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# Organocatalytic alkyne isomerizations under flow conditions using heterogeneous bifunctional polystyrene bearing phosphine and phenol groups

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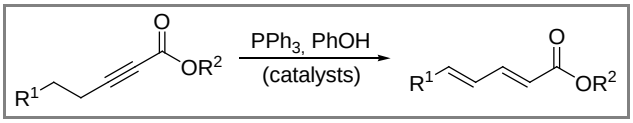
**Abstract:** A heterogeneous bifunctional polymer bearing phosphine and phenol groups was developed to catalyze the isomerization of electronically activated alkynes that yielded the corresponding (*E*,*E*)-dienes in an organocatalytic process. These reactions were shown to work both under batch and flow processes, respectively.

**Key words:** Rearrangement, organocatalysis, polymer-supported catalyst, phosphine, phenols, flow chemistry

The organocatalytic phosphine-catalyzed isomerization of electron-withdrawing group activated alkynes to the corresponding (*E*,*E*)-dienes is a highly stereoselective process that occurs under mild reaction conditions.[1,2] It was independently reported by the groups of Trost[3] and Lu[4] for the isomerization of alkynones. Shortly thereafter Rychnovsky and Kim reported that the addition of phenol as a co-catalyst allows this methodology to be extended to alkynoate substrates (Scheme 1),[5] and thereby greatly increasing its utility. Recently such reactions have been used in the synthesis of a series of different natural products.[6]




**Scheme 1.** The Trost-Lu isomerization of alkynes.

Several years ago we reported on the synthesis of **1**, a bifunctional non-cross-linked polystyrene bearing phosphine and phenol groups. This bifunctionalized polymer served as a catalyst for the Morita-Baylis-Hillman reaction.[7] The linear nature of the polymer backbone meant that it functions as a homogeneous catalyst, and thus it was difficult to recover and recycle. Nevertheless, we have more recently used **1** to efficiently catalyze the rearrangement of a wide range of ester group activated alkyne substrates (Figure 1).[8] We now wish to report the synthesis of heterogeneous analogue **2**, based on the rasta resin architecture (Figure 2), where the functional groups are attached to linear polystyrene grafts anchored onto a heterogeneous cross-linked polystyrene core,[9] and its use as a catalyst in the isomerization of alkynoates under flow conditions.

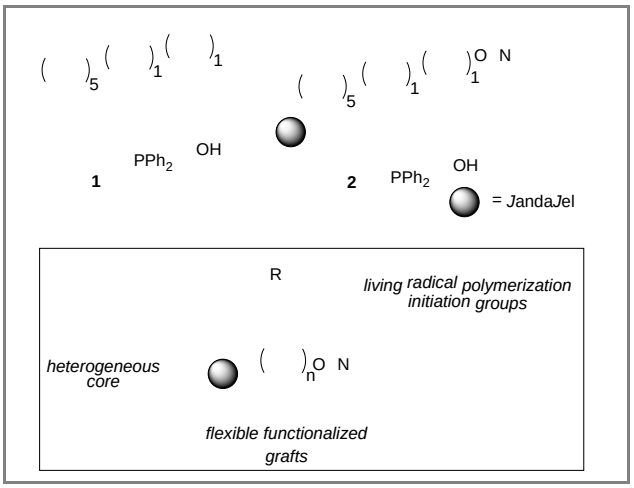
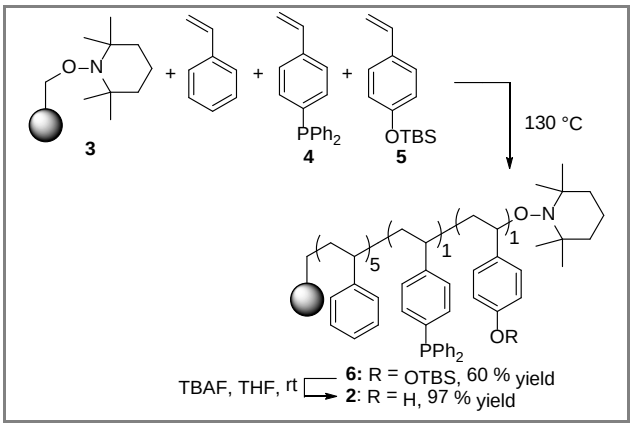



