(1R*,3R*,6R*,9S*,19R*,20S*)- and (1R*,3R*,6S*,9R*,19R*,20S*)-19-Methyl-4,11,17-trioxa-5,10,16-trioxo-7-cis-tetracyclo[17.2.1.0^{3,20}.0^{6,9}]docosene (23). The silyl acid **35** (154 mg, 0.312 mmol) and tetra-*n*-butylammonium fluoride (408 mg, 1.56 mmol) were stirred in THF (2 mL) at room temperature for 3 h. The mixture was then poured into 50% ethyl acetate–ether (180 mL), washed with 10% sodium bisulfate (40 mL) and water (40 mL), dried ($MgSO_4$), and concentrated in vacuo to yield a pale yellow oil. The oil was purified by chromatography (Florisil column, 3 × 25 cm) with 10% ethyl acetate–hexane, 50% ethyl acetate–hexane, and 50% ethyl acetate–hexane (with 2% formic acid). The latter fractions contained the product and were combined and concentrated in vacuo. To the residue was added toluene (10 mL), which was then removed in vacuo. This procedure was repeated twice to remove the last traces of formic acid (note: the water bath never exceeds 55 °C during this process). The resulting oil was placed under high vacuum (0.1 mm) for 18 h to yield the hydroxy acid (118 mg, 100% mass balance).

To the crude hydroxy acid (48 mg, 0.126 mmol) in benzene (25 mL) was added triphenylphosphine (66 mg, 0.252 mmol) and diethyl azodicarboxylate (43.8 mg, 0.262 mmol). The reaction was stirred at room temperature for 36 h and then concentrated in vacuo to yield an orange oil. The oil was purified by chromatography (silica gel plate, 15 × 20 cm) in 50% ethyl acetate–hexane to give the lactone **23** (32.7 mg, 71.6%) as a colorless oil: partial ^{1}H NMR (270 MHz, $CDCl_3$) [The spectrum of the diastereomeric mixture is complex so only a partial analysis is given.] δ 0.91 (d, J = 12 Hz), 1.11 (s, methyl group), 4.75 (bd, J = 6.5 Hz, CHOC(O)R for one of the two diastereomers), 4.80 (bd, J = 6.5 Hz, CHOC(O)R for one of the two diastereomers), 6.18 and 6.28 (both d (AB), J = 3.1 Hz, cyclobutene olefin protons for one of the two diastereomers), 6.25 (bs, cyclobutene olefin protons for one of the two diastereomers).

Thermolysis of Cyclobutene 23. The cyclobutene **23** (35 mg, 0.0966 mmol) in toluene-d_8 (0.55 mL) was heated at 87 °C for 4 h (^{1}H NMR analysis showed no reaction had occurred) and at 106 °C for 41 h. The ^{1}H NMR (270 MHz) spectrum showed a 63:37 mixture of the *E,Z* isomers **24** and **25**, with **24** predominating (integration of the signals at δ 7.80 (**25**) and 8.27 (**24**) was used to determine the isomer ratio). The toluene-d_8 was removed in vacuo and the residue purified by chromatography (silica gel plate, 20 × 20 cm) in 33% ethyl acetate–hexane (three elutions) to yield the *Z,E* isomer **24** (16.2 mg, 46.3%) and at a lower R_f the other *E,Z* isomer **25** (12.1 mg, 34.6%), both as colorless oils. Isomer **24** was identical with the previously prepared *E,Z* macrocycle (vide supra) by ^{1}H NMR (270 MHz), MS, and analytical TLC (25% ethyl acetate–hexane). **25**: IR (CCl_4) 1739, 1718 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.97 (1 d, dd, J = 12.0, 1.9 Hz), 1.18 (3 H, s), 1.1–1.98 (9 H, m), 2.20 (1 H, s), 2.29–2.50 (3 H, m), 3.72 (1 H, d (AB), J = 11.0 Hz), 4.13 (1 H, m), 4.29 (1 H, *d* (AB), J = 11.0 Hz), 4.48 (1 H, m), 4.71 (1 H, bd, J = 6.1 Hz), 5.95 (1 H, d, J = 11.1 Hz), 6.05 (1 H, d, J = 15.5 Hz), 6.68 (1 H, td, J = 11.1, 0.8 Hz), 7.80 (1 H, ddd, J = 15.5, 11.1, 12 Hz); MS, *m/e* (relative intensity) 137 (9.4), 121 (12.7), 108 (39.3), 101 (100), 93 (98.7), 80 (18.5), 55 (40.8), 43 (43.8); calcd for $C_{20}H_{26}O_6$ 362.1729, found 362.1730.

5-(*tert*-Butyldimethylsiloxy)pentanoic Acid (37). To the alcohol **36** (1 g, 8.13 mmol) in methylene chloride (15 mL) were added *tert*-butyldimethylsilyl chloride (1.34 g, 8.94 mmol) and DMAP (1.20 g, 9.83 mmol). The reaction was stirred at room temperature for 19 h, then diluted with ether (200 ml), washed with 10% aqueous sodium bisulfate (2 × 50 mL) and saturated aqueous sodium chloride (40 mL), dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was purified by chromatography (silica gel column 3 × 40 cm) with hexane to 25% ether–hexane to yield a silyl ether (1.21 g, 60.5%) as a colorless oil.

