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Selective Mono- and 1,2-Difunctionalisation of Cyclopentene Derivatives via Mg and Cu Intermediates

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Abstract: A single Br/Mg exchange of 1,2-dibromocyclopentene with *i*PrMgCl·LiCl provides the corresponding β-bromocyclopentenylmagnesium reagent, which can then be reacted with various electrophiles (yields: 65–82%). In the presence of a secondary alkylmagnesium halide and Li_2CuCl_4 (2 mol%), these 2-bromoalkenylmagnesium compounds undergo bromine substitution and can then further react with electrophiles to give 1,2-difunctionalised cyclopentenes (63–79%). The mechanism of this process is discussed.

Keywords: alkenylmagnesium reagents · cross-coupling · Cu catalysis · functionalized cyclopentenes · Grignard reaction

Introduction

Organomagnesium reagents are key organometallic intermediates in organic synthesis.[1,2] Recently, we have shown that I/Mg exchange using *i*PrMgCl·LiCl allows the stereoselective preparation of alkenylmagnesium reagents starting from polyfunctional alkenyl iodides.[3] Whereas this exchange proceeds at low temperatures, alkenyl bromides do not react with *i*PrMgCl·LiCl even at 40–50 °C.[4] The preparation of magnesium derivatives of 1,2-dibromocycloalkenes would be of special interest, since the corresponding lithium organometallics[5] are elusive intermediates. For example, single Br/Li exchanges of 2,3-dibromobicyclo[2.2.1]hept-2-ene and 1,2-dibromocyclopentene (**1**) using *n*BuLi at −78 °C lead to unstable organolithium compounds, which decompose at room temperature within 18 h.[6] Herein, we wish to report that the reaction of 1,2-dibromocyclopentene (**1**) with *i*PrMgCl·LiCl (1.1 equiv, 25 °C, 24–30 h) provides the corresponding magnesium reagent **2** bearing a β-bromo substituent. Remarkably, this new magnesium species shows no tendency to eliminate MgClBr at 25 °C and can be stored for more than a month at room temperature as a 1 M solution in THF under argon with only a minimal decrease in activity.

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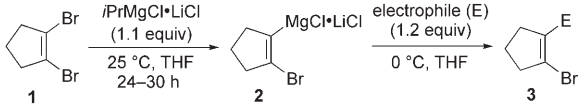
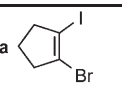
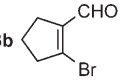
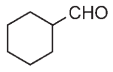
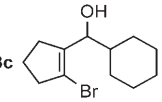
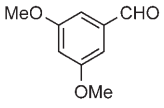
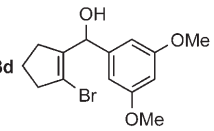
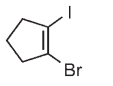
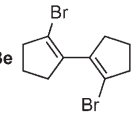
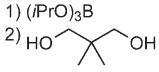
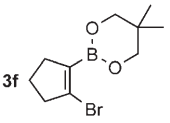
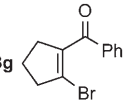
Results and Discussion

Reactions of the magnesium reagent **2** with various electrophiles produced the functionalised cyclopentenyl bromides **3a–g** in yields of 65–82% (Table 1).Treatment of the magnesium reagent **2** with iodine provided the unsymmetrical 1-bromo-2-iodocyclopentene (**3a**) in 82% yield (entry 1 in Table 1). Quenching of **2** with DMF gave the unsaturated β-bromo aldehyde **3b** (82%, entry 2). Reactions with aliphatic and aromatic aldehydes afforded the allylic alcohols **3c** and **3d** in yields of 80 and 77%, respectively (entries 3 and 4). Dimerisation of **2** was best performed by means of a palladium-catalysed Negishi cross-coupling reaction,[7] giving **3e** in 80% yield (entry 5). Reaction with $(iPrO)_3B$, followed by the addition of 2,2-dimethylpropane-1,3-diol, yielded the cycloalkenyl boronic ester **3f** in 72% yield (entry 6). Benzoylation of **2** after transmetallation with $ZnCl_2$ and addition of CuCN·2LiCl (20 mol%) provided the ketone **3g** in 65% yield (entry 7).[8]

In the presence of an excess of *i*PrMgCl·LiCl (2.4 equiv) and a catalytic amount of Li_2CuCl_4 (2 mol%, 0 °C, 8–12 h), the β-bromo substituent of the intermediate Grignard reagent **2** was substituted by an isopropyl group, furnishing the Grignard reagent **4a** (Scheme 1). After transmetallation with $ZnCl_2$, copper-catalysed acylation yielded the unsaturated ketone **5a** (entry 1 in Table 2). Quenching with alde-

Table 1. Reactions of β-bromoalkenylmagnesium chloride (**2**) prepared by a selective Br/Mg exchange reaction.

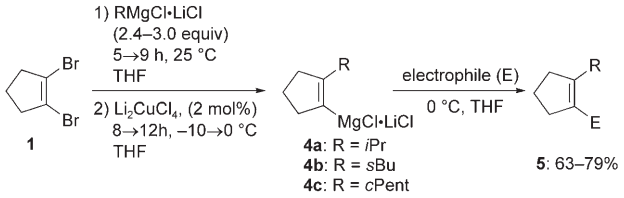


Entry	Electrophile	Product	Yield [%][a]
1	I_2	**3a** 	82
2	DMF	**3b** 	82
3		**3c** 	80
4		**3d** 	77
5		**3e** 	80[b]
6	1) $(iPrO)_3B$ 2) 	**3f** 	72
7	PhCOCl	**3g** 	65[c]

[a] Yield of analytically pure product. [b] **2** was transmetallated with $ZnCl_2$ (1 equiv), and then $[Pd(dba)_2]$ (5 mol%) and tfp (7 mol%) were added. [c] **2** was transmetallated with $ZnCl_2$ (1 equiv) at −20 °C, and then CuCN·2LiCl (20 mol%) was added.

hydes provided the allylic and benzylic alcohols **5b–g** in yields of 63–79% over three steps in a one-pot procedure (entries 2–7). An excess of alkylmagnesium reagent was necessary to overcome undesired homocoupling reactions; this was most prevalent when $cC_5H_9MgCl{\cdot}LiCl$ was used, three

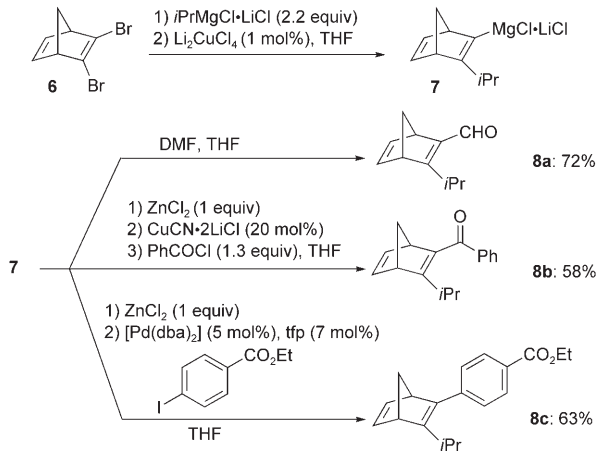
Abstract in German: *Durch einen Br/Mg-Austausch an 1,2-Dibromcyclopenten mit* i*PrMgCl·LiCl werden die entsprechenden β-Bromcyclopentenyl-magnesium-Verbindungen erhalten, die anschließend mit verschiedenen Elektrophilen umgesetzt werden (65–82%). Zusätzlich können diese 2-Bromalkenylmagnesium-Verbindungen in Anwesenheit eines sekundären Alkylmagnesiumhalogenids und Li_2CuCl_4 (2 mol%) eine Bromsubstitution eingehen und danach mit verschiedenen Elektrophilen abgefangen werden, sodass 1,2-difunktionalisierte Cyclopentenderivate (63–79%) erhalten werden. Zusätzlich wird der Mechanismus dieser Reaktion diskutiert.*



Scheme 1. Reaction of alkenylmagnesium reagents **4** prepared by a Cu-catalysed coupling starting from the Grignard reagent **2**.

equivalents of the reagent being required to complete both the exchange and coupling steps. Attempts to extend the scope of the reaction beyond secondary alkylmagnesium reagents proved unsuccessful. With *n*BuMgCl, *n*BuLi, *t*BuMgCl, PhMgCl, and PhLi, coupling between the alkenylmagnesium species (of both types **2** and **4**) was a major side reaction. Preliminary experiments also showed the same difficulties when allyl- and benzyl-organomagnesium reagents were used.

