Journal of Organometallic Chemistry, 402 (1991) 105–112
Elsevier Sequoia S.A., Lausanne
JOM 21384

Approaches to selective isoprenologation via reactions of $(\eta^3\text{-allyl})Fe(CO)_4^+$ with allyl nucleophiles

Zhong Li and Kenneth M. Nicholas *
Department of Chemistry and Biochemistry, University of Oklahoma, Norman, OK 73019 (USA)

(Received May 30th, 1990)

Abstract

The reactions of substituted $(\eta^3\text{-allyl})Fe(CO)_4BF_4$ complexes **1** with various allyl-metals [M = $SiMe_3$ (**2**), -$SnBu_3$ (**3**) and -$FeCp(CO)_2$ (**4**)] and dienolate derivatives [CH_2=C(CH_3)CH=COM(OR) (M = Li, $SiMe_3$)] have been investigated in search of a method for regio- and stereocontrolled allyl-allyl coupling. All three classes of allyl derivatives react with **1** in moderate to good yield with variable regioselectivity; the silyl derivatives **2** generally provide good regioselectivity for attack at the less substituted terminus of unsymmetrical derivatives of **1** but deprotonation of the 1,1-dimethylallyl complex **1e** prevents efficient isoprenylation. Although deprotonation of **1e** also dominates with the siloxydienes, the lithium dienolates couple efficiently with **1**; however, reaction at the α position of the dienolate dominates.

Introduction

There has been widespread interest in the reactivity of $(\eta^3\text{-allyl})ML_n$ complexes as a means for regio- and stereocontrolled introduction of the allyl unit. Complexes of Pd [1], Ni [2], Mo [3], W [4], Ti [5] and Fe [6] have proven to be particularly useful in this respect. In earlier studies we [6d] and others [6a,b] have shown that the readily available iron derivatives $(\eta^3\text{-allyl})Fe(CO)_4BF_4$ (**1**) undergo facile reactions with mild nucleophiles, generally to provide allyl coupled products in a stereospecific (with retention of the allyl fragment geometry) and regioselective (attack at the less substituted allyl terminus) manner.

A particularly important potential application of such allylic alkylation reactions lies in the generation of the 1,5-diene and polyene units characteristic of terpenoid natural products. Although considerable efforts and significant progress have been made to effect such "isoprenologation" reactions using allyl metal (and enolate) reactions with classical allyl electrophiles (e.g. halides, esters, etc.) [7,8], utilization of $(\eta^3\text{-allyl})ML_n$ complexes as either the electrophilic or nucleophilic component have been far more limited. Early studies involving nucleophilic $[(\eta^3\text{-allyl})NiX]_2$ met with some success but stereocontrol is problematic because of the facile *anti–syn* isomerization encountered with these complexes [2,9]. Following upon seminal studies by Tsuji [1a] and Trost [1b] of stoichiometric and catalytic Pd-mediated allylic alkylation, Keinan recently has reported [10] an impressive geranyl (C_{10})

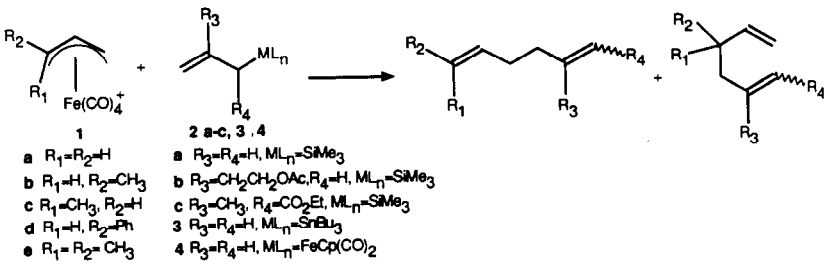
0022-328X/91/$03.50

extension methodology which features Pd-catalyzed coupling of allylic carbonates with stabilized allyl enolates. This method gives good yields, allows a high degree of regio- and stereocontrol, and can be carried out repeatedly to produce oligomeric products. The necessary removal in separate steps of the activating groups on the nucleophilic component detracts somewhat from the overall efficiency of the process.

