Efficient Cross-Coupling Reactions of (Pivaloyloxymethyl)zinc Chloride

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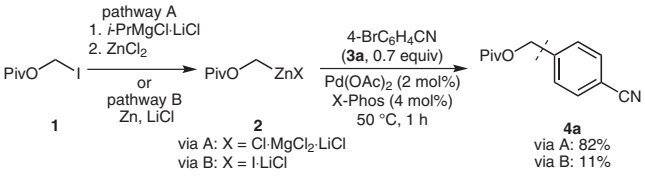
Abstract: (Pivaloyloxymethyl)zinc chloride, obtained by an iodine–magnesium exchange and subsequent transmetalation, shows a much higher reactivity in Negishi cross-couplings than the corresponding zinc organometallic, prepared by direct zinc insertion. Furthermore, a substituted derivative of (pivaloyloxymethyl)zinc chloride is prepared starting from pivaloyloxymethyl sulfoxide using TMPZnCl·LiCl (TMP = 2,2,6,6-tetramethylpiperidyl), followed by a sulfoxide–magnesium exchange.

Key words: organozinc reagents, carbenoids, cross-coupling, palladium, sulfoxides

Organometallic carbenoids are an important class of reagents with a range of applications in organic synthesis.[1] In particular, magnesium, zinc and copper carbenoids are valuable reagents used for homologations or cyclopropanations.[2] Several years ago, we reported the preparation of (pivaloyloxymethyl)zinc iodide by direct zinc insertion.[3] Although this zinc reagent participates efficiently in a range of reactions with electrophiles, such as acylations, allylations, 1,2- and 1,4-additions, an example of a palladium-catalyzed Negishi cross-coupling[4] with aryl halides has only been reported recently.[5] Thus, highly interesting structures, such as hydroxymethylated nucleosides can be prepared via a palladium-catalyzed cross-coupling using RCO_2-CH_2-ZnI, obtained by zinc dust insertion.[6] This method requires the use of an excess of the zinc reagent and only electron-poor electrophiles, especially 2-haloazines, show good reactivity.[7]

Herein, we report a new preparation of $PivOCH_2ZnX$ (Piv = *t*-BuCO, X = Cl-$MgCl_2$-LiCl), as well as the influence of this preparative method on the outcome of the subsequent cross-couplings. Although the preparation of (pivaloyloxymethyl)magnesium chloride ($PivOCH_2MgCl$) from iodomethyl pivalate (**1**) with isopropylmagnesium chloride (*i*-PrMgCl) has been reported,[8] a polar co-solvent was needed to solubilize the magnesium reagent at low temperature. We have found that the use of the lithium chloride (LiCl) complexed exchange reagent, *i*-PrMgCl·LiCl[9] (1.05 equiv) allows the preparation of well soluble $PivOCH_2MgCl$·LiCl in anhydrous tetrahydrofuran after 15 minutes at –78 °C. This reagent is stable at –40 °C for at least one hour. Transmetalation with zinc chloride ($ZnCl_2$) (1.1 equiv, –78 °C, 15 min) gave the (pivaloyloxymethyl)zinc reagent **2** (pathway A, X = Cl·$MgCl_2$·LiCl), which is comparable in stability at room temperature to the organometallic obtained by the insertion into **1** using zinc powder (2.0 equiv) in the presence of lithium chloride (1.0 equiv) (THF, 25 °C, 30 min, pathway B) (Scheme 1).



Scheme 1 Cross-coupling reaction of (pivaloyloxymethyl)zinc reagent **2** depending on the manner of preparation. *Reagents and conditions*: (A) (1) *i*-PrMgCl·LiCl (1.05 equiv), THF, –78 °C, 15 min; (2) $ZnCl_2$ (1.1 equiv), –78 °C, 15 min; (B) Zn (2.0 equiv), LiCl (1.0 equiv), THF, 25 °C, 30 min.

Comparing the zinc reagent **2**, obtained either by pathway A or B, in a palladium-catalyzed cross-coupling with, for example, 4-bromobenzonitrile (**3a**) (0.7 equiv) resulted in completely different reactivities (Scheme 1). Whereas the reaction of **2**, obtained via pathway A, in the presence of palladium(II) acetate [$Pd(OAc)_2$] (2%) and >2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos)[10] (4%) produced the desired product **4a** in 82% isolated yield after one hour at 50 °C, in the case of the zinc reagent **2**, prepared by zinc insertion (pathway B), only a low conversion of the electrophile was observed.[11] Studies regarding this difference in reactivity revealed that external addition of magnesium chloride ($MgCl_2$)[12] (1.0 equiv) and isopropyl iodide (*i*-PrI)[13] (1.0 equiv) to the insertion-derived $PivOCH_2ZnI$·LiCl species resulted in an increased yield of **4a** (50%), but still full conversion of the electrophile was not obtained after one hour at 50 °C. Furthermore, the zinc reagent counterion[14] seemed to influence the reactivity of **2** as the use of various zinc salts for the transmetalation, after iodine–magnesium exchange of **1**, gave varying yields of **4a** [$ZnCl_2$: 82%, $ZnBr_2$: 19%, ZnI_2: 46%, $Zn(OAc)_2$: 46%].

