Silaborative Carbocyclization of 1,6-Enynes

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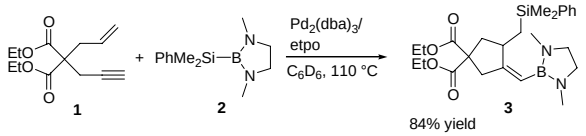
Summary: The silaboration of 1,6-enynes gives densely functionalized five-membered rings that offer promising reactivities for further synthetic manipulations. We have found that using silylborane ***4*** *silaborative carbocyclization reactions proceed in good to excellent yields, giving the product as a single diastereomer. Attempts to extend this methodology to include terminally substituted enynes and developing asymmetric versions were largely unsuccessful. The vinylboronates formed were employed in Suzuki cross-coupling reactions with a range of aryl bromides, furnishing arylated product in good yields.*

Introduction

The transition metal catalyzed carbocyclization of 1,6-enynes gives direct access to five-membered carbocycles and heterocycles.[1] These processes can be performed in tandem with addition reactions. Examples include the addition of aryl groups,[2] oxygen nucleophiles,[3] H-Si,[4] H-B,[5] H-H,[6] and H-Sn.[7] When compounds containing interelement linkages,[8,9] such as B-Sn,[10] Sn-Si,[11] and B-Si,[12] are added products containing two reactive functional groups are formed. These products offer promising reactivities for further synthetic elaborations. So far these reactivities have not been explored and only a limited number of substrates have been employed, leaving unanswered questions on the generality and applicability of these processes. We therefore decided to extend our studies on silaboration reactions[13] to the silaborative carbocyclization of 1,6-enynes, and to explore the utility of the products formed.

Scheme 1. Silaborative Carbocyclization of Enyne 1.



The silaborative carbocyclization of a 1,6-enyne (Scheme 1) was performed by Tanaka and co-workers as part of a study on silaborations of alkynes and diynes. Enyne **1** was reacted with silylborane **2** furnishing compound **3** in 84% yield using a $Pd_2(dba)_3$/etpo catalyst system (M/L ratio 1:2, C_6D_6, 110 °C, 2 h).[12] No other enynes were employed in this study. The silastannylative carbocyclization of 1,6-enynes has been more thoroughly studied. A number of 1,6-enynes were successfully employed using phosphine-free Pd-complexes as catalyst, giving the product in good to moderate yields. Terminally substituted enynes were generally less reactive than unsubstituted ones, resulting in moderate to poor yields. The reactivities of the products formed were not investigated.[11]

Results and Discussion

Palladium Catalyzed Silaborations. We started our investigation by examining the reaction of silylborane **4** and enyne **5**, derived from dimethyl malonate. Screening was performed on a 1:1 mixture of reactants using $Pd_2(dba)_3$ and various phosphane ligands[14] in toluene at 110 °C. Under these conditions the desired product was not formed, albeit some products derived from silaboration of the alkyne were observed. Fortunately the desired product could be obtained in 50% yield

(1) Michelet, V.; Toullec, P. Y.; Gent, J.-P. *Angew. Chem. Int. Ed*. **2008**, *47,* 4268-4315.

(2) Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094-1095.

(3) Galland, J.-C.; Dias, S.; Savignac, M.; Genêt, J.-P. *Tetrahedron* **2001**, 57, 5137-5148.

(4) (a) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580-6582. (b) Ojima, I.; Vu, A. T.; Lee, S.-Y.; McCullagh, J. V.; Moralee, A. C.; Fujiwara, M.; Hoang, T. H. *J. Am. Chem. Soc.* **2002**, *124*, 9164-9174. (c) Widenhoefer, R. A. *Acc. Chem. Res.* **2002**, *35*, 905-913. (d) Chakrapani, H.; Liu, C.; Widenhoefer, R. *Org. Lett.* **2003**, *5*, 157-159. (e) Park, K. H.; Kim, S. Y.; Son, S. U.; Chung, Y. K. *Eur. J. Org. Chem.* **2003**, 4341-4345. (f) Denmark, S. E.; Liu, J. H.-C. *J. Am. Chem. Soc.* **2007**, *129*, 3737-3744.

(5) (a) Widenhoefer, R. A.; Kinder, R. E. *Org. Lett.* **2006**, *8*, 1967-1969. (b) Marco-Martínez, J.; López-Carillo, V.; Bunuel, E.; Simancas, R.; Cárdenas, D. J. *J. Am. Chem. Soc.* **2007**, *129*, 1874-1875.

(6) (a) Trost, B. M.; Rise, F. *J. Am. Chem. Soc.***1987**, *109*, 3161-3163. (b) Chen, M.; Weng, Y.; Guo, M.; Zhang, H.; Lei, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 2279-2282.

(7) Lautens, M.; Mancuso, J. *Org. Lett.* **2000**, *2*, 671-673.

(8) Editorial *J. Organomet. Chem* **2000**, *611*, 3-4.

(9) For some reviews of interelement additions, see: (a) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221-3256. (b) Beletskaya, I.; Moberg, M. *Chem. Rev.* **2006**, *106*, 2320-2354.

(10) Onozawa, S.-y.; Hatanaka, Y, Choi, N; Tanaka, M *Organometallics* **1997**, *16*, 5389-5391.

(11) Mori, M.; Hirose, T.; Wakamatsu, H.; Imakuni, N.; Sato, Y. *Organometallics* **2001**, *20*, 1907-1909.

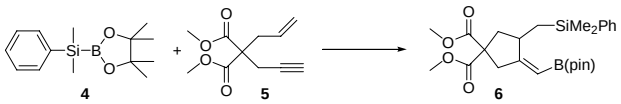
(12) Onozawa, S.-y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229-1230.