Given our modest understanding of the factors controlling regioselectivity of nucleophilic attack on (η^3-allyl)ML_n complexes and the continued need for new, alternative and efficient methods for allyl-allyl coupling, we have examined the reactions of representative (η^3-allyl)$Fe(CO)_4BF_4$ complexes with various σ-allyl-metal and dionolate derivatives and report our findings herein.

Results and discussion

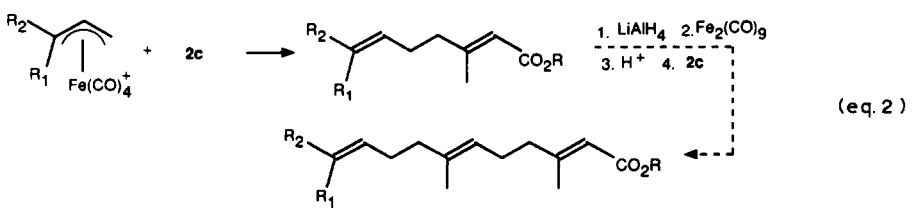
For our initial experiments we selected as reaction partners for the iron complexes **1a–d** representatives of three classes of nucleophilic σ-allyl-metals **2–4**. These species are known to react with a variety of electrophiles, typically γ- to the metal [11–13], and appeared to have appropriate reactivity to effect C–C bond formation with **1** under mild conditions. Indeed, such reactions were found to proceed according to Eq. 1 at room temperature in CH_3NO_2 solution to afford 1,5-diene products in moderate to good isolated yields (Eq. 1, Table 1).



a R_1=R_2=H
b R_1=H, R_2=CH_3
c R_1=CH_3, R_2=H
d R_1=H, R_2=Ph
e R_1=R_2=CH_3

a R_3=R_4=H, ML_n=$SiMe_3$
b R_3=CH_2CH_2OAc, R_4=H, ML_n=$SiMe_3$
c R_3=CH_3, R_4=CO_2Et, ML_n=$SiMe_3$
3 R_3=R_4=H, ML_n=$SnBu_3$
4 R_3=R_4=H, ML_n=$FeCp(CO)_2$

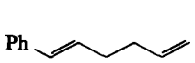
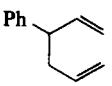
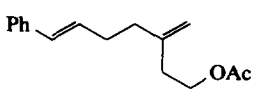
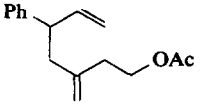
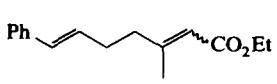
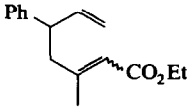
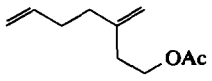
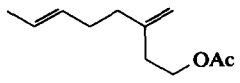
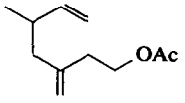
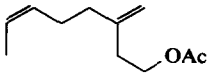
Interesting and unexpected regioselectivity was found in the reactions of the 1-phenylallyl complex **1d**, which previously was observed to undergo exclusive C-3 attack by aromatic nucleophiles [6e]. The allyl silanes **2a–c** all reacted with **1d** to produce a substantial (but minority) amount of the C-1 attack product. The coupling reaction of the pentenyl ester **2c** is also noteworthy since it not only demonstrates the expected (and desired) γ-to-Si attack [8c] but it also provides in the unsaturated ester product a prospective starting material for subsequent repetitive isoprenologation via ester reduction and recomplexation by iron according to Eq. 2.



The branched isomer (from C-1 attack), however, became the major product with the corresponding tin and iron allyls, **3** and **4**. Although we do not have a

Table 1

Allyl–allyl coupling reactions of $(\eta^3\text{-allyl})Fe(CO)_4BF_4$ complexes

Complex	Nucleophile	Time (h) [a]	Products [a]	Yield (%) [c]
1d	**2a**	4	 **5a** (73)  **5b** (27)	72
1d	**3**	4	**5a** (29) **5b** (71)	77
1d	**4**	4	**5a** (27) **5b** (73)	68
1d	**2b**	16	 **6a** (77)  **6b** (23)	67
1d	**2c**	16	 **7a** (72)  **7b** (28)	68
1a	**2b**	4	 **8**	47
1b	**2b**	16	 **9a** (80)  **9b** (20)	61
1c	**2b**	16	 **10**	41

