Iterative Synthesis of Alkenes by Insertion of Lithiated Epoxides into Boronic Esters

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Author contribution: S. Fritsch conducted experiments towards exploiting the different steric demand of alkyl substituents for the synthesis of 3f and 3g. All other experiments were conducted by K. Bojaryn. C. Hirschhäuser conceived the project and wrote the manuscript.

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(2R,3R)-2-butyl-2,3-diphenyloxiran (10b-cis)
(2R,3R)-2-Ethyl-2,3-diphenyloxiran (10c-cis)
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But-1-ene-1,1,2-triyltribenzene (11e)
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Alkene Formation from a lithiated Benzoate and an α-Halo Boronic Ester

In an attempt to react α-halo boronic esters with chiral carbanions generated by direct lithiation, we found that lithiated N,N-diisopropylcarbamates reacted poorly with α-haloboronic esters like S2. Although numerous different conditions were tested these reactions delivered poor yields (<20%) and were plagued by competing alkene formation. Lithiated benzoates (Li-S1) on the other hand performed much better in this type of reaction.

Benzoate S1 (1.42 equiv.) was lithiated at -78 °C with sBuLi (1.39 equiv.) and TMEDA (1.39 equiv.) in dry Et2O (3 h). A solution of S2 (1.00 equiv.) in Et2O was added at the same temperature and after 1 h a solution of ZnCl2 (3.9 equiv.) was added. The reaction mixture was stirred for 19 h during which the cooling bath was allowed to warm up to rt. After an aqueous workup (NH4Cl) a mixture of substitution products of type S3 was isolated. The 1H NMR (A, see next page) of the crude product in CDCl3 revealed a broad multiplet 5.32-5.39 ppm (highlighted in green), which was attributed to S3-anti and S3-syn, as well as a triplet at 4.34 ppm (highlighted in yellow), characteristic for S1.1 Based on later addition of an internal standard, yields of 18% for S1 and 65% for S3-anti and S3-syn were calculated. A ratio of diastereomers S3-anti and S3-syn could not be determined from the data.

As alkene formation was a major side reaction for N,N-diisopropylcarbamates we attempted to deliberately induce thermal syn-elimination for benzoates of type S3 by heating. Therefore, the complete sample was dried in vacuo to remove CDCl3 before redissolving it in THF. After heating at 60 °C for 2 h, the solvent was removed in vacuo and another 1H NMR (B) was recorded in CDCl3. It revealed a doublet of triplets at 5.44 ppm (J=4.8, 2.5 Hz, highlighted in dark blue),2 which is characteristic for the E-olefin S4-E. However, the corresponding signal for the Z-olefin S4-Z, a complex multiplet at 5.34-5.45 ppm (300 MHz CDCl3, highlighted in light blue),3 could not be assigned unambiguously as the broad multiplet assigned to S3 has a similar shift. In total the integral of signals in this area had increased by 150%, relative to the triplet at 4.34 ppm which had been assigned to S1. This is consistent with reaction of S3-syn to S4-E, while S3-anti remained. Since heating most likely induced a syn-elimination of S3, it is reasonably understandable that S3-anti reacts significantly slower than S3-syn. In S3-anti the alkyl substituents have to adopt a syn-periplanar orientation in order to accommodate the ecliptic conformation necessary. Based on these assumptions we attempted to convert left over S3-anti to S4-E as well using a base induced anti-elimination. Therefore, the complete sample was evaporated again to remove CDCl3.

1 R. Larouche-Gauthier, T. G. Elford, V. K. Aggarwal, J. Am. Chem. Soc. 2011, 133, 16794–16797.
2 X. Guo, J. Wang, C.-J. Li, Org. Lett. 2010, 12, 3176–3178. Here the relevant signal was reported as a multiplet from 5.38-5.46 ppm.
3 H. Dang, N. Cox, G. Lalic, Angew. Chem. Int. Ed. 2014, 53, 752–756.
The material was dissolved in THF and TBAF (6.25 equiv.) was added. After stirring at rt for 17 h and aqueous workup (CyHex−Et₂O/NH₄Cl) another ¹H NMR (C) of the crude material revealed formation of a 4.3:1 mixture of S₄−E/S₄−Z in 63% yield, judging by the internal standard. Purification by column chromatography delivered a 5:1 mixture of S₄−E/S₄−Z (36% isolated yield). The reduction in yield and increase in de upon isolation, could be due to rigorous drying in vacuo (Boiling points predicted by SciFinder: S₄−E 280 °C, S₄−Z, 260 °C). We briefly attempted to apply this reaction to the synthesis of trisubstituted alkenes but turned to the epoxide based strategy described in the main article after Blakemore's publication on the topic.

¹H NMR S₄−E (300 MHz, CHLOROFORM-d): δ = 0.79 - 0.95 (m, 3 H), 1.20 - 1.36 (m, 4 H), 1.90 - 2.05 (m, 2 H), 2.20 - 2.39 (m, 2 H), 2.58 - 2.83 (m, 2 H), 5.44 (dt, J = 4.8, 2.5 Hz, 2 H), 7.12 - 7.23 (m, 3 H), 7.23 - 7.35 (m, 2 H) ppm. c.f ref. 2

¹H NMR S₄−Z (300 MHz, CDCl₃): δ = 7.39 - 7.24 (m, 2 H), 7.24 - 7.11 (m, 3 H), 5.56 - 5.21 (m, 2 H), 2.66 (t, J = 7.7 Hz, 2 H), 2.46 - 2.23 (m, 2 H), 2.10 - 1.87 (m, 2 H), 1.41 - 1.15 (m, 4 H), 0.88 (t, J = 6.7 Hz, 3 H) ppm. Overlaying signals reproduced from ref. 3.

Wu, X. Sun, K. Potter, Y. Cao, L. N. Zakharov, P. R. Blakemore, Angew. Chem. Int. Edit. 2016, 55, 12285–12289.
Early Attempts at the Synthesis of Alkenes from Epoxide Insertion Products

**Comment:** (*) TBS-Cl was used with the intention to isolate the corresponding silyl ether. This was not achieved, but the free alcohol S6 was obtained instead.

| Entry | Elimination-precursor | Solvent | t\(^{(1)}\) | Reagent(s) | T   | t\(^{(2)}\) | Yield Alkene | E/Z-ratio |
|-------|------------------------|---------|-------------|------------|-----|-------------|--------------|------------|
| 1     | S5\(^{(0)}\)           | THF     | o.n.\(^{(8)}\) | MsCl        | 0 °C | 2 h         | 47%          | 16.2:1     |
| 2     | S5\(^{(0)}\)           | THF     | o.n.\(^{(8)}\) | AcCl        | 0 °C | 2 h         | 26%\(^{(A)}\) | 3:1        |
| 3     | S5\(^{(0)}\)           | THF     | o.n.\(^{(8)}\) | 1. nBuLi    | -78 °C | o.n.\(^{(8)}\) | 51%\(^{(A)}\) | only E-isomere |
|       |                        |         |             | 2. MsCl     |       |             |              |            |
|       |                        |         |             | 3. -78 °C   |       |             |              |            |
| 4     | S5\(^{(0)}\)           | THF     | 1 h         | 1. ZnCl\_2 | 1.0 °C | 1.1 h       | 73%          | 5.2:1      |
|       |                        |         |             | 2. nBuLi    | -78 °C | 2. 10 min   |              |            |
|       |                        |         |             | 3. MsCl     | 3. 1 h | 3. 1 h\(^{(C)}\) |              |            |
| 5     | S6\(^{(E)}\)           | THF     | /           | 1 M HCl\(^{(F)}\) | rt    | 7 d         | 95%\(^{(A)}\) | only E-isomere |
| 6     | S6\(^{(E)}\)           | MeCN    | /           | 1 M HCl\(^{(F)}\) | rt    | 7 d         | 41%\(^{(A)}\) | only E-isomere |
| 7     | S6\(^{(E)}\)           | THF     | /           | 1. TBAG     | 0 °C  | 7 d         | 34%          | 0.8:1      |
|       |                        |         |             | 2. 1 M HCl\(^{(F)}\) |       |             |              |            |
| 8     | S6\(^{(E)}\)           | MeCN    | /           | 1. TBAG     | 0 °C  | 7 d         | 33%          | 1.4:1      |
|       |                        |         |             | 2. 1 M HCl\(^{(F)}\) |       |             |              |            |

(A) Yield obtained by \(^1\)H NMR using dimethylbinol as an internal standard. (B) The reaction mixture was allowed to warm up to rt overnight. (C) The reaction mixture was allowed to warm up to rt within 1 h. (D) S5 was prepared from 4b and reacted directly to alkene 6a without any isolation. (E) S6 was isolated before the reaction. (F) Aqueous solution.
General Experimental Remarks

All reactions using dry solvents were carried out under argon in glassware dried with a heat gun under vacuum. Solvents for chromatography, unless purchased as pro analysi (p.a.) grade, were distilled over a rotary evaporator before use. THF was always freshly distilled from sodium/benzophenone, as was the case of Et₂O, when employed for reactions. Diisopropylamine and N,N,N,N-tetramethylpiperidine were distilled from CaH₂ and stored in a Schlenk tube under argon. nBuLi, sBuLi, tBuLi and ZnCl₂ were purchased as solutions and stored under argon at +7 °C or rt in the case of nBuLi. Aged BuLi solutions were titrated against N-benzylbenzamide. All other reagents were used as supplied from commercial sources and stored appropriately.

1H- and 13C NMR spectra were recorded in CDCl₃ on Bruker DMX 300 and Bruker DRX 500 spectrometers. IR spectra were measured on a Jasco FT/IR-430 with ATR attachment spectrometer. Low and High resolution ESI mass spectra were recorded with a Bruker amaZon SL and a Bruker maXis 4G spectrometer, respectively.

Experimental Procedures

Synthesis/Sources of monosubstituted Epoxides

2-Ethylxirane (4a-1) and 2-(t-Butyl)oxirane (4c) were obtained commercially. t-Butylidimethyl-(oxiran-2-ylmethoxy)-silane (4d) was prepared by silylation of commercially available rac-glycidol.

