reflections. Details of the data collection and processing as well as of the structure analysis and refinement calculations are given elsewhere.

Acknowledgment. Financial support from the Swedish Natural Science Research Council and the Swedish Board for Technical Development is gratefully acknowledged. We thank Prof. Margaret C. Etter (University of Minnesota) for valuable discussions concerning hydrogen bonding. I.C. and A. E. are also indebted to Prof. Peder Kierkegaard (Stockholm University) for his continuous interest and encouragement.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for compounds 3-7 (10 pages). Ordering information is given on any current masthead page.

Development of a Triply Convergent Aldol Approach to Prostanoids†

Carl R. Johnson* and Yung-Fa Chen

Department of Chemistry, Wayne State University, Detroit, Michigan 48202

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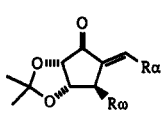
Various organocopper-mediated methods for the conjugate addition of alkyl and alkenyl groups to enone 1 to provide cyclopentanones 4 were studied. A variety of aldol-based procedures for the production of ketones 3 was evaluated, including a two-pot procedure involving generation of lithium enolates from 4, one-pot conjugate additions/aldol condensations methods, and methods involving the intermediate production of silyl enol ethers. The most promising procedure was found to be that involving trapping of the initial enolates from 1 as enol acetates and regeneration of enolates with methyllithium followed by aldol and dehydration reactions.

A triply convergent approach to PGE_2 has been developed in this laboratory based on enone (+)-1.[1] Conjugate addition followed by in situ electrophilic allylation afforded the desired ketone 2, which was converted to PGE_2 methyl ester, by hydrofluoric acid desilylation and aluminum amalgam deoxygenation (Scheme I). Variations on this approach, particularly involving the use of aldehydes as the electrophilic components,[2] provide the main theme of the present article.

We anticipated that cuprate additions followed by aldol condensations would result in enones 3, which would serve as intermediates to various types of prostanoids. The presence of the acetonide protecting group on 1 offers three advantages in this approach: (1) It should suppress enolate equilibration, which is the major obstacle in conjugate addition approachs to prostanoids. (2) It should allow regiospecific generation of the enolate from the corresponding ketone 4. (3) It offers a 10α-hydroxy (PG numbering) group for further manipulation.



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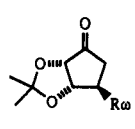

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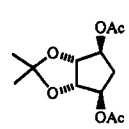

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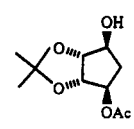

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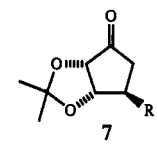
An efficient route to optically active (+)-1 has been developed in our laboratory by use of an enzymatic hydrolysis of diacetate 5 to furnish optically active monoacetate 6.[1,3] Oxidation of 6 provided enone (+)-1 with high optical purity (98% ee). The developmental chemistry described in the present paper was done with racemic 1.

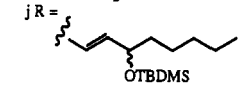
Results and Discussion

Cuprate Addition Reactions. Addition of lithium dibutylcuprate to enone 1 proceeded cleanly at −78 °C in THF to give a 92% yield of conjugate addition product



7

a R = *n*-Bu
b R = Me
c R = *n*-Oct
d R = *i*-Pr
e R = *t*-Bu
f R = $(CH_2)_7OTHP$
g R = $(CH_2)_7OTBDMS$
h R = $(CH_2)_6CH{=}CH_2$
i R = $CH{=}CH_2$
j R =



7a; the addition of lithium dimethylcuprate was equally successful in the production of ketone **7b** (90%). Cuprous bromide–dimethyl sulfide complex catalyzed addition of octylmagnesium bromide to enone 1 also results exclusively in conjugate addition to give ketone 7c in 87% yield. Recently, trimethylsilyl chloride has been noted to enhance the rate of additions of cuprates to enones.[4] Hexamethylphosphoric triamide (HMPA) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) in conjunction with TMSCl facilitate the addition of organocopper reagents to enones according to a report of Kuwajima and coworkers.[5] Utilization of tetramethylethylenediamine (TMEDA) as a promoter has been developed in this laboratory.[6] Indeed, 5% cuprous iodide in conjunction with TMSCl-promoted octylmagnesium bromide addition in conjugate fashion to enone 1 to give a mixture of ketone

† This paper is dedicated to Prof. Norman A. LeBel on the occasion of his 60th birthday.

(1) (a) Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 4726. (b) Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1986**, *108*, 5655.

(2) For other aldol approach to prostanoids, see: (a) Suzuki, M.; Yanagiwawa, A.; Noyori, R. *Tetrahedron Lett.* **1984**, *25*, 1384. (b) Suzuki, M.; Kawagishi, T.; Noyori, R. *Ibid.* **1982**, *23*, 5563. (c) Suzuki, M.; Kawagishi, T.; Suzuki, T.; Noyori, R. *Ibid.* **1982**, *23*, 4057. (d) Suzuki, M., Kawagishi, T.; Yanagiwawa, A.; Suzuki, T.; Okamura, N.; Noyori, R. *Bull Chem. Soc. Jpn.* **1988**, *61*, 1299. (e) Suzuki, M.; Koyano, H.; Morita, Y.; Noyori, R. *Synlett* **1989**, 22.

(3) For other examples of the synthesis of enone (+)-1, see: Hudlicky, T.; Luna, H.; Barbieri, G.; Kwart, L. D. *J. Am. Chem. Soc.* **1988**, *110*, 4735. Bélanger, P.; Prasit, P. *Tetrahedron Lett.* **1988**, *29*, 5521. Deardorff; D. R.; Shambayati, S.; Myles, D. C.; Heerding, D. *J. Org. Chem.* **1988**, *53*, 3614. See also: Bestman, H. J.; Roth, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 99; *Synlett* **1990**, 751. Flann, J. C.; Mash, E. A. *Synth. Commun.* **1988**, *18*, 391. Flann, J. C.; Mash, E. A. *Synth. Commun.* **1988**, *18*, 391. Ali, S. M.; Ramesh, K.; Borchardt, R. T. *Tetrahedrom Lett.* **1990**, *31*, 1509. Wolfe, M. S.; Anderson, B. L.; Borcherding, D. R.; Borchardt, R. T. *J. Org. Chem.* **1990**, *55*, 4712.

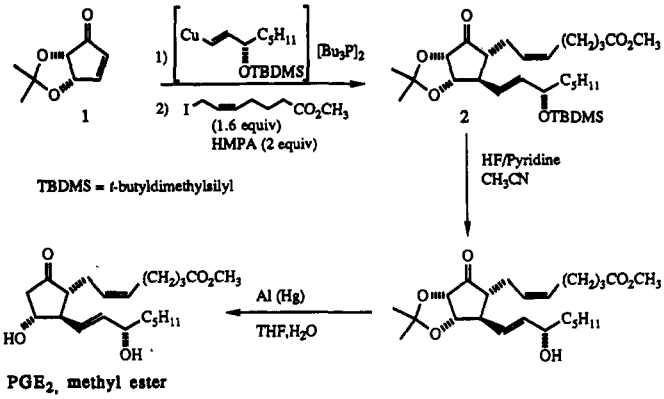
(4) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015.

(5) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025, 4029.

(6) Johnson, C. R.; Marren, T. J. *Tetrahedron Lett.* **1987**, *28*, 27.

0022-3263/91/1956-3344$02.50/0

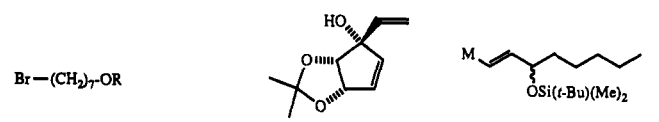
Scheme I



7c and its TMS enol ether. After hydrolysis of the mixture with K_2CO_3 in MeOH, ketone **7c** was isolated in 84% yield. The intermediate magnesium enolate generated under these conditions behaves quite differently from the corresponding lithium enolate. The trapping of the magnesium enolate with TMSCl does not go to completion even after warming the reaction mixture to room temperature.[7]

Secondary and tertiary alkyl groups also undergo conjugate addition to enone **1** cleanly. Isopropylmagnesium chloride gave ketone **7d** in 88% yield when 5% of CuI, 1.2 equiv of TMEDA, and 1.1 equiv of TMSCl were used. Conjugate addition of a *tert*-butyl group to enone **1** was achieved by using TMSCl, TMEDA, and *tert*-butylcopper, giving ketone **7e** in 66% yield. Higher order di-*tert*-butylcyanocuprate[8] was more successful for this purpose; conjugate addition product **7e** was obtained in 98% yield.

In order to synthesize prostanoids with a carboxylic group on the ω-side chain, cuprate addition of an alkyl group with a protected terminal alcohol as a masked COOH was investigated. Addition of the Grignard reagent prepared from **8** to enone **1** in the presence of 5% CuBr–Me_2S gave ketone **7f** in only 19% yield. The *tert*-butyldimethylsilyl-protected Grignard reagent derived from **9** gave ketone **7g** (34%). Varying reaction temperature or solvent, using the lithium reagents prepared from lithium halogen exchange on THP or TBDMS-protected iodides with *tert*-butyllithium or using TMSCl to promote conjugate addition all failed to increase the chemical yield. The reason for this deleterious effect in cuprate conjugate addition in the presence of a terminal alkoxy group is still unclear. Owing to this difficulty, a terminal double bond was used as a "masked" carboxylic acid. Addition to a Grignard reagent prepared from 8-bromo-1-octene to enone **1** in the presence of 5% CuBr–Me_2S catalyst afforded, after flash chromatography, a clean conjugate addition product **7h** in 73% yield. An even better result was obtained by promoting the conjugate addition with TMSCl. Under these conditions, ketone **7h** was obtained in 86% yield.



