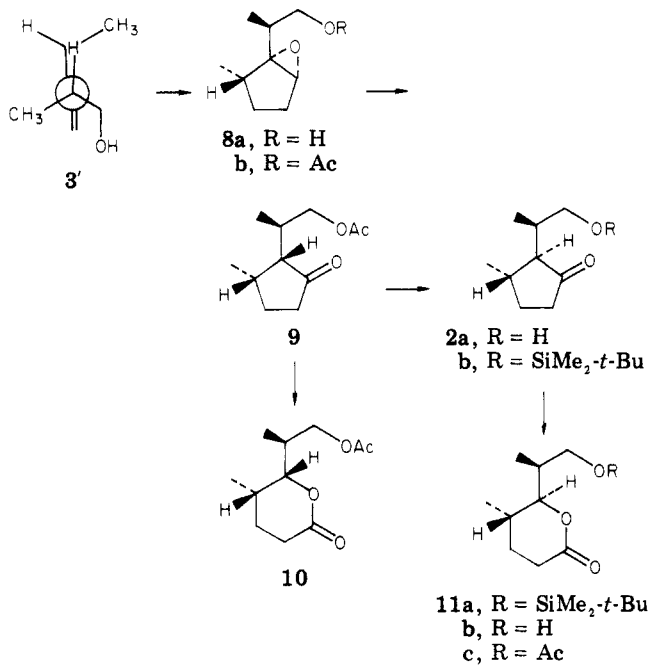
Scheme III



parisons.[16] Then **2b** was converted to the acetoxy lactone **11c** by Baeyer–Villiger oxidation (**11a**), removal of the silyl group (**11b**), and acetylation. Thin-layer chromatography (hexane/ethyl aceatate, 2:1) and ^{1}H NMR cleanly distinguish between the two epimeric lactones **10** and **11c**. Since there is only one epimerizable center in the conversion of **9** to **11c** the stereochemistry of **10** as well as **9** must be as depicted. Compound **2b** was previously converted to the Prelog–Djerassi lactone **1** via **11a** by Grieco.[3d]

In summary, the ene reaction of (*Z*)-1-ethylidene-2-methylcyclopentane **4** has been found to proceed with a high degree of regio- and stereoselectivity which appears to be controlled by a combination of steric interactions. A formal total synthesis of racemic Prelog–Djerassi lactone was completed by the conversion of the major ene adduct **3** to a known synthetic intermediate.

Acknowledgment. We are indebted to Professor P. Grieco for providing a generous sample of the alcohol precursor for racemic **2b**. We also express our gratitude to the members of the Physical Chemistry Department of Hoffmann-La Roche Inc. for determinations of spectral and analytical data.

Registry No. (±)-**1**, 56781-39-6; (±)-**2a**, 80866-35-9; (±)-**2b**, 71828-72-3; (±)-**3**, 80866-36-0; (±)-**4**, 80866-37-1; (±)-**5**, 80866-38-2; (±)-**6**, 80866-39-3; (±)-**7**, 80866-40-6; (±)-**8a** (isomer 1), 80866-41-7; (±)-**8a** (isomer 2), 80924-11-4; (±)-**8b**, 80866-42-8; (±)-**9**, 80866-43-9; (±)-**10**, 80866-44-0; (±)-**11a**, 71828-73-4; (±)-**11b**, 80866-45-1; (±)-**11c**, 80866-46-2; 2-methylcyclopentanone, 32854-37-8.

† This manuscript is dedicated the the memory of Dr. Willy Leimgruber, deceased, July 8, 1981.

(16) We are indebted to Professor P. Grieco for providing a generous sample of the alcohol precursor for racemic **2b** which was then oxidized to **2b** according to his procedure.[3d] The ^{13}C NMR comparison included obtaining the spectrum of a 1:1 mixture of authentic material with **2b** prepared by the process described in the text. No doubling of the 12 signals was observed.

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Synthesis and Transmetalation of Alkyl (*E*)-2,3-Bis(trimethylstannyl)-2-alkenoates, Novel Organotin Compounds

Summary: Reaction (THF, 0 °C) of α,β-acetylenic esters with 2.5 equiv of the (trimethylstannyl)copper reagents **3** or **5** provides, stereoselectively, the corresponding alkyl (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates. The potential synthetic utility of the latter substances is demonstrated by the conversion of ethyl (*E*)-2,3-bis(trimethylstannyl)-2-butenoate (**17**) into the stereochemically homogeneous compounds **25–30**, inclusive.

