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1,6-Addition of Organolithium Compounds to Acceptor-Substituted Enynes Catalyzed by a Copper(I) Arenethiolate

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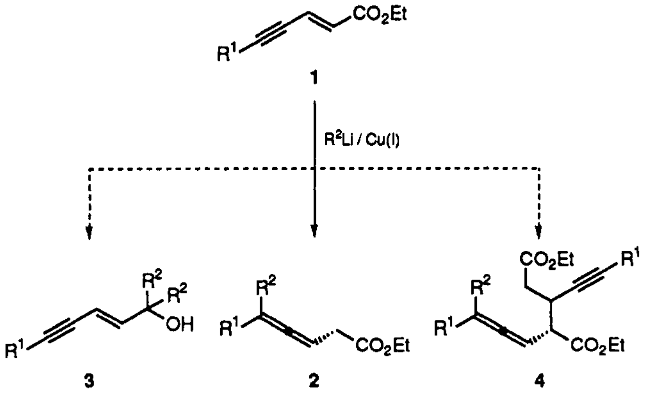
In recent organic synthesis the development of reactions proceeding with high degrees of chemo-, regio-, and stereoselectivity is of increasing importance.[1] A larger number of these processes involve the use of organometallic reagents,[2] and among those organocuprates play a prominent role.[3,4] Conjugate 1,4-additions of cuprates to Michael acceptors have been utilized extensively for the synthesis of natural products and other target molecules;[3] recently, the scope of conjugate cuprate additions has been extended by the introduction of 1,6- and 1,8-addition reactions to 2-en-4-ynoates and 2,4-dien-6-ynoates, respectively, which open a versatile access to richly functionalized allenes.[4]

An intriguing feature of conjugate 1,4-additions is that they can be performed not only with stoichiometric amounts of organocuprates R_2CuLi but also with organometallic compounds RM (usually Grignard reagents) in the presence of catalytic amounts of copper(I) salts.[3] Advantages of the latter method are a more economic use of the organometallic reagent (with cuprates R_2CuLi only one substituent R is transferred to the Michael acceptor whereas the second one is wasted[3]) and smaller waste disposal problems, since only minute amounts of copper salts are employed. Therefore, we considered it useful to develop a catalytic method for the 1,6-addition of organometallic reagents to 2-en-4-ynoates **1** in order to open a more efficient access to β-allenic carbonyl compounds **2**.



The 1,6-addition of cuprates to acceptor-substituted enynes is characterized by a much lower reactivity compared to 1,4-additions to Michael acceptors.[4] As a consequence of this, side reactions which are normally negligible compared to the desired conjugate addition might prevail. If the copper(I) catalyst is not efficient to promote the 1,6-addition, simple 1,2-addition of the organometallic reagent to the ester function of **1** to give tertiary alcohol **3** could take place. If the copper(I) salt does catalyze the 1,6-addition, but with too slow a rate, the allenyl enolate thus obtained could add to unreacted enyne to give adducts of type **4** and larger oligomerization products.[5] Recently, we demonstrated the importance of these effects, in particular the influence of the order of addition of the reagents, in the enantioselective Michael addition of MeMgI to benzylideneacetone catalyzed by chiral copper arenethiolates.[6] Here, we wish to present the results of our effort to fine-tune the copper catalyst and reaction conditions in order to realize a Cu(I)-catalyzed 1,6-addition of organometallic reagents to acceptor-substituted enynes.

Results

During our investigations, it turned out that the following parameters have to be taken into account: the copper(I) catalyst, the organometallic reagent, the mode of addition of the reactants, the stoichiometry of the reactants, and temperature and solvent.[6b,c] As test case we chose the reaction of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**, scale: 1 mmol) with methyllithium/methylmagnesium iodide; the analysis of the crude product mixture was performed by GC. With this system, the following observations concerning the reaction parameters mentioned above were made.

