



Tetrahedron Letters 44 (2003) 7723-7725

TETRAHEDRON LETTERS

## Bismuth compounds in organic synthesis. Synthesis of resorcinarenes using bismuth triflate

Katherine E. Peterson, Russell C. Smith and Ram S. Mohan\*

Laboratory for Environment Friendly Organic Synthesis, Department of Chemistry, Illinois Wesleyan University, Bloomington, IL 61701, USA

Received 6 August 2003; revised 21 August 2003; accepted 22 August 2003

Abstract—Bismuth triflate (5 mol%) smoothly catalyzes the condensation of aromatic and aliphatic aldehydes with resorcinol to give tetrameric cyclic products, resorcinarenes. With benzaldehyde, the product is obtained as a mixture of two diastereomers and the ratio of the diastereomers depends on reaction time. On the other hand, a single diastereomer is obtained with aliphatic aldehydes. The low toxicity and ease of handling of bismuth compounds coupled with fast reaction times make this method an attractive alternative to the existing methods for resorcinarene formation.

© 2003 Elsevier Ltd. All rights reserved.

As early as 1872, von Baeyer discovered that the condensation of benzaldehyde and resorcinol in the presence of concentrated sulfuric acid gave a red-colored product (Scheme 1).<sup>1</sup> It was not until 1968 that Erdtman established the structure of such condensation products by X-ray analysis.<sup>2</sup>

Recently, the name resorcinarenes has been suggested for such compounds.<sup>3</sup> Resorcinarenes are of considerable interest because (1) they serve as starting materials for a variety of cavitands or compounds that contain a cavity that can accommodate other ions or molecules<sup>4</sup> and (2) with appropriate choice of the R groups on the resorcinarene, they exhibit liquid crystalline behavior.<sup>5</sup> They have also found application as HPLC stationary phases.<sup>6</sup> They can be prepared by acid-catalyzed condensation of an aldehyde with resorcinol.<sup>7</sup> More recently, a Lewis acid, Yb(OTf)<sub>3</sub>, catalyzed condensation reaction between aldehydes and resorcinol has been reported.<sup>8</sup> A solvent-free synthesis of resorcinarenes using *p*-TsOH as the catalyst has also been reported.<sup>9</sup> A drawback of these procedures is that they suffer from either the use of large quantities of concentrated HCl, use toxic catalysts such as *p*-TsOH or require long reaction times, such as with Yb(OTf)<sub>3</sub> (48 h).

Our continued interest in bismuth compounds prompted us to investigate the utility of bismuth triflate



## Scheme 1.

*Keywords*: bismuth and compounds; resorcinarenes; Lewis acids; environment-friendly catalysts. \* Corresponding author. Tel.: 1-(309) 556 3829; fax: 1-(309) 556 3864; e-mail: rmohan@iwu.edu

<sup>0040-4039/\$ -</sup> see front matter © 2003 Elsevier Ltd. All rights reserved. doi:10.1016/j.tetlet.2003.08.093

as a catalyst for the formation of resorcinarenes. Bismuth compounds have recently attracted attention due to their low cost, ease of handling and remarkably low toxicity.<sup>10,11</sup> We now report that bismuth triflate,  $Bi(CF_3SO_3)_3$ · $4H_2O$  (5.0 mol%) is an efficient catalyst for the synthesis of resorcinarenes. Bismuth triflate has previously been used as a catalyst for Friedel–Crafts acylations,<sup>12</sup> sulfonylation of arenes,<sup>13</sup> Diels-Alder reactions,<sup>14</sup> aza-Diels–Alder reactions,<sup>15</sup> rearrangement of epoxides,<sup>16</sup> formation of acylals,<sup>17</sup> deprotection and formation of acetals.<sup>18,19</sup> Bismuth triflate is not commercially available but can be easily synthesized in the lab.<sup>20</sup>

Herein we report that the bismuth triflate (5 mol%) catalyzed condensation of aldehydes and resorcinol proceeds smoothly in ethanol to give the corresponding resorcinarenes in good yields (Scheme 2). The condensation of benzaldehyde with resorcinol required only 75 min for completion (as judged by disappearance of starting materials by TLC) while aliphatic aldehydes reacted in few hours to a day. With benzaldehyde, the product was obtained as a mixture of diastereomers 2a (all-cis) and **2b** (cis-trans-trans) (2a:2b=0.78:1.0) while aliphatic aldehydes gave only the thermodynamically favored all-cis diastereomer 2a. The tetrameric nature of the products was confirmed by FAB mass spectrometry analysis and the ratio of the diastereomers was determined by <sup>1</sup>H NMR analysis of the products in  $d^{6}$ -DMSO.<sup>21</sup> The absolute configuration of the two isomers has been previously determined by X-ray analysis of the corresponding octabutyrates and the NMR spectra observed by us is consistent with that reported in the literature.<sup>22</sup>