**Figure 1.** Bifunctional polymers **1** and **2** and the rasta resin concept.

For the synthesis of **2**, the rasta resin architecture was used since the attachment of the catalytic phosphine and phenol groups to the flexible grafts rather than the more rigid heterogeneous core would eliminate the need for swelling in the reaction solvent to achieve high catalytic efficiency. We felt that his was important since previous results from our group indicated that the presence of phenol groups in more traditional Merrifield-type resins reduced their ability to swell, and thus would reduce substrate accessibility to the catalytic sites.[10] Thus, heterogeneous core **3**[9] was heated in the presence of a ternary monomer mixture of styrene, phosphine monomer **4**[11] and phenol monomer **5**[9] (5:1:1 molar ratio) in order to initiate living radical polymerization to afford **6** (Scheme 2). Subsequent treatment of **6** with TBAF liberated the phenol groups to form **2**. The loading level of the phosphine groups was determined by elemental analysis to be 0.95 mmol $g^{-1}$, compared to a theoretical value of 0.90 mmol $g^{-1}$. Furthermore, gel-phase $^{31}$P-NMR analysis of **2** confirmed that the phosphine groups were not oxidized. Scanning electron microscopy images of the resins are shown in Figure 1. A dramatic increase in average bead size was observed in **6** compared to **3**

and the beads of **2** and **6** were approximately equal in size.




**Scheme 2.** Synthesis of rasta resin **2**.

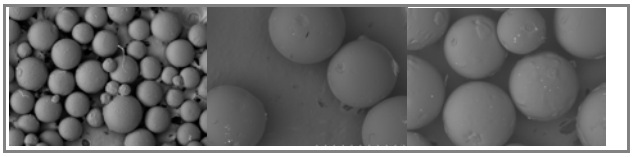
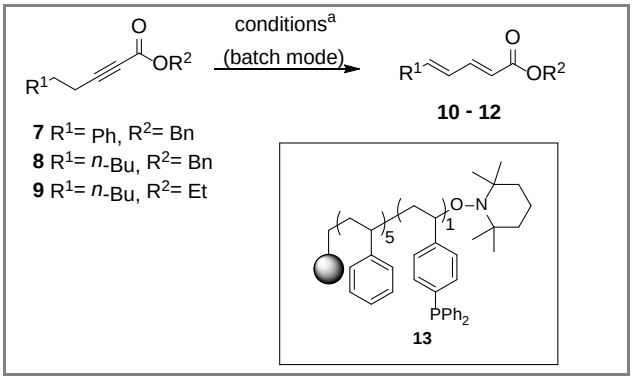


**Figure 2.** The SEM images of resins **3** (left), **6** (middle) and **2** (right).

Interest in miniaturized flow devices (meso- or microstructured reactors) has seen a dramatic increase lately.[12] By combining it with chemically functionalized fixed bed materials based on inorganic or polymeric supports synthetic technology platforms are created which simplify synthesis and work-up protocols.[13] Catalytic processes using heterogenized homogeneous catalysts are ideally suited for being operated under the regime of flow protocols. For example the catalytic reaction can be carried out in a continuous mode which is particularly beneficial when a chemically robust catalyst is immobilized. Importantly, the local catalyst concentration is very high which has an impact on the kinetics of a catalytic reaction allowing for high substrate concentrations and higher conversions with shorter reaction times.

In continuation of our work on flow chemistry and enabling techniques in organic synthesis[14] we investigated the performance of the bifunctional heterogeneous organocatalyst **2** as fixed bed material inside microstructured flow reactors. For this purpose we first had to optimize the catalytic process with respect to the nature of the immobilized catalyst, the amount of catalyst employed and the concentration of the solution (Table 1).