The cross-coupling of the (pivaloyloxymethyl)zinc reagent **2** prepared by pathway A was the most efficient. It provided excellent results in the cross-couplings with various aromatic halides of type **3** (Table 1). Using electron-poor aryl iodides bearing, for example, an ester, trifluoromethyl or amide function, resulted in the protected benzylic alcohols **4b–d** in good yields (Table 1, entries 1–3). Remarkably, electron-rich aryl substrates also underwent the cross-coupling with **2** when prepared according to

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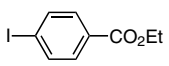
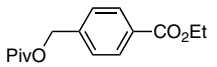
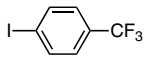
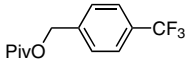
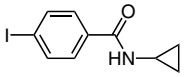
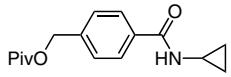
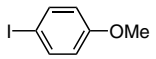
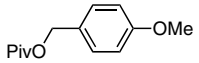
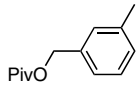
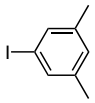
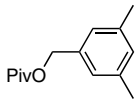
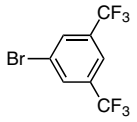
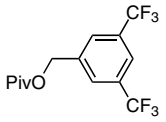
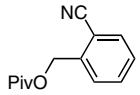
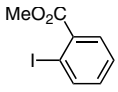
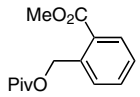
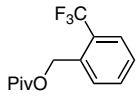
Table 1 Cross-Coupling of $PivOCH_2ZnCl{\cdot}MgCl_2{\cdot}LiCl$ (**2**) Obtained by Iodine–Magnesium Exchange and Subsequent Transmetalation with $ZnCl_2$

Entry	Electrophile	Product/Yield[a]
1		
	3b	**4b**: 75% (11%)[b]
2		
	3c	**4c**: 70%
3		
	3d	**4d**: 65%
4		
	3e	**4e**: 75%
5		
	3f	**4f**: 82%
6		
	3g	**4g**: 88%
7		
	3h	**4h**: 61%
8		
	3i	**4i**: 78%
9		
	3j	**4j**: 67%
10		
	3k	**4k**: 58%[c]

[a] Yield of isolated analytically pure product. *Reagents and conditions*: aryl halide **3** (0.7 equiv), $Pd(OAc)_2$ (2%), X-Phos (4%), THF, 50 °C, 1 h.
[b] Yield of **4b** by using zinc reagent **2** obtained by zinc insertion.
[c] Reaction time: 12 h.

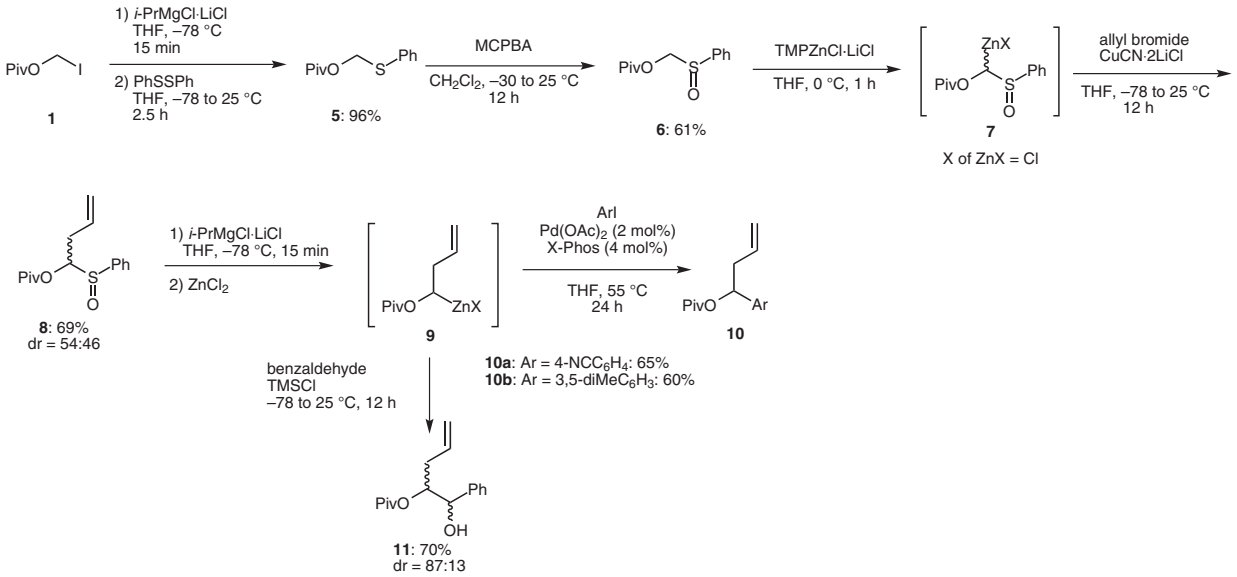
pathway A compared to that obtained via pathway B.[7] Thus, 4-iodoanisole (**3e**) underwent an efficient cross-coupling with **2** after one hour at 50 °C to give **4e** in 75% yield (Table 1, entry 4). Further evidence for the higher reactivity of the zinc reagent **2** prepared according to pathway A was obtained by the cross-couplings with 3-iodotoluene (**3f**) and xylene derivative **3g** (Table 1, entries 5 and 6). The aryl bromide **3h** also underwent a satisfactory cross-coupling with **2** leading to the benzylic pivalate **4h** in 61% yield (Table 1, entry 7).

In addition, *ortho*-substituted electrophiles such as **3i**–**k** could be used to give the 2-hydroxymethylated benzenes **4i**–**k** in 58–78% yield (Table 1, entries 8–10).

Besides an iodine–magnesium exchange reaction using *i*-PrMgCl·LiCl for the preparation of magnesium carbenoids, we have also used a sulfoxide–magnesium exchange[15] to prepare such organometallics.[8]