Extension of this reactivity pattern to the norbornadiene framework[5b,9] was effective, as shown in Scheme 2. Br/Mg

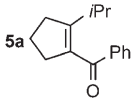
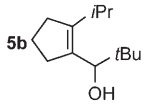
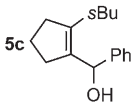
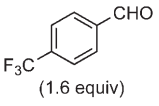
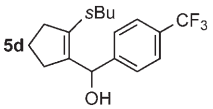
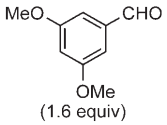
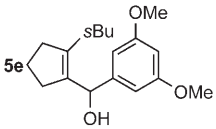
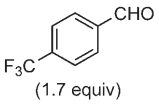
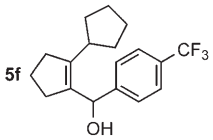
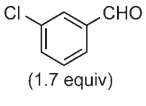
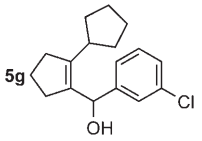


Scheme 2. Preparation and reactions of norbornadienylmagnesium reagent **7**.

exchange as in the case of 1,2-dibromocyclopentene (**1**) on 1,2-dibromonorbornadiene (**6**) proceeded at a similar rate (25 °C, 7 h) and coupling with *i*PrMgCl was accomplished using Li_2CuCl_4 (1 mol%). The reaction of **7** with DMF produced the unsaturated aldehyde **8a** in 72% yield. Transmetallation of **7** to give the corresponding zinc reagent, followed by copper-catalysed benzoylation, afforded the unsaturated ketone **8b**. Negishi cross-coupling with ethyl 4-iodobenzoate gave the arylated norbornadiene **8c** in 63% yield.

The mechanism of this copper-catalysed bromine substitution reaction was investigated. Under our standard conditions, the Grignard reagent **2** did not appear to eliminate MgClBr to provide cyclopentyne. No trapping of this highly reactive intermediate could be achieved by the addition of furan, 2,3,4,5-tetraphenylcyclopentadienone, or dihydropyr-

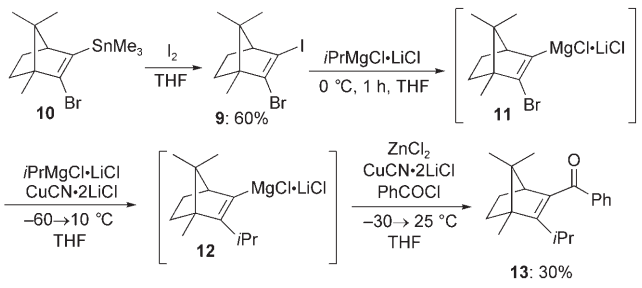
Table 2. Products of type **5** obtained by Cu-catalysed coupling.

Entry	RMgCl·LiCl	Electrophile	Product	Yield [%][a]
1	*i*PrMgCl·LiCl (2.4 equiv)	PhCOCl (1.5 equiv)	**5a** 	66[b]
2	*i*PrMgCl·LiCl (2.4 equiv)	*t*BuCHO (1.5 equiv)	**5b** 	74
3	*s*BuMgCl·LiCl (2.8 equiv)	PhCHO (1.6 equiv)	**5c** 	68
4	*s*BuMgCl·LiCl (2.8 equiv)	 (1.6 equiv)	**5d** 	79
5	*s*BuMgCl·LiCl (2.8 equiv)	 (1.6 equiv)	**5e** 	63
6	*c*PentMgCl·LiCl (3.0 equiv)	 (1.7 equiv)	**5f** 	73
7	*c*PentMgCl·LiCl (3.0 equiv)	 (1.7 equiv)	**5g** 	65

[a] Isolated, analytically pure product. [b] **4a** was transmetallated with $ZnCl_2$ (1 equiv) at −20 °C, and then CuCN·2 LiCl (20 mol %) was added.

an.[10] We therefore prepared the unsymmetrical bicyclo[2.2.1]alkenyl 2,3-dihalide **9** in order to determine the regioselectivity of the cross-coupling. The synthesis of the 2-bromo-3-iodocamphor derivative **9** was accomplished regioselectively in 40 % overall yield over four steps starting from D-camphor. The final step was an Sn/I exchange reaction on the cycloalkenyltin derivative **10** (Scheme 3).[11]

I/Mg exchange of the dihalide **9** with *i*PrMgCl·LiCl (1.1 equiv) proceeded within 1 h at 0 °C. The Grignard reagent **11** proved to be significantly less reactive than the corresponding norbornadiene derivative **7**. The best results in



Scheme 3. Regioselective Cu-catalysed cross-coupling of alkenyl- and alkylmagnesium species.

the copper-catalysed coupling of **11** with *i*PrMgCl were obtained by using a stoichiometric amount of CuCN·2 LiCl. Following completion of the coupling, transmetallation with zinc and copper-catalysed acylation with benzoyl chloride yielded the unsaturated ketone **13** in 30 % overall yield from **9**.[12] Characterisation by 1D and 2D NMR experiments, as well as by X-ray crystallographic analysis, confirmed the structure of **13**, proving that the new carbon–carbon bond to *i*Pr had indeed been formed at the carbon atom that initially bore the bromine atom (Figure 1).[13]

Therefore, we propose the mechanism shown in Scheme 4 for the copper-catalysed coupling. Transmetallation of *i*PrMgCl to *i*PrCu(CN)Li, followed by oxidative addition to the carbon–bromine bond in **11** is tentatively believed to generate intermediate **14**. Reductive elimination would then give intermediate **12**, which would be acylated with benzoyl chloride

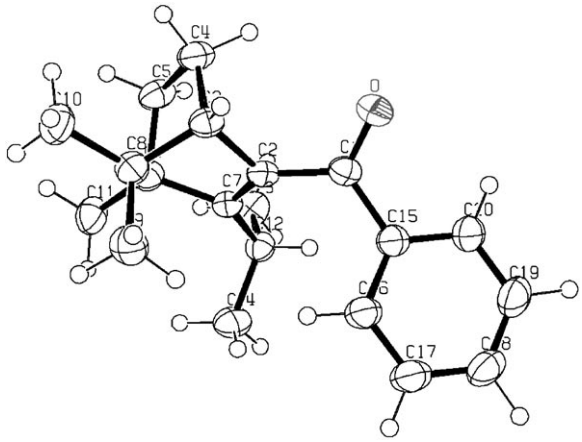
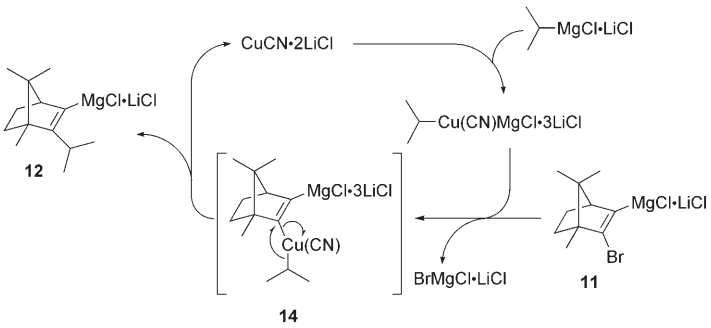


Figure 1. X-ray crystal structure of compound **13**.

upon transmetallation with CuCN·2 LiCl (1 equiv). Alternatively, the reaction may proceed through a copper(III)-cyclopropane intermediate,[14] from which the alkenylmagnesium reagent **12** would be obtained through β-elimination assisted by the polymetallic components of the organocuprate.



