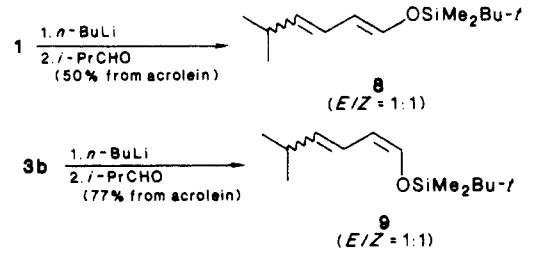
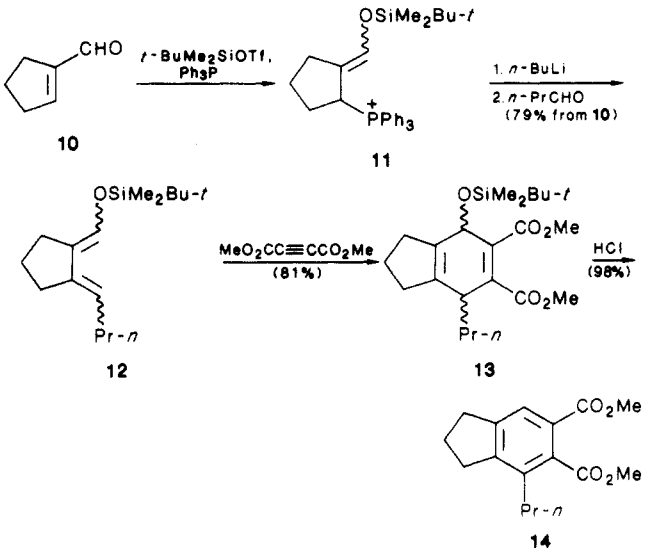
Certainly, the introduction of a host of other electrophiles into such dienol systems is feasible.

It is of further interest to point out here that the two silyloxy-bearing allylphosphonium salts **1** and **3b** can also be transformed to their corresponding phosphoranes. On reaction with isobutyraldehyde, each of these ylides gave rise to a 1:1 mixture of silyloxy dienes. In each case, the



stereochemistry about the silyl ether bearing double bond was retained, while formation of the new double bond proved indiscriminate. This Wittig process may prove valuable to the procurement of unusually substituted silyloxy dienes for the Diels–Alder process.[2,11]

The use of cyclopentene-1-carboxaldehyde in the phosphoniosilylation process was particularly intriguing, for it offered potentially a new approach to exocyclic 1,3-dienes for (4 + 2)-based molecular elaborations. Indeed, this aldehyde was found to readily yield the product of 1,4-addition. None of the alternative 1,2-addition product was observed. Subsequent Wittig condensation then led to the desired diene system **12**. While we have not yet



made a rigorous assignment of stereochemistry for this system, it was nonetheless encouraging to find that this new diene did react efficiently with dimethyl acetylenedicarboxylate. Acid treatment of the product **13** resulted in its conversion to the aromatic system **14**. Such methodology would appear to offer an attractive route to 1,4-cyclohexadienols and consequently a new means for effecting a benzannulation sequence.[12]

In summary, we suggest that this phosphoniosilylation reaction should commend itself for immediate use in the laboratory, for the techniques required for its execution are simple and the reagents needed are readily available.[13]

Acknowledgment. We are indebted to the donors of the Petroleum Research Fund, administered by the American Chemical Society and the National Institutes of Health (HL 20579) for support of these studies. We thank P.-W. Yuen for helpful suggestions and Dr. T. Caggiano of Ayerst Laboratories for some pertinent literature references.

Supplementary Material Available: Representative experimental procedures for the phosphoniosilylation reaction, Wittig condensation, and hydrolysis to β-substituted enone (2 pages). Ordering information is given on any current masthead page.

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Received April 1, 1986

(11) For a report on the preparation and use of (3-methoxyallylidene)triphenylphosphorane, see: Martin, S. F.; Garrison, P. J. *Tetrahedron Lett.* **1977**, 3875.

(12) Bauman, J. G.; Hawley, R. C.; Rapoport, H. *J. Org. Chem.* **1984**, *49*, 3791. Bauman, J. G.; Barber, R. B.; Gless, R. D.; Rapoport, H. *Tetrahedron Lett.* **1980**, *21*, 4777. Gesson, J. P.; Jacquesy, J. C.; Mondon, M. *Nouv. J. Chim.* **1983**, *7*, 205.

