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Concise synthesis and characterization of unsymmetric 1,3-benzoxazines by tandem reactions

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ABSTRACT

A new synthetic protocol for the preparation of unsymmetric 1,3-bisbenzoxazines using the combination of three-step synthesis and classical one-step benzoxazine synthesis strategies is described. For this purpose, 4-hydroxyphenylaminomethyl phenol (HPAMP) is synthesized as the intermediate and reacted with two different aliphatic amines to yield the desired unsymmetric bisbenzoxazines. The structures of the intermediates and products are confirmed by FT-IR and ^{1}H NMR spectral analysis. Curing behaviors of the bisbenzoxazines are studied by differential scanning calorimetry (DSC).

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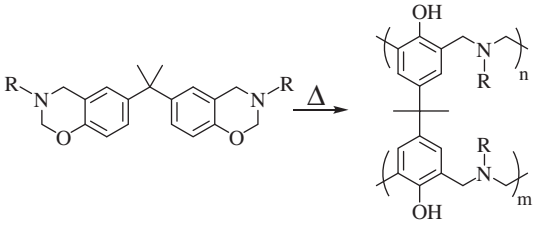
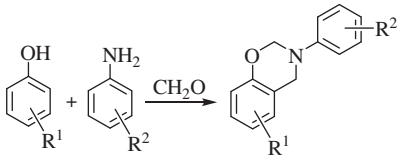
Benzoxazine-based phenolic thermosets, namely polybenzoxazines, have gained significant interest due to their superior properties compared to other resins such as epoxy and phenolic. Moreover, their convenient synthesis under catalyst- or initiator-free conditions is another noteworthy feature of polybenzoxazines.[1–3] Their synthesis is simply a thermally-induced ring-opening polymerization of the corresponding benzoxazine monomer (Scheme 1).

These materials have low water absorption, high char yield, modulus, strength, glass transition temperatures, resistance to flame, long shelf lives, and limited or no volumetric change during polymerization. The monomers are synthesized from a suitable phenol, primary amine (aliphatic or aromatic), and formaldehyde[4–11] (Scheme 2). The synthesis proceeds via a Mannich reaction and subsequent ring-closure process. Formaldehyde functions in both Mannich reaction and as a nitrogen–oxygen bridging reagent. Depending on the melting points of the reagents, the synthesis can be carried out even without solvent.[12] The overall process is relatively easy and generally results in high yields. Hence, various benzoxazine monomers were synthesized via this process.[13–18]

For example allyl,[19,20] acetylene,[21,22] nitrile,[23] propargyl,[24] coumarin,[25] alcohol,[26,27] and maleimide[28] functionalized benzoxazines were synthesized in order to insert additional cross-linking or post-modifiable sites. Typically, the hydroxyl functional



Scheme 1. Thermally-induced ring-opening polymerization of bisbenzoxazine monomers yielding a polybenzoxazine network.



Scheme 2. Synthesis of 1,3-benzoxazine monomers.

benzoxazines facilitate incorporation of polymeric segments through several chain and step-growth polymerization methods. In this way poly(methyl methacrylate),[29] poly(ε-caprolactone),[11] and polyesters[4,27] were combined successfully with benzoxazine structures to yield flexible and process curable resins. Similar polymeric materials were obtained through acetylene functionality via Huisgen-type click reactions and coupling reactions.[30–33]

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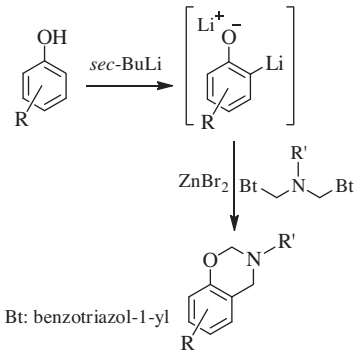
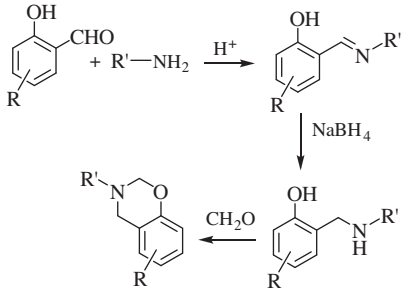


Scheme 3. Synthesis of 1,3-benzoxazines via a dilithiation approach using benzotriazoles.



