Synthesis of a Polymerizable Benzocyclobutene that Undergoes Ring-Opening Isomerization at Reduced Temperature

Coleen Pugh,* James S. Baker, William K. Storms
The University of Akron, Department of Polymer Science, Maurice Morton Institute of Polymer Science and Polymer Engineering, Akron, OH 44325-3909, USA
Fax +1(330)9725290; E-mail: cpugh@uakron.edu
Received: 04.09.2013; Accepted: 12.09.2013

Abstract: 1-Ethoxyvinylbenzocyclobutene is a substituted benzocyclobutene that undergoes radical polymerization to produce polymers that can be crosslinked at 100–150 °C. The 4- and 5-vinyl isomers are synthesized in a 1:4 ratio via a halogenated benzyne intermediate produced from anthranilic acid, followed by cycloaddition with ethyl vinyl ether and replacement of the halogen atom with a vinyl group.

Key words: benzocyclobutene, cycloaddition, ring-opening isomerization, Kumada coupling, benzyne

Bicyclo[4.2.0]octa-1,3,5-triene, or benzocyclobutene (BCB),1,2 has been widely used in polymer science based on the ring-opening ability of the strained cyclobutene ring.3 It is stable at room temperature, but undergoes an electrocyclic rearrangement at elevated temperature (>200 °C) to the highly reactive o-quinodimethane. The o-quinodimethane undergoes Diels–Alder reactions, and in the absence of an external dienophile, generates 1,2,5,6-dibenzocyclooctane (~25%) and higher oligomers (~75%) (Scheme 1).4,5 Since the thermally unstable spirodimer does not generate any 1,2,5,6-dibenzocyclooctane upon heating, it apparently forms by a different mechanism than the oligomers.5 This thermal activation and the lack of condensation byproducts makes benzocyclobutene chemistry especially attractive for crosslinking6 and for polymer-forming reactions7 by a step (condensation-like) mechanism. Benzocyclobutene-containing vinyl monomers have also been polymerized by chain mechanisms.7–10

Although the high temperature of the ring-opening isomerization reaction is useful for applications such as the crosslinking of engineering polymers, which are synthesized at elevated temperatures, it also limits the use of benzocyclobutene in other applications, such as those involving temperature-sensitive materials. For example, it would be difficult to exploit the benzocyclobutene crosslinking reaction to create nanostructured flexible films by field-assisted roll-to-roll processing if the glass transition temperature of the substrate polymer film and/or the available thermal field are significantly less than 200 °C. We are particularly interested in developing nanostructured flexible films using block copolymers that can be aligned and crosslinked at more reasonable temperatures than those used to crosslink benzocyclobutene.

4-Vinylbenzocyclobutene (VBCB) was first synthesized by a Wittig reaction starting from 4-chloromethylbenzocyclobutene,8 and subsequently from 4-bromobenzocyclobutene with conversion into the corresponding

Scheme 1 Electroyclic ring-opening of benzocyclobutene and its subsequent [4+2] cycloaddition with another o-quinodimethane

The ring-opening isomerization temperature of benzocyclobutenes can be lowered by introducing both electron-donating (raises the ground state energy) and electron-withdrawing (lowers the transition state energy) substituents onto the cyclobutene ring.7 For example, 1-methoxybenzocyclobutene isomerizes at ≥110 °C,11 and the cyclobutene rings of poly(1-benzocyclobutyl vinyl ether) isomerize at ≥60 °C.12 (The temperature range over which the exothermic isomerization transitions occur is usually broad.)

Block copolymers with controlled chain lengths are prepared by chain polymerizations, such as living anionic, cationic or radical polymerizations of vinyl monomers.13 Therefore, the preparation of well-defined block copolymers that can be aligned and crosslinked by benzocyclobutene chemistry at reduced temperatures requires the synthesis of a benzocyclobutene functionalized with both a polymerizable vinyl group, and a substituent that lowers the temperature of ring-opening isomerization, such as an ethyl ether moiety.

4-Vinylbenzocyclobutene (VBCB) was first synthesized by a Wittig reaction starting from 4-chloromethylbenzocyclobutene,8 and subsequently from 4-bromobenzocyclobutene with conversion into the corresponding
The cyclobutene ring to decrease its isomerization temperatures lower than 100 °C, and 100–150 °C is accessible for creating nanostructured flexible films, because many living chain polymerizations are performed at temperatures lower than 100 °C, and 100–150 °C is accessible in field-assisted roll-to-roll processing equipment.

Our goal was therefore to introduce an ethoxy group onto the cyclobutene; however, its synthesis was not reported. An ether-substituted vinylbenzocyclobutene with an isomerization temperature at approximately 100 °C would be ideal for creating nanostructured flexible films, because many living chain polymerizations are performed at temperatures lower than 100 °C, and 100–150 °C is accessible in field-assisted roll-to-roll processing equipment.

Our goal was therefore to introduce an ethoxy group onto the cyclobutene ring to decrease its isomerization temperature, and a halogen (Br or I) onto the aromatic ring to provide a site for attaching the polymerizable vinyl group. The most direct method for synthesizing 1-substituted benzocyclobutenes is by [2+2] cycloaddition of benzyne with an alkene, especially electron-rich alkenes such as vinyl ethers and vinyl acetate. Due to the many routes for converting 4-bromobenzocyclobutene into vinylbenzocyclobutene, we considered the three possible routes: (1) bromination of benzocyclobutenone, for example, reaction of 1-ethoxybenzocyclobutene into benzocyclobutenone. Other halogenation agents, such as fluoroiodobenzene and 2-bromofluorobenzene, in Scheme 2, with a 2-silylaryl triflate will lead to the same product. The Grignard route is not useful because the elimination step required a higher temperature than the boiling point of ethyl vinyl ether.