**Table 1**. Trost-Lu isomerization using mono and bifunctional organocatalysts **1**, **2**, and **13 (13** resembles functionalized polymer **2** but it is only monofunctionalized lacking the phenol moiety).

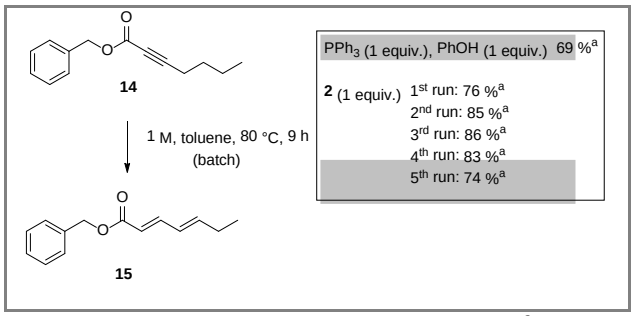



| | alkyne | conditions | product | yield [%][b] |
|---|---|---|---|---|
| 1 | **7** | **13**, PhOH, 29 h | **10** | 50 |
| 2 | **7** | **1**, 29 h | **10** | 75 |
| 3 | **7** | **2**, 24 h | **10** | 85 |
| 4 | **8** | **2** (0.5 eq.), 24 h | **11** | 90 |
| 5 | **9** | **2** (0.2 eq.), 24 h | **12** | 85 |
| 6 | **7** | **2**, 0.5 M, 24 h | **10** | 0 |
| 7 | **9** | 0.2 M, $PPh_3$, PhOH, 2 h | **12** | 91 |
| 8 | **8** | **2**, 2 h | **11** | 46 |
| 9 | **8** | **2**, 4 h | **11** | 81 |
| 10 | **9** | **2**, 7 h | **12** | 80 |

[a] Conditions if not otherwise stated: 1 M solution in toluene, 80 °C, 1 equiv. catalyst; [b] isolated yield.

We chose alkynes **7**-**9** as substrates and the reactions were conducted in the batch mode in a vial. Clearly, the insoluble rasta resin **2** showed superior activity compared to phosphine functionalized resin **13**[9] and soluble non-cross-linked bifunctional polymer **1**[7] (compare entries 1-3), which is a prerequisite for the flow experiments to follow. The reduced activity of the monofunctionalized resin in the presence of phenol indicates that both groups act cooperatively, when closely attached to the polymeric backbone. With respect to the catalyst concentration we investigated the possibility to lower the initial amount of stoichiometric amounts down to 0.2 equivalents (entries 3-5). Gratifyingly, we found that the catalyst truly acts as an organocatalyst and can be used at 20 mol% loading levels. Regarding the concentrations of the substrates we observed that concentrations below 1 M led to no conversion with catalyst **2** (entry 6). In contrast, the use of traditional conditions with PhOH and $PPh_3$ allowed the use of 0.2 M concentrations (entry 7). Obviously, catalyst **2** is limited to high concentrations although in the context of flow reactions this is not a concern as stated above. Next, we varied the reaction time to get a grip on the actual kinetics (entries 8-10). We found that after 4 to 7 h the conversion was almost as high as in the case of 20 h. Thus, we could collect important information and facts for the desired flow reactions described ín the following.

First, we studied the reusability of resin **2** and as a test reaction we chose the isomerization of alkyne **14** to diene **15** (Scheme 3). For being useful as fixed bed materials in flow processes heterogenized catalyst must prove to be robust with respect to loading which is an immense problem in metal-catalyzed reactions. We[15] and other groups[16] have encountered that the strong convective flow inside microstructured flow reactors leads to enhanced leaching of metals from its ligand, when attached to a solid phase compared to corresponding batch reactions. Mechanical stability and stress are other issues when low cross-linked polymers are exposed to different solvents because solvents cause swelling and shrinking.



