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S_N2' Reaction of Organozinc Reagents Activated by Catalytic *t*Bu-P4 Base in the Presence of LiCl

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Abstract: The *t*Bu-P4 base was found to be an excellent catalyst for the activation of organozinc reagents. The base was used to promote the S_N2' reaction of α,β-unsaturated esters bearing a γ-chloride in the reactions with various organozinc reagents in the presence of LiCl. The reactions proceeded in high yield with excellent chemo-and regioselectivity. The role of LiCl appears to be the activation of the γ-chloride of the α,β-unsaturated esters, which was confirmed by NMR spectroscopic study.

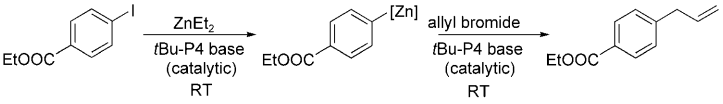
Keywords: lithium · nucleophilic substitution · phosphazene bases · zinc

Introduction

Organozinc reagents are one of the most useful class of organometallic reagents for organic synthesis.[1] The easy accessibility and high functional group compatibility of organozinc compounds allow numerous applications in synthetic chemistry. However, they occasionally require a catalyst to react smoothly with electrophiles. Many activation methods of organozinc reagents have been reported and one of the most prevalent activation methods is transmetalation using transition-metal catalysts.[2] However, transition metals are often expensive and sometimes their removal from the product after the reaction is detrimental, especially in multistep reactions in medicinal chemistry research. It seems still very important to provide a novel activation method without the help of transition-metal catalyst.

The S_N2' reaction is an important synthetic transformation for creating highly substituted sp^3 carbon centers effectively.[3] Recently, Lee and Hoveyda reported Cu-free allylic alkylation reactions with Grignard reagents using *N*-heterocyclic carbenes as Lewis base catalyst.[4] However, for the S_N2' reaction of organozinc reagents the use of transition-metal catalyst seemed still essential.[5]

We recently reported that the use of catalytic *t*Bu-P4 base[6] dramatically improved the performance of halogen-zinc exchange of aryl iodides (Scheme 1).[7] This activation is considered to closely relate to the donation of *t*Bu-P4 base to zinc atom of dialkylzinc reagents, which increases the electron density of alkyl group to enhance the reactivity. Herein we wish to report the *t*Bu-P4 base catalyzed S_N2' reaction of organozinc reagents in the presence of LiCl without using transition metal catalysts.[8]



Scheme 1. *t*Bu-P4 base catalyzed halogen–zinc exchange.

Results and Discussion

The S_N2' reaction was first examined with α,β-unsaturated esters bearing a γ-chloride (**1a**), two equivalents of diethylzinc, and 10 mol% of *t*Bu-P4 base in various organic solvents (Table 1, entries 1–4). It was suggested that the catalytic activity was solvent dependent; among the solvents, DMF was found to be the best for the catalytic activity (Table 1, entry 4). In this case, no S_N2 reaction product was detected in the NMR analysis of the crude material. By lowering the reaction temperature to 0°C, the yield of **2a** increased to 75% (Table 1, entry 5). The use of a weaker

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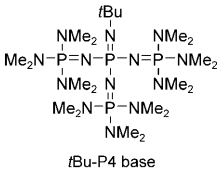
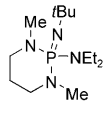
phosphazene base such as 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP; see below) resulted in lower yields (Table 1, entry 6); the reaction did not proceed in the absence of a phosphazene base (Table 1, entry 7). The use of an additive was then examined to facilitate the reaction. When LiCl was used as an additive, the reaction proceeded more smoothly, and the yield of **2a** was improved up to 90% (Table 1, entry 7).

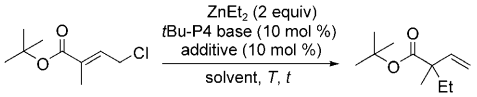


*t*Bu-P4 base



BEMP

Table 1. Optimization of S_N2' reaction conditions.



