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1,2-Asymmetric Induction in the Conjugate Addition of Organocopper Reagents to γ-Aryl α,β-Unsaturated Carbonyl Derivatives

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Abstract—The diastereoselectivity in the conjugate addition of organocopper reagents to γ-aryl α,β-unsaturated carbonyl derivatives 8–14 was investigated. The *syn*-diastereoselectivity was obtained irrespective of the reagents type in the addition of 8, while the *anti*-diastereoselectivity was obtained in the addition of 10–14 with RCu and RCu(CN)Li (R=Me and Bu) and the *syn*-selectivity was produced in the addition of 10–14 with R_2CuLi and $R_2Cu(CN)Li_2$. The reagent controlled and substrate dependent diastereoselectivity are explained by two different reaction pathways: either π-complex formation or ordinary nucleophilic addition. Reduction potentials of the Michael acceptors and electron donating ability of organocopper reagents control the reaction pathway.

Introduction

The diastereoselectivity of nucleophilic addition to α-alkoxy aldehydes having α-chiral center can be interpreted and predicted either by a Felkin–Anh transition state model **1**[1] or by a chelation model **2**[2] (Fig. 1). On the other hand, the diastereoselectivity of nucleophilic conjugate addition to γ-alkoxy α,β-unsaturated carbonyl derivatives having γ-chiral center was puzzling.[3] Previously we carried out a systematic study on this problem and reported that the diastereoselectivity of organocopper conjugate addition to such enoates depended on the substrate structure and the reagent type.[4] The alkylcopper addition to a *trans*-mono-enoate proceeds through the inside alkoxy model **3** to give the *anti*-adduct predominantly, while the addition to a *cis*-mono-enoate proceeds through the outside alkoxy model **4** to afford the *syn*-adduct preferentially. When stronger Michael acceptors and/or copper reagents having lower oxidation potentials are used, the π-complex model **5** is involved which gives the *syn*-adduct predominantly. The 1,2-asymmetric induction of γ-alkoxy-enoates could be elucidated by the above three different models. However, a chelation controlled addition of organocopper reagents may intervene, depending upon OR' group, in certain cases of those γ-alkoxy enoates, which makes it difficult to perform straightforward interpretation on the diastereoselectivity relationship between the reagent type and the substrate structure.

On the other hand, the 1,2-asymmetric induction of α-aryl substituted chiral aldehydes is straightforward, and can be explained by the Felkin–Anh model **6**: it is not necessary to consider other models such as a chelation model. It occurred to us that the 1,2-asymmetric induction of γ-aryl substituted α,β-enoates having γ-chiral center must also be straightforward in comparison with that of γ-alkoxy analogs and therefore more deep insight into the π-complex mechanism must be gained. We now detail the results for the diastereoselectivities on conjugate addition to γ-aryl substituted α,β-unsaturated carbonyl derivatives **7** and report that π-complex formation is in fact a key for dictating the direction of 1,2-asymmetric induction.

Results and Discussion

Diesters and related systems

Diesters **11**–**14** and other Michael acceptors **8**–**10** were prepared by the standard procedure.[5] All the Michael acceptors have a substituent (Me, CN, or CO_2Et) *cis* to the α-phenyl-ethyl group and therefore it is reasonable to assume that similar level of the allylic strain to the chiral center is operative. Although all the substrates are racemic, the structures **8**–**14** are drawn in (*S*) form for convenience.

Keywords: Michael reactions; copper and compounds; diastereoselectivity; substituent effects.
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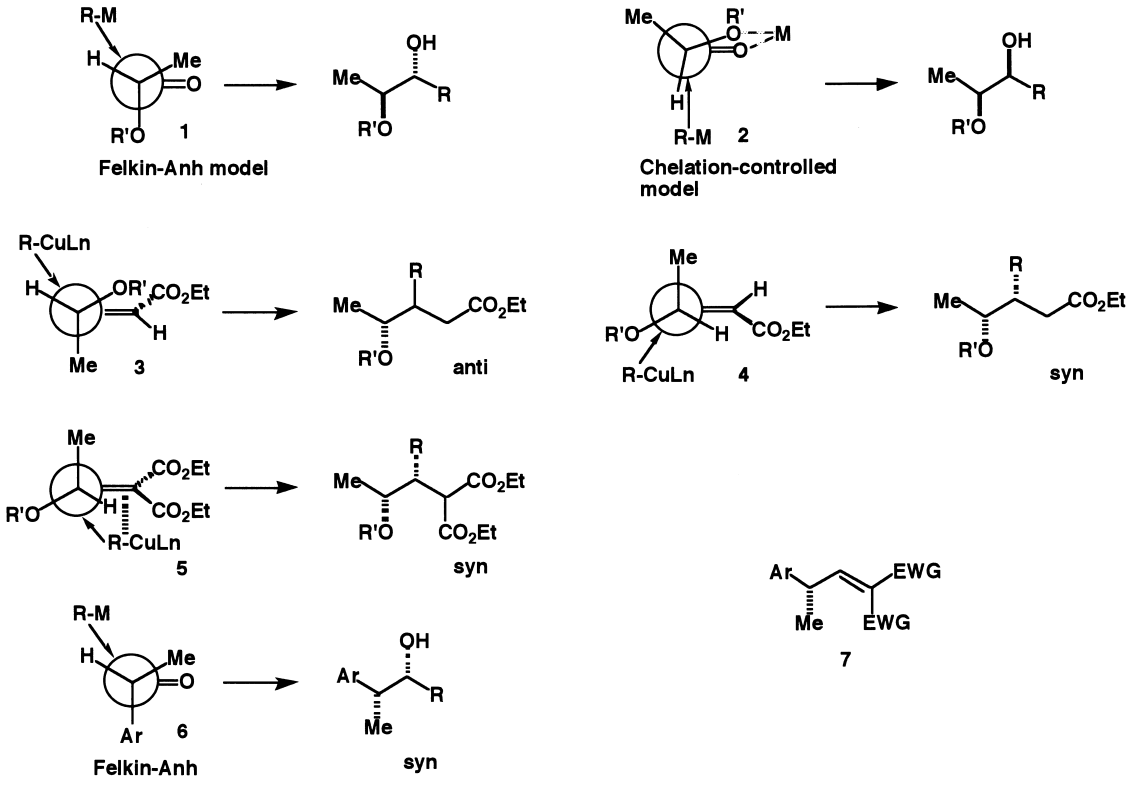

Figure 1.

Reduction potentials of **8**–**14** were measured by cyclic voltammetry and E_{red} values are shown in Fig. 2. Those of **12**–**14** were too low, i.e. below −2.0 V, to be measured exactly by this method. The reactions of 3 equiv. organocopper reagents with the Michael acceptors were carried out in diethyl ether at −78°C and then the mixtures were allowed to warm to ca. −20°C. The reactions were quenched with aqueous ammonium chloride solution, and the isomer distribution was investigated by GLC and/or ^{1}H NMR analysis. The stereochemistries of the conjugate adducts were determined unambiguously by the spectroscopic method (^{1}H NMR) and/or by correlation with their authentic compounds (see Experimental section). The results are summarized in Table 1.