8 R = THP
9 R = *t*-butyldimethylsilyl

10

11 M = Bu_3Sn
12 M = Li

The conjugate addition of vinylmagnesium bromide to enone **1** catalyzed by CuBr–Me_2S was less successful. With 5% of CuBr–Me_2S, a 3:1 ratio of ketone **7i** to allyl alcohol **10**, resulting from 1,4- and 1,2-addition, respectively, was isolated. When a stoichiometric amount of CuI was employed, the ratio dropped to 2:1 with lower chemical yield (53%). The use of a mixed higher order cuprate, prepared from a 4:3:1 mixture of vinylmagnesium bromide, cuprous iodide, and methyllithium,[9] gave an excellent chemical yield, but only slightly improved the ratio of products to 5:1. Trimethylsilyl chloride was found to promote the conjugate addition of vinylmagnesium bromide catalyzed by CuI; the reaction cleanly afforded ketone **7i** in 81% yield. Surprisingly, the corresponding TMS enol ether was not detected in the ^1H NMR spectrum of the crude product.

Mixed homocuprates and organocopper reagents, which contain only 1 equiv of the valuable ω-side chain have been examined extensively.[1,10] A tributylphosphine-stabilized organocopper reagent prepared from the *tert*-butyltrimethylsilyl-protected vinyllithium **12** furnished a 93% yield of **7j** as an inseparable mixture of two diastereomers.

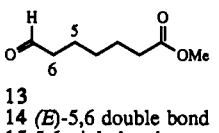
The best results were obtained when 2.5 equiv of tributylphosphine were used. In addition to the tetrabutyltin generated by transmetallation of the vinyltin compound **11**, the presence of a large amount of tributylphosphine caused difficulty in product isolation. The tin compounds are much less polar and can be easily separated by flash chromatography, but the presence of a large amount tributylphosphine made the separation quite tedious. The in situ transmetallation between a vinyl stannane and dimethylcyanocuprate developed by Lipshutz[11] was examined. The vinylstannane (mixture of isomers) was added to a solution of dimethylcyanocuprate in THF at room temperature and stirred for 1.5 h. The mixture was cooled to −78 °C, and enone **1** was added. The mixture was warmed to −30 °C for a few minutes and then was quenched with saturated aqueous ammonium chloride solution. The product isolated after flash chromatography was an inseparable mixture of diastereomers **7j** (88% yield).

The transmetallation of vinyltin isomers[11] with dimethylcyanocuprate is selective; only the trans isomer **11**[12] participated in this reaction. For an efficient transmetallation reaction, it is necessary to exclude oxygen and to use a slight excess of methyllithium in the preparation of dimethylcyanocuprate. In the presence of oxygen or other impurities the vinyltin compounds tend to dimerize, and significantly lower yields of conjugate addition products are observed.

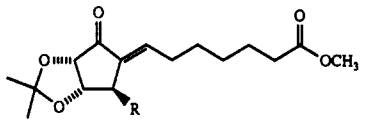
Direct Aldol Condensation. The initial aldol addition was performed with use of ketone **7a** and aldehyde **13**[13] since these materials are easily obtained. The desired lithium enolate of **7a** could be generated regiospecifically by LDA at −78 °C in THF. Treatment of the lithium enolate with aldehyde **13** at −78 °C and quenching at low temperature gave a mixture of diastereomeric ketols and starting ketone. The most convenient dehydration procedure found was stirring an ether solution of the crude reaction mixture with aluminum oxide G (type E, EM).

(7) Complete enolate trapping by TMSCl was achieved by adding 2 equiv of HMPA.
(8) Lipshutz, B. H. *Synthesis* **1987**, 325.
(9) Drouin, J.; Leyendecker, F.; Lonia, J. *Nouv. J. Chim.* **1977**, *2*, 267, 271.
(10) Suzuki, M.; Suzuki, T.; Kawagishi, T.; Morita, Y.; Noyori, R. *Isr. J. Chem.* **1984**, *24*, 118.
(11) Behling, J. R.; Babiak, K. A.; Ng, J. S.; Campbell, A. C.; Moretti, R.; Koerner, M.; Lipshutz, B. H. *J. Am. Chem. Soc.* **1988**, *110*, 2641.
(12) Vinylstannane **11** was prepared by irradiation of 3-(*tert*-butyldimethylsiloxy)-1-octyne with 1 equiv of tributyltin hydride in the absence of solvent. The product was a mixture of isomers consisting of ca. 85% of the desired *E* isomer.
(13) Aldehyde **13** was prepared from cycloheptene with use of Schreiber's procedure. (a) Schreiber, S. L.; Claus, R. E.; Reagan, J. *Tetrahedron Lett.* **1982**, *23*, 3867. (b) Schreiber, S. L.; Claus, R. E. *Org. Synth.* **1985**, *64*, 150.

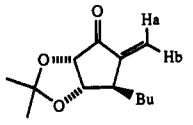
The dehydration was usually complete within 15 min at room temperature. The resulting mixture was easily separated by flash chromatography to furnish a 37% yield of enone **16a** and a 55% yield of recovered starting ketone **7a**.



13
14 (*E*)-5,6 double bond
15 5,6 triple bond



16



17

Enone **16a** was shown by ^{1}H NMR to be a single diastereomer with an olefinic proton resonance at δ 6.75. The stereochemistry of the double bond was assigned as *E* on the basis of the anisotropic effect of the carbonyl group. The ^{1}H NMR of the model enone **17** has olefinic proton resonances appearing at δ 6.25 (H_a) and 5.48 (H_b).[14]

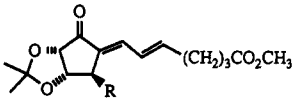
It has been found that the addition of zinc(II) chloride to the lithium enolate prior to aldehyde addition often improves the yield of the aldol products.[15,16] The $ZnCl_2$ is believed to intercept the intermediate ketoalkoxide as a chelate.[16] After addition of 1 equiv of anhydrous $ZnCl_2$ to the lithium enolate of **7a** at −78 °C followed by addition of aldehyde **13**, the TLC of the reaction mixture revealed the formation of ketol compounds. The reaction mixture was stirred at −78 °C for 15 min and allowed to slowly warm to room temperature while being monitored frequently by TLC. The dehydration of ketol compounds occurred around −10 °C. The reaction mixture was worked up and treated with aluminum oxide as described previously. Flash chromatography furnished a 76% yield of enone **16a**, and 18% of the starting ketone **7a** was recovered. All attempts to drive the reaction to completion failed. The solvent for this reaction also played a crucial role. When the reaction was carried out in diethyl ether, the result was a complex mixture and only 10% of the desired enone was isolated.

Aldol condensation of **7a** with unsaturated aldehyde **14**[17] in the presence of $ZnCl_2$ failed; the starting ketone was recovered in greater than 90% yield even after the reaction mixture had been warmed to room temperature. The reason for this failure is not clear.

One-Pot Conjugate Addition/Aldol Condensation Approach. On the basis of the results of direct aldol condensation, a more efficient one-pot conjugate addition/aldol condensation reaction[18] was examined. Addition of aldehyde **13** to the enolate generated from addition of lithium dibutylcuprate to enone **1** afforded a 35% yield of enone **16a** and a 49% yield of ketone **7a**. This result is consistent with that obtained by direct use of ketone **7a** in an aldol condensation. A one-pot reaction was carried out by adding 1 equiv of zinc chloride to the enolate prior to the aldehyde addition;[15] enone **16a** and ketone **7a** were obtained in 72 and 8% yield, respectively.

Encouraged by the success of trapping an enolate generated by lithium organocuprate conjugate addition, we turned to examine the enolates from copper-catalyzed Grignard reagent conjugate addition. Addition of aldehyde **13** to the enolate generated by CuBr–Me_2 complex-catalyzed conjugate addition of octylmagnesium bromide to enone **1** furnished, after dehydration, a 42% yield of enone **16c**. A 40% yield of untrapped ketone **7c** was also isolated. Addition of $ZnCl_2$ prior to the aldehyde provided enone **16c** in 48% yield along with 39% of untrapped ketone **7c**. The use of $ZnCl_2$ with a magnesium enolate seemed to be of no real advantage. Self-condensation products of aldehyde **13** were found in the reaction mixtures involving magnesium enolates; such side-products were not seen in the reaction mixtures involving lithium enolates.

A tributylphosphine-stabilized organocopper reagent from the *tert*-butyldimethylsilyl-protected vinyllithium **12** was added to enone **1**. This was followed by aldol condensation with aldehyde **13** in the presence of $ZnCl_2$ to furnish enone **16j** as a mixture of two inseparable C-15 epimers in 62% yield along with a 29% yield of untrapped ketone **7j**. The enolate generated from conjugate addition of cyanocuprate (from vinyltin **11** and $Me_2Cu(CN)Li_2$) to enone **1** reacted with aldehyde **13** in the presence of $ZnCl_2$ to afford a 73% yield of enone **16j** along with 20% of untrapped ketone **7j**.



