[Chem. Pharm. Bull. 34(6)2417—2427(1986)]

Reduction–Alkylation with Organocopper(I) Reagents–Alkyl Halides: Highly Regioselective α-Alkylation of γ-Acetoxy-α,β-enoates with Lithium Dibutylcuprate–Alkyl Halides and Difference in the Reactivity of Electron-Deficient Olefins with Organocopper(I)–Lewis Acid Reagents

TOSHIRO IBUKA,*,[a] TAKESHI AOYAGI,[a] and YOSHINORI YAMAMOTO[b]

Faculty of Pharmaceutical Sciences, Kyoto University,[a] Sakyo-ku, Kyoto 606, Japan and Department of Chemistry, Faculty of Science, Tohoku University,[b] Aobayama, Sendai 980, Japan

(Received December 3, 1985)

Reaction of γ-acetoxy-α,β-enoates with lithium dialkylcuprate followed by alkyl halides results in the predominant or exclusive formation of α-alkyl-β,γ-enoates in high yields under mild conditions, and a synthetic application to (±)-α-vetispirene is presented. Treatment of diethyl fumarate and triethoxycarbonylethylene with $Bu_2CuLi \cdot AlCl_3$ led to 1,4-addition to give conjugate adducts in high yields. In sharp contrast, diethyl maleate and tetraethoxycarbonylethylene predominantly gave the respective reduction products. Evidence for a presumed dianionic intermediate, based on trapping with some electrophiles, is also presented.

Keywords——γ-oxygenated α,β-enoate; β,γ-enoate; deconjugative reduction; α-vetispirene; lithium dialkylcuprate; organocopper(I)–Lewis acid

A New Regioselective α-Alkylation of γ-Acetoxy-α,β-enoates with Lithium Dibutylcuprate–Alkyl Halides

The regioselective α- or γ-alkylation of α,β-unsaturated carbonyl compounds and of allylic acetates and halides is a longstanding synthetic problem which continues to receive much attention.[1,2] γ-Oxygenated-α,β-unsaturated carbonyl compounds are extremely valuable sources for natural product syntheses, especially for compounds with high biological activities,[3-8] and the γ-oxygen functions are deconjugatively eliminated by reducing agents such as zinc amalgam in the presence of hydrogen chloride,[6] zinc in acetic acid,[7] and zinc–copper[8] to yield β,γ-unsaturated carbonyl compounds. However, none of the above methods seemed well suited to the direct regioselective alkylation. Trapping of an enolate intermediate by electrophiles would be impossible, since the above reduction conditions involve a proton source.

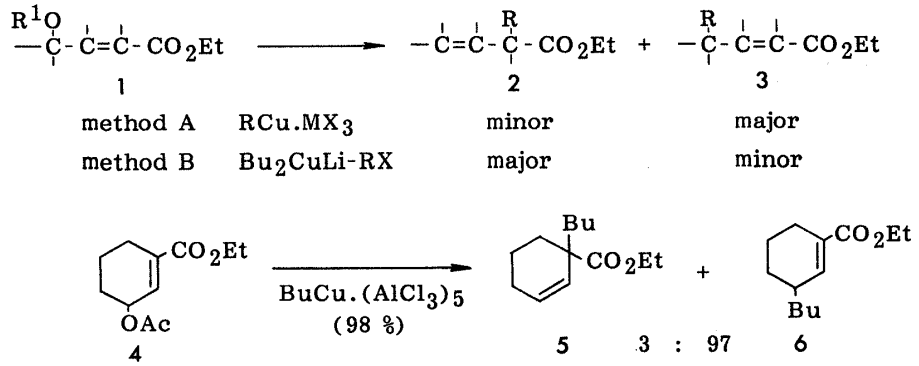


Chart 1

Previously, Yamamoto *et al.*[9] and we[10] reported the reaction of a γ-oxygenated α,β-enoate (**1**) with Lewis acid-mediated organocopper reagents to yield a mixture of the α-alkylated β,γ-enoate (**2**) and the γ-alkylated α,β-enoate (**3**) in favor of the γ-alkylated product (method A); *e.g.*, reaction of the enoate (**4**) with $BuCu \cdot (AlCl_3)_5$ complex afforded the γ-butylated product (**6**) as the major product. Such a substitution reaction of γ-oxygenated α,β-enoates could not be attained by using the ordinary organocopper reagents. However, no general method for the efficient regioselective α-alkylation of γ-oxygenated α,β-enoates by reduction–alkylation in a one-pot reaction was available.

We present here a new highly regioselective α-alkylation of the presumed copper enolates derived from γ-acetoxy-α,β-enoates (**1**) by treatment with lithium dibutylcuprate followed by alkyl halides in a one-pot reaction (method B). After several attempts by judicious selection of organometallic reagent and reaction conditions we found that good to excellent results could be obtained by using lithium dibutylcuprate as a reducing agents; this has the advantages of being more reliable than other methods based on zinc[6,7] and less hazardous than lithium in

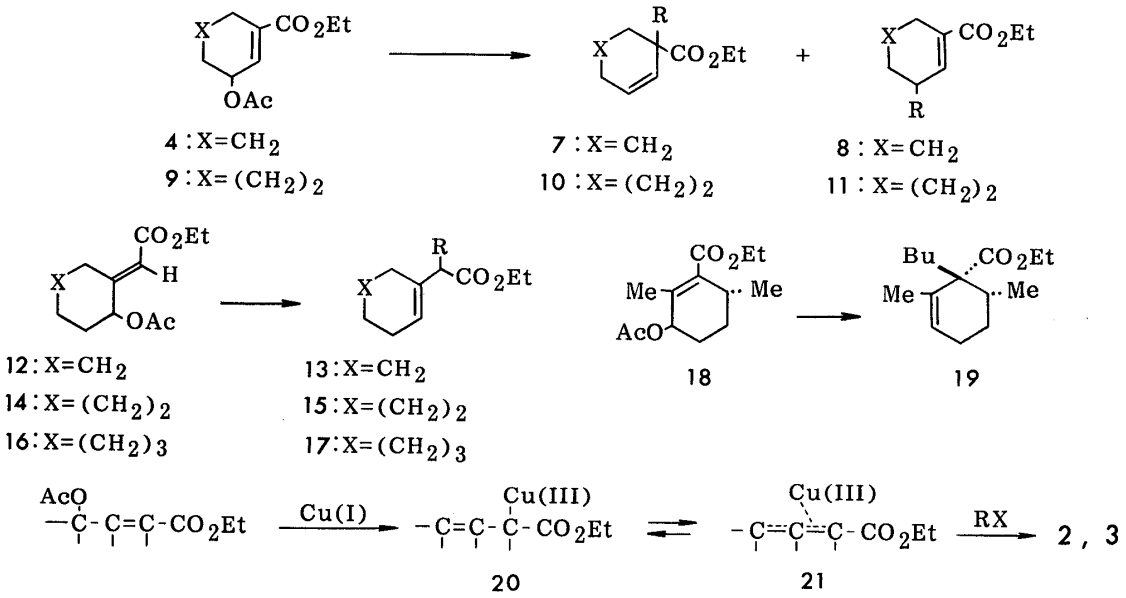


Chart 2

TABLE I. Yields of α- and γ-Alkylated Products in the Reaction of γ-Acetoxy-α,β-enoates with Lithium Dibutylcuprate and Alkyl Halides

Entry	Substrate	Alkyl halide	α-Alkylated product	Yield (%)
1	**4**	BuBr	**7**, R=Bu	92[a]
2	**4**	MeI	**7**, R=Me	94
3	**4**	$Br(CH_2)_3Br$	**7**, R=$(CH_2)_3Br$	75
4	**4**	$Br(CH_2)_3OTHP$	**7**, R=$(CH_2)_3OTHP$	52
5	**4**	$BrCH_2CH=CH_2$	**7**, R=$CH_2CH=CH_2$	91
6	**9**	BuBr	**10**, R=Bu	94[a]
7	**9**	MeI	**10**, R=Me	89
8	**12**	BuBr	**13**, R=Bu	91
9	**14**	BuBr	**15**, R=Bu	66
10	**14**	EtBr	**15**, R=Et	50
11	**16**	BuBr	**17**, R=Bu	87
12	**18**	BuBr	**19**	30

a) γ-Alkylated product (**8**, R=Bu, <0.8% yield) or (**11**, R=Bu, <0.8% yield) was also isolated. THP=tetrahydropyranyl.

