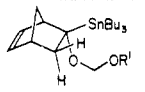
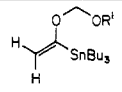
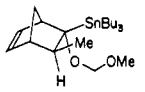
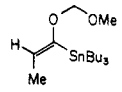
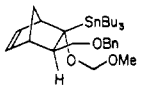
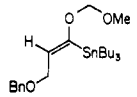
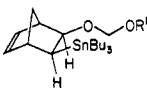
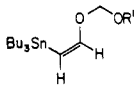
Table I. Pyrolytic Generation of Stannylated Vinyl Ethers

entry	bicyclic precursor	vinyl ether	yield
1	 **4a** : R^1 = Me	 **11a** : R^1 = Me	98 %
2	**4b** : R^1 = Bn	**11b** : R^1 = Bn	95 %
3	**4c** : R^1 = $(CH_2)_2OMe$	**11c** : R^1 = $(CH_2)_2OMe$	95 %
4	 **7**	 **12**	85 %
5	 **8**	 **13**	98 %
6	 **10a** : R^1 = Me	 **14a** : R^1 = Me	75 %
7	**10b** : R^1 = $(CH_2)_2OMe$	**14b** : R^1 = $(CH_2)_2OMe$	70 %

stereocontrolled fashion to serve as precursors to stannylated vinyl ethers.

As shown in Figure 3, this expectation was realized through straightforward elaboration of a simple common intermediate, bicyclo[2.2.1]hept-5-en-2-one (**3**).[6] α-Alkoxy stannanes were prepared as single isomers[8] through addition of tri-*n*-butylstannyllithium[7,9] to ketones **3**, **5**, and **6**, while the β-alkoxy species **10** could be realized through hydrostannation of silyl enol ether **9**.[8] The stereoselection in products **4** and **10** reflects the attachment of the stannyl group to the least hindered face of the π-system, whereas the formation of the tin bond in the most congested position in **7** and **8** may reflect the previously observed reversibility of such anionic additions.[9]

With suitable bicyclic alkoxymethyl-protected stannanes available in quantity, the critical thermolytic fragmentation was examined. The bicyclic stannanes (neat) were introduced dropwise to an evacuated, heated (0.25 torr, 400 °C) vertical quartz column packed with crushed quartz (34 cm × 2.6 cm).[12] The pyrolyzates, collected in a cooled round-bottomed receiver (CO_2(s)/acetone), were found to consist of nearly pure stannylated vinyl ethers in the yields given in Table I. The stereochemistries of products **12**, **13**, and **14** are supportive of the stereospecificity of the retro-Diels–Alder process.[3] Also of mechanistic note are the results of entries 6 and 7 wherein no norbornadiene formation via elimination of the β-alkoxy stannanes was observed to compete with the desired fragmentation reaction.[13]

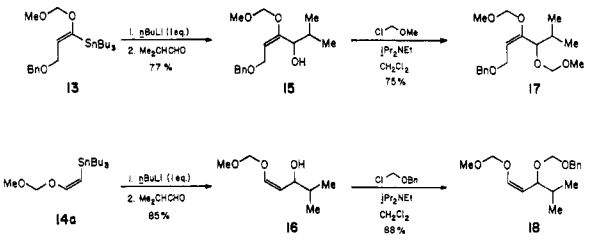


Figure 4.

As anticipated, compounds **11–14** participated in smooth tin–lithium exchange without loss of geometry by the action of *n*-BuLi (1 equiv in THF at −78 °C: 20 min for **11–13**, 90 min for **14**). The resulting vinyllithium species cleanly condensed with aldehydes to afford adducts of gratifying stability. To illustrate, isobutyraldehyde adducts **15** and **16** were isolated in the indicated yields following purification by flash chromatography (Figure 4).[14] Routine protections of the allylic alcohols affords derivatives **17** and **18** which exhibit still greater resistance to eliminative hydrolysis to the corresponding α,β-unsaturated aldehydes. Furthermore, the conversion of **18** → **16** may be effected by warming the protected compound in acetone with pyridinium tosylate.[14]

Having secured stereospecific access to metalated vinyl ethers and demonstrated the relative stability of alkoxymethyl substitution on the vinyl oxygen, completion of the strategy outlined in Figure 1 may be pursued. The stereoselective elaboration of compounds of the types **15–18** will be reported in due course.