1a **2a**

Entry	Base	Additive	Solvent	*T*	*t* [h]	Yield [%]
1	*t*Bu-P4 base	–	THF	RT	24	32[a]
2	*t*Bu-P4 base	–	toluene	RT	24	18[a]
3	*t*Bu-P4 base	–	DMF	RT	2	71
4	*t*Bu-P4 base	–	DMF	0°C	2	75
5	*t*Bu-P4 base	–	DMF	−40°C	12	63[a]
6	BEMP	–	DMF	0°C	2	29
7	–	–	DMF	0°C	2	0
8	*t*Bu-P4 base	LiCl	DMF	0°C	2	90

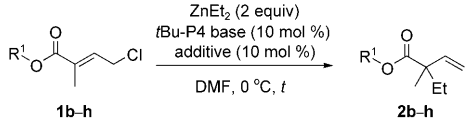
[a] Yield based on NMR peak analysis.

As shown in Table 1, it was found that *t*Bu-P4 base is an excellent catalyst for the S_N2' reaction of organozinc reagents; the presence of LiCl was also found to be favorable for a smooth conversion. With the aim to further develop the synthetic utility of this method, reactions with other substrates were investigated.

Other α,β-unsaturated esters bearing a γ-chloride substrate, such as phenyl and benzyl esters, were reacted with diethylzinc under the same conditions to give the corresponding esters in 87 (**2b**) and 93% (**2c**), respectively (Table 2, entries 1 and 2). Various substituents on the α,β-unsaturated esters bearing a γ-chloride were compatible in the S_N2' reaction. The substitution with metal coordinating functional groups such as a methoxy group did not affect the reaction, and the corresponding ester **2d** was obtained in good yields (Table 2, entry 3). The presence of electrophilic functional groups was examined and the tolerance of cyano, carbonyl, nitro and iodo groups during the S_N2' reaction is considered to be synthetically important and attractive (Table 2, entries 4–7). These highly chemoselective conversions in the presence of functional groups are considered to be difficult using conventional transition-metal catalyzed processes, especially in the presence of the iodo group.

Our next interest focused on the study of the substituent effect at the α-position of the α,β-unsaturated esters. Alkyl-, allyl-substituted substrates and an unsubstituted substrate were reacted with diethylzinc under the same conditions and the desired products were obtained in good yields (Table 3, entries 1–3). But, when phenyl-substituted substrate was used, the selectivity was siginificantly lowered and desired product was isolated in only 38% yield together with S_N2 product in 61% yield (Table 3, entry 4).

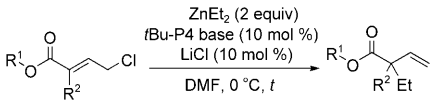
Table 2. S_N2' reaction of functionalized substrates.



1b–h **2b–h**

Entry	R^1	*t* [h]	Yield [%]
1	Ph	2	87
2	Bn	2	93
3	4-MeO-Bn	2	91
4	4-NC-Ph	2	84
5	4-Bz-Ph	2	88
6	4-O_2N-Ph	8	66
7	3-I-Bn	3	88

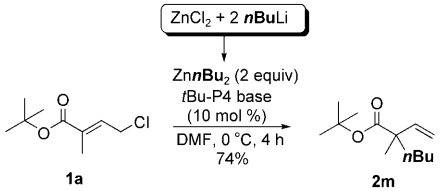
Table 3. Influence of α-substituents on S_N2' reaction.



1i–l **2i–l**

Entry	R^1	R^2	*t* [h]	Yield [%]
1	*t*Bu	*n*Bu	2	88
2	*t*Bu	Allyl	4	74
3	Bn	H	2	94
4	Me	Ph	2	38 (S_N2: 61)

We next examined the reaction of another alkylzinc with α,β-unsaturated esters bearing a γ-chloride. When di-*n*-butylzinc, prepared from *n*-butyllithium and zinc chloride, was used, the corresponding ester (**2m**) was obtained in 74% yield (Scheme 2).



1a **2m**

Scheme 2. Reaction using dibutylzinc.

^{1}H NMR spectra of dimethylzinc in the presence of *t*Bu-P4 base was measured for the preliminary estimation of the activation mechanism. As a result, the methyl signals of dimethylzinc in presence of *t*Bu-P4 base and no additive in THF at −20 °C were observed as sharp singlets at δ −1.06 and −0.89 ppm, respectively (Figure 1). This result suggested that dimethylzinc exist as the more anionically activated form in the presence of *t*Bu-P4 base by the electron-donating coordination to dimethylzinc. It has been known that the coodination of donors to alkylzinc compounds causes higher-field shifts of alkyl protons in ^{1}H NMR spectra.[9] It is assumed that the high reactivity in the presence of *t*Bu-P4 base is attributed to this enhanced anionic character.