Unfortunately, although benzocyclobutene is readily brominated using bromine in acetic acid, with only a minor amount of dealkylated (ring-opened) side product, the same conditions oxidize 1-ethoxybenzocyclobutene into benzocyclobutenone. For example, reaction of 1-ethoxybenzocyclobutene with 1.2 equivalents of bromine produced approximately equimolar amounts of benzocyclobutenone and unreacted 1-ethoxybenzocyclobutene. Other halogenation agents, such as PhCH2NMe3, ICl2/ZnCl2, PhCH3NMe3, Br3/CoCO3, and NH4I/H2O produced only a minor amount of side product with the remaining material unreacted. Therefore, the aromatic ring must be halogenated prior to functionalizing the cyclobutene ring. Note that although 2-(trimethylsilyl)aryl triflates generate arynes under very mild conditions, replacement of 4-bromo-2-fluoriodobenzene and 2-bromofluorobenzene, in Scheme 2, with a 2-silylaryl triflate will lead to the same problems for vinylation, either in the synthesis of the appropriately functionalized 2-silylaryl triflate, or in its use.

As outlined in Scheme 3, 1-ethoxyvinylbenzocyclobutene can be successfully synthesized by first regioselectively:

**Scheme 2** Potential synthetic routes to 4- and/or 5-bromo-1-ethoxybenzocyclobutenes via benzyne intermediates
iodinating anthranilic acid para to the amine group using ammonium iodide, similar to brominations using ammonium bromide, in combination with hydrogen peroxide. The corresponding benzenediazonium-2-carboxylates is then generated using isoamyl nitrite, and converted into the iodinated benzene at reflux in 1,4-dioxane or 1,2-dichloroethane in the presence of ethyl vinyl ether. Generation of the benzene intermediate is the yield-limiting step, both because of the lower yields of halogenated benzenediazonium-2-carboxylates, and due to the low boiling point of ethyl vinyl ether. 1-Ethoxy-4-vinylbenzocyclobutene and 1-ethoxy-5-vinylbenzocyclobutene are produced in approximately a 1:4 ratio using either a two-step Wittig reaction, or by a direct Kumada coupling with vinyl bromide as the final step. Figure 1 presents the 1H NMR spectrum of 1-ethoxy-5-vinylbenzocyclobutene produced by the Kumada coupling route and isolated from its product mixture with 1-ethoxy-4-vinylbenzocyclobutene. The resonance at 5.04 ppm corresponds to the methine proton, and those at 3.10 and 3.44 ppm correspond to the methylene protons of the benzocyclobutene ring.

In summary, we have established a synthetic route to 1-ethoxyvinylbenzocyclobutene. 1-Ethoxyvinylbenzocyclobutene is a polymerizable benzocyclobutene that undergoes ring-opening isomerization and crosslinking at 100–150 °C, which is ~100 °C lower than that of the unsubstituted vinylbenzocyclobutene-containing polymers. The vinyl group was introduced via a halogen functionality.
which must be introduced to the aromatic ring before forming the functionalized benzocyclobutene ring.

Acknowledgment

We acknowledge the National Science Foundation for support of this research through DMR-1006195 and a Special Creativity Award. We also gratefully acknowledge the Ohio Board of Regents for a partial matching award.

Supporting Information

for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

References and Notes

(17) For a review on arynes, see for example: Tadross, P. M.; Stolz, B. M. Chem. Rev. 2012, 112, 3550.
(28) CAUTION: Benzenediazonium-2-carboxylates can react explosively to shock, scraping, or heating when dry. These compounds must remain wet with solvent. Reactions using benzenediazonium-2-carboxylate reagents are most safely performed in a Parr reactor.

Chem. Abstr.

Synlett 2014, 25, 148–152

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.
7.0 Hz, 1 H, OC\(\text{H})\), 5.04 (dd, \(\beta J = 4.4\) Hz, \(\alpha J = 2.0\) Hz, 1 H, CH\(\text{OEt})\), 5.18 (dd, \(\beta J = 10.9\) Hz, \(\alpha J = 0.8\) Hz, 1 H, H\(\text{CH}_{2,\text{trans}}\)), 5.68 (dd, \(\beta J = 17.6\) Hz, \(\alpha J = 0.9\) Hz, 1 H, H\(\text{CH}_{2,\text{cis}}\)), 6.70 (dd, \(\beta J = 17.6\) Hz, \(\alpha J = 10.9\) Hz, 1 H, CH\(\text{X})\), 7.09 (d, \(\beta J_{\text{ortho}} = 8.4\) Hz, 1 H, aromatic C\(\text{H})\), 7.24 (s, aromatic C\(\text{H})\), 7.35 (d, \(\beta J_{\text{ortho}} = 8.5\) Hz, 1 H, aromatic C\(\text{H})\).

Anal. Calcd for C\(12\)H\(14\)O: C, 82.72; H, 8.10. Found: C, 82.46; H, 8.11.

(32) Alternatively, an inhibitor such as pyrogallol can be added to the crude product, which can then be purified by distillation at 77 °C/1 mmHg.