2-Octyloxiran (4a)

At room temperature a solution of mCPBA (14.00 g, 81.1 mmol) in DCM (120 mL) was added to a solution of Dec-1-en (5.0 mL, 48.2 mmol) in DCM (75 mL) in a dropwise manner through a dropping funnel. The reaction mixture was stirred overnight, after which it was quenched through the addition of a 1:1 mixture of sat. aq. NaHCO₃/Na₂S₂O₃. The organic layer was extracted with brine (200 mL) and the aqueous layer was re-extracted with DCM (3x200 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. After chromatography (SiO₂, CyHex/EtOAc 19:1) epoxide 4a (4.15 g, 26.5 mmol, 55 %) was obtained as a colorless oil.

Rᵣ = 0.40 (CyHex/EtOAc, 19:1).

1H-NMR (300 MHz, CHLOROFORM-d) δ = 2.85 - 2.96 (m, 1 H), 2.74 (dd, J=5.00, 4.06 Hz, 1 H), 2.46 (dd, J=5.16, 2.66 Hz, 1 H), 1.40 - 1.59 (m, 4 H), 1.17 - 1.40 (m, 10 H), 0.81 - 0.94 (m, 3 H) ppm.

13C-NMR (75 MHz, CHLOROFORM-d) δ = 52.6, 47.3, 32.7, 32.0, 29.7, 29.6, 29.4, 26.1, 22.8, 14.2 ppm.

1H- and 13C NMR data were consistent with those previously reported.²

² K. Yahata, N. Ye, K. Iso, Y. Ai, J. Lee, Y. Kishi, J. Org. Chem. 2017, 82, 8808–8830.
³ Y. Monguchi, T. Marumoto, T. Ichikawa, Y. Miyake, Y. Nagae, M. Yoshida, Y. Oumi, Y. Sawama, H. Sajiki, ChemCatChem 2015, 7, 2155–2160.
To a solution of cyclohexyl methyl ketone (10 mL, 72.6 mmol) in MeOH (60 mL) at 0 °C bromine (3.8 mL, 72.6 mmol) was added via a dropping funnel over the course of 1 h. The reaction mixture was stirred for 2 h at 0 °C before water (60 mL) was added and stirring was continued at rt overnight. The reaction mixture was diluted with Et₂O (100 mL) and the phases were separated. The aqueous phase was re-extracted with Et₂O (100 mL) and the combined organic layers were neutralized with aq. K₂CO₃ (10%, ca. 300 mL). The organic phase was separated, dried over MgSO₄ and concentrated in vacuo yielding 2-bromo-1-cyclohexylethanone (13.03 g, 63.9 mmol, 88%) as colorless oil. The crude product was dissolved in MeOH (136 mL) and cooled to 0 °C before NaBH₄ (3.63 g, 95.9 mmol) was added in small portions. The reaction mixture was stirred for 30 min at 0 °C and concentrated in vacuo. The residue was partitioned between water (270 mL) and Et₂O (3x70 mL). The combined organic layers were washed with sat. aq. NH₄Cl and brine, dried over MgSO₄ and concentrated in vacuo. The solvent was removed on a rotary evaporator and 2-cyclohexyloxirane (4b) (4.40 g, 34.9 mmol, 55%) was obtained as a colorless oil after distillation (7 mbar, 49 °C).

\[1^H\text{NMR (}300\text{ MHz, CDCl}_3\text{)} \delta = 2.56\text{ (dd, }J = 2.3, 4.2\text{ Hz, }2\text{ H}), 2.42 - 2.29\text{ (m, }1\text{ H}), 1.75\text{ (m, }1\text{ H}), 1.67 - 1.49\text{ (m, }4\text{ H}), 1.27 - 0.90\text{ (m, }6\text{ H}).\]

\[13^C\text{NMR (}75\text{ MHz, CDCl}_3\text{)} \delta = 56.6, 46.0, 40.4, 29.7, 28.8, 26.3, 25.7, 25.5.\]

\(^1H\text{- and }^{13}C\text{ NMR data were consistent with those previously reported.}\]

**CAUTION:** Although no toxicological data is available for the product, similar compounds (e.g. 2-ethyloxirane) are suspected carcinogens. Furthermore, the intermediate 2-bromo-1-cyclohexylethanone is a lacrimator. Handle both compounds in fume cupboard only.

\[\text{[**] We advise to use a rotary evaporator, which is positioned in a fume hood. Some of the volatile product can evaporate with the solvent.}\]

\[\text{[***] For the distillation a diaphragm pump positioned in fume hood was used to avoid exposure to the product.}\]

tert.-Butyldimethyl((8-(oxiran-2-yloxy))octyl)oxy)silan (4e)

To a solution of tert.-butyl(dec-9-en-1-yloxy)dimethylsilane\(^5\) (1.004 g, 3.70 mmol) in DCM (30 mL) were added NaHCO₃ (1.56 g, 18.5 mmol) and mCPBA (957 mg, 5.54 mmol) at rt and the reaction mixture was stirred overnight. An aq. solution of Na₂S₂O₃ (5%, 30 mL) was added at 0 °C over the course of five minutes, after which stirring was continued at rt for 15 min. The phases were separated,

\(^5\) Huang, K.; Wang, H.; Stepanenko, V.; De Jesús, M.; Torruellas, C.; Correa, W.; Ortiz-Marciales, M. J. Org. Chem. 2011, 76, 1883–1886.
and the aqueous layer was extracted with DCM (2x30 mL). The combined organic layers were washed with a 1:1 mixture of brine and saturated aq. NaHCO₃, dried over MgSO₄ and concentrated in vacuo. Chromatography (SiO₂, CyHex) yielded epoxide 4e (677 mg, 2.36 mmol, 64%) as a colorless oil.

Rᵣ = 0.22 (CyHex/EtOAc, 9:1).

¹H NMR (300 MHz, CHLOROFORM-d) δ = 3.59 (t, J=6.6 Hz, 2 H), 2.86 - 2.94 (m, 1 H), 2.74 (dd, J=5.2, 3.9 Hz, 1 H), 2.46 (dd, J=5.0, 2.8 Hz, 1 H), 1.21 - 1.58 (m, 14 H), 0.89 (s, 9 H), 0.03 (s, 6 H) ppm.

¹³C NMR (CHLOROFORM-d, 75 MHz): δ = 63.3, 52.4, 47.1, 32.9, 30.9, 29.5, 29.3, 25.8, 18.4, -5.3 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.⁹

2-(8-{Oxiran-2-yl}octyl)isoindolin-1,3-dion (4f)

To a solution of 1-phthalimido-dec-9-en (816 mg, 2.86 mmol) in DCM (40 mL) were added NaHCO₃ (752 mg, 9 mmol) and mCPBA (795 mg, 4.6 mmol) at rt and the reaction mixture was stirred overnight. An aq. solution of Na₂S₂O₃ (5%, 30 mL) was added at 0 °C over the course of five minutes, after which stirring was continued at rt for 15 min. The phases were separated, and the aqueous layer was extracted with DCM (2x30 mL). The combined organic layers were washed with a 1:1 mixture of brine and saturated aq. NaHCO₃ (30 mL), dried over MgSO₄ and concentrated in vacuo. Chromatography (SiO₂, CyHex/CHCl₃ 9:1) yielded epoxide 4f (644 mg, 2.03 mmol, 71%) as a colorless oil, containing 16% CyHex.

Rᵣ = 0.10 (CyHex/CHCl₃, 9:1).

¹H NMR (300 MHz, CHLOROFORM-d) δ = 7.80 - 7.87 (m, 2 H), 7.67 - 7.74 (m, 2 H), 7.64 (t, J=5.2, 2.7 Hz), 7.53 (dd, J=5.0, 3.8 Hz, 1 H), 2.45 (dd, J=5.2, 2.7 Hz, 1 H), 1.67 (t, J=7.04 Hz, 2 H), 1.27 - 1.59 (m, 12 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-d) δ = 143.6, 139.8, 130.8, 128.3, 126.5, 126.5, 32.0, 29.9, 29.8, 29.6, 29.4, 28.9, 22.8, 22.0, 14.6, 14.2 ppm.

IR: ν = 2927 (m, br), 2848 (m), 1770 (m), 1694 (s), 1611 (w), 1431 (m), 1398 (m), 1188 (s), 1055 (m), 875 (m), 718 (s) cm⁻¹.

MS m/z (ESI⁺): 324.2 (M+Na⁺, 100%), 242.2 (M+Na⁺+H₂O, 24%), 356.2 (M+Na⁺+MeOH, 18%).

HR-MS m/z (ESI⁺): found: [M+H⁺] 302.1759, C₁₂H₂₀NO₃Na calculated 302.1751 and [M+Na⁺] 324.1579, C₁₂H₂₃NO₃Na calculated: 324.1570.

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⁹ L. Balas, J. Bertrand-Michel, F. Viars, J. Faugere, C. Lefort, S. Caspar-Bauguil, D. Langin, T. Durand, Org. & Biomol. Chem. 2016, 14, 9012–9020.

¹⁰ C. Hirschhäuser, J. Velcicky, D. Schlawe, E. Hessler, A. Majdalani, J.-M. Neudörlfl, A. Prokop*, T. Wieder, H.-G. Schmalz*, Chem. Eur. J. 2013, 19, 13017-13029.
Synthesis of Disubstituted Alkenes

**General Procedure GP1: Synthesis of Disubstituted Alkenes**

A solution of LiTMP was freshly prepared in a dried Schlenk tube by addition of nBuLi in hexanes (2 equiv.) to 2,2,6,6-tetramethylpiperidin (TMP, 2.2 equiv.) in dry THF (1.7 – 2.1 mL/mmol of epoxide 4) at 0 °C and stirring for 30 min at rt. This LiTMP solution was added dropwise to a solution of epoxide 4 (1 equiv.) and boronic ester (2.0 equiv.) in dry THF (3.5 – 4.7 mL/mmol of epoxide 4) at 0 °C (GP1A and 1B) or -30 °C (GP1C). Stirring was continued for 2 h at the same temperature. The reaction mixture was allowed to warm up to room temperature for 30 min (GP1A and 1C) or overnight (GP1B) before the reaction mixture was heated to 60 °C for 2 h. The reaction mixture was cooled to room temperature, transferred into a separation funnel with Et₂O and washed (3x) with NaOH (1 M). The combined aqueous layers were re-extracted with Et₂O (2x). The combined organic layers were dried with Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography.