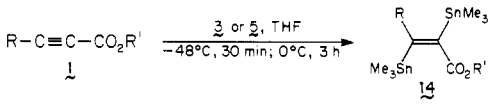
Sir: We have shown[1,2] recently that α,β-acetylenic esters **1** react smoothly with (trimethylstannyl)cuprate (**2–4**)[3] or copper (**5**)[3] reagents to produce, after protonation of the presumed intermediates **6**[4] and/or **7**[4], the conjugate addition products **8** and/or **9**. Clearly, the synthetic utility of this methodology would be enhanced significantly if **6** and/or **7** could be trapped with electrophiles ("E$^+$") other than proton. For example, reduction of the ester group of the resultant product(s) (general structures **10** and/or **11**), followed by sequential protection of the hydroxyl function and transmetalation (CH_3Li) of the Me_3Sn moiety, would provide organolithium reagents corresponding to the geometrically isomeric general synthons[5] **12** and/or **13**. We report herein that (a) although our attempts to trap **6** and/or **7** with electrophiles other than proton have been unsuccessful thus far, investigations into possibility have led to the discovery of an efficient method for the synthesis of alkyl (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates (**14**),[6] and (b) treatment of the latter substances with CH_3Li results in the selective transmetalation of the α-trimethylstannyl group to provide nucleophilic species which may be trapped by carbon electrophiles.

Treatment of a solution (THF, −78 or −48 °C)[1,2] of 1.2 equiv of the cuprate reagent **3** with 1.0 equiv of ethyl 2-butynoate (**15**),[9,10] followed by addition of methyl iodide, benzyl bromide, or cyclohexanone and stirring of the reaction mixture at −78 or −48 °C for 2–3 h, failed to provide any of the desired products **16** (E = CH_3, $C_6H_5CH_2$, or 1-hydroxycyclohexyl). In each case, appropriate workup gave only the product (**16**, E = H) resulting from protonation of the intermediate.[12] In efforts to find conditions

(1) Piers E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263.
(2) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron Lett.* **1981**, *22*, 4905.
(3) For the preparation of these reagents, see ref 2.
(4) The formulas **6** and **7** are not meant to imply actual structures, but are used only for the sake of clarity. See also Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851. Siddall, J. B.; Biskup, M.; Fried, J. H. *Ibid.* **1969**, *91*, 1853. Anderson, R. J.; Corbin, V. L.; Cotterrell, G.; Cox, G. R.; Henrick, C. A.; Schuab, F.; Siddall, J. B. *Ibid.* **1975**, *97*, 1197.
(5) Cf. Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
(6) Although 1,2-bis(trialkylstannyl)ethylenes are known,[7,8] to the best of our knowledge organotin compounds of general structure **14** have not been reported previously.
(7) Bulten, E. J.; Budding, H. A.; Noltes, J. G. *J. Organomet. Chem.* **1970**, *22*, C5.
(8) (a) Corey, E. J.; Wollenberg, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 5581. (b) *J. Org. Chem.* **1975**, *40*, 3788.
(9) The α,β-acetylenic esters employed in this work were prepared by reaction of the appropriate lithium acetylides with ethyl (or methyl) chloroformate. The required acetylenes are commercially available or were prepared via standard methods. Details will be given in a full paper.
(10) All compounds reported herein exhibited spectral data in full accord with structural assignments. New compounds gave satisfactory elemental analyses and/or high-resolution mass spectrometric measurements. Although the mass spectra of the organotin compounds did not exhibit molecular ion peaks, in accord with previous observations concerning trimethylstannyl compounds,[11] all showed $m/e = M^+ - 15$ peaks, and, in each case, the high-resolution measurement was carried out on this fragment.
(11) Kuivila, H. G.; Tsai, K.-H.; Kingston, D. G. I. *J. Organomet. Chem.* **1970**, *23*, 129.

