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Vinylalumination for the Synthesis of Functionalized Allyl Alcohols, Vinylepoxides, and α-Alkylidene-β-hydroxy-γ-lactones

P. Veeraraghavan Ramachandran,* Michael T. Rudd, Thomas E. Burghardt, and M. Venkat Ram Reddy

Department of Chemistry, Purdue University, 560 Oval Dr., West Lafayette, Indiana 47907-2084

chandran@purdue.edu

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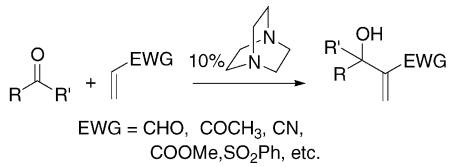
A modified hydroalumination protocol for the preparation of [α-(ethoxycarbonyl)vinyl]diisobutylaluminum and its β-methyl or -phenyl analogues was developed. These vinylaluminum reagents react with aldehydes and ketones to provide the corresponding functionalized allyl alcohols in good to excellent yields. Perfluoroalkyl and -aryl carbonyl compounds, α-keto esters, α-acyl cyanides, and α-acetylenic ketones provide the corresponding α-hydroxyalkenes in high yields. The allyl alcohol product ratios from the vinylalumination of unsymmetrical α-diketones with [α-(ethoxycarbonyl)-vinyl]diisobutylaluminum and its β-methyl or -phenyl analogues depend on the steric and electronic environments of the ketones as well as the reagents. The products from the vinylalumination of α-bromoaldehydes and -ketones were cyclized with K_2CO_3 or KF under nonaqueous conditions to provide functionalized vinylepoxides in high yields. Vinylaluminations of keto-protected pyruvaldehyde provided the products, which were converted to α-alkylidene-β-hydroxy-γ-lactones.

Introduction

Organoaluminum intermediates have been well studied in organic chemistry.[1] Hydroalumination of acetylenes to prepare vinylaluminum intermediates for application in organic syntheses has been known for decades.[2] In 1987, Tsuda, Saegusa, and co-workers reported the preparation of novel vinylaluminum reagents, [α-(alkoxycarbonyl)vinyl]diisobutylaluminum and aluminum allenoates by the hydroalumination of α,β-acetylenic carbonyl compounds with diisobutylaluminum hydride (DIBAL-H) in the presence of hexamethylphosphoric amide (HMPA).[3] They treated these aluminum intermediates with protic acid, allyl bromide, and carbonyl compounds.[3] The reaction with carbonyl compounds provides functionalized allyl alcohols.

The recent interest in the Baylis−Hillman (BH) reaction[4] (eq 1), which furnishes similar allylic alcohol products, attracted us to this vinylalumination reaction. The drawbacks of the DABCO-catalyzed BH reaction include its slow rate of reaction and the inapplicability to β-substituted olefins. We envisaged that appropriately substituted vinylaluminum reagents could overcome the deficiencies of the BH reaction. Accordingly, we undertook a project to prepare β-substituted vinylaluminums and treat them with a variety of carbonyl compounds as an efficient alternative to BH reaction.[5]



(1)

Our initial projects involved the application of [α-(alkoxycarbonyl)vinyl]diisobutylaluminums, prepared via the hydroalumination of propiolate esters in the presence of HMPA, for the vinylalumination of activated carbonyls, such as fluorocarbonyls, α-keto esters, etc.[5] Li and coworkers also reported similar observations on aldehydes and ketones.[6] Subsequently, we modified the hydroalumination procedure by replacing carcinogenic HMPA with 4-methylmorpholine *N*-oxide (NMO).[7] Apart from reexamining the earlier vinylaluminations, we included additional classes of carbonyl compounds, particularly those that could be readily converted to naturally occurring molecules. Our results are described herein.

* Corresponding author.

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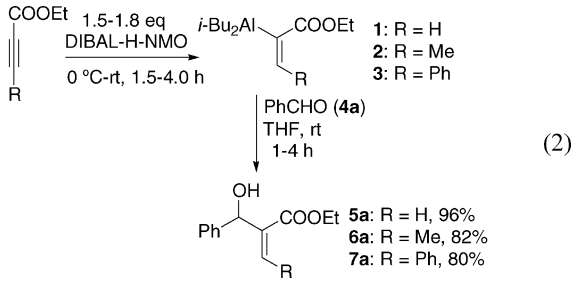
Results and Discussion