Scheme 4. Proposed mechanism for the regioselective Cu^{I}-catalysed cross-coupling reaction.

The presence of a carbon–magnesium bond in the β-position with respect to the carbon–bromine bond, as found in compound **11**, may have an accelerating effect on such cross-couplings.[15]

Conclusion

In conclusion, we have shown that the use of *i*PrMgCl·LiCl allows a simple, high-yielding preparation of previously unknown cyclic β-bromo-substituted alkenylmagnesium reagents. We have performed a copper-catalysed heterocoupling reaction, allowing the regioselective formation of a new β-alkylated cycloalkenylmagnesium compound that can be further reacted with a range of electrophiles. This sequence constitutes an effective one-pot cascade difunctionalisation of cycloalkenes. Extensions of this work, which include the investigation of this reaction pattern on 1,2-dibromocyclohexene, are currently underway in our laboratories.

Experimental Section

General: Unless otherwise indicated, all reactions were carried out with magnetic stirring in flame-dried glassware under argon. Syringes used to transfer reagents and solvents were purged with argon prior to use. Reactions were monitored by gas chromatography (GC and GC-MS) or thin-layer chromatography (TLC). TLC was performed on aluminium plates coated with SiO_2 (Merck 60, F-254); spots were visualised either by UV detection or following immersion in $KMnO_4$ solution ($KMnO_4$ (1.5 g), K_2CO_3 (10 g), and 10% NaOH solution (1.25 mL) in H_2O (200 mL)). Column chromatography was performed using Merck silica gel 60 (40–63 μm, 230–400 mesh ASTM). Melting points were measured using a Büchi B-540 apparatus and are uncorrected.

NMR spectra were recorded from samples in $CDCl_3$ or C_6D_6 solution; chemical shifts (δ) are reported in parts per million (ppm) relative to the residual solvent peak: $CDCl_3$ ($\delta = 7.25$ ppm (^1H) and $\delta = 77.0$ ppm (^{13}C)); C_6D_6 ($\delta = 7.16$ ppm (^1H) and $\delta = 128.0$ ppm (^{13}C)). Mass spectra and high-resolution mass spectra (HRMS) were recorded in electrospray ionisation (ESI) mode, except where otherwise noted. GC was performed on Hewlett-Packard 6890 or 5890 Series II chromatographs (column: 5% phenylmethylpolysiloxane, length: 10 m, diameter: 0.25 mm, film thickness: 0.25 μm). The method used to determine GC purity, referred to as "method 70", was as follows: 70 °C for 1 min, heating at a ramp rate of 50 °C min^{-1} to 250 °C, holding at 250 °C for 5 min, heating at a ramp rate of 50 °C min^{-1} to 300 °C, holding at 300 °C for 3 min.

Starting materials: The reagents *i*PrMgCl·LiCl and *s*-BuMgCl·LiCl were obtained from Chemetall as 14% and 15% solutions, respectively, in THF and were titrated with iodine prior to use. *c*-PentMgCl·LiCl was prepared from cyclopentyl chloride and Mg in the presence of LiCl according to the published procedure.[16]

A 1.0 M CuCN·2 LiCl solution was first prepared by heating 1 equiv of CuCN (100 mmol, 8.9 g) and 2 equiv of LiCl (200 mmol, 8.4 g) under vacuum at 130 °C for 6 h; THF (100 mL) was slowly added and the resulting solution was stirred overnight. Li_2CuCl_4 was purchased as a 0.1 M solution in THF from Acros Organics.

Acid chlorides, DMF, and liquid aldehydes were distilled under argon prior to use. Solid aldehydes were used without further purification.

1,2-Dibromocyclopentene **1** was prepared according to the published procedure.[17] 2,3-Dibromo-bicyclo[2.2.1]hepta-2,5-diene **6** was prepared following the published procedure.[5b]

Typical procedure A for the synthesis of compounds 3a–g: Dibromide **1** (1 equiv) was added to a flame-dried flask equipped with a magnetic stirring bar, an argon inlet, and a septum. *i*PrMgCl·LiCl (1.1 equiv in THF) was added at room temperature with stirring. Upon completion of the exchange (as determined by GC analysis of aliquots of the reaction mixture quenched with saturated aqueous NH_4Cl solution; 24–30 h), the reaction mixture was cooled to 0 °C in an ice bath. The electrophile was slowly added and the solution was warmed to 25 °C. After stirring for 2 h at room temperature, saturated aqueous NH_4Cl solution (5 mL) was added and the aqueous layer was extracted with Et_2O (3×10 mL). The combined organic extracts were washed with saturated NaCl solution, dried over $MgSO_4$, and filtered. Removal of the solvent in vacuo and purification of the residue by column chromatography (SiO_2, initially neutralised with 3% Et_3N) afforded the desired product.

Typical procedure B for the synthesis of compounds 5a and 8b: The appropriate dibromide **1** or **6** (1 equiv) was added to a flame-dried flask equipped with a magnetic stirring bar, an argon inlet, and a septum. *i*PrMgCl·LiCl (2.2–2.4 equiv) was added at room temperature with stirring. Upon completion of the exchange (as determined by GC analysis; 6 h), the solution was cooled to −10 °C. Li_2CuCl_4 (0.1 M in THF, 2 mol%) was added dropwise and the solution was slowly warmed to 0 °C. Upon completion of the coupling (as determined by GC analysis; 9 h), the solution was cooled to −30 °C and $ZnCl_2$ solution (1 M in THF, 1 equiv) was added. After stirring for 30 min, the solution was warmed to −20 °C and a solution of CuCN·LiCl (1.0 M in THF, 20 mol%) was added. After stirring for 5 min, the requisite acid chloride (1.2–1.5 equiv) was added and the solution was warmed to room temperature. The reaction mixture was stirred at room temperature for 2 h, then quenched with saturated aqueous NH_4Cl solution. The aqueous layer was extracted with Et_2O (3× 10 mL) and the combined organic extracts were washed with saturated NaCl solution, dried over $MgSO_4$, and filtered. Removal of the solvent in vacuo and purification of the residue by column chromatography (SiO_2, initially neutralised with 3% Et_3N) afforded the desired product.

Typical procedure C for the synthesis of compounds 5b–g, 8a, and 8c: The appropriate dibromide **1** or **6** (1 equiv) was added to a flame-dried flask equipped with a magnetic stirring bar, an argon inlet, and a septum. RMgCl·LiCl (2.2–3.0 equiv in THF) was added at room temperature with stirring. Upon completion of the exchange (as determined by GC analysis of hydrolysed aliquots of the reaction mixture; 6 h), the solution was cooled to −10 °C. Li_2CuCl_4 (0.1 M solution in THF, 2 mol%) was added dropwise and the solution was slowly warmed to 0 °C. Upon completion of the coupling (as determined by GC analysis; 9 h), the requisite electrophile (1.3–1.7 equiv) was slowly added and the solution was warmed to 25 °C. After stirring for 2 h at room temperature, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl solution and the aqueous layer was extracted with Et_2O (3×10 mL). The combined organic extracts were washed with saturated NaCl solution, dried over $MgSO_4$, and filtered. Removal of the solvent in vacuo and purification of the residue by column chromatography (SiO_2, initially neutralised with 3% Et_3N) afforded the desired product.