Acknowledgment is gratefully given to the National Institutes of Health for their generous support. We also thank Professor Timothy L. Macdonald for helpful discussions.

Registry No. **3**, 694-98-4; **4a**, 92012-59-4; **4b**, 92012-60-7; **4c**, 92012-61-8; **5**, 51100-02-8; **6**, 92012-62-9; **7**, 92012-63-0; **8**, 92012-64-1; **9**, 68364-22-7; **10a**, 92012-65-2; **10b**, 92012-66-3; **11a**, 92012-67-4; **11b**, 92012-68-5; **11c**, 92012-69-6; **12**, 92012-70-9; **13**, 92012-71-0; **14a**, 92012-72-1; **14b**, 92012-73-2; **15**, 92012-74-3; **16**, 92012-75-4; **17**, 92012-76-5; **18**, 92012-77-6; Me_2CHCHO, 78-84-2; *n*-Bu_3SnLi, 4226-01-1; chloromethoxymethane, 107-30-2; ((chloromethoxy)methyl)benzene, 3587-60-8.

Supplementary Material Available: Spectral data for compounds **11–14** (3 pages). Ordering information is given on any current masthead page.

(6) Freeman, P. K.; Balls, D. M.; Brown, D. J. *J. Org. Chem.* **1968**, *33*, 2211.
(7) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.
(8) The stereochemistry of product **4** was determined through stereospecific tin–proton exchange[9] and comparison of the result with both protected norbornenol isomers. Alkylation products **5** and **6** are obtained through expected exo selectivity.[10] Stannanes **7**, **8**, and **10** were analyzed by NMR comparisons with related bicycloheptenes.[11]
(9) Sawyer, J. S.; Macdonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 3376.
(10) (a) Corey, E. J.; Hartmann, R.; Vatakencherry, P. A. *J. Am. Chem. Soc.* **1962**, *84*, 2611. (b) Grieco, P. A.; Ohfune, Y.; Yokoyama, Y.; Owens, W. *J. Am. Chem. Soc.* **1979**, *101*, 4750.
(11) Marchand, A. P. "Stereochemical Applications of NMR Studies in Rigid Bicyclic Systems"; Verlag Chemie: Deerfield Beach, FL, 1982.
(12) This method is based upon the description given in Stork, G.; Guthikonda, R. N. *Tetrahedron Lett.* **1972**, 2755.
(13) (a) Kauffmann, T.; Kriegesmann, R.; Altepeter, B.; Steinseifer, F. *Chem. Ber.* **1982**, *115*, 1810. (b) Kauffmann, T.; Kriegesmann, R.; Hamsen, A. *Chem. Ber.* **1982**, *115*, 1818.
(14) For example, compare the acid stability of **16** with similar compounds in ref 2b.

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Palladium-Catalyzed Conversion of Esters of 4-(Trimethylsilyl)-2-buten-1-ol to Trimethylsilyl Esters. A New Carboxyl Protecting Group

Summary: Carboxylic acids protected as esters of 4-(trimethylsilyl)-2-buten-1-ol are catalytically converted by $Pd(PPh_3)_4$ to trimethylsilyl esters which are readily hydrolyzed by treatment with an alcohol.

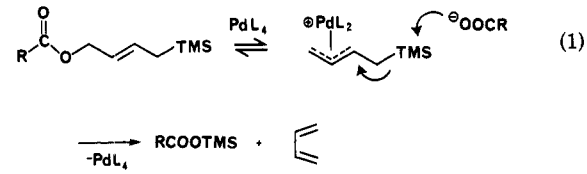
Scheme I[a]

1 2

[a] (a) BuLi, THF, −78 °C, then paraformaldehyde, −78 °C → room temperature. (b) LAH (2 molar equiv), THF, reflux, 1 h.