Environmentally Benign Vinylalumination. Although known for over a decade, the lack of extensive utilization of Tsuda's vinylalumination procedure[3] may be due to the presence of a carcinogenic material, HMPA,[8] as the complexing agent with DIBAL-H for the hydroalumination of propiolates. Several possible replacements for HMPA, such as 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU),[9] 1,3-dimethyl-2-imidazolidinone (DMEU or DMI),[10] and quinuclidine *N*-oxide (QNO),[11] have been reported in the literature. Since DMPU and DMI might undergo reduction with DIBAL-H and QNO is not economical, we studied a series of other amine oxides as a complexing agent. Although mixtures of DIBAL-H and aromatic amine oxides, such as pyridine and picoline *N*-oxides, did not provide the desired hydroalumination product, aliphatic trialkylamine oxides, such as trimethylamine *N*-oxide and NMO, were found to be suitable complexing agents for the hydroalumination of propargylic esters and ketones. Our study with the relatively inexpensive NMO revealed it to be an excellent HMPA-alternative for vinylaluminations, improving the reaction conditions and providing very good yields of the products.[7] It is very interesting that NMO aids in the formation of the vinylalanes cleanly and does not oxidize them.[12]

Vinylalumination of Aldehydes. The addition of DIBAL-H to a suspension of NMO in THF provided a clear solution. The reaction of ethyl propiolate in THF with 1.5 equiv of DIBAL-H/NMO complex at 0 °C provided the [α-(ethoxycarbonyl)vinyl]diisobutylaluminum (**1**). The corresponding *β*-substituted vinylaluminum reagents, [α-(ethoxycarbonyl)-*β*-methylvinyl]diisobutylaluminum (**2**) and the α-(ethoxycarbonyl)-*β*-phenyl]vinyldiisobutylaluminum (**3**), were prepared similarly with 1.8 equiv of DIBAL-H/NMO. Initially, we examined the reaction of aldehydes with these reagents. Benzaldehyde (**4a**) was added to **1** at 0 °C and warmed to rt. The reaction was complete within 4 h. Hydrolysis using 1.0 M HCl followed by chromatography provided 96% yield of the product **5a** (eq 2). We observed that the hydrolysis was much more facile when compared to the reactions using HMPA.



(2)

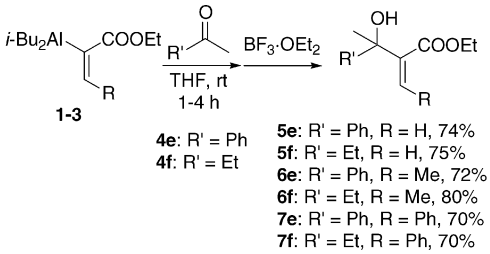
Reagent **2** reacted with **4a** smoothly to provide ethyl (2*Z*)-2-[hydroxy(phenyl)methyl]but-2-enoate (**6a**) in 82% yield (eq 2, Table 1, entry 2). The *β*-phenylvinyldiisobutylaluminum reagent **3** yielded 80% of the corresponding *Z*-product **7a**. In contrast to the previously reported procedure involving HMPA,[6] both of these reactions do not require the presence of Lewis acid or low temperatures (−78 °C). The reaction provided high yields of the products with all of the aldehydes examined, viz. butyraldehyde (**4b**), isobutyraldehyde (**4c**), and pivalaldehyde (**4d**). The results are summarized in Table 1 (entries 1−8).

TABLE 1. Vinylalumination of Aldehydes and Ketones[a]

	reagent		R′COR″			product	
entry	no.	R	no.	R′	R″	no.	yield[b] (%)
1	**1**	H	**4a**	Ph	H	**5a**	96
2	**2**	Me	**4a**	Ph	H	**6a**	82
3	**3**	Ph	**4a**	Ph	H	**7a**	80
4	**1**	H	**4b**	*n*-Pr	H	**5b**	90
5	**2**	Me	**4b**	*n*-Pr	H	**6b**	90
6	**3**	Ph	**4b**	*n*-Pr	H	**7b**	75
7	**1**	H	**4c**	*i*-Pr	H	**5c**	88
8	**1**	H	**4d**	*t*-Bu	H	**5d**	72
9	**1**	H	**4e**[c]	Ph	Me	**5e**	74
10	**2**	Me	**4e**[c]	Ph	Me	**6e**	72
11	**3**	Ph	**4e**[c]	Ph	Me	**7e**	70
12	**1**	H	**4f**[c]	Et	Me	**5f**	75
13	**2**	Me	**4f**[c]	Et	Me	**6f**	80
14	**3**	Ph	**4f**[c]	Et	Me	**7f**	70

[a] The reactions were carried out in THF at rt with 1.2 equiv of the carbonyl compound. [b] All of the yields are of isolated, purified products. [c] One equivalent of $BF_3{\cdot}OEt_2$ was added.