liquid ammonia.[11]

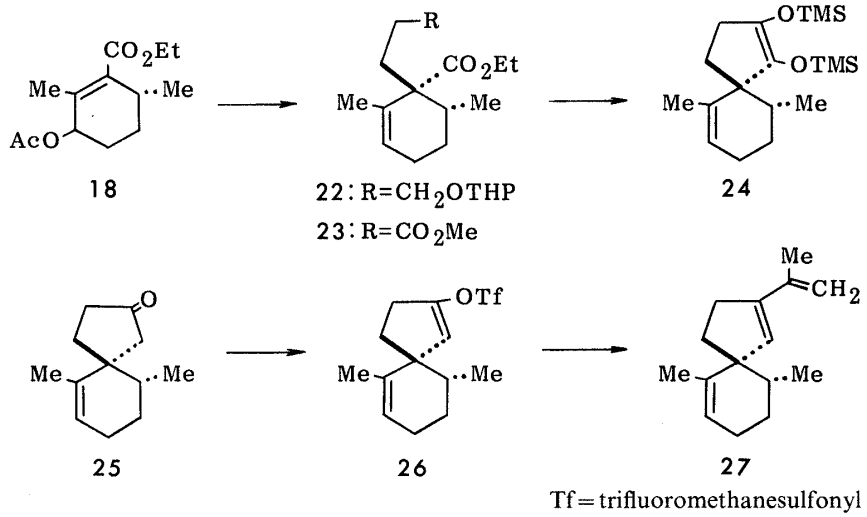
As can be seen from Chart 2 and Table I, reaction of a variety of γ-acetoxy-α,β-enoates (**4**, **9**, **12**, **14**, **16**, and **18**) with lithium dibutylcuprate at −70 to −40 °C for 10—30 min followed by alkyl halides at ambient temperature for 15—20 h afforded α-alkylated β,γ-enoates in high regioselectivity. The present α-alkylation is opposite to the selective γ-alkylation with Lewis acid-mediated organocopper reagents reported earlier.[9,10]

Despite the slow rate of reaction in the alkylation stage, successful reaction requires both an aprotic solvent, usually diethyl ether or, preferably, tetrahydrofuran, and hexamethyl phosphoric triamide (2—3 molar equiv. relative to the substrate).[12] Since a substantial amount of starting material was recovered with the use of 1 molar equiv. of the cuprate reagent, at least 2 molar equiv. of the cuprate is also necessary. The enoates (**4** and **9**) with an endocyclic double bond gave, in some cases (entries 1 and 6), a small amount of γ-alkylation product. In contrast, the substrates (**12**, **14**, and **16**) with an exocyclic double bond gave exclusively α-alkylation products (entries 8—11). The enoate (**18**) reacted rapidly with lithium dibutylcuprate, even at −60 °C, but failed to give significant amounts of the α-alkylated product (**19**) due to severe steric hindrance even after extended reaction periods. In fact, the major by-product was a reduction product, ethyl 2,6-dimethylcyclohex-2-enecarboxylate. The relative stereochemistry of the butyl group in **19** has tentatively been assigned as shown, based on the expected approach of the electrophile from the less hindered side.

Entry 3 shows regioselective α-monoalkylation of the substrate (**4**) with 9 molar equiv. of 1,3-dibromopropane. We were unable to detect any of the bis-alkylated product(s), although we can not conclusively rule out its presence. The reduction–alkylation with organocuprate–alkyl halides presumably proceeds *via* "tight" and "loose" intermediates (**20** and **21**) as shown in Chart 2.

We have recently embarked upon the development of new methods using organocopper and organocopper–Lewis acid reagents[3,10,13-15] for the synthesis of key intermediates of toxic alkaloids, and chose to demonstrate the viability of the methods by synthesizing alkaloids of Neotropical poison-dart frogs.[3a,4]

The utility of the present regioselective reduction–alkylation is demonstrated by its application to the synthesis of the constituents of vetiver oil. Thus, reduction–alkylation of **18** with lithium dibutylcuprate followed by 3-(tetrahydropyran-2-yloxy)propyl bromide gave the ester (**22**) as the sole isolable product in 25% yield. All attempts to enhance the yield of **22** were unsuccessful. The ester (**22**) was converted into the diester (**23**) (68% overall yield) by successive treatment with 5% hydrochloric acid in ethanol, oxalyl chloride–dimethyl sul-



Tf = trifluoromethanesulfonyl

Chart 3

foxide–triethylamine,[16] silver oxide in methanol, and diazomethane.

The acyloin condensation of **23** was carried out using sodium and chlorotrimethylsilane in refluxing toluene[17] to yield the rather labile bis(trimethylsilyl) ether (**24**) in 91% yield. Compound **24** was converted into the spiro-ketone (**25**)[18-20] by a standard procedure.[20] The synthesized ketone (**25**), one of the constituents of vetiver oil,[18] was characterized by comparison of its spectra with those of the authentic compound.[19] The ketone (**25**) was transformed into (±)-α-vetispirene (**27**) in a straightforward way. Thus, treatment of **25** with trifluoromethanesulfonic anhydridepyridine followed by silica gel column chromatography yielded the triflate (**26**) in 46% yield. Cross-coupling[21] of **26** with the reagent prepared from cuprous iodide and isopropenylmagnesium bromide gave **27**, whose spectral data were identical with those of an authentic sample.[19c,20,22,23]

Differences in the Reaction of Electron-Deficient Olefins with Organocopper(I)–Lewis Acid Reagents and Evidence for a Dianion Equivalent

Organocopper(I)–Lewis acid reagents have been acclaimed as one of the most useful of known organocopper reagents since the advent of organocopper(I)–boron trifluoride complex.[24] Considerable current interest is centered around the development of an effective method of using Lewis acid-mediated organocopper(I) reagents because of several drawbacks of the ordinary organocopper reagents.[3,4,9,10,13-15,25]

Although it has been reported by Petersen *et al.* that reactions of electron-deficient olefins with some organometallic reagents yield a complex mixture of products,[26] the reactions of Lewis acid-mediated organocopper(I) reagents with electron-deficient olefins remain to be explored systematically. In the present investigation, the following points have been examined using Lewis acid-mediated organocopper(I) reagents. 1) Does conjugate addition to the double bond or reduction of the double bond take place? 2) What is the orientation of addition to unsymmetrically substituted olefins? 3) Is there any difference in the above respects between geometrical isomers? 4) Does trapping of the presumed dianion by electrophiles take place? Typical results are shown in Chart 4 and Table II.