1-Bromo-2-iodocyclopentene (3a): According to typical procedure **A**, dibromide **1** (1.00 mmol, 226 mg) was reacted with *i*PrMgCl·LiCl (1.10 mmol, 1.24 M in THF, 0.89 mL). After completion of the exchange, the mixture was quenched with a solution of iodine (1.20 mmol, 305 mg) in THF (2.00 mL) at −20 °C. The product was purified according to typical procedure **A** (column chromatography eluting with pentane) to yield **3a** as a pale-yellow oil (223 mg, 82 %). GC purity ≥99 % (retention time: 2.92 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.67–2.59 (m, 4H), 2.05 ppm (quint, $^3J_{H,H}$ = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 130.2, 97.2, 43.5, 39.6, 24.1 ppm; IR (film): $\tilde{\nu}$ = 2951 (m), 2848 (m), 1604 (m), 1440 (m), 1382 (w), 1306 (m), 1287 (w), 1199 (w), 1132 (w), 1091 (s), 1042 (w), 1028 (w), 903 (w), 824 (s), 747 (w), 692 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 272 (100) [M^+], 206 (2), 193 (17), 145 (21), 127 (13), 65 (63); HRMS (EI): *m*/*z*: calcd for $C_5H_6{}^{79}BrI$: 271.8698; found: 271.8686.

2-Bromocyclopent-1-ene-1-carbaldehyde (3b): According to typical procedure **A**, *i*PrMgCl·LiCl (1.75 mmol, 1.06 M, 1.65 mL) was added to **1** (1.59 mmol, 359 mg). The alkenylmagnesium species **2** was quenched with DMF (1.91 mmol, 0.15 mL). Following work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 1:1) to give **3b** (228 mg, 82 %) as a pale-yellow oil. GC purity ≥99 % (retention time: 2.53 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.89 (s, 1H), 2.92–2.87 (m, 2H), 2.55–2.50 (m, 2H), 2.01 ppm (quint, $^3J_{H,H}$ = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 189.5, 141.6, 140.3, 42.8, 29.5, 21.6 ppm; IR (film): $\tilde{\nu}$ = 2925 (w), 1662 (s), 1599 (s), 1329 (w), 1240 (w), 1195 (w), 1074 (m), 909 (m), 720 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 174 (100) [M^+], 145 (10), 95 (45), 94 (12), 67 (90), 66 (41), 65 (73), 41 (20); HRMS (EI): *m*/*z*: calcd for $C_6H_7{}^{79}BrO$: 173.9680; found: 173.9681.

(2-Bromocyclopent-1-en-1-yl)(cyclohexyl)methanol (3c): According to typical procedure **A**, *i*PrMgCl·LiCl (1.01 mmol, 1.22 M, 0.83 mL) was added to **1** (0.92 mmol, 208 mg) and the newly formed alkenylmagnesium species **2** was quenched with cyclohexylcarbaldehyde (1.10 mmol, 0.13 mL). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **3c** (192 mg, 80 %) as a colourless oil. GC purity ≥99 % (retention time: 4.50 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.22 (d, $^3J_{H,H}$ = 9.0 Hz, 1H), 2.66–2.61 (m, 2H), 2.53–2.42 (m, 1H), 2.31–2.20 (m, 1H), 2.07–2.03 (m, 1H), 1.94 (quint, $^3J_{H,H}$ = 7.5 Hz, 2H), 1.78–1.62 (m, 3H), 1.56 (s, 1H), 1.48–1.38 (m, 2H), 1.26–1.15 (m, 3H), 1.08–0.87 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 141.8, 118.7, 74.4, 42.0, 40.4, 30.0, 29.7, 28.9, 26.6, 26.2, 26.0, 22.0 ppm; IR (film): $\tilde{\nu}$ = 3360 (s), 2929 (s), 2851 (s), 2668 (w), 2246 (w), 1712 (w), 1651 (m), 1448 (m), 1385 (w), 1317 (m), 1263 (m), 1205 (m), 1971 (m), 1013 (m), 961 (w), 893 (m), 844 (w), 734 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 258 (2) [M^+], 179 (40), 177 (96), 175 (100), 97 (23), 96 (19), 95 (10), 83 (10), 67 (37), 55 (15), 41 (15); HRMS (EI): *m*/*z*: calcd for $C_{12}H_{19}{}^{79}BrO$: 258.0619; found: 258.0608.

(2-Bromocyclopent-1-en-1-yl)(3,5-dimethoxyphenyl)methanol (3d): According to typical procedure **A**, *i*PrMgCl·LiCl (1.04 mmol, 1.22 M, 0.85 mL) was added to **1** (0.94 mmol, 213 mg) and the newly formed alkenylmagnesium species **2** was quenched with 3,5-dimethoxybenzaldehyde (1.13 mmol, 188 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **3d** (236 mg, 77 %) as a colourless oil. GC purity ≥99 % (retention time: 6.08 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.57 (d, $^4J_{H,H}$ = 2.2 Hz, 2H), 6.36 (t, $^4J_{H,H}$ = 2.2 Hz, 1H), 5.69 (s, 1H), 3.78 (s, 6H), 2.68–2.59 (m, 2H), 2.53–2.44 (m, 1H), 2.18–2.00 (m, 2H), 1.96–1.80 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 161.1, 144.4, 142.0, 118.4, 103.7, 99.6, 71.5, 55.6, 40.5, 29.6, 21.7 ppm; IR (film): $\tilde{\nu}$ = 3428 (s), 2956 (s), 2840 (m), 1651 (w), 1608 (s), 1464 (s), 1428 (m), 1319 (m), 1293 (m), 1204 (s), 1153 (s), 1088 (w), 1067 (m), 1038 (m), 925 (w), 895 (w), 848 (s), 743 (m), 704 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 314 (42), 312 (43) [M^+], 241 (60), 240 (15), 220 (12), 219 (67), 208 (30), 165 (74), 151 (26), 139 (100), 122 (11), 115 (12), 107 (12), 95 (67), 77 (17), 67 (36), 64 (25); HRMS (EI): *m*/*z*: calcd for $C_{14}H_{17}{}^{79}BrO_3$: 312.0361; found: 312.0360.

2,2′-Dibromo-1,1′-bi(cyclopent-1-en-1-yl) (3e): According to typical procedure **A**, *i*PrMgCl·LiCl (5.50 mmol, 1.22 M, 4.50 mL) was added to **1** (5.00 mmol, 1.13 g). The alkenylmagnesium species **2** was transmetallated with $ZnCl_2$ (1.00 M solution in THF, 2.75 mL) at −20 °C and the solution was stirred for 15 min. 1-Bromo-2-iodocyclopentene (**3a**) (5.00 mmol, 1.36 g) was then added to the reaction mixture at −20 °C, followed by [Pd(dba)$_2$] (5 mol %, 144 mg) and trifurylphosphine (tfp) (7 mol %, 81 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane) to give **3e** (1.16 g, 77 %) as a colourless oil. GC purity ≥99 % (retention time: 4.11 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.71–2.53 (m, 8H), 1.96 ppm (quint, $^3J_{H,H}$ = 7.6 Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.9, 119.0, 41.4, 35.0, 22.8 ppm; IR (film): $\tilde{\nu}$ = 4329 (w), 4250 (w), 2966 (m), 2946 (m), 2893 (m), 2846 (s), 1668 (w), 1615 (w), 1435 (m), 1308 (m), 1283 (m), 1202 (w), 1134 (w), 1118 (w), 1082 (m), 1033 (s), 998 (w), 922 (m), 907 (m), 876 (w), 784 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 292 (100) [M^+], 290 (47), 213 (32), 211 (32), 132 (58), 131 (61), 129 (10), 117 (28), 116 (11), 115 (14), 104 (16), 103 (14), 91 (30), 77 (17), 65 (23), 64 (25), 63 (10), 51 (16); HRMS (EI): *m*/*z*: calcd for $C_{10}H_{12}{}^{79}Br_2$: 289.9306; found 289.9316.