Sir: Elimination reactions in allylic systems which are initiated by the formation of an allylpalladium complex and then proceed with the loss of a proton or carbon dioxide to give dienes have been described.[1] Recently, Trost and Chan[2] demonstrated that a silyl group will also function as an electrofuge if situated α to the π-allyl complex. This suggested a new silicon-based carboxyl protecting group which is the subject of this communication.

It was thought that an ester of 4-(trimethylsilyl)-2-buten-1-ol would react with palladium(0) to form a π-allyl complex (eq 1). This should then undergo desilylation

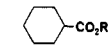
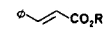
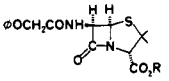
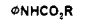
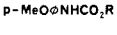
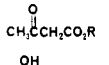
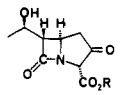
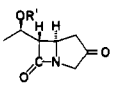


(1)

by the expelled carboxylate ion to give the trimethylsilyl ester and butadiene. This would amount to the catalytic conversion of a stable allyl ester to a very labile trimethylsilyl ester under neutral conditions without the addition of any nucleophilic species.[3] Since trimethylsilyl esters are readily hydrolyzed upon treatment with water or an alcohol,[4] this would constitute an exceptionally mild means of removing a carboxyl protecting group.

The required alcohol **2** was prepared as outlined (Scheme I). This involved hydroxymethylation of trimethylpropargylsilane[5] to give the alcohol[6] **1** followed by reduction to the *trans*-olefin **2**. Model esters were prepared[7,8] by standard esterification procedures where the carboxyl group is activated and then allowed to react with the alcohol **2** in the presence of a base.

Table I. Deprotection Results[a]

entry	substrate[j] (R = CH₂ / TMS)	product(s)	yield, %
1		R = H[b]	90
2		R = H[c]	98
3		R = K[d]	73[e]
4		$PhNH_2$[b,f]	96
5		p-$MeOC_6H_4NH_2$[b,f]	97
6		R = TMS[g]	80
7	 3  4, R' = H 5, R' = TMS		4 10, 5 71[h,b] 4 67, 5 5[i,b]

[a] Reactions were conducted under N_2 on a 0.5 → 1.0 mmol scale, 0.2 M in dry CH_2Cl_2 with 0.02 equiv of $Pd(Ph_3)_4$. [b] Workup involved transfer of the reaction mixture onto a silica gel column followed by isolation of the product. [c] Workup involved addition of MeOH (3 equiv, room temperature, 0.5 h) followed by chromatography. [d] After hydrolysis with methanol, potassim ethylhexanoate (1.1 equiv in EtOAc) was added and the product collected by filtration. [e] Yield of material recrystallized from acetone–H_2O; yield of crude material, 96%. [f] CO_2 evolution on contact with silica gel. [g] Isolated from the reaction mixture by Kugelrohr distillation. [h] Complete after 3 h. [i] Conversion conducted in the presence of MeOH (2.2 equiv), complete after 6 h. [j] TMS = trimethylsilyl.

Initial examination of the deprotection (Table I, entries 1 and 2) revealed that conversion of the allyl ester to a trimethylsilyl ester proceeds readily (within 2 h) at room temperature in CH_2Cl_2 with a catalytic amount of $Pd(PPh_3)_4$. The presence of additional PPh_3 or the use of solvents which can coordinate with palladium bring about a noticeable decrease in the rate of conversion.[9] The acid was isolated either by adding several equivalents of MeOH to hydrolyze the trimethylsilyl ester and then by filtering the reaction mixture through a silica gel column to remove the palladium catalyst or by pouring the reaction mixture directly onto a silica gel column and eluting the acid. The yields are very good even with highly functionalized and sensitive esters such as that of penicillin V (entry 3). In this latter case, precipitation of the potassium salt from the reaction mixture was the most convenient means of isolating the product.

It should also be possible to use this procedure to deprotect carbonates or carbamates which incorporate the alcohol **2**. This was only examined with carbamates[10] of aromatic amines (entries 4 and 5) but it was found that the conversion to the corresponding trimethylsilyl carba-

(1) Trost, B. M.; Verhoven, T. R. In "Comprehensive Organometallic Chemistry"; Wilkinson, G., Ed.; Pergamon Press: Oxford, 1982; Vol. 8, p 836.