To this oil (700 mg, 2.84 mmol) in HMPA (4 mL) was added lithium methyl mercaptide (500 mg, 9.25 mmol). The reaction was stirred at room temperature for 12 h, then poured into 10% chloroform–ethyl acetate (100 mL), and extracted with 10% potassium carbonate (2 × 70 mL). The base extractions were combined, neutralized at 0 °C with solid sodium bisulfate to pH 1, and extracted with ether (3 × 70 mL). The organic extracts were combined, dried ($MgSO_4$), and concentrated in vacuo to yield the acid **37** contaminated with 15–20% HMPA. The HMPA was removed under high vacuum (0.1 mm, 14 h) at 40 °C, leaving the acid **37** (524 mg, 78.8%) as a colorless oil: IR ($CHCl_3$) 3400–2900 (br), 1702 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.04 (6 H, s), 0.88 (9 H, s), 1.40–1.80 (4 H, m), 2.35 (2 H, t, J = 7.0 Hz), 3.60 (2 H, t, J = 7.0 Hz), 11.38 (1 H, bs).

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Registry No. **1**, 3148-09-2; **7**, 87729-18-8; **8**, 87729-19-9; **9**, 10374-07-9; (*E,Z*)-**10a**, 87729-20-2; (*E,E*)-**10b**, 87729-21-3; (*Z,E*)-**10b**, 87729-22-4; (*E,Z*)-**11a**, 79568-66-4; (*Z,E*)-**11b**, 87729-23-5; **12**, 87729-24-6; **14**, 6666-46-2; **15**, 22810-52-2; **16**, 13432-80-9; **17**, 7167-29-5; **19**, 87729-25-7; **20**, 38335-10-3; **21**, 87760-80-3; **22**, 87729-26-8; **23** (isomer 1), 87729-27-9; **23** (isomer 2), 87760-81-4; **24**, 87729-28-0; **25**, 87760-82-5; **29a**, 87729-29-1; **29b**, 87729-30-4; **30**, 87729-31-5; **31**, 87729-32-6; **32**, 87729-33-7; **33**, 87729-34-8; **34a**, 87729-35-9; **34b**, 87729-36-0; **35** (isomer 1), 87729-37-1; **35** (isomer 2), 87760-83-6; **36**, 14273-92-8; **36** *tert*-butyldimethylsilyl ether, 87729-38-2; **37**, 87729-39-3; ethanethiol, 75-08-1; δ-valerolactone, 542-28-9.

On the Palladium-Catalyzed Alkylation of Silyl-Substituted Allyl Acetates with Enolates

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Treatment of lithium enolates with trialkylstannyl trifluoroacetates permits their use as nucleophiles in allylic alkylations catalyzed by palladium with high regioselectivity and without polyalkylation. Alkylation without concomitant desilylation occurs for 3-acetoxy-1-(trimethylsilyl)-1-propene and *n*-butyl 2-acetoxy-4-(trimethylsilyl)-3-butenoate under these conditions. The choice of substituents on the tin does affect the rate of the alkylation; trimethyl substitution proceeds substantially faster than tri-*n*-butyl substitution.

Palladium-mediated formation of carbon–carbon bonds in allyl systems begins to emerge as a powerful tool for selective synthetic transformations.[1] In addition to the chemoselectivity, the ability to activate normally inert

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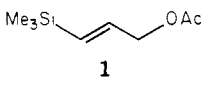
leaving groups, the ability to manipulate the regioselectivity independent of the regiochemistry of the starting allyl system, and the obtention of a complementary stereochemistry to normal displacements combine to offer a new dimension of control. The types of allylic substituents that succumb to palladium (0) catalysts now include acetate (or other carboxylate),[2] vinylogous carbonate,[3] phenoxide,[4,5] epoxide,[6] phosphate,[7] sulfone,[8] sulfide,[5,9] nitro,[10] and ammonium.[11] The nucleophilic partners can be classified into three groups:[1] (1) stabilized carbon nucleophiles among which fall malonic esters, β-keto esters, β-keto sulfones, bis sulfones, 1,3-diketones, and nitro compounds[12] which are characterized by an overall *retention* of stereochemistry;[2] (2) nonstabilized carbon and related nucleophiles among which fall vinyl,[13] aryl[9,13] methyl, and trimethylsilyl[14] organometallics as well as various hydride donors[15] which proceed with an overall *inversion* of stereochemistry; and (3) heteroatom nucleophiles like oxygen, nitrogen, and sulfur such as carboxylates,[16] alcoholates,[4a,17] amines,[18] and sulfones[19] which, while showing a preference for overall retention of stereochemistry, also can proceed via a net inversion pathway as well; the observed stereochemistry normally can be controlled to give either result. Allyl organometallics such as allylstannanes[20] have not yet been characterized.

Enolates form one of the most important classes of nucleophiles. Their suitability in palladium-catalyzed reactions appears somewhat confusing at present. In our early work with the lithium enolate of acetophenone, we encountered polyalkylation and elimination reactions competing with the desired simple alkylation[21]—an observation recently verified by Negishi.[22] Such an observation seems to agree with the vast body of work on alkylations of enolates with sluggish alkylating agents. Since the initial product of alkylation behaves as a carbon acid toward the unreacted enolate, equilibration between the product and the starting enolate which leads to loss of regioselectivity and to polyalkylation competes with the straight alkylation. Clearly, palladium-catalyzed reactions are relatively slow—an ideal case for such equilibration. Fiaud[23] and Hirao[11b] report good yields in such reactions. Nevertheless, all of our attempts to use lithium enolates proved less than successful.

