Pergamon

Tetrahedron Letters 39 (1998) 9649–9650

TETRAHEDRON LETTERS

Preparation of the First Polymeric, Chelating Proton Donors and their Use in Diastereoselective Protonations of Chiral Enolates

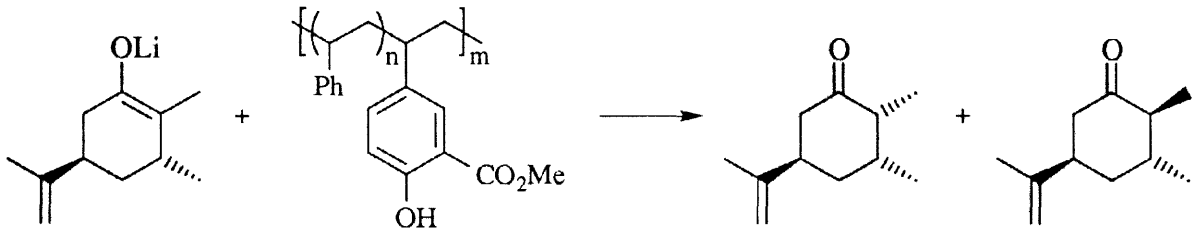
Norbert Krause*‡ and Marc Mackenstedt

Kekulé-Institut für Organische Chemie und Biochemie der Universität Bonn, Gerhard-Domagk-Strasse 1, D-53121 Bonn, Germany

Received 16 September 1998; revised 26 October 1998; accepted 27 October 1998

Abstract: The use of a homopolymer **2a** of methyl 5-vinylsalicylate, as well as of statistical copolymers **2b-f**, in the diastereoselective protonation of the chiral keto-enolate **1** leads to selectivities of up to 93:7 in favor of product **3**.

The use functionalized polymers as reagent is a fascinating aspect of modern preparative chemistry since it opens new perspectives for conducting reactions (e.g., in membrane reactors) and for the recovery and multiple use of the often very valuable reagents[1]. Whereas the application of this principle to stereoselective oxidations, reductions and cycloadditions has been described, there is hardly any precedent for the use of functionalized polymers in stereoselective protonations[2], a reaction that is of high current interest for the controlled construction of stereogenic centers[3]. Recently, we have shown that chiral endocyclic keto-enolates can be protonated with high cis-selectivities under reagent control when *chelating proton donors* such as salicylates are used as proton source[4,5]. This finding makes the usual trial and error search for stereoselective protonating agents unnecessary and allows the deliberate use of a certain class of proton sources, e.g. in natural product synthesis[5]. We now report the use of functionalized polymers **2** containing salicylate units in these stereoselective protonations; this facilitates the separation of the product from the proton source, and the multiple use of recycled polymeric protonating agents is also possible. To the best of our knowledge, there are no previous reports on the use of *polymeric chelating proton donors* in the literature.



1 **2** **3** **4**

‡ New address: Organische Chemie II, Universität Dortmund, D-44221 Dortmund, Germany; Fax: +49-231-7553884, e-mail: nkrause@pop.uni-dortmund.de

0040-4039/98/$ - see front matter
PII: S0040-4039(98)02326-0

The homopolymer **2a** (m ≈ 20, n = 0) was prepared by radicalic polymerization of methyl 5-vinylsalicylate in the presence of AIBN[6,7], and the statistical copolymers **2b-f** (n = 1-9) with a smaller "concentration" of salicylate units were obtained accordingly by polymerization with various amounts of styrene (yields: 77-94%). As substrate for the diastereoselective protonation, we chose the chiral enolate **1** which is readily accessible by anti-selective 1,4-addition of lithium dimethylcuprate to (R)-carvone in diethyl ether[5]. The protonation with monomeric chelating proton donors is carried out in diethyl ether at -80°C[5]; protonation of **1** with methyl salicylate under these conditions gives a diastereoselectivity of **3** : **4** = 98 : 2. The polymers **2**, however, are virtually unsoluble in diethyl ether, and the protonation of **1** with a slurry of polymers **2** in diethyl ether gave unsatisfactory product ratios. Therefore, dichloromethane or ethyl acetate were used as solvent for polymers **2** in the diastereoselective protonation of **1** (Table 1).

Table 1. Diastereoselective protonation of the chiral enolate **1** with polymeric chelating proton donors **2**[a].

Entry	Proton Source	n[b]	Eq.[c]	Solvent	Ratio **7** : **8**
1	**2a**	0	9	CH_2Cl_2	83 : 17
2	**2b**	1	15	CH_2Cl_2	88 : 12
3	**2d**	5	5	CH_2Cl_2	86 : 14
4	**2c**	3	5	EtOAc	83 : 17
5	**2d**	5	5	EtOAc	87 : 13
6	**2e**	7	5	EtOAc	87 : 13
7	**2f**	9	5	EtOAc	**93 : 7**

[a] The enolate **1** was prepared by addition of $Me_2CuLi \cdot LiI$ to (R)-carvone in diethyl ether, and this mixture was added at -80°C to a slurry or solution of the polymer in the appropriate solvent. The product ratio was determined by GC[4,5]. - [b] Ratio of styrene to salicylate units in the copolymers **2**. - [c] Equivalents of salicylate units in the polymer with regard to enolate **1**.

It turns out that a product ratio of **3** : **4** = 83 : 17 can be reached with homopolymer **2a** (entry 1), and the selectivity could be increased somewhat by using the copolymers **2**, but not beyond the value of 88 : 12 found with a large excess of **2b** (entry 2). This result seems to indicate that steric hindrance between neighboring salicylate moieties disfavors the formation of a chelate complex with the enolate which may be necessary for obtaining high stereoselectivities[4,5]. This trend was confirmed when ethyl acetate was used as solvent for the polymeric protonating agents (entries 4-7): the product ratio rose steadily from **3** : **4** = 83 :17 with **2c** up to 93 : 7 with **2f**, i.e. close to values obtained with monomeric chelating proton donors! The product can be separated from the proton source by extraction with an unpolar solvent like pentane or cyclohexane, and repeated use of the recovered polymers **2** in the protonation of enolate **1** gave consistingly high diastereoselectivities. Currently, we are extending this principle to other types of functionalized polymers which shall also be used as stereoselective protonating agents.

Acknowledgement. Financial support of this work by the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

References

[1] Review: Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217-1239.
[2] Cavelier, F.; Gomez, S.; Jacquier, R.; Verducci, J. *Tetrahedron Lett.* **1994**, *35*, 2891-2894
[3] Review: Fehr, C. *Angew. Chem.* **1996**, *108*, 2726-2748; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2566-2587.
[4] Krause, N. *Angew. Chem.* **1994**, *106*, 1845-1847; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1764-1765.
[5] Krause, N.; Ebert, S.; Haubrich, A. *Liebigs Ann./Recueil* **1997**, 2409-2418.
[6] Bailey, D.; Tirrell, D.; Vogl, O. *J. Polymer Sci.* **1976**, *14*, 2725-2747.
[7] Hartmann, M.; Riegel, B.; Wondraczek, H.; Geschwend, G. *Z. Chem.* **1978**, *18*, 95-96.