Vinylalumination of Ketones. Unactivated ketones fail to undergo BH reaction.[4] We extended the modified vinylalumination procedure to such ketones as an alternative to BH reaction. However, the reaction of acetophenone (**4e**) with **1** was sluggish. Workup of the reaction after 2 days yielded only 12% of the product **5e** along with 25% of recovered **4e** and a mixture of unidentified products. Addition of 10% of a Lewis acid, such as $BF_3{\cdot}OEt_2$, provided a small amount of the product with most of the ketone recovered. Upon addition of 1 equiv of $BF_3{\cdot}OEt_2$, the reaction was complete within 4 h, and workup provided a 74% yield of **5e** (eq 3). 2-Butanone (**4f**) reacted similarly, in the presence of 1 equiv of $BF_3{\cdot}OEt_2$, providing the product in 75% yield. Reagents **2** and **3** gave similar results with these ketones (Table 1, entries 9−14).



(3)

Reaction of Fluorocarbonyl Compounds. Due to the importance of fluoroorganic compounds[13] in agrochemistry, biochemistry, materials, and medicinal chemistry, we undertook the vinylalumination of fluorocarbonyl compounds.[5a] The difficulties encountered in the BH reaction of fluorocarbonyl compounds provided additional impetus to undertake this project.[14,15]

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(9) Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385.
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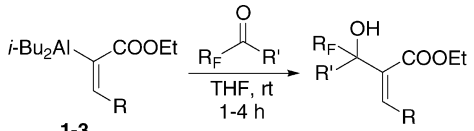
TABLE 2. Vinylalumination of Fluorocarbonyls[a]

	reagent		R_FCOR'			product	
entry	no.	R	no.	R_F	R′	no.	yield[b] (%)
1	**1**	H	**4g**	CF_3	H	**5g**	80
2	**2**	Me	**4g**	CF_3	H	**6g**	70
3	**3**	Ph	**4g**	CF_3	H	**7g**	75
4	**1**	H	**4h**	C_3F_7	H	**5h**	77
5	**2**	Me	**4h**	C_3F_7	H	**6h**	72
6	**3**	Ph	**4h**	C_3F_7	H	**7h**	76
7	**1**	H	**4i**	C_6F_5	H	**5i**	82
8	**2**	Me	**4i**	C_6F_5	H	**6i**	70
9	**3**	Ph	**4i**	C_6F_5	H	**7i**	78
10	**1**	H	**4j**	CF_3	Me	**5j**	65
11	**2**	Me	**4j**	CF_3	Me	**6j**	70
12	**3**	Ph	**4j**	CF_3	Me	**7j**	75
13	**1**	H	**4k**	CF_3	Ph	**5k**	95
14	**3**	Ph	**4k**	CF_3	Ph	**7k**	78
15	**1**	H	**4l**	CF_3	2-Thioph	**5l**	96

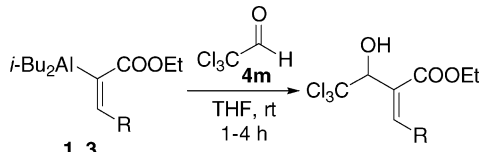
[a] The reactions were carried out in THF at rt with 1.2 equiv of the carbonyl compound. [b] All of the yields are of isolated, purified products.

Fluoral (**4g**) was added to **1**−**3** at −78 °C and was warmed to rt. The reactions were complete within 4 h (Table 2, entries 1−3). The generality of the reaction was examined by condensing a series of aliphatic and aromatic perfluorocarbonyl compounds, such as 2,2,3,3,4,4,4-heptafluorobutyraldehyde (**4h**), pentafluorobenzaldehyde (**4i**), 1,1,1-trifluoroacetone (**4j**), 2,2,2-trifluoroacetophenone (**4k**), and 2-trifluoroacetylthiophene (**4l**), with **1**−**3**. In all of the cases, high yields of the product alkenols were obtained (eq 4) (Table 2, entries 4−15). It is noteworthy that, unlike the hydrocarbon analogues,[7] the fluoro-ketones underwent reaction without the presence of any Lewis acid.



4g: $R_F = CF_3$, R' = H
4h: $R_F = C_3F_7$, R' = H
4i: $R_F = C_6F_5$, R' = H
4j: $R_F = CF_3$, R' = Me
4k: $R_F = CF_3$, R' = Ph
4l: $R_F = CF_3$, R' = 2-Thiophene (4)

The reaction of fluoral was compared with the chloro analogue, chloral (**4m**). We obtained similar results for the vinylalumination of **4m** with reagents **1** and **3** (eq 5).