A novel approach involved the simultaneous formation of an enolate and the π-allylpalladium intermediate in the palladium-assisted expulsion of carbon dioxide from 2-((allyloxy)carbonyl)cycloalkanones.[24] However, such an approach is restrictive due to the requirement for the (allyloxy)carbonyl derivative and does not show high stereocontrol. Due to the diverse methods to generate enolates directly from ketones, we focused on the attenuated of the reactivity of the enolate towards proton exchange. Indeed, we found that preformed enol stannanes did participate in such alkylations.[20] Negishi very recently reported that potassium enolates form borate salts that participate in such alkylations.[22]

In our exploration of bifunctional silicon conjunctive reagents such as **1**[25,26] or **2**,[25] we wished to initiate their



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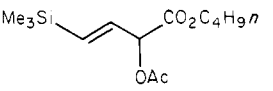

2

unravelling by alkylation of ketone enolates. Attempts to use the lithium enolate of cyclohexanone with **1** in the presence of a variety of palladium catalysts led, as now expected, to the desired mono- but also dialkylation. Our earlier observation regarding the use of enol stannanes attracted us except for the observation that we had to preform the enol stannane separately. Attempts to simply add tri-*n*-butyltin chloride to the lithium enolate and than perform the alkylation in situ did not yield completely satisfactory results.[21] In this paper, we wish to report a solution to this problem and to the use of the novel conjunctive reagents **1** and **2** in such *chemo-* and *regioselective* alkylations.

Results

Believing the source of the difficulty of using tri-*n*-butyltin chloride lay in the reactivity and bonding characteristics of the chloride ion and wishing to substitute at tin with a relatively hard nucleophile, an oxygen of an enolate, we chose tri-*n*-butyltin trifluoroacetate (**3**)[27] as our reagent. Generation of the enolate of 4-*tert*-butylcyclo-

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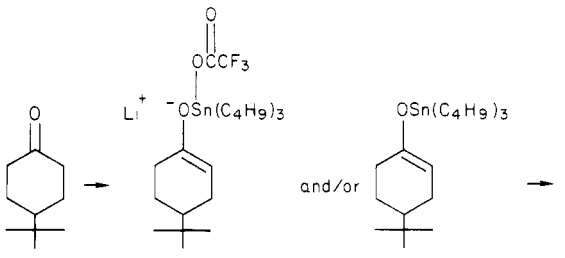
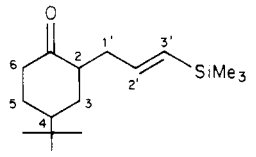
hexanone with lithium hexamethyldisilazide in THF at 0 °C followed by addition of **3** at room temperature produces in situ either the "ate" complex **4** or the enol stannane **5**.



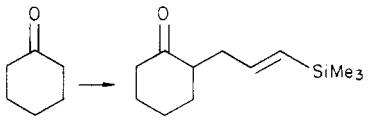
4 **5**



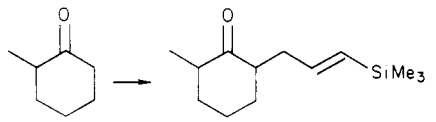
(1)

6a, *Z*, 2,4
b, *E*, 2,4

Simply adding 5.6 mol% of tetrakis(triphenylphosphine)palladium (**6**), 2.8 mol% of dppe, and a full equivalent of the allyl acetate **1** produces a 70% yield of approximately a 1:1 ratio of the *E* and *Z* isomers of **6** after 6 h at room temperature. The stereochemistry was assigned based upon the ^{1}H and ^{13}C NMR spectra. In the ^{1}H NMR spectra of **6a**, H-2 appears at δ 2.59 as a dtd (J = 13.9, 5.5, and 1.4 Hz); the 13.6 Hz coupling is consistent with a vicinal axial–axial coupling. In the ^{13}C NMR spectrum, the absorption for C-1' shifts from δ 36.6 in **6a** to δ 30.0 in **6b** in addition to the absorptions for C-4 and C-6 shifting from δ 47.2 and 41.6 in **6a** to δ 41.9 and 38.6 in **6b** in accord with the allyl group switching from equatorial in the former to axial in the latter. Alkylation of cyclohexanone under similar conditions gave a 61% yield of the expected alkylation product. Exposure of 2-



methylcyclohexanone to the same reaction conditions gives only alkylation at C-6 in 60% yield as a 1.4:1 ratio of diastereomers **7a**:**7b** (eq 2). The regiochemistry of each



(2)

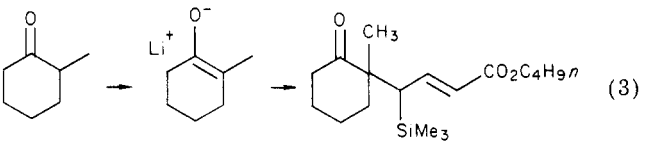
7a, *Z*, 2,6
b, *E*, 2,6

diastereomer is clearly established by the observation of a clean doublet for the methyl group (**7a** δ 0.98, J = 6.6 Hz; **7b** δ 1.01, J = 7 Hz). The absorptions for C-1', C-4, and C-6 shift from δ 36.6, 25.6, and 45.7, respectively, in **7a** to δ 31.6, 20.3, and 42.9 in **7b**, again suggesting an equatorial to axial shift of the allyl group. The appearance of the absorption for H-2 in **7a** at δ 2.60 as a dtd (J = 14.3, 5.5, and 1.5 Hz) further supports the diequatorial nature of **7a**.

Extension of this method to the less reactive allylating system **2** showed this alkylation to be sufficiently sluggish that we were led to search for an alternative stannylating agent. The simple change of the alkyl groups on tin from *n*-butyl to methyl makes the enol derivative sufficiently more reactive that normally 50–60% yields of the alkylated product are obtained at room temperature as summarized in Table I. Entries 3, 5, and 7 illustrate that high regioselectivity with respect to the unsymmetrical ketone is observed. Acetophenone, a system prone to polyalkylation, shows only the desired monoalkylated product (entry 4).