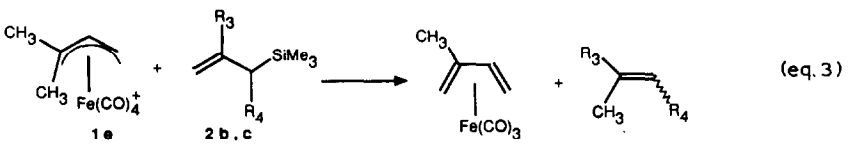
[a] Reaction carried out in CH_3NO_2 at 25 °C. [b] Isomer ratio determined by GC. [c] Isolated after chromatography.

convincing explanation for this interesting metal dependency, it is likely electronic in origin since no significant steric differences at the (presumably) reacting γ carbon of **2–4** are present. Highly nucleophile-dependent regioselectivity has been observed in many metal-mediated allylic alkylations [1–6,14] and appears to derive from a

delicate balance of steric and electronic effects. In some cases (including the present one) frontier orbital control may play a determinant role [14,15].

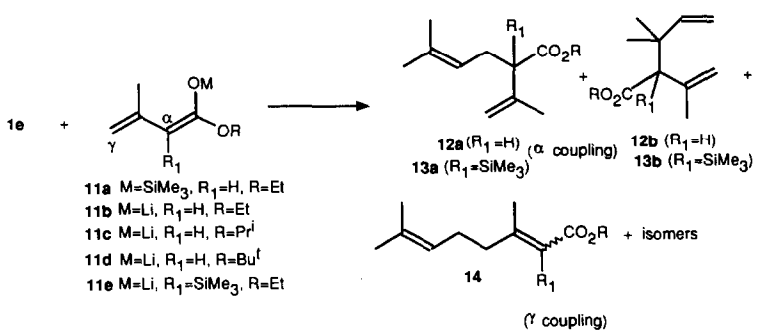
Regardless of the explanation for the above regioselectivities we concentrated our subsequent efforts on coupling reactions of the allyl silane derivatives since these appeared more likely to yield the linear head-to-tail selectivity needed for applications in isoprenologation. With the crotyl complexes **1b** and **1c** the acetoxysilane **2b** was indeed found to provide primarily (with **1b**) or exclusively (with **1c**) the linear dienes resulting from C-3 attack. This selectivity parallels that found previously for stabilized enolate additions to the substituted (η^3-allyl)$Fe(CO)_4BF_4$ complexes [6d].

Following these initial model studies we turned our attention to reactions of the allyl silane derivatives with the readily available 1,1-dimethylallyl complex **1e** [16] which we hoped would serve as an isoprenyl cation equivalent. To our disappointment, however, **1e** was found to be quantitatively deprotonated by either **2b** or **2c** under a variety of conditions ($T = 0$–$80\,^\circ C$, solvents = CH_3NO_2, THF, CH_3CN, CH_3COCH_3) giving the known isoprene complex [η^4-CH_2=C(CH_3)CH=CH_2]Fe-$(CO)_3$ [16] and the corresponding desilylated olefins (detected by GC/MS) (Eq. 3). Complex **1e** thus appears to be a surprisingly strong Bronsted–Lowry acid and the allyl silanes exhibit an inadequate nucleophilicity/basicity ratio to couple at carbon.



(eq. 3)

We also examined the reactions of **1e** with a set of isoprenyl dienolate derivatives in search of a reaction partner with a higher selectivity for C- vs H-attack (Eq. 4).



(eq. 4)

The siloxydiene derivative **11a** appeared to be a reasonable prospect since previous studies have shown that it can react with *C*-electrophiles via γ-attack [8e,f]. In the event **1e** was found to react with **11a** exclusively via the proton transfer pathway giving only (isoprene)$Fe(CO)_3$ and the methylacrylate ester under a variety of conditions. A more radical modification of the nucleophile's reactivity (both basicity and nucleophilicity) was then explored in the form of the lithium dienolates **11b–d**. These species, prepared by treatment of 3,3-dimethylacrylic acid esters with LDA, are known to undergo α- and γ-attack by *C*-electrophiles [8a]. Reaction between **1e** and **11b** (R = Et) occurred rapidly at $-78\,^\circ C$ to produce a mixture of coupled products (by GC/MS analysis) in approximately 65% yield. ^{1}H-NMR and GC/MS

