (h) Harada, N.; Yokota, Y.; Iwabuchi, J.; Uda, H.; Ochi, M. *J. Chem. Soc., Chem. Commun.* **1984**, 1220. (i) Ochi, M.; Asao, K.; Kotsuki, H.; Miura, I.; Shibata, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 661.

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(4) All compounds reported herein exhibited spectra in full accord with structural assignments. New compounds gave satisfactory molecular mass determinations (high resolution mass spectrometry).

(5) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979.

(6) We have found that palladium(0)-catalyzed ring closures of vinylstannane–enol triflates are, in general, faster in acetonitrile than in THF.[2]

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(8) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53. Miyano, S.; Hashimoto, H. *Chem. Commun.* **1971**, 1418.

(9) Saegusa, T.; Ito, Y.; Fujii, S. *J. Org. Chem.* **1976**, *41*, 2073.

(10) This material was accompanied by minor amounts of starting material, C-7 monoalkylation product(s), and C-2,C-7 dialkylation product(s).

(11) The yields associated with this one-pot procedure are significantly higher than those derived from a two-step process in which the vinylstannane–enol triflate is isolated prior to cyclization.

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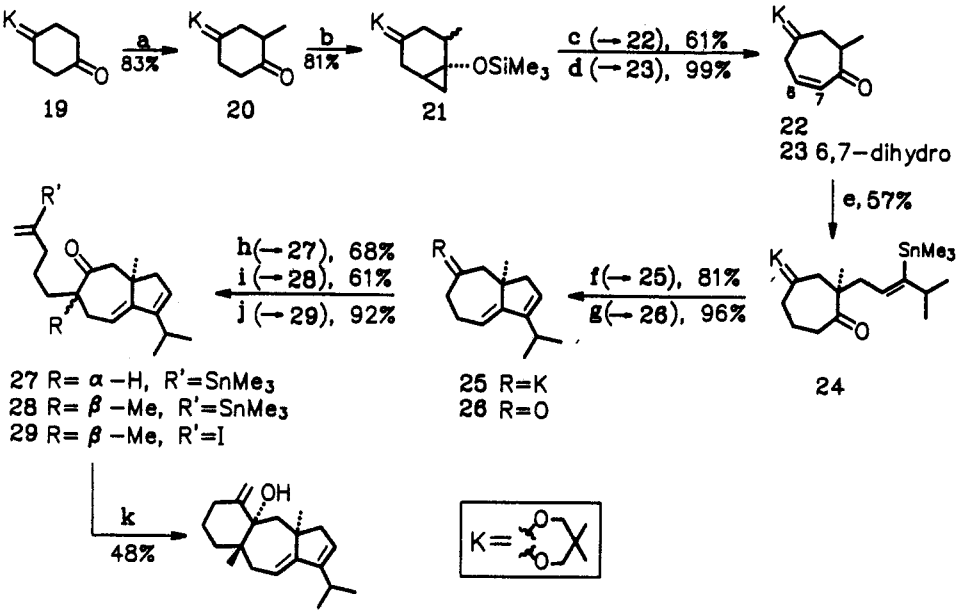
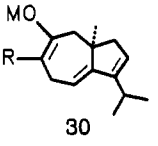
Scheme II[a]



[a](a) (i) H_2NNMe_2, PhH, reflux; (ii) LDA, THF, −78 °C to 0 °C, 1.5 h; MeI, room temperature, 2 h; (iii) $NaIO_4$, THF, pH 7 phosphate buffer, room temperature, 15 h; (b) (i) LDA, DME, 0 °C; Me_3SiCl, Et_3N, 0 °C to room temperature; (ii) CH_2I_2, Et_2Zn, PhMe, 55 °C, 15 h; (c) (i) $FeCl_3$, DMF, C_5H_5N, 0 °C, 2 h; room temperature, 2 h; (ii) NaOAc, MeOH, reflux, 3 h; (d) H_2, Pd–C, hexane; (e) (i) KOBu-*t*, HOBu-*t*, DME, room temperature, 45 min; (ii) **9**, room temperature, 15 min; (f) (i) LDA, THF, HMPA, −78 °C to 0 °C; (ii) $PhN(SO_2CF_3)_2$, room temperature, 2 h; (iii) catalytic $(Ph_3P)_4Pd$, room temperature to 30 °C, 5 min; (g) 1 N HCl, acetone, room temperature, 2 h; (h) (i) H_2NNMe_2, MeOH, 4-Å molecular sieves, reflux, 4.5 h; (ii) LDA, THF, −78 °C to 0 °C, 2 h; **31**, 0 °C to room temperature, 2 h; (iii) $NaIO_4$, THF, pH 7 phosphate buffer, 40 °C, 15 h; (i) KOBu-*t*, THF–HMPA, 60 °C, 1 h; MeI, 60 °C, 15 min; (j) I_2, CH_2Cl_2, room temperature; (k) Mg, THF, reflux, 2.5 h.