The reaction of diethyl fumarate (**28**) in ether with the reagent $Bu_2CuLi \cdot AlCl_3$ gave a conjugate adduct, diethyl butylsuccinate (**32**) (94% yield), and a trace amount of a reduction product, diethyl succinate (**33**) (entry 1). This selectivity is highly dependent upon the reagent used since, under the same reaction conditions, a complex mixture of products was obtained by reaction with $Bu_2CuLi \cdot BF_3$ or $Me_2CuLi \cdot AlCl_3$. In contrast, diethyl maleate (**29**) gave the reduction product (**33**) (92% yield) and a small amount of the conjugate adduct (**32**) (entry 2). Explanation of the different reactivities in the above reactions is rather difficult, since little structural information on the reagent is available. Nonetheless, it is of special interest to note that the direction of the reaction path is dependent upon the geometry of the substrate. Addition of a Lewis acid such as aluminum chloride to the Gilman reagent is essential for the completion of the above reaction (entries 4 and 5). Diethyl ether is the solvent of choice since reactions in a mixture of tetrahydrofuran and diethyl ether or in tetrahydrofuran were too sluggish to be practicable (entries 3 and 6).[27]

In the case of triethoxycarbonylethylene (**30**), the conjugate adduct (**34**) was isolated as a sole product in high yield by treatment with $Me_2CuLi \cdot AlCl_3$ or $Me_2CuLi \cdot BF_3$ (entries 7 and 8). Similarly, reaction of **30** with $Bu_2CuLi \cdot AlCl_3$ or $Bu_2CuLi \cdot BF_3$ gave the conjugate adduct (**35**) (78—80% yield) accompanied by a small amount of the reduction product (**36**) (7—8% yield) (entries 9 and 10). These results indicate that the unsymmetrical substrate (**30**) was regiospecifically attacked by the reagents at the less substituted position. In these reactions, an $R_2CuLi \cdot MX_3$-type organometallic is the reagent of choice, since reaction of **30** with $BuCu \cdot AlCl_3$ led to a complex mixture of products. The exclusive or predominant formation of the conjugate adducts (**34** and **35**) should be contrasted with the complete reduction of

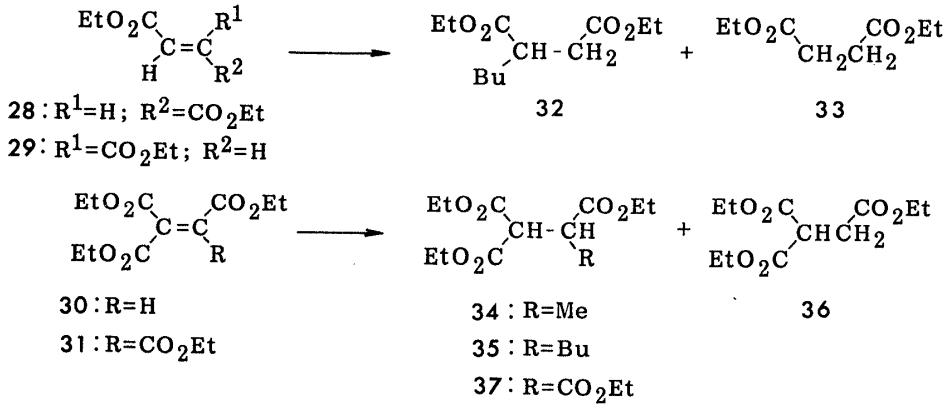


Chart 4

TABLE II. Yields of Products in the Reaction of Electron Deficient Olefins with Some Organocopper(I) Reagents[a]

Entry	Substrate	Reagent	Reaction condition	1,4-Adduct	Reduction product	Recovered
1	**28**	$Bu_2CuLi \cdot AlCl_3$ (4 eq)	−65——−40 °C, 1 h	**32** (94%)	**33** (Trace)	—
2	**29**	$Bu_2CuLi \cdot AlCl_3$ (4 eq)	−65——−40 °C, 1 h	**32** (1.8%)	**33** (92%)	—
3	**29**	$Bu_2CuLi \cdot AlCl_3$ (4 eq)	−65——−40 °C, 1 h	**32** (9%)	**33** (66%)	**29** (25%)
4	**28**	Bu_2CuLi (4 eq)	−65——−40 °C, 1 h	**32** (23%)	**33** (11%)	**28** (65%)
5	**29**	Bu_2CuLi (4 eq)	−65——−40 °C, 1 h	**32** (1%)	**33** (57%)	**29** (37%)
6	**29**	Bu_2CuLi (8 eq)	−70——−40 °C, 2 h	**32** (<5%)	**33** (<5%)	**29** (90%)
7	**30**	$Me_2CuLi \cdot AlCl_3$ (4 eq)	−70——−40 °C, 1 h	**34** (97%)	—	—
8	**30**	$Me_2CuLi \cdot BF_3$ (4 eq)	−70——−40 °C, 1 h	**34** (97%)	—	—
9	**30**	$Bu_2CuLi \cdot AlCl_3$ (4 eq)	−70——−40 °C, 1 h	**35** (80%)	**36** (7%)	—
10	**30**	$Bu_2CuLi \cdot BF_3$ (4 eq)	−65——−40 °C, 1 h	**35** (78%)	**36** (8%)	—
11	**31**	$BuCu \cdot AlCl_3$ (4 eq)	−65——−30 °C, 1 h	—	**37** (91%)	—
12	**31**	$BuCu \cdot BF_3$ (4 eq)	−65——−30 °C, 1 h	—	**37** (95%)	—
13	**31**	$MeCu \cdot AlCl_3$ (4 eq)	−65——−15 °C, 1.5 h	—	**37** (94%)	—
14	**31**	$MeCu \cdot BF_3$ (4 eq)	−65— 0 °C, 20 min	—	**37** (94%)	—
15	**31**	$Bu_2CuLi \cdot AlCl_3$ (4 eq)	−65——−40 °C, 1 h	—	**37** (100%)	—
16	**31**	$Bu_2CuLi \cdot BF_3$ (4 eq)	−65——−40 °C, 1 h	—	**37** (99%)	—

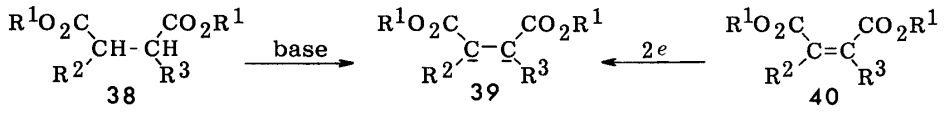
a) Except for the entries 3 and 6, all reactions were carried out in dry ether. Entry 3: solvent, ether–THF (3 : 2); entry 6: solvent, THF.

tetraethoxycarbonylethylene (**31**) described below.

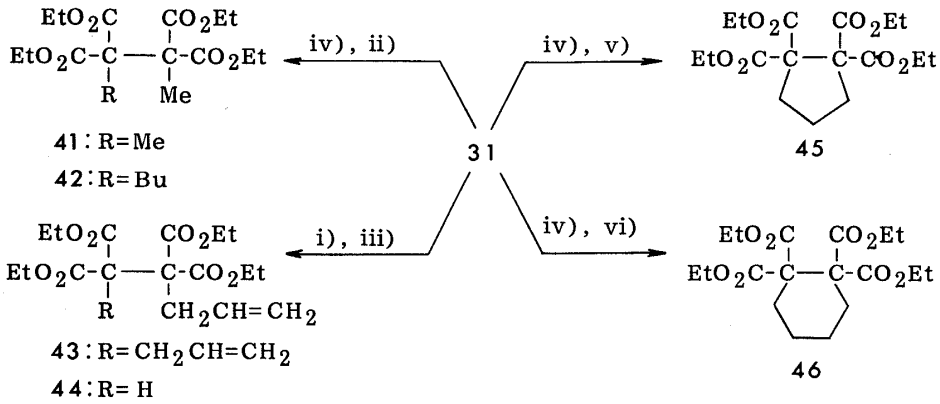
It has been reported that the most electron-deficient olefin, **31**, was reduced with the Gilman reagent to give the reduction product (**37**).[28] Likewise, the olefin **31** was reduced by treatment with the Lewis acid-mediated organocopper reagents to afford the product (**37**) (entries 11—16).