0022-3263/82/1947-1602$01.25/0

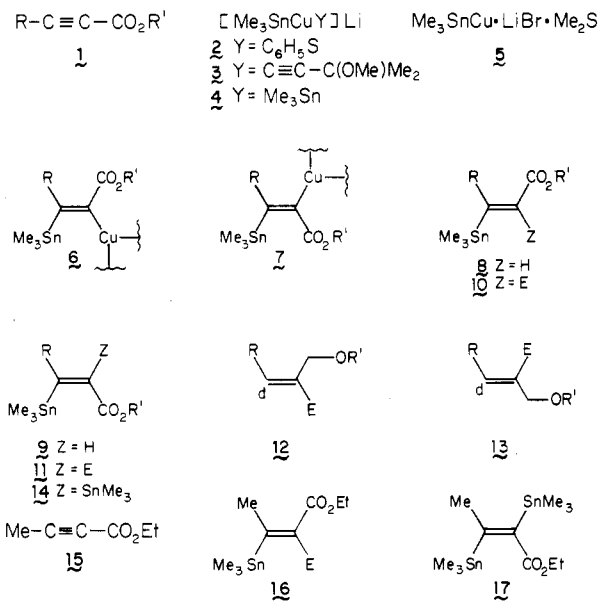
Table I. Preparation of (*E*)-α,β-Bis(trimethylstannyl) α,β-Unsaturated Esters



R	R′	% yield of 14[a] reagent 3	% yield of 14[a] reagent 5
Me	Et	74	73
Et	Et	76	79
i-Pr	Me	74	70
n-C_6H_{13}	Me	86	79
cyclopropyl	Me	73	77
2-(2-cyclopentenyl)ethyl	Me	71	76
(3-cyclohexenyl)methyl	Me	82	82
t-$BuMe_2SiOCH_2$	Et	70	74
t-$BuMe_2SiOCH_2CH_2$	Me	69	72

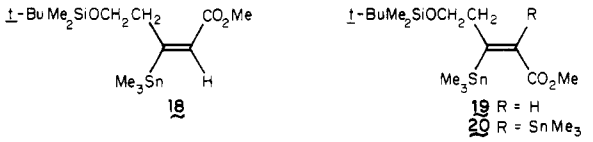
[a] Yield of distilled, purified product.

under which the desired trapping reactions would take place, the reaction temperature was increased. However, when methyl iodide was added to the reaction mixture obtained by allowing **15** to react with 1.2 equiv of reagent **3** and the temperature was allowed to rise from −48 to 0 °C, the material obtained upon workup contained none of the desired product **16** (E = CH_3). Instead, there was obtained, in addition to **16** (E = H), a low yield (~25% based on **15**) of a substance which contained *two* trimethylstannyl groups and which was subsequently identified as ethyl (*E*)-2,3-bis(trimethylstannyl)-2-butenoate (**17**).



Compound **17** represents a novel, new type of organotin derivative.[6] Therefore, we decided to try to improve the yield of this material and to determine whether or not this interesting reaction is generally applicable to other α,β-acetylenic esters. After some experimentation, it was found that when **15** was allowed to react (THF, −48 °C, 30 min; 0 °C, 3 h) with 2.5 equiv of the reagents **3** or **5**,[13] the bis(trimethylstannyl) ester **17** was produced in 70–75% yield. In essentially identical fashion, other α,β-acetylenic esters **1** could be transformed smoothly into the corresponding (*E*)-α,β-bis(trimethylstannyl) α,β-unsaturated esters **14** (see Table I). Although the results summarized in the table require little additional comment, it should be emphasized that, in each case, the indicated product was, in addition to Me_6Sn_2, essentially the only volatile substance obtained upon distillation of the crude material. Furthermore, the yields were consistently good, and the reaction was successful not only with "simple" α,β-acetylenic esters but also with functionalized substrates.

The stereochemical assignments with respect to the products **14** were made on the basis of ^1H NMR spectroscopy. For example, the γ protons of the α,β-unsaturated ester **18**[1] resonate ($CDCl_3$) at δ 3.10 (broad triplet), while the corresponding signal of the geometric isomer **19**[1] appears at δ 2.63. In comparison, the γ protons of the bis(trimethylstannyl) compound **20** give rise to a triplet at δ 2.72. Since the latter value is much closer to 2.63 than to 3.10, it seems highly likely that in compounds **19** and **20**, the stereochemical relationship between the CO_2Me group and the γ-methylene group is the same.[14] Similar comparisons were made for the other bis(trimethylstannyl) esters listed in Table I, and the results are completely consistent with the stereochemical assignments.