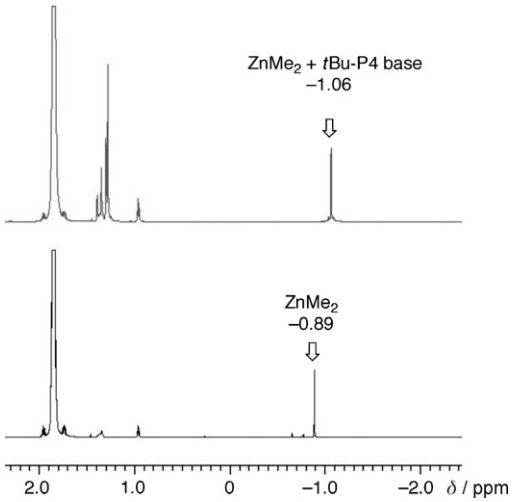


Figure 1. ^{1}H NMR spectra of dimethylzinc in the presence of *t*Bu-P4 base (THF, −20 °C).

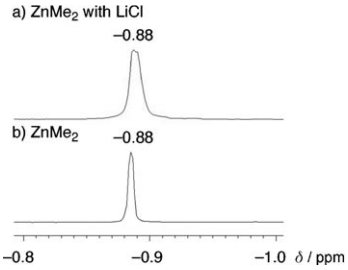


Figure 2. ^{1}H NMR spectra of dimethylzinc in the presence of LiCl (THF, −20 °C).

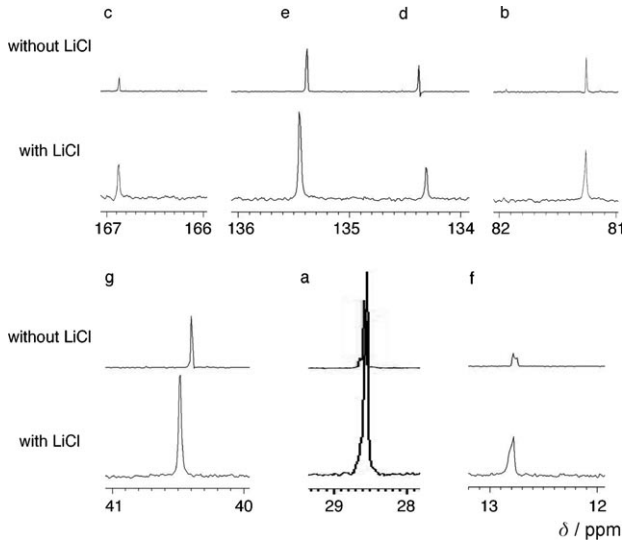


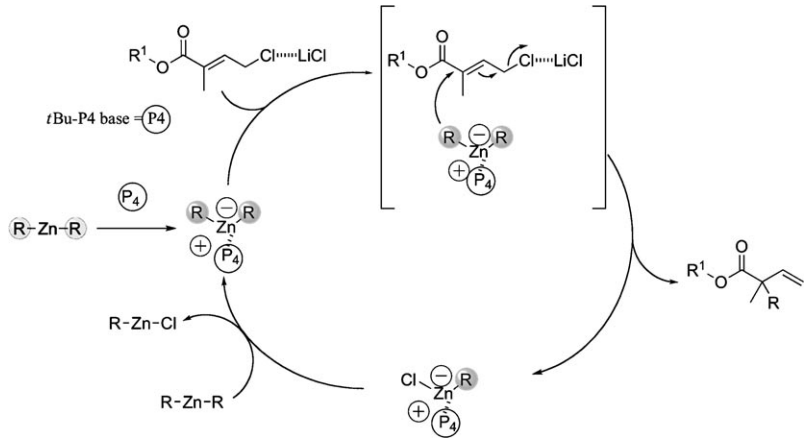
Figure 3. ^{13}C NMR spectra of substrate in the presence of LiCl (THF, RT).