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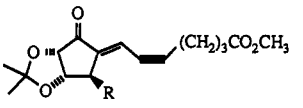


19

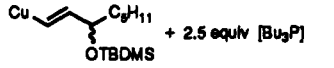
Unsaturated aldehyde **14**, which failed to react with the enolate generated from ketone **7a** with LDA, was examined. Addition of aldehyde **14** to the enolate generated from a tributylphosphine-stabilized vinylcopper reagent (from **12**) to enone **1** in the presence of $ZnCl_2$ afforded, after dehydration, a 51% yield of trienone **18j** (epimers at C-15) and a 34% yield of ketone **7j**. The new double bond on the α-side chain of **18j** has the *E* configuration as shown by the proton NMR resonance at δ 7.03. No conjugate addition product of the unsaturated aldehyde could be detected by ^{1}H NMR.

Enynone **19j** was obtained in 45% yield under the same reactions condition by using aldehyde **15** as the trapping reagent. The untrapped ketone **7j** was obtained in 38% yield.

Silyl Enol Ether Approach. Although the syntheses of various exocyclic enones **3** by aldol condensation or one-pot conjugate addition/aldol condensation procedures were successful, the results were not completely satisfactory due to significant amounts of recovered or "untrapped" ketones in the reaction mixtures. Indirect approaches involving silyl enol ethers[19,20] and enol acetates were therefore examined. Aldol condensation involving silyl enol ethers have been achieved by employing Lewis acid catalyzed reactions (Mukiyama procedure)[21] or by using fluoride ion.[22]

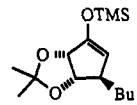
(14) Stork, G.; Isobe, M. *J. Am. Chem. Soc.* **1975**, *97*, 4745.
(15) (a) Heng, K. K.; Smith, R. A. J. *Tetrahedron* **1979**, *35*, 425. (b) Heng, K. K.; Smith, R. A. J. *J. Org. Chem.* **1981**, *46*, 2932.
(16) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310.
(17) Aldehydes **14** and **15** were prepared from PCC oxidation of the corresponding alcohols.
(18) For a review on organocopper conjugate addition–enolate trapping reaction, see: Taylor, R. J. K. *Synthesis* **1985**, 364.
(19) For reviews on the synthesis and reactin of silyl enol ethers, see: (a) Rasmussen, J. K. *Synthesis* **1977**, 91. (b) Brownbridge, P. *Synthesis* **1983**, *1*, 85. (c) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462. (d) Stork, G. *Pure Appl. Chem.* **1968**, *17*, 383.
(20) For silyl enol ether approaches to PG systems, see: Patterson, J. W.; Fried, J. H. *J. Org. Chem.* **1974**, *39*, 2506. Gooding, O. W. *Ibid.* **1990**, *55*, 4209.
(21) (a) Mukiyama, T.; Narasaka, K.; Banno, K. *Chem. Lett.* **1973**, 1011. (b) Mukiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (c) Mukiyama, T.; Izawa, T.; Saigo, K. *Chem. Lett.* **1974**, 323. (d) Mukiyama, T.; Ishida, A. *Chem. Lett.* **1975**, 319. (e) Mukiyama, T.; Ishida, A. *Bull Chem. Soc. Jpn.* **1977**, *50*, 1161.

Table I. Enol Acetates from Conjugate Addition/Enolate Acetylation of Enone 1

organocopper reagent	enol acetate	yield,[a] (%)
$LiMe_2Cu$	**21b**	97
n-OctMgBr	**21c**	88
5% CuBr–Me_2S		
i-PrMgCl	**21d**	90
5% CuI–TMEDA		
$Li_2Cu(CN)(t\text{-}Bu)_2$	**21e**	95
 + 2.5 equiv $[Bu_3P]$	**21j**	92

[a] Isolated yield of pure product.

Silyl enol ether **20** can be prepared in excellent yield by trimethylsilyl chloride promoted addition of lithium dibutylcuprate to enone **1**. As desilylation procedures using tetrabutylammonium fluoride were found to promote decomposition in our synthesis of PGE_2 (Scheme I), our efforts were focused on the regeneration of lithium enolates from silyl enol ethers by methyllithium and Lewis acid catalyzed approaches. Generation of the enolate from its silyl enol ether **20** and methyllithium failed. Lewis acids including $TiCl_4$, $ZnCl_2$, $SnCl_4$, and BF_3–Et_2O under a variety of conditions gave complex reaction mixtures.



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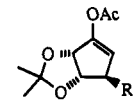


21

Enol Acetate Approach. Enolate acylation[18] is much more complicated than silylation. Acylation reactions can give enol esters by O-acylation or β-diketone compounds by C-acylation. Guidelines derived from the studies of the acylation of organocopper-generated enolates indicate the following: (1) Acid anhydrides give primarily O-acylation product;[23] acetyl chloride or bromide as acylating agent increases significantly the proportion of C-acylation.[24] (2) C-Acylation is favored by the presence of magnesium rather than lithium as the enolate counter ion.[24] (3) C-Acylation is favored by nonpolar solvents like ether, O-acylation is favored by polar solvents like THF and DME.[24] (4) C-Acylation is favored by low temperature and inverse addition.[25]

Addition of 5 equiv of freshly distilled acetic anhydride to the enolate generated by CuBr–Me_2S-catalyzed conjugate addition of octylmagnesium bromide to enone **1** furnished O-acylation product **21c** in 88% yield. Enol acetates are stable to silica gel flash chromatography and thus are much more easily purified than TMS enol ethers. Table I shows the yields of enol acetates prepared from organocopper conjugate addition/O-acylation reactions of enone **1**.

After addition of 2 equiv of MeLi to a THF solution of enol acetate **21c** at −78 °C, the regeneration of lithium enolate was complete in 15 min. After the reaction mixture was quenched with saturated aqueous ammonium chloride solution, ketone **7c** was obtained in quantitative yield. Encouraged by these results, aldol condensations utilizing the enolates generated from enol acetates and MeLi were examined. Addition of 1 equiv of $ZnCl_2$ to the enolate generated from enol acetate **21c** and 2 equiv of MeLi followed by aldol condensation with aldehyde **13** furnished, after dehydration with aluminum oxide, a 83% yield of enone **16c** and a 6% yield of ketone **7c**.

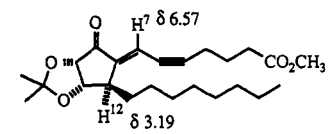
Table II. Enones 16 from Enol Acetates 21

enol acetate	aldehyde	aldol product (yield[a] (%))	recovered ketone (yield (%))
21b	**13**	**16b** (85)	**7b** (6)
21d	**13**	**16d** (68)	**7d** (13)
21e	**13**	**16e** (55)	**7e** (21)
21j	**13**	**16j** (81)	**7j** (4)
21c	**13**	**16c** (83)	**7c** (6)
21c	**14**	**18c** (68)	**7c** (22)
21c	**15**	**19c** (75)[b]	**7c** (12)

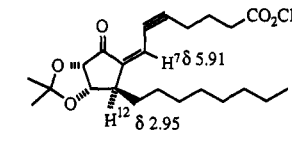
[a] Isolated yield of pure product. [b] About 3% of the 7*Z*, isomer (**22c**) was also isolated.

Table II gives the yields of enones prepared from enol acetates. These reactions usually proceeded more completely than the related reactions using enolates generated by LDA. A more important feature is that reactions with unsaturated aldehydes **14** and **15** give the aldol condensation products **18** and **19**, respectively, in moderate yield. As discussed previously, the enolate generated by LDA did not react with unsaturated aldehyde **14**. The presence of diisopropylamine in the latter aldol condensation reactions must have some kind of deleterious effects.

From the reaction of the lithium enolate derived from **21c** with aldehyde **15**, a 3% yield of 7*Z* product **22c** also isolated in addition to the normal 7*E* product **19c**. The ^1H NMR spectra of these two isomers are similar, with differences in the proton resonances of H-7 and H-12 only. The H-7 proton resonance of 7*E* isomer **19c** appears at δ 6.57, resulting from the deshielding effect of the carbonyl group. The H-12 resonance of the 7*Z* isomer appearing at 2.95 could be attributed to the shielding effect of the carbon–carbon triple bond. Compound **22c** is unstable at room temperature; a chloroform solution of **22c** completely isomerized to **19c** within 1 week.



19c



22c

By comparing the three procedures we examined, it is clear that the route employing enol acetates as intermediates is the most promising way to prepare the enones of interest. If the reactions that involve lithium cuprate conjugate additions, the one-pot procedure is a convenient and efficient route. The efficiency of the addition step varies litle with the various organocopper reagents; subsequent reactions of the intermediate enolate are highly sensitive to the nature of the initial organocopper reagent. The paper that follows describes the elaboration of ketones of type **3** to prostanoids.

Experimental Section

General Procedures. All air-sensitive reactions were conducted in flame- or oven-dried apparatus under a positive pressure of argon. Air-sensitive liquids were transferred by syringe or double-ended needle and introduced into the reaction vessel through rubber septum caps.[26] CuI was obtained from Fisher Scientific Co. and was purified by dissolution in a saturated

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aqueous solution of KI followed by treatment with charcoal, filtration, and dilution with water to reprecipitate the CuI.[27] CuBr was obtained from Fisher and was purified by continuous extraction with THF. CuI–Bu_3P was prepared according to a literature procedure.[27] CuCN obtained from Aldrich was used without further purification. CuBr–Me_2S was prepared by the literature method.[28] Flash chromatography[29] was performed with use of silica gel 60 (230–400 mesh, EM Reagents). In ^{13}C NMR data, * indicates a doublet due to the presence of two diastereomers.