Some efforts have been directed toward the preparation and reaction of dianions (**39**) having electron-withdrawing groups; these dianions are prepared exclusively from saturated diesters or their equivalents (**38**) by treatment with strong bases.[29,30]

In the present experiment (entries 2 and 11—16), the reduction intermediate(s) from the unsaturated substrates (**29** and **31**) must be generated by two-electron transfers (reduction)[28] from the organometallics. Because dianion species of type **39** formed by electron transfers from **40** have no precedent in terms of chemical evidence, an attempt to trap the reduction intermediate was made. Unfortunately, the presumed dianion species formed by reaction with organocopper(I)–Lewis acid reagents are limited by their low solubility for trapping with



R^2, R^3 = ester, ketone, alkyl, or ring residue



reagents: i) Me_2CuLi; ii) MeI; iii) $CH_2=CHCH_2Br$; iv) Bu_2CuLi; v) $Br(CH_2)_3Br$; vi) $Br(CH_2)_4Br$

Chart 5

electrophiles.[31] Therefore the presumed dianion intermediate, derived from **31** by treatment with the Gilman reagent, was treated with some electrophiles to yield the dialkylated or annulated products [**41** (84% yield), **43** (26% yield), **45** (71% yield), and **46** (40% yield)]. Some practical observations merit description. Reduction of **31** with $BuCu \cdot (Bu_3P)_2$[32] followed by trapping with 1,3-dibromopropane in the presence of hexamethylphosphoric triamide gave a poor result (40% yield). Somewhat surprisingly, reaction of **31** with lithium dibutylcuprate followed by methyl iodide gave the unexpected derivative (**42**, 11% yield) as a minor by-product for reasons that were not clear. Trapping of the presumed dianion from **31** with allyl bromide gave the diallyl product (**43**) accompanied by the monoallyl derivative (**44**, 23% yield).

The above trapping with electrophiles provided evidence that double bond reduction involves an intermediate dianion and the dialkylated products (**41** and **43**) and the annulated products (**45** and **46**) indicate that copper hydride[33] was not involved in the reduction.

The possibility that this reduction–alkylation could serve as a method for synthetic chemistry is under investigation.

Experimental

General Methods——All reactions were performed under an atmosphere of argon. Tetrahydrofuran (THF) was freshly distilled from lithium aluminum hydride. All melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. All infrared (IR) spectra were recorded on a Shimadzu IR-400 spectrometer. Nominal and accurate mass spectra (MS) were recorded on a JEOL JMS-01SG-2 mass spectrometer equipped with a direct inlet system. All proton magnetic resonance spectra (^{1}H-NMR) were recorded on one of the following spectrometers: Varian A-60, JEOL PMX-60, and JEOL FX-200. Chemical shifts are quoted in parts per million down-field from internal tetramethylsilane (s=singlet, d=doublet, dd=double doublet, t=triplet, q=quartet, m=multiplet). Elemental analyses were carried out by the Microanalytical Center of Kyoto University. For column chromatographies, silica gel (Wakogel C-200) or alumina (Merck, aluminum oxide 90, activity II-III) was employed.

Reduction–Alkylation of γ-Acetoxy-α,β-enoates with Lithium Dibutylcuprate–Alkyl Halides——The following procedure is representative. A solution of the γ-acetoxy-α,β-enoate (**4**) (0.5 mmol) in dry THF (2 ml) was added dropwise to a solution of Bu_2CuLi (1.5 mmol) in a mixture of dry THF (3 ml) and hexamethylphosphoramid (HMPA) (1.5 mmol) at −70 °C with stirring, and the mixture was stirred for 20 min. Butyl bromide (3 mmol) was

added to the stirred mixture at −70 °C, and the temperature was allowed to rise to room temperature, then the mixture was stirred for 20 h. Saturated NH_4Cl solution (2 ml) and 28% NH_4OH (3 ml) were added to the above mixture at −20 °C and the whole was stirred at ambient temperature for 30 min. The mixture was extracted with ether and the extract was washed successively with 5% $NaHCO_3$, 5% HCl, and water, dried over $MgSO_4$, and concentrated to leave a mixture of the α- and γ-butylated products. The mixture was separated by silica gel column chromatography with hexane–AcOEt (9:1) or by preparative gas chromatography (GC) (1.5% FFAP on Chromosorb W, 2 m, column temp., 130 °C) to yield the pure α-butyl (**7**, R = Bu) and γ-butyl derivatives (**8**, R = Bu).

7 (R = Bu): A colorless oil (92% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1713 (CO), 1646 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, tripletoid m, CH_3), 1.25 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 4.13 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.67—5.80 (2H, m, olefinic protons).

8 (R = Bu): A colorless oil (<0.8% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1698 (CO), 1645 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, tripletoid m, CH_3), 1.29 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 4.18 (2H, q, J = 7.1 Hz, $CO_2C\underline{H}_2CH_3$), 6.87 (1H, m, olefinic proton). Both **7** (R = Bu) and **8** (R = Bu) were identified by IR ($CHCl_3$), ^{1}H-NMR ($CDCl_3$), GC (1.5% FFAP on Chromosorb W, 2 m, 130 °C), and thin-layer chromatography (TLC) (silica gel) comparisons with authentic samples.[10]

Other alkylated products **7** [R = Me, $(CH_2)_3Br$, $(CH_2)_3OTHP$, and $CH_2CH{=}CH_2$], **10** (R = Bu and Me), **13** (R = Bu), **15** (R = Bu and Et), **17** (R = Bu), **19**, and **11** (γ-alkylated product) were similarly synthesized.

7 (R = Me): A colorless oil (94% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1655 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 1.250 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 1.253 (3H, s, CH_3), 4.13, 4.14 (each 1H, q, J = 7.1 Hz, $CO_2CH(\underline{H})CH_3 \times 2$), 5.6—5.8 (2H, m, olefinic protons). Accurate MS m/z Calcd for $C_{10}H_{16}O_2$: 168.1150. Found: 168.1157.

7 [R = $(CH_2)_3Br$]: A colorless oil (75% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1652 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 4.14 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.60—5.90 (2H, m, olefinic protons). Nominal MS m/z: 274 (M^+), 200 (base peak). Accurate MS m/z Calcd for $C_{12}H_{19}{}^{78}BrO_2$: 274.0568. Found: 274.0563.

7 [R = $(CH_2)_3OTHP$]: A colorless oil (52% yield). bp 140 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1718. ^{1}H-NMR ($CDCl_3$) δ: 1.25 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 4.13 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.56 (1H, m, ), 5.68—5.85 (2H, m, olefinic protons). Nominal MS m/z: 296 (M^+), 85 (base peak). Accurate MS m/z Calcd for $C_{17}H_{28}O_4$: 296.1988. Found: 296.1989.

7 (R = $CH_2CH{=}CH_2$): A colorless oil (91% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1645 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 1.25 (3H, t, J = 7.1 Hz, CH_3), 4.126, 4.130 (each 1H, q, J = 7.1 Hz, $CO_2CH(\underline{H})CH_3 \times 2$), 4.9—5.9 (5H, m, olefinic protons). Accurate MS m/z Calcd for $C_{12}H_{18}O_2$: 194.1306. Found: 194.1315.

10 (R = Bu): A colorless oil (94% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715 (CO), 1650 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, tripletoid m, CH_3), 1.26 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 5.64 (1H, q, of d, J = 1.0, 11.0 Hz, C-2-H), 5.82 (1H, dt, J = 11.0, 5.0 Hz, C-3-H). Accurate MS m/z Calcd for $C_{14}H_{24}O_2$: 224.1776. Found: 224.1782.

11 (R = Bu): A colorless oil (<0.8% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1694 (CO), 1644 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, tripletoid m, CH_3), 1.29 (3H, t, J = 7.0 Hz, $CO_2CH_2C\underline{H}_3$), 4.17 (2H, q, J = 7.0 Hz, $CO_2C\underline{H}_2CH_3$), 6.91 (1H, m, olefinic proton). This compound was identified by IR ($CHCl_3$), ^{1}H-NMR ($CDCl_3$), GC (1.5% FFAP on Chromosorb W, 2 m, 130 °C), and TLC (silica gel) comparisons with an authentic sample.[10]

10 (R = Me): A colorless oil (89% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, t, J = 7.0 Hz, $CO_2CH_2C\underline{H}_3$), 1.31 (3H, s, CH_3), 4.15 (2H, q, J = 7.0 Hz, $CO_2C\underline{H}_2CH_3$), 5.57 (1H, q of d, J = 1.0, 11.0 Hz, C-2-H), 5.78 (1H, dt, J = 11.0, 5.5 Hz, C-3-H). Nominal MS m/z: 182 (M^+), 109 (base peak). *Anal.* Calcd for $C_{11}H_{18}O_2$: C, 72.53; H, 9.89. Found: C, 72.94; H, 10.33.