Next, the effect of LiCl was investigated. The activating effect of LiCl to organometallic reagents was reported by Knochel et al.,[10] but the exact role of the salt still seemed unclear. To disclose the role of LiCl in our reaction, the ^{1}H and ^{13}C NMR spectrum of dimethylzinc or substrate with LiCl were examined carefully (Figures 2 and 3). The chemical shift of dimethylzinc in the presence of LiCl was the same chemical shift of dimethylzinc in the absence of LiCl (Figure 2). This result indicates that LiCl have little interaction with the organozinc reagents. On the other hand, the apparent changes of the chemical shifts of the substrate in the presence of LiCl were observed (Figure 3). In ^{13}C NMR spectra of the substrate with LiCl and without LiCl, the chemical shifts of carbonyl carbon were almost the same (Figure 3, c). However, the signals of alkenyl sp^2 carbons and allyl sp^3 carbon shifted (Figure 3, e, d and g). The signal shift of allyl sp^3 carbon was the largest (Figure 3g). This observation suggests that LiCl activates the substrate by coordinating to the γ-chloride of the substrate.

Based on these results which suggest that the *t*Bu-P4 base activates the organozinc reagents and LiCl activates the substrate, a possible catalytic cycle is proposed as shown in Scheme 3. First, *t*Bu-P4 base activates organozinc reagents anionically. Then, the activated organozinc reagents react with α,β-unsaturated esters bearing a γ-chloride coordinated by LiCl in a push–pull S_N2' fashion. The coordination of LiCl to the carbonyl of the substrates is also considered to be important, which would facilitate alkylation by the enhancement of electrophilicity at the α carbon.

Conclusions

The use of *t*Bu-P4 base as a catalyst was found to improve the performance of S_N2' reaction with organozinc reagents dramatically. ^{1}H NMR and ^{13}C NMR study suggested that this high reactivity is reflected by the coordination of *t*Bu-P4 base to organozinc and the activation of the substarate by LiCl, but the interaction of LiCl with organozinc reagents was not observed in our case. LiCl is known to change the aggregation state of organometallic compounds; an active species undetectable by NMR analysis may also be involved in the substitution. The efficient *t*Bu-P4 base and LiCl are considered to function independently, but still cooperatively in this S_N2' reaction. Further investigations on the scope and



Scheme 3. A possible catalytic cycle.

limitation of the *t*Bu-P4 base promoted reactions of organozinc compounds and mechanistic studies are currently underway.

Experimental Section

General methods: Reactions were carried out under Ar atmosphere using dry solvents. Melting points (m.p.) were determined with a Yazawa micro melting point apparatus and uncorrected. Infrared (IR) data were recorded on SensIR ATR (Attenuated Total Reflectance) FT-IR. The spectra were acquired in 32 scans per spectrum at a resolution of four using system ReactIR 2.20 software. Absorbance frequencies are reported in cm^{-1}. NMR data were recorded on either a JEOL AL400 spectrometer (395.75 MHz for ^1H, 99.50 MHz for ^{13}C). Chemical shifts are expressed in d (parts per million, ppm) values, and coupling constants are expressed in hertz (Hz). ^1H NMR spectra were referenced to a tetramethylsilane as an internal standard or to a solvent signal ($CDCl_3$: 7.26 ppm). ^{13}C NMR spectra were referenced to a tetramethylsilane as an internal standard or to a solvent signal ($CDCl_3$: 77.0 ppm). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, td = triple doublet, dq = double quartet, br = broad singlet. Low and high resolution mass spectra (LRMS and HRMS) were obtained from Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University, on a JEOL JMS-DX303 and JMS-700 spectrometer respectively.

Materials: Unless otherwise noted, materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used after appropriate purification (distillation or recrystallization). Flash column chromatographies were performed with Kanto silica gel 60N (spherical, neutral, 70–230 mesh).

General procedure: Under argon atmosphere, *t*Bu-P4 base (0.03 mL 1.0 M in hexane, 0.03 mmol) was added to a mixture of electrophile (0.3 mmol), diethyl zinc (0.60 mL 0.6 mmol), LiCl (1.3 mg 0.03 mmol) and dry DMF (0.4 mL) at 0 °C and the mixture was stirred 2–8 h at 0 °C. After the reaction, saturated aq. NH_4Cl and H_2O were added to the mixture. The mixture was extracted with AcOEt or Et_2O (3 × 30 mL). The combined organic layers were then washed with saturated aq. NaCl (50 mL). The solution was dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by SiO_2 column chromatography. All γ-chloro-α,β-unsaturated esters were synthesized using literature procedures.[4]

***tert*-Butyl 2-ethyl-2-methylbut-3-enoate (2a)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (49.8 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.85 (t, J = 7.5 Hz, 3H), 1.44 (s, 9H), 1.49 (s, 3H), 1.49–1.88 (m, 1H,), 1.68–1.80 (m, 1H), 5.02–5.09 (m, 2H), 5.98 ppm (dd, J = 18.1, 10.5 Hz, 1H); IR (neat): $\tilde{\nu}$ = 2973, 2933, 1725, 1459, 1368, 1246, 1136, 914, 850 cm^{-1}; LRMS (EI): m/z: 184 [M^+]; HRMS: m/z: calcd for $C_{11}H_{20}O_2$: 184.1463; found: 184.1447.