analysis indicated the mixture to be made up primarily of isomers **12a** and **12b** (ca. 54: 36%) resulting from preferred α-attack by **11b** at C3 of **1e** along with a small amount (ca. 10%) of the desired γ-attack product **14**. The somewhat surprising enhancement of *C*-coupling at the expense of simple deprotonation with the dienolate derivative **11b** encouraged us to attempt to improve the γ/α selectivity of the nucleophilic component by increasing the steric bulk of the ester function. Reactions of **1e** with the corresponding i-propyl and t-butyl ester enolates **11c** and **11d** did result in an increase of the relative amount of the γ-attack isomer (up to 20–40%) but the selectivity was still unsatisfactory. Reasoning further that a Si-substituent at the α-position of the enolate could discourage α attack sterically and encourage γ-attack electronically we carried out the reaction of enolate derivative **11e** (formed by deprotonation of the silyl ester **2c**) with **1e**. GC/MS and ^{1}H NMR analysis of the resulting product mixture, however, revealed nearly exclusive (ca. 90%) formation of the α-attack product **13a**. Finally, since it had been reported that greatly improved γ-alkylation selectivity can be obtained using copper dienolates [8b], a parallel set of reactions was conducted in which CuI was added to the preformed lithium dienolates **11b–d**, followed by addition of complex **1e**. Unfortunately, no significant improvement in γ/α selectivity was observed upon analysis of the product mixtures by GC/MS and NMR.

In conclusion, it has been found that allyl-allyl coupling can be accomplished in satisfactory yields using (η^3-allyl)Fe(CO)$_4$BF$_4$ complexes in combination with allyl-metal or dienolate derivatives. Reasonably efficient regio- and stereoselective coupling of two unsymmetrical allyl components can be achieved using complexes **1b–d**. The isoprenyl complex **1e** couples with good terminal attack (C3) selectivity using lithium dienolates but acceptable levels of terminal γ-attack have yet to be found. This study also has uncovered an interesting regioselectivity dependency on the nature of the metal fragment of the σ-allyl-metal and a surprising chemoselectivity (deprotonation vs. C–C coupling) dependency on the counterion (Li vs. SiMe$_3$) of the dienolate.

Experimental

General methods and reagents

Solvents and reagents were dried by distillation from the following drying agents: tetrahydrofuran (Na/benzophenone), acetone and nitromethane ($CaSO_4$), and acetonitrile, dichloromethane, diisopropyl amine and trimethylsilyl chloride (CaH_2). (η^3-Allyl)Fe(CO)$_4$BF$_4$ **1a–d** [17], CpFe(CO)$_2$(η^1-allyl) [18], allyl silanes **2b** [19] and **2c** [20], and siloxydiene **11a** [21] were prepared by previously reported procedures. Siloxydienes **11b,c** were obtained using the general method described earlier [22].

*General procedure for allylation of complexes **1a–d** with allyl-Si, -Sn and Fe reagents*

To a stirred solution containing the η^3-allyl complex (4 mmol) in 30 mL of CH_3NO_2 was added the nucleophile (3 mmol) at room temperature. The mixture was stirred for 4–16 h. Upon reaction completion (monitored by IR disappearance of **1**), the mixture was diluted with ether (50 ml) and washed with brine. The organic phase was treated with iodine, washed with aqueous sodium thiosulfate and dried over $MgSO_4$. The products were isolated by flash chromatography on silica gel

(elution with 1 : 10 ethyl acetate/hexane). Isomeric products were not separated but were analyzed as a mixture by IR, NMR and GC/MS.

5a / 5b. IR (neat, cm^{-1}) 3020, 1640, 990, 915; MS (EI, *m/e*) 158 (M^+), 117. ^{1}H-NMR ($CDCl_3$, δ ppm) (**5a**): 7.27 (m, 5H, arom), 6.42 (d, $J = 15.9$ Hz, 1H, Ph–C*H*=), 6.24 (dt, $J = 6.3$, 15.9 Hz, 1H, Ph–CH=C*H*), 5.8 (m, 1H, C*H*=CH_2), 5.0 (m, 2H, =CH_2), 2.26 (m, 2H, CH_2–CH=CH_2), 2.32 (m, 2H, CH=CH–CH_2); lit [23]. ^{1}H-NMR ($CDCl_3$, δ ppm) (**5b**): 7.27 (m, 5H, arom), 5.96 (m, 1H, Ph–CH–C*H*=), 5.72 (m, 1H, CH_2–C*H*=CH_2), 5.0 (m, 4H, 2CH=CH_2), 3.31 (m, 1H, Ph–C*H*), 2.50 (m, 2H, Ph–CHCH_2); lit [23].