(1) Copper(I) Catalyst. Several copper(I) compounds were tested for the reaction of **1a** with MeLi under optimum reaction conditions (see below). These can be classified into three groups: (i) Catalysts that give mainly 1,2-addition product **3** (besides starting material), such as CuI, $CuBr\cdot Me_2S$, CuCN, $CuI\cdot 2LiCl$, and $CuI\cdot (EtO)_3P$ (these are not efficient to promote the desired 1,6-addition); (ii) catalysts that give mixtures of 1,6-addition product **2**, 1,2-addition product **3**, and oligomers **4**, such as $CuI\cdot n\text{-}Bu_3P$, $CuI\cdot (Et_2N)_3P$, CuI + i-Pr_2NH, $CuCN\cdot 2LiCl$, CuSPh,

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CuSPh + Et_3N, and CuSCN (these catalyze the 1,6-addition at too slow a rate); and (iii) catalysts that give mainly the 1,6-addition product **2** (>80% of the crude mixture) and only small amounts of side products **3** and **4** (<20% of the crude mixture), such as trimeric copper(I) 2-[(dimethylamino)methyl]phenylthiolate (**5**).[7]

Having observed the nice chemoselectivity of catalyst **5**, further studies were concentrated on establishing the optimal reaction conditions for this catalyst.

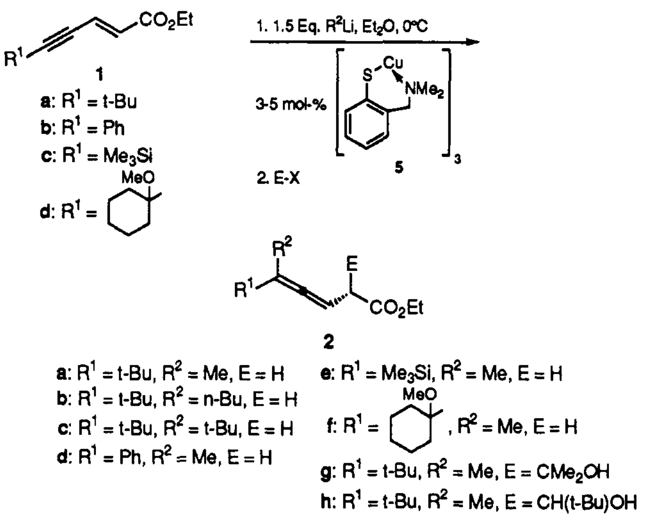
(2) Organometallic Reagent. Methyllithium is superior to methylmagnesium iodide; with the latter the 1,6-addition proceeds slower so that the starting enynoate is not consumed completely and large amounts of side products **4** are formed.

(3) Mode of Addition of the Reactants. Three different addition modes were tested (cf. ref 6b,c): (i) Addition of the organolithium compound to a mixture of the enyne **1** and catalyst **5**: Due to the high concentration of starting material in the mixture, addition of the allenyl enolate to unreacted enyne is prevailing, so that large amounts of side products **4** and oligomers are formed. (ii) Addition of the enyne **1** to a mixture of the organolithium compound and catalyst **5**: During the reaction the excess of organolithium reagent reacts most probably faster than the arenethiolate species (cf. experiments described in ref 6b) to the effect that the 1,2-addition product **2** is formed predominantly. (iii) Simultaneous addition of the organolithium compound and the enyne **1** to a suspension of the catalyst: Under these conditions the 1,6-addition product is the major product since both side reactions are suppressed. The reaction can be performed by using two dropping funnels (for large scale) or a syringe pump (for small scale).

(4) Stoichiometry of the Reactants. For the reactions with **5** 3–5 mol % of the trimeric catalyst with respect to enyne **1** was used; this is sufficient to achieve a complete consumption of the starting material and a clean conversion into the 1,6-addition product (>80% of the crude product). The ratio of the organolithium reagent to the Michael acceptor is of crucial importance; with small ratios (ca. 1:1) the formation of oligomers of type **4** is favored whereas with larger ratios (ca. 2:1) considerable amounts of 1,2-adduct **2** are formed. A ratio of RLi:**1** $\approx$ 1.5:1 gives the best results and was used throughout the following investigations.