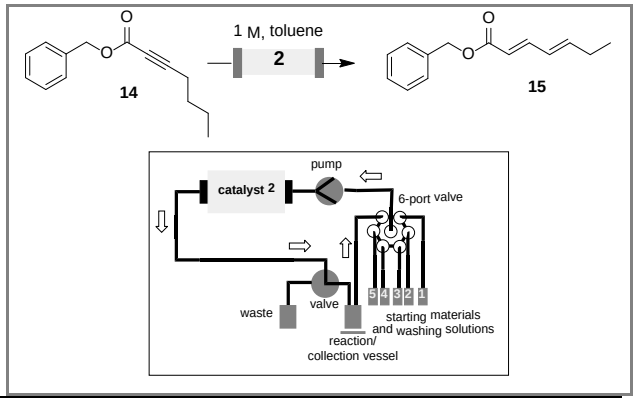

**Scheme 3**. Recyclability studies with rasta resin **2** ([a] full conversion, isolated yield).

When alkyne **14** was subjected to the homogeneous Trost-Lu conditions, diene **15** was isolated in 69 % yield. The rasta resin **2** gave a similar yield after filtration, removal of solvent and gel filtration. The polymer was resubjected to a new batch of alkyne furnishing diene **15** in 85 %. This procedure was repeated another three times with similar results. In essence, we did not observe any degradation or loss of activity of the functionalized polymer **2**.

Next, we optimized the reaction of alkyne **14** for applications under flow conditions. The technical setup is also depicted in Table 2; it allows conducting the flow synthesis in a circular mode or alternatively as a continuous process. In the present study we utilized a reactor design, based on glass rods, already been used earlier in our group.[14a] The flow reactor (length: 12 cm, I.D.: 5.0 mm, void volume when filled with catalyst **2**: 1 mL) was filled with the heterogeneous catalyst and heated by an external oil bath while the reaction mixture was pumped through and finally collected at the reactor outlet.

We optimized three reaction parameters to achieve full conversion in a single pass. The investigations included the impact of the flow rate, the reaction temperature and the influence of toluene. All reactions were conducted with the same fixed bed reactor; thus the same batch of functionalized polymer **2** was used for all reactions. The residence time which correlated with the flow rate has a strong influence on the degree of conversion (entries 1-4). Clearly, at a flow rate of 0.005 mL/min good results were obtained and the isolated yield of 82 % demonstrates that the transformation provides a true picture on the efficacy of the process. When the temperature was raised to 100 °C, good yields are achievable at higher flow rates (entry 5). At temperatures well above 100 °C we encountered degradation of the rasta resin **2** which led to reduced yields (compare entries 4, 6-8). Interestingly, the reaction can also be conducted in the absence of toluene as solvent at 100 °C and a flow rate of 0.005 mL/min (residence time approximately 200 min) which could be of particular importance for continuous industrial processes (entry 9).

**Table 2**: Isomerization of alkyne **15** under flow conditions and schematic presentation of flow set-up.[a]



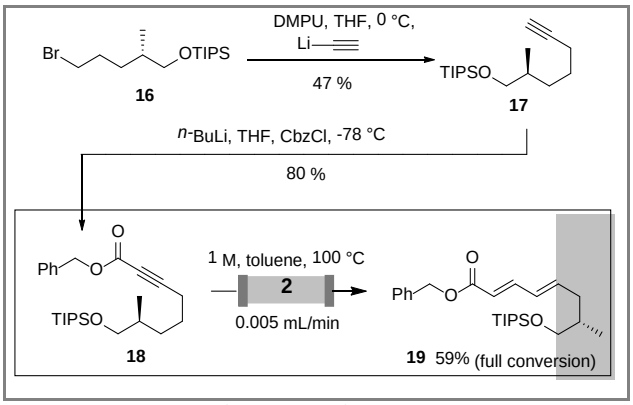

| | flow rate [mL/min] | residence time [min] | temp. [°C] | Transformation [%] |
|---|---|---|---|---|
| 1 | 0.05 | 20 | 80 | 43 |
| 2 | 0.02 | 50 | 80 | 55 |
| 3 | 0.01 | 100 | 80 | 81 |
| 4 | 0.005 | 200 | 80 | 87 (82)[b] |
| 5 | 0.02 | 50 | 100 | 78 |
| 6 | 0.005 | 200 | 100 | 92 |
| 7 | 0.005 | 200 | 105 | 60 |
| 8 | 0.005 | 200 | 110 | 69 |
| 9[c] | 0.005 | 200 | 100 | 86 |

