

## Investigations on the Giese Reaction Carried Out with Polymer-supported Organotin Reagents

Catharina Bokelmann, Wilhelm P. Neumann\* and Markus Peterseim

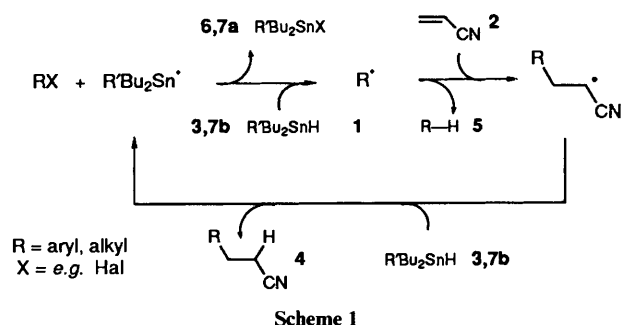
Department of Chemistry, University of Dortmund, Otto-Hahn-Str. 6, D-4600 Dortmund 50, Germany

Cyclohexyl halides undergo radical coupling with acrylonitrile in the presence of a new polymer-supported organotin reagent to give products which are free of tin by-products. This method has the additional advantage of easy processing and multiple regeneration of reagents.

The Giese reaction (see Scheme 1) is a kinetically sophisticated free-radical chain coupling of alkyl and aryl radicals **1** with electron-deficient olefins **2** mainly by means of tributyltin hydride **3** ( $R' = \text{Bu}$ ; TBTH)<sup>1,2</sup> leading to a broad variety of products, e.g. with acrylonitrile **2-4**. It is of great interest both with respect to theoretical aspects and synthetic applications.

To reduce the unwanted scavenging of **1** by the very strong H-donor TBTH **3** to give  $R-H$  **5**, the stationary concentration of **3** must be kept very low, either by syringe techniques or by *in situ* generation of the hydride.<sup>1,3</sup> The use of 'monomeric' tin reagents like TBTH, however, has a general and considerable drawback: namely, the difficult separation of the toxic tin by-products  $R_3\text{SnX}$  **6** from the product **4**.

Thus, it appeared challenging to us to test whether our polystyrene-supported tin reagents **7a, b**<sup>5,6</sup> could be applied to the Giese reaction thus resolving the cited problem (see Scheme 1,  $R' \text{Bu}_2\text{SnX} = \mathbf{7a, b}$ ,  $R' = \text{polystyryl}$ ).



Since it is essential to guarantee a very small stationary tin hydride concentration, the question arose as to whether the distance between two SnH groups inside the polymer beads

would be sufficient to allow the desired intermediate radical reactions. Since rate constants for the diffusions at or into the cross-linked, macroporous polymer (mean bead diameter: 0.5 mm; mean pore size: 800 Å) are not known, we developed three such polymers for different typical cases: (a) a polymer with a high functionality of tin hydride **7b**, for the case where diffusion is slower than the wanted radical steps; (b) a polymer with a low functionality of tin hydride **7b**, for the case where diffusion is faster, so there must be a long distance between two hydride sites; (c) a polymer with a high functionality of tin chloride **7a**, used in catalytic amounts together with a reducing agent for the case where the *in situ* generation of the hydride is slower than its subsequent reaction.

Although for method (c), sodium borohydride is regarded as the best suited reagent,<sup>3</sup> with the usual solvents such as dimethoxyethane, bis(2-methoxyethyl) ether or tetrahydrofuran we had only poor generation and rapid decomposition of SnH when starting from **7a** ( $X = \text{Cl}$ ), and additional problems with the polymer.<sup>5,7</sup> However, in alcohols such as ethanol the difficulties were resolved, and high transforming rates 90–95% **7a** to **7b** achieved (see Scheme 2).

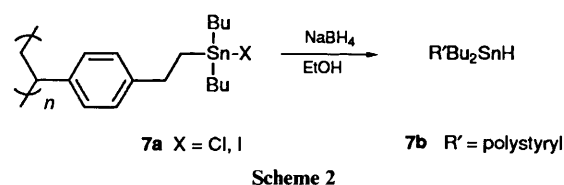


Table 1 lists the results we obtained with the model reaction of cyclohexyl halides with acrylonitrile (see Scheme 1,  $R' = \text{polystyryl}$ ) together with some experimental detail. The yields correspond to those at present achieved, although further

**Table 1** Conditions for and results of Giese reactions carried out with the polymer-supported tin hydride following Scheme 1