13 (R = Bu): A colorless oil (91% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J = 7.3 Hz, CH_3), 1.24 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 2.86 (1H, t, J = 8 Hz, $C_2H_5O_2C{-}C\underline{H}<$), 4.12 (2H, q, $CO_2C\underline{H}_2CH_3$), 5.57 (1H, m, olefinic proton). This compound was identified by IR ($CHCl_3$), ^{1}H-NMR ($CDCl_3$), and TLC (silica gel) comparisons with an authentic sample.[10]

15 (R = Bu): A colorless oil (66% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J = 6.9 Hz, CH_3), 1.24 (3H, t, J = 7.1 Hz, $CO_2CH_2CH_3$), 2.89 (1H, t, J = 7 Hz, $C_2H_5O_2C{-}C\underline{H}<$), 4.12 (2H, q, J = 7.1 Hz, $CO_2C\underline{H}_2CH_3$), 5.71 (1H, t, J = 6.6 Hz, olefinic proton). This compound was identified by IR ($CHCl_3$), ^{1}H-NMR ($CDCl_3$), and GC (1.5% FFAP on Chromosorb W, 2 m, 140 °C) comparisons with an authentic sample.[10]

15 (R = Et): A colorless oil (50% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (3H, t, J = 7.3 Hz, CH_3), 1.24 (3H, t, J = 7.1 Hz, $CO_2CH_2C\underline{H}_3$), 2.81 (1H, t, J = 7.6 Hz, $C_2H_5O_2{-}C\underline{H}<$), 4.12 (2H, q, J = 7.1 Hz, $CO_2C\underline{H}_2CH_3$), 5.71 (1H, t, J = 6.6 Hz, olefinic proton). Nominal MS m/z: 210 (M^+), 181 (base peak). Accurate MS m/z Calcd for $C_{13}H_{22}O_2$: 210.1619. Found: 210.1613.

17 (R = Bu): A colorless oil (87% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1721. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J = 7.1 Hz, CH_3), 1.24 (3H, t, J = 7.3 Hz, $CO_2CH_2C\underline{H}_3$), 2.91 (1H, dd, J = 6.5, 8.1 Hz, $C_2H_5O_2C{-}C\underline{H}<$), 4.11 (2H, q, J = 7.3 Hz, $CO_2C\underline{H}_2CH_3$), 5.54 (1H, t, J = 8.1 Hz, olefinic proton). Nominal MS m/z: 252 (M^+), 195 (base peak). Accurate MS m/z Calcd for $C_{16}H_{28}O_2$: 252.2089. Found: 252.2091.

19: A colorless oil (30% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, d, J = 6.4 Hz, $>CHC\underline{H}_3$),

0.91 (3H, t, $J=6.8$ Hz, CH_3), 1.53 (3H, m, vinylic CH_3), 4.14 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.67 (1H, m, olefinic proton). Nominal MS *m/z*: 238 (M^+). Accurate MS *m/z* Calcd for $C_{15}H_{26}O_2$: 238.1933. Found: 238.1934.

Reduction–Alkylation of 18 with Lithium Dibutylcuprate–3-(Tetrahydropyran-2-yloxy)propyl Bromide——A solution of the enoate (**18**) (120 mg, 0.5 mmol) in dry THF (3 ml) was added dropwise to a stirred solution of Bu_2CuLi (1.5 mmol) in 3.53 ml of THF–HMPA (6 : 1) at −70 °C, and the mixture was stirred for 30 min. The temperature was allowed to rise to −40 °C, and then cooled to −70 °C. 3-(Tetrahydropyran-2-yloxy)propyl bromide (934 mg, 4.2 mmol) was added to the above mixture with stirring, and the temperature was allowed to rise to ambient temperature, then the mixture was stirred for 16 h. Saturated NH_4Cl solution (2 ml) and 28% NH_4OH (2 ml) were added to the above solution at −40 °C under vigorous stirring. The mixture was extracted with ether and the extract was washed successively with 5% $NaHCO_3$, 5% HCl, and water, dried over $MgSO_4$, and concentrated to leave a colorless oil. The residual oil was chromatographed on a silica gel column with hexane–EtOAc (4 : 1) to give **22** (40 mg, 25% yield) as a colorless oil. bp 165 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, d, $J=6.4$ Hz, $C\underline{H}_3CH$<), 1.25 (3H, t, $J=7.1$ Hz, $CO_2CH_2C\underline{H}_3$), 1.54 (3H, m, vinylic CH_3), 4.14 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.58 (1H, m, ), 5.70 (1H, m, olefinic proton). Accurate MS *m/z* Calcd for $C_{19}H_{32}O_4$: 324.2300. Found: 324.2293.

Preparation of the Diester (23)——Compound **23** was obtained from **22** by the following successive reactions.

a) A solution of the THP–ether (**22**) (3 g, 9.3 mmol) in a mixture of EtOH (30 ml) and 5% HCl (10 ml) was heated for 2 h under reflux. The solvent was evaporated off under reduced pressure to leave an oily residue, which was extracted with $CHCl_3$. The extract was washed with brine, dried over $MgSO_4$, and concentrated to leave an oily residue which was purified by silica gel column chromatography with hexane–EtOAc (1 : 1) to yield a primary alcohol (2.11 g, 95% yield) as a colorless oil. bp 133 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1713 (CO). ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, d, $J=6.4$ Hz, >$CHC\underline{H}_3$), 1.26 (3H, t, $J=7.2$ Hz, $CO_2CH_2C\underline{H}_3$), 1.53 (3H, m, vinylic CH_3), 3.62 (2H, t, $J=6.7$ Hz, $C\underline{H}_2OH$), 4.14 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.71 (1H, m, olefinic proton). *Anal.* Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 70.14; H, 10.33.

b) A solution of DMSO (0.36 ml, 5 mmol) in dry CH_2Cl_2 (1 ml) was added dropwise to a solution of oxalyl chloride (0.21 ml, 2.4 mmol) in CH_2Cl_2 (0.5 ml) with stirring at −65 °C, and the mixture was stirred for 10 min. A solution of the above primary alcohol (120 mg, 0.5 mmol) in CH_2Cl_2 (2 ml) was added to the reagent at −65 °C and the mixture was stirred at −65 °C for 1 h and then at 0 °C for 5 min. Triethylamine (1.38 ml, 10 mmol) was added dropwise to the above mixture at −65 °C, and the temperature was allowed to rise to room temperature. The usual work-up of the reaction mixture led to a colorless oil which was chromatographed on a silica gel column with hexane–EtOAc (1 : 1) to yield an aldehyde (120 mg, quantitative yield) as a colorless oil. bp 118 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1722. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, d, $J=6.4$ Hz, >$CHC\underline{H}_3$), 1.26 (3H, t, $J=7.1$ Hz, $CO_2CH_2C\underline{H}_3$), 1.52 (3H, m, vinylic CH_3), 4.16 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.76 (1H, m, olefinic proton). Nominal MS *m/z*: 238 (M^+).

c) A mixture of the above aldehyde (38 mg, 0.16 mmol), MeOH (5 ml), and freshly prepared excess Ag_2O (*ca.* 200 mg) was stirred at ambient temperature for 30 min. The usual work-up of the reaction mixture led to a colorless oil, which was methylated with ethereal diazomethane followed by column chromatography on a silica gel to yield **23** (31 mg, 72% yield) as a colorless oil. bp 118 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1723. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, d, $J=6.3$ Hz, >$CHC\underline{H}_3$), 1.25 (3H, t, $J=7.1$ Hz, $CO_2CH_2C\underline{H}_3$), 1.54 (3H, m, vinylic CH_3), 3.67 (3H, s, CO_2CH_3), 4.15 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.74 (1H, m, olefinic proton). Accurate MS *m/z* Calcd for $C_{15}H_{24}O_4$: 268.1674. Found: 268.1677.