Thus, we first prepared the sulfoxide **6** from **1** (1.0 equiv) using an iodine–magnesium exchange reaction with *i*-PrMgCl·LiCl (1.05 equiv, –78 °C, 15 min), followed by the addition of phenyl disulfide (0.8 equiv, –78 °C, 2.5 h) to give the thioether **5** in 96% yield. Next, the oxidation of **5** using *m*-chloroperoxybenzoic acid (MCPBA) (1.0 equiv, –30 to 25 °C, 12 h) in dichloromethane gave the sulfoxide **6** in 61% yield. Treatment of **6** with TMPZnCl·LiCl[16] (TMP = 2,2,6,6-tetramethylpiperidyl, 1.05 equiv, 0 °C, 1 h) led to a complete zincation to give the zincated sulfoxide **7**. Subsequent allylation with allyl bromide (1.5 equiv, –78 °C, 15 min) in the presence of copper(I) cyanide di(lithium chloride) complex (CuCN·2LiCl) (1.0 equiv) gave the sulfoxide **8** in 69% yield (dr = 54:46). Sulfoxide **8** underwent a sulfoxide–magnesium exchange reaction using *i*-PrMgCl·LiCl (1.05 equiv, –78 °C, 15 min), followed by a transmetalation with zinc chloride (1.1 equiv, –78 °C, 15 min) to afford the (pivaloyloxymethyl)zinc species **9**. Finally, a palladium-catalyzed cross-coupling reaction with, for example, 4-bromobenzonitrile (**3a**) (0.7 equiv, 55 °C, 24 h) gave the product **10a** in 65% yield (Scheme 2). The same sequence was also performed from **6** with 5-iodo-*m*-xylene (**3g**) (0.7 equiv, 50 °C, 4 h) affording the corresponding product **10b** in 60% yield. Also, the sulfoxide–magnesium exchange reaction starting from the sulfoxide **6** using *i*-PrMgCl·LiCl, followed by trapping of the resulting magnesium compound with benzaldehyde (0.8 equiv, –78 °C, 12 h) in the presence of chlorotrimethylsilane (TMSCl) (2.4 equiv) led to the selectively protected 1,2-diol **11** in 70% yield (dr = 87:13).

In summary, we have shown that (pivaloyloxymethyl)zinc reagent **2** can be prepared using an iodine–magnesium exchange, followed by the addition of zinc chloride. In this case, this organometallic compound **2** constitutes a much better reagent for performing palladium-catalyzed cross-coupling reactions than the same reagent prepared by zinc insertion, especially with the electron-rich aryl substrates described in previous work.[7] Furthermore, substituted reagents of type **2** can be prepared using an intermediate sulfoxide of type **6**, which readily undergoes a sulfoxide–magnesium exchange. This zinc reagent also undergoes addition to an aldehyde as well as palladium-catalyzed cross-couplings. Additional studies on this topic are under way in our laboratory.



Scheme 2 Zincation, subsequent sulfoxide allylation, followed by sulfoxide–magnesium exchange and palladium-catalyzed cross-coupling reactions or addition to an aldehyde (complexed $MgCl_2$ and LiCl are omitted for clarity)

All reactions were carried out under an Ar atmosphere in flame-dried glassware. Syringes used to transfer anhydrous solvents or reagents were purged with Ar prior to use. All starting materials were purchased from commercial suppliers and were used without further purification unless otherwise stated. Iodomethyl pivalate (**1**) was prepared according to the literature procedure.[3b] THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under N_2 and stored over 4 Å molecular sieves. Column chromatographic purification was performed using Merck SiO_2 (0.040–0.063 mm, 230–400 mesh ASTM). Yields refer to those of isolated compounds estimated to be >95% pure as determined by ^{1}H NMR spectroscopy and capillary GC analyses. Melting points were obtained using a Buchi B540 melting point apparatus. IR spectra were recorded on a Perkin 218 IR spectrophotometer in ATR mode. NMR spectra were obtained using Bruker AC300 and WH400 spectrometers using samples as solutions in $CDCl_3$, with residual $CHCl_3$ (7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR) and $CFCl_3$ (0 ppm for ^{19}F NMR) as reference. Abbreviations for multiplicities are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. MS spectra were obtained using a Finnigan MAT95Q mass spectrometer. HRMS was performed using a Finnigan MAT90 mass spectrometer.

Pathway A: Iodine–Magnesium Exchange and Subsequent Transmetalation; Typical Procedure (TP1)

To an oven-dried, round bottom Schlenk flask, under Ar and equipped with a magnetic stir bar, was added iodomethyl pivalate (**1**;[17] 2.42 g, 10 mmol, 1.0 equiv) in anhydrous THF (10 mL). The solution was cooled to –78 °C and *i*-PrMgCl·LiCl (8.2 mL, 1.29 M in THF, 10.5 mmol, 1.05 equiv) was slowly added. The mixture was stirred for 15 min at –78 °C. Next, $ZnCl_2$ (11 mL, 1 M in THF, 11 mmol, 1.1 equiv) was slowly added and the mixture stirred for 15 min at the same temperature. The solution was allowed to warm to 25 °C and the resulting suspension was filtered using a syringe filter to obtain a clear solution. Finally, the zinc species **2** was concentrated to half the original volume and titrated with I_2 (0.5 M).[17]

Pathway B: Zn Insertion in the Presence of LiCl

LiCl (640 mg, 15.0 mmol) was placed in a dry Ar-flushed Schlenk flask and dried for 10 min at 450 °C (heat gun) under high vacuum. After addition of Zn powder (1.96 g, 30.0 mmol), the flask was evacuated again and refilled with Ar. THF (5.0 mL) was added, and after addition of TMSCl (2 drops) and 1,2-dibromoethane (2 drops), the suspension was heated until ebullition occurred. Next, iodomethyl pivalate (**1**; 3.63 g, 15.0 mmol) was added and the mixture was stirred at 25 °C for 30 min. The remaining Zn was separated by centrifugation (2000 rpm, 40 min) and the supernatant was carefully transferred via cannula into a dried Ar-flushed Schlenk flask and titrated with iodine.

Palladium-Catalyzed Cross-Coupling; Typical Procedure (TP2)

To an oven-dried, Ar-flushed Schlenk flask, equipped with a magnetic stir bar, was added a solution of Zn species **2** (2.0 mL, 0.5 M in THF, 1.0 mmol, 1.0 equiv). $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.02 equiv) and X-Phos (19 mg, 0.04 mmol, 0.04 equiv) were added, followed by aromatic halide substrate **3** (0.7 equiv). The mixture was stirred at 50 °C for 1 h and then poured into a solution of NH_4Cl–EtOAc (25 mL/25 mL). The crude product was separated and the aq phase extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo.