[a] Conditions if not otherwise stated: 1 M solution in toluene, 80 °C, 1 equiv. catalyst; [b] isolated yield; [c] neat conditions.

Compared to the reaction times for isomerisation under batch conditions, the residence time calculated for the optimized flow process (100 °C, 0.005 mL/min) is 3.5 times shorter which demonstrates another advantage of flow processes over the batch mode. This can be ascribed to the fact that catalyst concentration is higher when used as fixed bed material inside the flow device.

Finally, we planned to show that the Trost-Lu isomerization can be a powerful synthetic tool in natural product synthesis using more complex substrates. As a telling example we prepared alkyne **18** starting from bromide **16**[17] (Scheme 4). Alkynylation of bromide **16** with lithium acetylide gave alkyne **17**, which was further functionalized after

deprotonation and trapping of the acetylide with benzyloxycarbonyl chloride to afford alkyne **18**.




**Scheme 4**. Synthesis of alkyne **18** from bromide **16** and Trost-Lu isomerization of alkyne **18** under flow conditions using rasta resin **2**.

When alkyne **18** was subjected to the optimized isomerization conditions using rasta resin **2** full conversion at a flow rate of 0.005 mL/min under flow conditions. These conditions are comparable with those found for simpler alkynes (Scheme 4).

In conclusion, we described the first example of an organocatalytic flow process using a heterogeneous bifunctionalized polymer as catalyst. The process described paves the way to perform the Trost-Lu isomerization of alkynoates to dienoates under continuous flow conditions with minimum work up. We are currently developing heterogeneous bifunctional polymers that bear chiral catalytic groups in the hopes that we can apply this new methodology to asymmetric organocatalysis, and the results of these experiments will be reported in due course.

## Experimental

**General Methods.** $^{1}$H NMR spectra were recorded at 400 MHz with a Bruker AVS-400 spectrometer. $^{13}$C NMR spectra were recorded at 100 MHz with a Bruker AVS-400. Mass spectra (EI) were obtained at 70 eV with a type VG Autospec apparatus (Micromass) or with a type LCT (ESI) (Micromass). Analytical thin-layer chromatography was performed using precoated silica gel 60 $F_{254}$ plates (Merck, Darmstadt), and the spots were visualized with UV light at 254 nm or by staining with $H_2SO_4$/4-methoxybenzaldehyde in ethanol. Flash column chromatography was performed on Merck silica gel 60 (230-400 mesh). All reagents were used as received from the suppliers. THF was dried over sodium wire with benzophenone as indicator. Specific optical rotations [α] were measured at 20 °C with a polarometer type 341 from Perkin-Elmer with a 10 cm cuvette at λ = 589.3 mm (sodium-D-line). As HPLC pumps Smartline Pump 100 from Knauer were used. The employed glass reactors were constructed from commercially available parts. Analytical data of dienes **10**-**12** have been reported in reference 8.

**Preparation of catalyst 2**. A suspension of **3** (0.41 g, 1.5 mmol), **4** (4.2 g, 14.6 mmol), **5** (3.42 g, 14.6 mmol) and styrene (7.6 g, 72.9 mmol) was heated at 130 °C under $N_2$ for 48 h. After cooling to room temperature, the resulting polymer was shaken with $CH_2Cl_2$ (25 mL) for about 5 min until the resin beads floated freely. The resin was collected by filtration, placed in a Soxhlet extractor, and washed with refluxing THF for 24 h. The beads were then washed sequentially with methanol, THF, diethyl ether, and hexanes, and dried *in vacuo* to afford **6** (9.4 g, 60 %).