(13) (a) Gerdin, M.; Moberg, C. *Adv. Synth. Catal.* **2005**, *347*, 749-753. (b) Gerdin, M., Moberg, C. *Org. Lett.* **2006**, *8*, 2929. (c) Lüken, C.; Moberg, C. *Org. Lett.* **2008**, *10*, 2505-2508. (d) Durieux, G.; Gerdin, M.; Moberg. C.; Jutand, A. *Eur. J. Inorg. Chem.* **2008**, 4236-4241. (e) Gerdin, M.; Penhoat, M.; Zalubovskis, R.; Pétermann, C.; Moberg, M. *J. Organomet. Chem.* **2008**, *693*, 3519-3526.

(14) $P(OEt)_3$, $PPhMe_2$, $P(OPh)_3$, and PPh_3.

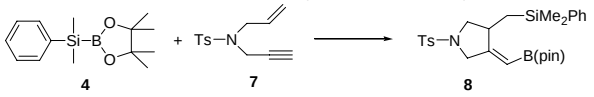
as a 5:1 mixture of isomers by switching to Pd-PEPPSI-IPr[15] catalyst in diethyl ether.

Scheme 2. Silaborative Carbocyclization of Enyne 5.



Using the same conditions the reaction could be extended to enyne **7**, forming pyrrolidine **8** in 31% yield as a 2:1 mixture of isomers (Table 2, entry 1). Although no by-products could be identified, enyne **7** was completely consumed during the reaction. The reaction temperature was decreased, and an optimum was found at 50 °C where decomposition was reduced, and the desired product was formed in 49% yield (entries 1–4). Gratifyingly, the selectivity of the reaction was also improved and the product was now obtained as a single detectable diastereomer (^{1}H NMR).

Table 1. Silaborative Carbocyclization of Enyne 7



Entry	Temp. (°C)	Time (h)	Yield (%)[a]	d.r.
1	110	24	31	2:1
2	80	24	42	5:1
3	50	24	49	> 98:2
4	r.t.	24	25	> 98:2

Reactions performed in Et_2O using 10 mol % Pd-PEPPSI-IPr. [a]Determined by ^{1}H NMR using 1-methoxynapthalene as internal standard.

Enyne **7** was added to silylborane **4** over 15 hours using a syringe pump. After 18 hours at 50 °C a disappointing 50% yield was recorded. Exchange of diethyl ether for THF gave 56% yield (Table 2, entry 1). As enyne decomposition seemed to be a major problem the amount of **7**, which is readily available from inexpensive starting materials, was increased to 2 equivalents, resulting in 84% yield (entry 2). The yield could be improved even further by reducing the amount of catalyst employed, underlining the importance of suppressing the decomposition pathways (entries 3 and 4).

Table 2. Silaborative Carbocyclization of Enyne 7

Entry	Catalyst (%)	Equiv. of **7**	Yield (%)[a]
1	10	1	56
2	10	2	84
3	5	2	93
4	1	2	96

Reactions performed in THF using Pd-PEPPSI-IPr catalysis for 24 h at 50 °C, yielding the product as a single detectable diastereomer (^{1}H NMR). [a]Determined by ^{1}H NMR using 1-methoxynapthalene as internal standard.

A scope and limitations study was performed. First enyne **5** was subjected to the optimized conditions, yielding the desired product in 98% isolated yield as a single isomer. Then a number of enynes were tested at 50, 80 and 110 °C employing 5 mol % Pd-PEPPSI-IPr. Any substituents introduced at the double or triple bond resulted in low or no yields (Figure 1). At 50 °C the enynes remained largely intact, but at 80 °C and 110 °C various amounts of decomposition occurred.

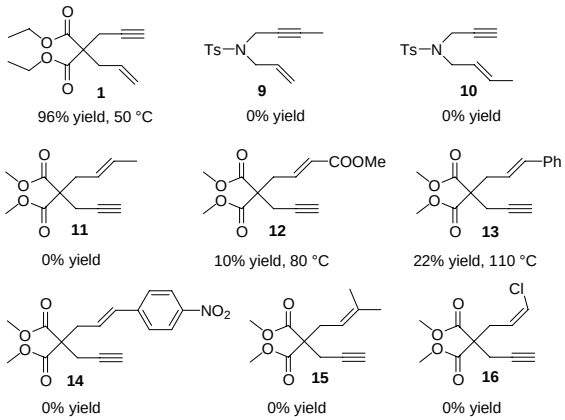


Figure 1. Enynes employed in scope and limitations study. Reactions performed for 24 h in THF using 5 mol % Pd-PEPPSI-IPr and 1.5 equivalents of the enyne.

Several attempts aimed at developing an asymmetric version of the reaction were performed, starting by the use of chiral NHC ligands (**17**–**20**). As none of these showed any significant chiral induction (Table 4, entries 1–4) we turned to substrate controlled reactions. Employing chiral silylboranes (**21**–**23**) was equally unsuccessful (entries 5–7), while chiral enynes (**24** and **25**) gave low but significant selectivities (entries 8–9).

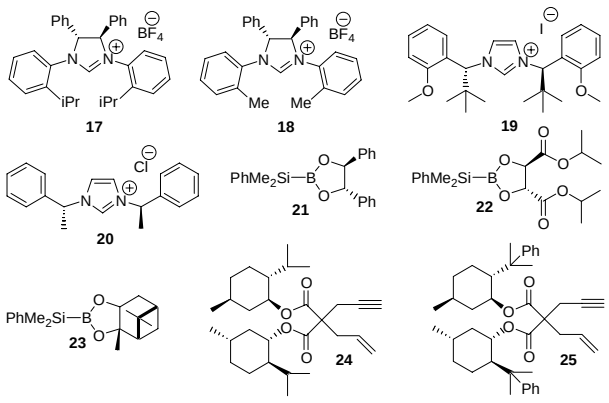
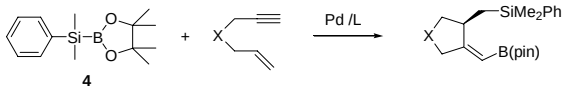


Figure 2. Chiral Compounds Employed in Silaborative Carbocyclizations of Enynes

(15) Organ, M. G.; Abdel-Hadi; M.; Avola, S.; Hadei, N.; Nasielski, J.; O'Brien, C. J.; Valente, C. *Chem. Eur. J.* **2007**, *13*, 150-157.