(13) For a recent report on the functionalization of enones using "bifunctional" reagents, see: Leonard, W. R.; Livinghouse, T. *J. Org. Chem.* **1985**, *50*, 730.

Stereoselective Acid-Catalyzed Claisen Rearrangements[1]

Summary: An alkyl substituent in the 2-position of an *E* trisubstituted allylic alcohol confers significant diastereoselectivity on ortho ester and ketal Claisen rearrangements of the system.

Sir: The Claisen rearrangement is an important synthetic tool, due in part to the stereochemical control it affords.[3] The olefinic geometries in the initial allyl vinyl ether dictate the relative stereochemistry of the carbon atoms α and β to the new carbonyl group.[4] The enolate Claisen[5] and the amide acetal Claisen[6] rearrangements are examples that allow control over this relative stereochemical relationship. In contrast, previous examples of the acid-catalyzed ortho ester[7] and ketal[8] Claisen rearrangements have shown no significant stereoselectivity. In this paper we report that the judicious choice of the allylic alcohol leads to a diastereoselective reaction.

The basis for predicting the stereoselectivity arises from a consideration of the transition states leading to the syn and anti products (Scheme I).[9] The transition-state model

(1) Presented in part at the 1985 Pacific Conference on Chemistry and Spectroscopy, San Francisco, CA, October 9–11, 1985.

(2) Camille and Henry Dreyfus Teacher-Scholar, 1982–1987.

(3) (a) Bennett, G. B. *Synthesis* **1977**, 589. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227.

(4) Hansen, H. J.; Schmid, H. *Tetrahedron* **1974**, *30*, 1959.

(5) (a) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. (b) Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155. (c) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1981**, *46*, 479.

(6) (a) Sucrow, W.; Richter, W. *Chem. Ber.* **1971**, *104*, 3679. (b) Welch, J. T.; Eswarakrishnan, S. *J. Org. Chem.* **1985**, *50*, 5909.

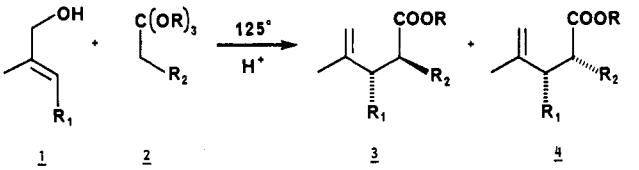
(7) For example: (a) Stork, G.; Raucher, S. *J. Am. Chem. Soc.* **1976**, *98*, 1583. (b) Raucher, S.; Hwang, K. J.; McDonald, J. E. *Tetrahedron Lett.* **1979**, 3057. (c) Raucher, S.; McDonald, J. E.; Lawrence, R. F. *Tetrahedron Lett.* **1980**, 4335. (d) Daub, G. W.; Teramura, D. H.; Bryant, K. E.; Burch, M. T. *J. Org. Chem.* **1981**, *46*, 1485.

(8) (a) Daub, G. W.; McCoy, M. A.; Sanchez, M. G.; Carter, J. S. *J. Org. Chem.* **1983**, *48*, 3876. (b) Daub, G. W.; Lunt, S. R. *Tetrahedron Lett.* **1983**, 4397.

(9) All structures, while drawn as a single enantiomer, represent racemates. The syn/anti stereostructural notation proposed by Masamune is used in this paper. Masamune, S.; Ali, S. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557.