Polymer **6** was mixed with 1.0 M TBAF solution in THF (34.4 mL, 34.4 mmol), shaken overnight at rt for 12 h, and then washed sequentially with methanol, THF, diethyl ether and hexane and dried *in vacuo* to afford **2** (9.1 g, 97 %). Elemental analysis was used to determine the phosphine content (3.0 %), and thus a loading level of 0.95 mmol $PPh_3$/g. Gel-phase $^{31}$P NMR of **2** indicated only the presence of unoxidized phosphine at -6.13 ppm.

**Benzyl hept-2-ynoate (14):** 1-Hexyne (5.2 mL, 3.6 g, 44.1 mmol) was dissolved in dry THF (140 mL) and cooled to -78 °C under an argon atmosphere. Subsequently, *n*-BuLi (2.5 M in hexane, 17.64 mL, 1.25 equiv.) was added dropwise over 30 min and the resulting solution further stirred for 30 min. Benzyl chloroformate (5.0 mL, 6.0 g, 35.3 mmol, 1.0 equiv.) was added dropwise and stirring was continued for 45 min. The reaction mixture was hydrolyzed by addition of a sat. $NH_4Cl$ solution, the organic phase separated and the aqueous one was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $Na_2SO_4$ and concentrated *in vacuo*. The crude product was purified by *Kugelrohr* distillation at 150 °C and **14** was obtained as a pale yellow oil (6.03 g, 27.9 mmol, 79 %).

$^{1}$H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm): δ = 7.38-7.33 (m, 5H, Ar-H), 5.19 (s, 2H, Bn-H), 2.33 (t, 2H, J = 7.0 Hz, H-4), 1.59-1.51 (m, 2H, H-5), 1.47-1.37 (m, 2H, H-6), 0.92 (t, 3H, J = 7.3 Hz, H-7). $^{13}$C-NMR (100 MHz, $CDCl_3$, $CHCl_3$ = 77.16 ppm): δ = 153.7 (q, C-1), 135.1 (q, Ar-C), 128.6 (t, Ar-C), 128.53 (t, Ar-C), 128.50 (t, Ar-C), 90.2 (q, C-3), 73.0 (q, C-2), 67.4 (s, Bn-C), 29.5 (s, C-5), 21.9 (s, C-6), 18.4 (s, C-4), 13.5 (p, C-7). HRMS (ESI): calc. for $C_{14}H_{16}O_2Na_1^+$: 239.1048 $[M+Na]^+$ found: 239.1053.

**Benzyl (2*E*,4*E*)-hepta-2,4-dienoate (15):** *Batch reaction*: Catalyst **2** (625 mg, 0.50 mmol) was added to a solution of **14** (108 mg, 0.50 mmol, 1 equiv.) in toluene (0.5 mL). The reaction mixture was shaken at 80 °C for 18 h. The polymer beads were filtered off and washed with ethyl acetate. The filtrate was concentrated *in vacuo* to afford **15** as a yellow oil (86.4 mg, 0.40 mmol, 80 %).

*Flow reaction*: A glass reactor (length: 12 cm, I.D.: 5.0 mm) was filled with catalyst **2** (1.6 g, 1.28 mmol) and flushed with toluene. The reactor was placed in a preheated oil bath (80 °C) and a flow rate of 0.005 mL/min was employed. After a steady state was reached **14** (215 mg, 1.0 mmol) in toluene (1 mL) was pumped through the reactor. The crude product was collected, concentrated *in vacuo* and purified by column chromatography (EtOAc/petroleum ether = 1:40) to afford **15** as a yellow oil (175 mg, 0.81 mmol, 81 %).