General Procedures for the Preparation of Organocopper Reagents and Their Reactions with Enone 1. (I) Lithium Dialkylcuprates. (a) Bu_2CuLi. To a 0.5 M slurry of purified CuI (1.2 equiv) in THF at −78 °C was added *n*-BuLi (hexane solution, 2.4 equiv); the resulting mixture was allowed to warm with stirring to −20 °C for 1–2 min and recooled to −78 °C. To this was added enone 1 (1 equiv) as a 1 M THF solution. The mixture was stirred at −78 °C for 30 min, and then the reaction was quenched with saturated aqueous NH_4Cl; workup was by procedure A (in the following text). **(b) Me_2CuLi.** The general procedure as shown for Bu_2CuLi was followed. Me_2CuLi was prepared by reaction of a CuI slurry in THF with MeLi at 0 °C for 3 min.

(II) Conjugate Addition of Grignard Reagents Catalyzed by CuBr–Me_2S (with or without TMSCl/HMPA). A THF suspension of CuBr–Me_2S complex (5 mol % based on Grignard reagent) was cooled to −78 °C, to which Grignard reagent (1.2 equiv) was added and the resulting mixture was allowed to warm to 0 °C and stirred for 3 min. The resulting mixture was recooled to −78 °C. TMSCl (1.2 equiv)/HMPA (1.2 equiv) was added at this time if needed. A solution of enone 1 in THF (1.0 equiv, 1 M solution) was added. The reaction mixture was maintained at −78 °C, and the reaction was monitored by TLC. Upon completion of the reaction, the mixture was worked up by one of the following procedures. For reactions without TMSCl/HMPA, procedure A was used. If the reaction mixture contained TMSCl/HMPA, procedure B gave ketone, while procedure C gave the corresponding TMS enol ether.

(III) CuI–TMEDA/TMSCl-Mediated Conjugate Addition of Grignard Reagents.[6] To a suspension of CuI (5 mol % based on Grignard reagent) in THF at 0 °C was added TMEDA (1.2 equiv). The mixture was stirred for 5 min and then cooled to −78 °C, and the Grignard reagent (1.1 equiv) was added. After 20 min at −78 °C, TMSCl (1.1 equiv) was added, followed by a THF solution of enone 1. The reaction was monitored by TLC. The workup procedures were the same as described in II.

(IV) Stabilized Organocopper Reagent: RCu–Bu_3P.[1] A solution of vinylstannane 11 (0.80 g, 1.50 mmol, 1.275 mmol of trans product) in dry THF (5 mL) at −78 °C was treated with *n*-BuLi (1.6 M in hexane, 0.8 mL, 1.275 mmol) for 20 min. A solution of CuI–Bu_3P (0.47 g, 1.20 mmol) and Bu_3P (0.35 mL, 1.4 mmol) in THF (5 mL) was added, and the reaction mixture was stirred at −78 °C for 30 min. After addition of a solution of enone 1 (0.154 g, 1 mmol) in dry ether (2 mL), the reaction mixture was stirred at −78 °C for 10 min and at −30 °C for 1 h. The reaction was then quenched with saturated aqueous NH_4Cl and worked up as described in procedure A.

(V) In Situ Cuprate Formation via Transmetallation between Vinylstannane and Higher Order Cyanocuprate.[11] Copper cyanide (63 mg, 0.7 mmol, flame dried under argon) in THF (1 mL) was treated with methyllithium (1 mL, 1.5 M in ether, 1 mmol) at 0 °C. The cooling bath was removed, and vinylstannane 11 (0.531 g, 0.7 mmol based on trans isomer) in THF (1 mL) was added. After 1.5 h at room temperature, the mixture was cooled at −78 °C and enone 1 (77 mg, 0.5 mol) in THF (1 mL) was added rapidly via syringe. After being stirred at −78 °C for 10 min and −30 °C for 10 min, the reaction was quenched with saturated aqueous NH_4Cl solution and worked up as described in procedure A.

Workup Procedures for Cuprate Addition Reactions. Procedure A. The reaction mixture was poured into a 1:1 (v/v) solution of saturated aqueous NH_4Cl and NH_4OH. The resulting mixture was then extracted with diethyl ether and the organic extracts were washed successively with water and brine, dried over $MgSO_4$, filtered, and concentrated by use of a rotary evaporator. The product was then purified by flash chromatography on silica gel. **Procedure B.**[6] The reaction mixture was quenched with saturated aqueous NH_4Cl, and the resulting mixture was allowed to warm to room temperature with stirring. The mixture was diluted with diethyl ether, washed with 0.5 N HCl and aqueous $NaHCO_3$, and dried over anhydrous $MgSO_4$. The ether solution was concentrated, and the residue was purified by flash chromatography on silica gel. **Procedure C.**[6] The reaction mixture was poured into a separatory funnel containing a mixture of ice cold 0.1 N HCl and pentane, and the contents were shaken briefly. The pentane solution was separated, washed with cold saturated $NaHCO_3$, and dried (Na_2SO_4). Further purification could be achieved by dissolution of the concentrated pentane extract in DMSO followed by extraction with pentane. The combined pentane extracts were then washed with saturated aqueous $NaHCO_3$ and dried (Na_2SO_4). Concentration of the resulting pentane extracts gave the pure TMS enol ether.

6-Butyl-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7a). Compound **7a** was obtained from the conjugate addition of Bu_2CuLi to enone 1 and workup as described in procedure A (flash chromatography (10:1 petroleum ether/EtOAc)) in 92% yield as a colorless oil: IR (neat) 2989, 2933 (s), 2960, 1757 (s), 1057 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.54 (d, J = 5.4 Hz, 1 H), 4.22 (d, J = 5.4 Hz, 1 H), 2.76 (dd, J_1 = 18.3 Hz, J_2 = 8.5 Hz, 1 H), 2.37 (dt, J_1 = 8.5 Hz, J_2 = 8.0 Hz, 1 H), 2.06 (d, J = 18.3 Hz, 1 H), 1.43 (s, 3 H), 1.35 (s, 3 H), 1.32 (m, 6 H), 0.91 (t, J = 6.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.04, 112.08, 82.10, 78.11, 39.97, 36.76, 33.30, 29.29, 26.79, 24.81, 22.45, 13.78; HRMS calcd for $C_{12}H_{20}O_3$ 212.1412 ($M^{\bullet+}$), found 212.1419.

2,2,6-Trimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7b). Compound **7b** was obtained from the conjugate addition of Me_2CuLi to enone 1 and workup as described in procedure A (flash chromatography using 5:1 petroleum ether/EtOAc)) in 90% yield as a colorless oil: IR (CCl_4) 2936, 2873, 1740 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.50 (d, J = 5.2 Hz, 1 H), 4.24 (d, J = 5.2 Hz, 1 H), 2.81 (dd, J_1 = 18.2 Hz, J_2 = 8.4 Hz, 1 H), 2.52 (p, J = 7.8 Hz, 1 H), 1.97 (d, J = 18.2 Hz, 1 H), 1.43 (s, 3 H), 1.35 (s, 3 H), 1.06 (d, J = 7.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.29, 112.16, 83.12, 78.00, 41.43, 31.08, 26.77, 24.79, 19.11; HRMS calcd for $C_9H_{14}O_3$ 170.0943 ($M^{\bullet+}$), found 170.0946.

6-Octyl-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7c). Compound **7c** was obtained from CuBr–Me_2S-catalyzed conjugate addition of OctMgBr to enone 1 after workup as described in procedure A and flash chromatography (10:1 petroleum ether/EtOAc) in 87% yield as a colorless oil: IR (neat) 2988 (w), 2929 (s), 2856 (s), 1757 (s), 1459, 1215 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.54 (d, J = 5.0 Hz, 1 H), 4.21 (d, J = 5.0 Hz, 1 H), 2.75 (dd, J_1 = 18.3 Hz, J_2 = 8.5 Hz, 1 H), 2.37 (dt, J_1 = 8.5 Hz, J_2 = 7.0 Hz, 1 H), 2.05 (d, J = 18.3 Hz, 1 H), 1.43 (s, 3 H), 1.35 (s, 3 H), 1.27 (m, 14 H), 0.88 (t, J = 6.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.0, 111.97, 82.05, 78.05, 39.91, 36.73, 33.56, 31.72, 29.35, 29.30, 29.11, 27.12, 26.75, 24.78, 22.53, 13.96; HRMS calcd for $C_{16}H_{28}O_3$ 268.2038 ($M^{\bullet+}$), found 268.2041.

6-Isopropyl-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7d). Compound **7d** was obtained from TMEDA/TMSCl-promoted conjugate addition of *i*-PrMgCl to enone 1. Hydrolysis of the resulting TMS enol ether with K_2CO_3/MeOH and flash chromatography (10:1 petroleum ether/EtOAc) gave **7d** in 88% yield as a colorless oil: IR (CCl_4) 1734 (s), 1243 (s), 1153 (w), 1062 (s), 1026 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.60 (d, J = 5.8 Hz, 1 H), 4.25 (d, J = 5.8 Hz, 1 H), 2.69 (dd, J_1 = 18.0 Hz, J_2 = 8.6 Hz, 1 H), 2.22 (m, 1 H), 2.16 (dd, J_1 = 18.0 Hz, J_2 = 4.5 Hz, 1 H) 1.72 (octet, J = 6.8 Hz, 1 H), 1.44 (s, 3 H), 1.35 (s, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 213.85, 111.84, 80.55, 78.64, 44.19, 38.12, 30.80, 26.82, 24.77, 20.03, 19.69; HRMS calcd for $C_{11}H_{18}O_3$ 198.1256 ($M^{\bullet+}$), found 198.1255.