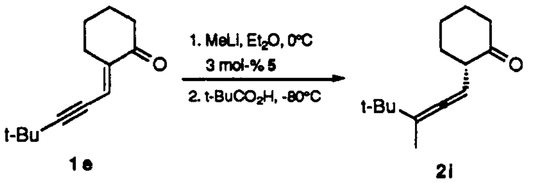
(5) Temperature and Solvent. Like the stoichiometry of the reactants, the temperature is of critical importance for the outcome of the reaction. The optimum temperature is 0 °C; at −20 °C the reaction is so slow that the 1,6-adduct, unconsumed starting material, and large amounts of side products **4** are found in the product mixture, whereas at +20 °C only starting material and oligomeric side products are formed. As was found previously for the stoichiometric 1,6-addition of organocuprates to acceptor-substituted enynes,[4] the best solvent for the Cu(I)-catalyzed reaction is diethyl ether; in THF no 1,6-addition is taking place (Scheme I).

Scheme I



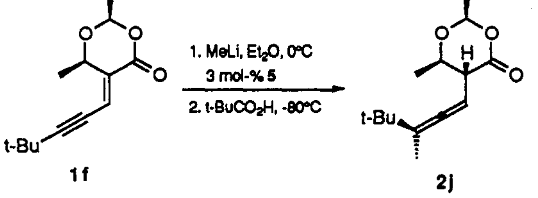
Having established the optimum conditions for the 1,6-addition of MeLi to enynoate **1a** catalyzed by copper(I) arenethiolate **5** (3–5 mol %), we next examined this reaction and the reactions of esters **1a–d** with different organolithium compounds and electrophiles on a preparative scale (2.5–10 mmol) in order to explore the efficiency of the catalytic process. The reaction of **1a** with MeLi/catalyst **5** on a 10 mmol scale furnished allene **2a** in 64% yield, i.e., with lower efficiency than achievable by using 2 equiv of $Me_2CuLi{\cdot}LiI$ (86% yield).[5] The relation is better for the reactions of **1a** with n-BuLi and t-BuLi, respectively, in the presence of catalyst **5** giving the β-allenic esters **2b** (59%) and **2c** (83%); the corresponding yields obtained with cyanocuprates $R_2Cu(CN)Li_2$ are 59% (**2b**)[5] and 91% (**2c**).[4b]

Enynoates with different substituents at C-5 were also tested; reaction of compounds **1b–d** bearing phenyl, trimethylsilyl, and 1-methoxycyclohexyl groups at this position with MeLi/catalyst **5** furnished the 1,6-adducts **2d** (51%; regioselective protonation of the allenyl enolate with pivalic acid[4a]), **2e** (57%), and **2f** (61%). The corresponding yields found with 1.5–2 equiv of $Me_2CuLi{\cdot}LiI$ are 79% (**2d**),[4a] 57% (**2e**),[4a] and 95% (**2f**).[5] As in the case of stoichiometric 1,6-additions of organocuprates to acceptor-substituted enynes,[4e,f] the allenyl enolate formed by treatment of **1a** with MeLi/catalyst **5** could also be reacted with carbonyl compounds; likewise, these trapping reactions take place regioselectively at C-2 of the allenyl enolate, but the diastereoselectivities are not as high as observed in the stoichiometric 1,6-addition reactions. Thus, reaction of **1a** with MeLi/catalyst **5** and acetone gave β-hydroxy ester **2g** (80% yield, ds = 2:1), and trapping with pivalic aldehyde furnished adduct **2h** (87%, ds = 37:33:22:8); with $Me_2CuLi{\cdot}LiI$, **2g** was obtained in 83% yield (ds = 4:1)[4e] and **2h** in 82% yield (ds = 50:38:9:3).[4e]