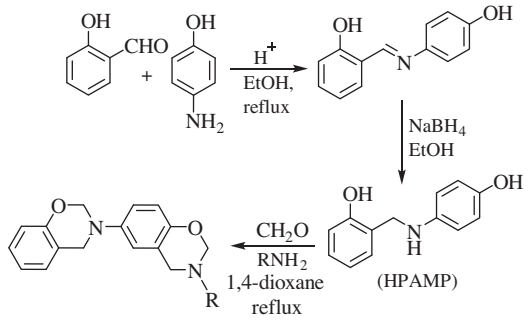
Scheme 4. Synthesis of 1,3-benzoxazines via a three-step approach.

Although the classical benzoxazine synthesis methodology is most commonly applied, step-wise procedures have received considerable interest. For example, *ortho*–metalation methodology used for the construction of heterocyclic compounds has been adapted successfully to benzoxazine synthesis. Accordingly, dilithiation of phenols and subsequent use of benzotriazoles with $ZnBr_2$ as the catalyst gave various benzoxazines (Scheme 3). However, low yields and difficulties in the isolation of the products, particularly when aliphatic amines were used have limited their wider application.[34]

Another stepwise strategy involves the use of 2-hydroxybenzaldehyde or similar structurally related compounds as starting reagents. Imine formation is accomplished between the aldehyde and amino compound, followed by reduction to form 2-aminomethylphenols, and finally ring closure takes place using formaldehyde (Scheme 4). This methodology is especially useful when the starting reagents possess groups that do not tolerate the Mannich reaction. For example, phenolic hydroxy functionalized benzoxazines, which cannot be synthesized by the classical method due to the high reactivity of the free phenolic groups at the *ortho* position toward the Mannich base, essentially yielding gels and side products, are readily obtained.

Due to its tolerance of various functional groups, this step-wise method was utilized for the synthesis of different benzoxazine or benzoxazine-based polymeric precursors.[35–40] The one-pot synthesis of benzoxazines using this strategy has also been reported.[41] We now report analogous investigations on the combination of this three-step approach with the one step classical method. As shown below, unsymmetric bisbenzoxazines can be synthesized via two tandem reactions.

The crucial component for the combined method is the preparation of 4-hydroxyphenylaminomethyl phenol (HPAMP), since the synthesis of the unsymmetric benzoxazine proceeds in preference to the ring-closure between the aminomethyl moiety and its neighboring phenolic OH, and at the same time the 4-hydroxyphenyl moiety undergoes the classical benzoxazine formation reaction. In order to synthesize HPAMP, a two-step reaction was performed. In the first step, 2-hydroxybenzaldehyde was reacted with 4-hydroxyaniline catalyzed by H_2SO_4 to yield a Schiff base. Next, reduction was carried out using sodium borohydride without any further purification to produce the starting material for the subsequent step in a good yield. Finally, the unsymmetric benzoxazines were obtained by the reaction of HPAMP with three equivalents of paraformaldehyde and one equivalent of a primary amine, namely *n*-hexyl or *n*-butylamines in chloroform for 24 h (Scheme 5).



Scheme 5. Synthesis of unsymmetric bisbenzoxazines.

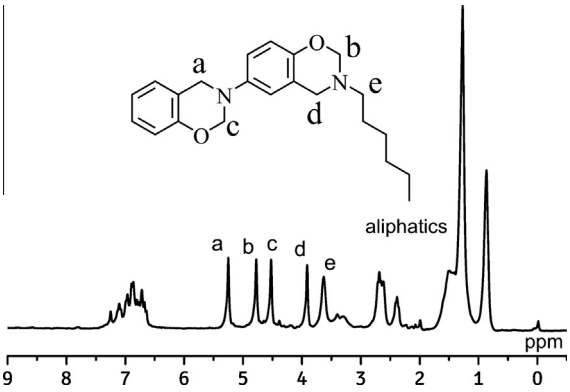


Figure 1. ^{1}H NMR spectrum of *u*-hexyl-benz.