30

On the basis of steric and stereoelectronic considerations, along with an examination of molecular models, it appeared that alkylation of the enolate anion **30** would take place preferentially from the side opposite the angular methyl group. Therefore, addition of the necessary appendages to the ketone **26** had to be done in a specific order. In the event, alkylation of the dimethylhydrazone[7,12] of **26** with 5-iodo-2-(trimethylstannyl)-1-pentene (**31**)[2] provided, after hydrolysis of the hydrazone moiety, a single product **27** (69%). Direct methylation of **27** afforded the desired ketone **28**, which, upon reaction with iodine in CH_2Cl_2, was transformed smoothly into the keto vinyl iodide **29**.

Although, on the basis of literature precedents, a number of methods for effecting ring closure of **29** might be contemplated, it was found that the desired conversion could be achieved simply by treatment of **29** with small pieces of magnesium metal in refluxing THF (reaction initiated by addition of 1,2-dibromoethane). It is evident (molecular models) that cyclization should occur in the desired stereochemical sense. Indeed, there was obtained, in addition to a small amount of uncyclized keto alkene (**29**, H in place of I), a single alcohol that proved to be spectrally identical with (14*S*)-dolasta-1(15),7,9-trien-14-ol (**2**).[1f,13] Racemic **2** exhibited the following: mp 105–106 °C (from heptane); ^1H NMR (C_6D_6, 400 MHz) δ 0.92 (s, 3 H), 1.11, 1.14 (d, d, 3 H each, J = 7.0, 7.0 Hz), 1.25–1.35 (m, 1 H), 1.39 (s, 3 H), 1.43–1.66 (diffuse m, 4 H), 1.97 (br d, 1 H, J = 12.5 Hz), 2.03 (d, 1 H, J = 14.5 Hz), 2.05–2.15 (m, 2 H), 2.22 (br d, 1 H, J = 17 Hz), 2.42 (septet, 1 H, J = 7.0 Hz), 2.60 (overlapped ddd, 1 H, J = 12.5, 12.5, 6 Hz), 3.22 (dd, 1 H, J = 4.5, 15 Hz), 4.61 (br s, 1 H), 4.78 (br s, 1 H), 5.46 (dd, 1 H, J = 4.5, 9.5 Hz), 5.54 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.8, 22.1, 22.2, 23.2, 25.6, 27.4, 32.0, 35.1, 37.2, 41.5, 43.4, 45.4, 50.9, 79.5, 108.4, 114.4, 124.7, 149,8, 153.9, 154.1.

Very recently, Pattenden and Robertson[14] described a total synthesis of the dolastane-type diterpenoid (±)-isoamijiol [(2*S*,14*R*)-dolasta-1(15),8-diene-2,14-diol]. Other approaches to the synthesis of the dolastanes have also been reported.[15]

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(12) Attempted alkylation of **26** under a variety of conditions, with the enolate anion being formed under kinetically (e.g., LDA, THF) or thermodynamically (e.g., KOBu-*t*, HOBu-*t*–DME) controlled conditions, failed to give useful yields of desired product.

(13) We are grateful to Professor P. Crews for sending us copies of spectra (mass, ^1H NMR, ^{13}C NMR) of compound **2**.

(14) Pattenden, G.; Robertson, G. M. *Tetrahedron Lett.* **1986**, *27*, 399.

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