6a / 6b. IR (neat, cm^{-1}) 3020, 1740, 1650, 1235, 1040, 967, 900; MS (*m/e*) 244 (M^+), 184, 117. ^{1}H-NMR ($CDCl_3$, δ ppm) (**6a**): 7.30 (m, 5H, arom), 6.41 (d, $J = 15.9$ Hz, 1H, Ph–C*H*=CH), 6.22 (dt, $J = 6.4$, 15.9 Hz, 1H, Ph–CH=C*H*), 4.89 (s, 1H, =CH_2), 4.83 (s, 1H, =CH_2), 4.20 (t, $J = 7.0$ Hz, 2H, OCH_2), 2.38 (t, $J = 7.0$ Hz, 2H, OCH_2CH_2), 2.2 (m, 4H, CH_2CH_2), 2.05 (s, 3H, $COCH_3$). ^{1}H-NMR ($CDCl_3$, δ ppm) (**6b**): 7.30 (m, 5H, arom), 5.96 (ddd, $J = 7.1$, 10.2, 17.1 Hz, 1H, C*H*=CH_2), 5.04 (m, 2H, CH=CH_2), 4.80 (s, 1H, =CH_2), 4.78 (s, 1H, =CH_2), 4.15 (t, $J = 7.0$ Hz, 2H, OCH_2), 3.5 (m, 1H, Ph–C*H*), 2.48 (d, $J = 7.7$ Hz, 2H, Ph–CH=CH_2), 2.38 (t, $J = 7.0$ Hz, 2H, OCH_2CH_2), 2.05 (s, 3H, $COCH_3$).

E-***7a****, inter alia.* ^{1}H-NMR ($CDCl_3$, δ ppm) 7.25 (m, 5H, arom), 6.42 (d, $J = 15.9$ Hz, 1H, Ph–C*H*=), 6.25 (dt, $J = 6.0$, 15.9 Hz, 1H, Ph–CH=C*H*), 5.71 (q, $J = 1.2$ Hz, 1H, CH_3C=C*H*), 4.14 (q, $J = 6.0$ Hz, 2H, $COOCH_2$), 2.81 (t, $J = 7.0$ Hz, 2H, =$CHCH_2$–CH_2), 2.40 (m, 2H, =CH–CH_2), 2.20 (d, $J = 1.2$ Hz, 3H, CH_3C=CH), 1.24 (t, $J = 6.0$ Hz, 3H, $COOCH_2CH_3$); MS (*m/e*) 244 (M^+), 199, 171, 117; lit [24].

Z-***7a****, inter alia.* ^{1}H-NMR ($CDCl_3$, δ ppm) 7.25 (m, 5H, arom); 6.42 (d, $J = 15.9$ Hz, 1H, Ph–C*H*=), 6.25 (dt, $J = 15.9$, 6.8 Hz, 1H, Ph–CH=C*H*), 5.70 (q, $J = 1.2$ Hz, 1H, =C*H*CO_2Et), 4.14 (q, $J = 6.0$ Hz, 2H, $COOCH_2$), 2.81 (t, $J = 7.0$ Hz, 2H, =CH–CH_2–CH_2), 2.40 (m, 2H, =CH–CH_2), 1.92 (d,, $J = 1.3$ Hz, 3H, CH_3=CHCOOC_2H_5), 1.24 (t, $J = 6.0$ Hz, 3H, $COOCH_2CH_3$); MS (*m/e*) 244 (M^+), 199, 171, 117; lit [24].

E-***7b****, inter alia.* ^{1}H-NMR ($CDCl_3$, δ ppm) 7.25 (m, 5H, arom), 5.95 (m, 1H, PhCHC*H* = CH_2), 5.61 (m, 1H, =C*H*CO_2Et), 5.05 (m, 2H, CH=CH_2), 4.14 (q, $J = 6.0$ Hz, 2H, CO_2CH_2), 3.30 (m, 1H, PhC*H*), 2.56 (d, $J = 7.0$ Hz, 2H, PhCHCH_2), 2.14 (d, $J = 1.2$ Hz, 3H, CH_3C=), 1.24 (t, $J = 6.0$ Hz, 3H, $CO_2CH_2CH_3$); MS (*m/e*) 199 ($M^+ - OCH_2CH_3$), 171, 117.