0022-3263/86/1951-3402$01.50/0

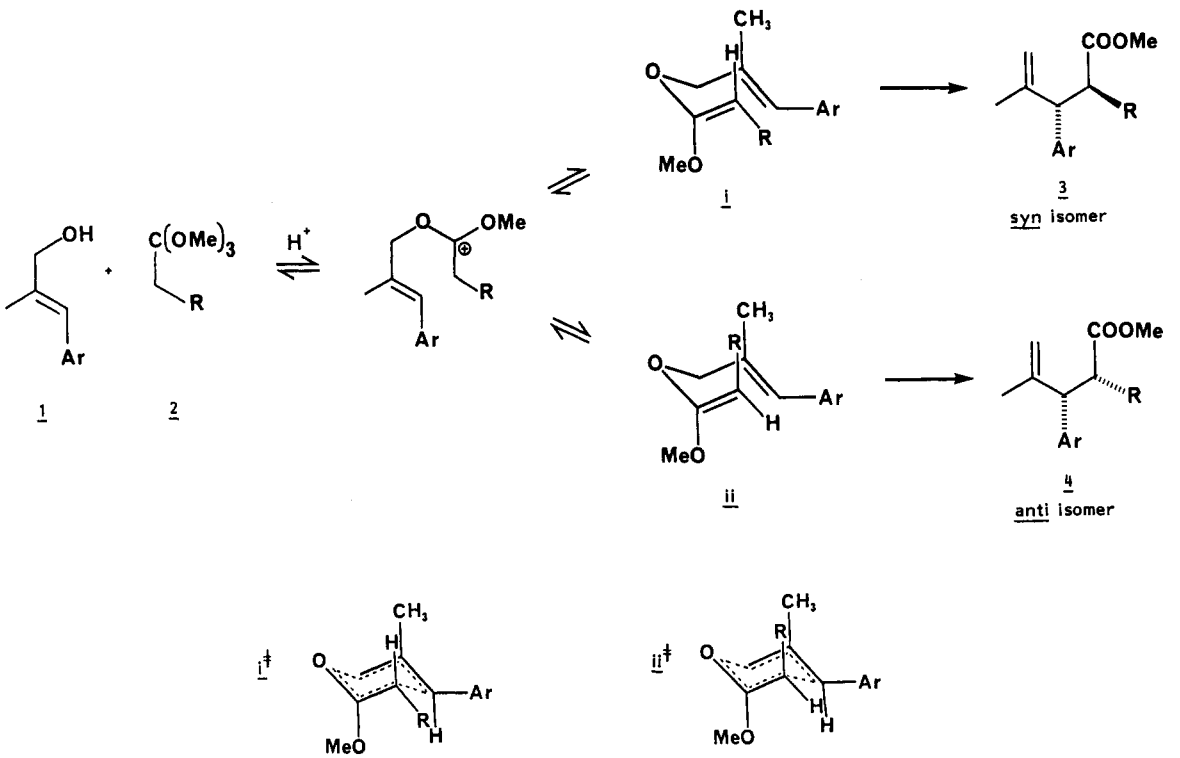
Table I



example	R_1	R_2	R	ratio 3:4[a]	yield, %
a	C_6H_5	CH_3	Me	84:16	80
b	C_6H_5	CH_3	Et	84.7:15.3	65
c	C_6H_5	CH_2CH_3	Me	83.5:16.5	60
d	C_6H_5	$CH_2CH_2CH_3$	Me	82.1:17.9[b]	70
e	p-$C_6H_4OCH_3$	CH_3	Et	82.7:17.3	73,[c] 62[d]
f	p-$C_6H_4OCH_3$	CH_2CH_3	Me	81.4:18.6	55
g	p-C_6H_4Cl	CH_3	Et	83.4:16.6	40

[a] Uncertainties are 0.5%. [b] 3 and 4 did not resolve on capillary GC. Ratio determined by integration of ^1H NMR spectrum at 200 MHz. [c] Acid catalyst was propionic acid. [d] Acid catalyst was mesitoic acid.

Scheme I

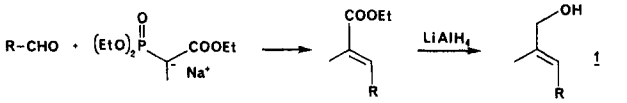


of the Claisen rearrangement developed by Perrin and Faulkner[10] suggests that alkyl groups at C_1 and C_5 would interact more strongly in the Z ketene acetal transition state (ii‡) than the E ketene acetal transition state (i‡). In particular, a 1–3 diaxial-like interaction exists in the transition state leading to **4** (ii‡) between the methyl and R groups, which suggests that a preference for the syn isomer might be observed. Parker[11] has suggested that a similar interaction is responsible for the regioselectivity observed in Claisen rearrangements of some bisallylic alcohols. In contrast, Ziegler[12] has indicated that processes involving such a 1–3 diaxial-like interaction are not precluded as long as other possible pathways are more sterically demanding.

The results of our study for the ortho ester Claisen rearrangements of three (E)-allylic alcohols[13] **1** are presented in Table I. All reactions were performed according to the procedure of Johnson (2 h at 125 °C, 3 equiv of ortho ester, and a catalytic amount of $CH_3CH_2CO_2H$).[14] The syn/anti ratios in the reaction mixtures were determined by capillary gas chromatography.[15] The syn isomer was favored in all cases, and selectivities of about 5:1 were