The most striking aspect of this table is the regioselectivity with respect to the electrophilic partner. In all cases, except one (entry 3), a bias for formation of the new C–C bond α to the silicon substituent exists. In entries 4–7, this selectivity is exclusive. Assignment of the regioselectivity relies upon NMR spectroscopy. For example, **8** (n = 2) shows widely separated vinyl absorptions for the two diastereomers at δ 7.02 (dd, J = 15.8 and 10.7 Hz), 6.81 (dd, J = 15.4 and 11.4 Hz), 5.67 (d, J = 15.4 Hz), and 5.56 (d, J = 15.8 Hz) in accord with the anisotropic effect of the carbomethoxy group on the double bond, whereas, **9** (n = 2) shows only one set of closely spaced vinyl absorptions (one diastereomer?) at δ 5.83 (d, J = 18 Hz) and 5.73 (dd, J = 18 and 7.7 Hz) in accord with the minimal effect of the trimethylsilyl group on chemical shifts.

A dramatic change occurs in the case of entry **3** where only alkylation α to the ester group occurs [δ 5.82 (d, J = 18.7 Hz) and 5.71 (dd, J = 18.7 and 7.5 Hz)]. As in the case of **9**, only one set of peaks is observed in the ^{1}H NMR spectrum of **10**. Furthermore, the ^{13}C NMR spectrum also shows only 15 peaks (one identity). These observations suggest that the reaction gives only *one geometric isomer and only one diastereomer*! The closer correspondence of the ^{13}C absorptions of the ring methyl carbon, C(4) and C(6) of **10** [δ 16.1, 20.9, and 44.2], to the corresponding absorption of **7b** [δ 15.6, 20.4, and 42.9] compared to those of **7a** [δ 14.5, 25.6, and 45.7] suggest it is the *E* isomer. A preliminary experiment with the thermodynamic enolate derived from 2-methylcyclohexanone led to the "normal" type of alkylation product **11** (eq 3) as a mixture of dia-



(3)

11

stereomers (δ 6.86 (dd, J = 19.5 and 11.7 Hz), 6.83 (dd, J = 18.8 and 11.5 Hz), 6.53 (d, J = 18.8 Hz), and 6.31 (d, J = 19.5 Hz)]. In the cases of **13** and **14**, a mixture of geometric isomers in addition to the diastereomers resulted as evidenced by the NMR spectra. On the other hand, 5α-cholestanone forms a single geometric isomer at C-2 which was tentatively assigned the 2α configuration, but it is a mixture of diastereomers at the side chain carbon.

Discussion

This method for palladium-catalyzed alkylation of enolates is simple to execute. While the yields normally range from 40–70%, no attempt has been made to optimize the alkylation conditions for any example. Thus, further improvement for a particular case of importance appears likely. In this regard, special note should be taken that this study was limited to the silyl substituted allyl acetates. The silicon substituent can have a deleterious effect on the rate of the reaction due to its steric size.[28] It is anticipated that allyl acetates or other types of substrates lacking such a substituent will behave even better. Even contrasting the reactions of **1** vs. **2** the yields of alkylation with the former proceeded in somewhat higher yields with the more

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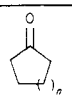
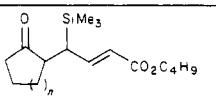
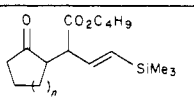
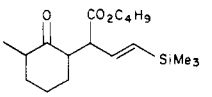
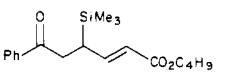
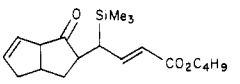
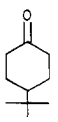
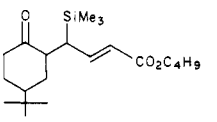
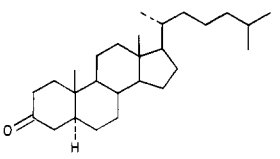
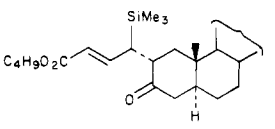
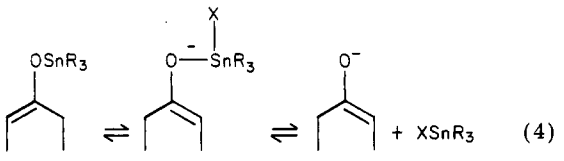
Table I. Palladium-Catalyzed Alkylation of Trimethyltin Enolates with 2[a]

entry	ketone	product		isolated yield, %
		 8	 9	
1	$n = 1$	82	18	55
2	$n = 2$	67	33	37
3		 10		49
4	$PhCOCH_3$	 12		52
5		 13		26
6		 14		61
7		 15		61

[a] All reactions were performed using 1–7 mol % of $(Ph_3P)_4Pd$ + dppe in THF at room temperature.

sluggish tri-*n*-butylstannane derivatives than the latter did with the more reactive trimethylstannane derivatives. The destabilizing influence of the carbo-*n*-butoxy group on the π-allylpalladium cationic intermediate from **2** accounts for this behavior.

The effect of the alkyl substituents on tin on the rate of the reaction is normally ignored.[29] The fact that a rate acceleration is experienced in going from the tri-*n*-butyl to the trimethyl group is expected if we consider an alkylation mechanism requiring attack of a nucleophile on tin as in eq 4 in which an "ate" complex such as **17**, rather



16 **17** (4)

than the enol stannane **16**, undergoes alkylation or dissociates to the enolate prior to alkylation. The retention of regioselectivity and the lack of polyalkylation speaks against a free enolate. Thus, we suggest that **17** is the likely intermediate for alkylation.