Z-***7b****, inter alia.* ^{1}H-NMR ($CDCl_3$, δ ppm) 7.25 (m, 5H, arom), 5.95 (m, 1H, PhCHC*H*=), 5.68 (m, 1H, =C*H*CO_2Et), 5.00 (m, 2H, CH=CH_2), 4.14 (q, $J = 6.0$ Hz, 2H, CO_2CH_2), 3.30 (m, 1H, PhC*H*), 2.56 (d, $J = 7.0$ Hz, 2H, PhCHCH_2), 1.74 (d, $J = 1.3$ Hz, 3H, CH_3C=), 1.24 (t, $J = 6.0$ Hz, 3H, $COOCH_2CH_3$); MS (*m/e*) 199 ($M^+ - OC_2H_5$), 171, 117.

8. IR (neat, cm^{-1}) 3080, 1740, 1642, 1235, 1040, 910; ^{1}H-NMR ($CDCl_3$, δ ppm) 5.0 (m, 2H, CH_2=CH), 5.80 (m, 1H, CH_2=C*H*), 4.83 (s, 1H, =CH_2), 4.80 (s, 1H, =CH_2), 4.18 (t, $J = 7.0$ Hz, 2H, OCH_2), 2.34 (t, $J = 7.0$ Hz, 2H, OCH_2CH_2), 2.15 (m, 4H, CH_2CH_2), 2.04 (s, 3H, $COCH_3$); MS (CI, *m/e*) 169 ($M^+ + 1$) 109.

9a / 9b. IR (neat, cm^{-1}) 3080, 1740, 1645, 1235, 1040, 970, 900; MS (*m/e*) 122 (M^+ – HOAc), 107, 93. ^{1}H-NMR ($CDCl_3$, δ ppm) (**9a**) 5.43 (m, 2H, C*H*=C*H*), 4.82 (s, 1H, =CH_2), 4.78 (s, 1H, =CH_2), 4.17 (t, $J = 7.0$ Hz, 2H, OCH_2), 2.34 (t, $J = 7.0$ Hz, 2H, OCH_2CH_2), 2.10 (m, 4H, CH_2CH_2), 2.04 (s, 3H, $COCH_3$), 1.64 (d,

$J = 6.4$ Hz, 3H, CH_3). ^{1}H-NMR ($CDCl_3$, δ ppm) (**9b**) 5.67 (ddd, $J = 7.1$, 10.2, 17.3 Hz, 1H, $CH{=}CH_2$), 4.9 (m, 2H, $CH{=}CH_2$), 4.81 (s, 1H, ${=}CH_2$), 4.80 (s, 1H, $={CH_2}$), 4.17 (t, $J = 7.0$ Hz, 2H, OCH_2), 2.34 (t, $J = 7.0$ Hz, 2H, OCH_2CH_2), 2.10 (m, 1H, CH_3CH), 2.04 (s, 3H, $COCH_3$), 0.98 (d, $J = 6.7$ Hz, 3H, CH_3CH); MS (m/e) 122 ($M^+ -$ HOAc), 107, 93.

10. IR (neat, cm^{-1}) 3080, 1740, 1650, 1235, 1040, 910; ^{1}H-NMR ($CDCl_3$, δ ppm) 5.45 (m, 1H, CH_3CH), 5.39 (m, 1H, $CH_3CH{=}CH$), 4.84 (s, 1H, $={CH_2}$), 4.80 (s, 1H, $={CH_2}$), 4.18 (t, 7.1 Hz, 2H, OCH_2), 2.35 (t, $J = 7.1$ Hz, 2H, OCH_2CH_2), 2.18 (m, 2H, $=CH{-}CH_2$), 2.06 (m, 2H $=CH{-}CH_2CH_2$), 2.05 (s, 3H, $COCH_3$), 1.61 (d, $J = 6.0$ Hz, 3H, CH_3); MS (m/e) 122 ($M^+ -$ HOAc), 107, 93.

