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2-ARYLBENZOTHIAZOLES AND 2-ARYLBENZOXAZOLES FROM α,α,α-TRIHALOMETHYL AROMATIC COMPOUNDS

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Abstract: α,α,α-Trichloromethyl and α,α,α-trifluoromethyl aromatic compounds react with *o*-aminothiophenol and *o*-aminophenol in polyphosphoric acid (PPA) to produce 2-arylbenzothiazoles and 2-arylbenzoxazoles in high yields.

INTRODUCTION

Benzothiazoles and benzoxazoles are the basis of numerous optical brighteners and dyes.[1,2] Poly(*p*-phenylenebenzobisthiazole) (PBT) and Poly(*p*-phenylenebenzoxazole) (PBO) are rigid-rod polymers with excellent thermal and oxidative stability, and good hydrolytic and chemical resistance. The synthesis, process and characterization of PBT and PBO have been actively pursued. [3,4]

Two of the most important benzothiazole and benzoxazole compounds, 2-phenylbenzothiazole and 2-phenylbenzoxazole, are prepared by the condensation

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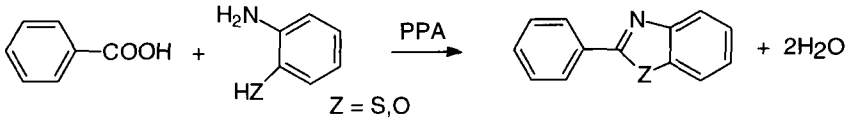
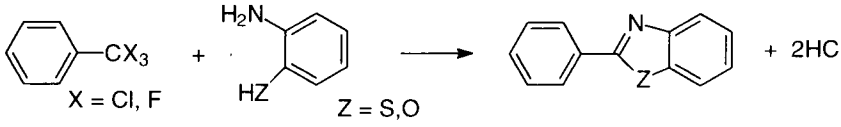
of *o*-aminothiophenol or *o*-aminophenol with benzoic acid or its derivatives in polyphosphoric acid (PPA),[5] polyphosphate ester,[6] or a mixture of methanesulfonic acid and phosphorous pentoxide.[7] This reaction in PPA has been extended to large-scale preparation of PBO and PBT polymers.[3,4]



2-Arylbenzothiazoles and 2-arylbenzoxazoles can also be made by palladium-catalyzed condensation of aryl halides with *o*-aminothiophenol or *o*-aminophenol followed by dehydrative cyclization,[8] reaction of copper(I) thiobenzoate and 2-iodoanilines,[9] the Beckman rearrangement of oximes of *o*-hydoxybenzophenones,[10] the action of selenoamides on *o*-aminophenol or *o*-aminothiophenol,[11] and condensation of *o*-aminothiophenol or *o*-aminophenol with carboxylic acids in polyphosphoric acid trimethylsilyl ester.[12, 13]

In this paper, 2-arylbenzothiazoles and 2-arylbenzoxazoles are prepared in good yields from trihalomethyl aromatics with *o*-aminothiophenol and *o*-aminophenol in PPA. Trihalomethyl is a common functional group in herbicide intermediates, and this method provides a convenient approach to converting trihalomethyls to thiazoles and oxazoles. High product yield makes it effective to extend this method to PBT and PBO synthesis. When PPA is used as the solvent to make these polymers, solid P_2O_5 has to be added to adjust the P_2O_5 content of the system to ensure high molecular weight. Since water is not evolved when

trihalomethyls are converted to benzothiazole or benzoxazole, adjustment of P_2O_5 content in PPA with solid P_2O_5 is not needed.[14, 15]



RESULTS AND DISCUSSION

o-Aminothiophenol and a trihalomethyl aromatic compound were heated with stirring in PPA. Products were isolated by precipitation in water. Good product yields were achieved as shown in Table 1.