Table 4. Attempts at Asymmetric Silaborative Carbocyclization Reactions



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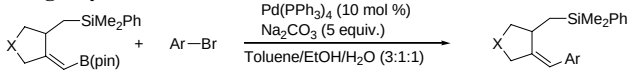
Entry	Catalyst	Ligand	Si-B	Enyne	Yield (%)[a]	Selectivity
1[b]	$Pd(acac)_2$	**17**	**4**	**7**	60	52:48[f]
2[c]	$Pd(acac)_2$	**18**	**4**	**7**	65	50:50[f]
3[d]	$Pd_2(dba)_3$	**19**	**4**	**7**	0	-
4[e]	$Pd_2(dba)_3$	**20**	**4**	**7**	41	52:48[f]
5	PEPPSI	-	**21**	**7**	72	50:50[g]
6	PEPPSI	-	**22**	**7**	67	52:48[g]
7	PEPPSI	-	**23**	**7**	68	50:50[g]
8	PEPPSI	-	**4**	**24**	95	61:39[g]
9	PEPPSI	-	**4**	**25**	98	59:41[g]

Reactions performed in THF for 24 h at 50 °C. [a]Determined by ^{1}H NMR using 1-methoxynapthalene as internal standard. [b]Reaction performed in toluene. THF, Et_2O and DCM were also employed without improving yield or selectivity. [c]DIBALH used to reduce Pd(II) and deprotonate the imidazolinium salt. [d]NaO*t*Bu used to deprotonate imidazolium salt. [e]NaH/NH_3 used to deprotonate imidazolium salt. [f]Determined by chiral HPLC; CHIRALCEL OD-H, 12% *i*PrOH in hexane, flow rate 0.25 mL/min. [g]Determined from crude ^{1}H NMR spectrum.

Palladium Catalyzed Arylations. To explore the reactivity of the vinylboronates formed, the Suzuki cross-coupling reaction between vinylpyrrolidine **8** and bromobenzene was investigated. After an initial screening of reaction conditions we found that the best result was obtained by using $Pd(PPh_3)_4$ as catalyst in a mixture of toluene, ethanol and water. Next, the substrate scope was examined using various aryl bromides and two types of vinylboronates. The results are summarized in Table 5.

Table 5: Suzuki Cross-Coupling of Vinyl Boronate 8 or 26 using Aryl Bromides.



X = NTs **8**
X = $C(CO_2Et)_2$ **26**

X = NTs **27**
X = $C(CO_2Et)_2$ **28**

Entry	Substrate	Ar	Product	Yield (%)[a]
1[b]	**8**	Ph	**27a**	87
2	**8**	4-$MeOC_6H_4$	**27b**	77
3	**8**	3-$MeOC_6H_4$	**27c**	78
4	**8**	2-$MeOC_6H_4$	**27d**	80
5	**8**	4-CNC_6H_4	**27e**	83
6	**8**	4-ClC_6H_4	**27f**	88
7	**8**	3-Pyridyl	**27g**	77
8	**8**	2,4,6-$Me_3C_6H_2$	**27h**	77
9	**8**	1-Naphthyl	**27i**	86
10	**26**	4-$MeOC_6H_4$	**28a**	80
11	**26**	4-CNC_6H_4	**28b**	85

All reactions were performed on a 0.20 mmol scale using substrate **8** or **26** (1.0 equiv.), aryl bromide (1.2 equiv.), Na_2CO_3 (5 equiv.), and $Pd(PPh_3)_4$ (10 mol %), in toluene/ethanol/water (3:1:1), at 80 °C for 18 h. Concentration 0.05 M with respect to the substrate **8** or **26**. [a]Isolated yield. [b]Reaction was performed using 2.0 equiv. of bromobenzene.

The optimized conditions for the Suzuki cross-coupling of vinyl pyrrolidine **8** and bromobenzene proved to be efficient for all other aryl bromides, and the corresponding arylated products were isolated in good yields. Neither electron-donating nor electron-withdrawing substituents on the aryl bromides seemed to have a significant influence on the yield of the reaction (entries 2 and 6). Moreover, it was possible to couple even sterically demanding aryl bromides such as 2-bromomesitylene (entry 7) and 1-bromonaphthalene (entry 8) in good yields. Not only vinylpyrrolidine **8** but also vinylcyclopentane **26** turned out to be suitable substrates for the Suzuki cross-coupling (entries 10 and 11).

Conclusions

A high-yielding silaborative carbocyclization reaction using silylborane **4** was developed, selectively furnishing functionalized five-membered derivatives. The reaction shows little tolerance to substituents at the double or triple bond of the enyne. Attempts to perform the reaction in an enantio- or diastereoselective fashion were unsuccessful.

A protocol for the Suzuki cross-coupling of the vinylboronates formed was also developed. Using a range of aryl bromides the corresponding arylated products were formed in good yields.

Experimental Section

General Considerations. All transition metal catalyzed reactions were prepared inside a nitrogen filled glovebox using oven dried glassware. After the reaction flask had been sealed, heating was performed outside the glovebox. Toluene, THF, Et_2O, and CH_2Cl_2 were dried using a Glass-contour solvent dispensing system. Compounds **1**,[16] **4**,[17] **7**,[18] **5**,[19] **9**,[20] **10**,[21] **11**,[22]

(16) Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kiyomi, K. *J. Am. Chem. Soc.* **2002**, *124*, 3806-3807.

(17) Suginome, M.; Matsuda, T.; Ito, Y. *Organometallics* **2000**, *19*, 4647-4649.

13,[23] **14**,[5b] **15**,[24] **17**–**18**,[25], **20**,[26] and **21**–**23**,[27] were synthesized according to literature procedures. All other chemicals were of at least 97% purity and used as received. ^{1}H NMR spectra were recorded at 500 or 400 MHz and ^{13}C spectra at 125 or 100 MHz. The ^{1}H and ^{13}C chemical shifts are reported relative to $CHCl_3$.