Phenyl 2-ethyl-2-methyl-3-enoate (2b): The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (53.3 mg, 87%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.98 (t, J = 7.2 Hz, H), 1.38 (s, 3H), 1.70–1.82 (m, 1H), 1.90–2.11 (m, 1H), 5.17–5.27 (m, 2H), 6.14 (dd, J = 17.6, 10.8 Hz, 1H), 7.04 (d, J = 7.6 Hz, 2H), 7.21 (t, J = 7.6 Hz, 1H), 7.35 ppm (t, J = 7.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 9.1, 20.0, 31.9, 49.2, 114.2, 121.4, 125.6, 129.2, 141.0, 150.9, 174.2 ppm; IR (neat): $\tilde{\nu}$ = 2977, 1723, 1640, 1457, 1368, 1167, 1136, 914, 849, 766 cm^{-1}; LRMS (EI): m/z: 204 [M^+]; HRMS: m/z: calcd for $C_{13}H_{16}O_2$: 204.1150; found: 204.1149.

Benzyl 2-ethyl-2-methylbut-3-enoate (2c): The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as yellowish oil (60.9 mg, 93%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.83 (t, J = 7.6 Hz, 3H), 1.28 (s, 3H), 1.58–1.69 (m, 1H), 1.74–1.83 (m, 1H), 5.05–5.19 (m, 2H), 5.12 (s, 2H), 6.03 (dd, J = 17.4 Hz, J = 10.8 Hz, 1H), 7.27–7.38 ppm (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 8.9, 19.9, 31.9, 49.0, 66.2, 113.7, 127.7, 128.4, 136.1, 141.3, 175.4 ppm; LRMS (EI): m/z: 218 [M^+]; HRMS: Calcd. for $C_{14}H_{18}O_2$: 218.1307, Found: 218.1325. IR (neat): $\tilde{\nu}$ = 2970, 1727, 1457, 1231, 1133, 1003, 916, 731, 696 cm^{-1}.

***para*-Methoxybenzyl 2-ethyl-2-methylbut-3-enoate (2d)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (67.8 mg, 91%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.81 (t, J = 7.2 Hz, 3H), 1.26 (s, 3H), 1.55–1.67 (m, 1H), 1.71–1.83 (m, 1H), 3.81 (s, 3H), 5.01–5.12 (m, 4H), 6.01 (dd, J = 17.6 Hz, J = 11.2 Hz, 1H), 6.87 (d, J = 8.4 Hz, 2H), 7.27 ppm (d, J = 8.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 8.9, 19.9, 31.9, 49.0, 55.2, 66.1, 113.5, 113.8, 128.3, 129.6, 141.4, 159.3, 175.5 ppm; IR (neat): $\tilde{\nu}$ = 2966, 1725, 1613, 1515, 1459, 1245, 1133, 1034, 920, 822 cm^{-1}; LRMS (EI): m/z: 248 [M^+]; HRMS: m/z: calcd for $C_{15}H_{20}O_3$: 248.1412; found: 248.1395.

***para*-Cyanophenyl 2-ethyl-2-methylbut-3-enoate (2e)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (57.8 mg, 84%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.97 (t, J = 7.2 Hz, 3H), 1.40 (s, 3H), 1.71–1.82 (m, 1H), 1.90–2.00 (m, 1H), 5.19–5.26 (m, 2H), 6.09 (dd, J = 17.2 Hz, J = 10.4 Hz, 1H), 7.19 (d, J = 8.8 Hz, 2H), 7.68 ppm (d, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 9.0, 19.9, 31.8, 49.3, 109.5, 114.8, 118.1, 122.6, 133.5, 140.2, 154.2, 173.4 ppm; IR (neat): $\tilde{\nu}$ = 2970, 2231, 1752, 1602, 1497, 1206, 1167, 1092, 901, 862 cm^{-1}; LRMS (EI): m/z: 229 [M^+]; HRMS: m/z: calcd for $C_{14}H_{15}NO_2$: 229.1103; found: 229.1103.