4-Cyanobenzyl Pivalate (4a)[18]

The organozinc reagent **2** was prepared from iodomethyl pivalate (**1**) according to TP1. A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 4-bromobenzonitrile (**3a**; 127 mg, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 4:1), the desired product **4a** (124 mg, 82%) was obtained as a brown liquid.

IR (ATR): 2973 (w), 2229 (w), 1728 (s), 1480 (m), 1280 (m), 1138 (vs), 1035 (w), 817 (s), 733 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.6 Hz, 2 H, 2 × CH_{Ar}), 7.44 (d, J = 7.4 Hz, 2 H, 2 × CH_{Ar}), 5.15 (s, 2 H, CH_2), 1.24 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (C), 141.9 (C_{Ar}), 132.5 (2 × CH_{Ar}), 128.0 (2 × CH_{Ar}), 118.7 (C_{Ar}), 112.0 (C_{Ar}), 65.0 (CH_2), 39.0 (C), 27.3 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 217 (2), 116 (45), 89 (19), 57 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}NO_2$: 217.1103; found: 217.1089.

Ethyl 4-[(Pivaloyloxy)methyl]benzoate (4b)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and ethyl 4-iodobenzoate (**3b**; 193 mg, 0.12 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 9:1), the desired product **4b** (139 mg, 75%) was obtained as a brown liquid.

IR (ATR): 2975 (w), 1716 (s), 1615 (w), 1479 (w), 1366 (m), 1270 (vs), 1140 (vs), 1101 (vs), 1021 (m), 753 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.0 Hz, 2 H, 2 × CH_{Ar}), 7.39 (d, *J* = 7.4 Hz, 2 H, 2 × CH_{Ar}), 5.15 (s, 2 H, CH_2), 4.37 (q, *J* = 7.2 Hz, 2 H, CH_2), 1.39 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.23 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.2 (C), 166.4 (C), 141.5 (C_{Ar}), 132.2 (C_{Ar}), 129.9 (2 × CH_{Ar}), 127.4 (2 × CH_{Ar}), 65.5 (CH_2), 61.1 (CH_2), 39.0 (C), 27.3 (3 × CH_3), 14.5 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 264 (5), 219 (10), 163 (36), 135 (10), 118 (9), 107 (17), 90 (18), 54 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{20}O_4$: 264.1362; found: 264.1356.

4-(Trifluoromethyl)benzyl Pivalate (4c)[18]
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 1-iodo-4-(trifluoromethyl)benzene (**3c**; 190 mg, 0.10 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 9:1), the desired product **4c** (128 mg, 70%) was obtained as a brown liquid.

IR (ATR): 2975 (w), 1731 (m), 1323 (vs), 1280 (m), 1210 (w), 1122 (vs), 1110 (vs), 1065 (vs), 1019 (s), 821 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 7.5 Hz, 2 H, 2 × CH_{Ar}), 7.45 (d, *J* = 7.4 Hz, 2 H, 2 × CH_{Ar}), 5.16 (s, 2 H, CH_2), 1.24 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3 (C), 140.6 (C_{Ar}), 130.3 (d, J_{C-F} = 32.4 Hz, C_{Ar}), 127.8 (2 × CH_{Ar}), 125.6 (q, J_{C-F} = 3.8 Hz, 2 × CH_{Ar}), 124.0 (q, J_{C-F} = 272.1 Hz, CF_3), 65.3 (CH_2), 39.0 (C), 27.3 (3 × CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –66.6 (3 F, CF_3).

MS (EI, 70 eV): *m*/*z* (%) = 260 (4), 241 (4), 159 (66), 109 (12), 85 (18), 57 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}F_3O_2$: 260.1024; found: 260.1019.

4-(Cyclopropylcarbamoyl)benzyl Pivalate (4d)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and *N*-cyclopropyl-4-iodobenzamide (**3d**; 201 mg, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 1:1), the desired product **4d** (179 mg, 65%) was obtained as a white solid; mp 88–90 °C.

IR (ATR): 3242 (w), 2959 (w), 1729 (s), 1621 (s), 1548 (m), 1324 (m), 1282 (m), 1149 (vs), 1019 (m), 864 (m), 756 (m), 673 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.74–7.71 (m, 2 H, 2 × CH_{Ar}), 7.37–7.34 (m, 2 H, 2 × CH_{Ar}), 6.34 (br s, 1 H, NH), 5.12 (s, 2 H, CH_2), 2.81 (oct, *J* = 3.2 Hz, 1 H, CH), 1.22 (s, 9 H, 3 × CH_3), 0.87–0.82 (m, 2 H, CH_2), 0.64–0.59 (m, 2 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3 (C), 168.6 (C), 140.1 (C_{Ar}), 134.1 (C_{Ar}), 127.7 (2 × CH_{Ar}), 127.2 (2 × CH_{Ar}), 65.4 (CH_2), 38.9 (C), 27.3 (3 × CH_3), 23.3 (CH), 6.9 (2 × CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 275 (11), 220 (12), 219 (100), 89 (8), 57 (12).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{21}NO_3$: 275.1521; found: 275.1521.

4-Methoxylbenzyl Pivalate (4e)[18]
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 4-iodoanisole (**3e**; 163.8 mg, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 9:1), the desired product **4e** (167 mg, 75%) was obtained as a colorless liquid.

IR (ATR): 2958 (w), 1724 (s), 1613 (m), 1514 (s), 1280 (m), 1246 (s), 1141 (vs), 1032 (s), 820 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.28 (m, 2 H, 2 × CH_{Ar}), 7.27–7.25 (m, 2 H, 2 × CH_{Ar}), 5.04 (s, 2 H, CH_2), 3.81 (s, 3 H, CH_3), 1.24 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.5 (C), 159.6 (C_{Ar}), 129.7 (2 × CH_{Ar}), 128.7 (C_{Ar}), 114.0 (2 × CH_{Ar}), 65.6 (CH_2), 55.4 (CH_3), 38.9 (C), 27.3 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 222 (12), 121 (100), 57 (10), 43 (33).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{18}O_3$: 222.1256; found: 222.1255.