5m: R = H, 87%
7m: R = Ph, 75% (5)

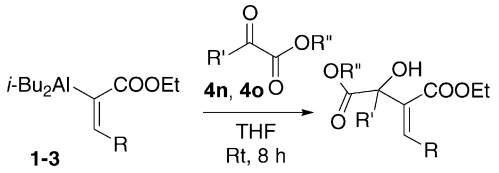
Vinylalumination of Activated Carbonyl Compounds. The vinylalumination of fluorocarbonyl compounds without the addition of a Lewis acid prompted us to examine the reaction of other activated carbonyls, such as α-keto esters, α-acyl cyanides, α-acetylenic ketones, and α-diketones. Although α-keto esters[16] and nonenolizable α-diketones undergo the BH reaction, other activated ketones, such as α-acetylenic and acyl cyanides, fail to provide the products.[17] We envisaged vinylalumination of these activated carbonyls as a general reaction to provide BH products.

TABLE 3. Vinylalumination of Activated Carbonyl Compounds

	reagent		R-C(O)-R″			product	
entry	no.	R	no.	R′	R″	no.	yield[a] (%)
1	**1**	H	**4n**	C(O)Me	OEt	**5n**	95
2	**2**	Me	**4n**	C(O)Me	OEt	**6n**	70
3	**3**	Ph	**4n**	C(O)Me	OEt	**7n**	81
4	**1**	H	**4o**	C(O)Ph	OMe	**5o**	80
5	**2**	Me	**4o**	C(O)Ph	OMe	**6o**	60
6	**3**	Ph	**4o**	C(O)Ph	OMe	**7o**	75
7	**1**	H	**4p**	Me	CN	**5p**	72[b]
8	**2**	Me	**4p**	Me	CN	**6p**	70[b]
9	**3**	Ph	**4p**	Me	CN	**7p**	72[b]
10	**1**	H	**4q**	Me	C≡CH	**5q**	51
11	**2**	Me	**4q**	Me	C≡CH	**6q**	45
12	**3**	Ph	**4q**	Me	C≡CH	**7q**	46

[a] All of the yields are of isolated, purified products. [b] Yields obtained from the reaction with HMPA.

Ethyl pyruvate (**4n**) was added to **1** at rt, and the reaction was complete within 4 h. Hydrolysis using 1.0 M HCl followed by chromatography provided an almost quantitative yield of the product **5n** (eq 6). An aromatic keto ester, methyl benzoylformate (**4o**), also underwent ready reaction with **1** to form the product **5o** in 80% yield (Table 3, entry 4). We then extended this reaction to the β-substituted vinylaluminums. Reagent **2** also reacted with **4n** and **4o** smoothly to provide the corresponding hydroxyalkenyl diester products **6n** and **6o**. Reagent **3** provided the products **7n** and **7o** from the α-keto esters **4n** and **4o**. It is noteworthy that unlike the BH reaction, the vinylalumination is very facile with both aliphatic and aromatic keto esters and the yields of the products are consistent (eq 6, Table 3, entries 1−6).



5n: R = H, R' = Me, R" = Et, 95%
5o: R = H, R' = Ph, R" = Et, 80%
6n: R = Me, R' = Me, R" = Et, 70%
6o: R = Me, R' = Ph, R" = Me, 60%
7n: R = Ph, R' = Me, R" = Me, 81%
7o: R = Ph, R' = Ph, R" = Me, 75% (6)

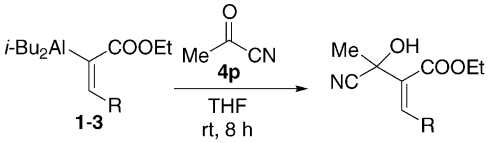
Although we succeeded in carrying out the vinylalumination of α-keto esters with reagents derived from

(13) For several recent reviews, see: (a) *Asymmetric Fluoroorganic Chemistry: Synthesis, Applications, and Future Directions;* Ramachandran, P. V., Ed.; ACS Symposium Series 746; American Chemical Society: Washington, DC, 2000. (b) *Enantiocontrolled synthesis of fluoro-organic compounds: stereochemical challenges and biomedical targets*; Soloshonok, V. A., Ed.; J. Wiley: Chichester, NY, 1999. (c) *Biomedicinal Frontiers in Fluorine Chemistry*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; ACS Symposium Series 639; American Chemical Society: Washington, DC, 1996.

(14) Fluoral and 1,1,1-trifluoroacetone polymerize instantaneously in the presence of amines: (a) Busfield, W. K.; Whalley, E. *Polymer* **1966**, *7*, 541. (b) Dhingra, M. M.; Tatta, K. R. *Org. Magn. Reson.* **1977**, *9*, 23.

propiolates and DIBAL-H/NMO, we failed to achieve the vinylalumination of acyl cyanides with this reagent. The reaction mixture darkened upon addition of acyl cyanide, and TLC analysis indicated no clean product formation. However, we encountered no problems in obtaining the products when the vinylalumination of acyl cyanides was carried out using reagents prepared from propiolates and DIBAL-H/HMPA.