Table 1. Synthesis of 2-Arylbenzothiazoles from Trihalomethyl Aromatic Compounds and *o*-Aminothiophenol

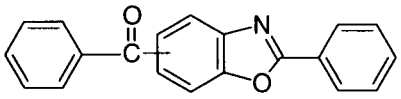
Run	Trihalomethyl Compound	Product	Yield %
1	α, α, α-Trichlorotoluene	2-Phenylbenzothiazole	98
2	1,4-Bis(α, α, α–trichloromethyl)benzene	1,4-Bis(2-benzothiazole)benzene	93
3	α, α, α-Triflorotoluene	2-Phenylbenzothiazole	92
4	4-Methylbenzotrifloride	2-(4-Methylphenyl)benzothiazole	92

Reaction results of trihalomethyl aromatic compounds with *o*-aminophenol in PPA are shown in Table 2. α,α,α-Trichlorotoluene and α,α,α-trifluorotoluene reacted with *o*-aminophenol to produce 2-phenylbenzoxazole and

2-phenyl-5(or 6)-benzoylbenzoxazole (Compound **1**). Compound **1** was also a side product in the reaction of benzoic acid and *o*-aminophenol.[16]

Table 2. Synthesis of 2-Arylbenzoxazoles from Trihalomethyl Aromatic Compounds and *o*-Aminophenol

Run	Trihalomethyl Compound	Product	Yield %
1	α, α, α-Trichlorotoluene	2-Phenylbenzoxazole	62
		Compound **1**	15
2	1,4-Bis(α, α, α–tri-chloromethyl)benzene	1,4-Bis(2-benzoxazole)benzene	96
3	α, α, α-Triflorotoluene	2-Phenylbenzoxazole	35
		Compound **1**	25
4	4-Chlorobenzotrichloride	2-(4-Chlorophenyl)benzoxazole	60



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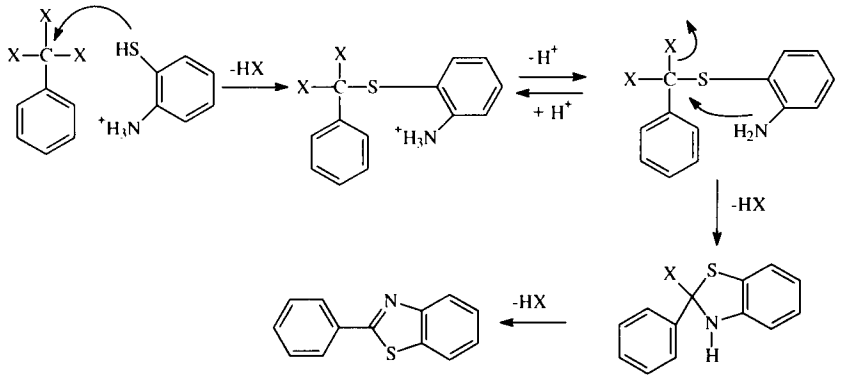
Higher reaction temperatures were required for the reactions of trihalomethyl aromatic compounds with *o*-aminophenol than with *o*-aminothiophenol. α,α,α-Trichlorotoluene started to react with *o*-aminothiophenol in PPA at room temperature. The reaction was completed at 50°C overnight. *o*-