***para*-Benzoylphenyl 2-ethyl-2-methylbut-3-enoate (2f)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (81.4 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.99 (t, J = 7.6 Hz, 3H), 1.42 (s, 3H), 1.73–1.84 (m, 1H), 1.92–2.02 (m, 1H), 5.21–5.28 (m, 2H), 6.13 (dd, J = 17.6 Hz, J = 10.4 Hz, 1H), 7.17 (d, J = 8.8 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.79 (d, J = 7.6 Hz, 2H), 7.85 ppm (d, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 9.0, 20.0, 31.8, 49.3, 114.6, 121.3, 128.2, 129.8, 131.5, 132.3, 134.8, 137.6, 140.5, 154.1, 173.7, 195.2 ppm; IR (neat): $\tilde{\nu}$ = 2968, 1750, 1657, 1598, 1275,

1200, 1148, 1098, 924, 735, 704 cm^{-1}; LRMS (EI): m/z: 308 [M^+]; HRMS: m/z: calcd for $C_{20}H_{20}O_3$: 308.1412; found: 308.1399.

***para*-Nitrobenzyl 2-ethyl-2-methylbut-3-enoate (2g)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a yellow oil (52.1 mg, 66%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.84 (t, J=7.6 Hz, 3H), 1.31 (s, 3H), 1.61–1.72 (m, 1H), 1.77–1.87 (m, 1H), 5.09–5.29 (m, 2H), 5.21 (s, 2H), 6.02 (dd, J=17.6 Hz, 10.8 Hz, 1H), 7.49 (d, J=9.2 Hz, 2H), 8.22 ppm (d, J=9.2 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS): δ = 8.92, 19.80, 31.78, 49.02, 64.77, 114.12, 123.64, 127.98, 140.86, 143.36, 147.44, 175.14 ppm; IR (neat): $\tilde{\nu}$ = 3085, 2970, 1729, 1607, 1520, 1345, 1229, 1111, 735 cm^{-1}; LRMS (EI): m/z: 263 [M^+]; HRMS: m/z: calcd for $C_{14}H_{17}NO_4$: 263.1158; found 263.1158.

***ortho*-Iodobenzyl 2-ethyl-2-methylbut-3-enoate (2h)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 8:2) to give the title compound as a colorless oil (90.9 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.85 (t, J=7.6 Hz, 3H), 1.31 (s, 3H), 1.61–1.72 (m, 1H), 1.78–1.88 (m, 1H), 5.08–5.20 (m, 2H), 5.12 (s, 2H), 6.65 (dd, J=17,6 Hz, J=10.8 Hz, 1H), 7.01 (td, J=6.8 Hz, J= 2.4 Hz, 1H), 7.31–7.39 (m, 2H), 7.84 ppm (d, J=7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS): δ = 8.93, 19.83, 31.83, 49.11, 70.10, 98.14, 113.89, 128.23, 129.26, 129.66, 138.52, 139.42, 141.32, 175.30 ppm; IR (neat): $\tilde{\nu}$ = 3064, 2970, 1727, 1459, 1437, 1229, 1129, 1015, 918, 746 cm^{-1}; LRMS (EI): m/z: 344 [M^+]; HRMS: m/z: calcd for $C_{14}H_{17}IO_2$: 344.0273; found 344.0287.

***tert*-Butyl 2-butyl-2-ethylbut-3-enoate (2i)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (59.8 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.89 (t, J=7.2 Hz, 3H), 1.16–1.35 (m, 4H), 1.21 (s, 3H), 1.43 (s, 9H), 1.49–1.58 (m, 2H), 1.62–1.72 (m, 1H), 5.01–5.08 (m, 2H), 5.99 ppm (dd, J=17.6 Hz, J=10.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS): δ = 14.04, 20.49, 23.23, 26.84, 28.02, 39.03, 49.08, 80.11, 112.72, 142.44, 174.98 ppm; IR (neat): $\tilde{\nu}$ = 2958, 2933, 1725, 1459, 1366, 1272, 1254, 1135, 914, 850 cm^{-1}; LRMS (EI): m/z: 212 [M^+]; HRMS: m/z: calcd for $C_{13}H_{24}O_2$: 212.1776; found 212.1774.