The conjugate addition to the nitro-olefin **8**, which has the highest reduction potential (E_{red}=−1.33 V) among the substrates, gave the *syn*-adduct **16** predominantly regardless of the reagent type (entries 1–5). The yields of the conjugate adducts **15** and **16** were low; the starting material was recovered in most cases and, for example, **8** was recovered in 54% yield in entry 1. The reagent controlled diastereoselectivity was observed in the conjugate addition to **9** (E_{red}=−1.43 V). The addition with MeCu(CN)Li and BuCu(CN)Li gave the *anti*-adduct **17** predominantly, whereas the reaction with MeCu, $Me_2Cu(CN)Li_2$, Me_2CuLi, BuCu, $Bu_2Cu(CN)Li_2$, and Bu_2CuLi afforded the *syn*-adduct **18** preferentially (entries 6–13). The diastereoselectivity of **10** (E_{red}=−1.68 V) is very interesting in comparison with that of **9**; here also the reagent controlled diastereoselectivity was observed, but MeCu and BuCu gave the *anti*-isomer **19** predominantly whereas Me_2CuLi and Bu_2CuLi afforded the *syn*-isomer **20** preferentially (entries 14–17). The electronic effect of the *para*-substituent of

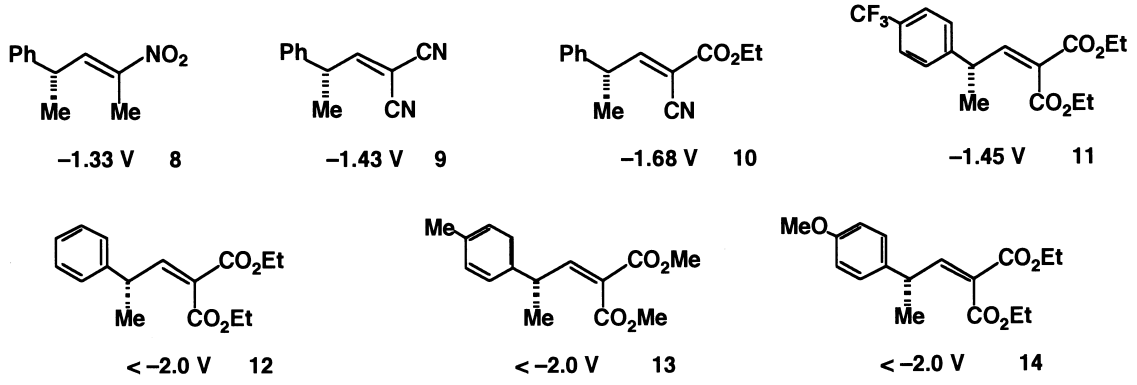

Figure 2.

Table 1. Conjugate addition of RCuLn to Michael acceptors **8**–**14** in diethyl ether (all reactions were carried out in diethyl ether at −78°C with Michael acceptor (0.3 mmol) and organocopper (0.9 mmol))

Entry	Michael acceptor	Reagent	Conjugate adduct (%)[a]	Isomer ratio[b] *anti*:*syn*
				15:**16**
1	**8**	MeCu	27	33:67
2		MeCu·TMSCl	47	24:76
3		Me_2CuLi	35	21:79
4		BuCu	45	13:87
5		Bu_2CuLi	28	19:81
				17:**18**
6	**9**	MeCu(CN)Li	81	69:31
7		MeCu	72	23:77
8		$Me_2Cu(CN)Li_2$	79	21:79
9		Me_2CuLi	73	13:87
10		BuCu(CN)Li	81	62:38
11		BuCu	89	23:77
12		$Bu_2Cu(CN)Li_2$	77	14:86
13		Bu_2CuLi	79	9:91
				19:**20**
14	**10**	MeCu	92	62:38
15		Me_2CuLi	91	38:62
16		BuCu	79	75:25
17		Bu_2CuLi	68	25:75
				21:**22**
18	**11**	MeCu(CN)Li	58	26:74
19		MeCu	58	21:79
20		$Me_2Cu(CN)Li_2$	62	26:74
21		Me_2CuLi	64	35:65
				23:**24**
22	**12**	MeCu(CN)Li	88	83:17
23		MeCu	93	75:25
24		$Me_2Cu(CN)Li_2$	94	23:77
25		Me_2CuLi	87	32:68
26		BuCu(CN)Li	92	73:27
27		BuCu	83	69:31
28		$Bu_2Cu(CN)Li_2$	88	26:74
29		Bu_2CuLi	90	33:67
30		$Bu_2CuLi{\cdot}BF_3$	95	7:93
				25:**26**
31	**13**	MeCu(CN)Li	70	90:10
32		MeCu	87	81:19
33		$Me_2Cu(CN)Li_2$	81	17:83
34		Me_2CuLi	81	24:76
				27:**28**
35	**14**	MeCu(CN)Li	67	63:37
36		MeCu	64	77:23
37		$Me_2Cu(CN)Li_2$	59	27:73
38		Me_2CuLi	63	29:71

[a] Isolated yield.
[b] By ^1H NMR and/or GLC analysis.

phenyl ring was investigated with four different diesters **11**–**14**. The *para*-CF_3, as an electron withdrawing group, substituted diester **11** (E_{red}=−1.45 V) produced the *syn*-adduct **22** predominantly irrespective of the reagent type (entries 18–21). Diester **12** (E_{red}=<−2.0 V), non-substituted at the *para*-position, exhibited the reagent controlled diastereoselectivity; MeCu and BuCu afforded the *anti*-isomer **23** preferentially, while Me_2CuLi and Bu_2CuLi gave the *syn*-isomer **24** predominantly (entries 22–29). In the case of the Michael acceptor **13** (E_{red}=<−2.0 V) having the *para*-Me, as an electron donating group, substituted phenyl group, the reactions with MeCu(CN)Li and MeCu gave the *anti*-isomer **25** preferentially, whereas those with Me_2CuLi and $Me_2Cu(CN)Li_2$ afforded the *syn*-isomer **26** predominantly (entries 31–34). The *para*-MeO, as an electron donating group, substituted phenyl derivative **14** (E_{red}=<−2.0 V) exhibited a reagent-controlled diastereoselectivity similar to **12** and **13**; the addition of MeCu(CN)Li and MeCu produced the *anti*-adduct **27** as a major isomer whereas that of $Me_2Cu(CN)Li_2$ and Me_2CuLi gave the *syn*-adduct **28** predominantly (Fig. 3) (entries 35–38).

A clear-cut trend on the diastereoselectivity was observed and it depended upon both the reagent type and the substrate structure. The relationships between reagents type, substrate structures and diastereoselectivities are summarized in Table 2 (for MeCuLn) and in Table 3 (for BuCuLn). The Michael acceptor **8** having the highest reduction potential gave the *syn*-diastereoselectivity regardless of the reagent

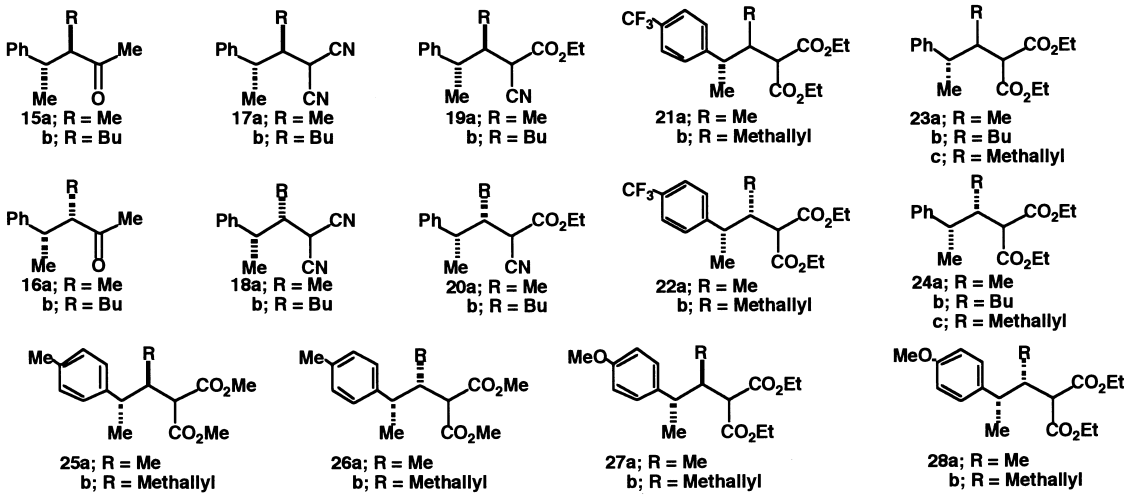

Figure 3.