(2) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315, 2326.

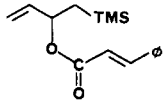
(3) For the palladium-catalyzed deprotection of allylic esters with potassium ethyl hexanoate, see: Jeffrey, P. D.; McCombie, S. W. *J. Org. Chem.* **1982**, *47*, 587.

(4) Greene, T. W. "Protecting Groups in Organic Synthesis"; Wiley-Interscience: New York, 1981; p 178.

(5) Prepared from propargyl bromide using the procedure of Slutsky and Kwart: Slutsky, J.; Kwart, H. *J. Am. Chem. Soc.* **1973**, *95*, 8678. Material obtained in this manner also contained trimethylallenylsilane and was used as such without complications.

(6) Satisfactory elemental analyses were obtained for all new compounds. Selected physical and spectral data: **1**, bp 94–96 °C at 20 mm; δ ($CDCl_3$ + D_2O) 0.08 (s, 9 H), 1.45 (t, 2 H, J = 2.4 Hz), 4.18 (t, 2 H, J = 2.4 Hz); **2**, bp 87–89 °C at 20 mm; δ ($CDCl_3$ + D_2O) ca. 0, (s, 9 H), 1.48 (d, 2 H, J = 6.9 Hz), 4.04 (d, 2 H, J = 5.1 Hz), 5.6 (complex multiplet, 2 H, from decoupling experiments the vicinal olefinic coupling is 15.4 Hz); **5**, oil; IR (neat) 3450, 1750 (br) cm^{-1}; δ ($CDCl_3$ + D_2O), 1.36 (d, 3 H, J = 6.4 Hz), 2.56, (dq, 2 H, δ_A = 2.77, δ_B = 2.34, J_{AB} = 18.7 Hz, J_{AX} = 6.6 Hz, J_{BX} = 8.1 Hz), 3.15 (dd, 1 H, J = 1.8, 6.3 Hz), 3.61 (q, 2 H, δ_A = 4.02, δ_B = 3.20, J_{AB} = 18.1 Hz), 3.99 (ddd, 1 H, J = 1.8, 6.6, 8.1 Hz), 4.27 (dq, 1 H, J = 6.4, 6.3 Hz).

(7) Interestingly, esterification via activation of the allylic alcohol (see: Mitsunobu, O. *Synthesis* **1981**, 1) is possible, although under standard conditions with cinnamic acid, the yield is somewhat low (58%) and allylic isomerization is observed (ca. 1:2 mixture of the expected ester and i was obtained).



(8) As an indication of the resistance of these esters toward protodesilylation, it is noted that one survived treatment with 1 N aqueous HCl–MeOH (1:5) at 5 °C for 16 h, conditions required for the hydrolysis of a TBDMS ether.

(9) The results of a qualitative TLC determination of solvent effects on the time required for complete conversion of the cinnamate ester (room temperature, 0.2 M, 0.05 equiv of $Pd(PPh_3)_4$, 0.1 equiv of PPh_3) are CH_2Cl_2, 1 h; benzene, 6 h; THF, 14 h; CH_3CN, precipitate formation with essentially no conversion over 2 days.

(10) Prepared by allowing the appropriate isocyanate to react with the alcohol **2** in the presence of a catalytic amount of triethylamine.

mate is very rapid (complete within 20 min at room temperature) and that the free amine could be obtained in good yield after chromatography. Competing N-allylation[3] is apparently not a problem since the deprotected material exists in the reaction mixture as a silylated carbamate[11] rather than the free amine.