The Bis(trimethylsilyl) Ether (24)——A solution of **23** (427 mg, 1.6 mmol) in toluene (3 ml) was added dropwise to a refluxing suspension of sodium (221 mg, 9.6 mmol) in a mixture of toluene (5 ml) and chlorotrimethylsilane (1.22 ml, 9.6 mmol), and the mixture was refluxed for 2 h. After cooling, the suspension was filtered and the filtrate was concentrated *in vacuo* to leave **24** (485 mg, 91% yield) as a rather labile colorless oil. The product was immediately used for the next step.

The Spiro-ketone (25)——The spiro-ketone (**25**) was obtained from **24** by the following successive reactions.

a) (1*R**,5*R**,10*R**)-6,10-Dimethyl-1-hydroxyspiro[4.5]deca-6-en-2-one: A solution of **24** (560 mg, 1.6 mmol) in THF (6 ml) was treated with 5% HCl (15 drops) at ambient temperature and the mixture was stirred for 15 min. The solvent was evaporated off under reduced pressure, and the residual oil was extracted with $CHCl_3$. The extract was washed with water, dried over $MgSO_4$, and concentrated to leave a semisolid. Recrystallization from hexane–ether (3 : 1) gave (1*R**,5*R**,10*R**)-6,10-dimethyl-1-hydroxyspiro[4.5]deca-6-en-2-one (53 mg, 18% yield) as colorless crystals. mp 113—116 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH), 1742 (CO). ^{1}H-NMR ($CDCl_3$) δ: 1.12 (3H, d, $J=6.6$ Hz, >$CHC\underline{H}_3$), 1.52 (3H, m, vinylic CH_3), 4.01 (1H, s, OH), 5.55 (1H, m, olefinic proton). *Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.19; H, 9.57.

b) (5*R**,10*R**)-6,10-Dimethylspiro[4.5]deca-6-en-2-one (**25**): Methanesulfonyl chloride (1 ml) was added dropwise to a stirred solution of the above spiro compound (200 mg, 1.0 mmol) in 5 ml of $CHCl_3$–pyridine (3 : 2) at −40 °C. The temperature was allowed to rise to 0 °C and the mixture was stirred for 3 h. The usual work-up of the

reaction mixture led to a crystalline mass. Recrystallization from ether–hexane (5 : 1) gave (1*R**,5*R**,10*R**)-6,10-dimethyl-1-methanesulfonyloxyspiro[4.5]deca-6-en-2-one (280 mg, 99% yield) as colorless crystals, mp 123—125 °C. This product was used for the next step. Zinc dust (3 g) and NH_4Cl (1 g) were added portionwise to a solution of the above mesylate in a mixture of THF (1 ml) and MeOH (9 ml) with stirring. The mixture was stirred at ambient temperature for 1.5 h, and then at 55 °C for 6.5 h. The inorganic precipitate was filtered off and the filtrate was concentrated *in vacuo* to leave an oily residue which was chromatographed on a silica gel with hexane–EtOAc (4 : 1) to yield **25** (92 mg, 52% yield) as a colorless oil. bp 130 °C (5 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, d, J=7.0 Hz, >CHC$\underline{H}_3$), 1.65 (3H, m, vinylic CH_3), 5.41 (1H, m, olefinic proton). Accurate MS *m/z* Calcd for $C_{12}H_{18}O$: 178.1358. Found: 178.1368.

(5*R,10*R**)-6,10-Dimethyl-2-trifluoromethanesulfonyloxyspiro[4.5]deca-1,6-diene (26)**——Trifluoromethanesulfonic anhydride (0.5 ml) was added dropwise to a solution **25** (132 mg, 0.74 mmol) in a mixture of CH_2Cl_2 (3 ml) and pyridine (0.4 ml) at −70 °C with stirring. The temperature was allowed to rise to ambient temperature, and the mixture was stirred for 76 h. Saturated NH_4Cl solution (2 ml) was added with stirring to the above mixture at −30 °C. The mixture was extracted with ether and the extract was washed successively with 5% HCl, 5% $NaHCO_3$, and water, dried over $MgSO_4$, and concentrated to leave an oily residue, which was purified by silica gel column chromatography with hexane to give **26** (105 mg, 46% yield) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1665, 1416, 1138, 909. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, d, J=6.5 Hz, >CHC$\underline{H}_3$), 1.61 (3H, m, vinylic CH_3), 5.42 (1H, m, C-7-H), 5.44 (1H, t, J=1.8 Hz, C-1-H). Nominal MS *m/z*: 310 (M^+).

(±)-α-Vetispirene (27)——Isopropenylmagnesium bromide (0.4 mmol) in THF (2 ml) was added dropwise to a suspension of CuI (38 mg, 0.2 mmol) in THF (1 ml) with stirring at −70 °C, and the temperature was allowed to rise gradually to −40 °C. Then a solution of **26** (16 mg, 0.05 mmol) in 1 ml of THF was added with stirring and the whole was stirred at −20 to −15 °C for 2.5 h. The usual work-up of the reaction mixture led to an oily product which was chromatographed on a silica gel column with hexane to yield **27** (2 mg, 21% yield) as a colorless oil. The synthesized compound (**27**) was identified by ^{1}H-NMR ($CDCl_3$), GC, and TLC comparisons with an authentic sample.[20] ^{1}H-NMR ($CDCl_3$), δ: 0.87 (3H, d, J=6.0 Hz, >CHC$\underline{H}_3$), 1.93 (3H, m, vinylic CH_3), 4.90 (2H, m, >C=C$\underline{H}_2$), 5.38 (1H, m, C-7-H), 5.50 (1H, m, C-1-H). Accurate MS *m/z* Calcd for $C_{15}H_{22}$: 202.1721. Found: 202.1704.

General Procedure for the Reaction of Electron-Deficient Olefins (28, 29, 30, and 31) with Lewis Acid-Mediated Organocopper(I) Reagents——The following procedure is representative for all reactions. Reaction of the diethyl fumarate (**28**) with $Bu_2CuLi \cdot AlCl_3$: A solution of aluminum chloride (266 mg, 2 mmol) in ether (4 ml) was added dropwise to a solution of Bu_2CuLi (2 mmol) in ether (4 ml) at −65 °C with stirring and the temperature was allowed to rise to −40 °C, and then reduced to −65 °C. A solution of **28** (86 mg, 0.5 mmol) in ether (4 ml) was added dropwise to the above reagent at −65 °C with stirring and the temperature was allowed to rise to −40 °C. Stirring was continued for 1 h at −40 °C. Saturated NH_4Cl solution (2 ml) was added to the above mixture and the whole was extracted with ether. The extract was washed successively with 5% HCl, 5% $NaHCO_3$, and water, dried over $MgSO_4$, and concentrated to leave a colorless oil. The oily mixture was separated by silica gel column chromatography with hexane–EtOAc (2 : 1) or preparative gas chromatography (1.5% FFAP on Chromosorb W, 2 m, column temp., 120 °C) to give the pure conjugate adduct (**32**) and the reduction product (**33**).

32: A colorless oil (108 mg, 94% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1724. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, tripletoid m, CH_3), 1.25, 1.26 (each 3H, t, J=7.1 Hz, $CO_2CH_2C\underline{H}_3 \times 2$), 1.45—1.75 (6H, m, $CH_2 \times 3$), 2.41 (1H, dd, J=16.0, 4.6 Hz, Bu–C$\underline{H}$–CO_2Et), 4.13, 4.14 (each 2H, q, J=7.1 Hz, $CO_2C\underline{H}_2CH_3 \times 2$). Nominal MS *m/z*: 230 (M^+). Accurate MS *m/z* Calcd for $C_{12}H_{22}O_4$: 230.1517. Found: 230.1498.