6-*tert*-Butyl-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7e). Compound **73** was obtained from the conjugate addition of $(t\text{-Bu})_2Cu(CN)Li_2$ to enone 1. Workup as described in procedure A and flash chromatography (10:1 petroleum ether/EtOAc) gave the product as a colorless oil (98% yield): IR (neat) 2961 (s), 2935 (s), 2872, 1757 (s), 1473,

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1372 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.66 (dd, J_1 = 6.0 Hz, J_2 = 1.6 Hz, 1 H), 4.26 (d, J = 6.0 Hz, 1 H), 2.62 (dd, J_1 = 18.6 Hz, J_2 = 10.0 Hz, 1 H), 2.29 (ddd, J_1 = 18.6 Hz, J_2 = 5.7 Hz, J_3 = 1.7 Hz, 1 H), 2.17 (ddd, J_1 = 10.0 Hz, J_2 = 5.7 Hz, J_3 = 1.7 Hz, 1 H), 1.44 (s, 3 H), 1.36 (s, 3 H), 0.94 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 213.67, 111.58, 78.86, 78.57, 48.66, 36.86, 31.59, 27.07, 26.75, 24.71; HRMS calcd for $C_{12}H_{20}O_3$ 212.1412 ($M^{\cdot+}$), found 212.1409.

6-[7′-(Tetrahydropyran-2″-yloxy)heptyl]-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7f). Compound **7f** was obtained from CuBr–Me_2S-catalyzed conjugate addition of THP-protected (7-hydroxyheptyl)magnesium bromide to enone **1** after workup as described in procedure A and flash chromatography (10:1 petroleum ether/ETOAc) in 19% yield as a colorless oil (two inseparable diastereomers): ^1H NMR ($CDCl_3$) δ 4.58 (t, J = 3.7 Hz, 1 H) 4.54 (d, J = 5.3 Hz, 1 H), 4.21 (d, J = 5.3 Hz, 1 H), 3.87 (td, J_1 = 7.3 Hz, J_2 = 3.3 Hz, 1 H), 3.73 (dt, J_1 = 9.4 Hz, J_2 = 6.8 Hz, 1 H), 3.50 (m, 1 H), 3.38 (dt, J_1 = 9.4 Hz, J_2 = 6.6 Hz, 1 H), 2.76 (dd, J_1 = 18.4 Hz, J_2 = 9.8 Hz, 1 H), 2.37 (d, J = 9.8 Hz, 1 H), 2.05 (d, J = 18.4 Hz, 1 H), 1.43 (s, 3 H), 1.35 (s, 3 H), 1.85–1.20 (m, 18 H); ^{13}C NMR ($CDCl_3$) δ 214.03, 112.03, 98.81, 82.04, 78.07, 67.49, 62.29, 39.94, 36.75, 33.56, 30.71, 29.62, 29.29, 29.17, 27.09, 26.77, 26.08, 25.43, 24.80, 19.63.

6-[7′-(*tert*-Butyldimethylsiloxy)heptyl]-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7g). Compound **7g** was obtained from CuBr–Me_2S-catalyzed conjugate addition of TBDMS-protected (7-hydroxyheptyl)magnesium bromide to enone **1** after workup as described in procedure A and flash chromatography (20:1 petroleum ether/EtOAc) in 34% yield as a colorless oil: ^1H NMR ($CDCl_3$) δ 4.51 (d, J = 5.1 Hz, 1 H), 4.18 (d, J = 5.1 Hz, 1 H), 3.58 (t, J = 6.4 Hz, 2 H), 2.73 (dd, J_1 = 18.3 Hz, J_2 = 8.5 Hz, 1 H), 2.23 (d, J = 7.0 Hz, 1 H), 2.03 (d, J = 18.3 Hz, 1 H), 1.48 (m, 2 H), 1.41 (s, 3 H), 1.32 (s, 3 H), 1.29 (m, 10 H), 0.87 (s, 9 H), 0.24 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 210.95, 112.07, 82.08, 78.11, 63.14, 39.99, 36.79, 33.61, 32.75, 29.38, 29.16, 27.12, 26.81, 25.92, 25.66, 24.84, 18.29, –5.33

6-(7′-Octenyl)-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7h). Compound **7h** was obtained from TMEDA/TMSCl-promoted conjugate addition of 7-octen-1-yl-copper to enone **1**. Hydrolysis of the resulting TMS enol ether with K_2CO_3/MeOH and flash chromatography (5:1 petroleum ether/EtOAc) gave **7h** in 86% yield as a colorless oil: IR (neat) 3078 (w), 2992, 2931 (s), 2855, 1758 (s), 1641 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.82 (ddt, J_1 = 17.1 Hz, J_2 = 10.3 Hz, J_3 = 6.6 Hz, 1 H), 5.02 (dq, J_1 = 17.1 Hz, J_2 = 1.7 Hz, 1 H), 4.95 (ddt, J_1 = 10.3 Hz, J_2 = 1.7 Hz, J_3 = 1.2 Hz, 1 H), 4.55 (d, J = 5.3 Hz, 1 H), 4.23 (d, J = 5.3 Hz, 1 H), 2.77 (dd, J_1 = 18.4 Hz, J_2 = 8.4 Hz, 1 H), 2.39 (m, 1 H), 2.07 (m, 3 H), 1.45 (s, 3 H), 1.36 (s, 3 H), 1.33 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 214.09, 139.01, 114.39, 112.17, 82.20, 78.22, 40.09, 36.93, 33.72, 29.35, 28.93, 28.86, 27.24, 26.92, 24.95; HRMS calcd for $C_{16}H_{26}O_3$ 266.1882 ($M^{\cdot+}$), found 266.1876. Anal. Calcd: C, 72.14; H, 9.84. Found: C, 71.86; H, 9.68.

6-Vinyl-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7i). Compound **7i** was obtained from TMEDA/TMSCl-promoted conjugate addition of vinylmagnesium bromide to enone **1**. Hydrolysis of the resulting TMS enol ether with K_2CO_3/MeOH and flash chromatography (10:1 petroleum ether/EtOAc) gave **7i** in 81% as a colorless oil: ^1H NMR ($CDCl_3$) δ 5.75 (ddd, J_1 = 17.2 Hz, J_2 = 10.6 Hz, J_3 = 6.5 Hz, 1 H), 5.06 (d, J = 10.6 Hz, 1 H), 5.01 (d, J = 17.2 Hz, 1 H), 4.55 (d, J = 5.2 Hz, 1 H), 4.11 (d, J = 5.2 Hz, 1 H), 3.00 (t, J = 6.9 Hz, 1 H), 2.72 (dd, J_1 = 18.2 Hz, J_2 = 8.5 Hz, 1 H), 2.18 (d, J = 18.2 Hz, 1 H), 1.34 (s, 3 H), 1.25 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.94, 137.34, 116.31, 112.34, 81.42, 77.88, 39.87, 38.61, 26.84, 24.90.

(1′*E*)-6-[3′-(*tert*-Butyldimethylsiloxy)-1′-octenyl]-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-cyclopenta-1,3-dioxol-4-one (7j). Compound **7j** was obtained from conjugate addition of Bu_3P-stabilized vinylcopper reagent prepared from **12** to enone **1** after workup as described in procedure A and flash chromatography (elution with petroleum ether then 10:1 petroleum ether/EtOAc) in 93% yield as a colorless oil (inseparable mixture of C-15 epimers): IR (neat) 2956 (s), 2932 (s), 2857 (s), 1759 (s), 1067 (s), 836 (s), 775 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.49 (m, 2 H), 4.56 (d, J = 5.0 Hz, 1 H), 4.14 (d, J = 5.0 Hz, 1 H), 4.01 (m, 1 H), 3.05 (m, 1 H), 2.80 (ddd, J_1 = 18.1 Hz, J_2 = 8.4 Hz, J_3 = 0.8 Hz, 1 H), 2.19 (dd, J_1 = 18.1 Hz, J_2 = 0.8 Hz, 1 H), 1.51–1.13 (m, 8 H), 1.40 (s, 3 H), 1.31 (s, 3 H), 0.84 (2s, t, J = 6.8 Hz, 12 H), –0.01 (s, 3 H), –0.05 (S, 6 h); ^{13}C NMR ($CDCl_3$) δ 213.03*, 135.76, 127.92, 112.30, 81.73*, 77.86, 72.77*, 39.01, 38.48*, 38.08, 31.64, 26.77, 25.76, 24.82, 24.70, 22.47, 18.11, 13.89, –4.41, –4.86.

4α-Hydroxy-4-vinyl-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (10). This compound, the result of 1,2-addition of a vinylcopper reagent to enone **1**, was obtained in various amounts depending on the type of reagent that had been used: ^1H NMR ($CDCl_3$) δ 5.90 (dd, J_1 = 5.8 Hz, J_2 = 1.7 Hz, 1 H), 5.89 (dd, J_1 = 17.4 Hz, J_2 = 10.7 Hz, 1 H), 5.72 (d, J = 5.8 Hz, 1 H), 5.21 (dd, J_1 = 17.4 Hz, J_2 = 1.2 Hz, 1 H), 5.13 (dd, J_1 = 10.7 Hz, J_2 = 1.2 Hz, 1 H), 5.07 (dd, J_1 = 5.3 Hz, J_2 = 1.7 Hz, 1 H), 4.37 (d, J = 5.3 Hz, 1 H), 3.31 (br, 1 H), 1.44 (s, 3 H), 1.38 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 140.73, 137.98, 131.96, 114.90, 112.91, 83.75, 82.82, 82.45, 27.91, 26.90.