Conversion of the acetoacetate ester (entry 6) to a trimethylsilyl ester is interesting in light of results[12] obtained from the reaction of allyl acetoacetate with palladium catalysts in the absence of nucleophiles. It appears that in the present instance, desilylation of the π-allyl complex by the acetoacetate ion occurs more readily than decarboxylation and subsequent alkylation. This result encouraged an examination of the deprotection of the β-keto ester **3**, a key intermediate in the synthesis of thienamycin.[13] However under standard conditions it was predominantly converted to the novel ketone **5** (entry 7). Indications of the origin of this compound came from the following observations. If the reaction were stopped prior to reaching completion (after 40 min) an intermediate, the silyl ether of **3**, could be isolated (20% yield at 54% conversion). When the reaction was conducted in the presence of MeOH, the hydroxy ketone **4** was obtained as the major product. These results suggest that a trimethylsilyl ester is formed in the usual manner but that the silyl group is then transferred intermolecularly to any alcohol present. The β-keto acid then formed undergoes a facile decarboxylation to give the observed products.

Registry No. **1**, 90933-84-9; **2**, 92097-18-2; **3**, 92097-19-3; **3** (TMS ether), 92097-28-4; **4**, 92097-20-6; **5**, 92097-21-7; (*E*)-PhCH=CHCOCl, 17082-09-6; (*E*)-PhCH=CHCO$_2$H (1 ester), 92097-23-9; (*E*)-PhCH=CHCO$_2$H, 140-10-3; PhNCO, 103-71-9; PhNHCO$_2$H (1 ester), 92097-25-1; PhNH$_2$, 62-53-3; *p*-MeOC$_6$H$_4$NCO, 5416-93-3; *p*-MeOC$_6$H$_4$NHCO$_2$H (1 ester), 92097-26-2; *p*-MeOC$_6$H$_4$NH$_2$, 104-94-9; CH$_3$COCH$_2$CO$_2$H (1 ester), 92097-27-3; CH$_3$COCH$_2$CO$_2$TMS, 18457-02-8; CH$_3$COC(=N$_2$)CO$_2$H (1 ester), 92097-29-5; HC≡CCH$_2$TMS, 13361-64-3; CH$_2$O, 50-00-0; Pd(PPh$_3$)$_4$, 14221-01-3; cyclohexanecarbonyl chloride, 2719-27-9; cyclohexanecarboxylic acid (1 ester), 92097-22-8; cyclohexanecarboxylic acid, 98-89-5; Penicillin V (1 ester), 92097-24-0; Penicillin V (K salt), 132-98-9; diketene, 674-82-8; (3*S*,4*R*)-3-[(1*R*)-1-[(*tert*-butyldimethylsilyl)oxy]ethyl]-4-acetoxyazetidin-2-one, 76855-69-1.

(11) For practical reasons, these intermediates were not isolated but their existence was inferred from the gas evolution observed when the reaction mixture was poured onto a silica gel column.

(12) Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381. Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199.

(13) Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. C.; Bouffard, F. A.; *J. Am. Chem. Soc.* **1980**, *102*, 6161.

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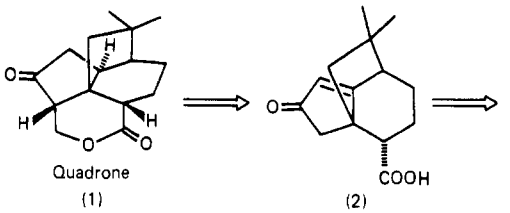
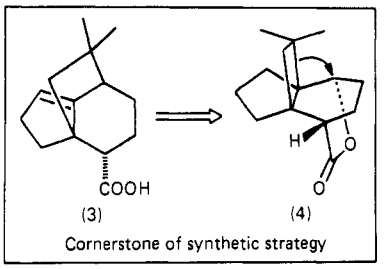
Total Synthesis of (+)-Quadrone: Assignment of Absolute Stereochemistry

Summary: The first total synthesis of quadrone in chiral nonracemic form is disclosed; assignment of the absolute stereochemistry is thereby secured.

Sir: Quadrone (**1**), a biologically active sesquiterpene, has been the focus of intense synthetic interest since its structure elucidation in 1978.[2] We also were enchanted with the quadrone architecture and report here the first total synthesis of quadrone in chiral nonracemic form. We note in advance that our approach is both short and highly efficient and permits for the first time assignment of the absolute stereochemistry.