Table 2. Diastereoselectivities of MeCuLn addition

Reagent	Substrate (E_{red})						
	8 (−1.33)	**9** (−1.43)	**11** (−1.45)	**10** (−1.68)	**12** (<−2.0)	**13** (<−2.0)	**14** (<−2.0)
MeCu(CN)Li		*anti*	*syn*		*anti*	*anti*	*anti*
MeCu	*syn*	*syn*	*syn*	*anti*	*anti*	*anti*	*anti*
$Me_2Cu(CN)Li_2$	*syn*	*syn*	*syn*		*syn*	*syn*	*syn*
Me_2CuLi	*syn*	*syn*	*syn*	*syn*	*syn*	*syn*	*syn*

type. With decrease of reduction potential of substrates, the *anti*-selectivity appears in the table. Previously, we proposed the order of the oxidation potential of alkylcopper reagents by using a certain chemical scale.[6] The electron transfer ability of methylcopper reagents is in the following order: $Me_2CuLi \gg Me_2Cu(CN)Li_2 > MeCu > MeCu(CN)Li$; and that of butylcopper reagents is in the following order: $Bu_2CuLi > Bu_2Cu(CN)Li_2 \approx BuCu(CN)Li > BuCu$. Table 2 clearly shows that methylcopper reagents with higher electron transfer ability are prone to produce *syn*-selectivity. Thus, Me_2CuLi and $Me_2Cu(CN)Li_2$ produce *syn*-diastereoselectivity irrespective of the substrate structures. MeCu reagent gives *anti*-selectivity in the case of the Michael acceptors with lower reduction potentials, while it affords *syn*-selectivity in the case of those with higher reduction potentials. The diastereoselectivities of **11** seem to be not straightforward and, if we count that this is an exceptional case, the addition of MeCu(CN)Li to most Michael acceptors produces *anti*-selectivity. The addition of MeCu(CN)Li to **8** was so sluggish, and essentially no reaction took place even after prolonged reaction times. A similar trend was observed in the case of BuCu reagents although fewer examples were studied (Table 3). Bu_2CuLi produces *syn*-selectivity regardless of the substrate structure, and BuCu affords *syn*-selectivity in the case of the Michael acceptors (**8** and **9**) with higher reduction potentials while it gives *anti*-selectivity in the case of **10** and **12** with lower potentials. The diastereoselectivity of the cyanocuprates, $Bu_2Cu(CN)Li_2$ and BuCu(CN)Li, is not straightforward. In the case of **9**, its diastereoselectivity trend is the same as that of methylcopper reagents, but the order of electron transfer ability of butyl cyanocoppers is a bit different from that of methyl cyanocoppers; according to the chemical scale,[6b] the order of electron transfer ability of BuCu(CN)Li is higher than that of BuCu.

Table 3. Diastereoselectivities of BuCuLn addition

Reagent	Substrate (E_{red})			
	8 (−1.33)	**9** (−1.43)	**10** (−1.68)	**12** (<−2.0)
BuCu(CN)Li		*anti*		*anti*
BuCu	*syn*	*syn*	*anti*	*anti*
$Bu_2Cu(CN)Li_2$		*syn*		*syn*
Bu_2CuLi	*syn*	*syn*	*syn*	*syn*

The *syn*-diastereoselectivity of **8**–**14** can be explained by the π-complex model **29** (Fig. 4). 'Hydrogen' should be inside in order to alleviate both an allylic strain and steric repulsion of the R group approaching the β-carbon. The formation of the π-complex would become much easier when the 'matched' combination between Michael acceptors having higher reduction potentials and organocopper reagents having higher electron donating ability was used. Even with enoates having lower reduction potentials, such as **12**–**14**, the organocuprate reagents having higher electron donating ability would be able to form such π-complex, leading to the *syn*-diastereoselectivity. On the other hand, even with the alkylcopper and alkylcyanocopper reagents having lower electron donating ability, the Michael acceptor **8** having the highest reduction potential would also be able to form π-complex, leading to *syn*-diastereoselectivity. However, in the case of 'mismatched' combination, π-complex formation would

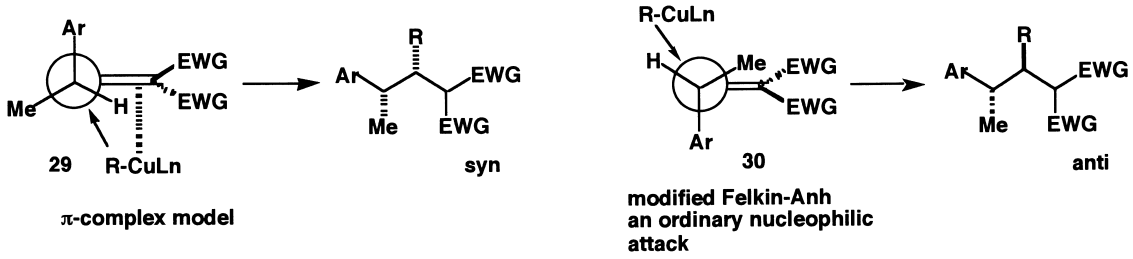

Figure 4.

Table 4. Reaction of mono-esters (in the case of mono-esters, the use of Me- and Bu-organocopper reagents in the absence of $BF_3{\cdot}OEt_2$ resulted in very low yields of the conjugate adducts)

Entry	Mono-ester	Reagent	Conjugate adduct (%)[a]	Isomer ratio[b] *anti*:*syn*
				33:**34**
1	**31**	$MeCu{\cdot}BF_3$	10	85:15
2		$Me_3CuLi_2{\cdot}BF_3$	46	87:13
3		$BuCu{\cdot}BF_3$	82	88:12
4		$Bu_2Cu(CN)Li_2{\cdot}BF_3$	29	80:20
5		$Bu_2CuLi{\cdot}BF_3$	90	70:30
6	**32**	$Me_3CuLi_2{\cdot}BF_3$	67	21:79
7		$Bu_2Cu(CN)Li_2{\cdot}BF_3$	26	33:67
8		$Bu_2CuLi{\cdot}BF_3$	89	30:70

[a] Isolated yield.
[b] By ^1H NMR and/or GLC analysis.

be not possible but an ordinary nucleophilic attack **30** from the outside would intervene in the conjugate addition, giving the *anti*-diastereoselectivity. 'Hydrogen' should be outside in order to diminish the steric repulsion of the incoming R group and 'Me' may be inside since its steric demand is rather small (*A*-value of Me=1.70 and that of Ph=3.0).[7] The pairs between Michael acceptors **10**–**14** having relatively lower reduction potentials and RCu (and/or RCu(CN)Li) having relatively lower electron donating ability area 'mismatched' combination.

The comparison of the diastereoselectivity difference among **11**–**14** is especially noteworthy. Only structural difference of these substrates is their *para*-substitutents of the aromatic ring and therefore it is clear that there is no difference among the substrates on the steric effect such as allylic strain. The reduction potential of **11** is the highest among them. Although the exact data on the reduction potentials of **12**–**14** could not be obtained due to their lower values, the ^{13}C-chemical shifts at the β-carbons suggested the order of the electron density of the olefinic bond; 150.48 ppm for **11**, 151.74 ppm for **12**, 153.06 ppm for **13**, and 158.61 ppm for **14**. Accordingly, it is not unreasonable to assume that the order of electron accepting ability is **11**>**12**>**13**>**14**. With **11**, the *syn*-selectivity was obtained irrespective of the reagent type. On the other hand, in the case of **12**–**14**, the *anti*-selectivity was produced with MeCu and the *syn*-selectivity was obtained with Me_2CuLi. It is now clear that only the electronic effect of the phenyl ring dictates the diastereoselectivity, and this can be explained either by π-complex formation or by an ordinary nucleophilic mechanism.