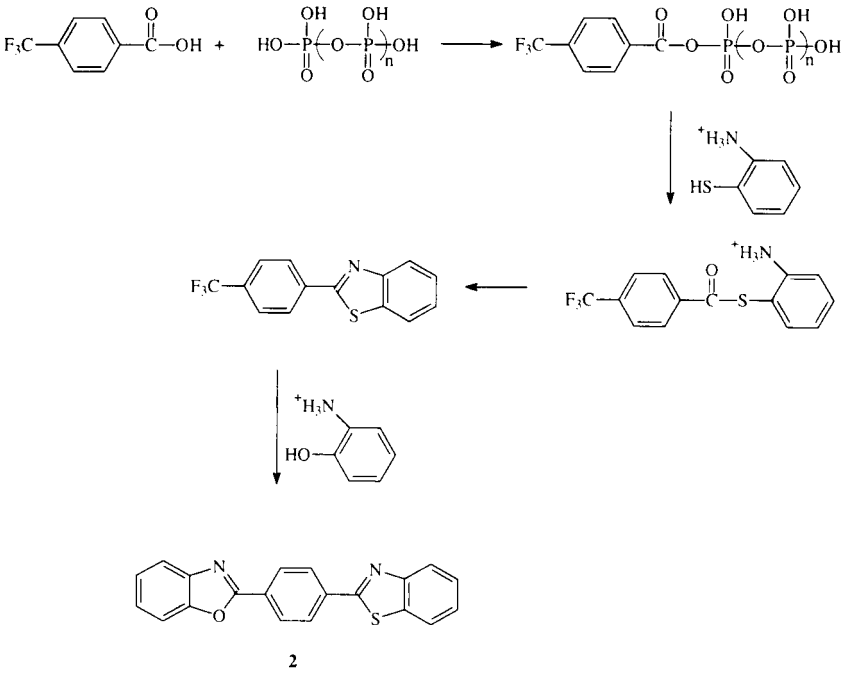
Aminophenol and α,α,α-trichlorotoluene in PPA remained essentially unreacted after 16 h at 50°C. Hydrogen chloride started to evolve, and products were observed at 70°C. A significant amount of 2-phenylbenzothiazole was formed when α,α,α-trifluorotoluene was stirred with *o*-aminothiophenol in PPA at 100°C. *o*-Aminophenol did not react with α,α,α-trifluorotoluene at 100°C and reaction products were only detected at temperatures above 120°C.

Lower reaction temperatures and better product yields for *o*-aminothiophenol, which is a better nucleophile than *o*-aminophenol, suggest nucleophilic attack of the -SH group on -CX_3. A proposed mechanism for *o*-aminothiophenol is shown below.



Benzothiazole and benzoxazole were subsequently formed from α,α,α-trifluoro-*p*-toluic acid. When 1 mole each of *o*-aminothiophenol and *o*-aminophenol were allowed to react with 1 mole of α,α,α-trifluoro-*p*-toluic acid in PPA at 80°C, the ratio of 2-(α,α,α-trifluoro-*p*-tolyl)benzothiazole to 2-(α,α,α-trifluoro-*p*-tolyl)benzoxazole was 96 to 4. After the reactor was further heated at

170°C for 16 h, 2-(4-(2-benzothiazolyl)phenyl)-benzoxazole (Compound **2**) was formed as the major product. The higher reactivity of *o*-aminothiophenol with carboxylic acid in PPA is consistent with the previously reported formation of ester as the first reaction intermediate in this reaction.[16]



2

α,α,α-Tribromoquinaldine did not react with *o*-aminothiophenol or *o*-aminophenol to form benzothiazole or benzoxazole in PPA. The reaction products were not identified.

In summary, 2-arylbenzothiazoles and 2-arylbenzoxazoles are prepared from α,α,α-trichloromethyl or α,α,α-trifluoromethyl aromatic compounds with *o*-aminothiophenol and *o*-aminophenol in PPA in good yield. Reaction temperatures for the formation of benzothiazoles are lower than those for benzoxazoles.

EXPERIMENTAL

NMR spectra were recorded at 300 MHz with a Varian VXR-300 instrument. Mass spectra were recorded on a Finnigan 4600 quadruple system in the EI mode. Gas chromatographic analysis was performed on a HP5840A chromatograph with a 30-m J&W fused-silica capillary column. Trihalomethyl aromatic compounds, 2-phenylbenzothiazole, and 2-phenylbenzoxazole were purchased from Aldrich Chemical Company. Melting points were measured in sealed and evacuated capillary tubes on a Syblon thermolyne apparatus with polarizing microscope and were not corrected.