Previous studies have shown that the ratio of the diastereomers depends on reaction time suggesting that isomerization via ring opening of the tetrameric product occurs.<sup>8</sup> In light of this observation, the reac-

tion between benzaldehyde and resorcinol catalyzed by bismuth triflate was allowed to proceed for 8 days. The product of this reaction was the all *cis* diastereomer **2a**. None of the other isomer **2b** could be detected by NMR spectroscopy. The diastereomeric mixture of **2a**/ **2b**, isolated from the 75 min reaction was also subjected to the reaction conditions (5 mol% bismuth triflate, ethanol, 80°C) for 10 days. The resulting product mixture consisted primarily of the *cis*-isomer **2a** (**2a**:**2b** = 1.0:0.11). A systematic study of the bismuth triflate catalyzed reaction of a variety of aldehydes with various substituted resorcinols is now underway.

A representative procedure is given here: A solution of resorcinol (2.095 g, 19.03 mmol) and benzaldehyde (2.019 g, 19.03 mmol) in 35 mL of absolute ethanol was stirred as bismuth triflate (0.624 g, 5 mol%) was added. The reaction was then heated in an oil bath at 80°C for 75 min under N<sub>2</sub>, cooled and poured onto 80 mL of ice-cold water. The resulting precipitate was collected by suction filtration, washed with water and dried at 90°C under vacuum to yield 2.50 g (66%) of a tan colored solid that was characterized by NMR spectroscopy and FAB-MS analysis.

In conclusion, bismuth triflate smoothly catalyzes the condensation of aldehydes with resorcinol. The advantages of this method include fast reaction times and the use of a relatively non-toxic and easy to handle catalyst.

## Acknowledgements

We wish to thank the National Science Foundation for an RUI grant (# 0078881). R.M. is also indebted to The Camille Henry Dreyfus foundation for the Henry Dreyfus Teacher Scholar award.



## References

- 1. Baeyer, A. Ber. Dtsch. Chem. Ges. 1872, 5, 25.
- Erdtman, H.; Hogberg, S.; Abrahamsson, S.; Nilsson, B. Tetrahedron Lett. 1968, 1679.
- For a review on resorcinarenes, see: Timmerman, P.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* 1996, 52, 2663.
- (a) Cram, D. J.; Karbach, S.; Kim, H.-E.; Knobler, C. B.; Maverick, E. F.; Ericson, J. L.; Helgeson, R. C. J. Am. Chem. Soc. 1988, 110, 2229; (b) Tunstad, L. M.; Tucker, J. A.; Dalcanale, E.; Weiser, J.; Bryant, J. A.; Sherman, J. C.; Helgeson, R. C.; Knobler, C. B.; Cram, D. J. J. Org. Chem. 1989, 54, 1305.
- (a) Bonsignore, S.; Cometti, G.; Dalcanale, E.; Du Vosel, A. Liquid Crystals 1990, 8, 639; (b) Cometti, G.; Dalcanale, E.; Du vosel, A.; Levelut, A.-M. J. Chem. Soc., Chem. Commun. 1990, 163; (c) Purse, B. W.; Shivanyuk, A.; Rebek, J. Chem. Commun. 2002, 2612.
- Pietraszkiewicz, O.; Pietraszkiewicz, M. Polish J. Chem. 1998, 72, 2418.
- 7. Högberg, A. G. S. J. Am. Chem. Soc. 1980, 102, 6046.
- Barrett, A. G. M.; Braddock, D. C.; Henschke, J. P.; Walker, E. R. J. Chem. Soc., Perkin Trans. 1 1999, 873.
- Roberts, B. A.; Cave, G. W. V.; Raston, C. L.; Scott, J. L. Green Chem. 2001, 3, 280.
- (a) Irwing-Sax, N.; Bewis, R. J. Dangerous Properties of Industrial Materials; Van Nostram Reinhold: New York, 1989; pp. 283–284; (b) Irwing-Sax, N.; Bewis, R. J. Dangerous Properties of Industrial Materials; Van Nostrand Reinhold: New York, 1989; pp. 522–523; (c) Wormser, U.; Nir, I. In The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds; Patai, S., Ed.; Wiley: New York, 1994; pp. 715–723; (d) Dill, K.; McGowan, E. L. In The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds; Patai, S., Ed.; Wiley: New York, 1994; pp. 695–713; (e) Maeda, S. In The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds; Patai, S., Ed.; Wiley: New York, 1994; pp. 725–759.
- (a) Reglinski, J. In *Chemistry of Arsenic, Antimony and Bismuth, Chapter 8*; Blackie Academic and Professional: London, 1998; pp. 403-440; (b) The LD<sub>50</sub> values of some bismuth compounds are given here to illustrate their low toxicity. Bi<sub>2</sub>O<sub>3</sub> (5g/kg, rat, oral); BiOCl (22 g/kg, rat,