Mono-esters

α,β-Unsaturated mono-esters **31** and **32** were prepared by the standard procedures (Fig. 5).[8] The reduction potentials of those mono-esters must be lower than those of diester **12**, and therefore it is reasonable to assume that π-complex formation becomes more difficult for these mono-esters in comparison with the corresponding diester. Since the reaction of the mono-esters was more sluggish even with reactive cuprate reagents than that of the di-esters, the Lewis acid mediated addition was used.[4,9–11] The presence of $BF_3{\cdot}OEt_2$ as a Lewis acid in these reactions did not exert significant influence upon the diastereoselectivity of the conjugate adducts (entry 30, Table 1). The results are summarized in Table 4. The *trans* ester **31** produced the *anti*-adduct **33** predominantly irrespective of the reagent type (entries 1–5), while *cis* ester **32** afforded the

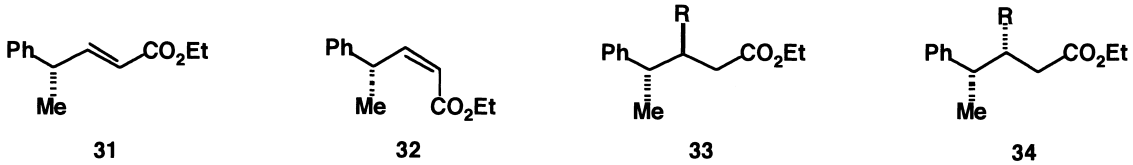

Figure 5.

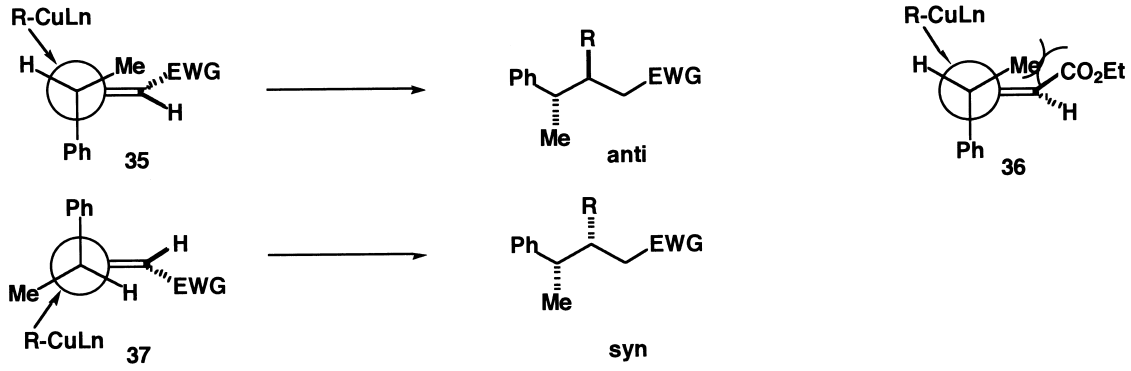

Figure 6.

syn-isomer **34** preferentially (Fig. 5) regardless of the reagents (entries 6–8).

It is now clear that the double bond geometry plays an important role in controlling the diastereoselectivity of the conjugate addition to mono olefins (Fig. 6). The reactions of the monoesters (**31** and **32**) with alkyl copper reagents must proceed via the ordinary nucleophilic attack. The addition of the copper reagents proceeds through a Bürgi–Dunitz trajectory[1c,g] from the outside position of a transition state geometry **35** in which phenyl group is *anti* and methyl group is inside, giving the *anti* isomer predominantly. If the double bond geometry changes from *trans* to *cis*, the inside methyl conformation would be destabilized due to the steric repulsion between the ester and phenyl group (as shown in **36**), and thus the transition state geometry **37** would become more favorable in order to minimize the allylic strain. The *syn* isomer is produced from **37**, and this mechanism is in good agreement with the diastereoselectivity observed in the reaction between alkyl cooper reagents and the *cis* enoate **32**, and with the stereoselectivity switch from *anti* to *syn* upon changing the enoate from the *trans* **31** to the *cis* enoate **32**.

Conjugate addition of methallylcopper reagents

The conjugate additions of methallylcopper reagents to **11**–**14** were investigated. The results are summarized in Table 5. The reactions with methallylcopper reagents afforded the *syn* isomer preferentially regardless of the reagent type and the *para*-substituents of the substrates, except for one case (entry 6). The reason for this exception is not clear at present. The reaction of **11**–**14** with methallylcopper reagents would proceed through π-complex formation **29** irrespective of the reagent type since the methallylcopper reagents may possess higher electron donating ability than the corresponding methylcopper reagents.[4b] A hydrogen is on the inside position because nucleophile attacks from inside. It is further confirmed by the result of methallylcopper reagents that

Table 5. Conjugate addition of methallylcopper reagents to Michael acceptors **11**–**14** in diethyl ether (all reactions were carried out in diethyl ether at −40°C with Michael acceptor (0.3 mmol) and organocopper (0.9 mmol))

Entry	Michael acceptor	Reagent	Conjugate adduct (%)[a]	Isomer ratio[b] *anti*:*syn*
				21:**22**
1	**11**	(Methallyl)Cu(CN)Li	77	43:57
2		(Methallyl)Cu	75	24:76
3		$(Methallyl)_2Cu(CN)Li_2$	77	12:88
4		$(Methallyl)_2CuLi$	87	43:57
				23:**24**
5	**12**	(Methallyl)Cu(CN)Li	72	48:52
6		(Methallyl)Cu	75	67:33
7		$(Methallyl)_2Cu(CN)Li_2$	87	30:70
8		$(Methallyl)_2CuLi$	78	44:56
				25:**26**
9	**13**	(Methallyl)Cu(CN)Li	80	32:68
10		(Methallyl)Cu	75	31:69
11		$(Methallyl)_2Cu(CN)Li_2$	69	29:71
12		$(Methallyl)_2CuLi$	63	23:77
				27:**28**
13	**14**	(Methallyl)Cu(CN)Li	65	34:66
14		(Methallyl)Cu	75	14:86
15		$(Methallyl)_2Cu(CN)Li_2$	77	34:66
16		$(Methallyl)_2CuLi$	87	42:58

[a] Isolated yield.
[b] By ^1H NMR and/or GLC analysis.

a 'matched pair' produces *syn*-diastereoselectivity via π-complex formation.

Conclusion

The 1,2-asymmetric induction in the conjugate addition of organocopper reagents to γ-aryl α,β-unsaturated carbonyl derivatives is rather straightforward in comparison with that of the addition to γ-alkoxy-analogs. Two different types of transition state geometries are involved: an ordinary nucleophilic addition and π-complex formation. If the combination between organocopper reagents and Michael acceptors is 'matched pair', π-complex formation takes place, giving the *syn*-diastereoselectivity. In the case of 'mismatched pair', the *anti*-diastereoselectivity is produced through the ordinary nucleophilic addition. 'Matched pair' implies the reaction between organocopper reagents having higher electron donating ability and Michael acceptors having higher reduction potentials. 'Mismatched pair' implies the reaction between organocoppers having lower electron donating ability and Michael acceptors having lower reduction potentials.

Experimental

General methods

Melting points were determined on either a Yamoto MP-21 capillary melting point apparatus or a MRK No. 8026. Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated silica gel $60F_{254}$ plates. Solvents for extraction and chromatography were reagent grade. THF and diethyl ether were distilled from benzophenone ketyl under argon immediately prior to use. Butyllithium and methyllithium were obtained from the Kanto Chemical Co., Inc. and Aldrich Chemical Company, respectively, as standardized solutions. In vacuo removal of solvent refers to the use of a rotary operating aspirator and then rotary pump pressure. Column chromatography was carried out with E. Merck silica gel 60 (70–230 mesh ASTM). Flush chromatography was carried out with E. Merck silica gel 60 (230–400 mesh ASTM). HPLC was performed on a HITACHI L-6000 model using a GASUKURO KOGYO HPLC Packed Column Intertisil SIL (5 μm 4.6×250 nm^2). GC analysis was carried out on a Shimadzu 14A model equipped with a fused silica-capillary column (Shimadzu CPB1-M25-025). Infrared spectra were recorded on a HITACHI model 260-10. Peaks are recorded (in cm^{-1}). NMR spectra were recorded on a JEOL GSX-270 and GSX-400 spectrometers. Low-resolution mass spectra were obtained on a HITACHI M-2500S spectrometer using electron impact (EI) obtained at 13.5 eV. High-resolution mass spectra were obtained on JEOL JMS-HX 110. Combustion analyses were performed by the Analytical Center of the Graduate School of Science at Tohoku University.