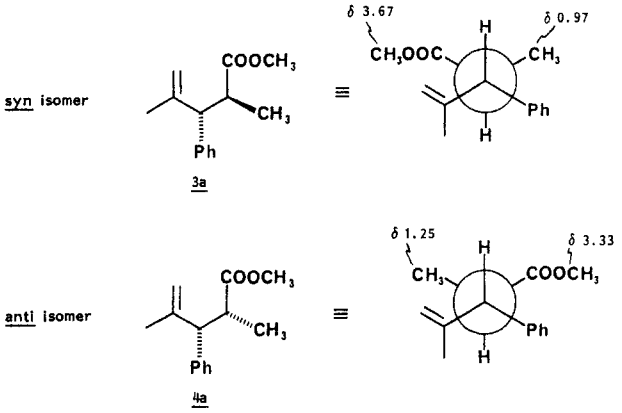
(10) Perrin, C. L.; Faulkner, D. J. *Tetrahedron Lett.* **1969**, 2873.
(11) Parker, K. A.; Farmar, J. G. *Tetrahedron Lett.* **1985**, 3655.
(12) See Claisen rearrangement strategy for quassinoid synthesis: Ziegler, F. E.; Klein, S. I.; Pati, U. K.; Wang, T.-F. *J. Am. Chem. Soc.* **1985**, *107*, 2730.

(13) The E alcohols were prepared according to the following sequence.[24] These alcohols (1) were shown to be a single isomer by capillary GC, ^1H NMR, and ^{13}C NMR. NOE experiments indicate that the hydroxymethylene group is cis to the vinyl hydrogen in the products. The alcohols are therefore assigned E geometry.[25]



(14) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
(15) Capillary GC was performed on a 30-m WCOT DB-1 column as supplied by J. and W. Scientific.

Scheme II



obtained. In accord with our previous observations in the ketal Claisen rearrangment,[8a] neither the acid catalyst nor the nature of the ortho ester (methoxy vs. ethoxy) had any observable effect on the syn/anti selectivity.

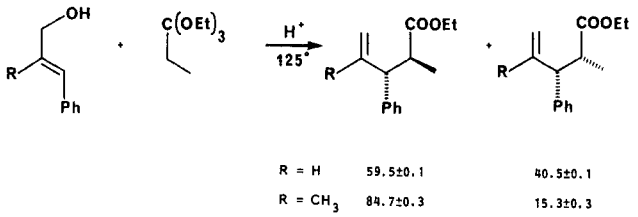
The observed selectivity, while much improved over previous examples in the ortho ester Claisen series, is still less than might be expected considering that an interaction resembling a 1,3-diaxial methyl–methyl interaction is involved. The selectivity exhibited in example b, Table I corresponds to a difference in transition-state free energies of ≈1.4 kcal/mol at 125 °C. This is less than might be expected for such an interaction based on a model of a cis 3,5-disubstituted tetrahydropyran.[16] The fact that the Claisen rearrangement is judged to have an early transition state[17] probably accounts for the bulk of the attenuated selectivity.

The esters **3** and **4**[18] were isolated and purified by preparative chromatography.[19] In some cases both the syn and anti isomers could be obtained in pure form (entries e and f, Table I). In the other cases only the syn isomer was obtained pure, and the anti isomer was characterized as a syn/anti mixture.

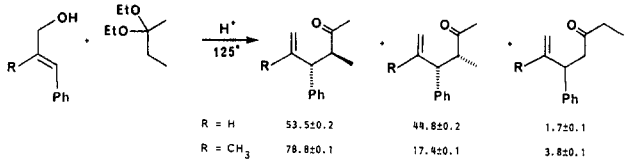
Distinct differences between the syn and the anti isomers can be observed in the ^1H NMR spectra. The anisotropy introduced by the aromatic group leads to specific upfield shifts of the α-alkyl group in the syn isomer and corresponding upfield shifts of the ester alkoxy group in the anti isomer. Scheme II indicates these differences for **3a** and **4a**. These results are consistent with the interpretation of Heathcock for aldols with two stereogenic centers.[20]

Equilibration studies established that the sigmatropic rearrangement is not reversible and that enolization processes are not affecting the observed syn/anti ratio. A pure sample of **3e** was subjected to the original reaction conditions, and no **4e** could be detected by capillary GC.[21] Similarly, no evidence of equilibration could be discerned when **4e**, **3f**, and **4f** were subjected to the original reaction conditions. Evidently enolization of the carbonyl group in **3** and **4** is slow under the reaction conditions.