**Comments:** The difference between GP1A and GP1B, i.e. whether the reaction is warmed up to room temperature for 30 min or overnight respectively, is a matter of convenience. For comparison 6a (R¹=R²=Cy) was prepared according to GP1A and GP1B with 68% and 62% yield, respectively. When necessary, brine was added to aid phase separation.

**Sample Procedure:** A solution of LiTMP was prepared by addition of nBuLi in hexanes (2.8 mL, 4.49 mmol, 1.55 mol/L) to 2,2,6,6-tetramethylpiperidin (0.83 mL, 5.39 mmol) in dry THF (6 mL) at 0 °C. After stirring for 0.5 h at room temperature, this mixture was added dropwise to a solution of epoxide 4a (280 mg, 2.25 mmol) and octylboronic acid pinacol ester (1.08 g, 4.49 mmol) stirred at 0 °C in dry THF (8 mL). Stirring at 0 °C continued for 2 h. The reaction mixture was allowed to warm up to room temperature overnight, after which the reaction mixture was heated to 60 °C for 2 h. The reaction mixture was cooled to room temperature, transferred into a separation funnel with Et₂O and washed with aq. NaOH (1 M, 2x50 mL) and brine (50 mL). The combined aqueous layers were re-extracted with Et₂O (2x50 mL). The combined organic layers were dried with Na₂SO₄ and concentrated in vacuo. Column chromatography (SiO₂, CyHex/EtOAc, 9:1) afforded alkene 6c (272 mg, 1.23 mmol, 55%) as a colorless oil. Rf = 0.72 (CyHex/EtOAc, 9:1). **1H NMR** (300 MHz, CHLOROFORM-d) δ = 5.27 - 5.42 (m, 2 H), 1.85 - 2.02 (m, 3 H), 1.59 - 1.74 (m, 5 H), 0.80 - 1.40 (m, 20 H) ppm. **13C NMR** (75 MHz, CHLOROFORM-d): δ = 136.4, 127.8, 40.7, 33.3, 32.7, 31.9, 29.7, 29.5, 29.3, 29.1, 26.3, 26.2, 22.7, 14.1 ppm. **1H- and 13C NMR data were consistent with those previously reported.**

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11 G. Cahiez, O. Gager, J. Buendia, C. Patinote, Chem. Eur. J. 2012, 18, 5860–5863.
Following GP1A a solution of LiTMP (0.88 mmol), was reacted with epoxide 4b (0.40 mmol) and cyclohexyl pinacol boronic ester (0.80 mmol) to yield 6a (52 mg, 0.27 mmol, 68%) as a colorless oil after chromatography (SiO\textsubscript{2}, CyHex).

\( R_f = 0.61 \) (CyHex).

\( ^1\text{H NMR} \) (300 MHz, CHLOROFORM-d) \( \delta = 5.30 \) (dd, \( J=3.60, 1.72 \) Hz, 2 H), 0.93 - 1.92 (m, 22 H) ppm.

\( ^{13}\text{C NMR} \) (75 MHz, CHLOROFORM-d) \( \delta = 133.8, 40.7, 33.4, 26.3, 26.2 \) ppm.

\(^1\text{H}-\) and \(^{13}\text{C NMR data were consistent with those previously reported.}^{12}

Following GP1B a solution of LiTMP (0.40 mmol) and octyl pinacol boronic ester (4.50 mmol) to yield 6c (272 mg, 1.22 mmol, 55%) as a colorless oil after chromatography (SiO\textsubscript{2}, CyHex/EtOAc, 19:1). Also see sample procedure on page 7.

\( R_f = 0.72 \) (CyHex/EtOAc, 19:1).

\( ^1\text{H NMR} \) (300 MHz, CHLOROFORM-d) \( \delta = 5.27 - 5.42 \) (m, 2 H), 1.85 - 2.02 (m, 3 H), 1.59 – 1.74 (m, 5 H), 0.80 - 1.40 (m, 20 H) ppm.

\( ^{13}\text{C NMR} \) (75 MHz, CHLOROFORM-d): \( \delta = 136.4, 127.8, 40.7, 33.3, 32.7, 31.9, 29.7, 29.5, 29.3, 29.1, 26.3, 26.2, 22.7, 14.1 \) ppm.

\(^1\text{H- and}^{13}\text{C NMR data were consistent with those previously reported.}^{13}

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\(^{12}\) G. Opitz, T. Ehlis, K. Rieth, \textit{Chem. Ber.} \textbf{1990}, 123, 1989–1998.

\(^{13}\) G. Cahiez, O. Gager, J. Buendia, C. Patinote, \textit{Chem. Eur. J.} \textbf{2012}, 18, 5860–5863.
(E)-3,3-Dimethyl-1-butene-1-ylcyclohexan (6d)

Following GP1B a solution of LiTMP (5.24 mmol), was reacted with epoxide 4c (2.38 mmol) and cyclohexyl pinacol boronic ester (4.76 mmol) to yield 6d (173 mg, 0.64 mmol, 27%) as a colorless oil after chromatography (SiO\textsubscript{2}, CyHex/EtOAc, 19:1). Yield corrected for 40 % of impurity based on subsequent transformations.

R\textsubscript{f} = 0.71 (Cyhex/EtOAc, 9:1).

\textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): \( \delta = 0.97 \) (s, 9 H), 1.05-1.80 (m, 11 H), 5.25 (dd, \( J = 15.6, 6.6 \) Hz, 1 H), 5.36 (d, \( J = 15.6, 1 \) H) ppm.

\textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}): \( \delta = 138.9, 130.8, 40.7, 33.4, 32.5, 26.9, 26.3, 26.3 \) ppm.

\textsuperscript{1}H- and \textsuperscript{13}C NMR data were consistent with those previously reported.\textsuperscript{14}

(E)-2,2-Dimethyl-3-dodecen (6e)

Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide 4c (0.40 mmol) and octyl pinacol boronic ester (0.80 mmol) to yield 6e (35 mg, 0.18 mmol, 45%) as a colorless oil after chromatography (SiO\textsubscript{2}, CyHex/EtOAc, 19:1).

R\textsubscript{f} = 0.67 (Cyhex/EtOAc, 9:1).

\textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): \( \delta = 5.25-5.46 \) (m, 2 H), 1.93-1.99 (m, 2 H), 1.26 (m, 12 H), 0.98 (s, 9 H), 0.88 (l, \( J = 6.87 \) Hz, 3 H) ppm.

\textsuperscript{13}C-NMR (75 MHZ, CDCl\textsubscript{3}): \( \delta = 141.4, 124.8, 32.7, 31.9, 29.8, 29.7, 29.5, 29.4, 29.3, 29.1, 22.7, 14.1 \) ppm.

\textsuperscript{1}H- and \textsuperscript{13}C NMR data were consistent with those previously reported.\textsuperscript{15}

\textsuperscript{14} T. M. Yuan, T. Y. Luh, J. Org. Chem. 1992, 57, 4550–4552.

\textsuperscript{15} First report of compound: G.H. Posner, K.A. Babiak, J. Organomet. Chem. 1979, 177, 299-307. NMR Data was compared to the octen-congener: G. Cahiez, H. Avedissian, Synthesis 1998, 1998, 1199–1205.
Following GP1A a solution of LiTMP (0.88 mmol), was reacted with epoxide 4b (0.46 mmol) and phenyl pinacol boronic ester (0.80 mmol) to yield 6f (70 mg, 0.38 mmol, 82%) as a colorless oil after chromatography (SiO₂, CyHex).

R_f = 0.38 (CyHex).

^1H-NMR (300 MHz, CHLOROFORM-d) δ = 7.23 - 7.44 (m, 4 H), 7.09 - 7.22 (m, 1 H), 6.35 (d, J=15.6 Hz, 1 H), 6.18 (dd, J=15.9, 6.9 Hz, 1 H), 2.02 - 2.26 (m, 1 H), 1.61 - 1.88 (m, 4 H), 1.09 - 1.45 ppm (m, 4 H) ppm.

^13C NMR (75 MHz, CHLOROFORM-d) δ = 138.22, 137.02, 128.60, 127.37, 126.87, 126.09, 41.31, 33.12, 26.34, 26.20 ppm.

^1H- and ^13C NMR data were consistent with those previously reported.¹⁶

*Comment:* Prolonged heating at 60 °C lead to a reduction in yield in this case, probably due to decomposition of the styrene derivative.

Following GP1C a solution of LiTMP (0.70 mmol), was reacted with epoxide 4a (0.35 mmol) and phenyl pinacol boronic ester (0.64 mmol) to yield 6g (67 mg, 0.31 mmol, 88%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1).

R_f = 0.62 (CyHex/EtOAc, 19:1).

^1H NMR (300 MHz, CHLOROFORM-d) δ = 7.27 - 7.38 (m, 4 H), 7.14 - 7.22 (m, 1 H), 6.38 (d, J=16.3 Hz, 1 H), 6.16 - 6.29 (m, 1 H), 2.15 - 2.26 (m, 2 H), 1.41 - 1.53 (m, 2 H), 1.17 - 1.40 (m, 10 H), 0.80 - 0.95 (m, 3 H) ppm.

^13C NMR (75 MHz, CHLOROFORM-d) δ = 138.1, 131.4, 129.8, 128.6, 126.9, 126.1, 33.2, 32.1, 29.7, 29.6, 29.5, 29.4, 22.8, 14.3 ppm.

^1H- and ^13C NMR data were consistent with those previously reported.¹⁷

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¹⁶ M. J. Rawling, J. H. Rowley, M. Campbell, A. R. Kennedy, J. A. Parkinson, N. C. O. Tomkinson, *Chem. Sci.* 2014, 5, 1777–1785.

¹⁷ P. Andrews, C. M. Latham, M. Magre, D. Willcox, S. Woodward, *Chem. Comm.* 2013, 49, 1488.
(E)-But-1-en-1-ylbenzen (6h)

Following GP1B a solution of LiTMP (10.78 mmol), was reacted with epoxide 4a-1 (4.90 mmol) and phenyl pinacol boronic ester (9.80 mmol) to yield 6h (393 mg, 2.97 mmol, 54%) as a colorless oil after chromatography (SiO₂, CyHex).

R₂ = 0.50 (CyHex/EtOAc, 19:1).