General Procedure for the Preparation of 5-Alkylidene-6-alkyl-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxol-4-ones (3). Methyl (7*E*)-7-(6′-Butyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidine)heptanoate (16a). Method A: Direct Aldol Condensation. A solution of ketone **7a** (106 mg 0.5 mmol) in dry THF (2 mL) was added to a solution of LDA. The latter was prepared by adding *n*-BuLi (0.6 mL, 1.6 M in hexane, 0.58 mmol) to a solution of diisopropylamine (0.09 mL, 0.64 mmol) in THF (4 mL) at 0 °C; the resulting mixture was stirred fo 5 min and cooled to –78 °C. After being stirred at –78 °C for 30 min, $ZnCl_2$ (0.5 mL of a 1 M ether solution) and a solution of aldehyde **13** (119 mg, 0.75 mmol) in dry THF (1 mL) was added. The reaction mixture was stirred at –78 °C for 15 min and was allowed to warm to 0 °C in 1 h. The mixture was poured into water (10 mL) and ether (15 mL). The organic layer was separated and washed with three 10-mL portions of water. The ether layer was dried ($MgSO_4$) and filtered. The filtrate was stirred with alumina G (200 mg, type E, EM) for 15 min at room temperature. The alumina was removed by filtration, and filtrate was concentrated by rotary evaporation. Flash chromatography eluted by 10:1 petroleum ether/EtOAc furnished **16a** (134 mg, 76% yield) and recovered ketone **7a** (19 mg, 18% yield). Compound **16a** was obtained as a colorless oil: IR (neat) 2934, 2860, 1735 (s), 1646, 1457, 1382, 1218, 1157, 1085, 865 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.75 (t, J = 7.3 Hz, 1 H), 4.51 (d, J = 5.0 Hz, 1 H), 4.43 (d, J = 5.0 Hz, 1 H), 3.67 (s, 3 H), 3.05 (t, J = 5.6 Hz, 1 H), 2.31 (t, J = 7.4 Hz, 2 H), 2.21 (q, J = 7.3 Hz, 2 H), 1.36 (s, 3 H), 1.34 (s, 3 H), 1.42–1.39 (m, 12 H), 0.91 (t, J = 6.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.20, 173.86, 141.57, 138.34, 111.48, 79.50, 51.35, 41.06, 33.75, 32.97, 29.19, 29.08, 28.73, 28.06, 27.22, 25.42, 24.57, 22.65, 13.78; HMRS calcd for $C_{20}H_{32}O_5$ 352.2250 ($M^{\cdot+}$), found 252.2253.

Method B: From Enol Acetates. To a solution of enol acetate (0.5 mmol) in dry THF (2 mL) at –78 °C was added MeLi (0.67 mL, 1.5 M THF solution, 1.0 mmol), and the reaction mixture was stirred for 20 min. To the resulting mixture was added successively $ZnCl_2$ (0.5 mL of a 1.0 M solution in ether, 0.5 mmol) and a THF (1 mL) solution of aldehyde (0.75 mmol). The reaction mixture after stirring at –78 °C for 15 min was allowed to warm to 0 °C over 30 min. The reaction mixture was poured into water (10 mL) and ether (15 mL). The organic layer was separated, washed with three 10-mL portions of water, and dried ($MgSO_4$). To the filtrate was added alumina G (200 mg, type E, EM), and the mixture was stirred for 15 min at room temperature. The alumina was removed by filtration, and the filtrate was concentrated by rotary evaporation. The products were purified by flash chromatography on silica gel.

Method C: One-Pot Procedure. The procedure of the preparation and conjugate addition of organocopper reagent to enone **1** described previously was followed. After TLC showed enone **1** was completely consumed, the reaction mixture from the cuprate conjugate addition was cooled to –78 °C. To the reaction mixture was then added successively $ZnCl_2$ (1 equiv, 1 M ether solution) and a solution of aldehyde (1.5–2.0 equiv in THF). The reaction mixture was stirred at –78 °C for 15 min and was allowed to warm to 0 °C over 30 min. The reaction mixture was quenched with saturated aqueous NH_4Cl, poured into a 1:1 mixture of saturated aqueous NH_4Cl and aqueous NH_4OH, and extracted with ether. The combined ether extracts were washed by water, dried over $MgSO_4$, and filtered. To the filtrate was added alumina G (200 mg, type E, EM), and the mixture was stirred for 15 min

at room temperature. The alumina was removed by filtration, and the filtrate was concentrated by rotary evaporation. The products were purified by flash chromatography on silica gel.

Methyl (7*E*)-7-(2′,2′,6′-Trimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)heptanoate (16b). Compound **16b** was obtained from enol acetate **21b** and aldehyde **13** after flash chromatography (10:1 petroleum ether/EtOAc) in 85% yield as a colorless oil: IR (neat) 2988, 2936 (s), 2863, 1735 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.69 (t, J = 7.2 Hz, 1 H), 4.43 (d, J = 4.8 Hz, 1 H), 4.38 (d, J = 4.8 Hz, 1 H), 3.63 (s, 3 H), 3.10 (q, J = 7.6 Hz, 1 H), 2.27 (t, J = 7.5 Hz, 2 H), 2.19 (q, J = 7.4 Hz, 2 H), 1.61 (p, J = 7.4 Hz, 2 H), 1.47 (p, J = 7.4 Hz, 2 H), 1.33 (p, J = 7.5 Hz, 2 H), 1.32 (s, 3 H), 1.31 (s, 3 H), 1.11 (d, J = 7.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.05, 173.88, 141.28, 139.25, 111.68, 81.15, 79.47, 51.36, 35.52, 33.75, 28.87, 28.76, 28.06, 27.27, 25.49, 24.57, 18.57; MS 310 ($M^{\bullet+}$), 295 ($M^+ - CH_3$), 252, 205, 109, 95, 81, 69, 59, 55, 43 (100).

Methyl (7*E*)-7-(6′-Octyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)heptanoate (16c). Compound **16c** was obtained from enol acetate **21c** and aldehyde **13** after flash chromatography (10:1 petroleum ether/EtOAc) in 83% yield as a colorless oil: IR (neat) 2929 (s), 2856, 1739 (s), 1644 (w), 1215 (s), 1171, 1083 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.62 (t, J = 7.1 Hz, 1 H), 4.40 (d, J = 4.9 Hz, 1 H), 4.31 (d, J = 4.9 Hz, 1 H), 3.54 (s, 3 H), 2.94 (t, J = 5.5 Hz, 1 H), 2.19 (t, 7.3 Hz, 2 H), 2.10 (q, J = 7.2 Hz, 2 H), 1.24 (s, 3 H), 1.21 (s, 3 H), 1.53 (p, J = 7.4 Hz, 2 H), 1.39–1.16 (m, 20 H), 0.76 (t, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.08, 173.74, 141.38, 138.37, 111.40, 79.48, 79.44, 51.24, 41.07, 33.68, 33.23, 31.67, 29.26, 29.15, 29.06, 28.68, 28.03, 17.16, 16.91, 25.36, 14.53, 22.46, 13.89; HRMS calcd for $C_{24}H_{40}O_5$ 408.2875 ($M^{\bullet+}$), found 408.2870.

Methyl (7*E*)-7-(6′-Isopropyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)heptanoate (16d). Compound **16d** was obtained from enol acetate **21d** and aldehyde **13** after flash chromatography (10:1 petroleum ether/EtOAc) in 68% yield as a colorless oil: IR (neat) 2937, 2873, 1734 (s), 1643 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.74 (td, J_1 = 7.7 Hz, J_2 = 1.7 Hz, 1 H), 4.53 (d, J = 5.3 Hz, 1 H), 4.31 (d, J = 5.3 Hz, 1 H), 3.61 (s, 3 H), 2.91 (d, J = 3.3 Hz, 1 H), 2.25 (t, J = 7.4 Hz, 2 H), 2.16 (q, J = 7.4 Hz, 2 H), 1.83 (m, 1 H), 1.58 (p, J = 7.7 Hz, 2 H), 1.45 (p, J = 7.3 Hz, 2 H), 1.30 (p, J = 7.8 Hz, 2 H), 1.31 (s, 3 H), 1.28 (s, 3 H), 0.99 (d, J = 6.9 Hz, 3 H), 0.76 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.15, 173.91, 142.63, 137.51, 111.04, 79.66, 76.99, 51.40, 47.76, 33.80, 30.92, 29.62, 28.74, 28.14, 27.12, 25.33, 24.61, 20.64, 18.92; HRMS calcd for $C_{19}H_{30}O_5$ 338.2093 ($M^{\bullet+}$), found 338.2088.

Methyl (7*E*)-7-(*tert*-Butyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)heptanoate (16e). Compound **16e** was obtained from enol acetate **21e** and aldehyde **13** after flash chromatography (10:1 petroleum ether/EtOAc) in 55% yield as a colorless oil: IR (neat) 2951 (s), 2871, 1734 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.82 (t, J = 7.3 Hz, 1 H), 4.72 (d, J = 5.3 Hz, 1 H), 4.35 (d, J = 5.3 Hz, 1 H), 3.67 (s, 3 H), 2.81 (s, 1 H), 2.30 (t, J = 7.4 Hz, 2 H), 2.22 (q, J = 7.3 Hz, 2 H), 1.63 (p, J = 7.5 Hz, 2 H), 1.56–1.30 (m, 4 H), 1.36 (s, 3 H), 1.32 (s, 3 H), 0.92 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 203.16, 173.91, 143.99, 136.92, 110.75, 78.61, 77.59, 52.01, 51.37, 34.13, 33.78, 30.34, 28.62, 28.08, 27.21, 27.05, 25.18, 24.57; HRMS calcd for $C_{20}H_{32}O_5$ 352.2246 ($M^{\bullet}$+), found 352.2254.