3-Methylbenzyl Pivalate (4f)[19]
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 3-iodotoluene (**3f**; 152.6 mg, 0.90 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 85:15), the desired product **4f** (170 mg, 82%) was obtained as an orange liquid.

IR (ATR): 2971 (w), 1727 (s), 1611 (w), 1479 (m), 1280 (m), 1140 (vs), 1032 (m), 770 (m), 696 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.29–7.22 (m, 1 H, CH_{Ar}), 7.17–7.10 (m, 3 H, 3 × CH_{Ar}), 5.08 (s, 2 H, CH_2), 2.37 (s, 3 H, CH_3), 1.24 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.5 (C), 138.3 (C_{Ar}), 136.5 (C_{Ar}), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 128.5 (CH_{Ar}), 124.9 (CH_{Ar}), 66.2 (CH_2), 38.9 (C), 27.3 (3 × CH_3), 21.5 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 206 (23), 122 (13), 105 (89), 77 (13), 70 (11), 61 (14), 57 (74), 45 (13), 43 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{18}O_2$: 206.1307; found: 206.1300.

3,5-Dimethylbenzyl Pivalate (4g)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 1-iodo-3,5-dimethylbenzene (**3g**; 162.4 mg, 0.101 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 95:5), the desired product **4g** (194 mg, 88%) was obtained as an orange liquid.

IR (ATR): 2972 (w), 1728 (s), 1480 (m), 1143 (vs), 1034 (m), 843 (m), 691 (w) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.96 (s, 3 H, 3 × CH_{Ar}), 5.05 (s, 2 H, CH_2), 2.33 (s, 6 H, 2 × CH_3), 1.25 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.5 (C), 138.2 (2 × C_{Ar}), 136.5 (C_{Ar}), 129.7 (CH_{Ar}), 125.6 (2 × CH_{Ar}), 66.3 (CH_2), 38.9 (C), 27.3 (3 × CH_3), 21.4 (2 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 221 (11), 220 (60), 136 (25), 120 (13), 118 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{20}O_2$: 220.1463; found: 220.1458.

3,5-Bis(trifluoromethyl)benzyl Pivalate (4h)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 1-bromo-3,5-bis(trifluoromethyl)benzene (**3h**; 205.1 mg, 0.121 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 8:2), the desired product **4h** (200 mg, 61%) was obtained as a slightly brown liquid.

IR (ATR): 2977 (vw), 1733 (m), 1359 (w), 1275 (vs), 1170 (s), 1110 (s), 887 (m), 704 (m), 682 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (s, 1 H, CH_{Ar}), 7.78 (s, 2 H, 2 × CH_{Ar}), 5.21 (s, 2 H, CH_2), 1.25 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (C), 139.3 (C_{Ar}), 132.1 (q, $J_{C–F}$ = 33.5 Hz, 2 × C_{Ar}), 127.6 (d, $J_{C–F}$ = 3.7 Hz, 2 × CH_{Ar}), 123.3 (q, $J_{C–F}$ = 272.6 Hz, 2 × CF_3), 122.1 (CH_{Ar}), 64.5 (CH_2), 39.0 (C), 27.3 (3 × CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –63.1 (6 F, 2 × CF_3).

MS (EI, 70 eV): *m*/*z* (%) = 328 (8), 309 (18), 227 (100), 205 (16), 177 (10), 57 (46).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}F_6O_4$: 328.0898; found: 328.0905.

2-Cyanobenzyl Pivalate (4i)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 2-iodobenzonitrile (**3i**; 160.3 mg, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 85:15), the desired product **4i** (195 mg, 78%) was obtained as a brown liquid.

IR (ATR): 2973 (m), 2227 (m), 1730 (s), 1279 (m), 1137 (vs), 1033 (m), 761 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.67 (m, 1 H, CH_{Ar}), 7.64–7.56 (m, 1 H, CH_{Ar}), 7.51–7.39 (m, 2 H, 2 × CH_{Ar}), 5.27 (s, 2 H, CH_2), 1.24 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (C), 140.0 (C_{Ar}), 133.2 (CH_{Ar}), 133.0 (CH_{Ar}), 129.3 (CH_{Ar}), 128.8 (CH_{Ar}), 117.1 (C), 112.2 (C_{Ar}), 64.0 (CH_2), 39.1 (C), 27.3 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 217 (6), 133 (11), 132 (14), 117 (18), 116 (31), 89 (12), 57 (100), 43 (15), 41 (25).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}NO_2$: 217.1103; found: 217.1103.

Methyl 2-[(Pivaloyloxy)methyl]benzoate (4j)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and methyl 2-iodobenzoate (**3j**; 183.4 mg, 0.103 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 85:15), the desired product **4j** (168 mg, 67%) was obtained as an orange liquid.

IR (ATR): 2972 (w), 1717 (vs), 1603 (w), 1480 (m), 1434 (m), 1261 (s), 1135 (vs), 1082 (s), 736 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.98 (br d, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.55–7.46 (m, 2 H, 2 × CH_{Ar}), 7.37 (br t, *J* = 7.8 Hz, 1 H, CH_{Ar}), 5.49 (s, 2 H, CH_2), 3.90 (s, 3 H, CH_3), 1.25 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (C), 167.4 (C), 138.3 (C_{Ar}), 132.4 (CH_{Ar}), 131.0 (CH_{Ar}), 128.9 (C_{Ar}), 128.1 (CH_{Ar}), 127.7 (CH_{Ar}), 64.7 (CH_2), 52.2 (CH_3), 39.0 (C), 27.4 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 165 (77), 149 (31), 133 (100), 118 (10), 91 (12), 57 (59), 41 (13).