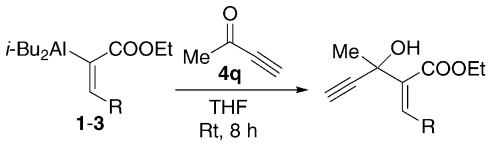
The results noted below are those obtained with the reagent prepared using HMPA as the additive. No difficulty was experienced in condensing pyruvonitrile (**4p**) with all of the three vinylaluminum reagents **1**−**3** (eq 7). The reactions were complete within 4 h, and acidic workup provided the α-alkenyl-*β*-cyano-*β*-hydroxy esters in 70−72% yields (Table 3, entries 7−9). The BH reaction of this class of carbonyl compounds is too slow to be of any practical use.



(7)

5p: R = H, 72%
6p: R = Me, 70%
7p: R = Ph, 72%

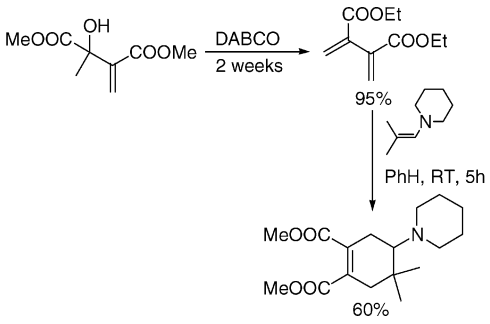
However, the reagents **1**−**3** prepared with NMO reacted readily with another class of activated carbonyls, α-acetylenic ketones. 3-Butyn-2-one (**4q**) provided the products in 45−51% yields (eq 8) (Table 3, entries 10−12). Addition of a Lewis acid (BF_3·OEt_2) did not improve the yields. The results for the vinylalumination of activated carbonyls are summarized in Table 3.



(8)

5q: R = H, 51%
6q: R = Me, 45%
7q: R = Ph, 46%

Hoffmann[18] and Basavaiah[16] had reported the preparation of activated dienes for the Diels−Alder reaction from similar products obtained from the BH reaction of α-keto esters (eq 9).[18] The dienes could be converted into many useful synthons, including substrates for the preparation of molecular rods, which has applications in nanotechnology.[19]



(9)

Stereoelectronic Effects in the Vinylalumination of α-Diketones with [α-(Ethoxycarbonyl)vinyl]di-isobutylaluminum. The BH reaction of α-diketones is limited to only nonenolizable diketones.[20] Enolizable and nonenolizable α-diketones were subjected to vinylalumination to show the generality of this process. In addition, the possibility of studying the effect of sterics and electronics in the case of unsymmetrical α-diketones[21] persuaded us to undertake such a study.

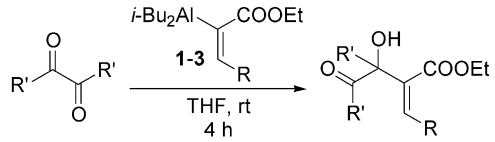
TABLE 4. Vinylalumination of Diketones

	reagent		R′-C(O)-C(O)R″			product(s)		
entry	no.	R	no.	R′	R″	no.	ratio	yield[a] (%)
1	**1**	H	**4r**	Me	Me	**5r**		70
2	**2**	Me	**4r**	Me	Me	**6r**		60
3	**3**	Ph	**4r**	Me	Me	**7r**		72
4	**1**	H	**4s**	Et	Et	**5s**		81
5	**1**	H	**4t**	Ph	Ph	**5t**		78
6	**1**	H	**4u**	Me	Et	**5u**/**5′u**	45:55[b]	80[c]
7	**2**	Me	**4u**	Me	Et	**6u**/**6′u**	39:61[b]	66[c]
8	**3**	Ph	**4u**	Me	Et	**7u**/**7′u**	20:80[b]	80[c]
9	**1**	H	**4v**	Me	Ph	**5v**/**5′v**	75:25	88[c]
10	**2**	Me	**4v**	Me	Ph	**6v**/**6′v**	65:35	71[c]
11	**3**	Ph	**4v**	Me	Ph	**7v**/**7′v**	52:48	83[c]

[a] All of the yields are of isolated, purified products. [b] The products could not be separated. Ratios given were obtained from ^{1}H NMR analysis. [c] Combined yield.

Enolizable and nonenolizable α-diketones were subjected to vinylalumination to show the generality of this process. In addition, the possibility of studying the effect of sterics and electronics in the case of unsymmetrical α-diketones[21] persuaded us to undertake such a study.