General procedure for silaborative carbocyclization of enynes using Pd-PEPPSI-IPr as catalyst Inside a nitrogen filled glovebox MeMgCl in THF (3 M, 13.3 μL, 0.04 mmol) was added to a THF solution (400 μL) of Pd-PEPPSI-IPr (13.6 mg, 0.02 mmol) at –35 °C, and the solution allowed to reach rt over 1 h. The resulting solution (0.05 M in Pd, 10–100 μL) was added to silylborane **4** (26.2 mg, 0.1 mmol), the enyne (1–2 eq), and 1-methoxynapthalene (15.8 mg, 0.1 mmol) in THF (300 μL). The vial was capped and heating performed outside the glovebox. The reaction was monitored by taking out 20 μL samples, evaporating the solvent and recording the ^{1}H NMR spectrum. NMR yields were calculated by comparing the integral of the olefinic proton in the product and the methoxygroup in 1-methoxynapthalene. Purification was performed by evaporating the solvents, adding the crude product onto a SiO_2 column and eluting with an appropriate eluent. *p*-Anisaldehyde solution was used to develop TLC plates.

(*E*)-Dimethyl-3-((dimethylphenylsilyl)methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-cyclopentane-1,1-dicarboxylate (6). The reaction was performed using 2 equiv. of enyne **5** and 1 mol % Pd-PEPPSI-IPr catalyst at 50 °C for 24 h. After flash chromatography on SiO_2 (gradient of 5–20% Et_2O in hexane) the product was isolated as a colorless oil in 98% yield. *E* configuration of the double bond was assigned by NOESY spectroscopy. ^{1}H NMR ($CDCl_3$) δ 0.338 (s, 3H), 0.346 (s, 3H), 0.87 (dd, J = 14.3, 12.8 Hz, 1H), 1.21 (s, 6H), 1.23 (s, 6H), 1.39 (dd, J = 14.3, 2.4 Hz, 1H), 1.83 (dd, J = 13.5, 5.7 Hz, 1H), 2.60 (ddd, J = 13.5, 8.3, 1.0 Hz, 1H), 2.80 (d, J = 16.6 Hz), 3.13 (m, 1H), 3.26 (app. dt, J = 16.6, 2.1 Hz, 1H), 3.67 (s, 3H), 3.68 (s, 3H), 5.18–5.21 (m, 1H), 7.31–7.36 (m, 3H), 7.51–7.55 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –2.3, –2.0, 24.7, 24.9, 38.4, 40.9, 43.8, 52.67, 52.69, 58.6, 82.8, 109.6 (br), 127.6, 128.7, 133.5, 139.6, 172.0, 172.4, 173.0; Anal Calc. for $C_{25}H_{37}BO_4Si$: C, 63.55; H, 7.89. Found: C, 63.48, H, 7.73%

(*E*)-3-((Dimethylphenylsilyl)methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-1-tosylpyrrolidine (8). The reaction was performed using 2 equiv. of enyne **7** and 1 mol % Pd-PEPPSI-IPr catalyst at 50 °C for 24 h. After flash chromatography on SiO_2 (1:1 DCM/hexane) the product was isolated as a white solid in 81% yield. *E* configuration of the double bond was assigned by NOESY spectroscopy. ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 3H), 0.34 (s, 3H), 0.88-0.96 (m, 2H), 1.213 (s, 6H), 1.216 (s, 6H), 2.40 (s, 3H), 2.97 (dd, J = 9.0, 6.0 Hz, 1H), 3.08 (dd, J = 9.6, 1.8 Hz, 1H), 3.17–3.27 (m, 1H), 3.58 (dd, J = 15.0, 1.8 Hz, 1H), 4.03 (app. dt, J = 15.0, 1.7 Hz, 1H), 5.08–5.12 (m, 1H), 7.26–7.30 (m, 2H), 7.33–7.39 (m, 3H), 7.47–7.53 (m, 2H), 7.58–7.64 (m, 2H); ^{13}C NMR ($CDCl_3$) δ -2.18, -2.15, 21.5, 22.6, 24.7, 24.8, 39.2, 53.3, 54.0, 83.1, 109.0 (br), 127.80, 127.82, 129.0, 129.54, 129.59, 132.6, 133.6, 138.8, 143.5,167.6.

(*E*)-Dimethyl-3-((dimethylphenylsilyl)-phenyl-methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-cyclopentane-1,1-dicarboxylate. The reaction was performed using 1.5 equiv. of enyne **13** and 5 mol % Pd-PEPPSI-IPr catalyst at 80 °C for 24 h. After flash chromatography on SiO_2 (gradient of 5–20% Et_2O in hexane) the product could be isolated as a colorless oil in ~70% purity, dr 95:5. Major contaminant was what seem to be products of alkyne silaboration. ^{1}H NMR ($CDCl_3$) δ 0.37 (s, 3H), 0.40 (s, 3H), 1.29 (s, 12H), 2.09 (app. dt, J = 15.6, 2.3 Hz, 1H), 2.34 (dd, J = 13.8, 7.2 Hz, 1H), 2.48 (d, J = 15.6 Hz, 1H), 2.68 (ddd, J = 13.8, 8.8, 1.2 Hz, 1H), 3.15 (d, J = 5.1 Hz, 1H), 3.64 (s, 3H), 3.65 (s, 3H), 6.97–7.02 (m, 2H), 7.08–7.17 (m, 3H), 7.24–7.34 (m, 3H), 7.42–7.46 (m, 2H).