2-(2-Bromocyclopent-1-en-1-yl)-5,5-dimethyl-1,3,2-dioxaborinane (3f): According to typical procedure **A**, *i*PrMgCl·LiCl (1.10 mmol, 1.22 M, 0.90 mL) was added to **1** (1.00 mmol, 226 mg) at room temperature. The alkenylmagnesium species **2** was reacted with (iPrO)$_3$B (1.20 mmol, 0.28 mL) at −20 °C and the reaction mixture was slowly warmed to 25 °C. Neat 2,2-dimethylpropane-1,3-diol (1.50 mmol, 156 mg) was then added to the solution. After standard work-up, the resultant oil was purified by column chromatography (pentane/diethyl ether 7:3) to give **3f** (185 mg, 72 %) as a brown oil. GC purity ≥99 % (retention time: 4.08 min, measured by method 70). ^{1}H NMR (C_6D_6, 300 MHz): δ = 3.34 (s, 4H), 2.61–2.53 (m, 4H), 1.58 (quint, $^3J_{H,H}$ = 7.6 Hz, 2H), 0.57 ppm (s, 6H); ^{13}C NMR (C_6D_6, 75 MHz): δ = 132.2, 71.9, 44.0, 36.3, 31.3, 23.4, 21.5 ppm (olefinic C attached to B not observed due to quadropolar coupling); IR (film): $\tilde{\nu}$ = 2958 (m), 2926 (m), 1731 (m), 1616 (m), 1476 (m), 1418 (w), 1318 (s), 1253 (s), 1118 (s), 1073 (w), 840 (w), 696 (m), 672 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 258 (100) [M^+], 180 (40), 179 (63), 135 (46), 93 (62), 79 (28); HRMS (EI): *m*/*z*: calcd for $C_{10}H_{16}{}^{11}B^{79}BrO_2$: 258.0427; found 258.0433.

(2-Bromocyclopent-1-en-1-yl)phenylmethanone (3g): According to typical procedure **A**, *i*PrMgCl·LiCl (1.10 mmol, 1.30 M, 0.85 mL) was added to **1** (1.00 mmol, 226 mg). After the exchange was complete, the solution was cooled to −30 °C and $ZnCl_2$ solution (1.00 M in THF, 1.00 mmol, 1.00 mL) was added. After stirring for 30 min, the solution was warmed to −20 °C and a solution of CuCN·2LiCl (1.00 M in THF, 1.00 mmol, 1.00 mL) was added. After stirring for 5 min, benzoyl chloride (1.20 mmol, 0.14 mL) was added and the solution was warmed to 25 °C. After stirring for 2 h at 25 °C, saturated aqueous NH_4Cl solution (5 mL) was added and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with saturated NaCl solution, dried over $MgSO_4$, and filtered. Removal of the solvent in vacuo and purification of the residue by column chromatography (pentane/diethyl ether 9:1) afforded **3g** (162 mg, 65 %) as a pale-yellow oil. GC purity ≥99 % (retention time: 4.58 min, measured by method 70). ^{1}H NMR (C_6D_6, 400 MHz): δ = 7.92 (d, $^3J_{H,H}$ = 7.0 Hz, 2H), 7.20–7.12 (m, 3H), 2.49–2.40 (m, 4H), 1.50 ppm (quint, $^3J_{H,H}$ = 7.6 Hz, 2H); ^{13}C NMR (C_6D_6, 75 MHz): δ = 194.0, 140.7, 136.7, 133.0, 129.6, 128.6, 123.4, 41.9, 35.5, 22.1 ppm; IR (film): $\tilde{\nu}$ = 1653 (s), 1616 (m), 1595 (m), 1451 (m), 1321 (s), 1283 (s), 1072 (m), 955 (m), 840 (m), 792 (m), 713 (s), 687 (s), 675 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 252 (64), 251 (17), 250 (66) [M^+], 175 (23), 173 (23), 172 (13), 171 (100), 170 (11), 143 (32), 128 (15), 105 (47), 77 (22); HRMS (EI): *m*/*z*: calcd for $C_{12}H_{11}{}^{79}BrO$: 249.9993; found 249.9992.

(2-Isopropylcyclopent-1-en-1-yl)phenylmethanone (5a): According to typical procedure **B**, *i*PrMgCl·LiCl (2.30 mmol, 1.22 M, 1.90 mL) was added to **1** (0.96 mmol, 218 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, 0.10 M in THF, 0.19 mL) was added. The newly formed alkenylmagnesium species **4a** was transmetallated with a solution of $ZnCl_2$ (0.96 mmol, 1.00 M in THF, 0.96 mL) and then CuCN·2LiCl (0.19 mmol, 1.00 M in THF, 0.19 mL) was added; the resultant copper–zinc reagent was then quenched with benzoyl chloride (1.40 mmol, 0.17 mL). Following work-up, the resultant oil was purified by column chromatography (pentane) to give **5a** (137 mg, 66 %) as a colourless oil.

GC purity ≥99% (retention time: 4.34 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.79 (d, $^3J_{H,H}$=7.0 Hz, 2H), 7.55–7.41 (m, 3H), 2.71–2.62 (m, 3H), 2.54–2.49 (m, 2H), 1.91 (quint, $^3J_{H,H}$= 7.4 Hz, 2H), 0.95 ppm (d, $^3J_{H,H}$=6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=198.3, 157.4, 139.0, 134.7, 132.8, 129.0, 128.6, 36.2, 32.3, 28.6, 22.7, 21.3 ppm; IR (film): $\tilde{\nu}$=3392 (s), 3063 (w), 2961 (s), 2932 (m), 2871 (m), 1649 (s), 1598 (m), 1578 (m), 1464 (w), 1448 (m), 1384 (w), 1340 (m), 1263 (s), 1175 (w), 1099 (m), 1072 (m), 1024 (m), 891 (w), 796 (m), 715 (m), 697 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 214 (26) [M^+], 199 (100), 184 (10), 171 (10), 105 (28), 77 (25); HRMS (EI): *m*/*z*: calcd for $C_{15}H_{18}O$: 214.1358; found: 214.1352.

1-(2-Isopropylcyclopent-1-en-1-yl)-2,2-dimethylpropan-1-ol (5b): According to typical procedure **C**, *i*PrMgCl·LiCl (2.40 mmol, 1.06 M, 2.27 mL) was added to **1** (1.00 mmol, 226 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, 0.10 M in THF, 0.20 mL) was added. The newly formed alkenylmagnesium species **4a** was quenched with pivaldehyde (1.20 mmol, 0.13 mL). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **5b** (146 mg, 74%) as a colourless oil. GC purity ≥99% (retention time: 3.32 min, measured by method 70); ^{1}H NMR (C_6D_6, 400 MHz): δ=4.14 (s, 1H), 2.72 (sept, $^3J_{H,H}$=6.7 Hz, 1H), 2.53–2.15 (m, 5H), 1.73–1.56 (m, 2H), 0.98 (s, 9H), 0.95 (d, $^3J_{H,H}$=7.0 Hz, 3H), 0.92 ppm (d, $^3J_{H,H}$=6.7 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz): δ=145.4, 135.0, 75.8, 35.9, 33.6, 30.6, 27.1, 26.9, 22.9, 21.5, 20.9 ppm; IR (film): $\tilde{\nu}$=3628 (w), 3460 (s), 2956 (s), 2868 (s), 1649 (w), 1480 (s), 1464 (s), 1392 (m), 1381 (m), 1362 (s), 1329 (w), 1292 (w), 1240 (m), 1190 (m), 1167 (w), 1100 (w), 1047 (s), 998 (s), 956 (m), 935 (w), 898 (m), 861 (w), 769 (w), 753 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 196 (2) [M^+], 163 (16), 139 (100), 121 (15), 95 (15), 93 (12), 81 (82), 69 (12), 67 (11), 43 (24), 41 (14); HRMS (EI): *m*/*z*: calcd for $C_{13}H_{24}O$: 196.1827; found: 196.1823.