The resulting unsymmetric benzoxazines were isolated simply by washing the chloroform solution with 0.2 M NaOH solution to remove the unreacted phenolics. After neutralization of the chloroform phase by several washings with distilled water, a second extraction with benzonitrile-hexane mixture was performed. Following evaporation of the benzonitrile phase, relatively pure compounds were obtained. The '*u*-hexyl-benz' and '*u*-butyl-benz' abbreviations are used for unsymmetric bisbenzoxazines from *n*-hexylamine and *n*-butylamine, respectively. The characterization of the unsymmetric bisbenzoxazines was achieved by spectral methods. The ^{1}H NMR spectra of the unsymmetric bisbenzoxazines exhibited two different types of 1,3-oxazine rings. In Figure 1, the protons of the u-hexyl-benz oxazine rings emerge at 5.25 (O–CH_2–N–Ph), 4.78 (O–CH_2–N–hexyl), 4.52 (Ph–CH_2–N–Ph), and 3.91 ppm (Ph–CH_2–N–hexyl), respectively. Aromatic and aliphatic protons were also detectable. Similarly, in Figure 2, the protons of the *u*-butyl-benz oxazine rings appeared at 5.32 (O–CH_2–N–Ph), 4.70 (O–CH_2–N–butyl), 4.54 (Ph–CH_2–N–Ph), and 3.86 ppm (Ph–CH_2–N–butyl), respectively.

The structures of the unsymmetric bisbenzoxazines were also confirmed by IR analysis (Fig. 3). The IR spectra of both *u*-hexyl-benz and *u*-butyl-benz revealed asymmetric stretching

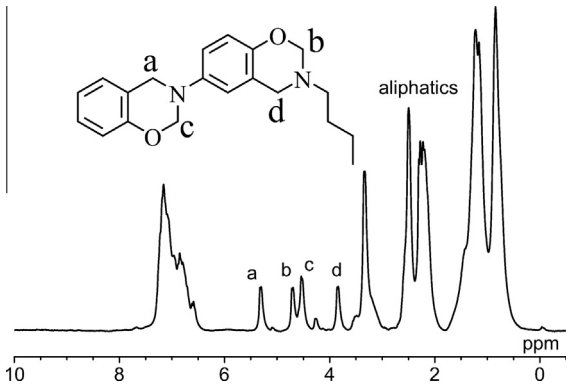


Figure 2. ^{1}H NMR spectrum of *u*-butyl-benz.

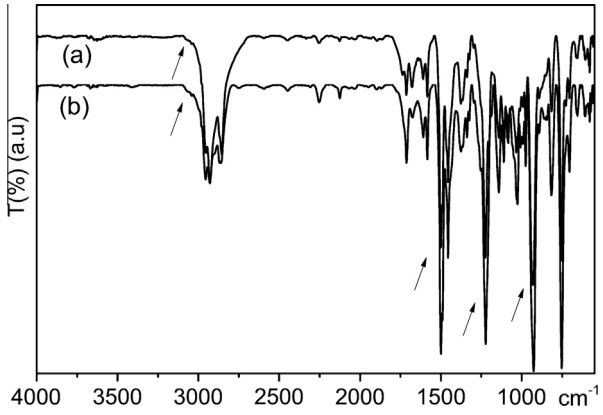


Figure 3. FT-IR spectra of *u*-hexyl-benz (a) and *u*-butyl-benz (b).

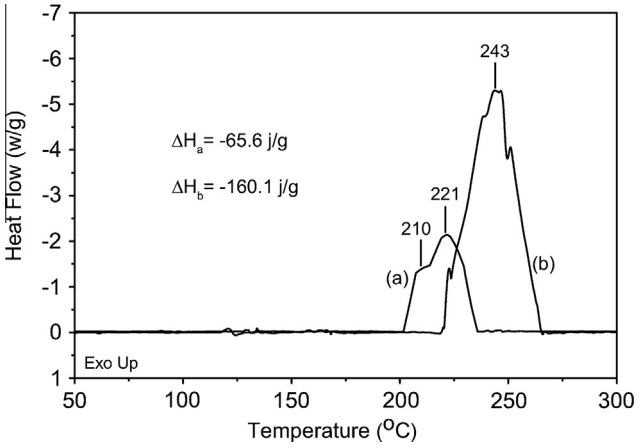


Figure 4. DSC traces of *u*-hexyl-benz (a), and *u*-butyl-benz (b).

for the C–O–C groups at ca. 1231 cm^{-1} and trisubstituted benzene ring modes at 932 cm^{-1} and 1495 cm^{-1}, which are characteristic absorptions of benzoxazines. Moreover, both compounds showed asymmetric Ar-H stretching vibration bands at 3058 cm^{-1} and aliphatic CH_2 stretching bands between 2971 and 2829 cm^{-1}.