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{19}O_4$: 251.1284; found: 251.1287.

2-(Trifluoromethyl)benzyl Pivalate (4k)
The organozinc reagent **2** was prepared according to TP1 from iodomethyl pivalate (**1**). A cross-coupling reaction was performed according to TP2 between organozinc reagent **2** (2.0 mL, 0.5 M in THF, 1 mmol) and 1-iodo-2-(trifluoromethyl)benzene (**3k**; 190.4 mg, 0.098 mL, 0.7 mmol). After purification by flash column chromatography (*i*-hexane–Et_2O, 95:5), the desired product **4k** (151 mg, 58%) was obtained as a brown liquid.

IR (ATR): 2976 (w), 1731 (m), 1599 (vw), 1587 (vw), 1481 (w), 1314 (s), 1280 (m), 1142 (s), 1114 (vs), 1061 (m), 1039 (s), 767 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.4 Hz, 1 H, CH_{Ar}), 7.58–7.52 (m, 2 H, 2 × CH_{Ar}), 7.46–7.41 (m, 2 H, CH_{Ar}), 5.29 (s, 2 H, CH_2), 1.24 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (C), 134.8 (q, $J_{C–F}$ = 1.4 Hz, C_{Ar}), 132.1 (CH_{Ar}), 129.7 (CH_{Ar}), 128.4 (t, $J_{C–F}$ = 30.9 Hz, CH_{Ar}), 128.2 (CH_{Ar}), 126.2 (t, $J_{C–F}$ = 5.6 Hz, C_{Ar}), 124.3 (q, $J_{C–F}$ = 273.9 Hz, CF_3), 62.8 (CH_2), 39.0 (C), 27.3 (3 × CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –60.1 (3 F, CF_3).

MS (EI, 70 eV): *m*/*z* (%) = 260 (10), 159 (87), 109 (15) 85 (8).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}F_3O_2$: 260.1024; found: 260.1024.

(Phenylthio)methyl Pivalate (5)
To an oven-dried, Ar-flushed Schlenk flask, equipped with a magnetic stir bar, was added iodomethyl pivalate (**1**; 15.0 g, 62 mmol) in anhydrous THF (26 mL). The solution was cooled to –78 °C and a solution of *i*-PrMgCl·LiCl (53 mL, 1.29 M in THF, 68.3 mmol, 1.1 equiv) was slowly added. The mixture was stirred for 15 min at –78 °C. In an another oven-dried Schlenk flask, under Ar and equipped with a magnetic stir bar, was placed phenyldisulfide (10.8 g, 49.6 mmol, 0.8 equiv) in anhydrous THF (20 mL). This solution was slowly added to the magnesium carbenoid solution at –78 °C. The mixture was stirred for 15 min at the same temperature, and then allowed to warm slowly to 25 °C. The progress of the reaction was followed by GC. After the total disappearance of the starting material (2.5 h), the mixture was hydrolyzed with sat. NH_4Cl solution. The layers were separated and the aq phase extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash column chromatography (*i*-hexane–Et_2O, 8:2) to afford pure product **5** (10.75 g, 96%) as a colorless liquid.

IR (ATR): 2973 (w), 1734 (s), 1584 (w), 1480 (m), 1272 (m), 1119 (vs), 1026 (m), 954 (m), 939 (m), 739 (s), 690 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.44 (m, 2 H, 2 × CH_{Ar}), 7.35–7.23 (m, 3 H, 3 × CH_{Ar}), 5.40 (s, 2 H, CH_2), 1.20 (s, 9 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8 (C), 135.0 (C_{Ar}), 130.7 (2 × CH_{Ar}), 129.2 (2 × CH_{Ar}), 127.5 (CH_{Ar}), 68.3 (CH_2), 39.0 (C), 27.1 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 224 (12), 194 (11), 123 (16), 70 (10), 61 (13), 57 (100), 45 (12), 43 (81), 41 (13).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{16}O_2S$: 224.0871; found: 224.0867.

(Phenylsulfinyl)methyl Pivalate (6)
To an oven-dried Schlenk flask, under Ar and equipped with a magnetic stir bar, was added (phenylthio)methyl pivalate (**5**; 3.0 g, 13.37 mmol, 1 equiv) in CH_2Cl_2 (50 mL). The solution was cooled to –30 °C and MCPBA (2.3 g, 13.37 mmol, 1 equiv) was carefully added in three portions over 10 min. The mixture was stirred at –30 °C for 4 h, and then allowed to warm to 25 °C and stirred at this temperature for 12 h. The crude product was hydrolyzed with sat. $NaHCO_3$ solution and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash column

chromatography (*i*-hexane–Et_2O, 1:1) to afford **6** (1.97 g, 61%) as a slightly yellow liquid.

IR (ATR): 2975 (w), 1741 (s), 1480 (m), 1444 (w), 1114 (vs), 1086 (s), 1073 (m), 1050 (s), 1037 (s), 748 (s), 691 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.72–7.64 (m, 2 H, 2 × CH_{Ar}), 7.59–7.49 (m, 3 H, 3 × CH_{Ar}), 5.05 (d, *J* = 10.3 Hz, 1 H, C*H*H), 4.87 (d, *J* = 10.3 Hz, 1 H, CH*H*), 1.20 (s, 9 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (C), 140.5 (C_{Ar}), 131.8 (CH_{Ar}), 129.5 (2 × CH_{Ar}), 124.7 (2 × CH_{Ar}), 82.0 (CH_2), 39.1 (C), 27.1 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 211 (24), 210 (100), 167 (25).

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{17}O_3S$: 241.0899; found: 241.0878.