General method for alkylation of ester lithium dienolates

Under a nitrogen atmosphere, 0.5 mmol of n-butyllithium in hexane was added to a solution of 55 mg (0.5 mmol) of diisopropylamine in 4 ml of THF at $-78°$C. To this solution was then added 0.5 mmol of the 1,1-dimethylacrylate ester and the solution was stirred for 2 h. The 1,1-dimethylallyl complex **1e** (163 mg, 0.50 mmol) was then added. After stirring at $-78°$C for 1–2 h, the reaction was warmed to room temperature and stirred several hours. The mixture was then diluted with ethyl ether and washed with brine. The organic phase was treated with iodine, washed with aqueous thiosulfate, dried, and the products were isolated by flash chromatography on silica gel and analyzed by NMR and GC/MS.

12a. ^{1}H-NMR ($CDCl_3$, δ ppm) 5.66 (m, 1H, $=CHCH_2$), 5.0 (m, 2H, $={CH_2}$), 4.13 (q, $J = 7.0$ Hz, 2H, $COOCH_2$), 3.0 (t, $J = 7.4$ Hz, 1H, $CH_2CHCOOC_2H_5$), 2.15 (m, 2H, $CH_2CHCOOC_2H_5$), 1.75 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 1.12 (t, $J = 7.0$ Hz, 3H, $COOCH_2CH_3$); MS (m/e) 196 (M^+); 181, 167, 151, 123; lit [24].

12b. ^{1}H-NMR ($CDCl_3$, δ ppm) 5.86 (m, 1H, $CH{=}CH_2$), 5.0 (m, 2H, $CH_2{=}$), 4.96 (m, 2H, $CH{=}CH_2$), 4.13 (q, $J = 7.0$ Hz, 2H, $COOCH_2$), 2.97 (s, 1H, $CHCOOC_2H_5$), 1.82 (s, 3H, $=CCH_3$), 1.13 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.12 (t, $J = 7.0$ Hz, 3H, $COOCH_2CH_3$); MS (m/e) 196 (M^+), 181, 167, 151, 123; lit [24].

13a. ^{1}H-NMR ($CDCl_3$, δ ppm) 5.15 (m, 1H, $=CHC$), 4.94 (s, 1H, $={CH_2}$), 4.75 (s, 1H, $={CH_2}$), 4.01 (q, $J = 7.1$ Hz, 2H, OCH_2), 2.5 (m, 2H, $=CHCH_2$), 1.67 (s, 3H, $=CCH_3$), 1.62 (s, 3H, $=CCH_3$), 1.26 (t, $J = 7.1$ Hz, 3H, CH_2CH_3), 0.11 (s, 9H, $Si(CH_3)_3$); MS (m/e) 268 (M^+), 253, 223, 107.

14. ^{1}H NMR ($CDCl_3$, δ ppm) 5.72 (brs, 1H, $=CHCO_2Et$), 5.6 (m, 1H, $=CHCH_2$), 4.13 (q, $J = 7.0$ Hz, 2H, OCH_2), 2.63 (t, $J = 7.0$ Hz, $CH_2C(CH_3)$), 2.50 (m, 2H, $CH_2CH{=}$), 1.88 (d, $J = 1.2$ Hz, 3H, $CH_3C{=}CH$), 1.67 (s, 3H, $CH_3C(CH_3){=}$), 1.60 (s, 3H, $CH_3C(CH_3){=}$), 1.22 (t, $J = 7.0$ Hz, 3H, CH_2CH_3); lit [24].

General method for alkylation of ester monocopper dienolates.

Under a nitrogen atmosphere, 0.5 mmol of 2.0 *M* n-butyllithium was added to a solution of 55 mg (0.50 mmol) of diisopropylamine in 4 mL of THF at $-78°$C. To this was added 0.5 mmol of 1,1-dimethylacrylate and the solution was stirred for 2 h. Copper iodide (5 mg, 0.5 mmol) was then added. The reaction was stirred for 2 h at $-78°$C, then 163 mg (0.50 mmol) of 1,1-dimethylallyl complex **1e** was added. After stirring at $-78°$C for 1–2 h, the reaction was warmed to room temperature and stirred for several hours. The mixture was then diluted with ethyl ether and washed with brine. The organic phase was treated with iodine, washed with aqueous

thiosulfate, dried, and the products as isomeric mixtures were isolated by flash chromatography on silica gel. The isomeric mixtures were analyzed (partially) by ^1H NMR and GC/MS.