(*E*)-2-Nitro-4-phenyl-2-pentene (8). The nitroolefine **8** was prepared by the reaction of 2-phenylpropionaldehyde with nitroethane according to the literature[5] in 64% yield. ^{1}H NMR ($CDCl_3$) δ 1.46 (d, *J*=7 Hz, 3H), 2.17 (d, *J*=1 Hz, 3H), 3.63 (dq, *J*=7 and 11 Hz, 1H), 7.00–7.30 (m, 6H); IR (neat) 3040, 2980, 2950, 1670, 1610, 1520, 1500, 1450, 1390, 1330, 1020, 980, 910, 850, 760, 720, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{11}H_{13}NO_2$:191.0946. Found: 191.0944.

Ethyl 2-cyano-4-phenyl-2-pentenoate (10). The nitrile **10** was prepared by the reaction of 2-phenylpropionaldehyde with ethyl cyanoacetate according to the literature[5] in 87% yield. ^{1}H NMR ($CDCl_3$) δ 1.35 (t, *J*=7.5 Hz, 3H), 1.55 (d, *J*=7 Hz, 3H), 4.10 (dq, *J*=7 and 11 Hz, 1H), 4.25 (q, *J*=7.5 Hz, 2H), 7.21 (m, 5H), 7.45 (d, *J*=11 Hz, 1H); IR (neat) 3040, 2980, 2940, 2240, 1730, 1620, 1600, 1490, 1450, 1370, 1300, 1280, 1250, 1100, 1080, 1020, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{14}H_{15}NO_2$:229.1103. Found: 229.1103.

Ethyl 4-methyl-2-(ethoxycarbonyl)-4-*p*-trifluoromethylphenyl-2-butenoate (11). (α,α,α-Trifluoro-*p*-tolyl)acetic acid was converted to the methyl ester with diazomethane according to the literature procedure (97% yield).[12] To a THF (140 mL) solution of diisopropylamine (3.14 mL, 22.1 mmol) cooled at 0°C under Ar was added slowly a *n*-hexane solution of *n*-BuLi (20.1 mmol), and the mixture was stirred at 0°C for 15 min and then cooled to −78°C. A THF (10 mL) solution of the methyl ester obtained above (4.38 g, 20.1 mmol) was slowly added, and the mixture was stirred for 30 min at −78°C. To this solution was slowly added a HMPA (4.5 mL) solution of methyl iodide (1.4 mL, 22.1 mmol), and the mixture was stirred for 30 min at −78°C. Addition of saturated NH_4Cl aqueous solution at 0°C, extraction three times with diethyl ether, washing the organic layer with brine, drying with anhydrous $MgSO_4$, concentration under vacuum, and purification two times by flash column chromatography (*n*-hexane:CH_2Cl_2:AcOEt=100:10:5 and 100:20:10) gave methyl 2-(α,α,α-trifluoro-*p*-tolyl)propionate (3.50 g) in 74% yield. To lithium aluminum hydride (0.85 g, 22.4 mmol) in diethyl ether (25 mL) at 0°C was added a diethyl ether solution (5 mL) of the ester obtained. The mixture was stirred for 2 h at room temperature and then cooled to 0°C. The reaction was quenched with 1N HCl. Extraction with CH_2Cl_2, washing with brine, drying with anhydrous Na_2SO_4, concentration, and purification with flash column chromatography (*n*-hexane:AcOEt=5:1) gave 2-(α,α,α-trifluoro-*p*-tolyl)propan-1-ol in 74% yield. To a CH_2Cl_2 solution (25 mL) of PDC (7.65 g, 20 mmol) was added a CH_2Cl_2 solution (5 mL) of the alcohol, and the mixture was stirred for 16 h. Filtration with Celite followed by purification with a short column (*n*-pentane:diethyl ether=20:1) gave 2-(α,α,α-trifluoro-*p*-tolyl)propanal. To diethyl malonate in benzene (8 mL) at 50°C was added a benzene solution (2.5 mL) of the aldehyde obtained (0.3 g, 2.12 mmol). Piperidine (0.01 mL, 0.08 mmol), acetic acid (0.01 mL, 0.4 mmol) and benzene (20 mL) were added. The mixture was heated at 105°C for 4 h with Dean-Stark distillation head to remove water produced in the reaction, and then stirred for 12 h at 80°C. Addition of ether (10 mL), 1% HCl (5 mL) and 1% $NaHCO_3$ aqueous solution (5 mL) at 0°C, washing two times with water, extraction three times with ether, drying with anhydrous Na_2SO_4, concentration under vacuum, and purification two times by flash column chromatography (*n*-hexane: CH_2Cl_2:AcOEt=50:1:2 and 20:1:2) gave **11** in

38% yield from 2-(α,α,α-trifluoro-*p*-tolyl)propan-1-ol: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, *J*=7.0 Hz, 3H), 1.36 (t, *J*=7.0 Hz, 3H), 1.48 (d, *J*=7.3 Hz, 3H), 3.94–4.05 (m, 1H), 4.23 (q, *J*=7.0 Hz, 2H), 4.32 (q, *J*=7.0 Hz, 2H), 6.95 (d, *J*=10.8 Hz, 1H), 7.38 (d, *J*=7.8 Hz, 2H), 7.58 (d, *J*=7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.11, 14.19, 26.73, 39.42, 61.57, 125.76, 127.66, 127.93, 128.72, 150.48, 163.94, 165.33; IR (neat) 3026, 2928, 2854, 1733, 1646, 1449, 1437, 1367, 1255, 1233, 1194, 1156, 1066, 1055, 999, 949, 932, 838, 758, 729, 669 cm^{-1}; HRMS *m/z* Calcd for $C_{17}H_{19}O_4F_3$:344.1235. Found: 344.1229. The general procedure mentioned above for the preparation of trifluoro ester was applied for the synthesis of **13** (from ethyl *p*-tolylacetate) and **14** (from ethyl *p*-methoxyphenylacetate).

Ethyl 2-ethoxycarbonyl-4-phenyl-2-butenoate (12). The diester **12** was prepared by the reaction of 2-phenylpropionaldehyde with diethyl malonate under the Lehnert's condition[5] in 70% yield: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, *J*=7.0 Hz, 3H), 1.31 (t, *J*=7.0 Hz, 3H), 1.44 (d, *J*=7.0 Hz, 3H), 3.87 (dq, *J*=7 and 11 Hz, 1H), 4.16 (q, *J*=7 Hz, 2H), 4.24 (q, *J*=7 and 11 Hz, 2H), 6.85 (d, *J*=11 Hz, 1H), 7.22 (m, 5H); IR (neat) 2980, 1730, 1640, 1600, 1500, 1450, 1370, 1250, 1220, 1140, 1100, 1070, 1020, 860, 760, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{16}H_{20}O_4$:276.1362. Found: 276.1363.

Methyl 4-methyl-2-(methoxycarbonyl)-4-*p*-tolyl-2-butenoate (13). Purification of the crude product two times by flash column chromatography (*n*-hexane:AcOEt=50:1 and 20:1) gave **13** in 10% yield from 2-(*p*-tolyl)propan-1-ol: ^{1}H NMR ($CDCl_3$) δ 1.43 (d, *J*=7.0 Hz, 3H), 2.32 (s, 3H), 3.75 (s, 3H), 3.85 (s, 3H), 3.81–3.89 (m, 1H), 7.01 (d, *J*=10.8 Hz, 1H), 7.13 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 20.27, 20.99, 39.27, 52.29, 52.34, 125.90, 126.99, 129.48, 136.63, 193.36, 153.06, 164.49, 165.86; IR (neat) 3025, 2954, 2927, 2875, 2849, 1735, 1644, 1514, 1437, 1364, 1309, 1275, 1248, 1223, 1195, 1143, 1077, 1047, 1017, 988, 942, 843, 812, 768, 668, 540 cm^{-1}; HRMS *m/z* Calcd for $C_{15}H_{18}O_4$:262.1205. Found: 262.1206.