33: A colorless oil (<0.8% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (6H, t, J=7.1 Hz, $CH_3 \times 2$), 2.62 (4H, s, CH_2CH_2), 4.15 (4H, q, J=7.1 Hz, $CO_2C\underline{H}_2CH_3 \times 2$). *Anal.* Calcd for $C_8H_{14}O_4$: C, 55.16: H, 8.10. Found: C, 55.19: H, 8.25.

Spectral and physical data for other reaction products from the electron-deficient olefins listed in the Table II are given below.

34: A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, d, J=7.1 Hz, >CHC$\underline{H}_3$), 1.25, 1.26, 1.28 (each 3H, t, J=7.2 Hz, $CO_2CH_2C\underline{H}_3 \times 3$), 3.16 (1H, q of d, J=7.1, 9.5 Hz, $CH_3C\underline{H}$<), 3.70 [1H, d, J=9.5 Hz, $(C_2H_5O_2C)$=C$\underline{H}$–], 4.20 (6H, m, $CO_2C\underline{H}_2CH_3 \times 3$). Accurate MS *m/z* Calcd for $C_{12}H_{20}O_6$: 260.1258. Found: 260.1265.

35: A colorless oil. bp 145 °C (4 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728. ^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, tripletoid m, CH_3), 1.24, 1.27, 1.28 (each 3H, t, J=7.1 Hz, $CO_2CH_2C\underline{H}_3 \times 3$), 3.10 (1H, t of d, J=6.3, 10.5 Hz, Bu–C$\underline{H}$<), 3.74 [1H, d, J=10.5 Hz, (EtO_2C)=C$\underline{H}$–], 4.20 (6H, m, $CO_2C\underline{H}_2CH_3 \times 3$). Nominal MS *m/z*: 302 (M^+), 160 (base peak). Accurate MS *m/z* Calcd for $C_{15}H_{26}O_6$: 302.1728. Found: 302.1745.

36: A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1731. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, t, J=7.3 Hz, $CO_2CH_2C\underline{H}_3$), 1.28 (6H, t, J=7.1 Hz, $CO_2CH_2C\underline{H}_3 \times 2$), 2.92 (2H, d, J=7.3 Hz, $C\underline{H}_2CO_2C_2H_5$), 3.83 [1H, t, J=7.3 Hz, $(C_2H_5O_2C)_2$=C$\underline{H}$–], 4.20 (6H, m, $CO_2C\underline{H}_2CH_3 \times 3$). Nominal MS *m/z*: 246 (M^+), 173 (base peak). Accurate MS *m/z* Calcd for $C_{11}H_{18}O_6$: 246.1102. Found: 246.1124.

37: Colorless prisms [recrystallized from $CHCl_3$–ether (1 : 10)]. mp 74—75 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1734. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (12H, t, J=7.1 Hz, $CO_2CH_2C\underline{H}_3 \times 4$), 4.13 [2H, s, $C\underline{H}(CO_2C_2H_5)_2 \times 2$], 4.218, 4.223 (each 4H, q,

$J=7.1$ Hz, $CO_2CH_2CH_3 \times 4$). *Anal.* Calcd for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97. Found; C, 52.82; H, 7.12.

Reaction of the Presumed Dianion from the Olefin (31) with Electrophiles——The following procedure for the trapping reaction is typical. A solution of **31** (158 mg, 0.5 mmol) in THF (3 ml) was added dropwise to a stirred solution of Bu_2CuLi (2 mmol) in 7 ml of THF–HMPA (6 : 1) at -70 °C, and the mixture was stirred for 30 min. 1,3-Dibromopropane (0.5 ml, 5 mmol) was added to the mixture at -70 °C with stirring and the temperature was allowed to rise to ambient temperature, then the mixture was stirred for 18 h. Saturated NH_4Cl solution (2 ml) and 28% NH_4OH (2 ml) were added to the above mixture at -40 °C. The usual work-up of the reaction mixture led to a colorless oil, which was chromatographed on a silica gel column with hexane–$CHCl_3$ (9 : 1) to yield the annulated product (**45**) (122 mg, 71% yield) as a colorless oil. bp 170 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1724. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (12H, t, $J=7.1$ Hz, $CO_2CH_2CH_3 \times 4$), 1.93 (2H, m, CH_2), 2.54 (4H, t, $J=7.7$ Hz, $CH_2 \times 2$), 4.17 (8H, q, $J=7.1$ Hz, $CO_2CH_2CH_3 \times 4$). Nominal MS *m/z*: 358 (M^+), 285 (base peak). Accurate MS *m/z* Calcd for $C_{17}H_{26}O_8$: 358.1626. Found: 358.1636.

Spectral and physical data for other trapping reaction products are given below.

41: A colorless oil (84% yield). bp 145 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (12H, t, $J=7.1$ Hz, $CO_2CH_2CH_3 \times 4$), 1.63 (6H, s, $CH_3 \times 2$), 4.12, 4.19 (each 4H, q, $J=7.1$ Hz, $CO_2CH_2CH_3 \times 4$). Nominal MS *m/z*: 346 (M^+).

42: A colorless oil (11% yield). bp 145 °C (1 Torr) (Büchi Kugelrohrofen apparatus). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1727. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, $J=7.1$ Hz, CH_3), 1.26, 1.27 (each 6H, t, $J=7.2$ Hz, $CO_2CH_2CH_3 \times 4$), 1.65 (3H, s, CH_3), 4.20 (8H, m, $CO_2CH_2CH_3 \times 4$). Nominal MS *m/z*: 388 (M^+).

43: A colorless oil (26% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1723 (CO), 1644 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 1.260, 1.262 (each 6H, t, $J=7.2$ Hz, $CO_2CH_2CH_3 \times 4$), 2.87 (4H, doubletoid m, $CH_2CH=CH_2 \times 2$), 4.19 (8H, m, $CO_2CH_2CH_3 \times 4$), 5.02—5.15 (4H, m, $CH=CH_2 \times 2$), 5.95 (2H, m, $CH=CH_2 \times 2$). Nominal MS *m/z*: 398 (M^+), 199 (base peak). Accurate MS *m/z* Calcd for $C_{20}H_{30}O_8$: 398.1938. Found: 398.1937.

44: A colorless oil (23% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1731. ^{1}H-NMR ($CDCl_3$) δ: 1.272, 1.276 (each 6H, t, $J=7.2$ Hz, $CO_2CH_2CH_3 \times 4$), 2.72 (4H, doubletoid m, $CH_2CH=CH_2 \times 2$), 4.05 [1H, s, $(C_2H_5O_2C)=CH-$], 4.22 (8H, m, $CO_2CH_2CH_3 \times 4$), 5.06—5.15 (4H, m, $CH_2CH=CH_2 \times 2$), 5.95 (2H, m, $CH=CH_2 \times 2$). Nominal MS *m/z*: 358 (M^+), 199 (base peak). Accurate MS *m/z* Calcd for $C_{17}H_{26}O_8$; 358.1627. Found: 358.1600.

46: A colorless oil (40% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1727. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (12H, t, $J=7.1$ Hz, $CH_3 \times 4$), 1.61 (4H, m, $CH_2 \times 2$), 2.25 (4H, m, $CH_2 \times 2$), 4.19 (8H, q, $J=7.1$ Hz, $CO_2CH_2CH_3 \times 4$). Nominal MS *m/z*: 372 (M^+). Accurate MS *m/z* Calcd for $C_{18}H_{28}O_8$: 372.1784. Found: 372.1800.