Acknowledgments

We are grateful for financial support provided by the National Institutes of Health (GM34799).

References

1 (a) J. Tsuji, Organic Synthesis with Palladium Complexes, Springer-Verlag, Berlin, 1980; (b) B.M. Trost, Acc. Chem. Res., 12 (1980) 198.
2 P.W. Jolly, in G. Wilkinson, F.G.A. Stone and E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, Vol. 8, Chap. 56.5, Pergamon Press, Oxford, 1982.
3 B.M. Trost and M. Lautens, J. Am. Chem. Soc., 105 (1983) 3343.
4 B.M. Trost and M.-H. Hung, J. Am. Chem. Soc., 105 (1983) 7757.
5 Y. Kobayashi, K. Umeyana and F. Sato, J. Chem. Soc., Chem. Commun., (1984) 621.
6 (a) T.H. Whitesides and R.W. Arhardt, J. Am. Chem. Soc., 93 (1971) 5297; (b) A.J. Pearson, Tetrahedron Lett., (1971) 3617; (c) J.L. Roustan, J.Y. Merour and F. Houlihan, ibid., (1979) 3721; (d) S.J. Ladoulis and K.M. Nicholas, J. Organomet. Chem., 285 (1985) C13; (e) J.W. Dieter, Z. Li and K.M. Nicholas, Tetrahedron Lett., 28 (1987) 5415.
7 G. Cainelli and G. Cardillo, Acc. Chem. Res., 14 (1981) 89.
8 (a) J.A. Katzenellenbogen and A.L. Crumrine, J. Am. Chem. Soc., 98 (1976) 4925; (b) P.A. Savu and J.A. Katzenellenbogen, J. Org. Chem., 46 (1980) 239; (c) P. Albaugh-Robertson and J.A. Katzenellenbogen, Tetrahedron Lett., 23 (1982) 723; (d) P. Albaugh-Robertson and J.A. Katzenellenbogen, J. Org. Chem., 48 (1983) 5288; (e) T. Mukaiyama and I. Ishida, Chem. Lett., (1977) 467 and references therein; (f) I. Fleming and T.V. Lee, Tetrahedron Lett., 22 (1981) 705 and references therein.
9 K. Sato, S. Inoue, S. Kijima and S. Hamamura, German Patent 2,416,035 (1974).
10 E. Keinan and D. Eren, Pure Appl. Chem., 60 (1988) 89.
11 E.W. Colvin in Silicon Reagents in Organic Synthesis, Academic Press, London, 1988, pp. 25–38.
12 M. Pereyre, J.-P. Quintard and A. Rahm, Tin in Organic Synthesis, Chap. 10, Butterworths, London, 1987, pp. 185–230.
13 M. Rosenblum, Acc. Chem. Res., 7 (1974) 122.
14 E. Keinan and Z. Roth, J. Org. Chem., 48 (1983) 1769.
15 M.D. Curtis and O. Eisenstein, Organometallics, 3 (1984) 887.
16 J. Dieter and K.M. Nicholas, J. Organomet. Chem., 212 (1981) 107.
17 R.B. King, T.A. Manuel and F.G.A. Stone, J. Inorg. Nucl. Chem., 16 (1961) 233.
18 P.A. Lennon, A. Rosan, M. Rosenblum, J. Tancrede and P. Waterman, J. Am. Chem. Soc., 102 (1980) 7033.
19 M. Ochiai, E. Fugita, M. Arimoto and H. Yamaguchi, Chem. Phar. Bull., 31 (1983) 86.
20 A.A. Millard and M.W. Rathke, J. Am. Chem. Soc., 99 (1977) 4833.
21 K. Krohn, Ann. Chem., (1981) 2285.
22 C. Raha, Org. Syn., Coll. Vol. 4, 1963, p. 264.
23 H. Levy and A.C. Cope, J. Am. Chem. Soc., 66 (1944) 1684.
24 Y. Yamamoto, K. Marayama and K. Matsumoto, Tetrahedron Lett., 25 (1984) 1075.