1e **2i**

54% Yield (ds = 1 : 1)



1f **2j**

57% Yield (ds = 4 : 1)

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Finally, we examined structurally more complex Michael acceptors, i.e., lactone **1e** and dioxanone **1f**, in the reaction with MeLi/catalyst **5**. Also in these cases the reaction proceeded as expected; 1,6-adducts **2i** (54% yield, ds ≈ 1:1) and **2j** (57% yield, ds = 4:1, regio- and stereoselective protonation of the allenyl enolate with pivalic acid[4a,5,8]) were obtained. The corresponding yields and selectivities found with stoichiometric amounts of $Me_2CuLi{\cdot}LiI$ are 67% (ds ≈ 1:1)[5] for **2i** and 78% (ds = 4:1)[5] for **2j**, i.e., the yields of the catalytic reaction are somewhat lower, but the stereoselectivities are unchanged.

Discussion

Of the 10 allenes synthesized by 1,6-addition of organolithium reagents to acceptor-substituted enynes under catalysis with the copper(I) arenethiolate **5**, five (**2b**, **2c**, **2e**, **2g**, **2h**) could be obtained with yields comparable to those achieved with stoichiometric amounts of organocuprates whereas in the other cases the yields are somewhat lower. The advantages of the catalytic method are lower costs and diminished waste disposal problems since smaller amounts of organolithium and copper(I) reagents can be used. Thus, in terms of efficiency the catalytic method with copper(I) arenethiolate **5** can well compete with the use of organocuprates, in particular if large-scale preparations are carried out.

In terms of stereoselectivity it is interesting to note that the diastereoselectivity of the cuprate addition to dioxanone **1f** is not changed by use of the catalytic instead of the stoichiometric copper precursor. However, it is clear from the results that the diastereoselectivities of trapping reactions with carbonyl compounds are lower if the allenyl enolate is formed by the catalytic method. One explanation for this behavior is that the *E*/*Z*-ratio of the metal enolate, which has been shown to influence the stereochemistry of the trapping reactions,[4e] depends on the method used for the generation of the enolate. In this context, it has to be taken into account that copper-containing clusters might be coordinated to the allenyl enolate. However, when copper is used in catalytic amounts, the lithium enolate will be present mainly. Accordingly, the differences in stereoselectivity could be caused by the different amounts and reactivities of copper species present in the reaction mixtures.

From the mechanistic point of view the question arises why the trimeric copper(I) arenethiolate **5** is an efficient catalyst for the 1,6-addition of organolithium compounds to acceptor-substituted enynes whereas all other copper(I) salts tested in this work are not. It seems that the presence of a hard donor (nitrogen) and a soft donor (sulfur)[6d] with a favorable geometry enables the bonding of one or more molecules of the organolithium reagent to the copper cluster to give a cuprate-like reagent which is sufficiently reactive to undergo the desired 1,6-addition to the enyne (an open-chain simulation of this situation, a mixture of copper(I) thiophenolate and triethylamine, is not an efficient catalyst for the 1,6-addition; see above). In this context it is interesting to note that a trimeric copper(I) arenethiolate analogous to **5** bearing a chiral 1-[2-(dimethylamino)ethyl] substituent instead of the achiral (dimethylamino)methyl group is able to bind up to six molecules of methyllithium and that with this catalyst highly enantioselective 1,4-addition reactions of Grignard reagents to benzylideneacetone could be realized.[6,9] Further work will have to show if other catalysts with this motiv are also suitable to promote conjugate addition reactions of organometallic compounds.

Experimental Section

General Information. See ref 4a. The NMR data for the major isomer of a mixture are marked with an asterisk. Ratios of diastereomers were determined by GC using a 30 m OV-1701 capillary column and hydrogen as carrier gas.