Ethyl 4-methyl-2-(ethoxycarbonyl)-4-*p*-methoxylphenyl-2-butenoate (14). Purification of the crude product two times by flash column chromatography (CH_2Cl_2:diethyl ether=200:1 and 100:1) gave **14** in 35% yield from 2-(*p*-methoxyphenyl)propan-1-ol: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, *J*=7.3 Hz, 3H), 1.34 (t, *J*=7.3 Hz, 3H), 1.42 (d, *J*=7.0 Hz, 3H), 3.78 (s, 1H), 3.81–3.88 (m, 1H), 4.21 (q, *J*=7.0 Hz, 2H), 4.33 (q, *J*=7.0 Hz, 1H), 6.86 (d, *J*=8.9 Hz, 2H), 6.93 (d, *J*=10.5 Hz, 1H), 7.18 (d, *J*=8.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.11, 14.20, 38.71, 55.29, 61.31, 114.20, 126.53, 128.12, 134.52, 152.03, 158.61, 164.10, 165.55; IR (neat) 2983, 2938, 2909, 2838, 1733, 1608, 1514, 1465, 1445, 1369, 1307, 1251, 1181, 1118, 1096, 1072, 1033, 858, 831, 808, 756, 669 cm^{-1}; HRMS *m/z* Calcd for $C_{17}H_{22}O_5$:306.1468. Found: 306.1470.

Reaction of methylcopper reagents

To a diethyl ether solution of 3 equiv. of the copper reagents, cooled at −78°C, was slowly added a diethyl ether (2 mL) solution of substrate (0.3 mmol); the mixture was stirred for 1 or 2 h at −78°C. The usual workup gave the products, whose diastereomer ratios were determined by a GLC and by ^{1}H NMR. Methylcopper reagents were prepared as follows. MeCu: A diethyl ether solution of MeLi·LiBr (0.86 M×1.05 mL, 0.9 mmol) was slowly added to a precooled diethyl ether (3 mL) suspension of CuI (171.4 mg, 0.9 mmol) at 0°C, stirring was continued for 5 min at this temperature, and then the mixture was cooled to −78°C. Me_2CuLi: a procedure similar to above, except for the use of 2 equiv. MeLi·LiBr, was used. MeCu(CN)Li: a diethyl ether solution of MeLi·LiBr (0.86 M×1.05 mL, 0.9 mmol) was added slowly to a precooled diethyl ether (3 mL) suspension of CuCN (80.6 mg, 0.9 mmol) at −78°C. The mixture was allowed to warm to 0°C, and a homogeneous solution was obtained. After a few minutes, the solution was cooled to 78°C. $Me_2Cu(CN)Li_2$: a procedure similar to above, except for the use of 2 equiv. of MeLi·LiBr.

Reaction of butylcopper reagents

A procedure similar to that above, except for the use of BuLi-hexane solution instead of MeLi·LiBr and for the use of −50°C instead of 0°C.

Reaction of methallylcopper reagents

To a diethyl ether solution of 3 equiv. of the copper reagents, cooled at −40°C, was added a diethyl ether (2 mL) solution of substrate (0.3 mmol), and the mixture was stirred for 1 h at −40°C. The usual workup followed by a short silica-gel column chromatography (*n*-hexane as an eluent) to remove tributyltin residues gave the products, which were analyzed by a capillary GLC. Methallyllithium was prepared from methallyltributyltin and *n*-BuLi according to the literature procedure.[13] Methallylcopper reagents were prepared in the following way. (Methallyl)Cu: Methallyllithium (0.9 mmol) was slowly added to a diethyl ether (3 mL) suspension of CuI (171.4 mg, 0.9 mmol) at −40°C, and the mixture was stirred for 10 min. (Methallyl)$_2$CuLi: 2 equiv. of methallyllithium were used at −40°C. (Methallyl)Cu(CN)Li: Methallyllithium (0.9 mmol) was slowly added to a diethyl ether (3 mL) solution of CuCN (80.6 mg, 0.9 mmol), cooled at −40°C, and the mixture was stirred for 10 min at this temperature. (Methallyl)$_2$Cu(CN)Li$_2$: a procedure similar to above, except for the use of 2 equiv. of methallyllithium.

3-Methyl-4-phenyl-2-pentanone (15a and 16a). 15a: ^{1}H NMR ($CDCl_3$) δ 1.25 (d, *J*=6.6 Hz, 3H), 1.31 (d, *J*=7.0 Hz, 3H), 2.19 (s, 3H), 2.79 (m, 1H), 3.00 (m, 1H), 7.15–7.33 (m, 5H); **16a:** ^{1}H NMR ($CDCl_3$) δ 1.11 (d, *J*=6.6 Hz, 3H), 1.24 (d, *J*=7.0 Hz, 3H), 1.88 (s, 3H), 2.79 (m, 1H), 3.00 (m, 1H), 7.15–7.33 (m, 5H); IR (neat) 2990, 2950, 1710, 1550, 1500, 1460, 1360, 1170, 1080, 770, 710 cm^{-1}; HRMS *m/z* Calcd for $C_{12}H_{16}O$: 176.1201. Found: 176.1197.

3-Butyl-4-phenyl-2-pentanone (15b and 16b). 15b: ^{1}H NMR ($CDCl_3$) δ 0.77–0.96 (m, 3H), 1.05–1.57 (m, 9H), 2.14 (s, 3H), 2.30–2.95 (m, 2H), 7.09 (m, 5H); **16b:** ^{1}H NMR ($CDCl_3$) δ 0.77–0.96 (m, 3H), 1.05–1.57 (m, 9H), 1.25 (d, *J*=7.0 Hz, 3H), 1.74 (s, 3H), 2.30–2.95 (m, 2H), 7.09 (m, 5H); IR (neat) 2980, 2940, 1710, 1550, 1500, 1460,

1360, 1160, 770, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{15}H_{22}O$: 218.1671. Found: 218.1672.

Ethyl 2-cyano-3-methyl-4-phenylpentanoate (19a and 20a). ^1H NMR ($CDCl_3$); The following signals were of four diastereomeric mixtures. δ 0.86 (d, J=6.6 Hz)+0.90 (d, J=6.6 Hz) (3H), 1.19–1.36 (m, 3H), 2.42 (m, 1H), 2.72–3.02 (m, 1H), 3.21 (d, J=3.3 Hz) +3.37 (d, J=6.2 Hz) +3.84 (d, J=4.0 Hz) (1H), 4.21 (d, J=7.0 Hz) +4.29 (d, J=7.0 Hz) (2H), 7.28 (m, 5H); IR (neat) 2990, 2950, 2270, 1740, 1610, 1500, 1460, 1380, 1310, 1260, 1200, 1100, 1030, 860, 780, 710 cm^{-1}; HRMS *m/z* Calcd for $C_{15}H_{19}NO_2$: 245.1416. Found: 245.1416.

Ethyl 3-butyl-2-cyano-4-phenylpentanoate (19b and 20b). ^1H NMR ($CDCl_3$); the following signals were of four diastereomeric mixtures. δ 0.77–0.91 (m, 3H), 1.15–1.66 (m, 12H), 2.41 (m, 1H), 2.75–2.99 (m, 1H), 3.24 (d, J=3.3 Hz) +3.56 (d, J=3.3 Hz) +3.64 (d, J=2.9 Hz) +3.70 (d, J=2.9 Hz) (1H), 4.20–4.28 (m, 2H), 7.24 (m, 5H); IR (neat) 2970, 2880, 2260, 1740, 1610, 1500, 1470, 1460, 1380, 1250, 1030, 770, 410 cm^{-1}; HRMS *m/z* Calcd for $C_{18}H_{25}NO_2$: 287.1885. Found: 287.1890.