1-(Phenylsulfinyl)but-3-en-1-yl Pivalate (8)

To an oven-dried round bottom Schlenk flask, under Ar and equipped with a magnetic stir bar, was added (phenylsulfinyl)methyl pivalate (**6**; 240 mg, 1 mmol, 1 equiv) in THF (2 mL). The solution was cooled to 0 °C and a solution of TMPZn·LiCl (1 mL, 1.06 M in THF, 1.05 mmol, 1.05 equiv) was slowly added. The mixture was stirred at 0 °C for 2 h and then cooled to –78 °C. A solution of CuCN·2LiCl (1 mL, 1 M in THF, 1 mmol, 1 equiv) and allyl bromide (0.130 mL, 1.5 mmol, 1.5 equiv) were added and the resulting mixture stirred for 15 min at the same temperature. The mixture was allowed to warm to 25 °C overnight and then poured into a solution of NH_4Cl–NH_3 (10:1, 25 mL) and EtOAc (25 mL). The layers were separated and the aq phase was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash column chromatography (*i*-hexane–Et_2O, 9:1) to afford **8** [193 mg, 69%, mixture of two diastereomers (54:46)] as a yellow liquid.

IR (ATR): 2975 (w), 1740 (s), 1656 (w), 1479 (m), 1273 (m), 1124 (vs), 1089 (s), 1049 (s), 746 (s), 689 (s) cm^{-1}.

^1H NMR (300 MHz, C_6D_6): δ (major diastereomer) = 7.73–7.61 (m, 2 H, 2 × CH_{Ar}), 7.07–6.90 (m, 3 H, 3 × CH_{Ar}), 5.61 (dd, *J* = 9.9, 3.3 Hz, 1 H, CH), 5.52–5.32 (m, 1 H, CH), 4.92–4.86 (m, 1 H, CH), 4.84–4.78 (m, 1 H, CH), 2.89–2.73 (m, 1 H, C*H*H), 2.47–2.34 (m, 1 H, CH*H*), 1.09 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, C_6D_6): δ (major diastereomer) = 177.2 (C), 142.1 (C_{Ar}), 131.9 (CH), 131.0 (CH_{Ar}), 129.2 (2 × CH_{Ar}), 124.9 (2 × CH_{Ar}), 119.0 (CH_2), 90.2 (CH), 39.0 (C), 29.5 (CH_2), 27.1 (3 × CH_3).

^1H NMR (300 MHz, C_6D_6): δ (minor diastereomer) = 7.52–7.50 (m, 2 H, 2 × CH_{Ar}), 7.04–6.96 (m, 3 H, 3 × CH_{Ar}), 5.76 (dd, *J* = 9.4, 4.3 Hz, 1 H, CH), 5.59–5.49 (m, 1 H, CH), 4.93 (dq, *J* = 15.2, 2.9 Hz, 1 H, CH), 4.90 (dq, *J* = 7.9, 2.9 Hz, 1 H, CH), 2.69–2.62 (m, 1 H, C*H*H), 2.44–2.36 (m, 1 H, CH*H*), 0.97 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, C_6D_6): δ (minor diastereomer) = 176.3 (C), 141.3 (C_{Ar}), 132.0 (CH), 131.1 (CH_{Ar}), 129.0 (2 × CH_{Ar}), 125.6 (2 × CH_{Ar}), 119.5 (CH_2), 85.9 (CH), 39.1 (C), 33.5 (CH_2), 27.2 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 218 (62), 185 (14), 154 (20), 109 (100), 77 (12), 65 (43).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{20}O_3SNa$: 303.1031; found: 303.1024.

1-(4-Cyanophenyl)but-3-en-1-yl Pivalate (10a)

To an oven-dried round bottom Schlenk flask, under Ar and equipped with a magnetic stir bar, was added pivalate **8** (171 mg, 0.610 mmol, 1 equiv) in anhydrous THF (1.2 mL). The solution was cooled to –78 °C and a solution of *i*-PrMgCl·LiCl (0.543 mL, 1.19 M in THF, 0.641 mmol, 1.05 equiv) was slowly added. The resulting mixture was stirred for 30 min at –78 °C. Next, $ZnCl_2$ (0.671 mL, 1 M in THF, 0.671 mmol, 1.1 equiv) was slowly added, and the mixture stirred for 30 min at the same temperature and then warmed to –20 °C. $Pd(OAc)_2$ (2.7 mg, 0.012 mmol, 0.02 equiv) and X-Phos (11.6 mg, 0.024 mmol, 0.04 equiv) were added, followed by 4-bromobenzonitrile (**3a**; 78 mg, 0.427 mmol, 0.7 equiv). The mixture was stirred at 55 °C for 24 h and then poured into a solution of NH_4Cl–EtOAc (25 mL/25 mL). The layers were separated and the aq phase was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (*i*-hexane–EtOAc, 95:5) to afford **10a** as a brown oil (71 mg, 65%).

IR (ATR): 2974 (w), 2228 (m), 1728 (s), 1479 (m), 1280 (m), 1146 (vs), 1085 (w), 834 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.6 Hz, 2 H, 2 × CH_{Ar}), 7.40 (d, *J* = 8.3 Hz, 2 H, 2 × CH_{Ar}), 5.77 (dd, *J* = 7.2, 5.8 Hz, 1 H, CH), 5.68 (ddd, *J* = 10.5, 7.2, 3.3 Hz, 1 H, CH), 5.09 (m, 1 H, C*H*H), 5.04 (dq, *J* = 7.5, 3.0 Hz, 1 H, CH*H*), 2.66–2.49 (m, 2 H, CH_2), 1.21 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.5 (C), 145.9 (C_{Ar}), 132.5 (2 × CH_{Ar}), 132.4 (CH), 127.0 (2 × CH_{Ar}), 119.0 (CH_2), 118.8 (C), 111.8 (C_{Ar}), 74.1 (CH), 40.9 (CH_2), 39.0 (C), 27.3 (3 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 156 (13), 116 (10), 85 (21), 57 (100), 41 (26).

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{20}O_2N$: 258.1494; found: 258.1489.