Methyl (1″*E*,7*E*)-7-[6′-[3″-(*tert*-Butyldimethylsiloxy)-1″-octenyl]-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene]heptanoate (16j). Compound **16j** was obtained from enol acetate **21j** and aldehyde **13** after flash chromatography (20:1 petroleum ether/EtOAc) in 81% yield as a colorless oil: IR (CCl_4) 2986 (s), 2958 (s), 2858 (s), 1735 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.87 (t, J = 7.1 Hz, 1 H), 5.57 (dd, J_1 = 15.6 Hz, J_2 = 6.0 Hz, 1 H), 5.42 (ddd, J_1 = 15.6 Hz, J_2 = 5.6 Hz, J_3 = 4.6 Hz, 1 H), 4.46 (d, J = 4.8 Hz, 1 H), 4.37 (d, J = 4.8 Hz, 1 H), 4.04 (d, J = 5.6 Hz, 1 H), 3.75 (m, 1 H), 3.65 (s, 3 H), 2.28 (t, J = 7.1 Hz, 2 H), 2.13 (q, J = 7.3 Hz, 2 H), 1.61 (p, J = 7.2 Hz, 2 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 1.50–1.23 (m, 12 H), 0.85 (2s, t, J = 6.7 Hz, 12 H), –0.04–0.00 (4s, 6 H); ^{13}C NMR ($CDCl_3$) δ 202.73, 173.86, 143.22, 136.44*, 135.79, 126.18*, 111.98, 79.91*, 79.58, 72.68*, 29.29, 28.88, 28.56, 27.88, 27.39, 25.81, 25.64, 24.78, 24.66, 24.52, 22.55, 18.17, 13.91, –4.40, –4.80; MS 479 ($M^{\bullet+}$ – t-Bu 100), 421, 379, 337, 279, 215, 73, 43.

Methyl (1″*E*,5*E*,7*E*)-7-[6′-[3″-(*tert*-Butyldimethylsiloxy)-1″-octenyl]-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene]-5-heptenoate (18j). Compound **18j** was obtained from the one-pot conjugate addition of Bu_3P-stabilized vinylcopper reagent prepared from **12** to enone **1** and trapping the resulting enolate with aldehyde **14**. Flash chromatography (10:1 petroleum ether/EtOAc) gave **18j** in 51% yield as a colorless oil: IR (CCl_4) 3029 (w), 2956 (s), 2938 (s), 2861 (s), 1742 (s), 1726 (s), 1632(s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19 (d, J = 10.7 Hz, 1 H), 6.18 (m, 2 H), 5.60 (m, 1 H), 5.40 (m, 1 H), 4.47 (d, J = 4.5 Hz, 1 H), 4.40 (dd, J_1 = 4.5 Hz, J_2 = 1.3 Hz, 1 H), 4.03 (m, 1 H), 3.77 (m, 1 H), 3.64 (s, 3 H), 2.30 (t, J = 7.5 Hz, 2 H), 2.22 (q, J = 7.3 Hz, 2 H), 1.75 (p, J = 7.5 Hz, 2 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 1.21 (m, 8 H), 0.85–0.84 (s, 9 H), 0.82 (t, J = 6.7 Hz, 3 H), –0.007 (2s, 3 H), –0.048 (2s, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.41, 173.38, 147.12, 137.74, 136.56, 133.06, 127.10, 126.54*, 111.92, 79.96, 79.67, 72.68*, 51.42, 43.86, 38.18*, 33.24, 32.71, 31.65, 27.36, 25.75, 25.60, 24.69, 23.78, 22.49, 18.10, 13.86, –4.44, –4.88; HRMS calcd for $C_{30}H_{50}O_6Si$ 534.3376 ($M^{\bullet+}$), found 534.3381.

Methyl (1″*E*,7*E*)-7-[6′-[3″-(*tert*-Butyldimethylsiloxy)-1″-octenyl]-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene]-5-heptynoate (19j). Compound **19j** was obtained from the one-pot conjugate addition of Bu_3P-stabilized vinylcopper reagent prepared from **12** to enone **1** and trapping the resulting enolate with aldehyde **15**. Flash chromatography (20:1 petroleum ether/EtOAc) gave **19j** in 45% yield as a colorless oil: IR (CCl_4) 2991, 2957 (s), 2938 (s), 2858 (s), 2240, 2214, 1742 (s), 1729 (s), 1616, 1257 (s), 1224 (s), 1158 (s), cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.65 (t, J = 2.2 Hz, 1 H), 5.50 (m, 2 H), 4.50 (dd, J_1 = 5.2 Hz, J_2 = 4.4 Hz, 1 H), 4.41 (dd, J_1 = 4.4 Hz, J_2 = 1.9 Hz, 1 H), 4.04, (t, J = 5.3 Hz, 1 H), 3.82 (dd, J_1 = 4.4 Hz, J_2 = 0.8 Hz, 1 H), 3.65 (s, 3 H), 2.41 (m, 4 H), 1.86 (p, J = 7.3 Hz, 2 H), 1.34 (s, 3 H), 1.32 (s, 3 H), 1.22 (m, 8 H), 0.84 (2s, t, J = 6.7 Hz, 12 H), –0.075 (2s, 3 H), –0.045 (2s, 3 H); ^{13}C NMR ($CDCl_3$) δ 202.01, 173.07, 136.64*, 124.94*, 119.47, 112.07, 105.08, 79.56*, 78.85, 72.65, 51.49, 44.88*, 38.25*, 32.96, 32.68, 32.46, 31.69, 29.58, 27.32, 25.76, 25.52, 24.76*, 23.48, 22.65*, 19.50, 18.13*, 13.89, –4.42, –4.92; HRMS calcd for $C_{30}H_{48}O_6Si$ 532.3220 ($M^{\bullet+}$), 475.2516 ($M^{\bullet+}$ – t-Bu), found 475.2521.

Methyl (5*E*,7*E*)-7-(6′-Octyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)-5-heptenoate (18c). Compound **18c** was obtained from enol acetate **21c** and aldehyde **14** after flash chromatography (10:1 petroleum ether/EtOAc) in 68% yield as a colorless oil: IR (CCl_4), 2990, 2929 (s), 2929 (s), 2858 (s), 1742 (s), 1723 (s), 1631, 1608, cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.03 (m, 1 H), 6.18 (m, 2 H), 4.49 (d, J = 5.1 Hz, 1 H), 4.39 (d, J = 5.1 Hz, 1 H), 3.61 (s, 3 H), 3.09 (t, J = 6.1 Hz, 1 H), 2.28 (t, J = 7.4 Hz, 2 H), 2.23 (q, J = 7.5 Hz, 2 H), 1.74 (p, J = 7.4 Hz, 2 H), 1.30 (s, 3 H), 1.27 (s, 3 H), 1.40 (p, J = 6.4 Hz, 2 H), 1.20 (m, 12 H), 0.82 (t, J = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.79, 173.39, 146.41, 136.23, 135.92, 126.83, 11.43, 79.59, 79.66, 51.38, 41.48, 33.69, 33.10, 32.60, 31.66, 29.51, 29.24, 29.04, 27.20, 26.97, 25.38, 23.68, 22.45, 13.89; HRMS calcd for $C_{24}H_{38}O_5$ 406.2719 ($M^{\bullet+}$), found 406.2722.

Methyl (7*E*)-7-(6′-Octyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)-5-heptynoate (19c). Compound **19c** was obtained from enol acetate **21c** and aldehyde **15** after flash chromatography (10:1 petroleum ether/EtOAc) in 75% yield as a colorless oil: R_f = 0.590 (5:1 petroleum ether/EtOAc); IR (neat) 2988, 2929 (s), 2856, 2210, 1740 (s), 1725 (s), 1611 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.57 (q, J = 2.2 Hz, 1 H), 4.50 (d, J = 5.1 Hz, 1 H), 4.45 (d, J = 5.1 Hz, 1 H), 3.68 (s, 3 H), 3.19 (td, J_1 = 6.9 Hz, J_2 = 2.4 Hz, 1 H), 2.52 (td, J_1 = 6.9 Hz, J_2 = 2.4 Hz, 2 H), 2.45 (t, J = 7.3 Hz, 2 H), 1.90 (p, J = 7.1 Hz, 2 H), 1.36 (s, 3 H), 1.34 (s, 3 H), 1.62–1.29 (m, 14 H), 0.87 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 202.44, 173.08, 147.44, 118.08, 111.75. 104.64, 79.62, 79.35, 68.87, 51.49, 42.90, 32.64, 32.30, 31.74, 23.48, 22.53, 19.45, 13.96; HRMS calcd for $C_{24}H_{36}O_5$ 404.2562 ($M^{\bullet+}$), found 404.2565.

Methyl (7*Z*)-7-(6′-Octyl-2′,2′-dimethyl-4′-oxo-3′aβ,5′,6′α,6′aβ-tetrahydro-4′*H*-cyclopenta-1′,3′-dioxol-5′-ylidene)-5-heptynoate (22c). Compound **22c**, a minor product obtained from synthesis of **19c**, was a colorless oil (3% yield): R_f = 0.483 (5:1 petroleum ether/EtOAc); ^1H NMR ($CDCl_3$) δ 5.91 (q, J = 2.0 Hz, 1 H), 4.42 (d, J = 5.0 Hz, 1 H), 4.41 (d, J = 5.0

Hz, 1 H), 3.67 (s, 3 H), 2.95 (m, 1 H), 2.56 (m, 4 H), 1.92 (p, J = 7.0 Hz, 2 H), 1.37 (s, 3 H), 1.35 (s, 3 H), 1.71–1.26 (m, 14 H), 0.88 (t, J = 7.0 Hz, 3 H).