(2-*sec*-Butylcyclopent-1-en-1-yl)phenylmethanol (5c): According to typical procedure **C**, *s*BuMgCl·LiCl (2.93 mmol, 1.08 M, 2.71 mL) was added to **1** (1.04 mmol, 236 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, 0.10 M in THF, 0.21 mL) was added. The newly formed alkenylmagnesium species **4b** was quenched with benzaldehyde (1.66 mmol, 0.17 mL). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **5c** (164 mg, 68%) as a colourless oil. GC purity ≥99% (retention time: 4.58 min, measured by method 70). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.34–7.21 (m, 5H), 5.70 (s, 1H), 2.70 (sext, $^3J_{H,H}$=7.1 Hz, 1H), 2.51–2.41 (m, 1H), 2.29 (t, $^3J_{H,H}$= 7.4 Hz, 2H), 2.09–1.98 (m, 1H), 1.77–1.69 (m, 3H), 1.45–1.35 (m, 2H), 1.03 (d, $^3J_{H,H}$=6.8 Hz, 3H), 0.87 ppm (t, $^3J_{H,H}$=7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=144.5, 143.3, 136.7, 128.4, 127.1, 125.9, 70.1, 34.6, 31.4, 31.0, 28.4, 21.9, 19.8, 12.8 ppm; IR (film): $\tilde{\nu}$=3392 (s), 3066 (w), 2954 (s), 2868 (s), 1661 (w), 1596 (w), 1473 (m), 1451 (m), 1384 (m), 1336 (w), 1261 (w), 1187 (m), 1095 (w), 1077 (w), 1035 (m), 973 (m), 895 (w), 854 (w), 791 (w), 723 (w), 698 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 230 (10) [M^+], 212 (32), 183 (17), 173 (100), 155 (19), 105 (14); HRMS (EI): *m*/*z*: calcd for $C_{16}H_{22}O$: 230.1671; found: 230.1661.

(2-*sec*-Butylcyclopent-1-en-1-yl)[4-(trifluoromethyl)phenyl]methanol (5d): According to typical procedure **C**, *s*-BuMgCl·LiCl (3.02 mmol, 1.08 M, 2.80 mL) was added to **1** (1.08 mmol, 244 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, 0.10 M in THF, 0.22 mL) was added. The newly formed alkenylmagnesium species **4b** was quenched with 4-(trifluoromethyl)benzaldehyde (1.73 mmol, 301 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **5d** (254 mg, 79%) as a white solid. GC purity ≥99% (retention time: 4.55 min, measured by method 70); m.p. 96.9–100.4 °C; ^{1}H NMR (C_6D_6, 400 MHz): δ=7.41 (d, $^3J_{H,H}$=8.4 Hz, 2H), 7.32 (d, $^3J_{H,H}$=8.4 Hz, 2H), 5.40 (s, 1H), 2.45 (sext, $^3J_{H,H}$=7.1 Hz, 1H), 2.38–2.28 (m, 1H), 2.23–2.05 (m, 2H), 1.93–1.83 (m, 1H), 1.63–1.48 (m, 2H), 1.31–1.22 (m, 3H), 0.94 (d, $^3J_{H,H}$=6.8 Hz, 3H), 0.76 ppm (t, $^3J_{H,H}$=7.4 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz): δ=147.7, 144.9, 136.4, 129.0 (q, $^2J_{C,F}$= 32.2 Hz), 126.3, 125.1 (q, $^3J_{C,F}$=3.7 Hz), 124.9 (q, $^1J_{C,F}$=277.0 Hz), 68.8, 34.2, 31.3, 30.9, 28.4, 21.7, 19.7, 12.7 ppm; ^{19}F NMR (C_6D_6, 282 MHz): δ= −62.2 ppm (s); IR (film): $\tilde{\nu}$=3369 (s), 2961 (s), 1620 (m), 1461 (w), 1413 (m), 1321 (s), 1164 (s), 1126 (s), 1068 (s), 1017 (m), 854 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 298 (9) [M^+], 280 (30), 251 (26), 241 (100), 223 (18), 173 (46), 145 (12); HRMS (EI): *m*/*z*: calcd for $C_{17}H_{21}F_3O$: 298.1544; found: 298.1553.

(2-*sec*-Butylcyclopent-1-en-1-yl)(3,5-dimethoxyphenyl)methanol (5e): According to typical procedure **C**, *s*BuMgCl·LiCl (3.50 mmol, 1.08 M, 3.25 mL) was added to **1** (1.25 mmol, 283 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, ≈0.10 M in THF, 0.25 mL) was added. The newly formed alkenylmagnesium species **4b** was quenched with 3,5-dimethoxybenzaldehyde (2.00 mmol, 333 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **5e** (229 mg, 63%) as a pale-yellow oil. GC purity ≥99% (retention time: 6.06 min, measured by method 70); ^{1}H NMR (C_6D_6, 400 MHz): δ=6.80 (d, $^4J_{H,H}$=2.0 Hz, 2H), 6.51 (t, $^4J_{H,H}$=2.3 Hz, 1H), 5.58 (s, 1H), 3.40 (s, 6H), 2.58–2.51 (m, 2H), 2.25–2.14 (m, 3H), 1.67–1.56 (m, 2H), 1.36–1.24 (m, 3H), 0.97 (d, $^3J_{H,H}$=6.7 Hz, 3H), 0.82 ppm (t, $^3J_{H,H}$=7.2 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz): δ=161.4, 146.5, 143.0, 137.6, 104.1, 99.1, 69.7, 54.7, 34.3, 31.2, 31.0, 28.3, 21.9, 19.6, 12.6 ppm; IR (film): $\tilde{\nu}$=3431 (w), 2957 (m), 1595 (s), 1458 (m), 1427 (m), 1293 (w), 1203 (m), 1154 (s), 1035 (m), 830 (w), 689 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 290 (50) [M^+], 272 (98), 257 (11), 243 (53), 233 (100), 215 (44), 165 (30), 152 (24), 151 (32), 139 (25), 121 (12), 95 (24); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{26}O_3$: 290.1882; found: 290.1889.

1,1′-Bi(cyclopentan)-1-en-2-yl[4-(trifluoromethyl)phenyl]methanol (5f): According to typical procedure **C**, *c*-PentMgCl·LiCl (3.08 mmol, 0.81 M, 3.80 mL) was added to **1** (1.03 mmol, 232 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, 0.10 M in THF, 0.20 mL) was added. The newly formed alkenylmagnesium species **4c** was quenched with 4-(trifluoromethyl)benzaldehyde (1.75 mmol, 304 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **5f** (234 mg, 73%) as a pale-yellow oil. GC purity ≥99% (retention time: 5.18 min, measured by method 70); ^{1}H NMR ($CDCl_3$, 600 MHz): δ=7.56 (d, $^3J_{H,H}$=8.2 Hz, 2H), 7.45 (d, $^3J_{H,H}$=7.9 Hz, 2H), 5.76 (s, 1H), 3.05 (quint, $^3J_{H,H}$=9.0 Hz, 1H), 2.45–2.30 (m, 3H), 1.97–1.91 (m, 1H), 1.84 (br s, 1H), 1.76–1.66 (m, 6H), 1.66–1.58 (m, 2H), 1.53–1.43 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ=147.2, 144.6, 135.7, 129.2 (q, $^2J_{C,F}$=32.3 Hz), 126.1, 125.5 (q, $^1J_{C,F}$=272.0 Hz), 125.3 (q, $^3J_{C,F}$=3.9 Hz), 69.6, 38.9, 32.4, 31.9, 31.7, 30.9, 26.1, 26.0, 21.9 ppm; IR (film): $\tilde{\nu}$=3348 (w), 2952 (m), 1326 (s), 1161 (m), 1121 (s), 1066 (s), 1016 (m), 852 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 310 (12) [M^+], 292 (80), 252 (10), 251 (13), 250 (10), 249 (16), 241 (100), 223 (27), 173 (25), 159 (10), 133 (19), 91 (11); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{21}F_3O$: 310.1544; found: 310.1546.