The observed regioselectivity with respect to the allylic acetates **1** and **2** merits comment. Regioselectivity appears to depend upon (1) steric hindrance to attack by the nucleophile, (2) the charge distribution in the intermediate π-allylpalladium complex which can also relate to the symmetry of this complex, and (3) the stability of the olefin–palladium(0) complex of the alkylated product which is the primary product. For all of these reasons, allyl acetate **1** should and does alkylate at the unsubstituted end of the π-allyl unit. On the other hand, for **2**, steric hindrance should lead to attack α to the ester, but charge distribution and stability of the primary alkylation product should lead to attack α to the silicon. That a competition exists is evident in the cases of alkylation of cyclopentanone and cyclohexanone in which both products are seen; nevertheless, the latter two factors are clearly dominant. In most cases, alkylation α to silicon is the exclusive product.

The exception of 2-methylcyclohexanone is striking. In an "ate" complex, $A^{1,3}$ strain should favor an axial methyl group as in **19**.[30] The presence of the axial methyl group should force the bulky alkylating agent into topside (pseudoequatorial) approach. For stereoelectronic reasons, a twist boat **21** must be the kinetic product.[31] The bow interactions in such a twist boat would increase the steric demands of the substituent on the carbon of the allyl fragment that is bonding to the "ate" complex. This enhanced steric effect presumably accounts for the odd behavior of 2-methylcyclohexanone. This rationale accommodates the high selectivity for one ring isomer in contrast to the 4-*tert*-butylcyclohexanone case and agrees with our assignment of this stereochemistry as *E*. While we have not established which diastereomer at the side chain is

(29) See however Abraham, M. H.; Hill, J. A. *J. Organomet. Chem.* **1967**, *7*, 11. Gielen, M.; Nasielski, J. *Ibid.* **1963**, *1*, 173. Boie, S.; Gielen, M.; Nasielski, J. *Ibid.* **1967**, *9*, 443. Abraham, M. H.; Spalding, T. R. *J. Chem. Soc. A* **1969**, 399. Cochran, J. C. et al. *Organomet.* **1982**, *1*, 586.

(30) Malhotra, S. K.; Johnson, F. *J. Am. Chem. Soc.* **1965**, *87*, 5493.

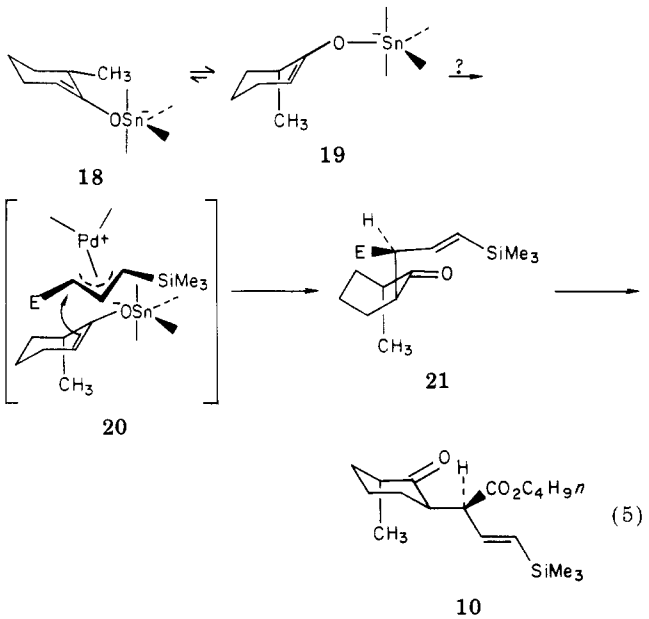
(31) For an excellent discussion of this effect see House, H. O. "Modern Synthetic Reactions"; W. A. Benjamin, Inc.: Menlo Park, 1972; pp 586–595.

Table II. Reaction Details for Alkylation Reactions

entry	allyl acetate, mg, mmol	ketone, mg, mmol	$R_3SnO_2CCF_3$, R, mg, mmol	$(Ph_3P)_4Pd$, mg, mol %	dppe, mg, mol %	time, h	product, mg, % yield
1	1, 172 mg, 1.0	4-*tert*-butylcyclohexanone, 169.9, 1.1	R = C_4H_9-*n*, 403, 1.0	64.7, 5.6	71., 2.8	4	**6a**,[a] 67.6, 25.4 **6b**,[a] 70.9, 26.6
2	1, 172, 1.0	4-*tert*-butylcyclohexanone, 150.0, 0.97	R = C_4H_9-*n*, 440, 1.09	43.9, 3.8	4.8, 1.9	6.3	**6a**+**b**[b] 181.4, 70
3	1	cyclohexanone	see text				
4	1, 172, 1.0	2-methylcyclohexanone, 116, 1.04	R = C_4H_9-*n*, 415, 1.03	54.1, 4.7	6.0, 2.4	4.25	**7a**,[c] 80.1, 34.5 **7b**,[c] 58.7, 25.3
5	2, 272, 1.0	cyclopentanone, 84.1, 1.0	R = CH_3, 286.4, 1.03	43.3, 3.7	4.8, 1.2	9	**8**[d] (*n* = 1) 133.7, 45 **9**[d] (*n* = 1) 28.9, 10
6	2, 136, 0.5	cyclohexanone, 48.0, 0.49	R = CH_3, 160.4, 0.58	46.0, 8	2.0, 2	18	**8**+**9** (*n* = 2) 54.4, 37
7	2, 272, 1.0	2-methylcyclohexanone, 112, 1.0	R = CH_3, 297.8, 1.08	74.4, 6.4	10, 2.5	ON[e]	**10**,[f] 158, 49
8	2, 136, 0.5	acetophenone, 60, 0.49	R = CH_3, 180.1, 0.65	39, 6.7	2.5, 1.3	6	**12**,[a], 86, 52
9	2, 136, 0.5	bicyclo[3.3.0]oct-7-en-2-one, 61, 0.50	R = CH_3, 165.4, 0.59	36.2, 6.3		20	**13**,[a] 42.7, 26
10	2, 272, 1.0	4-*tert*-butylcyclohexanone, 152.7, 0.99	R = CH_3, 289.2, 1.05	48.7, 4.2	3.3, 0.8	6	**14**,[a] 219.7, 61
11	2, 136, 0.5	5α-cholestanone, 193.3, 0.5	R = CH_3, 167, 0.6	28.1, 4.9		20	**15**,[g] 182.1, 61