Starting Materials. The syntheses of enynes **1a**,[10] **1b**,[4a] and **1c**,[10,11] and of copper(I) arenethiolate **5**[7] have been described. Enynoate **1d** was prepared by formylation of 1-ethinyl-1-methoxycyclohexane with n-BuLi/DMF[12] and subsequent Wittig–Horner olefination as described previously.[4a,e] Lactone **1e** and dioxanone **1f** were synthesized by treatment of δ-valerolactone and (2*R*,6*R*)-6-methyl-2-(1,1-dimethylethyl)-1,3-dioxan-4-one,[13] respectively, with LDA and 4,4-dimethyl-2-pentynal,[12] mesylation of the resulting alkynol and mesylate elimination with DBU.[5,14] Details of these procedures will be published elsewhere.

General Procedure for the 1,6-Addition of Organolithium Reagents to Acceptor-Substituted Enynes Catalyzed by Copper(I) Arenethiolate 5. A suspension of **5** (3–5 mol % with respect to **1**) in diethyl ether is cooled to 0 °C, and solutions of the enyne **1** in diethyl ether and of MeLi (1.5 M in diethyl ether, diluted with diethyl ether), n-BuLi (1.5 M in hexane, diluted with hexane), or t-BuLi (1.7 M in pentane) are added dropwise simultaneously (using two dropping funnels or a syringe pump) within ca. 1 h. In the case of MeLi and n-BuLi, yellow or orange homogeneous solutions are formed during the addition, whereas a black suspension results with t-BuLi. After the addition the mixture is stirred for 30–60 min prior to workup.

Workup Procedure A. Ca. 10 mL of a saturated NH_4Cl solution is added, and the mixture is filtered through Celite. The solvent is removed in vacuo, and the crude product is purified by column chromatography.

Workup Procedure B. The mixture is cooled to −80 °C and added via teflon tubing to a cold (−80 °C) solution of pivalic acid in diethyl ether. After the mixture is warmed to room temperature ca. 10 mL of water is added, and the mixture is filtered through Celite. The solvent and excess of pivalic acid are removed in vacuo, and the crude product is purified by column chromatography.

Workup Procedure C. A solution of the electrophile is added at 0 °C, and stirring is continued for 30–60 min. After addition of ca. 10 mL of a saturated NH_4Cl solution the mixture is filtered through Celite. The solvent is removed in vacuo, and the crude product is purified by column chromatography.

Ethyl 5,6,6-Trimethyl-3,4-heptadienoate (2a). From 1.66 g (9.2 mmol) of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**) in 30 mL of diethyl ether, 10.0 mL (15.0 mmol) of MeLi diluted with 20 mL of diethyl ether, and 204 mg (0.30 mmol) of **5** in 200 mL of diethyl ether; workup procedure A. After column chromatography of the crude product (SiO_2, 70–230 mesh, hexane/diethyl ether (20:1)) 1.16 g (64%) of **2a** was obtained as a slightly yellow liquid.

IR: ν = 1960 cm^{-1} (m, C=C=C), 1730 (s, C=O). ^1H-NMR: δ = 1.04 (s, 9H), 1.26 (t, 3H, *J* = 7.1 Hz), 1.68 (d, 3H, *J* = 2.9 Hz),

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[8] The conjugate addition to **1f** takes place preferably anti with respect to the methyl group at C-6; this could be established with an X-ray analysis of an allenic dioxanone bearing a methyl group instead of a hydrogen atom at C-5.[5] Details will be published elsewhere.

[9] This chiral copper(I) arenethiolate also catalyzes the 1,6-addition of methylmagnesium iodide to enynoate **1a**; however, the allene **2a** could only be obtained in racemic form (van Klaveren, M. Unpublished results).