***tert*-Butyl 2-ethyl-2-(2-propenyl) but-3-enoate (2j)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as an yellow oil (46.7 mg, 74%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.83 (t, J=7.2 Hz, 3H), 1.44 (s, 9H), 1.69 (q, J=7.2 Hz, 2H), 2.42 (d, J=7.2 Hz, 2H), 5.00–5.20 (m, 4H), 5.64–5.76 (m, 1H), 5.94 ppm (dd, J=17.6 Hz, J=10.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 8.6, 28.1, 28.6, 39.9, 52.7, 80.4, 114.3, 117.4, 134.1, 139.9, 173.8 ppm; IR (neat): $\tilde{\nu}$ = 2977, 1723, 1640, 1368, 1243, 1167, 1136, 914, 849 cm^{-1}; LRMS (EI): m/z: 210 [M^+]; HRMS: m/z: calcd for $C_{13}H_{22}O_2$: 210.1620; found: 210.1578.

Benzyl 2-ethylbut-3-enoate (2k): The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (57.6 mg, 94%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.90 (t, J=7.6 Hz, 3H), 1.54–1.65 (m, 1H), 1.75–1.87 (m, 1H), 2.97 (dt, J=8.3 Hz, J=7.3 Hz, 1H), 5.10–5.20 (m, 4H), 5.76–5.88 (m, 1H), 7.30–7.39 ppm (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 11.6, 25.4, 51.9, 66.2, 117.2, 127.9, 128.0, 128.4, 135.7, 135.9, 173.7 ppm; IR (neat): $\tilde{\nu}$ = 2694, 1733, 1457, 1167, 1144, 991, 920, 735, 696 cm^{-1}; LRMS (EI): m/z: 204 [M^+]; HRMS: m/z: calcd for $C_{13}H_{16}O_2$: 204.1150; found: 204.1137.

Methyl 2-ethyl-2-phenylbut-3-enoate (2l): The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 20:1) to give the title compound as a colorless oil (23.3 mg, 38%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.83 (t, J=7.6 Hz, 3H), 2.07–2.27 (m, 2H), 3.69 (s, 3H), 5.02 (d, J=18.0 Hz, 1H), 5.31 (d, J=10.8 Hz, 1H), 6.38 (dd, J=18.0, 10.8 Hz, 1H), 7.20–7.27 (m, 3H), 7.29–7.35 ppm (m, 5H); IR (neat): $\tilde{\nu}$ = 3087, 2950, 1731, 1459, 1434, 1227, 1123, 739, 698 cm^{-1}; LRMS (EI): m/z: 204 [M^+]; HRMS: m/z: calcd for $C_{13}H_{16}O_2$: 204.1150; found 204.1149.

Methyl 2-phenyl-2-hexenoate: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 20:1) to give the title compound as a colorless oil (37.4 mg, 61%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.87 (t, J=7.2 Hz, 3H), 1.44 (m, 2H), 2.05 (q, J= 7.6 Hz, 2H), 3.72 (s, 3H), 7.08 (t, J=7.6 Hz, 1H), 7.13–7.19 (m, 2H), 7.30–7.40 ppm (m, J=3H); IR (neat): $\tilde{\nu}$ = 2958, 1715, 1495, 1434, 1245, 1223, 1023, 764, 700 cm^{-1}; LRMS (EI): m/z: 204 [M^+]; HRMS: m/z: calcd. for $C_{13}H_{16}O_2$: 204.1150; found 204.1144.

***tert*-Butyl 2-butyl-2-ethylbut-3-enoate (2m)**: The crude material was purified by column chromatography on silica gel (hexane/ethyl acetate 10:1) to give the title compound as a colorless oil (47.1 mg, 74%). ^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.89 (t, J=7.2 Hz, 3H), 1.16–1.35 (m, 4H), 1.21 (s, 3H), 1.43 (s, 9H), 1.49–1.58 (m, 2H), 1.62–1.72 (m, 1H), 5.01–5.08 (m, 2H), 5.99 ppm (dd, J=17.6, 10.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS): δ = 14.04, 20.49, 23.23, 26.84, 28.02, 39.03, 49.08, 80.11, 112.72, 142.44, 174.98 ppm; IR (neat): $\tilde{\nu}$ = 2958, 2933, 1725, 1459, 1366, 1272, 1254, 1135, 914, 850 cm^{-1}; LRMS (EI): m/z: 212 [M^+]; HRMS: m/z: calcd for $C_{13}H_{24}O_2$: 212.1776; found 212.1774.

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