References and Notes

1) For recent reports on the alkylation of α,β-unsaturated carbonyl compounds, see: *a*) P. T. Lunsbury, G. E. Bebernitz, S. C. Maynard, and C. J. Spagnuolo, *Tetrahedron Lett.*, **26**, 169 (1985); *b*) W. G. Dauben, G. Shapiro, and L. Luders, *ibid.*, **26**, 1429 (1985); *c*) A. J. Birch and L. F. Kelly, *J. Org. Chem.*, **50**, 712 (1985); *d*) R. H. van der Veen and H. Cerfontain, *ibid.*, **50**, 342 (1985); *e*) M. Majewski, G. B. Mpango, M. T. Thomas, A. Wu, and S. Snieckus, *ibid.*, **46**, 2029 (1981); *f*) P. M. Savu and J. A. Katzenellenbogen, *ibid.*, **46**, 239 (1981).
2) For recent reports on the alkylation of allylic compounds, see: *a*) H. L. Goering and C. C. Tseng, *J. Org. Chem.*, **50**, 1597 (1985); *b*) I. Fleming and A. P. Thomas, *J. Chem. Soc., Chem. Commun.*, **1985**, 411.
3) *a*) T. Ibuka, G.-N. Chu, and F. Yoneda, *J. Chem. Soc., Chem. Commun.*, **1984**, 597; *b*) T. Ibuka, G.-N. Chu, and F. Yoneda, *Tetrahedron Lett.*, **25**, 3247 (1984).
4) *a*) T. Ibuka, H. Minakata, Y. Mitsui, E. Tabushi, T. Taga, and Y. Inubushi, *Chem. Lett.*, **1981**, 1409; *b*) T. Ibuka, Y. Mitsui, K. Hayashi, H. Minakata, and Y. Inubushi, *Tetrahedron Lett.*, **22**, 4425 (1981).
5) *a*) F. Freeman and K. D. Robarge, *Tetrahedron Lett.*, **26**, 1943 (1985); *b*) C. K. H. Tseng and V. E. Marquez, *ibid.*, **26**, 3669 (1985).
6) E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Samuelsson, and S. Hammarström, *J. Am. Chem. Soc.*, **102**, 1436 (1980).
7) L. E. Overman and C. Fukaya, *J. Am. Chem. Soc.*, **102**, 1454 (1980).
8) M. Isobe, Y. Ichikawa, D.-I. Bai, and T. Goto, *Tetrahedron Lett.*, **26**, 5203 (1985).
9) Y. Yamamoto, S. Yamamoto, H. Yatagai, Y. Ishihara, and K. Maruyama, *J. Org. Chem.*, **47**, 119 (1982).
10) T. Ibuka and H. Minakata, *Synth. Commun.*, **10**, 119 (1980).
11) R. Howe, F. J. McQuillin, and R. W. Temple, *J. Chem. Soc.*, **1959**, 363.
12) Recently, alkylation of a presumed copper enolate in the presence of triphenyltin chloride has been reported: M. Suzuki, A. Yanagisawa, and R. Noyori, *J. Am. Chem. Soc.*, **107**, 3348 (1985).
13) T. Ibuka, H. Minakata, Y. Mitsui, K. Kinoshita, and Y. Kawami, *J. Chem. Soc., Chem. Commun.*, **1980**, 1193.
14) T. Ibuka and E. Tabushi, *J. Chem. Soc., Chem. Commun.*, **1982**, 703.
15) T. Ibuka, H. Minakata, Y. Mitsui, K. Kinoshita, Y. Kawami, and N. Kimura, *Tetrahedron Lett.*, **21**, 4073 (1980).
16) K. Omura and D. Swern, *Tetrahedron*, **34**, 1651 (1978).

17) J. J. Bloomfield, D. C. Owsley, and J. M. Nelke, "Organic Reactions," Vol. 23, Academic Press, New York, 1976, pp. 259—404.
18) G. Büchi, *Koryo*, **1978**, 99.
19) *a*) E. Piers and C. K. Lau, *Synth. Commun.*, **1977**, 495; *b*) G. Büchi, D. Derthet, R. Decorzant, A. Grieder, and H. Hauser, *J. Org. Chem.*, **41**, 3208 (1976); *c*) D. Caine, A. A. Boucugnani, and W. R. Pennington, *ibid.*, **41**, 3632 (1976).
20) T. Ibuka, K. Hayashi, H. Minakata, Y. Ito, and Y. Inubushi, *Can. J. Chem.*, **57**, 1579 (1979).
21) J. E. McMurry and W. J. Scott, *Tetrahedron Lett.*, **21**, 4313 (1980).
22) A part of this work has appeared in a preliminary communication. T. Ibuka, T. Aoyagi, and F. Yoneda, *J. Chem. Soc., Chem. Commun.*, **1985**, 1452.
23) For recent reports on syntheses of (±)-α-vetispirene, see: G. Balme, *Tetrahedron Lett.*, **26**, 2309 (1985); L. A. Paquette, T. H. Yan, and G. J. Wells, *J. Org. Chem.*, **49**, 3610 (1984).
24) Y. Yamamoto and K. Maruyama, *J. Am. Chem. Soc.*, **100**, 3240 (1978).
25) For reports on organocopper(I)–BF_3, see: *a*) Ref. 9 and 24; *b*) M. Wada, Y. Sakurai, and K. Akiba, *Tetrahedron Lett.*, **25**, 1079 (1984); *c*) A. B. Smith, III and P. J. Jerris, *J. Am. Chem. Soc.*, **103**, 194 (1981); *d*) R. K. Olsen, W. J. Hennan, and R. B. Wardle, *J. Org. Chem.*, **47**, 4606 (1982); *e*) W. Oppolzer and H. J. Löher, *Helv. Chim. Acta*, **64**, 2808 (1981); *f*) Y. Yamamoto and K. Maruyama, *J. Chem. Soc., Chem. Commun.*, **1984**, 904. For reports on organocopper(I)–$AlCl_3$, see: ref. 3, 4, 11, and 13—15.
26) E. B. Nielsen, J. M.-Petersen, P. M. Jorgensen, and S. Refn, *Acta Chem. Scand.*, **13**, 1943 (1959); V. K. Andersen and J. M.-Petersen, *ibid.*, **16**, 947 (1962); J. M.-Petersen, *Bull. Soc. Chim. Fr.*, **1966**, 471.
27) THF is well-known to decrease the rate of organocopper reactions with enones relative to diethyl ether, presumably as the result of competitive complexation. *a*) B. H. Lipschutz, R. S. Wilhelm, and J. A. Kozlowski, *J. Org. Chem.*, **49**, 3938 (1984); *b*) C. R. Johnson, R. W. Herr, and D. M. Wieland, *ibid.*, **38**, 4263 (1973).
28) *a*) H. O. House and M. J. Umen, *J. Org. Chem.*, **38**, 3893 (1973); *b*) H. O. House, D. G. Melillo, and F. J. Sauter, *ibid.*, **38**, 741 (1973); *c*) H. O. House, *Acc. Chem. Res.*, **9**, 59 (1976).
29) *a*) W. Wilkening and B. P. Mundy, *Tetrahedron Lett.*, **25**, 4619 (1984); *b*) K. G. Bilyard, P. G. Garratt, R. Hunter, and E. Lete, *J. Org. Chem.*, **47**, 4731 (1982).
30) *a*) K. Furuta, N. Ikeda, and H. Yamamoto, *Tetrahedron Lett.*, **25**, 675 (1984); *b*) K. Furuta, A. Misumi, A. Mori, N. Ikeda, and H. Yamamoto, *ibid.*, **25**, 669 (1984).
31) B. H. Lipschutz, D. A. Parker, J. A. Kozlowski, and S. L. Nguyen, *Tetrahedron Lett.*, **25**, 5959 (1984).
32) M. Suzuki, T. Suzuki, T. Kawagishi, and R. Noyori, *Tetrahedron Lett.*, **21**, 1247 (1980).
33) S. H. Bertz and G. Dabbagh, *J. Chem. Soc., Chem. Commun.*, **1982**, 1030.