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2.97 (d, 2H, J = 7.0 Hz), 4.14 (q, 2H, J = 7.1 Hz), 5.14 (tq, 1H, J = 7.0/2.9 Hz). ^{13}C-NMR: δ = 14.1 (+), 14.7 (+), 28.9 (+), 33.3 (×), 35.5 (–), 60.4 (–), 83.4 (+), 109.6 (×), 171.8 (×), 201.5 (×). MS: m/z = 196 (17, M$^+$), 57 (100). Anal. Calcd for $C_{12}H_{20}O_2$ (196.3): C, 73.43; H, 10.27. Found: C, 73.45; H, 10.52.

Ethyl 5-(1,1-Dimethylethyl)-3,4-nonadienoate (2b). From 0.90 g (5.0 mmol) of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**) in 30 mL of diethyl ether, 5.0 mL (7.5 mmol) of n-BuLi diluted with 25 mL of hexane, and 125 mg (0.18 mmol) of **5** in 100 mL of diethyl ether; workup procedure A. Column chromatography of the crude product (SiO_2, 70–230 mesh, hexane/diethyl ether (20:1)) gave 0.70 g (59%) of **2b** as a slightly yellow liquid.

IR: ν = 1960 cm^{-1} (m, C=C=C), 1735 (s, C=O). ^{1}H-NMR: δ = 0.90 (t, 3H, J = 7.1 Hz), 1.03 (s, 9H), 1.21–1.43 (m, 4H), 1.29 (t, 3H, J = 7.1 Hz), 1.87–1.98 (m, 2H), 2.97 (d, 2H, J = 7.2 Hz), 4.14 (q, 2H, J = 7.1 Hz), 5.24 (tt, 1H, J = 3.5/7.2 Hz). ^{13}C-NMR δ = 14.0 (+), 14.2 (+), 22.5 (–), 26.6 (–), 29.2 (+), 30.3 (–), 33.5 (×), 35.8 (–), 60.4 (–), 86.1 (+), 115.2 (×), 171.9 (×), 201.0 (×). MS m/z = 238 (3, M$^+$), 57 (100). Anal. Calcd for $C_{15}H_{26}O_2$ (238.4): C, 75.58; H, 10.99. Found: C, 75.67; H, 11.32.

Ethyl 5-(1,1-Dimethylethyl)-6,6-dimethyl-3,4-heptadienoate (2c). From 0.54 g (3.0 mmol) of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**) in 3 mL of diethyl ether, 2.6 mL (4.5 mmol) of t-BuLi, and 75 mg (0.11 mmol) of **5** in 60 mL of diethyl ether; workup procedure A. Purification of the crude product by column chromatography (SiO_2, 70–230 mesh, hexane/diethyl ether (20:1)) furnished 0.59 g (83%) of **2c** as a slightly yellow liquid.

Spectroscopic data: see ref 4b.

Ethyl 5-Phenyl-3,4-hexadienoate (2d). From 1.00 g (5.0 mmol) of ethyl 5-phenyl-2-penten-4-ynoate (**1b**) in 25 mL of diethyl ether, 5.0 mL (7.5 mmol) of MeLi diluted with 20 mL of diethyl ether, 100 mg (0.15 mmol) of **5** in 100 mL of diethyl ether, and 1.02 g (10.0 mmol) of pivalic acid in 20 mL of diethyl ether; workup procedure B. After column chromatography of the crude product (SiO_2, 70–230 mesh, hexane/diethyl ether (14:1)) 0.55 g (51%) of **2d** was isolated as a slightly yellow liquid.

Spectroscopic data: see ref 4a.

Ethyl 5-(Trimethylsilyl)-3,4-hexadienoate (2e). From 0.59 g (3.0 mmol) of ethyl 5-(trimethylsilyl)-2-penten-4-ynoate (**1c**) in 20 mL of diethyl ether, 3.0 mL (4.5 mmol) of MeLi diluted with 20 mL of diethyl ether, and 68 mg (0.10 mmol) of **5** in 60 mL of diethyl ether; workup procedure A. Column chromatography of the crude product (SiO_2, 70–230 mesh, hexane/diethyl ether (10:1)) gave 0.36 g (57%) of **2e** as a slightly yellow liquid.