(*E*)-Dimethyl-3-((dimethylphenylsilyl)-methoxycarbonyl-methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-cyclopentane-1,1-dicarboxylate. The reaction was performed using 1.5 equiv. of enyne **12** and 5 mol % Pd-PEPPSI-IPr catalyst at 110 °C, 24 h. After flash chromatography on SiO_2 the product was isolated as a colorless oil contaminated by what seems to be by-products formed via alkyne silaboration (purity ~80%, dr 14.3:1). ^{1}H NMR ($CDCl_3$) δ 0.43 (s, 3H), 0.45 (s, 3H), 1.26 (s, 12H), 2.44 (ddd, J = 12.5, 8.8, 1.7 Hz, 1H), 2.64 (dd, J = 12.5, 10.0 Hz, 1H), 2.82 (d, J = 15.9 Hz, 1H), 2.9–3.0 (m, 1H), 3.33 (app. dt, J = 15.9, 2.6 Hz, 1H), 3.51 (s, 3H), 3.61 (s, 1H), 3.70 (s, 1H), 5.26 (app. s, 1H), 7.32–7.40 (m, 3H), 7.54–7.59 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –3.0, –2.3, 24.8, 25.0, 36.7, 39.7, 40.2, 46.2, 50.6, 52.58, 52.64, 58.9, 83.0, 127.7, 129.4, 133.9, 136.7, 170.7, 171.5, 172.0, 174.5.

(*E*)-Diethyl-3-((dimethylphenylsilyl)methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-cyclopentane-1,1-dicarboxylate (26). The reaction was performed using 1.5 equiv. of enyne **1** and 5 mol % Pd-PEPPSI-IPr catalyst at 50 °C for 24 h. After flash chromatography on SiO_2 the product was isolated as a colourless oil. *E* configuration of the double bond was assigned by NOESY spectroscopy. ^{1}H NMR ($CDCl_3$) δ 0.34 (s, 3H), 0.35 (s, 3H), 0.89 (t, J = 3.1 Hz, 1H), 1.19 (app. td, J = 7.1, 2.9 Hz, 6H), 1.21 (s, 6H), 1.22 (s, 6H), 1.40 (dd, J = 14.4, 2.2 Hz, 1H), 1.77 (dd, J = 13.5, 5.8 Hz), 2.59 (dd, J = 13.5, 8.3 Hz, 1H), 2.78 (d, J = 16.5 Hz, 1H), 3.08–3.18 (m, 1H), 3.25 (app. dt, J = 16.5, 2.0 Hz, 1H), 4.05–4.21 (m, 4H), 5.19 (app. s, 1H), 7.30–7.35 (m, 3H), 7.50–7.56 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –2.1, –1.8, 14.12, 14.13, 24.93, 25.08, 25.15, 38.6, 41.1, 44.0, 59.0, 61.5, 61.6, 83.0, 109.7, 127.8, 128.9, 133.7, 139.8, 171.7, 172.1, 173.5.

(*E*)-3-((Dimethylphenylsilyl)methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-cyclopentane-1,1-dicarboxylic acid bis-((−)-menthol) ester. The reaction was performed using 1.2 equiv. of enyne **24** and 5 mol % Pd-PEPPSI-IPr catalyst at 50 °C for 24 h, yielding the cyclized product as two diastereomers (dr 61:39) in 95% yield (^{1}H NMR). After flash chromatography on SiO_2, using 5% Et_2O in hexane as eluent, a mixture of the two products were isolated as a colourless oil (78% yield, dr 60:40). The diastereomers were separated using a Biotage SP1 employing a gradient of 1–10% Et_2O in pentane as eluent. Major isomer R_f = 0.32 (10% Et_2O/pentane); ^{1}H NMR ($CDCl_3$) δ 0.34 (s, 3H), 0.35 (s, 3H), 0.70 (app. t, J = 7.0 Hz, 6H), 0.78–0.90 (m, 18H), 1.21 (s, 6H), 1.22 (s, 6H), 1.30–1.53 (m, 4H), 1.64–1.71 (m, 4H), 1.78–1.87

(18) Patel, M.; Livinghouse, T.; Pagenkopf, B. L. *Organic Syntheses* **2003**, *80*, 93-103.

(19) Miura, K.; Saito, H.; Fujisawa, N.; Hosomi, A. *J. Org. Chem.* **2000**, *65*, 8119-8122.

(20) Ishizaki, M.; Suzuki, D.; Hoshino, O. *J. Fluorine Chem.* **2001**, *111*, 81-90.

(21) Gibson, S. E.; Kaufmann, K. A. C.; Haycock, P. R.; White, A. J. P.; Hardick, D. J.; Tozer, M. J. *Organometallics* **2007**, *26*, 1578-1580.

(22) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036.

(23) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590-9600.

(24) Nishizawa, M.; Yadav, V. K.; Skwarczynski, M.; Takao, H.; Imagawa, H.; Sugihara, T. *Org. Lett.* **2003**, *5*, 1609-1611.

(25) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225-3228.

(26) Hermann, W. A.; Goossen, L. J.; Artus, G. R. J.; Köcher, C. *Organometallics* **1997**, *16*, 2472-2477.

(27) Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174-11175.

(m, 3H), 1.88–1.95 (m, 2H), 2.51 (ddd, *J* = 13.3, 8.1, 1.4 Hz, 1H), 2.88–3.08 (m, 3H), 4.59–4.71 (m, 2H), 5.22 (app. s, 1H), 7.30–7.35 (m, 3H), 7.51–7.57 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –2.4, – 2.0, 15.8, 15.9, 20.86, 20.91, 21.99, 22.00, 23.00, 23.06, 24.7, 25.0, 25.3, 25.9, 31.3, 34.2, 37.9, 40.4, 40.5, 41.6, 44.4, 46.8, 46.9, 59.5, 75.33, 75.35, 82.7, 109.8 (br), 127.7, 128.8, 133.6, 139.7, 170.9, 171.3, 173.5. Anal. Calc. for $C_{43}H_{69}BO_6Si$: C, 71.64, H, 9.65. Found: C, 71.55, H, 9.79%