6-Butyl-5-methylene-2,2-dimethyl-3aβ,5,6α,6aβ-tetrahydro-4*H*-1,3-dioxol-4-one (17). To a solution of lithium dibutylcuprate (Bu_2CuLi, 1.5 mmol in THF (5 mL)) at −78 °C was added a solution of enone 1 (154 mg, 1.0 mmol) in THF (1 mL). After the solution was stirred for 15 min at −78 °C, freshly cracked formaldehyde (from 5 equiv of paraformaldehyde) was carried into the reaction mixture by a stream of argon. The reaction mixture was then allowed to warm to room temperature over 30 min and then was quenched with saturated aqueous NH_4Cl. The resulting mixture was poured into 5 mL of aqueous NH_4OH and extracted with 20 mL of ether. The ether extract was washed with 10 mL of water and dried over $MgSO_4$. After removal of the $MgSO_4$ by filtration, the filtrate was stirred overnight with 200 mg of alumina G (type E, EM reagent). The alumina was removed by filtration, and the filtrate was concentrated by rotary evaporation. Flash chromatography with 5:1 petroleum ether/EtOAc as eluant afforded ketone **7a** (114 mg, 54%) and the desired enone **17** (67 mg, 30%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.25 (d, J = 1.0 Hz, 1 H), 5.48 (d, J = 1.0 Hz, 1 H), 4.50 (d, J = 4.5 Hz, 1 H), 4.44 (d, J = 4.5 Hz, 1 H), 2.97 (m, 1 H), 1.37 (s, 6 H), 1.60–1.35 (m, 6 H), 0.92 (t, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.52, 145.79, 122.33, 111.89, 79.90, 79.15, 43.62, 33.71, 28.80, 27.24, 25.38, 22.44, 13.77.

4β-Butyl-6-(trimethylsiloxy)-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (20). Compound **20** was obtained from TMSCl-promoted conjugate addition of Bu_2CuLi to enone 1 after workup as described in procedure C in 95% yield as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 4.65 (dd, J_1 = 6.1 Hz, J_2 = 1.4 Hz, 1 H), 4.56 (d, J = 2.1 Hz, 1 H), 4.13 (d, J = 6.1 Hz, 1 H), 2.44 (m, 1 H), 1.32 (s, 3 H), 1.21 (s, 3 H), 1.21–1.13 (m, 6 H), 0.77 (t, J = 6.0 Hz, 3 H), 0.17 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 152.39, 110.24, 107.86, 82.55, 82.08, 46.57, 34.69, 29.43, 27.25, 25.52, 22.61, 13.86, −0.09.

General Procedure for the Preparation of Enol Acetates by One-Pot Conjugate Addition and Enolate Acylation. The preparation and conjugate addition of organocopper reagent to enone 1 was described previously. After TLC showed the starting material (enone 1) had been completely consumed, the reaction mixture was cooled to −78 °C and freshly distilled acetic anhydride (5 equiv based on enone) was added neat. The mixture was stirred at −78 °C for 15 min. The dry ice bath was removed, and the reaction mixture was warmed to room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl and worked up as described in procedure A.

6-Acetoxy-2,2,4β-trimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (21b). Addition of Me_2CuLi to enone 1 gave, after flash chromatography (5:1 petroleum ether/EtOAc), product **21b** as a colorless oil (97% yield): IR (neat) 2988, 2961, 2933, 2873 (w), 1773 (s), 1654 (w), 1372 (s), 1205 (s), 1176 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.51 (d, J = 2.5 Hz, 1 H), 5.08 (dd, J_1 = 6.0 Hz, J_2 = 1.6 Hz, 1 H), 4.20 (d, J = 6.0 Hz, 1 H), 2.71 (qt, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 1 H), 2.11 (s, 3 H), 1.36 (s, 3 H), 1.26 (s, 3 H), 1.04 (d, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.27, 148.01, 119.71, 110.96, 83.30, 81.42, 41.72, 27.33, 25.79, 21.10, 19.49; HRMS calcd for $C_{11}H_{16}O_4$ 212.1049 ($M^{\bullet+}$), found 212.1052.

6-Acetoxy-4β-isopropyl-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (21d). CuI/TMEDA-catalyzed addition of *i*-PrMgCl to enone 1 gave, after flash chromatography (10:1 petroleum ether/EtOAc), product **21d** as a colorless oil (90% yield): IR (neat) 2961, 2875, 1772 (s), 1665, 1466, 1371 (s), 1205 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.52 (d, J = 2.4 Hz, 1 H), 5.01 (dd, J_1 = 6.0 Hz, J_2 = 1.5 Hz, 1 H), 4.34 (d, J = 6.0 Hz, 1 H), 2.54 (m, 1 H), 2.14 (s, 3 H), 1.67 (octet, J = 6.6 Hz, 1 H), 1.39 (s, 3 H), 1.30 (s, 3 H), 0.89 (d, J = 6.8 Hz, 3 H), 0.85 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.18, 145.58, 116.44, 110.60, 81.22, 79.96, 53.95, 30.74, 27.20, 25.59, 20.96, 20.04, 19.56; HRMS calcd for $C_{13}H_{20}O_4$ 240.1362 ($M^{\bullet+}$), found 240.1363.

6-Acetoxy-4β-*tert*-butyl-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (21e). Addition of *t*-$Bu_2Cu(CN)Li_2$ to enone 1 gave, after flash chromatography (10:1 petroleum ether/EtOAc), product **21e** as a colorless oil (95% yield): IR (neat) 2963 (m), 2872, 1772 (s), 1667, 1473, 1370 (s), 1250, 1204 (s), 1176 (s), 1056 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.58 (s, 1 H), 5.03 (d, J = 6.0 Hz, 1 H), 4.45 (d, J = 6.0 Hz, 1 H), 2.52 (s, 1 H), 2.19 (s, 3 H), 1.44 (s, 3 H), 1.35 (s, 3 H), 0.91 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 168.27, 148.95, 116.14, 110.57, 81.53, 78.53, 58.45, 32.42, 27.30, 25.67, 21.03; HRMS calcd for $C_{14}H_{22}O_4$ 252.1518 ($M^{\bullet+}$), 239.1283 ($M^{\bullet+}$ − CH_3), found 239.1285.

6-Acetoxy-4β-octyl-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (21c). CuBr–Me_2S-catalyzed addition of OctMgBr to enone 1 gave, after flash chromatography (10:1 petroleum ether/EtOAc), product **21c** as a colorless oil (88% yield): IR (neat) 2926 (s), 2855, 1768 (s), 1666 (w), 1204 (s), 1174, 1057 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.60 (d, J = 2.5 Hz, 1 H), 5.10 (dd, J_1 = 6.1 Hz, J_2 = 1.6 Hz, 1 H), 4.31 (d, J = 6.1 Hz, 1 H), 2.68 (m, 1 H), 2.17 (s, 3 H), 1.43 (s, 3 H), 1.33 (s, 3 H), 1.25 (m, 14 H), 0.86 (t, J = 6.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.30, 148.10, 118.37, 110.87, 81.85, 81.23, 47.22, 34.08, 31.81, 29.57, 29.42, 29.20, 27.30, 27.25, 25.68, 22.59, 21.10, 14.02; HRMS calcd for $C_{18}H_{30}O_4$ 310.2144 ($M^{\bullet+}$) 295.1902 ($M^{\bullet+}$ − CH_3), found 295.1911.

(1′*E*)-6-Acetoxy-4β-[3′-(*tert*-butyldimethylsiloxy)-1′-octenyl]-2,2-dimethyl-3aβ,6aβ-dihydro-4*H*-cyclopenta-1,3-dioxole (21j). Addition of Bu_3P-stabilized vinylcopper reagent prepared from **12** to enone 1 gave, after flash chromatography (elution with petroleum ether then with 20:1 petroleum ether/EtOAc), product **21j** (mixture of C-15 epimers) as a colorless oil (92% yield): IR (neat) 2958, 2934 (s), 2858, 1772 (s), 1370 (s), 1253, 1201 (s), 1076 (s), 837 (s), 774 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.52 (t, J = 4.5 Hz, 3 H), 5.11 (d, J = 5.4 Hz, 1 H), 4.34 (d, J = 5.4 Hz, 1 H), 4.03 (m, 1 H), 3.36 (m, 1 H), 2.18 (s, 3 H), 1.43 (s, 3 H), 1.33 (s, 3 H), 1.24 (m, 8 H), 0.86 (2s, t, J = 6.7 Hz, 12 H), −0.01 (4s, 6 H); ^{13}C NMR ($CDCl_3$) δ 168.09, 148.86, 135.72*, 128.93*, 116.39*, 111.17*, 81.94, 81.26, 73.17*, 49.41*, 38.15, 31.71, 27.33, 25.84, 24.84, 22.52, 21.05, 18.17, 13.92, −4.82, −4.25; MS 423 ($M^{\bullet+}$ − CH_3), 381 (100; $M^{\bullet+}$ − CH_3-*t*-Bu), 321, 281 (56), 249 (45), 207 (34), 117, 57.

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Supplementary Material Available: ^{1}H NMR spectra at 300 MHz of **7a–j**, **10**, **16a–e**, **16j**, **17**, **18c**, **18j**, **19c**, **19j**, **20**, **21b–e**, **21j**, and **22c** (15 pages). Ordering information is given on any current masthead page.