[a] Purified by PLC using 15% ether in pentane. [b] Purified by flash chromatography using 15% ether in pentane. [c] Purified by flash chromatography using 3.2% ethyl acetate in hexane. [d] Purified by flash chromatography using 7.5% ethyl acetate in hexane. [e] ON = overnight. [f] Purified by flash chromatography using 4% ethyl acetate in hexane. [g] Purified by flash chromatography using 5% ethyl acetate in hexane.

produced, the rationale suggests the one depicted in eq 5 for **10**.



(5)

This approach permits a regiocontrolled alkylation of allylic substrates under very mild conditions. All alkylations have been performed at room temperature even using tetrakis(triphenylphosphine)palladium as the catalyst. We have not found advantages in using other catalysts at this point although there may be specific examples where such will be the case. It is tempting to speculate that such an approach may also be useful to minimize polyalkylation and loss of regioselectivity in nonmetal-catalyzed reactions since enol stannanes have been useful in alkylation reactions.[32] The perceived ability of transition metal templates to overwhelm the electronic bias of the π-allyl unit by steric effects suggests a new and more direct approach to enolonium equivalents.

(32) Odii, Y.; Pereyre, M. *J. Organomet. Chem.* **1973**, *55*, 273. Tardella, P. A. *Tetrahedron Lett.* **1969**, 1117.

Experimental Section

All reactions were carried out under a positive pressure of dry nitrogen. In some cases, the nitrogen was purified by bubbling through a triglyme solution of potassium benzophenone ketyl and activated 13X molecular sieves. Anhydrous reactions were performed in flame-dried glassware which was cooled under nitrogen. THF was freshly distilled from sodium benzophenone ketyl.

Silica gel (Machery Nagel P/UV_{254}) was used for PLC (1.5 mm thickness) and activated at 120 °C. Flash chromatography was accomplished with Merck Kieselgel (GF_{60} 230–400 mesh).

Proton NMR spectra were determined in $CDCl_3$ (unless otherwise stated) on an IBM WP200 or Brucker WM270 instrument and chemical shifts are recorded in δ relative to an internal standard of Me_4Si. Carbon NMR spectra were determined on a Jeol FX 60 or FX 200 instrument.

The stannyl trifluoroacetates were prepared according to literature procedures.[27]

General Alkylation Reaction. The lithium enolate of the ketone was generated at 0 °C by addition of a 1 M THF solution of 0.95–1.0 equiv of the ketone to 1 equiv of a 5 M THF solution of lithium hexamethyldisilazide. After concentrating in vacuo and warming to room temperature, 1 equiv of the stannyl trifluoroacetate was added and stirring was continued for 30 min to 1 h. The resultant solution was cannulated into a solution of 1–7 mol% of $(Ph_3P)_4Pd$, 0.5–3.5 mol% of dppe, and the allyl acetate. The resultant solution was stirred at room temperature until TLC monitoring indicated completion. Workup consisted of partitioning between ether and water, drying the ether layer over Na_2SO_4, removal of the ether by distillation, and purification of the residue by PLC. The reaction details are summarized in Table II. A typical procedure follows.

To a solution of 1 mmol of lithium hexamethyldisilazide in 1 mL of THF at 0 °C was added 94.7 mg (0.96 mmol) of cyclohexanone. After 30 min at 0 °C, the solution was concentrated in vacuo and 420 mg (1.04 mmol) of tri-*n*-butylstannyl trifluoroacetate in 1 mL of THF was added. The reaction was allowed to warm to room temperature over 1.5 h and cannulated into a solution of 68.3 mg (5.9 mol%) of tetrakis(triphenylphosphine)palladium, 8 mg (2 mol%) of 1,2-bis(diphenyl-

phosphino)ethane (dppe), and 200 mg (1.16 mmol) of 3-acetoxy-1-(trimethylsilyl)-1-propene in 2 mL of THF. After stirring overnight at room temperature, it was partitioned between 150 mL of ether and 30 mL of water. The water layer was washed with 3 × 20 mL of ether and the combined organic layers were dried. The solvent was removed by distillation and the residue subjected to PLC eluting with 15% ether in pentane to yield 124.4 mg (61%): ^{1}H NMR (270 MHz) δ 6.01 (1 H, ddd, J = 18.4, 7.4, 5.5 Hz), 5.50 (1 H dt, J = 18.4, 1.5 Hz), 2.57 (1 H, dtd, J = 14.0, 5.5, 1.5 Hz), 1.31-2.32 (8 H, m), -0.01 (9 H, s); ^{13}C NMR (50.1 MHz) δ 211.8, 144.2, 131.9, 50.2, 42.1, 36.8, 33.5, 28.0, 25.1, -1.0; calcd for $C_{12}H_{22}OSi$, 210.1439; found, 210.1441.