Minor isomer R_f = 0.28 (10% Et_2O/Pentane), ^{1}H NMR ($CDCl_3$) δ 0.326 (s, 3H), 0.331 (s, 3H), 0.66 (d, *J* = 6.9 Hz, 3H), 0.70 (d, *J* = 6.9 Hz, 3H), 0.80–0.92 (m, 18H), 1.20 (s, 6H), 1.22 (s, 6H), 1.27–1.37 (m, 2H), 1.40–1.50 (m, 4H), 1.60–1.95 (m, 9H), 2.70 (ddd, *J* = 12.9, 8.2, 1.7 Hz, 1H), 2.74 (d, *J* = 16.7 Hz, 1H), 3.07–3.17 (m, 1H), 3.22 (app. dt, *J* = 15.5, 2.2 Hz, 1H), 4.60–4.72 (m, 2H), 5.17 (app. s, 1H), 7.31–7.35 (m, 3H), 7.51–7.56 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –2.3, –2.0, 15.9, 16.1, 20.76, 20.85, 21.96, 22.00, 23.0, 23.2, 24.7, 24.9, 25.7, 25.8, 26.0, 31.3, 34.2, 37.9, 40.5, 40.6, 41.7, 44.6, 46.9, 47.0, 59.7, 75.07, 75.16, 82.7, 127.7, 128.7, 133.6, 139.7, 170.6, 171.0, 173.1.

***E*)-3-((Dimethylphenylsilyl)methyl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-cyclopentane-1,1-dicarboxylic acid bis-((−)-8-phenylmenthol) ester.** The reaction was performed using 1.2 equiv. of enyne **25** and 5 mol % Pd-PEPPSI-IPr catalyst at 50 °C for 24 h, yielding the cyclized product as a mixture of two diastereomers (dr 59:41) in 98% yield (^{1}H NMR). After flash chromatography on SiO_2, using a gradient of Et_2O in hexane (5–10%) as eluent, the product was isolated as a white fluffy solid (68% yield, 59:41 mixture of isomers). Major (maj) + minor isomer (min) ^{1}H NMR ($CDCl_3$) δ 0.31 (s, 3H, min), 0.338 (s, 3H, min), 0.344 (s, 3H, maj), 0.35 (s, 3H, maj), 0.62–0.78 (m, 2H), 0.80–1.02 (m, 12H), 1.18–1.63 (m, 32H), 1.75–2.05 (m, 5H), 2.41 (dd, *J* = 13.0, 7.8 Hz, 1H, maj), 2.60–2.78 (m, 2H), 2.98–3.20 (m, 1H maj, 2H min), 4.79–4.96 (m, 2H), 5.19 (app. s, 1H, min), 5.21 (app. s, 1H, maj), 7.14–7.19 (m, 2H), 7.22–7.37 (m, 11H), 7.52–7.59 (m, 2H); ^{13}C NMR ($CDCl_3$) δ -2.3, -2.1, -1.8, -1.7, 21.8, 21.9, 23.4, 23.5, 23.6, 24.1, 24.81, 24.84, 24.87, 24.91, 25.3, 25.5, 27.31, 27.35, 27.37, 27.42, 30.1, 30.7, 30.8, 30.9, 31.2, 31.3, 34.43, 34.47, 34.5, 37.8, 38.2, 40.36, 40.41, 41.2, 41.36, 41.48, 41.64, 43.4, 44.4, 50.1, 50.3, 50.42, 50.45, 59.7, 59.9, 76.50, 46.53, 46.6, 82.7, 125.36, 125.39, 125.41, 125.66, 125.7, 125.8, 125.9, 127.67, 127.70, 128.02, 128.06, 128.09, 128.78, 128.82, 133.59, 133.62, 139.6, 139.7, 150.2, 150.3, 150.39, 150.44, 170.77, 170.82, 170.9, 172.9, 173.9.

General Procedure for Suzuki Cross-coupling of Vinyl Boronate 8 and 26. $Pd(PPh_3)_4$ (0.02 mmol), sodium carbonate (1.00 mmol), ethanol (0.8 mL), dist. water (0.8 mL) and aryl bormide (0.24 mmol) were added to a solution of vinylboronate **8** or **26** (1.0 equiv., 0.20 mmol) in toluene (2.4 mL) in a Schlenk tube under nitrogen atmosphere. The reaction mixture was heated for 18 h to 80 °C, and then taken up in dichloromethane (10 mL), and the organic layer was separated. The aqueous phase was extracted with dichloromethane (2 x 10 mL), and the combined organic layers dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. The products were purified by column chromatography furnishing the corresponding pyrrolidine **27a–i** or cyclopentane **28a–b**.

***E*)-3-Benzylidene-4-((dimethylphenylsilyl)methyl)-1-tosylpyrrolidine (27a).** Compound **27a** was isolated after flash chromatography on silica gel (pentane:Et_2O = 5:1, R_f = 0.17) as a yellow oil in 87% yield. ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 3H), 0.32 (s, 3H), 0.80–0.95 (m, 2H), 2.42 (s, 3H), 3.07–3.15 (m, 3H), 3.81 (dd, *J* = 13.7, 1.7 Hz, 1H), 4.12 (d, *J* = 13.7 Hz, 1H), 6.15 (s, 1H), 6.99–7.04 (m, 2H), 7.14–7.18 (m, 3H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.37–7.42 (m, 3H), 7.42–7.46 (m, 2H), 7.69 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ –2.6, –2.5, 20.0, 21.5, 36.0, 52.8, 54.8, 121.2, 126.8, 127.8, 128.0, 128.1, 128.3, 129.3, 129.6, 133.0, 133.6, 136.2, 138.0, 143.5, 143.7.

***E*)-3-((Dimethylphenylsilyl)methyl)-4-(4-methoxybenzylidene)-1-tosylpyrrolidine (27b).** Compound **27b** was isolated after flash chromatography on silica gel (pentane:Et_2O = 4:1, R_f = 0.15) as a yellow oil in 77% yield. ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 3H), 0.34 (s, 3H), 0.80–0.95 (m, 2H), 2.42 (s, 3H), 3.05–3.14 (m, 3H), 3.75–3.80 (m, 4H), 4.10 (d, *J* = 13.6 Hz, 1H), 6.07 (s, 1H), 6.64–6.68 (m, 2H), 6.90–6.94 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.37–7.44 (m, 3H), 7.45–7.48 (m, 2H), 7.68 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ = –2.6, –2.4, 19.9, 21.5, 35.9, 52.8, 54.9, 55.2, 113.7, 120.5, 127.7, 128.0, 128.8, 129.2, 129.3, 129.6, 133.0, 133.6, 138.1, 141.5, 143.5, 158.3.