The cornerstone of our strategy was envisioned to be the acid-catalyzed rearrangement of propellane **4** to olefin **3** (or a closely related derivative).[3] Allylic oxidation would then afford **2**, an advanced intermediate in the Danishefsky synthesis.[2c]





Our synthesis begins with the [2 + 2]-photochemical cycloaddition of isobutylene to bicyclic enone **5**[4] to afford a mixture of isomeric propellanes **6**[5] and **7**[5] (2:1, 74%). Treatment of this mixture with sodium methoxide in methanol leads via epimerization at C(5) to a new mixture enriched in the desired *anti*-propellanone **7** (1:5 of **6** to **7**, 84%), from which pure **7** could be obtained by crystallization (mp 48–50 °C). Reduction of **7** with NaBH$_4$, followed by reaction of the resulting alcohol with methanesulfonyl chloride and pyridine, afforded trans-substituted **8**[5,6] in quantitative yield from **7**.

Treatment of **8** with lithium methanethiolate in HMPA[7] afforded lactone **4**,[5] substrate for the key acid-catalyzed rearrangement; the yield was 65%.[8] To our delight,

(1) Camille and Henry Dreyfus Teacher–Scholar, 1978–1983; National Institute of Health (National Cancer Institute) Career Development Award, 1980–1985.

(2) For the isolation of quadrone, see: (a) Ranieri, R. L.; Calton, G. J. *Tetrahedron Lett.* **1978**, 499–502. (b) Calton, G. J.; Ranieri, R. L.; Espenshade, M. A. *J. Antibiot.* **1978**, *31*, 38–42. For total synthesis of *racemic* quadrone, see: (c) Danishefsky, S.; Vaughan, K.; Gadwood, R. C.; Tsuzuki, K. J. *J. Am. Chem. Soc.* **1981**, *103*, 4136–4141; **1980**, *102*, 4262–4263. (d) Bornack, W. K.; Bhagwat, S. S.; Ponton, J.; Helquist, P. *Ibid.* **1981**, *103*, 4647–4648. (e) Burke, S. D.; Murtiashaw, C. W.; Saunders, J. O.; Dike, M. S. *Ibid.* **1982**, *104*, 872–874. (f) Takeda, K.; Shimono, Y.; Yoshii, E. *Ibid.* **1983**, *105*, 563–568. (g) Kende, A. S.; Roth, B.; Sanfilippo, P. J.; Blacklock, T. J. *Ibid.* **1982**, *104*, 5808–5810. (h) Schlessinger, R. H.; Wood, J. L.; Poss, A. J.; Nugent, R. A.; Parsons, W. H. *J. Org. Chem.* **1983**, *48*, 1146–1147. (i) Dewanckele, J. M.; Zutterman, F.; Vandewalle, M. *Tetrahedron* **1983**, *39*, 3235–3244.

(3) For a discussion of the stereoelectronic requirements for this rearrangement, see: Smith, A. B., III; Wexler, B. A. *Tetrahedron Lett.* **1984**, *25*, 2317–2320.

(4) Smith, A. B.; Jerris, P. J. *J. Org. Chem.* **1982**, *47*, 1845–1855.

(5) All new compounds gave 250-MHz ^{1}H NMR, IR, high-resolution mass spectra and/or satisfactory C, H combustion analysis in accord with the structure given. All yields recorded here are based upon isolated material which was 97% pure.

(6) Reduction occurs stereoselectivity from the anti face of the molecule.

(7) Kelly, T. R.; Dali, H. M.; Tsang, W.-G. *Tetrahedron Lett.* **1977**, 3859–3860.

(8) We have also explored the reaction of **8** with KO$_2$/18-crown-6. While we obtained yields of **4** as high as 70%, the reaction proved capricious and was abandoned for the methanethiolate procedure. For the use of KO$_2$/18-crown-6, see: Corey, E. J.; Nicolaou, K. C.; Shibasaki, M.; Machida, Y.; Shiner, C. S. *Tetrahedron Lett.* **1975**, 3183–3186.

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