Interestingly, the α-Me_3Sn group of the bis(trimethylstannyl) esters **14** can be removed directly and selectively by transmetalation, without interference from either the ester moiety or the β-Me_3Sn group. Furthermore, the resultant nucleophilic intermediates react smoothly with a variety of electrophiles. For example, transmetalation (THF, −98 °C, 20 min) of compound **17** with 1.1 equiv of CH_3Li, followed by treatment of the resultant solution with methyl iodide (−98 °C, 30 min; −78 °C, 1 h), allyl bromide (−98 °C, 30 min; −78 °C, 3 h), benzyl bromide (−98 °C, 30 min; −78 °C, 1 h), *n*-butyl iodide (−78 °C, 1 h; room temperature, 3 h), or cyclohexanone (−98 °C, 30 min; −78 °C, 1 h) provided the corresponding products **25**–**29**, in (isolated) yields of 84%, 79%, 76%, 50%,[17] and 71%, respectively. In each case, the product consisted of only one geometric isomer and the fact that the overall process took place with retention of configuration with respect to the olefinic linkage was shown as follows. Reduction (diisobutylaluminum hydride, ether) of **25** afforded the alcohol **30** which, upon transmetalation–protonation (2 equiv of CH_3Li, THF, 0 °C; NH_4Cl–H_2O) gave (*E*)-2-methyl-2-bu-

(12) Similar results were obtained when the cuprate reagent **2** was employed.

(13) Preliminary experiments indicate that reagents **2** and **4** give similar results. However, we have employed primarily reagents **3** and **5**, since (a) the reaction products derived from these reagents are cleaner than those obtained from **2**, and (b) only 1 equiv of Me_3SnLi is required to prepare reagents **3** and **5**, while preparation of **4** requires 2 equiv of Me_3SnLi.

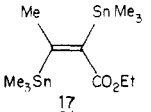
(14) It should be noted that the protons of the vinyl methyl groups of compounds **21**–**24** resonate at δ 1.88,[15] 1.90,[16] 2.14,[15] and 2.05,[16] respectively. Therefore, a cis or trans Me_3Sn group has only a small effect on the chemical shift of γ protons in α-trimethylstannyl α,β-unsaturated esters.

(15) Fraser, R. R.; McGreer, D. E. *Can. J. Chem.* **1961**, *39*, 505.

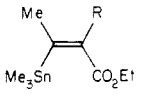
(16) Leusink, A. J.; Budding, H. A.; Marsman, J. W. *J. Organomet. Chem.* **1967**, *9*, 285.

(17) This product was accompanied by a significant amount (40%) of the protonated material (H in place of *n*-butyl).

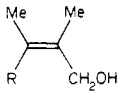
ten-1-ol (31), which was identical with an authentic sample of the same compound obtained by reduction of tiglic aldehyde.



17



25 R = Me
26 R = $CH_2CH=CH_2$
27 R = $CH_2C_6H_5$
28 R = n-Bu
29 R = 1-hydroxycyclohexyl



30 R = $SnMe_3$
31 R = H

Although direct trapping of intermediates 6 and/or 7 with electrophiles was not successful, it is clear that the methodology described above allows for a two-step conversion of α,β-acetylenic esters into compounds of general structure 11. The latter substances should be readily transformed into highly substituted vinyllithium reagents corresponding to the generalized unsaturated d^3-synthon 13. Work in this area is continuing.

Acknowledgment. Financial support from the Natural Sciences and Engineering Research Council of Canada (NSERCC) and a NSERCC postgraduate scholarship to (J.M.C.) are gratefully acknowledged.

Registry No. 1 (R = Me; R′ = Et), 4341-76-8; 1 (R = Et; R′ = Et), 55314-57-3; 1 (R = *i*-Pr; R′ = Me), 80866-47-3; 1 (R = *n*-C_6H_{13}; R′ = Me), 111-80-8; 1 (R = cyclopropyl; R′ = Me), 80866-48-4; 1 (R = 2-(2-cyclopentyl)ethyl; R′ = Me), 80866-49-5; 1 (R = (3-cyclohexenyl)methyl; R′ = Me), 80866-50-8; 1 (R = *t*-$BuMe_2SiOCH_2$; R′ = Et), 80866-51-9; 1 (R = *t*-$BuMe_2SiOCH_2CH_2$; R′ = Me), 74854-49-2; 14 (R = Me; R′ = Et), 80866-52-0; 14 (R = Et; R′ = Et), 80866-53-1; 14 (R = *i*-Pr; R′ = Me), 80879-50-1; 14 (R = *n*-C_6H_{13}; R′ = Me), 80866-54-2; 14 (R = cyclopropyl; R′ = Me), 80866-55-3; 14 (R = α-(2-cyclopentyl)ethyl; R′ = Me), 80866-56-4; 14 (R = (3-cyclohexenyl)methyl; R′ = Me), 80866-57-5; 14 (R = *t*-$BuMe_2SiOCH_2$; R′ = Et), 80866-58-6; 14 (R = *t*-$BuMe_2SiOCH_2CH_2$; R′ = Me), 80866-59-7; 16 (E = H), 74854-51-6; 25, 80866-60-0; 26, 80866-61-1; 27, 80866-62-2; 28, 80866-63-3; 29, 80866-64-4; 30, 80866-65-5; 31, 497-02-9.