Entry	1	2	3	4	5
Halide	<i>c</i> -C <sub>6</sub> H <sub>11</sub> Br	<i>c</i> -C <sub>6</sub> H <sub>11</sub> Br	<i>c</i> -C <sub>6</sub> H <sub>11</sub> I	<i>c</i> -C <sub>6</sub> H <sub>11</sub> I	<i>c</i> -C <sub>6</sub> H <sub>11</sub> I
Reactive group <b>7a, b</b>	<b>7b</b>	<b>7b</b>	<b>7b</b>	<b>7a</b> /NaBH <sub>4</sub>	<b>7a</b> /NaBH <sub>4</sub>
Content of reactive tin species [mmol/g polymer]	1.3	0.4	0.5 <sup>a</sup>	1.6	1.6
Molar ratio of starting materials and reagents	(b) 1:20:2	(b) 1:10:1.5	(b) 1:20:1.5	(c) 1:10:0.4:3	(c) 1:10:0.4:3
Initiation	80 °C; AIBN	80 °C; AIBN	80 °C; AIBN	20 °C; <i>hν</i>	78 °C; AIBN
Solvent (cm <sup>3</sup> )	Toluene (50)	Toluene (50)	Toluene (50)	Ethanol (20)	Ethanol (20)
Time of reaction (h)	4	1	3	23	18
Unchanged halide RX <sup>d</sup>	38	35	22	78	2
Reduction product <b>5</b> <sup>d</sup>	38	10	23	12	25
Addition product <b>4</b> <sup>d</sup>	24	55	55	10	73
Yield of <b>4</b> obtained with Bu <sub>3</sub> SnH <sup>2</sup>	80	80	95	95	95

<sup>a</sup> This polymer was recycled twice before the present use without loss of tin or active SnH. <sup>b</sup> Halide (2 mmol), acrylonitrile and tin hydride **7b**. <sup>c</sup> Halide (1 mmol), acrylonitrile, tin chloride **7a** and sodium borohydride. <sup>d</sup> Yield in %; determined by quantitative gas chromatography.

optimization by improvement of the processing seems possible.

Entry 1 shows the best result with the highly functionalized polymer, method (a). A large excess of acrylonitrile **2** is needed to scavenge the cyclohexyl radicals **1** although nearly 40% of the bromide ended up as unwanted cyclohexane **5**. Coupling with formation of **4** is disfavoured. Entry 2, method (b), seems more promising. The amount of reduction to **5** is small, and the quantity of unchanged halide gives room for further optimization. The more reactive iodide required a 20-fold excess of the olefin **2** even when the low functional polymer, method (b), is used (entry 3). Thus, in the case of the tin hydride reagent **7b** (X = H) the use of bromides is essential. Using method (c), at room temp., and with irradiation, the result was unsatisfactory (entry 4). The best yield of the addition product is achieved with the *in situ* method (c) (see Scheme 2), used in connection with thermal initiation at 78 °C (entry 5). In summary, entries 2 and 5 are the most encouraging at the present time and offer further improvement in yields.

Finally, two additional advantages of the polymers **7** are already obvious. (a) Since the products can be isolated from the tin compounds **6** (R' = polystyryl) by simple filtration of the reaction mixtures, no precipitation of tin fluorides *etc.* is necessary and no waste has to be deposited. (b) The used polymers can be regenerated,<sup>4,5</sup> multiple use of **7** yielding the same result as given in Table 1.

### Experimental

The following detail is in addition to that given in Table 1. All reactions were performed under argon using Duran glassware

and with slow magnetic stirring (max. 60 rpm). Irradiation means the use of two sun lamps (Philips HP1-N 125W). The reaction mixtures were checked by quantitative GLC with alkanes as internal standards.

*Method (a) and (b).* All components (see Table 1) and AIBN (5–10 mg) were mixed and heated to 80 °C. The reaction was monitored by GLC.

*Method (c).* Analogously to (a) and (b), but with irradiation at 20 °C or reflux together with AIBN.

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### References

- 1 B. Giese, *Angew. Chem. Internat. Ed. Engl.*, 1985, **24**, 553.
- 2 B. Giese, *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*, Pergamon Press, Oxford, 1986.
- 3 E. J. Corey and J. W. Suggs, *J. Org. Chem.*, 1975, **40**, 2554.
- 4 R. Scheffold, *Nachr. Chem. Tech. Lab.*, 1988, **36**, 261.
- 5 U. Gerigk, M. Gerlach, W. P. Neumann, R. Vieler and V. Weintritt, *Synthesis*, 1990, 448.
- 6 M. Gerlach, F. Joerdens, H. Kuhn, W. P. Neumann and M. Peterseim, *J. Org. Chem.*, 1991, **56**, 5971.
- 7 U. Gerigk, Diploma Thesis and Dr. rer. nat. Thesis, Univ. of Dortmund, 1987 and 1990.

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