¹H NMR (300 MHz, CHLOROFORM-d) δ = 7.21 - 7.35 (m, 4 H), 7.12 - 7.20 (m, 1 H), 6.36 (d, J=16.0 Hz, 1 H), 6.18 - 6.29 (m, 1 H), 2.14 - 2.27 (m, 2 H), 1.07 (t, J=7.3 Hz, 3 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-d) δ = 138.12, 132.80, 128.96, 128.62, 126.89, 126.06, 26.21, 13.81 ppm.

¹H NMR data was consistent with a previous report.¹⁸

Comment: The reaction was conducted several times on different scales and isolated yields varied considerably as the product is volatile.

tert.-Butyl(cinnamyloxy)dimethylsilan (6i)

Following GP1C a solution of LiTMP (0.66 mmol), was reacted with epoxide 4d (0.30 mmol) and phenyl pinacol boronic ester (0.53 mmol) to yield 6i (53 mg, <0.21 mmol, <70%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1). The product contained a R-OTBS type impurity, which could not be removed by repeated chromatography. NMR signals were obtained from mixture (see appendix for spectra).

Rᵣ = 0.40 (CyHex/EtOAc, 19:1).

¹H-NMR (300 MHz, CHLOROFORM-d): δ = 7.21 - 7.41 (m, 5 H), 6.59 (d, J=16.0 Hz, 1 H), 6.29 (dt, J=15.0, 5.0 Hz, 1 H), 4.36 (dd, J=5.0, 1.6 Hz, 2 H), 0.95 (s, 9 H), 0.12 (s, 6 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-d) δ = 137.1, 129.5, 129.2, 128.5, 127.3, 126.4, 63.9, 26.0, 18.4, -5.1 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.¹⁹

¹⁸ J. Li, J. Peng, Y. Bai, L. Chen, G. Lai, Phosphorus Sulfur 2011, 186, 1621–1625.
¹⁹ J. J. Loman, V. A. Pistritto, C. B. Kelly, N. E. Leadbeater, Synlett 2016, 27, 2372–2377.
(E)-tert.-Butyldimethyl((10-phenyldec-9-en-1-yl)oxy)silan (6k)

Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide 4e (0.41 mmol) and phenyl pinacol boronic ester (0.80 mmol) to yield 6k (104 mg, 0.31 mmol, 75%) as a colorless oil after chromatography (SiO₂, CyHex).

R_f = 0.58 (CyHex/EtOAc, 19:1).

1H NMR (300 MHz, CHLOROFORM-d) δ = 7.24 - 7.37 (m, 4 H), 7.14 - 7.22 (m, 1 H), 6.38 (d, J=15.6 Hz, 1 H), 6.17 - 6.28 (m, 1 H), 3.56 - 3.64 (t, 2 H), 2.15 - 2.27 (m, 2 H), 1.41 - 1.59 (m, 2 H), 1.23 - 1.41 (m, 10 H), 0.87 - 0.98 (m, 9 H), 0.03 - 0.12 (m, 6 H) ppm.

13C-NMR (75 MHz, CHLOROFORM-d) δ = 138.0, 131.2, 129.7, 128.4, 126.7, 125.9, 63.3, 33.0, 32.9, 29.5, 29.4, 29.4, 29.2, 26.0, 25.8, 18.4, -5.3 ppm.

IR: ν̃ = 2925 (m), 2854 (m), 1458 (w), 2160 (w), 2027 (w, br.), 1973 (w, br.), 1506 (w), 1458 (w), 1253 (m), 1097 (s), 966 (w), 833 (s), 773 (s), 741 (m), 690 (m) cm⁻¹.

HR-MS m/z (ESI⁺): found: [M+H⁺] 347.2767, C₂₂H₃₈O₇SiH calculated 347.2765 and [M+Na⁺] 369.2587, C₂₂H₃₈OSiNa calculated 369.2584.

(E)-tert.-Butyl((10-cyclohexyldec-9-en-1-yl)oxy)dimethylsilan (6l)

Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide 4e (0.40 mmol) and cyclohexyl pinacol boronic ester (0.80 mmol) to yield 6l (109 mg, 0.31 mmol, 77%) as a colorless oil after chromatography (SiO₂, CyHex).

R_f = 0.64 (CyHex/EtOAc, 19:1).

1H NMR (300 MHz, CHLOROFORM-d) δ = 5.31 - 5.37 (m, 2 H), 3.60 (t, J=6.57 Hz, 2 H), 1.44 - 2.01 (m, 11 H), 0.96 - 1.39 (m, 16 H), 0.90 (s, 9 H), 0.06 (s, 6 H) ppm.

13C-NMR (75 MHz, CHLOROFORM-d) δ = 136.5, 127.8, 63.4, 40.8, 33.4, 33.0, 32.7, 29.8, 29.6, 29.5, 29.1, 27.0, 26.3, 26.2, 26.1, 25.9, 18.4, -5.0 ppm.

IR: ν̃ = 2924 (s), 2852 (m), 1449 (w), 2160 (w), 2027 (w, br.), 1977 (w, br.), 1506 (w), 1458 (w), 1253 (m), 1097 (s), 966 (w), 833 (s), 773 (s) cm⁻¹.

HR-MS m/z (ESI⁺): found: [M+H⁺] 353.3239, C₂₂H₄₄OSiH calculated: 353.3234 and [M+Na⁺] 375.3056, C₂₂H₃₈OSiNa calculated: 375.3054.
Following GP1B a solution of LiTMP (1.76 mmol), was reacted with epoxide 4b (0.86 mmol) and ortho-methoxyphenyl pinacol boronic ester (1.60 mmol) to yield 6n (75 mg, 0.36 mmol, 40%) as a yellow oil after chromatography (SiO$_2$, CyHex/EtOAc, 19:1). The material obtained after chromatography contained 71% of 6n, 15.5% of boronic ester and 13.5% epoxide 4b starting material. The yield was corrected accordingly.

R$_f$ = 0.42 (CyHex/EtOAc, 19:1).

$^1$H NMR (300 MHz, CHLOROFORM-d) $\delta$ = 7.25 - 7.32 (m, 2 H), 6.81 - 6.87 (m, 2 H), 6.29 (d, $J$=15.9 Hz, 1 H), 6.04 (dd, $J$=15.9, 6.9 Hz, 1 H), 3.80 (s, 3 H), 2.03 - 2.19 (m, 1 H), 1.62 - 1.93 (m, 5 H), 1.08 - 1.43 (m, 5 H) ppm.

$^{13}$C NMR (75 MHz, CHLOROFORM-d) $\delta$ = 158.6, 134.8, 130.9, 127.0, 126.5, 113.9, 55.3, 41.1, 33.1, 26.2, 26.1 ppm.

$^1$H- and $^{13}$C NMR data were consistent with those previously reported.\textsuperscript{20}

\textsuperscript{20} C. Wang, Y. Lei, M. Guo, Q. Shang, H. Liu, Z. Xu, R. Wang, Org. Lett. 2017, 19, 6412–6415.
Synthesis/Sources of Disubstituted Epoxides

General Procedure GP2: Epoxidation of Di- and Trisubstituted Alkenes

NaHCO₃ (3 equiv.) and mCPBA (1.95 equiv.) were added to a solution of alkene in DCM (ca. 13 ml/mmol of alkene) and the mixture was stirred overnight at room temperature. Afterwards the reaction mixture was cooled to 0 °C before an equal volume of aq. Na₂S₂O₃ (5%) was added. Stirring was continued for 5 min. at 0 °C and 15 min. at room temperature. The mixture was washed with equal volumes of brine, saturated aq. NaHCO₃. The combined aqueous phases were re-extracted with DCM (3x) and the combined organic extracts were dried over MgSO₄. The solvent was removed in vacuo and the crude product was purified by column chromatography.

Comment: Although this is a known problem, it should be mentioned that such epoxides, which can open up and form stabilized cations, are particularly vulnerable to acid mediated epimerization. This tendency is reduced by the addition of base (here NaHCO₃, which intercepts meta-chlorobenzoic acid) and no epimerization was observed for the compounds reported below. However, attempts to epoxidize e.g. 6n with this (and a comparable biphasic) system consistently led to epimerization.

(2R,3R)-2-Ethyl-3-phenyloxiran (9a)

According to GP2 alkene 6h (210 mg, 1.59 mmol) was transformed into epoxide 9a (180 mg, 1.21 mmol, 76%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 19:1).

\[ R_f = 0.42 \text{ (CyHex/EtOAc, 19:1).} \]

\[ ^1H\text{-NMR (300 MHz, CHLOROFORM-d)} \delta = 7.24 - 7.38 \text{ (m, 5 H), 3.63 (d, J=2.2 Hz, 1 H), 2.95 (td, J=5.5, 2.2 Hz, 1 H), 1.67 - 1.79 \text{ (m, 2 H), 1.07 (t, J=7.5 Hz, 3 H) ppm.} \]

\[ ^13C\text{-NMR (75 MHz, CHLOROFORM-d)} \delta = 137.9, 128.4, 127.9, 125.5, 64.1, 58.3, 25.4, 9.8 \text{ ppm.} \]

\[ ^1H\text{- and } ^13C\text{ NMR data were consistent with those previously reported.}^{23} \]

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21 R. S. Mohan, K. Gavardinas, S. Kyere, D. L. Whalen, J. Org. Chem. 2000, 65, 1407–1413.
22 G. Moyna, H. J. Williams, A. I. Scott, Synthetic Commun. 1996, 26, 2235–2239.
23 H. Mang, J. Gross, M. Lara, C. Goessler, H. E. Schoemaker, G. M. Guebitz, W. Kroutil, Angew. Chem. Int. Edit. 2006, 45, 5201–5203.
trans-2,3-Diphenyloxirane (9b-trans)

According to GP2 stilbene (3.00 g, 16.6 mmol) was transformed into epoxide 9b-trans (2.96 g, 7.23 mmol, 91%), isolated as a colorless oil after column chromatography (SiO$_2$, CyHex/EtOAc 30:1).

$R_f = 0.34$ (CyHex/EtOAc, 19:1).

$^1$H-NMR (300 MHz, CHLOROFORM-d): $\delta = 7.28$ - 7.49 (m, 10 H), 3.89 (s, 2 H) ppm.