2,3-Butanedione (**4r**) was added to **1**, and the reaction was complete within 4 h. Hydrolysis using 1.0 M HCl and purification on silica gel provided 70% of the product **5r** (eq 10). The *β*-substituted vinylaluminum reagents **2** and **3** reacted with **4r** smoothly to provide the *β*-hydroxy-*γ*-keto esters **6r** and **7r** in 60% and 72% yields, respectively. 3,4-Hexanedione (**4s**) furnished a slightly better yield (81%) of the product **5s** for a reaction with **1**. An aromatic diketone, benzil (**4t**), afforded 78% yield of the corresponding α-keto α′-ethoxycarbonyl allylic alcohol **5t**. The results are summarized in Table 4 (entries 1−5).



(10)

4r: R′ = Me
4s: R′ = Et
4t: R′ = Ph

5r: R = H, R′ = Me, 70%
6r: R, R′ = Me, 60%
7r: R = Ph, R′ = Me, 72%
5s: R = H, R′ = Et, 81%
5t: R = H, R′ = Ph, 78%

The reaction of an unsymmetrical α-diketone, 2,3-pentanedione (**4u**), with **1** followed by workup provided an 80% yield of a mixture of alcohols, **5u** and **5′u**, that were difficult to separate by column chromatography. A

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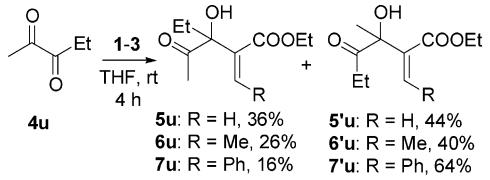
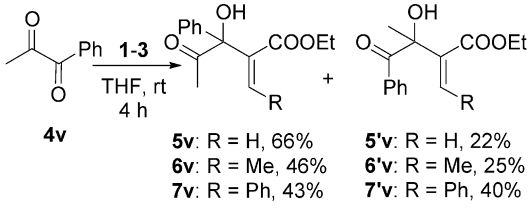
^{1}H NMR examination revealed modest preferential vinylalumination of the carbonyl bearing the methyl group (55%) over the carbonyl bearing the ethyl group (45%) (eq 11). When the β-methyl-substituted reagent **2** was used, the corresponding products **6u** and **6′u** were formed in a 2:3 ratio. The preference toward the methyl side increased considerably with reagent **3**. The corresponding products **7u** and **7′u** were formed in a 1:4 ratio. Clearly, the steric interactions of the reagent and the carbonyl group determine the outcome of the vinylalumination. The results are shown in Table 4 (entries 6−8).



(11)

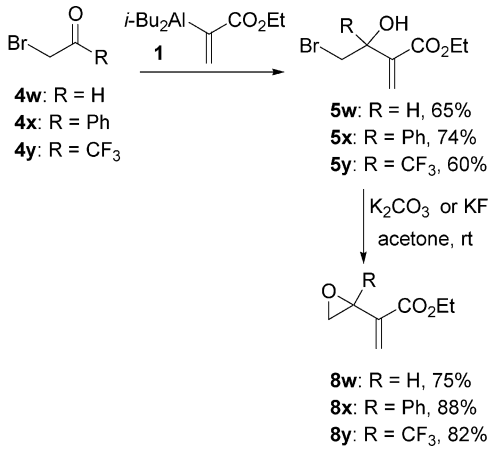
We then studied the vinylalumination of an unsymmetrical α-diketone with differing electronic surroundings. With 1-phenyl-1,2-propanedione (**4v**), reagent **1** reacted preferentially with the carbonyl adjacent to the phenyl ring to give a 3:1 ratio of **5v** and **5′v** (eq 12). However, β-methyl substitution of the reagent (**2**) decreases the preference for the aryl carbonyl. The bulkier β-phenyl-substituted reagent (**3**) provides the products in an almost 1:1 ratio. These results reveal that steric as well as electronic factors play a role in the regiochemical outcome of the reaction. Unlike in the case of **4u**, the products from **4v** could be readily separated by column chromatography. The results of vinylalumination of diketones are summarized in Table 4 (entries 6−11).



(12)

Vinylalumination of α-Halocarbonyls: Synthesis of Functionalized Vinylepoxides. Vinylepoxides are an important class of synthons in organic chemistry.[22] They constitute an important component of natural molecules, such as carotenoids.[23] Vinylepoxides have been utilized in the preparation of molecules with pharmaceutical applications[24] and are commonly used in polymer chemistry.[25] The importance of vinylepoxides in organic syntheses prompted us to examine the preparation of the vinyl halohydrin precursors from α-haloaldehydes and -ketones via vinylalumination.[26] Similar to several activated carbonyls, the vinylalumination of α-bromocarbonyls also proceeds without Lewis acid catalysis and the products were readily converted to functionalized vinylepoxides.

Vinylalumination of bromoacetaldehyde (**4w**) was complete in 15 h at rt. Dilute HCl workup provided 65% yield of the product bromohydrin **5w** (eq 13). The reaction was then extended to representative bromo ketones. Phenacyl bromide (**4x**) and 1-bromo-3,3,3-trifluoro-2-propanone (**4y**) provided the corresponding bromohydrins **5x** and **5y** in 74% and 60% yields, respectively (eq 13).