Scheme III



Scheme IV



The selectivity realized in example b in Table I is significantly better than the results for the reaction of an allylic alcohol containing no methyl at C_2 (see Scheme III). It seems quite likely that there is some, if not complete, equilibration of the intermediate ketene acetals under the reaction conditions. If there were no equilibration, similar syn/anti ratios would be expected for the examples in Scheme III. The question of whether the intermediate ketene acetals are in equilibrium is much clearer for the ketal Claisen rearrangement. We have previously demonstrated that the corresponding isomeric ketene acetals generated in the ketal Claisen rearrangement do equilibrate under the reaction conditions.[8a] The ketal Claisen rearrangement of alcohol **1** (R = C_6H_5) shows an improvement in its syn/anti ratio (Scheme IV) relative to the unsubstituted system comparable to the improvement observed in the examples in Scheme III. All of these facts suggest that the product ratio is only a function of the transition-state free energies and that the 1,3-diaxial-like interaction in transition state ii‡ determines the product distribution of the reaction.

Finally, one must consider whether any of the reaction is partitioned through a boat–like transition state.[22] Any boat-like participation significantly alters the interpretation of the results. In particular, the relative stereochemical orientations of the products are reversed when boat transition states are invoked: the *E* ketene acetal i rearranges to give the anti isomer, and the Z ketene acetal ii gives the syn isomer. The participation of boat transition states may be attenuating the stereoselectivity observed in this study.[23]

These results demonstrate that the ortho ester and ketal Claisen rearrangements of the appropriate *E* trisubstituted allylic alcohols lead to significant diastereoselection in good yield. Syn/anti ratios of 5:1 can generally be obtained in contrast to previous reports on these acid-catalyzed processes. We are currently defining the limits of the selectivity and applying the reaction to the synthesis of naturally occurring materials.

Acknowledgment. Financial support for this work was kindly provided by the donors of the Petroleum Research Fund, administered by the American Chemical Society,

(16) If *cis*-3,5-dimethyltetrahydropyran were a valid model for the transition-state ii‡, the difference in free energy between i‡ and ii‡ could be as large as 5 kcal/mol. This corresponds to a syn/anti selectivity of ≈550:1 at 125 °C. (a) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Wiley-Interscience: New York, 1966. (b) Eliel, E. L.; Hargrave, K. D.; Pietrusiewicz, K. M.; Manoharan, M. *J. Am. Chem. Soc.* **1982**, *104*, 3635.

(17) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 2747.

(18) (a) All new compounds exhibited spectral characteristics (^1H and ^{13}C NMR, IR) consistent with the assigned structures. (b) Satisfactory combustion analyses were obtained for all new compounds.

(19) Flash chromatography or medium-pressure liquid chromatography.

(20) Heathcock, C. H.; Kiyooka, S.; Blumenkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4214 and references cited therein.

(21) Limits of detection were <1%.

(22) (a) Lythgoe, B.; Metcalf, D. A. *Tetrahedron Lett.* **1975**, 2447. (b) Ireland, R. E.; Vevert, J. P. *J. Org. Chem.* **1980**, *45*, 4259.

(23) Experiments are currently in progress to clarify this question.

(24) Mori, K.; Matsui, M. *Tetrahedron* **1970**, *26*, 2801.

(25) Tokuyuma, F.; Shimada, K.; Uemura, M. *Tetrahedron Lett.* **1982**, 2121.

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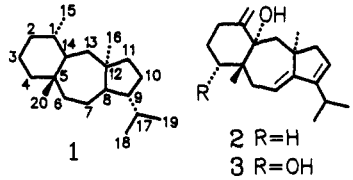
Annulations Leading to Diene Systems. Total Synthesis of the Diterpenoid (±)-(14*S*)-Dolasta-1(15),7,9-trien-14-ol

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

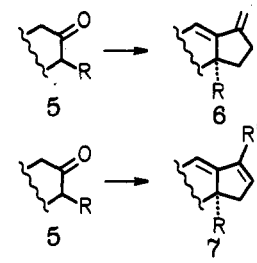


1

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.



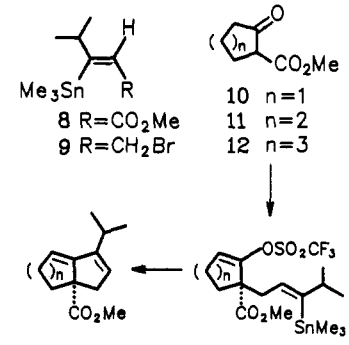
5 **6**

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.

(2) Piers, E.; Friesen, R. W.; Keay, B. A. *J. Chem. Soc., Chem. Commun.* **1985**, 809.

(3) Piers, E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263.

(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]

(7) Corey, E. J.; Enders, D. *Chem. Ber.* **1978**, *111*, 1337.

(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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