Ethyl 2-ethoxycarbonyl-3-methyl-4-*p*-trifluoromethylphenylpentanoate (21a and 22a). 21a: ^1H NMR ($CDCl_3$) δ 0.83 (d, J=7.0 Hz, 3H), 1.22–1.33 (m, 9H), 2.48–2.54 (m, 1H), 2.83–2.96 (m, 1H), 3.23 (d, J=6.8 Hz, 1H), 4.13–4.24 (m, 4H), 7.34 (d, J=7.8 Hz, 2H), 7.66 (d, J=7.8 Hz, 2H); **22a:** ^1H NMR ($CDCl_3$) δ 1.00 (d, J=7.0 Hz, 3H), 1.22–1.33 (m, 9H), 2.48–2.54 (m, 1H), 2.83–2.96 (m, 1H), 3.21 (d, J=6.8 Hz, 1H), 4.13–4.24 (m, 4H), 7.34 (d, J=7.8 Hz, 2H), 7.66 (d, J=7.8 Hz, 2H); IR (CCl_4) 2981, 2938, 2879, 1752, 1734, 1619, 1369, 1326, 1131, 1072, 1036, 1017 cm^{-1}; HRMS *m/z* Calcd for $C_{18}H_{23}O_4F_3$: 360.1548. Found: 360.1541.

Ethyl 2-ethoxycarbonyl-3-methallyl-4-*p*-trifluoromethylphenylpentanoate (21b and 22b): 21b. ^1H NMR ($CDCl_3$) δ 1.16–1.65 (m, 12H), 1.95–2.35 (m, 2H), 2.62–2.80 (m, 1H), 3.00–3.20 (m, 1H), 3.51 (d, J=4.7 Hz, 1H), 3.96–4.24 (m, 4H), 4.69–4.77 (m, 2H), 7.32 (d, J=7.8 Hz, 2H), 7.55 (d, J=8.1 Hz, 2H); **22b:** ^1H NMR ($CDCl_3$) δ 1.16–1.65 (m, 12H), 1.95–2.35 (m, 2H), 2.62–2.80 (m, 1H), 3.00–3.20 (m, 1H), 3.33 (d, J=6.5 Hz, 1H), 3.96–4.24 (m, 4H), 4.69–4.77 (m, 2H), 7.39 (d, J=8.1 Hz, 2H), 7.55 (d, J=8.1 Hz, 2H); IR (CCl_4) 2981, 2962, 2931, 1749, 1733, 1619, 1465, 1446, 1376, 1327, 1168, 1131, 1071, 1017 cm^{-1}; HRMS *m/z* Calcd for $C_{21}H_{27}O_4F_3$: 400.1861 Found: 400.1859.

Ethyl 2-ethoxycarbonyl-3-methyl-4-phenylpentanoate (23a and 24a). 23a: ^1H NMR ($CDCl_3$) δ 0.83 (d, J=7.0 Hz, 3H), 1.29 (t, J=7.0 Hz, 6H), 1.31 (d, J=7.0 Hz, 3H), 2.36 (m, 1H), 2.81 (m, 1H), 3.30 (d, J=6.0 Hz, 1H), 4.12 (q, J=7.0 Hz, 4H), 7.12 (m, 5H); **24a:** ^1H NMR ($CDCl_3$) δ 1.01 (d, J=7.0 Hz, 3H), 1.23 (d, J=7.0 Hz, 3H), 1.25 (t, J=7.0 Hz, 6H), 2.36 (m, 1H), 2.81 (m, 1H), 3.07 (d, J=6.0 Hz, 1H), 4.08 (q, J=7.0 Hz, 4H), 7.12 (m, 5H); IR (CCl_4) 2980, 1750, 1730, 1600, 1500, 1460, 1370, 1310, 1260, 1230, 1170, 1150, 1030, 860, 770, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{17}H_{24}O_4$: 292.1675. Found: 292.1676.

Ethyl 3-butyl-2-ethoxycarbonyl-4-phenylpentanoate (23b and 24b). 23b: ^1H NMR ($CDCl_3$) δ 0.75–0.87 (m, 3H), 1.16–1.35 (m, 15H), 2.23 (m, 1H), 2.86 (m, 1H), 3.35 (d, J=6.0 Hz, 1H), 4.06 (q, J=7.0 Hz, 4H), 7.08 (m, 5H); **24b:** ^1H NMR ($CDCl_3$) δ 0.75–0.87 (m, 3H), 1.16–1.35 (m, 15H), 2.23 (m, 1H), 2.86 (m, 1H), 3.08 (d, J=6.0 Hz, 1H), 4.03 (q, J=7.0 Hz, 4H), 7.08 (m, 5H); IR (CCl_4) 2970, 2890, 1750, 1730, 1600, 1500, 1470, 1460, 1380, 1300, 1250, 1160, 1040, 860, 770, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{20}H_{30}O_4$: 334.2144. Found: 334.2147.

Ethyl 2-ethoxycarbonyl-3-methallyl-4-phenylpentanoate (23c and 24c). 23c: ^1H NMR ($CDCl_3$) δ 1.18–1.32 (m, 11H), 1.64 (s, 3H), 2.01 (d, J=17.6 Hz, 1H), 2.81–3.05 (m, 2H), 2.15–2.38 (m, 1H), 2.61–2.79 (m, 1H), 2.94–3.09 (m, 1H), 3.52 (d, J=5.1 Hz, 1H), 3.99–4.20 (m, 4H), 4.71 (d, J=7.6 Hz, 2H), 5.48 (dt, J=10.8 and 16.2 Hz, 1H), 7.18–7.29 (m, 5H); **24c:** ^1H NMR ($CDCl_3$) δ 1.18–1.32 (m, 11H), 1.56 (s, 3H), 2.01 (d, J=17.6 Hz, 1H), 2.81–3.05 (m, 2H), 2.15–2.38 (m, 1H), 2.61–2.79 (m, 1H), 2.94–3.09 (m, 1H), 3.33 (d, J=6.5 Hz, 1H), 3.99–4.20 (m, 4H), 4.71 (d, J=7.6 Hz, 2H), 5.48 (dt, J=10.8 and 16.2 Hz, 1H), 7.18–7.29 (m, 5H); IR (CCl_4) 3076, 3029, 2982, 2938, 1749, 1732, 1495, 1452, 1373, 1252, 1222, 1174, 1156, 1038, 849, 701 cm^{-1}; HRMS *m/z* Calcd for $C_{20}H_{28}O_4$: 322.1987. Found: 322.1982.

Methyl 2-methoxycarbonyl-3-methyl-4-*p*-tolylpentanoate (25a and 26a). 25a: ^1H NMR ($CDCl_3$) δ 0.81 (d, J=7.0 Hz, 3H), 1.28 (d, J=7.3 Hz, 3H), 2.31 (s, 3H), 2.41–2.50 (m, 1H), 2.73–2.80 (m, 1H), 3.45 (d, J=7.6 Hz, 1H), 3.69 (d, J=1.4 Hz, 6H), 7.00–7.10 (m, 4H); **26a:** ^1H NMR ($CDCl_3$) δ 1.00 (d, J=6.8 Hz, 3H), 1.21 (d, J=7.0 Hz, 3H), 2.31 (s, 3H), 2.41–2.50 (m, 1H), 2.73–2.80 (m, 1H), 3.30 (d, J=6.5 Hz, 1H), 3.69 (d, J=1.4 Hz, 6H), 7.00–7.10 (m, 4H); IR (CCl_4) 2973, 2953, 2927, 1756, 1738, 1515, 1456, 1436, 1363, 1311, 1264, 1232, 1195, 1160, 1033, 1021, 545 cm^{-1}; HRMS *m/z* Calcd for $C_{16}H_{22}O_4$: 278.1518. Found: 278.1521.