(13)

We avoided strong aqueous alkaline conditions for the cyclization of these bromohydrins due to the presence of the ester moiety. The epoxide formation from **5w** and **5x** was successfully carried out with K_2CO_3 as base (eq 13). We conducted the cyclizations in dry acetone and obtained 75−88% yields of the vinylepoxides. However, the trifluoromethyl bromohydrin **5y** afforded only 65% yield of the corresponding epoxide **8y**, and we improved the yield to 82% by replacing K_2CO_3 with KF.[27]

Vinylalumination of Keto-Protected Pyruvaldehyde: Synthesis of α-Alkylidene-β-hydroxy-γ-lactones. Several natural products contain α-alkylidene-β-hydroxy-γ-methylbutyrolactone moiety.[28] Listenolides are a group of such molecules; they have been isolated in the 1970s from the roots and leaves of *Listea japonica* belonging to Lauraceae family.[29] Listenolides are divided into two series: X_1 and X_2, having *Z* and *E* alkylidene units, respectively. Several syntheses of these molecules have been reported.[30] We applied our vinylalumination protocol for the synthesis of representative α-methylene-β-hydroxy-γ-butyrolactone **9** and its β-substituted analogue listenolide A_1 (**10**).

Our protocol is shown in Scheme 1. β-Substituted substrate for the hydroalumination, ethyl tetradec-13-

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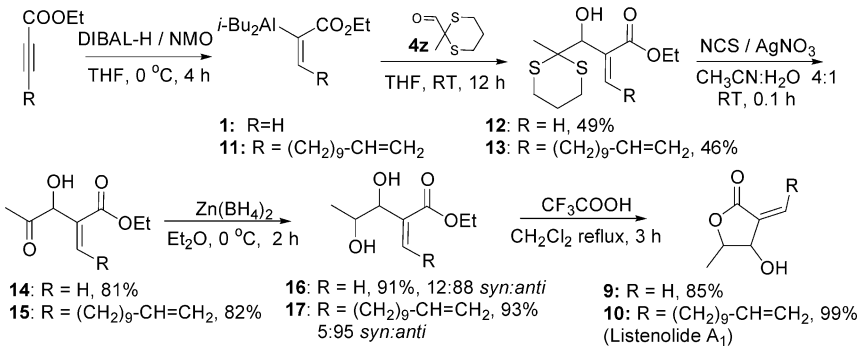
SCHEME 1



en-2-ynoate, was prepared by treatment of 1-bromo-11-undecene with sodium acetylide, followed by the addition of ethyl chloroformate according to a literature procedure.[31] The carbonyl substrate, 2-methyl-1,3-dithiane-2-carbaldehyde (**4z**), was made from acetaldehyde and 1,3-propanedithiol using the literature protocols.[32]

Addition of **4z** to the vinylaluminum reagents **1** and **11** and stirring overnight at room temperature, followed by workup with aq NH_4Cl and filtration through silica gel, afforded the desired dithiane hydroxy esters **12** and **13** in moderate yields (46−49%). A minor difficulty was experienced during the deprotection of the dithianes.[33] Deprotection with $HgCl_2$ required heating of the substrate and was proceeding only in ∼50% yield. Use of ceric ammonium nitrate[34] made the deprotection and workup easier; however, the yields were still unsatisfactory and inconsistent (43−70%). Fortunately, deprotection with *N*-chlorosuccinimide in the presence of $AgNO_3$[35] afforded the desired ketones **14** and **15** in good yields. Reduction of the ketones with $Zn(BH_4)_2$ furnished the desired diols **16** and **17** in excellent yields and good anti diastereoselectivities. Lactonization by refluxing in CH_2Cl_2 in the presence of CF_3COOH yielded the desired lactone **9** and listenolide A_1 (**10**). Comparison with the ^1H NMR spectral values reported by Ishii and coworkers[29a] confirmed that the desired *Z* stereochemistry was obtained in the case of **10**.