Spectral Data. 6a: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.95 (1 H, ddd, J = 18.4, 7.7, 5.5 Hz), 5.59 (1 H, dt, J = 18.4, 1.4 Hz), 2.59 (1 H, dtd, J = 13.9, 5.5, 1.4 Hz), 1.3-2.4 (9 H, m), 0.86 (9 H, s), -0.01 (9 H, s); ^{13}C NMR (FX 200) δ 212.3, 144.7, 132.0, 49.2, 47.2, 41.6, 36.6, 34.7, 32.5, 28.7, 27.6, -1.2; calcd for $C_{16}H_{30}OSi$, 266.2058; found, 266.2065.

6b: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.82 (1 H, ddd, J = 18.4, 7.4, 5.2 Hz), 5.56 (1 H, d, J = 18.4 Hz), 1.4-2.4 (10 H, m), 0.84 (9 H, s), -0.01 (9 H, s); ^{13}C NMR (FX 200) δ 214.6, 143.2, 133.4, 48.3, 41.9, 38.6, 38.3, 32.5, 30.0, 27.4, 26.6, -1.3; calcd for $C_{16}H_{30}OSi$, 266.2058; found, 266.2065.

7a: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.94 (1 H, ddd, J = 18.4, 7.4, 5.5 Hz), 5.59 (1 H, dt, J = 18.4, 1.5 Hz), 2.60 (1 H, dtd, J = 14.3, 5.5, 1.5 Hz), 2.2-2.5 (9 H, m), 0.98 (3 H, d, J = 6.6 Hz), -0.00 (9 H, s); ^{13}C NMR (FX 200) δ 213.1, 144.9, 131.8, 50.3, 45.7, 37.4, 36.6, 34.7, 25.6, 14.5, -1.15; calcd for $C_{13}H_{24}OSi$, 224.1590; found, 224.1596.

7b: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.84 (1 H, ddd, J = 18.8, 6.6, 5.5 Hz), 5.6 (1 H, d, J = 18.8 Hz), 2.45-1.46 (10 H, m), 1.01 (3 H, d, J = 7 Hz), -0.02 (9 H, s); ^{13}C NMR (FX 200) δ 215.3, 143.7, 132.5, 48.2, 42.9, 37.6, 34.9, 31.6, 20.4, 15.6, -1.3; calcd for $C_{13}H_{24}OSi$, 224.1590; found, 224.1596.

8 (n = 1): ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.91 (dd, J = 15.4, 10.1 Hz) and 6.8 (dd, J = 15.4, 11.4 Hz) total 1 H, 5.68 and 5.62 (total 1 H, each d, J = 15.4 Hz), 4.06 (2 H, m), 2.44 (1 H, dd, J = 11.4 and 3.2 Hz), 1.2-2.4 (11 H, m), 0.89 and 0.88 (total 3 H, each t, J = 8 Hz), 0.017 (9 H, s); ^{13}C NMR (50.1 MHz) δ 219.1, 218.3, 166.5, 149.8, 146.9, 120.7, 119.0, 63.9, 50.4, 48.9, 37.8, 37.6, 35.6, 33.7, 30.8, 29.8, 26.7, 20.7, 19.1, 13.6, -1.5, -2.3; calcd for $C_{16}H_{28}O_3Si$, 296.1806; found, 296.1806.

9 (n = 1): ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.04 (1 H, dd, J = 18.7, 7.4 Hz), 5.77 (1 H, dd, J = 18.7, 1.1 Hz), 4.04 (2 H, m), 3.61 (1 H, dd, J = 9.5, 5.5 Hz), 1.2-2.8 (11 H, m), 0.88 (3 H, t, J = 8 Hz), 0.01 (9 H, s); ^{13}C NMR (50.1 MHz) δ 217.9, 172.0, 141.0, 134.0, 64.6, 51.5, 50.6, 38.0, 32.5 30.7, 26.2, 20.7, 19.1, 13.6, -1.4.

8 and 9 (n = 2): (270 MHz, $CDCl_3$) δ 7.02 (dd, J = 15.8, 10.7 Hz), 6.81 (dd, J = 15.4, 11.4 Hz), 5.83 (d, J = 18 Hz), 5.73 (dd, J = 18, 7.7 Hz), 5.67 (d, J = 15.4 Hz), 5.56 (d, J = 15.8, Hz) [total 2 H], 4.05 (2 H, m), 3.10 (dd, J = 9.5, 5.5 Hz), 2.81 (m), 2.56 (m), 1.25-2.45 (m) [14 H], 0.88 (3 H, m), -0.01 (s) and -0.04 (s) [9 H]; ^{13}C NMR (50.1 MHz) δ 212.2, 211.5, 167.5, 151.3, 150.6, 141.7, 137.3, 119.5, 118.7, 63.9, 51.6, 42.0, 36.1, 34.1, 30.8, 28.0, 25.2, 25.0, 19.2, 13.7, -1.2, -1.8.

10: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.82 (1 H, d, J = 18.7 Hz), 5.71 (1 H, dd, J = 18.7, 7.5 Hz), 4.03 (2 H, m), 3.16 (1 H, dd, J = 10.3, 7.5 Hz), 2.93 (1 H, dt, J = 10.3, 5.2), 2.55 (1 H, m), 1.25-1.99 (10 H, m), 1.12 (3 H, d, J = 7 Hz), 0.87 (3 H, t, J = 7 Hz), 0.12 (9 H, s); ^{13}C NMR (50.1 MHz) δ 214.3, 172.9, 140.8, 136.2, 64.4, 53.6, 48.6, 44.2, 34.0, 30.6 (2C), 20.1, 19.1, 16.1, 13.6, -1.32; calcd for $C_{18}H_{32}O_3Si$, 324.2119; found, 324.2120.