1-(3,5-Dimethylphenyl)but-3-en-1-yl Pivalate (10b)

To an oven-dried round bottom Schlenk flask, under Ar and equipped with a magnetic stir bar, was added pivalate **8** (194 mg, 0.690 mmol, 1 equiv) in anhydrous THF (1.4 mL). The solution was cooled to –78 °C and a solution of *i*-PrMgCl·LiCl (0.693 mL, 1.18 M in THF, 0.73 mmol, 1.05 equiv) was slowly added. The resulting mixture was stirred for 30 min at –78 °C. Next, $ZnCl_2$ (0.759 mL, 1 M in THF, 0.759 mmol, 1.1 equiv) was slowly added, and the mixture stirred for 30 min at the same temperature and then warmed to –20 °C. $Pd(OAc)_2$ (3 mg, 0.014 mmol, 0.02 equiv) and X-Phos (13 mg, 0.028 mmol, 0.04 equiv) were added, followed by 1-iodo-3,5-dimethylbenzene (**3g**; 112 mg, 0.483 mmol, 0.7 equiv). The mixture was stirred at 50 °C for 4 h and then poured into a solution of NH_4Cl–EtOAc (25 mL/25 mL). The layers were separated and the aq phase was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (*i*-hexane–EtOAc, 98:2) to afford **10b** as a slightly yellow oil (74 mg, 60%).

IR (ATR): 2971 (w), 1727 (s), 1479 (m), 1459 (w), 1282 (m), 1032 (m), 846 (m), 803 (w), 770 (w), 702 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.92 (br s, 2 H, 2 × CH_{Ar}), 6.91 (br s, 1 H, CH_{Ar}), 5.76–5.69 (m, 2 H, 2 × CH), 5.08 (d, *J* = 17.0 Hz, 1 H, C*H*H), 5.05 (d, *J* = 9.3 Hz, 1 H, CH*H*), 2.63–2.50 (m, 2 H, CH_2), 2.31 (s, 6 H, 2 × CH_3), 1.21 (s, 9 H, 3 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C), 140.7 (C_{Ar}), 138.0 (2 × C_{Ar}), 133.9 (CH), 129.5 (CH_{Ar}), 124.1 (2 × CH_{Ar}), 117.8 (CH_2), 74.9 (CH), 41.4 (CH_2), 38.9 (C), 27.3 (3 × CH_3), 21.5 (2 × CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 219 (22), 135 (25), 125 (26), 97 (32), 95 (28), 83 (25), 71 (45), 57 (100), 55 (36), 42 (38).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{24}O_2Na$: 283.1674; found: 283.2642.

1-Hydroxy-1-phenylpent-4-en-2-yl Pivalate (11)

To an oven-dried round bottom Schlenk flask, under Ar and equipped with a magnetic stir bar, was added pivalate **8** (160 mg, 0.57 mmol, 1 equiv) in anhydrous THF (1.2 mL). The solution was cooled to –78 °C and a solution of *i*-PrMgCl·LiCl (0.464 mL, 1.29 M in THF, 0.6 mmol, 1.05 equiv) was slowly added. The mixture was stirred for 15 min at –78 °C. Next, benzaldehyde (0.046 mL, 0.456 mmol, 0.8 equiv) and TMSCl (0.174 mL, 1.37 mmol, 2.4

equiv) were added. The mixture was allowed to warm to 25 °C and stirred until the starting material had been consumed completely (3 h). The crude product was hydrolyzed with a mixture of NH_4Cl–EtOAc (25 mL/25 mL). The layers were separated and the aq phase was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (*i*-hexane–Et_2O, 9:1) to afford **11** [105 mg, 70%, mixture of two inseparable diastereomers (87:13)] as a yellow liquid.

IR (ATR): 3474 (w), 2974 (w), 1709 (s), 1480 (m), 1282 (m), 1154 (vs), 1036 (m), 983 (m), 915 (m), 762 (m), 700 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.28 (m, 2 H, 2 × CH_{Ar}, major), 7.23–7.21 (m, 2 H, 2 × CH_{Ar}, minor), 7.17–7.01 (m, 6 H, 6 × CH_{Ar}), 5.71 (dt, *J* = 17.0, 7.0 Hz, 1 H, CH, major), 5.70 (dt, *J* = 17.0, 7.0 Hz, 1 H, CH, minor), 5.33–5.24 (m, 2 H, 2 × CH), 5.03–4.95 (m, 2 H, 2 × CH), 4.94–4.90 (m, 2 H, 2 × CH), 4.58 (d, *J* = 5.6 Hz, 1 H, CH), 4.53 (d, *J* = 5.7 Hz, 1 H, CH), 2.46–2.38 (m, 4 H, 2 × CH_2), 1.11 (s, 9 H, 3 × CH_3, minor), 1.04 (s, 9 H, 3 × CH_3, major).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C, minor), 177.3 (C, major), 141.3 (C_{Ar}, minor), 141.2 (C_{Ar}, major), 134.4 (CH, major), 134.1 (CH, minor), 128.5 (2 × CH_{Ar}, minor), 128.4 (2 × CH_{Ar}, major), 128.04 (CH_{Ar}, major), 128.02 (CH_{Ar}, minor), 127.4 (2 × CH_{Ar}, major), 127.1 (2 × CH_{Ar}, minor), 117.8 (CH_2, minor), 117.7 (CH_2, major), 76.1 (CH, minor), 76.0 (CH, major), 75.4 (CH, major), 75.2 (CH, minor), 39.0 (C, minor), 38.9 (C, major), 35.5 (CH_2, minor), 34.8 (CH_2, major), 27.4 (3 × CH_3, minor), 27.3 (3 × CH_3, major).

MS (EI, 70 eV): *m*/*z* (%) = 177 (13), 160 (10), 107 (100), 105 (20), 85 (29), 79 (13), 57 (98), 40 (11).

HRMS (EI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{22}O_3Na$: 285.1467; found: 285.2642.

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