$^{1}$H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm): $\delta$ = 7.38-7.28 (m, 6H, Ar-H und H-3), 6.18-6.17 (m, 2H, H-2 und H-4), 5.84 (d, 1H, *J* = 15.0 Hz, H-5), 5.19 (s, 2H, Bn-H), 2.23-2.16 (m, 2H, H-6), 1.05 (t, 3H, H-7). $^{13}$C-NMR (100 MHz, $CDCl_3$, $CHCl_3$ = 77.16 ppm): $\delta$ = 167.1 (q, C-1), 146.4 (q, C-Ar), 145.7 (t, C-3), 136.3 (t, C-5), 128.5 (t, Ar-C9, 128.2 (t,Ar-C), 128.1 (t, Ar-C), 127.4 (t, C-4), 118.8 (t, C-2), 66.0 (s, Bn-C), 26.1 (s, C-6), 12.9 (p, C-7). HRMS (ESI): calc. for $C_{14}H_{16}O_2Na_1^+$: 239.1048 $[M+Na]^+$ found: 239.1047.

**(*S*)-Tri*iso*propyl-(2-methylhept-6-ynyloxy)silane (17):** Lithium acetylide ethylenediamine complex (85 %, 105 mg, 1.13 mmol, 2.0 equiv.) was suspended in dry THF (5 mL) under an argon atmosphere and cooled to 0 °C. 2-Methylhept-6-ynyl bromide (**16**, 190 mg, 0.57 mmol, 1 equiv.) in DMPU (1.5 mL) was added dropwise and stirring was continued at room temperature for 17 h. The reaction mixture was hydrolyzed by addition of ice cold water and extracted with diethyl ether. The combined organic phases were washed with

water, dried over $Na_2SO_4$ and concentrated *in vacuo*. Purification by column chromatography (EtOAc/petroleum ether = 1:50) afforded **17** as a colorless oil (75 mg, 0.27 mmol, 47 %).

$^1$H-NMR (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): $\delta$ = 3.55-3.46 (m, 2H, H-1), 2.19-2.16 (m, 2H, H-5), 1.94-1.93 (m, 1H, H-7), 1.66-1.49 (m, 4H, H-3 und H-4), 1.23-1.16 (m, 1H, H-2), 1.06 (s, 18H, TIPS-H), 0.90 (d, 3H, *J* = 6.5 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $CHCl_3$ = 77.16 ppm): $\delta$ = 84.9 (q, C-6), 68.6 (s, C-1), 68.3 (t, C-7), 35.8 (t, C-2), 32.6 (s, C-3), 26.3 (s, C-4), 18.9 (s, C-5), 18.2 (p, TIPS-C), 16.9 (p, $CH_3$), 12.2 (t, TIPS-C). HRMS (ESI): calc. for $C_{17}H_{35}O_1Si_1^+$: 283.2457 $[M+H]^+$ found: 283.2543. $[\alpha]_D$ = -43.4° (*c* 1.1, $CH_2Cl_2$).

**Benzyl (*S*)-7-methyl-8-(tri*iso*propylsilyloxy)oct-2-ynoate (18):** Alkyne **17** (35 mg, 0.12 mmol, 1.0 equiv.) was dissolved in dry THF (0.5 mL) under an argon atmosphere and cooled to -78 °C. *n*-BuLi (2.5 M in hexane, 53 µL, 0.13 mmol, 1.1 equiv.) was added dropwise and stirring was continued for 40 min. Benzylchloroformiate (21 µL, 24.6 mg, 0.14 mmol, 1.2 equiv.) was subsequently added dropwise and the reaction mixture was stirred for additional 90 min at -78 °C. The reaction mixture was hydrolyzed by addition of sat. $NH_4Cl$ solution and extracted with ethyl acetate. The combined organic phases are washed with brine, dried over $Na_2SO_4$ and concentrated *in vacuo*. Purification by column chromatography (EtOAc/petroleum ether = 1:50) afforded **18** as a colorless oil (21 mg, 0.05 mmol, 40 %).