$^{13}$C NMR (75 MHz, CHLOROFORM-d): $\delta = 137.1$, 128.6, 128.3, 125.5, 62.8 ppm.

$^1$H- and $^{13}$C NMR data were consistent with those previously reported.$^{24}$

2-Cyclohexyl-3-octyloxiran (9c)

According to GP2 alkene 6b/c (140 mg, 0.63 mmol) was transformed into epoxide 9c (112 mg, 0.47 mmol, 75%), isolated as a colorless oil after column chromatography (SiO$_2$, CyHex/EtOAc 7:3).

$R_f = 0.74$ (Cyhex/EtOAc, 7:3).

$^1$H-NMR (300 MHz, CHLOROFORM-d): $\delta = 2.68$-2.73 (m, 1 H), 2.42-2.47 (dd, $J = 8.8$, 2.2 Hz, 1 H), 1.80-1.90 (m, 1 H), 1.00-1.69 (m, 24 H), 0.88 (t, $J = 6.9$ Hz, 3 H) ppm.

$^{13}$C-NMR (75 MHZ, CDCl$_3$): $\delta = 63.3$, 57.7, 40.2, 32.2, 31.8, 29.8, 29.5, 29.4, 29.2, 29.1, 26.3, 26.1, 25.7, 25.6, 22.6, 14.1 ppm.

IR: $\tilde{\nu} = 2925$ (s), 2853 (m), 2360 (m), 2339 (m), 1652 (w), 1559 (w), 1539 (w), 1456 (w), 668 (s), 625 (w), 619 (w) cm$^{-1}$.

MS m/z (ESI$^{+/-}$): Compound was not detected by ESI. Identity was confirmed by comparison to data reported for 2-cyclohexyl-3-hexyloxiran.$^{25}$

(*) Comment: In divergence from GP2, the product was isolated after stirring for only 3 h.

$^{24}$ G. Anilkumar, S. Bhor, M. K. Tse, M. Klawonn, B. Bitterlich, M. Beller, Tetrahedron-Asymmetry 2005, 16, 3536–3561.

$^{25}$ T. Satoh, Y. Kaneko, K. Yamakawa, Bull. Chem. Soc. Jpn. 1986, 59, 2463–2470.
2-Cyclohexyl-3-(2-methyl-2-propanyl) oxiran (9d)

According to GP2\(^{(a)}\) alkene 6d (104 mg, 1.04 mmol) was transformed into epoxide 9d (84 mg, 0.46 mmol, 44%), isolated as a colorless oil after column chromatography (SiO\(_2\), CyHex/EtOAc 7:3).

\(R_I = 0.70\) (Cyhex/EtOAc, 7:3).

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 2.56\) (dd, \(J=6.6, 2.5\) Hz, 1 H), 2.47 - 2.53 (m, 1 H), 1.82 - 1.95 (m, 1 H), 1.56 - 1.80 (m, 4 H), 1.01 - 1.31 (m, 6 H), 0.91 (s, 9 H) ppm.

\(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta = 66.0, 59.9, 40.4, 30.5, 29.9, 29.1, 26.3, 25.8, 25.7, 25.5\) ppm.

IR: \(\tilde{\nu} = 2360\) (s), 2341 (s), 1653 (w), 668 (s) cm\(^{-1}\).

MS m/z (ESI\(^{+/-}\)): Compound was not detected by ESI. Identity was confirmed by comparison to other compounds of this series.

\(^{(a)}\) Comment: In divergence from GP2, the product was isolated after stirring for only 3 h.

2-Octyl-3-(2-methyl-2-propanyl) oxiran (9e)

According to GP2\(^{(a)}\) alkene 6e (15 mg, 0.077 mmol) was transformed into epoxide 9e (12 mg, 0.031 mmol, 40%), isolated as a colorless oil after column chromatography (SiO\(_2\), CyHex/EtOAc 7:3). Yield corrected for grease impurity.

\(R_I = 0.80\) (Cyhex/EtOAc, 7:3).

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 2.74-2.82\) (m, 1 H), 2.46 (d, \(J = 2.49\) Hz, 1 H), 1.35-1.65 (m, 14 H), 0.88-0.91 (m, 12 H) ppm.

\(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta = 67.0, 55.5, 32.3, 31.8, 30.7, 29.7, 29.4, 29.2, 26.2, 25.9, 22.6, 14.1\) ppm.

IR: \(\tilde{\nu} = 3744\) (w), 2923 (s), 2854 (m), 2360 (m), 1700 (w), 1652 (w), 668 (s) cm\(^{-1}\).

MS m/z (ESI\(^{+/-}\)): Compound was not detected by ESI. Identity was confirmed by comparison to data reported for 2-Propyl-3-(2-methyl-2-propanyl) oxiran\(^{26}\)

\(^{(a)}\) Comment: In divergence from GP2, the product was isolated after stirring for only 3 h.

\(^{26}\) A. K. Yudin, J. P. Chiang, H. Adolfsson, C. Copéret, J. Org. Chem. 2001, 66, 4713–4718.
Synthesis of Trisubstituted Alkenes from trans-Epoxides

General Procedure Optimized for reaction of 9a (GP3A)

At -110 °C sBuLi in hexanes (1.2 equiv.) was added dropwise to a solution of epoxide 9a and TMEDA (3 equiv.) in dry Et₂O (1.5 mL/mmol of 9a). After stirring for 10 min at the same temperature, a solution of appropriate boronic ester in Et₂O (2.2 equiv., 0.34 M) was added and stirring was continued for 2 h at -110 °C. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 38 °C overnight. The solvent was removed in vacuo and the residue was purified by column chromatography (Al₂O₃, CyHex).

(Z)-1-Methoxy-4-[(1-phenylbut-1-en-1-yl)benzen (3a)

According to GP3A epoxide 9a (154 mg, 1.04 mmol) was reacted with p-methoxyphenyl neopentyl boronic ester to yield 3a (156 mg, 0.65 mmol, 63%).

R_f = 0.60 (CyHex/EtOAc, 19:1).

^1^H-NMR (300 MHz, CHLOROFORM-d) δ = 7.29 - 7.50 (m, 5 H), 7.17 - 7.29 (m, 2 H), 6.95 - 7.10 (m, 2 H), 6.15 (t, J=7.3 Hz, 1 H), 3.97 (s, 3 H), 2.27 (quin, J=7.5 Hz, 2 H), 1.17 ppm (t, J=7.5 Hz, 3 H) ppm.

^1^C NMR (75 MHz, CHLOROFORM-d) δ = 158.5, 143.2, 140.5, 132.6, 131.5, 131.0, 128.0, 127.3, 126.7, 113.5, 55.2, 23.2, 14.5 ppm.

^1^H- and ^1^C NMR data were consistent with those previously reported.27

27 K. Mondal, S. C. Pan, Eur. J. Org. Chem. 2015, 2015, 2129–2132.
(E)-4-Phenyl-3-dodecene (3b)

According to GP3A epoxide 9a (52 mg, 0.35 mmol) was reacted with octyl pinacol boronic ester to yield 3b (56 mg, 0.23 mmol, 65%). When the reaction was conducted with octyl neopentyl boronic ester 3b was obtained in 53% yield.

\[ R_f = 0.71 \text{ (CyHex/EtOAc, 19:1).} \]

\[ ^{1}H\text{-NMR} \text{ (300 MHz, CHLOROFORM-d) } \delta = 7.14 - 7.44 \text{ (m, 5 H), 5.66 (t, } J=7.2 \text{ Hz, 1 H), 2.42 - 2.60 \text{ (m, 2 H), 2.24 (quin, } J=7.4 \text{ Hz, 2 H), 1.18 - 1.46 \text{ (m, 12 H), 1.09 (t, } J=7.5 \text{ Hz, 3 H), 0.73 - 0.96 \text{ (m, 3 H) ppm.} } \]

\[ ^{13}C\text{-NMR} \text{ (75 MHZ, CHLOROFORM-d) } \delta = 143.5, 139.7, 130.6, 128.1, 126.3, 126.3, 31.9, 29.7, 29.6, 29.4, 29.3, 28.8, 22.6, 21.9, 14.4, 14.1 \text{ ppm.} \]

\[ ^{1}H \text{- and } ^{13}C \text{ NMR data were consistent with those previously reported for (E)-4-Phenyl-3-octene.}^{28} \]

Identity was further confirmed after subsequent epoxidation (v.i.).

**General Procedure Optimized for reaction of 9b-trans (GP3B)**

At -60 °C nBuLi in hexanes (1.5 equiv.) was added dropwise to a solution of epoxide 9b-trans and TMEDA (3 equiv.) in dry THF (6.5 – 7.8 mL/mmol of 9b-trans). After stirring for 2 h at the same temperature, a solution of appropriate boronic ester in THF (2 equiv., 0.61 – 1.0 M) was added and stirring was continued for 2 h at -60 °C. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 60 °C overnight. The reaction mixture was transferred with a small amount of EtO into a separation funnel and extracted with aqueous NaOH (1 M, 3x). The aqueous layers were re-extracted with EtO (2x) and the combined organic layers were dried over Na₂SO₄, concentrated in vacuo and purified by chromatography.

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28 J. Gerard, L. Hevesi, *Tetrahedron* 2001, 57, 9109-9121.
According to GP3B epoxide 9b-trans (104 mg, 0.53 mmol) was reacted with cyclohexyl pinacol boronic ester to yield 3c-E (60 mg, 0.23 mmol, 44%, de 95%), as a colorless oil after chromatography (SiO₂, CyHex).

\[ R_f = 0.58 \text{ (CyHex/EtOAc, 19:1).} \]

\(^1\)H-NMR (300 MHz, CHLOROFORM-d) \( \delta = 7.07 - 7.48 \text{ (m, 10 H), 6.31 (s, 1 H), 2.79 - 3.05 (m, 1 H), 0.92 - 1.85 ppm (m, 10 H)} \) ppm.

\(^{13}\)C NMR (75 MHz, CHLOROFORM-d) \( \delta = 149.4, 143.3, 137.9, 128.9, 128.8, 128.4, 128.2, 127.5, 126.5, 126.4, 40.4, 32.1, 26.3, 25.9 \) ppm.