Methyl 2-methoxycarbonyl-3-methallyl-4-*p*-tolylpentanoate (25b and 26b). 25b: ^1H NMR ($CDCl_3$) δ 1.22 (d, J=6.8 Hz, 3H), 1.65 (s, 3H), 2.08–2.28 (m, 2H), 2.31 (s, 3H), 2.59–2.72 (m, 1H), 2.89–3.02 (m, 1H), 3.52 (d, J=6.5 Hz, 1H), 3.62 (s, 3H), 3.71 (s, 3H), 4.71 (t, J=8.6 Hz, 2H), 7.11 (d, J=8.6 Hz, 2H); **26b:** ^1H NMR ($CDCl_3$) δ 1.22 (d, J=7.3 Hz, 3H), 1.65 (s, 3H), 2.08–2.28 (m, 2H), 2.31 (s, 3H), 2.59–2.72 (m, 1H), 2.89–3.02 (m, 1H), 3.37 (d, J=6.2 Hz, 1H), 3.57 (s, 3H), 3.68 (s, 3H), 4.71 (t, J=8.6 Hz, 2H), 7.11 (d, J=8.6 Hz, 2H); IR (CCl_4) 2969, 2952, 2924, 1754, 1739, 1647, 1514, 1458, 1435, 1159, 894 cm^{-1}; HRMS *m/z* Calcd for $C_{19}H_{26}O_4$: 318.1831. Found: 318.1835.

Ethyl 2-ethoxycarbonyl-3-methyl-4-*p*-methoxyphenylpentanoate (27a and 28a). 27a: ^1H NMR ($CDCl_3$) δ 0.81 (d, J=6.8 Hz, 3H), 0.83–1.90 (m, 11H), 2.63–2.73 (m, 1H), 3.07 (dt, J=5.4 and 10.8 Hz, 1H), 3.60 (d, J=10.3 Hz, 1H), 3.70 (s, 3H), 3.73 (s, 3H), 4.97–5.12 (m, 2H), 5.93 (dt, J=10.8 and 16.2 Hz, 1H); **28a:** ^1H NMR ($CDCl_3$) δ 0.81 (d, J=6.8 Hz, 3H), 0.83–1.90 (m, 11H), 2.63–2.73 (m, 1H), 3.07 (dt, J=5.4 and 10.8 Hz, 1H), 3.70 (d, J=3.0 Hz, 1H), 3.70 (s, 3H), 3.73 (s, 3H), 4.97–5.12 (m, 2H), 5.68 (dt,

J=8.1 and 16.2 Hz, 1H); IR (CCl_4) 2952, 2927, 2854, 1761, 1741, 1457, 1449, 1435, 1261, 1196, 1146, 924 cm^{-1}; HRMS *m/z* Calcd for $C_{18}H_{26}O_5$: 322.1780. Found: 322.1783.

Ethyl 2-ethoxycarbonyl-3-methallyl-4-*p*-methoxyphenylpentanoate (27b and 28b). 27b: ^1H NMR ($CDCl_3$) δ 1.18–1.31 (m, 9H), 1.52 (s, 3H), 2.01–2.28 (m, 2H), 3.49 (d, J=5.1 Hz, 1H), 3.79 (s, 3H), 4.02–4.19 (m, 4H), 4.59–4.64 (m, 2H), 6.83 (d, J=8.9 Hz, 2H), 7.11 (d, J=8.6 Hz, 2H); **28b:** ^1H NMR ($CDCl_3$) δ 1.18–1.31 (m, 9H), 1.52 (s, 3H), 2.01–2.28 (m, 2H), 3.33 (d, J=6.8 Hz, 1H), 3.79 (s, 3H), 4.02–4.19 (m, 4H), 4.59–4.64 (m, 2H), 6.83 (d, J=8.9 Hz, 2H), 7.16 (d, J=8.4 Hz, 2H); IR (CCl_4) 2982, 2937, 2909, 2836, 1748, 1733, 1612, 1513, 1464, 1443, 1373, 1303, 1249, 1177, 1155, 1041, 894 cm^{-1}; HRMS *m/z* Calcd for $C_{21}H_{30}O_5$: 362.2093. Found: 362.2094.

trans Ester **31** and *cis* ester **32** were prepared by the reaction of commercially available 2-phenylpropanal with $(MeO)_2POCH_2CO_2Et$ according to the general procedure.[8] The 77:23 mixture of *trans* and *cis* ester was easily separated by column chromatography on silica gel (hexane: diethyl ether=20:1). *trans* Ester **31** was obtained in 76% yield, and *cis* ester **32** was gained 22% yield.

(*E*)-Ethyl 4-phenyl-2-pentenoate (31). ^1H NMR ($CDCl_3$) δ 1.24 (t, J=7 Hz, 3H), 1.40 (d, J=7 Hz, 3H), 3.57 (dq, J=7 and 7 Hz, 1H), 4.11 (q, J=7 Hz, 2H), 5.72 (dd, J=2 and 16 Hz, 1H), 7.05 (dd, J=7 and 16 Hz, 1H), 7.18 (m, 5H); IR (neat) 2980, 1720, 1650, 1600, 1495, 1450, 1370, 1270, 1170, 1030, 980, 860, 760, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{13}H_{16}O_2$: 204.1150. Found: 204.1150.

(*Z*)-Ethyl 4-phenyl-2-pentenoate (32). ^1H NMR ($CDCl_3$) δ 1.28 (t, J=7 Hz, 3H), 1.39 (d, J=7 Hz, 3H), 4.14 (q, J=7 Hz, 2H), 4.94 (dq, J=7 and 11 Hz, 1H), 5.65 (d, J=11 Hz, 1H), 6.16 (dd, J=11 and 11 Hz, 1H), 7.25 (m, 5H); IR (neat) 2980, 2940, 1720, 1640, 1450, 1410, 1390, 1200, 1110, 1080, 1030, 830, 740, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{13}H_{16}O_2$: 204.1150. Found: 204.1151.

Ethyl 3-methyl-4-phenylpentanoate (33 and 34, R=Me). 33: ^1H NMR ($CDCl_3$) δ 0.81 (d, J=6.6 Hz, 3H), 1.25 (t, J=7.3 Hz, 3H), 1.27 (d, J=7.0 Hz, 3H), 2.05 (dd, J=9.0 and 14.3 Hz, 1H), 2.21 (m, 1H), 2.44 (dd, J=4.8 and 14.3 Hz, 1H), 2.65 (m, 1H), 4.12 (q, J=7.3 Hz, 1H), 7.15–7.31 (m, 5H); **34:** ^1H NMR ($CDCl_3$) δ 0.97 (d, J=6.6 Hz, 3H), 1.24 (t, J=7.3 Hz, 3H), 1.25 (d, J=7.0 Hz, 3H), 2.05 (dd, J=9.0 and 14.3 Hz, 1H), 2.21 (m, 1H), 2.44 (dd, J=4.8 and 14.3 Hz, 1H), 2.65 (m, 1H), 4.12 (q, J=7.3 Hz, 1H), 7.15–7.31 (m, 5H); IR (neat) 2980, 1730, 1600, 1500, 1450, 1380, 1260, 1170, 1030, 770, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{14}H_{20}O_2$: 220.1463. Found: 220.1466.

Ethyl 3-butyl-4-phenylpentanoate (33 and 34, R=Bu). 33: ^1H NMR ($CDCl_3$) δ 0.82–0.91 (m, 3H), 1.12–1.40 (m, 12H), 2.11–2.30 (m, 3H), 2.84 (dq, J=7.0 and 7.0 Hz, 1H), 4.08 (q, J=7.1 Hz, 2H), 7.17–7.29 (m, 5H); **34:** ^1H NMR ($CDCl_3$) δ 0.82–0.91 (m, 3H), 1.12–1.40 (m, 12H), 2.11–2.30 (m, 3H), 2.77 (dq, J=7.0 and 7.0 Hz, 1H), 4.08 (q, J=7.1 Hz, 2H), 7.17–7.29 (m, 5H); IR (neat) 2980, 2950, 1730, 1460, 1380, 1170, 1040, 770, 700 cm^{-1}; HRMS *m/z* Calcd for $C_{17}H_{26}O_2$: 262.1939. Found: 262.1936.

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