$^1$H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm): $\delta$ = 7.40-7.33 (m, 5H, Ar-H), 5.18 (s, 2H, Bn-H), 3.53-3.46 (m, 2H, H-4), 2.34-2.30 (m, 2H, H-8), 1.66-1.50 (m, 5H, H-5 und H-6 und H-7), 1.05 (s, 18H, TIPS-H), 0.89 (d, 3H, J = 8.0 Hz, C*H*$_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $CHCl_3$ = 77.16 ppm): $\delta$ = 153.8 (q, C-1), 135.2 (q, Ar-C), 128.7 (Ar-C), 128.67 (Ar-C), 128.64 (Ar-C), 90.3 (q, C-3), 73.1 (q, C-2), 68.5 (s, Bn-*C*H$_2$), 67.5 (s, C-8), 35.7 (t, C-7), 32.7 (s, C-6), 25.4 (s, C-5), 19.2 (s, C-4), 18.2 (p, TIPS-C), 12.1 (t, TIPS-C). HRMS (ESI): calc. for $C_{25}H_{41}O_3Si_1^+$: 417.2825 $[M+H]^+$ found: 417.2839. $[\alpha]_D$ = -34.0° (*c* 0.9, $CH_2Cl_2$).

**Benzyl (*S*,2*E*,4*E*)-7-methyl-8-(tri*iso*propylsilyloxy)octa-2,4-dienoate (19):** *Batch reaction*: Catalyst **2** (30 mg, 0.024 mmol) was added to a solution of **18** (10 mg, 0.024 mmol, 1 equiv.) in toluene (24 µL). The reaction mixture was shaken at 80 °C for 20 h. The polymer beads were filtered and washed by ethyl acetate. The filtrate was concentrated *in vacuo* and after purification by column chromatography (EtOAc/petroleum ether = 1:50) **19** as a colorless oil (86.4 mg, 0.40 mmol, 80 %).

*Flow reaction*: A glass reactor (length: 12 cm, I.D.: 5.0 mm) was filled with catalyst **2** (1.6 g, 1.28 mmol) and flushed with toluene. The reactor was placed in a preheated oil bath (80 °C) and a flow rate of 0.005 mL/min was employed. After a steady state was reached **18** (39 mg, 0.094 mmol) in toluene (0.1 mL) was pumped through the reactor. The crude product was collected, concentrated *in vacuo* and purified by column chromatography (EtOAc/petroleum ether = 1:50) to afford **19** as a colorless oil (23 mg, 0.055 mmol, 59 %).

$^1$H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm): $\delta$ = 7.38-7.30 (m, 6H, Ar-H und H-3), 6.22-6.10 (m, 2H, H-5 und H-4), 5.83 (d, 1H, J = 15.7 Hz, H-2), 5.19 (s, 2H, Bn-H), 3.56-3.47 (m, 2H, H-8a und H-8b), 2.40-2.34 (m, 1H, H-6a), 2.05-1.97 (m, 1H, H-6b), 1.80-1.72 (m, 1H, H-7), 1.05 (s, 18H, TIPS-H), 0.89 (d, 3H, J = 6.5 Hz, C*H*$_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $CHCl_3$ = 77.16 ppm): $\delta$ = 167.3 (q, C-1), 145.7 (t, C-3), 143.8 (t, C-5), 136.4 (q, Ar-C), 129.8 (t, C-4), 128.7 (t, Ar-C), 128.3 (t, Ar-C), 128.2 (t, Ar-C), 118.9 (t, C-2), 68.0 (s, C-8), 66.2 (s, Bn-C), 37.0 (s, C-6), 36.3 (t, C-7), 18.2 (p, TIPS-C), 16.6 (p, *C*H$_3$), 12.3 (t, TIPS-C). HRMS (ESI): calc. for $(C_{25}H_{41}O_3Si)^+$: 417.2825 $[M+H]^+$ found: 417.2839; $[\alpha]_D^{20}$= -21.6° (*c* 0.6, $CH_2Cl_2$).

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## Graphical abstract