***E*)-3-((Dimethylphenylsilyl)methyl)-4-(3-methoxybenzylidene)-1-tosylpyrrolidine (27c).** Compound **27c** was isolated after flash chromatography on silica gel (pentane:Et_2O = 4:1, R_f = 0.15) as a yellow oil in 78% yield. ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 3H), 0.30 (s, 3H), 0.81–0.88 (m, 1H), 0.93 (d, *J* = 15.0 Hz, 1H), 2.42 (s, 3H), 3.05–3.16 (m, 3H), 3.76 (s, 3H), 3.80 (dd, *J* = 13.8, 1.1 Hz, 1H), 4.09 (d, *J* = 13.8 Hz, 1H), 6.13 (s, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 6.64–6.66 (m, 1H), 6.72–6.75 (m, 1H), 7.05–7.09 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.35–7.44 (m, 5H), 7.68 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ –2.6, –2.5, 20.0, 21.5, 36.2, 52.8, 54.8, 55.1, 111.9, 114.4, 120.2, 121.1, 127.7, 127.9, 129.2, 129.3, 129.6, 132.9, 133.5, 137.6, 138.1, 143.6, 144.2, 159.6.

***E*)-3-((Dimethylphenylsilyl)methyl)-4-(2-methoxybenzylidene)-1-tosylpyrrolidine (27d).** Compound **27d** was isolated after flash chromatography on silica gel (pentane:Et_2O = 4:1, R_f = 0.15) as a yellow oil in 80% yield. ^{1}H NMR ($CDCl_3$) δ = 0.22 (s, 3H), 0.25 (s, 3H), 0.70–0.77 (m, 1H), 0.87 (d, *J* = 15.0 Hz, 1H), 2.42 (s, 3H), 2.97 (d, *J* = 9.7 Hz, 1H), 3.03–3.09 (m, 1H), 3.16–3.21 (m, 1H), 3.77 (s, 3H), 3.89 (d, *J* = 13.7 Hz, 1H), 4.07 (d, *J* = 13.6 Hz, 1H), 6.39 (s, 1H), 6.70–6.75 (m, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 7.16–7.21 (m, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.33–7.41 (m, 5H), 7.66 (d, *J* = 7.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ = –2.7, –2.6, 19.9, 21.5, 36.0, 52.8, 54.9, 55.3, 110.4, 116.3, 120.2, 125.3, 127.8, 127.9, 128.2, 128.7, 129.1, 129.6, 133.1, 133.5, 138.1, 143.4, 143.6, 156.5.

***E*)-4-((4-((Dimethylphenylsilyl)methyl)-1-tosylpyrrolidin-3-ylidene)methyl)benzonitrile (27e).** Compound **27e** was isolated after flash chromatography on silica gel (pentane:Et_2O = 2:1, R_f = 0.14) as a yellow oil in 83 % yield. ^{1}H NMR ($CDCl_3$) δ = 0.27 (s, 3H), 0.34 (s, 3H), 0.76–0.91 (m, 2H), 2.42 (s, 3H), 3.01–3.07 (m, 3H), 3.12–3.19 (m, 2H), 3.80 (dd, *J* = 14.4, 1.6 Hz, 1H), 4.12–4.16 (m, 1H), 6.12 (s, 1H), 7.01 (d, *J* = 8.3 Hz, 2H), 7.31–7.35 (m, 2H), 7.38–7.48 (m, 5H), 7.68–7.71 (m, 2H). ^{13}C NMR ($CDCl_3$) δ = –2.7, –2.5, 20.2, 21.5, 36.2, 52.9, 54.7, 110.0, 118.7, 119.7, 127.8, 128.1 , 128.4 , 129.5, 129.7, 132.1, 132.8, 133.5, 137.6, 140.6, 143.8, 148.0.

***E*)-3-(4-Chlorobenzylidene)-4-((dimethylphenylsilyl)methyl)-1-tosylpyrrolidine (27f).** Compound **27f** was isolated after flash chromatography on silica gel (pentane:Et_2O = 5:1, R_f = 0.14) as a yellow oil in 88 % yield. ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 3H), 0.33 (s, 3H), 0.83–0.86 (m, 2H), 2.42 (s, 3H), 3.01–3.07 (m, 1H), 3.10–3.16 (m, 2H), 3.78 (dd, *J* = 13.9, 1.4 Hz, 1H), 4.08–4.12 (m, 1H), 6.08 (s, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.38–7.45 (m, 5H), 7.69 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ –2.7, –2.5, 20.1, 21.5, 36.0, 52.8, 54.8, 120.0, 127.8, 128.0, 128.4, 129.3, 129.4, 129.6, 132.4, 132.9, 133.5, 134.6, 137.8, 143.6, 144.6.

***E*)-3-((4-((Dimethylphenylsilyl)methyl)-1-tosylpyrrolidin-3-ylidene)methyl)pyridine (27g).** Compound **27g** was isolated after flash chromatography on silica gel (pentane:EtOAc = 1:1, R_f = 0.26) as a colourless oil in 77% yield. ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 3H), 0.31 (s, 3H), 0.79–0.93 (m, 2H), 2.42 (s, 3H), 3.00–3.08 (m, 1H), 3.09–3.17 (m, 2H), 3.81 (dd, *J* = 14.1, 1.5 Hz, 1H), 4.12 (d, *J* = 14.1 Hz, 1H), 6.11 (s, 1H), 6.99 (dd, *J* =

7.9, 4.8 Hz ,1H), 7.19–7.23 (m, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.35–7.45 (m, 5H), 7.68 (d, *J* = 8.2 Hz, 2H), 8.34–8.36 (m, 1H), 8.37–8.40 (m, 1H). ^{13}C NMR ($CDCl_3$) δ = –2.7, –2.6, 20.2, 21.5, 36.2, 52.8, 54.7, 117.5, 123.1, 127.8, 128.0, 129.4, 129.7, 131.9, 132.8 , 133.5, 134.4, 137.7 , 143.7 , 146.7, 147.7, 149.6.