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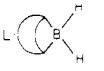
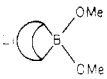
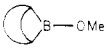
New Powerful Catalysts for the Reduction of Esters by Lithium Borohydride

Summary: The presence of 10 mol % of lithium 9-boratabicyclo[3.3.1]nonane, LiH·9-BBN, or lithium triethylborohydride, $LiEt_3BH$, strongly catalyzes the reduction of esters by lithium borohydride in ether at 25 °C. The corresponding Lewis acid, *B*-methoxy-9-borabicyclo[3.3.1]nonane, B-OMe-9-BBN, also permits the rapid and quantitative reduction of esters by $LiBH_4$ and provides a practical method for the reduction of esters in the presence of reducible groups, such as chloro and nitro.

Sir: We have recently developed an improved conversion of sodium borohydride into lithium borohydride in both diethyl ether (EE) and tetrahydrofuran (THF).[1] A major advantage of lithium borohydride over sodium borohydride is its ready solubility in simple ether solvents.[2] Also, lithium borohydride possesses a much greater selectivity than lithium aluminum hydride so that it is more suitable for selective reductions.[3] One important application appeared to be the reduction of esters, especially in the presence of other reducible groups. Accordingly, we explored this application.

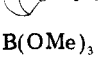
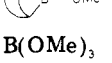
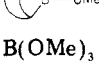
The reduction of esters proceeds smoothly but relatively slowly. The reaction is considerably faster in EE than in THF. However, even in refluxing EE, typical esters such as ethyl caproate required 5 h and ethyl benzoate ~24 h to go to completion. On the other hand, lithium triethylborohydride[4] and lithium 9-boratabicyclo[3.3.1]no-

Table I. Rate of Reduction of Ethyl Caproate by $LiBH_4$ in the Presence of Various Catalysts in Ether at 25 °C[a]

	% reaction					
catalyst	0.5 h	1 h	2 h	4 h	8 h	24 h
no catalyst	17	28	41	65	100	100
$LiEt_3BH$	80	100	100			
	100	100				
$LiEt_3BOMe$	83	98	100			
	100	100				
$BF_3\cdot OEt_2$	21	35	50	73	100	100
$BH_3\cdot THF$	10	14	18	26	53	62
n-Bu_3B	22	98	100			
	100	103				
n-OctB$(OMe)_2$	92	100				
$(MeO)_3B$	52	100				
$(PhO)_3B$	14	30	45	68	98	
$(n$-$DodO)_3B$[b]		26	46		100	

[a] [Ester] = 1.0 M; [$LiBH_4$] = 1.0 M; [catalyst] = 0.1 M. [b] *n*-Dod = *n*-dodecyl.

Table II. Reduction of Esters by $LiBH_4$ in Refluxing Ether[a]

		% reaction					
ester	catalyst	0.5 h	1 h	2 h	4 h	8 h	24 h
ethyl caproate	none	26	41	61	90	99[b]	
		100[c]	101				
	$B(OMe)_3$	100[d]	100				
ethyl benzoate	none	12	20	30	44	67[e]	
		60	100[e]	102			
	$B(OMe)_3$	29	46	65	86[e]	100	
ethyl pivalate	none	9	15	20	29	45	
		39	74	93	104	104	
	$B(OMe)_3$	68	102	104			

[a] [Ester] = 1.0 M; [$LiBH_4$] = 1.0 M; [catalyst] = 0.1 M. [b] 5 h. [c] 0.25 h. [d] 0.75 h. [e] Solution turns cloudy.

(1) Brown, H. C.; Choi, Y. M.; Narasimhan, S. *Inorg. Chem.* **1981**, *20*, 4454.

(2) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975; P 258.

(3) (a) Schlesinger, H. I.; Brown, H. C. *J. Am. Chem. Soc.* **1940**, *62*, 342. (b) Nystrom, R. F.; Chaikin, S. W.; Brown, W. G. *Ibid.* **1949**, *71*, 3245.

0022-3263/82/1947-1604$01.25/0