\(^1\)H- and \(^{13}\)C NMR data for the Z-isomer were previously reported and examination of the spectra published by Zhang et al. revealed contamination with the E-isomer (3c-E). The de for our reaction was determined through integration of the olefinic signals at 6.31 (s, 1H, E-isomer) ppm and 6.38 (s, 1H, Z-isomer) ppm.\(^29\) The reaction was also conducted using GP1A and GP3A delivering 3c in 29% and 9% yield, respectively.

According to GP3B epoxide 9b-trans (300 mg, 1.53 mmol) was reacted with butyl pinacol boronic ester to yield 3d-E (111 mg, 0.47 mmol, 31%, de 94%) as a colorless oil after chromatography (SiO₂, CyHex).

\[ R_f = 0.52 \text{ (CyHex/EtOAc, 19:1).} \]

\(^1\)H-NMR (300 MHz, CHLOROFORM-d) \( \delta = 7.20 - 7.51 \text{ (m, 10 H), 6.70 (s, 1 H), 2.64 - 2.76 (m, 2 H), 1.27 - 1.46 (m, 4 H), 0.81 - 0.88 (m, 3 H)} \) ppm.

\(^{13}\)C NMR (75 MHz, CHLOROFORM-d) \( \delta = 143.4, 143.2, 138.4, 128.8, 128.6, 128.3, 128.2, 128.1, 127.1, 126.6, 126.5, 125.5, 30.9, 30.0, 22.8, 13.9 \) ppm.

\(^1\)H- and \(^{13}\)C NMR data were consistent with those previously reported.\(^30\) The de was determined through integration of olefinic signals at 6.70 (s, 1H, E-isomer) ppm and 6.44 (s, 1H, Z-isomer) ppm.\(^31\)

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\(^29\) Q.-Q. Wang, Z.-X. Wang, X.-Y. Zhang, X.-S. Fan, Asian J. Org. Chem. 2017, 6, 1445–1450.

\(^30\) F. Xue, J. Zhao, T. S. A. Hor, Chem. Commun. 2013, 49, 10121.

\(^31\) E/Z Relationship according to: D. M. Hodgson, M. J. Fleming, S. J. Stanway, J. Org. Chem. 2007, 72, 4763–4773.
Synthesis of Trisubstituted Alkenes from cis-Stilbene Oxide – General Procedure (GP3C)

At -98 °C nBuLi in hexanes (1.5 equiv.) was added dropwise to a solution of epoxide 9b-cis and TMEDA (1.5 equiv.) in dry THF (8 mL/mmol of 9b-cis). After stirring for 0.5 h at the same temperature, a solution of appropriate boronic ester in THF (2.0 equiv., 0.50 M) was added and stirring was continued for 10 min at -98 °C. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 60 °C overnight. The reaction mixture was transferred with a small amount of Et₂O into a separation funnel and extracted with aqueous NaOH (1 M, 3x). The aqueous layers were re-extracted with Et₂O (2x) and the combined organic layers were dried over Na₂SO₄, concentrated in vacuo and purified by chromatography over Al₂O₃.

(Z)-(1-Cyclohexylethen-1,2-diyl)dibenzen (3c-Z)

According to GP3C epoxide 9b-cis (49 mg, 0.25 mmol) was reacted with cyclohexyl pinacol boronic ester to yield 3c-Z (58 mg, 0.22 mmol, 88%), as a colorless oil after chromatography (Al₂O₃, CyHex/EtOAc, 20:1).

Rₓ = 0.76 (Al₂O₃, CyHex/EtOAc, 20:1).

1H NMR (300 MHz, CHLOROFORM-d) δ = 7.20 - 7.36 (m, 3 H), 6.92 - 7.18 (m, 5 H), 6.71 - 6.91 (m, 2 H), 6.39 (s, 1 H), 2.19 - 2.44 (m, 1 H), 1.54 - 1.96 (m, 5 H), 1.03 - 1.40 (m, 5 H) ppm.

13C NMR (75 MHz, CHLOROFORM-d) δ = 148.9, 141.6, 137.7, 129.0, 128.9, 128.3, 127.7, 126.6, 125.9, 124.5, 47.7, 32.3, 26.8, 26.3 ppm.

1H- and 13C NMR data were consistent with those previously reported.32

32 Q.-Q. Wang, Z.-X. Wang, X.-Y. Zhang, X.-S. Fan, Asian J. Org. Chem. 2017, 6, 1445–1450.
According to GP3C epoxide 9b-cis (49 mg, 0.25 mmol) was reacted with butyl pinacol boronic ester to yield 3d-Z (56 mg, 0.24 mmol, 95%) as a colorless oil after chromatography (Al$_2$O$_3$, CyHex).

$R_f$ = 0.74 (Al$_2$O$_3$, CyHex/EtOAc, 20:1).

$^1$H-NMR (300 MHz, CHLOROFORM-d) $\delta$ = 7.19 - 7.39 (m, 3 H), 7.10 - 7.18 (m, 2 H), 6.97 - 7.11 (m, 3 H), 6.81 - 6.96 (m, 2 H), 6.42 (s, 1 H), 2.48 (td, $J$=7.3, 1.3 Hz, 2 H), 1.16 - 1.46 (m, 4 H), 0.89 (t, $J$=7.2 Hz, 2 H) ppm.

$^{13}$C NMR (75 MHz, CHLOROFORM-d) $\delta$ = 143.6, 141.5, 137.6, 129.0, 128.5, 128.4, 127.8, 126.8, 126.1, 126.0, 40.4, 30.1, 22.3, 13.9 ppm.

$^1$H- and $^{13}$C NMR data were consistent with those previously reported.$^{33}$

According to GP3C epoxide 9b-cis (50 mg, 0.25 mmol) was reacted with octyneopentyl boronic ester to yield 3e-Z (57 mg, 0.19 mmol, 78%) as a colorless oil after chromatography (Al$_2$O$_3$, CyHex/EtOAc, 20:1).

$R_f$ = 0.80 (Al$_2$O$_3$, CyHex/EtOAc, 20:1).

$^1$H-NMR (300 MHz, CHLOROFORM-d) $\delta$ = 7.22 - 7.36 (m, 3 H), 7.00 - 7.22 (m, 5 H), 6.86 - 6.98 (m, 2 H), 6.44 (s, 1 H), 2.27 - 2.66 (m, 2 H), 1.06 - 1.49 (m, 12 H), 0.73 - 0.98 (m, 3 H) ppm.

$^{13}$C NMR (75 MHz, CHLOROFORM-d) $\delta$ = 143.6, 141.5, 137.6, 129.0, 128.5, 128.4, 127.8, 126.8, 126.1, 126.0, 40.7, 31.9, 29.4, 29.3, 29.2, 27.9, 22.6, 14.1 ppm.

$^1$H- and $^{13}$C NMR data were consistent with those previously reported.$^{34}$

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$^{33}$ B. C. Chary, S. Kim, D. Shin, P. H. Lee, Chem. Comm. 2011, 47, 7851.

$^{34}$ G. Liu, L. Kong, J. Shen, G. Zhu, Org. Biomol. Chem. 2014, 12, 2310–2321.
Synthesis of Trisubstituted Epoxides

(2R,3R)-2-Cyclohexyl-2,3-diphenyloxiran (10a-trans)

According to GP2 alkene 3c-E (200 mg, 0.76 mmol) was transformed into epoxide 10a-trans (200 mg, 0.60 mmol, 83%), isolated as a white solid after column chromatography (SiO₂, CyHex/EtOAc 19:1).

Rf = 0.41 (CyHex/EtOAc, 19:1).

1H-NMR (600 MHz, CHLOROFORM-d) δ = 7.30 - 7.60 (m, 10 H), 4.11 (s, 1 H), 1.87 - 2.01 (m, 1 H), 1.63 - 1.73 (m, 1 H), 1.37 - 1.52 (m, 3 H), 1.31 (tt, J=12.1, 3.3 Hz, 1 H), 1.13 (qt, J=13.0, 3.4 Hz, 1 H), 0.97 (qd, J=12.5, 3.5 Hz, 1 H), 0.83 - 0.93 (m, 2 H), 0.73 - 0.82 (m, 1 H) ppm

13C-NMR (75 MHz, CHLOROFORM-d) δ = 139.2, 135.5, 130.5, 128.2, 128.0, 127.6, 127.5, 127.4, 126.6, 70.7, 64.7, 39.8, 28.9, 28.2, 26.0, 25.8 ppm.

IR: ν̃ = 3086 (w), 3064 (w), 3032 (w), 2929 (m), 2855 (m), 2360 (w), 2161 (w, br.), 2024 (w, br.), 1967 (w, br.), 1446 (m), 882 (m), 767 (m), 754 (s), 693 (s) cm⁻¹.

MS (ESI⁺): found: [M+Na⁺] 301.2 (100%), calculated: 301.1.

HR-MS m/z (ESI⁺): found: [M+H⁺] 279.1744, C20H22O calculated: 279.1743.

(2R,3R)-2-Cyclohexyl-2,3-diphenyloxiran (10a-cis)

According to GP2 alkene 3c-Z (58 mg, 0.22 mmol) was transformed into epoxide 10a-cis (58 mg, 0.21 mmol, 94%), isolated as a white solid after column chromatography (Al₂O₃, CyHex).

Rf = 0.67 (Al₂O₃, CyHex/EtOAc, 20:1).

1H-NMR (300 MHz, CHLOROFORM-d) δ = 7.02 - 7.20 (m, 32 H), 6.87 - 7.19 (m, 10 H), 4.16 (s, 1 H), 1.57 - 2.15 (m, 6 H), 0.97 - 1.36 (m, 5 H) ppm.

13C-NMR (75 MHz, CHLOROFORM-d) δ = 136.0, 135.6, 128.9, 127.5, 127.2, 127.1, 126.9, 126.4, 72.3, 63.5, 46.4, 29.3, 28.4, 26.3, 26.1, 26.0 ppm.

IR: ν̃ = 3086 (w), 3060 (w), 3028 (w), 2927 (w), 2852 (w), 2360 (s), 2339 (s), 1446 (w), 754 (w), 717 (w), 698 (m), 667 (w) cm⁻¹.