oral);  $Ph_3Bi$  (180 g/kg, dog, oral); NaCl (3.75 g/kg, rat, oral); InCl<sub>3</sub> (10.2 mg/kg).

- (a) Desmurs, J. R.; Labrouillère, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1997**, *38*, 8871; (b) Répichet, S.; Le Roux, C.; Dubac, J.; Desmurs, J. R. *Eur. J. Org. Chem.* **1998**, 2743.
- Répichet, S.; Le Roux, C.; Hernandez, P.; Dubac, J. J. Org. Chem. 1999, 64, 6479.
- (a) Garrigues, B.; Gonzaga, F.; Robert, H.; Dubac, J. J. Org. Chem. 1997, 62, 4880; (b) Robert, H.; Garrigues, B.; Dubac, J. Tetrahedron Lett. 1998, 39, 1161.
- Laurent-Robert, H.; Garrigues, B.; Dubac, J. Synlett 2000, 1160.
- Bhatia, K. A.; Eash, K. J.; Leonard, N. M.; Oswald, M. C.; Mohan, R. S. *Tetrahedron Lett.* **2001**, *42*, 8129.
- Carrigan, M. D.; Eash, K. J.; Oswald, M. C.; Mohan, R. S. *Tetrahedron Lett.* 2001, 42, 8133.
- (a) Carrigan, M. C.; Sarapa, D.; Smith, R. C.; Wieland, L. C.; Mohan, R. S. J. Org. Chem. 2002, 67, 1027–1030;
   (b) Leonard, N. M.; Oswald, M. C.; Freiberg, D. A.; Nattier, B. A.; Smith, R. C.; Mohan, R. S. J. Org. Chem. 2002, 67, 5202–5207.
- For a review on bismuth compounds, see: (a) Marshall, J. A. Chemtracts 1997, 1064–1075; (b) Suzuki, H.; Ikegami, T.; Matano, Y. Synthesis 1997, 249–267; (c) Organobismuth Chemistry; Suzuki, H.; Matano, Y., Ed.; Elsevier: Amsterdam, 2001; (d) Leonard, N. M.; Wieland, L. C.; Mohan, R. S. Tetrahedron 2002, 58, 8373.
- Labrouillère, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J.; Desmurs, J. R. *Tetrahedron Lett.* **1999**, 40, 285–286. Bismuth triflate synthesized by this procedure is reported to be mainly the tetrahydrate. Recently, another procedure for the synthesis of bismuth triflate has been reported. Répichet, S.; Zwick, A.; Vendier, L.; Le Roux, C.; Dubac, J. *Tetrahedron Lett.* **2002**, 43, 993.
- 21. The ratio of the diastereomers **2a** and **2b** was determined by analysis of the <sup>1</sup>H NMR spectrum (270 MHz,  $d_6$ -DMSO) of the crude product mixture. The ratio was obtained by integration of the signals at  $\delta$  5.64 (4H, benzylic hydrogens of **2a**) versus the signals at  $\delta$  5.54 (4H, benzylic hydrogens of **2b**) and  $\delta$  5.57 (2H, *ortho* to OH in **2b**).
- 22. (a) Högberg, A. G. S. J. Am. Chem. Soc. 1980, 102, 6046;
  (b) Weinelt, F.; Schneider, J.-J. J. Org. Chem. 1991, 56, 5527.