Conclusions

We have described a significantly improved procedure for the vinylalumination of a variety of carbonyl compounds with [α-(ethoxycarbonyl)vinyl]diisobutylaluminum. Replacement of carcinogenic HMPA with readily available and inexpensive NMO in the hydroalumination step makes this procedure environmentally benign. The workup is simpler, and the yields of the products are very good in most cases. Activated carbonyl compounds, such as α-keto esters, acyl cyanides (with HMPA), and α-acetylenic ketones undergo facile condensation with unsubstituted and *β*-methyl- or -phenyl-substituted [α-(ethoxycarbonyl)vinyl]diisobutylaluminum to provide the corresponding hydroxyalkenyl products in moderate to high yield. We extended the vinylalumination of activated carbonyl compounds to enolizable and nonenolizable α-diketones. Unsubstituted and *β*-methyl- and -phenyl-substituted [α-(ethoxycarbonyl)vinyl]diisobutylaluminum provide the corresponding α-methylene-*β*-hydroxy-*γ*-keto esters in moderate to high yields. In the case of unsymmetrical α-diketones, the regioselectivity of the reaction depends on the steric and electronic surroundings of the carbonyl groups and the vinylaluminum reagent. A convenient synthesis of functionalized vinylepoxides via the vinylalumination of α-bromocarbonyls has also been developed. The products from the vinylalumination of keto-protected pyruvaldehyde were converted to α-alkylidene-*β*-hydroxy-*γ*-lactones, such as listenolide A_1. We believe that this modified environmentally benign vinylalumination will find applications in organic synthesis.[36]

Experimental Section

General procedures for vinylalumination using NMO are described below. Other experimental procedures, the reaction yields, and physical data of individual reaction products are provided in the Supporting Information.

Experimental Procedure for Vinylalumination Using *β*-Unsubstituted Reagent (1): Preparation of Ethyl 2-(Hydroxyphenylmethyl)acrylate (5a). To a stirred suspension of NMO (2.3 g, 20 mmol) in anhydrous THF (50 mL) was added DIBAL-H (2.7 mL, 15 mmol) at 0 °C and the mixture stirred for 0.5 h. Ethyl propiolate (1.0 mL, 10 mmol) was added, and the mixture was stirred at 0 °C for 1 h, followed by the addition of benzaldehyde (**4a**) (1.2 mL, 12 mmol). The mixture was warmed to rt, stirred for 4 h, and quenched with 10 mL of aq 1.0 M HCl, and the product was extracted with ether (3 × 50 mL). The combined ether layers were washed with brine and dried over $MgSO_4$. Removal of the solvents and purification by column chromatography over silica gel (95:5, hexanes/ethyl acetate) provided 2.5 g (9.5 mmol, 95%) of **5a**.

Experimental Procedure for Vinylalumination Using *β*-Substituted Reagents (2, 3, and 11): Preparation of Ethyl (2*Z*)-2-(Hydroxyphenylmethyl)-3-phenylacrylate (7a). To NMO (2.3 g, 20 mmol) slurried in anhydrous THF (50 mL) was added DIBAL-H (2.7 mL, 15 mmol) at 0 °C, and the mixture was stirred for 0.5 h. Ethyl 3-phenylprop-2-ynoate (1.4 mL, 8.5 mmol) was added, and the mixture was warmed to rt and stirred for 4 h, followed by the addition of benzaldehyde (**4a**) (1.0 mL, 10 mmol) and overnight stirring. The reaction was quenched with 10 mL of 1.0 M HCl, and the product was extracted with ether (3 × 50 mL). The combined ether layers were washed with brine and dried over $MgSO_4$. Removal of the solvents and purification by column chromatography over

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silica gel (95:5, hexanes/ethyl acetate) provided 1.8 g (6.8 mmol, 80%) of **7a**.

Experimental Procedure for Vinylalumination of Unactivated Ketones: Preparation of Ethyl 2-(1-Hydroxy-1-phenylethyl)acrylate (5e). To a stirred suspension of NMO (4.17 g, 35.6 mmol) in anhydrous THF (30 mL) was added DIBAL-H (1 M in hexanes; 32 mL, 32 mmol) at 0 °C, and the mixture was stirred for 0.5 h. Ethyl propiolate (2.8 mL, 27.5 mmol) was added, and the mixture was stirred at 0 °C for 1 h. Next, acetophenone (**4e**) (1.8 mL, 15.3 mmol) was added, followed by addition of $BF_3{\cdot}OEt_2$ (1.9 mL, 15.3 mmol). The mixture was warmed to rt, stirred for 4 h, and quenched with 10 mL of 1.0 M HCl, and the product was extracted with ether (3 × 50 mL). The combined ether layers were washed with brine and dried over $MgSO_4$. Removal of the solvents and purification by column chromatography over silica gel (95:5, hexanes/ethyl acetate) provided 2.5 g (11.3 mmol, 74%) of **5e**.

Note: For the β-substituted vinylaluminum reagents (**2**, **3**), the solution has to be stirred for 4 h at rt prior to addition of the ketones.

Acknowledgment. The financial assistance from Eastman Kodak Co. is gratefully acknowledged.

Supporting Information Available: Additional experimental procedures, the spectral data (^1H, ^{13}C, and ^{19}F NMR spectra), and other physical characteristics of the compounds described. This material is available free of charge via the Internet at http://pubs.acs.org.

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