MS (ESI, 70 eV): found: [M+H⁺] 279.1740, calculated: [M+H⁺] 279.1743.
According to GP2 alkene 3d-Z (46 mg, 0.19 mmol) was transformed into epoxide 10b-cis (53 mg, 0.16 mmol, 84%, yield corrected for 12% CyHex), isolated as a colorless oil after column chromatography (Al₂O₃, CyHex).

\[ R_f = 0.60 \text{ (Al}_2\text{O}_3, \text{CyHex/EtOAc, 20:1).} \]

\[ \text{^1H-NMR (300 MHz, CHLOROFORM-d)} \delta = 7.04 - 7.22 (m, 8 H), 6.91 - 7.06 (m, 2 H), 4.15 (s, 1 H), 2.01 - 2.24 (m, 1 H), 1.75 - 1.95 (m, 1 H), 1.13 - 1.59 (m, 4 H), 0.89 (t, \text{J}=6.9 \text{ Hz}, 3 H) \text{ ppm.} \]

\[ \text{^13C-NMR (75 MHz, CHLOROFORM-d)} \delta = 137.1, 135.7, 127.7, 127.6, 127.5, 127.2, 127.0, 126.5, 69.3, 64.6, 38.7, 27.0, 22.8, 14.0 \text{ ppm.} \]

\[ \text{IR: } \tilde{\nu} = 3032 \text{ (w), 2954 \text{ (w), 2937 \text{ (w), 2870 \text{ (w), 2160 \text{ (w), 2027 \text{ (w, br.), 1977 \text{ (w, br.), 1496 \text{ (w), 1456 \text{ (w), 1201 \text{ (w), 1076 \text{ (w), 912 \text{ (w), 885 \text{ (w), 860 \text{ (w), 754 \text{ (m), 698 (s) cm}^{-1}.} } \}

\[ \text{MS m/z (ESI\textsuperscript{+}): 253.0 (M+H\textsuperscript{+}, 100%).} \]

\[ \text{HR-MS m/z (ESI\textsuperscript{+}): found: [M+H\textsuperscript{+}] 253.160, C_{18}H_{20}OH calculated 253.159.} \]

**Comment:** Using butyl iodide instead of ethyl iodide, the conditions reported below for the synthesis of 10c-cis were also used for preparation of 10b-cis in 96% yield.

\[ (2R,3R)-2-\text{butyl-2,3-diphenyloxirane (10b-cis)} \]

To a solution of 9b-cis (202 mg, 1.03 mmol) in THF (8 mL) at -98 °C was added sBuLi in Hexanes (0.9 mL, 1.35 M, 1.22 mmol) in a drop wise manner. After stirring for 0.5 h ethyl iodide (0.1 mL, 1.22 mmol) was added. The reaction mixture was allowed to reach rt and stirred overnight after which saturated aq. NH₄Cl (4 mL) was added and the mixture was transferred into a separation funnel containing brine (10 mL). After extraction with EtOAc (3x10 mL) the combined organic phases were dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by chromatography (Al₂O₃, CyHex/EtOAc 30:1), yielding 10c-cis (216 mg, 0.96 mmol, 94%) as a colorless oil.[x]

\[ R_f = 0.70 \text{ (Al}_2\text{O}_3, \text{CyHex/EtOAc, 10:1).} \]

\[ \text{^1H-NMR (300 MHz, CDCl}_3\text{): } \delta = 7.03 - 7.41 (m, 10 H), 4.27 (s, 1 H), 2.28 (dq, \text{J}=14.1, 7.5 \text{ Hz}, 1 H), 2.01 (dq, \text{J}=14.3, 7.2 \text{ Hz, 1 H), 1.10 (t, J=7.5 Hz, 3 H) ppm.} \]

\[ \text{^13C-NMR (75 MHz, CDCl}_3\text{): } \delta = 136.8, 135.7, 127.8, 127.6, 127.2, 127.0, 126.5, 69.9, 64.4, 31.8, 9.1 \text{ ppm.} \]
Comments:

[*] These conditions were also used to prepare the other diastereomer (10c-trans) from trans-stilbene oxide (9b-trans). This delivered a 7:1 mixture of 10c-trans and the ortho-lithiation product in 57% yield.

[**] Resolution of this signal in a 300 MHz NMR required application of a Lorenz-Gaussian window function upon Fourier-Transformation.

(2R,3R)-3-Ethyl-2-octyl-2-phenyloxirane (10d)

According to GP2 alkene 3b (56 mg, 0.23 mmol) was transformed into epoxide 10d (42 mg, 0.16 mmol, 67%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 19:1).

R_f = 0.57 (CyHex/EtOAc, 9:1).

^1H-NMR (300 MHz, CHLOROFORM-d) δ = 7.12 - 7.42 (m, 5 H), 2.78 (t, J=6.4 Hz, 1 H), 1.98 - 2.22 (m, 1 H), 1.59 - 1.83 (m, 3 H), 1.15 - 1.48 (m, 12 H), 1.10 (t, J=7.5 Hz, 3 H), 0.87 (t, J=6.6 Hz, 3 H) ppm.

^13C-NMR (75 MHz, CHLOROFORM-d) δ = 141.8, 128.2, 127.0, 125.9, 67.7, 64.7, 31.8, 31.1, 29.8, 29.4, 29.2, 25.1, 22.6, 22.0, 14.1, 10.6 ppm.

IR: ṽ = 3064 (w), 3035 (w), 2955 (m), 2924 (m), 2855 (m), 2360 (s), 2341 (s), 2158 (w, br.), 2026 (w, br.), 1653 (m), 1559 (m), 1507 (m), 1457 (m), 905 (w), 744 (m), 698 (s), 668 (s) cm⁻¹.

MS m/z (ESI⁺): 283.2 (M+Na⁺, 100%).

HR-MS m/z (ESI⁺): found: [M+Na⁺] 283.2038, C_{18}H_{28}ONa calculated: 283.2032.

Comment: This compound was prepared to confirm structure 3b.

35 S. Oudeyer, E. Léonel, J. P. Paugam, J.-Y. Nédélec, Synthesis 2004, 389–400.
Synthesis of Tetrasubstituted Alkenes – General Procedure (GP4)

At -78 °C tBuLi in pentane (1.1-1.3 equiv.) was added dropwise to a solution of epoxide 10-cis and TMEDA (6 equiv.) in dry Et₂O (9-10 mL/mmol of 10-cis). After stirring for 15 min. at the same temperature, a solution of appropriate boronic ester in Et₂O (2.0 equiv., 0.40-0.44 M) was added. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 38 °C overnight. The reaction mixture was transferred with a small amount of Et₂O into a separation funnel and extracted with aqueous NaOH (1 M, 3x). The aqueous layers were re-extracted with Et₂O (2x) and the combined organic layers were dried over Na₂SO₄, concentrated in vacuo and purified by chromatography.

Hex-1-ene-1,1,2-triyltribenzene (11b)

According to GP4 epoxide 10b-cis (50 mg, 0.20 mmol) was transformed into alkene 11b (20 mg, 0.06 mmol, 32%) at -78 °C, isolated as a white solid after column chromatography (Al₂O₃, CyHex).

R_f = 0.55 (SiO₂, CyHex/EtOAc, 20:1).

¹H-NMR (300 MHz, CHLOROFORM-d) δ = 7.33 - 7.38 (m, 2 H), 7.24 - 7.31 (m, 3 H), 7.10 - 7.18 (m, 5 H), 6.97 - 7.05 (m, 3 H), 6.86 - 6.95 (m, 2 H), 2.45 (t, J=7.5 Hz, 2 H), 1.17 - 1.37 (m, 4 H), 0.79 (t, J=7.2 Hz, 3 H) ppm.

¹³C-NMR (75 MHz, CHLOROFORM-d) δ = 143.5, 143.1, 142.5, 141.1, 139.0, 130.7, 129.6, 129.5, 128.1, 127.8, 127.3, 126.5, 126.1, 125.7, 35.6, 31.1, 22.8, 13.9 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.³⁶

Comment: When deprotonation was attempted at -98 °C the product was isolated in 22% yield.

³⁶ C. Zhou, R. C. Larock, J. Org. Chem. 2005, 70, 3765–3777.
(Z)-{1-Cyclohexyl-1-ene-1,2-diyl)dibenzene (11c)

According to GP4 epoxide 10b-cis (50 mg, 0.20 mmol) was transformed into alkene 11c (36 mg, 0.11 mmol, 56%) at -78 °C, isolated as a colorless oil after column chromatography (Al₂O₃, CyHex).

Rᵣ = 0.62 (CyHex/EtOAc, 20:1).

1H-NMR (300 MHz, CHLOROFORM-d) δ = 6.81 - 7.08 (m, 10 H), 2.81 (tt, J=11.3, 3.3 Hz), 2.45 - 2.63 (m, 2 H), 1.56 - 1.84 (m, 5 H), 1.25 - 1.46 (m, 5 H), 0.95 - 1.22 (m, 4 H), 0.91 (t, J=6.9 Hz, 3 H) ppm.

13C-NMR (75 MHz, CHLOROFORM-d) δ = 143.9, 143.4, 141.2, 138.1, 130.7, 129.4, 127.1, 126.7, 125.2, 125.1, 41.3, 33.4, 32.2, 31.0, 26.8, 25.9, 22.7, 14.0 ppm.

IR: ν̃ = 3078 (w), 3057 (w), 3020 (w), 2924 (m), 2856 (w), 1441 (w), 769 (m), 896 (s) cm⁻¹.

HR-MS m/z (ESI⁺): found: [M+Na⁺] 341.2240, C₂₄H₃₀Na calculated: 341.2240.

Stereochemical assignment: A clear nOe signal between the allylic cyclohexyl CH (2.81, tt, J=11.3, 3.3 Hz), and the allylic butyl CH₂ (2.55, m) confirmed formation of the Z-olefin 11c.

Comment: When deprotonation was attempted at -98 °C the product was isolated in 28% yield.

(Z)-Tetradec-5-ene-5,6-diylldibenzene (11d)

According to GP4 epoxide 10b-cis (50 mg, 0.20 mmol) was transformed into alkene 11d (45 mg, 0.13 mmol, 64%) at -78 °C, isolated as a colorless oil after column chromatography (Al₂O₃, CyHex).

Rᵣ = 0.58 (CyHex/EtOAc, 20:1).