It is well known that 1,3-benzoxazines can be cured by thermally-activated ring-opening polymerization. The polymerization can be monitored using differential scanning calorimetry (DSC) since the ring-opening is exothermic with a curing maximum at around 200–250 °C, depending on the functionalities present on the benzoxazines. Figure 4 shows the DSC profiles of *u*-hexyl-benz and *u*-butyl-benz. Both monomers are curable and their curing temperatures were in accordance with many classical bisbenzoxazine monomers. Notably, the benzoxazine with a hexyl substituent had a lower curing temperature and exotherm. Bulky alkyl groups decrease the polymerization rate and curing temperatures of benzoxazines as previously reported in the literature.[42] In our case, a similar bulkiness effect was observed for u-hexyl-benz. Moreover, it can be seen from the DSC traces that both monomers have shoulders in their curing exotherms. These shoulders would be expected since each monomer contains two different oxazine rings on their structure. The data show that each oxazine ring has its own curing maximum over a short temperature range. The inner oxazine rings are expected to have higher ring-opening temperatures compared to terminal oxazines, because inner core is more rigid. The relatively more flexible terminal benzoxazines favorably interact with the neighboring oxazine ring at lower temperatures. However, when the ring-opening process starts, the phenolic OH groups formed on the terminals could promote ring-opening reaction of the inner oxazines, thus merging of the exotherms is detected. The detailed curing data for both monomers are listed in Table 1.

Table 1
Curing characteristics of *u*-hexyl-benz and *u*-butyl-benz

Monomer	Onset Temp. (°C)	End-set Temp. (°C)	Maximum curing Temp. (°C)	Amount of exotherm (J/g)
u-Hexyl-benz	203	236	210, 221	−65.6
u-Butyl-benz	218	265	243	−160.1

In conclusion, we have demonstrated that unsymmetric bisbenzoxazine compounds can be prepared by combining the three-step approach with classical benzoxazine synthesis. The crucial intermediate is HPAMP, which creates the possibility of synthesizing many different unsymmetric benzoxazines by changing the amines in the final step of the synthesis. This methodology can also synthesize unsymmetric trisbenzoxazines by designing suitable intermediates. Unsymmetric benzoxazines have shown similar thermal properties compared to classical benzoxazines, hence they can be used in applications where a particular second functional group is needed on the benzoxazine structure.

Further studies including the design of novel unsymmetric bisbenzoxazines based on the same strategy are in progress in this laboratory to tune the property-structure relationships of these monomers and their polymers.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.07.041.

References and notes

1. Yagci, Y.; Kiskan, B.; Ghosh, N. N. J. Polym. Sci. Part A: Polym. Chem. **2009**, *47*, 5565–5576.
2. Kiskan, B.; Ghosh, N. N.; Yagci, Y. *Polym. Intern.* **2011**, *60*, 167–177.
3. Ghosh, N. N.; Kiskan, B.; Yagci, Y. *Prog. Polym. Sci.* **2007**, *32*, 1344–1391.
4. Tuzun, A.; Kiskan, B.; Alemdar, N.; Erciyes, A. T.; Yagci, Y. J. Polym. Sci. Part A: Polym. Chem. **2010**, *48*, 4279–4284.
5. Gulia, N.; Ejfler, J.; Szafert, S. *Tetrahedron Lett.* **2012**, *53*, 5471–5474.
6. Kiskan, B.; Koz, B.; Yagci, Y. J. Polym. Sci. Part A: Polym. Chem. **2009**, *47*, 6955–6961.