1,1′-Bi(cyclopentan)-1-en-2-yl(3-chlorophenyl)methanol (5g): According to typical procedure **C**, *c*-PentMgCl·LiCl (3.07 mmol, 0.81 M, 3.79 mL) was added to **1** (1.02 mmol, 231 mg). After the exchange was complete, Li_2CuCl_4 (0.02 mmol, 0.10 M in THF, 0.20 mL) was added. The newly formed alkenylmagnesium species **4c** was quenched with 3-chlorobenzaldehyde (1.74 mmol, 245 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane/CH_2Cl_2 4:1) to give **5g** (184 mg, 65%) as a pale-yellow oil. Note: this compound decomposed after two days. GC purity ≥99% (retention time: 6.04 min, measured by method 70); ^{1}H NMR (C_6D_6, 400 MHz): δ=7.43 (s, 1H), 7.11–7.04 (m, 3H), 6.93 (t, $^3J_{H,H}$=7.5 Hz, 1H), 5.41 (s, 1H), 2.84 (quint, $^3J_{H,H}$=9.0 Hz, 1H), 2.40–2.29 (m, 2H), 2.26–2.11 (m, 2H), 1.97–1.89 (m, 1H), 1.68–1.48 (m, 7H), 1.43–1.29 ppm (m, 2H); ^{13}C NMR (C_6D_6, 100 MHz): δ=143.0, 136.3, 134.4, 129.4, 126.9, 126.1, 123.9, 69.0, 38.7, 32.2, 31.7, 31.5, 30.8, 26.0, 25.9, 21.7 ppm; IR (film): $\tilde{\nu}$=3392 (s), 2946 (s), 1661 (w), 1596 (m), 1575 (m), 1472 (w), 1426 (w), 1187 (m), 1035 (m), 790 (w), 699 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 276 (1) [M^+], 260 (30), 258 (100), 223 (10), 217 (26), 215 (10), 191 (11), 189 (33), 165 (16), 154 (15), 153 (16), 152 (12), 133 (37), 125 (13), 115 (10), 91 (20); HRMS (EI): *m*/*z*: calcd for $C_{17}H_{21}ClO$: 276.1281; found: 276.1284.

3-Isopropylbicyclo[2.2.1]hepta-2,5-diene-2-carbaldehyde (8a): According to typical procedure **C**, *i*PrMgCl·LiCl (2.20 mmol, 1.22 M, 1.80 mL) was added to **6** (1.00 mmol, 250 mg). After the exchange was complete, Li_2CuCl_4 (0.01 mmol, 0.10 M in THF, 0.1 mL) was added. The newly formed alkenylmagnesium species **7** was quenched with DMF (1.50 mmol, 0.12 mL). After standard work-up, the resultant oil was purified by column chromatography (pentane/ethyl acetate 9:1) to give **8a**

(116 mg, 72%) as a yellow oil. GC purity ≥99% (retention time: 3.07 min, measured by method 70); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=9.87 (s, 1H), 6.65–6.63 (m, 1H), 6.38–6.36 (m, 1H), 4.09 (s, 1H), 3.22 (s, 1H), 2.93 (sept, $^3J_{H,H}$=6.8 Hz, 1H), 1.77 (d, $^3J_{H,H}$=6.7 Hz, 1H), 1.63 (d, $^3J_{H,H}$=6.7 Hz, 1H), 0.81 (d, $^3J_{H,H}$=6.8 Hz, 3H), 0.63 ppm (d, $^3J_{H,H}$=6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ=183.5, 182.5, 147.0, 143.7, 141.0, 70.0, 51.8, 47.7, 27.0, 19.0 ppm; IR (film): $\tilde{\nu}$=3437 (w), 2966 (s), 1659 (s), 1465 (m), 1332 (w), 1291 (m), 701 (w), 664 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 162 (45) [M^+], 147 (16), 133 (10), 129 (12), 119 (21), 105 (17), 96 (10), 92 (12), 91 (52), 77 (14), 67 (10), 66 (100), 65 (13), 41 (13); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{14}O$: 162.1045; found: 162.1035.

(3-Isopropylbicyclo[2.2.1]hepta-2,5-dien-2-yl)phenylmethanone (8b): According to typical procedure **B**, *i*PrMgCl·LiCl (2.20 mmol, 1.22 M, 1.80 mL) was added to **6** (1.00 mmol, 250 mg). After the exchange was complete, Li_2CuCl_4 (0.01 mmol, 0.10 M in THF, 0.10 mL) was added. The newly formed alkenylmagnesium species **7** was transmetallated with $ZnCl_2$ (1.0 mmol, 1.00 M in THF, 1.00 mL) and then CuCN·2LiCl (0.20 mmol, 1.00 M, 0.20 mL), and the resultant copper–zinc reagent was quenched with benzoyl chloride (1.50 mmol, 0.17 mL). After standard work-up, the resultant oil was purified by column chromatography (pentane/ethyl acetate 9:1) to give **8b** (138 mg, 58%) as a pale-yellow solid. GC purity ≥99% (retention time: 4.73 min, measured by method 70); m.p. 47.8–50.4 °C; ^{1}H NMR (C_6D_6, 400 MHz): δ=7.76 (d, $^3J_{H,H}$=6.7 Hz, 2H), 7.14–7.07 (m, 3H), 6.90–6.88 (m, 1H), 6.52–6.50 (m, 1H), 3.86 (s, 1H), 3.38 (s, 1H), 2.87 (sept, $^3J_{H,H}$=6.7 Hz, 1H), 1.89 (d, $^3J_{H,H}$=6.5 Hz, 1H), 1.85 (d, $^3J_{H,H}$=6.5 Hz, 1H), 0.91 (d, $^3J_{H,H}$=3.3 Hz, 3H), 0.62 ppm (d, $^3J_{H,H}$=3.3 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ=193.0, 172.3, 145.4, 143.4, 141.0, 140.4, 131.8, 128.7, 128.2, 69.6, 53.0, 51.7, 28.2, 20.4, 18.7 ppm; IR (film): $\tilde{\nu}$=2966 (m), 2868 (w), 1628 (s), 1334 (m), 1288 (m), 1250 (m), 999 (w), 884 (w), 808 (w), 725 (s), 696 (m), 662 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 238 (39) [M^+], 223 (11), 195 (11), 173 (17), 172 (34), 115 (10), 105 (100), 91 (22), 78 (11), 77 (80), 66 (41), 65 (14), 51 (31), 43 (11), 41 (37); HRMS (EI): *m*/*z*: calcd for $C_{17}H_{18}O$: 238.1358; found 238.1344.