1H-NMR (300 MHz, CHLOROFORM-d) δ = 6.86 - 7.12 (m, 10 H), 2.47 - 2.60 (m, 4 H), 1.16 - 1.40 (m, 16 H), 0.89 (t, J=6.6 Hz, 6 H) ppm.

13C-NMR (75 MHz, CHLOROFORM-d) δ = 143.6, 138.3, 138.3, 129.8, 127.3, 125.3, 34.3, 34.1, 31.9, 30.7, 29.6, 29.5, 29.3, 28.4, 22.7, 22.6, 14.1, 14.0 ppm.

IR: ν̃ = 3078 (w), 3057 (w), 3020 (w), 2924 (m), 2856 (w), 1441 (w), 769 (m), 896 (s) cm⁻¹.

HR-MS m/z (ESI⁺): found: [M+Na⁺] 371.2710, C₁₈H₃₀ONa calculated: 371.2709.

Comment: When deprotonation was attempted at -98 °C the product was isolated in 36% yield. As the allylic signals overlapped, no confirmation of the configuration by nOe was possible in this case.
But-1-ene-1,1,2-triyltribenzene (11e)

According to GP4 epoxide 10c-cis (50 mg, 0.22 mmol) was transformed into alkene 11e (26 mg, 0.09 mmol, 41%) at -78 °C, isolated as a white solid after column chromatography (Al₂O₃, CyHex).

R_f = 0.70 (Al₂O₃, CyHex/EtOAc, 20:1).

^1H-NMR (300 MHz, CHLOROFORM-d) δ = 7.23 - 7.39 (m, 5 H), 7.07 - 7.20 (m, 5 H), 6.94 - 7.05 (m, 3 H), 6.85 - 6.94 (m, 2 H), 2.49 (q, J=7.5 Hz, 2 H), 0.95 (t, J=7.5 Hz, 3 H) ppm.

^13C-NMR (75 MHz, CHLOROFORM-d) δ = 143.5, 143.0, 142.2, 142.2, 138.8, 130.7, 129.7, 129.4, 128.1, 127.8, 127.3, 126.6, 126.1, 125.7, 29.0, 13.5 ppm.

^1H- and ^13C NMR data were consistent with those previously reported.⁴⁷

Comment: When deprotonation was attempted at -98 °C the product was isolated in 35% yield.

(E)-(1-(4-Methoxyphenyl)but-1-ene-1,2-diyl)dibenzene (11f)

According to GP4 epoxide 10c-cis (51 mg, 0.23 mmol) was transformed into alkene 11e (69 mg,* 0.20 mmol, 87%) at -78 °C, isolated as a white solid after column chromatography (Al₂O₃, CyHex).

R_f = 0.57 (Al₂O₃, CyHex/EtOAc, 20:1).

^1H-NMR (300 MHz, CHLOROFORM-d) δ = 6.97 - 7.21 (m, 10 H), 6.83 - 6.95 (m, 4 H), 3.84 (s, 3 H), 2.53 (q, J=7.5 Hz, 2 H), 0.96 (t, J=7.5 Hz, 3 H) ppm.

^13C-NMR (75 MHz, CHLOROFORM-d) δ = 158.3, 143.4, 142.4, 141.9, 138.4, 136.0, 130.8, 130.6, 129.7, 127.7, 127.3, 126.0, 125.6, 55.2, 29.0, 13.6 ppm.

^1H- and ^13C NMR data were consistent with those previously reported.³⁸

Comment: When deprotonation was attempted at -98 °C the product was isolated in 61% yield. (*) Sample initially contaminated with 10% starting material. Yield corrected accordingly.

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³⁷ Z. He, S. Kirchberg, R. Fröhlich, A. Studer, Angew. Chem., Int. Ed. 2012, 51, 3699–3702.

³⁸ B. X. Li, D. N. Le, K. A. Mack, A. McClory, N.-K. Lim, T. Cravillion, S. Savage, C. Han, D. B. Collum, H. Zhang, et al., J. Am. Chem. Soc. 2017, 139, 10777–10783.
(E)-2-{4-(1,2-diphenylbut-1-en-1-yl)phenoxy}-N,N-dimethylethanamine (11g)

According to GP4 epoxide 10c-cis (47 mg, 0.21 mmol) was transformed into alkene 11g (49 mg, 0.13 mmol, 63%) at -78 °C, isolated as a white solid after column chromatography (Al₂O₃, DCM/MeOH 99:1).

R_f = 0.25 (Al₂O₃, DCM/MeOH, 9:1).

\(^1\text{H-NMR}\) (300 MHz, CHLOROFORM-d) \(\delta = 6.96 - 7.21 \text{ (m, 10 H)}\), 6.85 - 6.94 (m, 4 H), 4.12 (t, J=5.8 Hz, 2 H), 2.79 (t, J=5.6 Hz, 2 H), 2.52 (q, J=7.3 Hz, 2 H), 2.39 (s, 6 H), 0.95 (t, J=7.4 Hz, 3 H) ppm.

\(^{13}\text{C-NMR}\) (75 MHz, CHLOROFORM-d) \(\delta = 157.7, 143.5, 142.6, 142.1, 138.6, 136.3, 130.9, 130.7, 129.9, 127.9, 127.4, 126.2, 125.8, 114.3, 65.9, 58.4, 46.0, 29.2, 13.7 \text{ ppm.}\)

\(^1\text{H- and }^{13}\text{C NMR data were consistent with those previously reported.}\)

**Comment:** The boronic ester employed was not completely soluble in Et₂O and added as a suspension in 1 mL dry Et₂O. Therefore the flask and syringe were rinsed with additional Et₂O (1 mL).

**Optimization Experiments**

The following experiments were carried out in order to optimize GP 4 using a mixture of 10b/c-cis. These experiments indicate that lithiation times of 15-30 min at -98 °C are optimal. While shorter lithiation times led to incomplete conversion, longer lithiation times could very well lead to decomposition of the formed carbenoids.

| Entry | t     | Yield Alkene |
|-------|-------|--------------|
| 1     | 5 min | 48%          |
| 2     | 15 min| 60%          |
| 3     | 30 min| 62%          |
| 4     | 60 min| 50%          |

39 K. Itami, T. Kamei, J. Yoshida, J. Am. Chem. Soc. 2003, 125, 14670–14671.
Failed Attempts at Quaternary Alkene Synthesis from 10-trans

| Entry | Base           | Solvent | $T^{(1)}$ | $t^{(1)}$ | Boronate            | R     | $T^{(2)}$ | Result                  |
|-------|----------------|---------|----------|----------|---------------------|-------|-----------|-------------------------|
| 1     | LiTMP          | THF     | 0 °C     | 30 min.  | PMP-B(neo) (in situ) | Cyclohexyl | 60 °C     | no conversion of 10a-trans |
| 2     | sBuLi (TMEDA 3 equiv.) | EtO | -110 °C  | 10 min.  | PMP-B(pin)              | Cyclohexyl | 38 °C     | no conversion of 10a-trans |
| 3     | tBuLi (TMEDA 3 equiv.) | EtO | -110 °C  | 10 min.  | PMP-B(neo)              | Cyclohexyl | 38 °C     | no conversion of 10a-trans |
| 4     | nBuLi (TMEDA 3 equiv.) | THF | -60 °C   | 2 h      | PMP-B(neo)              | Cyclohexyl | 60 °C     | no conversion of 10a-trans |
| 5     | sBuLi (TMEDA 3 equiv.) | PhMe | -50 °C   | 30 min.  | PMP-B(neo)              | Cyclohexyl | 100 °C    | no conversion of 10a-trans |
| 6     | sBuLi (TMEDA 3 equiv.) | PhMe | -50 °C   | 2 h      | PMP-B(neo)              | Cyclohexyl | 100 °C    | no conversion of 10a-trans |
| 7     | tBuLi (TMEDA 6 equiv.) | EtO | -98 °C   | 5 min    | Ph-B(neo)               | Ethyl   | 38 °C     | no conversion of 10c-trans |
| 8     | tBuLi (TMEDA 6 equiv.) | EtO | -78 °C   | 2 h      | Ph-B(neo)               | Ethyl   | 38 °C     | no conversion of 10c-trans |
| 9     | tBuLi (TMEDA 6 equiv.) | EtO | -50 °C   | 2 h      | Ph-B(neo)               | Ethyl   | 38 °C     | no conversion of 10c-trans |
| 10    | KOT-Bu n-BuLi(a) | THF | -78 °C to -48 °C | 2 h | Ph-B(neo) | Cyclohexyl | 60 °C | (>95%)* |
| 11    | KOT-Bu n-BuLi(b) | THF | -78 °C to -48 °C | 2 h | Ph-B(neo) | Cyclohexyl | 60 °C | (>95%)* |

(*) Yield of 13 was obtained by $^1$H NMR using methyl benzoate as an internal standard.
Selected NMR-Spectra

Chemical Shift (ppm)

Normalized Intensity

KB149b.001.esp

KB149b.002.esp
Selected NMR-Spectra

contains ca. 40% of an inseparable contaminant (yield corrected for impurity)
Selected NMR-Spectra

KB112a.2.001.esp

Chemical Shift (ppm)

KB112a.002.esp

Chemical Shift (ppm)

KB112a.002.esp

Chemical Shift (ppm)
Selected NMR-Spectra

71% pure
impurities:
15.5% boronic ester
13.5% epoxide starting material
(yield corrected for impurity)
Selected NMR-Spectra

![NMR Spectra](image1.png)

- **Chemical Shift (ppm):**
  - 7.270

![NMR Spectra](image2.png)

- **Chemical Shift (ppm):**
  - 77.000
  - 63.334
  - 57.730
  - 40.169
  - 32.240
  - 29.758
  - 29.511
  - 29.199
  - 26.093
  - 25.723
  - 22.642
Selected NMR-Spectra

KB146b.2.001.esp

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)

KB146b.2.002.esp

176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)
Selected NMR-Spectra

KB210b 500.001.esp

KB210b 500.002.esp

Chemical Shift (ppm)

Normalized Intensity

KB210b 500.002.esp

Chemical Shift (ppm)
10b-cis
yield corrected for 12%
CyHex-residue
Selected NMR-Spectra

KB324b.001.esp

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0

Chemical Shift (ppm)

KB324b.002.esp

176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0

Chemical Shift (ppm)