Spectroscopic data: see ref 4a.

Ethyl 5-(1-Methoxycyclohex-1-yl)-3,4-hexadienoate (2f). From 0.71 g (3.0 mmol) of ethyl 5-(1-methoxycyclohex-1-yl)-2-penten-4-ynoate (**1d**) in 20 mL of diethyl ether, 3.0 mL (4.5 mmol) of MeLi diluted with 20 mL of diethyl ether, and 90 mg (0.13 mmol) of **5** in 60 mL of diethyl ether; workup procedure A. Purification of the crude product by column chromatography (SiO_2, 70–230 mesh, hexane/diethyl ether (2:1)) provided 0.46 g (61%) of **2f** as a slightly yellow liquid.

IR: ν = 1960 cm^{-1} (m, C=C=C), 1730 (s, C=O). ^{1}H-NMR: δ = 1.19–1.59 (m, 8H), 1.27 (t, 3H, J = 7.1 Hz), 1.63 (d, 3H, J = 2.8 Hz), 1.68–1.81 (m, 2H), 3.01 (d, 2H, J = 7.2 Hz), 3.08 (s, 3H), 4.16 (q, 2H, J = 7.1 Hz), 5.24 (tq, 1H, J = 7.2/2.8 Hz). ^{13}C-NMR: δ = 13.5 (+), 14.2 (+), 22.1 (–), 25.9 (–), 33.3 (–), 35.3 (–), 49.1 (+), 60.8 (–), 76.9 (×), 84.3 (+), 103.3 (×), 171.7 (×), 204.2 (×). MS: m/z = 252 (2, M$^+$), 81 (100). Anal. Calcd for $C_{15}H_{24}O_3$ (252.4); C, 71.39;H, 9.59. Found: C, 71.21;H, 9.99.

Ethyl 2-(1-Hydroxy-1-methylethyl)-5,6,6-trimethyl-3,4-heptadienoate (2g). From 0.54 g (3.0 mmol) of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**) in 20 mL of diethyl ether, 3.0 mL (4.5 mmol) of MeLi diluted with 20 mL of diethyl ether, 93 mg (0.13 mmol) of **5** in 60 mL of diethyl ether, and 0.58 g (10.0 mmol) of acetone in 5 mL of diethyl ether; workup procedure C. Column chromatography of the crude product (SiO_2, 70–230 mesh, hexane/diethyl ether (1:1)) yielded 0.61 g (80%) of **2g** as a slightly yellow liquid (2:1 mixture of diastereomers).

Spectroscopic data: see ref 4e.

Ethyl 2-(1-Hydroxy-1,1-dimethylpropyl)-5,6,6-trimethyl-3,4-heptadienoate (2h). From 0.90 g (5.0 mmol) of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**) in 30 mL of diethyl ether, 5.0 mL (7.5 mmol) of MeLi diluted with 25 mL of diethyl ether, 112 mg (0.16 mmol) of **5** in 100 mL of diethyl ether, and 0.86 g (10.0 mmol) of pivalic aldehyde in 5 mL of diethyl ether; workup procedure C. After column chromatography of the crude product (SiO_2, 70–230 mesh, hexane/diethyl ether (4:1)) 1.23 g (87%) of **2h** was obtained as a slightly yellow liquid (37:33:22:8 mixture of diastereomers).

Spectroscopic data: see ref 4e.