7. Burke, W. J. *J. Am. Chem. Soc.* **1949**, *71*, 609–612.
8. Kiskan, B.; Yagci, Y. *Polymer* **2008**, *49*, 2455–2460.
9. Burke, W. J.; Weatherbee, C. *J. Am. Chem. Soc.* **1950**, *72*, 4691–4694.
10. Ning, X.; Ishida, H. J. Polym. Sci. Part A Polym. Chem. **1994**, *32*, 1121–1129.
11. Kiskan, B.; Yagci, Y. *Polymer* **2005**, *46*, 11690–11697.
12. Brunovska, Z.; Liu, J. P.; Ishida, H. *Macromol. Chem. Phys.* **1999**, *200*, 1745–1752.
13. Baqar, M.; Agag, T.; Ishida, H.; Qutubuddin, S. J. Polym. Sci. Part A: Polym. Chem. **2012**, *50*, 2275–2285.
14. Yen, Y.-C.; Cheng, C.-C.; Chu, Y.-L.; Chang, F.-C. *Polym. Chem.* **2011**, *2*, 1648–1653.
15. Wu, X.; Zhou, Y.; Liu, S.-Z.; Guo, Y.-N.; Qiu, J.-J.; Liu, C.-M. *Polymer* **2011**, *52*, 1004–1012.
16. Zuniga, C.; Lligadas, G.; Carlos Ronda, J.; Galia, M.; Cadiz, V. *Polymer* **2012**, *53*, 3089–3095.
17. Andreu, R.; Reina, J. A.; Ronda, J. C. J. Polym. Sci. Part A: Polym. Chem. **2008**, *46*, 6091–6101.
18. Andreu, R.; Espinosa, M. A.; Galia, M.; Cadiz, V.; Ronda, J. C.; Reina, J. A. J. Polym. Sci. Part A: Polym. Chem. **2006**, *44*, 1529–1540.
19. Agag, T.; Takeichi, T. *Macromolecules* **2003**, *36*, 6010–6017.
20. Aydogan, B.; Sureka, D.; Kiskan, B.; Yagci, Y. J. Polym. Sci. Part A: Polym. Chem. **2010**, *48*, 5156–5162.
21. Kim, H. J.; Brunovska, Z.; Ishida, H. *Polymer* **1999**, *40*, 1815–1822.
22. Agag, T.; Takeichi, T. *Macromolecules* **2001**, *34*, 7257–7263.
23. Chaisuwan, T.; Ishida, H. *J. Appl. Polym. Sci.* **2006**, *101*, 548–558.
24. Kiskan, B.; Demiray, G.; Yagci, Y. J. Polym. Sci. Part A: Polym. Chem. **2008**, *46*, 3512–3518.
25. Kiskan, B.; Yagci, Y. J. Polym. Sci. Part A: Polym. Chem. **2007**, *45*, 1670–1676.
26. Kudoh, R.; Sudo, A.; Endo, T. *Macromolecules* **2010**, *43*, 1185–1187.
27. Kiskan, B.; Yagci, Y.; Ishida, H. J. Polym. Sci. Part A: Polym. Chem. **2008**, *46*, 414–420.
28. Ishida, H.; Ohba, S. *Polymer* **2005**, *46*, 5588–5595.
29. Koz, B.; Kiskan, B.; Yagci, Y. *Polym. Bull.* **2011**, *66*, 165–174.
30. Nagai, A.; Kamei, Y.; Wang, X. S.; Omura, M.; Sudo, A.; Nishida, H.; Kawamoto, E.; Endo, T. J. Polym. Sci. Part A: Polym. Chem. **2008**, *46*, 2316–2325.
31. Demir, K. D.; Kiskan, B.; Latthe, S. S.; Demirel, A. L.; Yagci, Y. *Polym. Chem.* **2013**, *4*, 2106–2114.
32. Chernykh, A.; Agag, T.; Ishida, H. *Polymer* **2009**, *50*, 382–390.
33. Demir, K. D.; Kiskan, B.; Yagci, Y. *Macromolecules* **2011**, *44*, 1801–1807.
34. Katritzky, A. R.; Xu, Y. J.; Jain, R. *J. Org. Chem.* **2002**, *67*, 8234–8236.
35. Chang, H. C.; Lin, C. H.; Tian, Y. W.; Feng, Y. R.; Chan, L. H. J. Polym. Sci. Part A: Polym. Chem. **2012**, *50*, 2201–2210.
36. Andreu, R.; Reina, J. A.; Ronda, J. C. J. Polym. Sci. Part A: Polym. Chem. **2008**, *46*, 3353–3366.
37. Oie, H.; Sudo, A.; Endo, T. J. Polym. Sci. Part A: Polym. Chem. **2011**, *49*, 3174–3183.
38. Andreu, R.; Ronda, J. C. *Synth. Commun.* **2008**, *38*, 2316–2329.
39. Lin, C. H.; Feng, Y. R.; Dai, K. H.; Chang, H. C.; Juang, T. Y. J. Polym. Sci. Part A: Polym. Chem. **2013**, *51*, 2686–2694.
40. Lin, C. H.; Chang, S. L.; Lee, H. H.; Chang, H. C.; Hwang, K. Y.; Tu, A. P.; Su, W. C. J. Polym. Sci. Part A: Polym. Chem. **2008**, *46*, 4970–4983.
41. Chang, S. L.; Lin, C. H. J. Polym. Sci. Part A: Polym. Chem. **2010**, *48*, 2430–2437.
42. Sudo, A.; Du, L.-C.; Hirayama, S.; Endo, T. J. Polym. Sci. Part A: Polym. Chem. **2010**, *48*, 2777–2782.