Ruthenium-catalysed cross metathesis binding of functionalized olefins to polystyrene resin *via* a novel allylsilyl linker suitable for electrophilic cleavage

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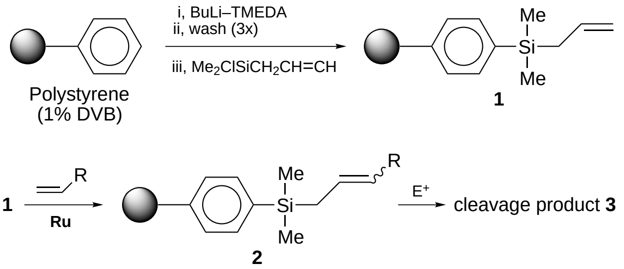
1% Divinylbenzene-crosslinked allyldimethylsilyl polystyrene 1 undergoes highly efficient ruthenium-catalysed cross-metathesis with functionalized terminal olefins and allows electrophilic cleavage of the resulting functionalized allylsilane.

During the last decade, olefin metathesis has emerged as a powerful synthetic tool for the formation of C=C double bonds.[1] Most recently, it has been demonstrated that highly selective cross-coupling[2] between functionalized terminal olefins can be performed under catalysis of well defined metathesis catalysts.[3] In the advent of combinatorial chemistry there is an increasing demand for innovative chemistry on solid supports including novel linker concepts. Cross metathesis involving polymer-supported olefins should enable the binding of target molecules *via* the highly stable C=C double bond in a catalytic manner. In an initial report[4] we described the catalytic immobilisation of several small nonpolar molecules to a modified trityl polystyrene resin using Grubbs' ruthenium initiator[3] $Cl_2(PCy_3)_2$-Ru=CHPh **Ru** (Cy = cyclohexyl). Cross metathesis products were characterized after cleavage from the acid-labile trityl linker.

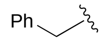
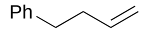
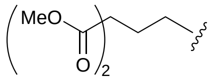
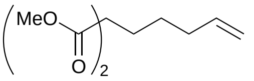
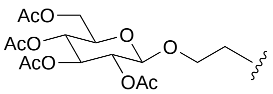
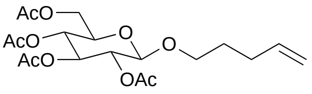
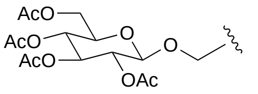
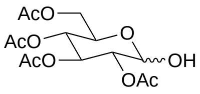
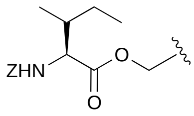
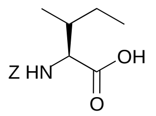
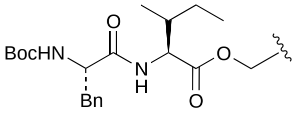
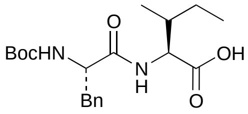
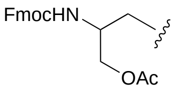
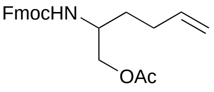
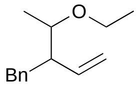
Here we present allyldimethylsilyl polystyrene **1**, which upon ruthenium-catalysed cross metathesis with terminal olefins yields immobilized products **2** (Scheme 1). Products **2** can be subject to electrophilic attack[5] resulting in C–Si cleavage and, thus, the formation of soluble products **3**. Cleavage can be performed either as protodesilylation or in combination with an additional synthetic step, when electrophiles other than H^+ are employed.

Polystyrene **1** closely resembles soluble allyltrimethylsilane, which was found to be an excellent cross metathesis partner by us and others.[2] The synthesis of **1** by treatment of polystyrene (1% DVB-crosslinked) (DVB = divinylbenzene) with BuLi–TMEDA and subsequently with allyldimethylsilyl chloride is based on the observation[6] that under these conditions metallation occurs in the *para*-position of the phenyl ring, exclusively.‡ The silicon content of **1** was determined by Inductive Coupled Plasma-Optical Emission Spectroscopy (ICP-OES) of sodium tertaborate melt samples. We found that removal of excess BuLi–TMEDA by repeated washing of the lithiated polymer ensures high loading capacities and significantly decreases the amount of the electrophile required. The resin employed throughout this study had a silicon content of 1.3 mmol g^{-1}. Cross metathesis was performed in refluxing dichloromethane using 0.05 mmol of **Ru** and 1.0–2.0 mmol of terminal olefin per gram of resin.§ Loadings of cross metathesis

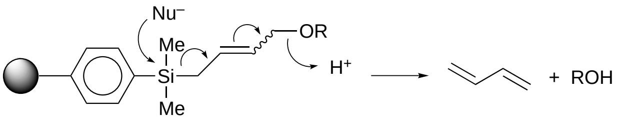


Scheme 1 Synthesis of, **Ru**-catalysed cross-metathesis with, and electrophilic cleavage from polystyrene-supported allylsilane **1**

Table 1 Results of the electrophilic cleavage of metathetically obtained polystyrene-supported allylsilanes **2**