(*E*)-3-((Dimethylphenylsilyl)methyl)-1-tosyl-4-(2,4,6-trimethylbenzylidene)pyrrolidine (27h). Compound **27h** was isolated after flash chromatography on silica gel (pentane:Et_2O = 9:1, R_f = 0.10) as a yellow oil in 77% yield. ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 3H), 0.02 (s, 3H), 0.46–0.52 (m, 2H), 2.02 (br s, 6H), 2.29 (s, 3H), 2.41–2.49 (m, 4H), 2.79 (dd, *J* = 9.8, 4.2 Hz, 1H), 3.23 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.91–4.01 (m, 2H), 6.13 (s, 1H), 6.82 (s, 2H), 7.09–7.12 (m, 2H), 7.24–7.28 (m, 2H), 7.31–7.35 (m, 3H), 7.68 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ –3.0, –2.8, 18.9, 20.1, 20.9, 21.5, 36.9, 51.8, 54.9, 120.0, 127.7, 127.8, 128.0, 128.9, 129.6, 132.7, 132.8, 133.2, 135.3, 136.3, 138.0, 143.5, 144.2.

(*E*)-3-((Dimethylphenylsilyl)methyl)-4-(naphthalen-1-ylmethylene)-1-tosylpyrrolidine (27i). Compound **27i** was isolated after flash chromatography on silica gel (pentane:Et_2O = 5:1, R_f = 0.13) as a colourless oil in 86% yield. ^{1}H NMR ($CDCl_3$) δ 0.016 (s, 3H), 0.020 (s, 3H), 0.59–0.69 (m, 2H), 2.45 (s, 3H), 2.88–2.98 (m, 2H), 3.21 (dd, *J* = 9.6, 6.4 Hz, 1H), 4.06 (dd, *J* = 13.6, 1.4 Hz, 1H), 4.14–4.18 (m, 1H), 6.72 (s, 1H), 7.12–7.16 (m, 3H), 7.24–7.37 (m, 6H), 7.45–7.52 (m, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.84–7.87 (m, 1H). ^{13}C NMR ($CDCl_3$) δ –2.9, –2.8, 20.3, 21.5, 36.2, 52.5, 54.9, 119.3, 124.4, 125.2, 125.7, 125.9, 126.0, 127.5, 127.76, 128.80, 128.4, 129.0, 129.7, 131.4, 133.0, 133.3, 133.5, 133.8, 137.9, 143.6, 145.9.

(*E*)-Diethyl 3-((dimethylphenylsilyl)methyl)-4-(4-methoxybenzylidene)cyclopentane-1,1-dicarboxylate (28a). Compound **28a** was isolated after flash chromatography on silica gel (pentane:Et_2O = 10:1, R_f = 0.12) as a colourless oil in 80% yield. ^{1}H NMR ($CDCl_3$) δ 0.31 (s, 3H), 0.36 (s, 3H), 0.81 (dd, *J* = 14.9, 12.4 Hz, 1H), 1.15–1.27 (m, 7H), 1.87 (dd, *J* = 13.3, 5.7 Hz, 1H), 2.68 (ddd, *J* = 13.3, 8.1, 1.2 Hz, 1H), 2.88 (d, *J* = 15.6 Hz, 1H), 3.13–3.22 (m, 1H), 3.25 (dt, *J* = 15.6, 2.2 Hz, 1H), 3.79 (s, 3H), 4.08–4.26 (m, 4H), 6.16 (s, 1H), 6.67–6.72 (m ,2H), 6.98–7.03 (m, 2H), 7.35–7.40 (m, 3H), 7.47–7.51 (m, 2H). ^{13}C-NMR ($CDCl_3$) δ –2.4, –2.2, 14.0, 21.7, 35.4, 42.1, 42.8, 55.2, 58.5, 61.4, 61.5, 113.5, 120.7, 127.8, 129.0, 129.4, 129.9, 133.6, 138.8, 146.6, 157.8, 171.6, 172.0. Anal. Calcd for $C_{28}H_{36}O_5Si$: C, 69.97; H, 7.55. Found: C, 69.62; H, 7.55%

(*E*)-Diethyl 3-(4-cyanobenzylidene)-4-((dimethylphenylsilyl)methyl)cyclopentane-1,1-dicarboxylate (28b) Compound **28b** was isolated after flash chromatography on silica gel (pentane:Et_2O = 8:1, R_f = 0.13) as a colourless oil in 85% yield. ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 3H), 0.36 (s, 3H), 0.82 (dd, *J* = 14.9, 12.4 Hz, 1H), 1.02 (dd, *J* = 14.9, 1.8 Hz 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.93 (dd, *J* = 13.3, 5.6 Hz, 1H), 2.70 (ddd, *J* = 13.3, 8.1, 1.2 Hz, 1H), 2.92 (d, *J* = 16.1 Hz, 1H), 3.10–3.20 (m, 1H), 3.30 (dt, *J* = 6.1, 2.2 Hz, 1H), 4.10–4.28 (m, 4H), 6.21 (s, 1H), 7.09 (d, *J* = 8.3 Hz, 2H), 7.35–7.43 (m, 5H), 7.44–7.48 (m, 2H) ^{13}C NMR ($CDCl_3$) δ –2.5, –2.3, 14.0, 22.2, 35.8, 41.9, 43.0, 58.3, 61.6, 61.7, 109.2, 119.1, 120.0, 128.0, 128.6, 129.3, 131.9, 133.6, 138.2, 141.7, 153.4, 171.4, 171.6.

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Supporting Information Available: Experimental procedures for compounds **12**, **16**, **24**, and **25**. ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge from the corresponding author.

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