3-(3,4,4-Trimethyl-1,2-pentadien-1-yl)-tetrahydro-2H-pyran-2-one (2i). From 0.48 g (2.5 mmol) of 3-(4,4-dimethyl-2-pentinylidene)tetrahydro-2*H*-pyran-2-one (**1e**) in 30 mL of diethyl ether, 2.5 mL (3.8 mmol) of MeLi diluted with 30 mL of diethyl ether, and 67 mg (0.10 mmol) of **5** in 50 mL of diethyl ether; workup procedure A. Purification of the crude product by column chromatography (SiO_2, 70–230 mesh, hexane/diethyl ether (2:1)) furnished 0.28 g (54%) of **2i** as a slightly yellow liquid (1:1 mixture of diastereomers).

IR: ν = 1960 cm^{-1} (m, C=C=C), 1730 (s, C=O). ^{1}H-NMR: δ = 1.03/1.04 (2s, 9H), 1.69 (d, 3H, J = 2.9 Hz), 1.73–2.14 (m, 4H), 3.12–3.24 (m, 1H), 4.32 (t, 2H, J = 5.8 Hz), 5.40 (m, 1H). ^{13}C-NMR: δ = 14.9 (+), 15.2 (+), 21.4 (–), 21.6 (–), 24.3 (–), 24.8 (–), 29.0 (+), 33.3 (×), 33.4 (×), 40.0 (+), 40.1 (+), 68.9 (–), 69.0 (–), 89.3 (+), 89.4 (+), 111.8 (×), 112.1 (×), 172.4 (×), 200.2 (×). MS: m/z = 208 (6, M$^+$), 151 (100). Anal. Calcd for $C_{13}H_{20}O_2$ (208.3): C, 74.96; H, 9.68. Found: C, 74.26; H, 9.77.

(2*R*,5*R*,6*R*)-6-Methyl-2-(1,1-dimethylethyl)-5-(3,4,4-trimethyl-1,2-pentadien-1-yl)-1,3-dioxan-4-one (2j). From 0.66 g (2.5 mmol) of (*E*,2*R*,6*R*)-6-methyl-2-(1,1-dimethylethyl)-5-(4,4-dimethyl-2-pentinylidene)-1,3-dioxan-4-one (**1f**) in 30 mL of diethyl ether, 2.5 mL (3.8 mmol) of MeLi diluted with 30 mL of diethyl ether, 59 mg (0.09 mmol) of **5** in 50 mL of diethyl ether, and 0.51 g (5.0 mmol) of pivalic acid in 20 mL of diethyl ether; workup procedure B. Column chromatography (SiO_2, 70–230 mesh, hexane/diethyl ether (2:1)) of the crude product gave 0.40 g (57%) of **2j** as slightly yellow crystals (4:1 mixture of diastereomers). Mp: 67–68 °C.

IR: ν = 1960 cm^{-1} (m, C=C=C), 1735 (s, C=O). ^{1}H-NMR: δ = 0.97 (s, 9H), 1.05/1.07* (2s, 9H), 1.36/1.37* (2d, 3H, 2 × J = 6.1 Hz), 1.71*/1.72 (2d, 3H, 2 × J = 2.9 Hz), 2.91* (dd, 1H, J = 6.9/9.7 Hz), 2.91 (dd, 1H, J = 6.3/9.7 Hz), 3.83*/3.86 (2dq, 1H, 2 × J = 9.7/6.1 Hz), 4.91/4.92* (2s, 1H), 5.22* (dq, 1H, J = 6.9/2.9 Hz), 5.34 (dq, 1H, J = 6.3/2.9 Hz). ^{13}C-NMR: δ = 14.8/14.9* (2+), 20.3 (+), 23.9 (+), 29.0 (+), 33.6 (×), 35.2 (×), 48.0/48.8* (2+), 75.0/75.4 (2+), 85.8 (+), 108.0*/108.2 (2+), 111.6*/111.7 (2×), 169.6 (×), 201.0/201.8* (2×). MS: m/z = 223 (<1, M$^+$ – *t*-Bu), 179 (100). Anal. Calcd for $C_{17}H_{28}O_3$ (280.4): C, 72.82; H, 10.07. Found: C, 72.80; H, 9.78.