Metathesis product **2**	Cleavage product **3**[a]
R =  **2a**[b]	 **3a**[d] (0.5 mmol g^{-1})
 **2b**[b]	 **3b**[d] (0.43 mmol g^{-1})
 **2c**[c]	 **3c**[d] (0.34 mmol g^{-1})
 **2d**[c]	 **3d**[d] (0.41 mmol g^{-1})
 **2e**[c]	 **3e**[d] (0.59 mmol g^{-1})
 **2f**[c]	 **3f**[e] (0.38 mmol g^{-1})
 **2g**[c]	 **3g**[d] (<0.1 mmol g^{-1})
2a[b]	 **3h**[f] (0.50 mmol g^{-1})

[a] Isolated yield of cleavage product **3** per gram of **2** given in parentheses. [b] Methathesis conditions: 300 mg **1**; 0.6 mmol terminal olefin; 0.015 mmol **Ru**; 5 ml CH_2Cl_2 (reflux); 18 h. [c] Metathesis conditions: 300 mg **1**; 0.3 mmol terminal olefin; 0.015 mmol **Ru**; 5 ml CH_2Cl_2 (reflux); 18 h. [d] Cleavage conditions: 3% TFA in CH_2Cl_2, 18 h. [e] Cleavage conditions: 1.5% TFA in CH_2Cl_2, 24 h. [f] To 500 mg of **2a** in 20 ml CH_2Cl_2 was added 1.3 mmol 1,1-diethoxypropane and 1.3 mmol $TiCl_4$ at −78 °C. After 22 h aqueous work-up ($NaHCO_3$) and flash chromatography of the CH_2Cl_2 phase gave the product.



Scheme 2 Proposed mechanism for the protodesilylation of allysilanes **2** with oxygen in the allyl position

immobilisation products **2** were calculated from the amount of soluble cleavage products **3**, liberated from **2** by protodesilylation with TFA (3% in CH_2Cl_2).

As shown in Table 1, protodesilylation of **2a** furnished the homologized product **3a**;¶ 0.5 mmol was released per gram of **2a**. This modification level indicates a highly effective metathesis reaction. A diester function does not affect the immobilisation reaction as demonstrated by the synthesis of **2b** with 0.43 mmol g^{-1}. Protodesilylation yields the expected product **3b**. A major goal of this study was to demonstrate that polyfunctional molecules of biological interest such as glycosides and amino acid derivatives can also be effectively coupled to **1**. Indeed **2c** was formed with a capacity of 0.34 mmol g^{-1}. Protodesilylation to **3c** proceeded with complete retention of the acetal, thus underlining the exceptionally mild cleavage conditions. However, cleavage of **2d** under identical conditions furnished tetra-*O*-acetyl glucose **3d** instead of the expected homoallyl glycoside. Possibly, deglycosylation of **2b** proceeds through a modified protodesilylation mechanism as shown in Scheme 2.

The same cleavage pattern should be obsered when allyl esters are used in the metathesis reaction. Indeed, cleavage of **2e** and **2f** furnished the respective free carboxylic acids **3e** and **3f**. This special type of allyl ester is even more acid sensitive than the Boc group, which remains intact when the cleavage reaction is performed using 1.5% TFA for 24 h. The scope of this unexpected cleavage reaction remains to be investigated. In contrast to isoleucin allyl ester derivatives the metathetical immobilisation of the protected *C*-allylglycinol was less successful, as demonstrated by the amount of **3g** that could be released from **2g**. Eventually, we wished to demonstrate the utility of solid phase-bound allylsilanes **2** as starting materials for C–C bond formation. To give a first example of the addition of a carbon electrophile to a polymer-supported allylsilane, a mixture of **2a** and 1,1-diethoxyethane was treated with $TiCl_4$. The yield of product **3h** proved comparable to the yield of the corresponding protodesilylation product **3a**.

In conclusion, we have presented a novel polystyrene resin containing an allylsilyl linker moiety. The linker enables both binding of functionalized olefins by catalytic cross metathesis and cleavage under exceptionally mild acidic conditions. The linker allows the cleavage to be performed under formation of an additional C–C bond. A cyclisation–cleavage strategy employing intramolecular electrophilic attack is currently being developed.

Footnotes

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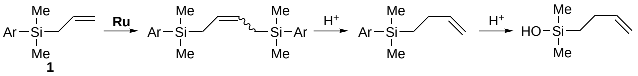
‡ Synthesis of **1**: 8 g of polystyrene (1% DVB) was suspended in 12 ml of cyclohexane, 12 ml (80 mmol) TMEDA and 48 ml (1.6 m in hexane, 77 mmol) BuLi were added and the suspension was gently shaken for 3 d at ambient temperature under exclusion of moisture and air. The supernatant was removed through a septum and replaced by 30 ml cyclohexane. This procedure was repeated twice, before 12 ml (80 mmol) allyldimethylsilyl chloride was added under shaking. After 1 h the reaction was quenched with 40 ml methanol, the resin was quickly filtered off, washed repeatedly with methanol, dichloromethane and $MeOBu^t$ and dried under vacuum.

§ Synthesis of **2b**: to 300 mg of **1** in 5 ml absolute dichloromethane was added 120 mg (0.6 mmol) of **2a** and 12 mg (0.015 mmol) of **Ru**. The resulting suspension was refluxed under argon atmosphere (glove box) for 18 h. The resin was filtered off and washed with 20 volumes each of DMF, chloromethane, methanol and diethyl ether. Residual diethyl ether was removed under high vacuum.

¶ After acidic cleavage homoallyldimethylsilanol was isolated as a minor byproduct. Its formation can be rationalized by the following reaction sequence:



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