Ethyl 4-(3-isopropylbicyclo[2.2.1]hepta-2,5-diene-2-yl)benzoate (8c): According to typical procedure **C**, *i*PrMgCl·LiCl (2.20 mmol, 1.22 M, 1.80 mL) was added to **6** (1.00 mmol, 250 mg). After the exchange was complete, Li_2CuCl_4 (0.01 mmol, 0.10 M in THF, 0.10 mL) was added. The newly formed alkenylmagnesium species **7** was coupled with 4-iodoethyl benzoate (1.50 mmol, 414 mg) in the presence of 5% [Pd(dba)$_2$] (0.05 mmol, 29 mg) and 7% tfp (0.07 mmol, 16 mg). After standard work-up, the resultant oil was purified by column chromatography (pentane/ethyl acetate 19:1) to give **8c** (177 mg, 63%) as a white solid. GC purity ≥99% (retention time: 5.45 min, measured by method 70); m.p. 42.3–43.7 °C; ^{1}H NMR (C_6D_6, 400 MHz): δ=8.24 (d, $^3J_{H,H}$=8.4 Hz, 2H), 7.21–7.19 (m, 2H), 6.79–6.77 (m, 1H), 6.66–6.64 (m, 1H), 4.15 (q, $^3J_{H,H}$=7.0 Hz, 2H), 3.52 (s, 1H), 3.44 (s, 1H), 2.93 (sept, $^3J_{H,H}$=6.7 Hz, 1H), 1.93 (s, 2H), 1.08–1.03 (m, 6H), 0.72 ppm (d, $^3J_{H,H}$=6.7 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ=166.1, 158.4, 144.6, 142.5, 142.1, 129.9, 128.6, 126.2, 69.9, 60.5, 55.0, 51.1, 27.3, 21.4, 19.0, 14.2 ppm; IR (film): $\tilde{\nu}$=2960 (m), 1712 (s), 1604 (m), 1463 (w), 1365 (w), 1268 (s), 1176 (m), 1103 (s), 1022 (m), 857 (w), 808 (w), 772 (s), 724 (s), 708 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 283 (20), 282 (100) [M^+], 259 (12), 235 (17), 215 (35), 214 (55), 171 (10), 167 (11), 165 (10), 143 (52), 128 (12); HRMS (EI): *m*/*z*: calcd for $C_{19}H_{22}O_2$: 282.1620; found: 282.1635.

(*R*)-2-Bromo-3-iodo-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene (9): (*R*)-2-Bromo-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene (10 mmol, 2.15 g), obtained by a Shapiro reaction from the camphor hydrazone according to the published procedure,[18] was deprotonated at the vinylic position with LDA (25 mmol, 1 M in THF) and the anion was trapped in situ with trimethyltin chloride (10 mmol, 2 g) as described by De Lucchi.[11] The product **10** was not isolated, but was quenched in situ with a solution of iodine (11.0 mmol, 2.79 g) in THF (20 mL) to yield **9**. The reaction mixture was concentrated under high vacuum to remove Me_3SnI, the product was extracted with pentane, and the combined extracts were washed with saturated $Na_2S_2O_3$ solution and water. The resultant oil was purified by column chromatography (pentane) to give **9** (1.68 g, 60%) as a pale-yellow oil. GC purity ≥99% (retention time: 3.71 min, measured by method 70); ^{1}H NMR (C_6D_6, 400 MHz): δ=2.34 (d, $^3J_{H,H}$=3.5 Hz, 1H), 1.42–1.36 (m, 1H), 1.23–1.18 (m, 1H), 1.04–0.97 (m, 2H), 0.94 (s, 3H), 0.76 (s, 3H), 0.47 ppm (s, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ=139.2, 99.2, 63.8, 59.5, 56.8, 31.8, 25.0, 19.6, 18.9, 13.4 ppm; IR (film): $\tilde{\nu}$=2958 (s), 2871 (m), 1574 (m), 1472 (w), 1441 (w), 1388 (w), 1300 (w), 1152 (w), 1111 (w), 1013 (s), 969 (m), 815 (m), 773 (m), 730 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 342 (36), 340 (41) [M^+], 314 (12), 216 (12), 215 (98), 214 (12), 213 (96); HRMS (EI): *m*/*z*: calcd for $C_{10}H_{14}{}^{79}BrI$: 339.9324; found 339.9335.

(*R*)-(3-Isopropyl-4,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl)phenylmethanone (13): According to typical procedure **C**, *i*PrMgCl·LiCl (2.20 mmol, 1.22 M, 1.80 mL) was added to **9** (1.00 mmol, 340 mg). After the exchange was complete (1 h, 0 °C), a solution of CuCN·2LiCl (1.00 mmol, 1 M in THF, 1.00 mL) was added at −60 °C. The newly formed alkenylmagnesium species **12** was first transmetallated with $ZnCl_2$ (1.00 mmol, 1.00 M in THF, 1.00 mL) and then, after 10 min, a solution of CuCN·2LiCl (1.00 mmol, 1.00 M in THF, 1.00 mL) was added and the mixture was quenched with benzoyl chloride (1.50 mmol, 0.17 mL) at −30 °C. After standard work-up, the resultant oil was purified by column chromatography (pentane/ethyl acetate 19:1) to give **13** (85 mg, 30%), which was recrystallised from heptane to give colourless crystals. GC purity ≥99% (retention time: 5.28 min, measured by method 70); m.p. 61.7–64.5 °C; ^{1}H NMR (C_6D_6, 400 MHz): δ=7.97–7.95 (m, 2H), 7.13–7.10 (m, 3H), 2.76 (sept, $^3J_{H,H}$=7.0 Hz, 1H), 2.64 (d, $^3J_{H,H}$=3.5 Hz, 1H), 1.86–1.79 (m, 1H), 1.59–1.43 (m, 2H), 1.29–1.22 (m, 1H), 1.03–0.95 (m, 12H), 0.62 ppm (s, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ=195.7, 159.9, 140.6, 140.1, 132.1, 129.1, 128.4, 58.2, 56.1, 55.6, 33.1, 29.1, 26.3, 20.8, 20.5, 20.0, 19.3, 13.2 ppm; IR (film): $\tilde{\nu}$=2962 (s), 2872 (w), 1629 (s), 1595 (m), 1446 (m), 1331 (m), 1272 (m), 1249 (m), 809 (m), 778 (w), 720 (s), 692 (s), 660 cm^{-1} (s); MS (EI, 70 eV): *m*/*z* (%): 283 (23), 282 (100) [M^+], 280 (28), 279 (18), 267 (22), 265 (20), 254 (10), 239 (25), 237 (11), 105 (35); HRMS (EI): *m*/*z*: calcd for $C_{20}H_{26}O$: 282.1984; found 282.1992.

Kinetic measurements: A mixture of 1-bromocyclopentene[19] (1.0 equiv) and 1-(trimethylstannyl)-2-bromocyclopentene[20] (1.0 equiv) was cooled to −65 °C. *i*PrMgCl·LiCl (2.0 equiv) and CuCN·2LiCl (4 mol%) were added, and the reaction mixture was slowly allowed to warm to 5 °C over 5 h. The progress of the reaction was monitored by GC analysis of hydrolysed aliquots of the reaction mixture, taken at intervals of 30 min. It was observed that the reaction of 1-(trimethylstannyl)-2-bromocyclopentene ($t_{1/2}$=60 min) with *i*PrMgCl·LiCl and catalytic CuCN·2LiCl was much faster than that of 1-bromocyclopentene ($t_{1/2}$=135 min); 1-(trimethylstannyl)-2-bromocyclopentene was fully consumed within 150 min. The results are summarized in Figure 2.

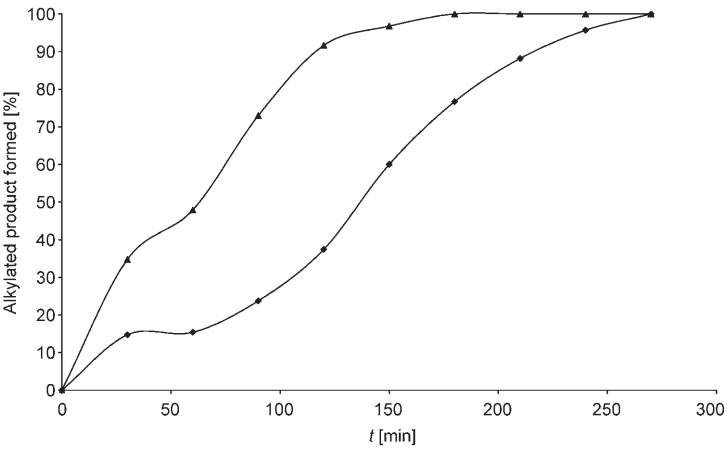


Figure 2. Rates of copper-catalysed alkylation of two bromocyclopentene derivatives: ◆: 1-bromocyclopenten, ▲: 1-(trimethylstannyl)-2-bromocyclopentene.

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