12: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.92 (2 H, m), 7.50 (3 H, m), 7.02 (1 H, dd, J = 15.4, 8.7 Hz), 5.60 (1 H, dd, J = 15.4, 1.2 Hz), 4.05 (2 H, t, J = 6.3 Hz), 3.22 (1 H, dd, J = 17.3, 9.6 Hz), 3.08 (1 H, dd, J = 17.3, 4.4 Hz), 2.59 (1 H, m), 1.28-1.61 (4 H, m), 0.89 (3 H, t, J = 6.3 Hz), 0.06 (9 H, s); ^{13}C NMR (50.1 MHz) δ 197.9, 166.5, 150.8, 136.6, 132.8, 129.1, 128.4, 128.1, 127.8, 117.6, 63.9, 37.2, 30.8, 29.6, 26.5, 19.3, 13.7, -2.8; calcd for $C_{19}H_{28}O_3Si$, 332.1806; found, 332.1807.

13: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.83 (dd, J = 15.5, 11.2 Hz) and 6.72 (dd, J = 15.2, 10.5 Hz) [total 1 H], 5.64 (3 H, m), 4.08 (2 H, m), 1.18-3.22 (12 H, m), 0.89 (3 H, t, J = 6 Hz), 0.08 (9 H, s); calcd for $C_{19}H_{30}O_3Si$, 334.1962; found, 334.1963.

14: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.10 (dd, J = 15.6, 10.8 Hz), 6.85 (dd, J = 15.4, 11.4 Hz) and 6.723 (dd, J = 15.4, 11.0 Hz) [total 1 H]; 5.70 (d, J = 15.4 Hz) and 5.57 (d, J = 15.4 Hz) [total 1 H]; 4.07 (2 H, t, J = 5.9 Hz), 1.36-2.68 (13 H, m), 0.895 (3 H, t, J = 5.9 Hz); 0.894 (s), 0.87 (s), 0.80 (s) [total 9 H], 0.005 (s), -0.016 (s), -0.024 (s) [total 9 H]; calcd for $C_{21}H_{38}O_3Si$, 366.2588; found, 366.2589.

15: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.99 (dd, J = 15.4, 11 Hz), 6.82 (dd, J = 15.4, 11.2 Hz) [total 1 H]; 5.69 (d J = 15.4 Hz), 5.54 (d, J = 15.4 Hz) [total 1 H]; 4.04 (2 H, m), 2.60 (1 H, m), 2.45 (1 H, dd, J = 11.4, 4.4 Hz), 2.22 (1 H, m), 0.60-1.98 (50 H, m) with methyl peaks at δ 0.61, 0.79, 0.81, 0.83, 0.85; -0.02 (s) and -0.04 (s) [9 H]; ^{13}C NMR (50.1 Hz) δ 210.2, 210.0, 166.6, 150.5, 149.1, 119.6, 118.7, 63.7, 56.2, 53.9, 47.5, 46.5, 44.7, 44.3, 42.6, 39.9, 39.5, 36.6, 36.2, 35.7, 35.2, 33.3, 31.7, 30.8, 28.7, 28.2, 27.9, 24.2, 23.8, 22.7, 22.5, 21.5, 19.1, 18.6, 13.6, 12.3, 12.0, -1.24, -1.71; calcd for $C_{38}H_{66}O_3Si$, 598.4778; found, 598.4778.

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Registry No. **1**, 80401-14-5; **2**, 86970-26-5; **3**, 7299-28-7; **6a**, 87729-60-0; **6b**, 87729-61-1; **7a**, 87729-62-2; **7b**, 87729-63-3; **8** (n = 1), 87729-64-4; **8** (n = 2), 87729-65-5; **9** (n = 1), 87729-66-6; **9** (n = 2), 87729-67-7; **10**, 87729-68-8; **11**, 87729-69-9; **12**, 87729-70-2; **13**, 87729-71-3; **14**, 87729-72-4; **15**, 87729-73-5; $Me_3SnO_2CCF_3$, 6430-48-4; 4-*tert*-butylcyclohexanone, 98-53-3; cyclohexanone, 108-94-1; 2-methylcyclohexanone, 583-60-8; cyclopentanone, 120-92-3; acetophenone, 98-86-2; bicyclo[3.3.0]oct-7-en-2-one, 56138-05-7; 5α-cholestanone, 566-88-1; lithium hexamethyldisilazide, 4039-32-1; 1,2-bis(diphenylphosphino)ethane, 1663-45-2; tetrakis(triphenylphosphine)palladium, 14221-01-3.

Strong Base Induced Cycloaddition of Homophthalic Anhydrides Leading to *peri*-Hydroxy Polycyclic Compounds

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A new and exceptionally facile cycloaddition of the alkaline metal salt of homophthalic anhydrides (**1a,b**) is described. The anions of the anhydrides **1a,b** undergo cycloadditions with various dienophiles (**5-14**) to give the corresponding *peri*-hydroxy polycyclic compounds (**15-26**) in good yields under extremely mild conditions, whereas thermal cycloaddition of **1a,b** requires high temperatures.

We recently reported[1] that homophthalic anhydrides (**1a,b**) undergo thermal cycloaddition to carbon-carbon multiple bonds to afford biologically important *peri*-hydroxyanthraquinones[2] in a single step. The cyclo-

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