General procedure. *o*-Aminothiophenol or *o*-aminophenol, the equivalence of a trihalomethyl aromatic compound, and PPA were loaded in a 100-mL reactor that was equipped with a mechanical stirrer, a nitrogen inlet and an outlet connected to a trap for acidic gases. The mixture was heated with stirring. Evolution of acidic gases was monitored with blue litmus paper. When the evolution of acidic gases stopped, the PPA solution was poured into ice water. In experiment numbers 1, 3, and 4 in Tables 1 and 2, products were extracted with ethyl acetate twice. The combined ethyl acetate solution was dried with anhydrous sodium sulfate, and ethyl acetate was removed by a rotary-evaporator. When 1,4-bis(trichloromethyl)benzene was used as the starting material, the precipitated product was collected with a sintered glass filter, washed thoroughly with water, and dried.

2-Phenylbenzothiazole from α,α,α-trichlorotoluene and *o*-aminothiophenol: α,α,α-Trichlorotoluene (2.20 g, 0.0113 mol) and *o*-aminothiophenol

(1.41 g, 0.0113 mol) were stirred in 60 g PPA at 50°C overnight. The crude product was purified by column chromatography (ethyl acetate) to afford 2-phenylbenzothiazole (2.31 g, 97%) as a light yellow crystalline solid: mp 113-115°C (lit.[7] 113-115°C). The ^{1}H NMR and mass spectra of the product were identical to those of a commercial sample.

1,4-Bis(2-benzothiazole)benzene from 1,4-bis(α,α,α-trichloromethyl)benzene and *o*-aminothiophenol: 1,4-Bis(α,α,α-trichloromethyl)benzene (2.13 g, 6.81 mmol) and *o*-aminothiophenol (1.70 g, 13.6 mmol) were stirred in 60 g PPA. Hydrogen chloride was detected at 85°C. The reactor was heated at 100°C for 2 h and 150°C for 4 h. The crude product was purified by sublimation to afford 1,4-bis(2-benzothiazole)benzene as a yellow solid (2.20 g, 94%). The compound decomposed before melting. The isolated product had identical ^{1}H NMR and mass spectra to those of a sample prepared from terephthalic acid and *o*-aminothiophenol in PPA. Anal. Calcd. for $C_{20}H_{12}N_2S_2$: C, 69.77; H, 3.49; N, 8.14. Found: C, 69.66; H. 3.51; N, 8.12.

2-Phenylbenzothiazole from α,α,α-trifluorotoluene and *o*-aminothiophenol: α,α,α-Trifluorotoluene (1.65 g, 0.0113 mol) and *o*-aminothiophenol (1.41 g, 0.0113 mol) were stirred in 60 g PPA. Some 2-phenylbenzothiazole was formed at 60°C. The reactor was heated at 100°C for 4 h and 120°C for 10 h. The crude product was purified by column chromatography (ethyl acetate) to afford 2-phenylbenzothiazole as a light yellow solid (2.14 g, 90%; mp 113-115°C; lit.[7] 113-115°C). The ^{1}H NMR spectrum of the product was identical to that of a commercial sample.

2-(4-Methylphenyl)benzothiazole from 4-methylbenzotrifluoride and *o*-aminothiophenol: 4-Methylbenzotrifluoride (2.56 g, 0.016 mol) and *o*-aminothiophenol (2.00 g, 0.016 mol) were stirred in 60 g PPA. The reactor was heated at 100°C for 4 h and 120°C for 10 h. The crude product was purified by column chromatography (ethyl acetate) to afford 2-(4-methylphenyl)benzothiazole as a light yellow solid (3.24 g, 90%; mp 84°C; lit.[17] 86°C). IR (KBr) 1610, 1486 cm^{-1}; ^1H NMR (300 MHz, acetone-d6) δ 8.03-8.01 (m, 2H), 7.96 (d, J=8.2 Hz, 2H), 7.52-7.35 (m, 2H), 7.28 (d, J=8.2 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d6) δ 170.0, 156.6, 143.8, 137.3, 133.3, 132.1, 129.6, 128.7, 127.5, 125.3, 124.2, 23.05: MS *m/z* (relative intensity) 225(100). Anal. Calcd. for $C_{14}H_{11}NS$: C, 74.67; H, 4.89; N, 6.22. Found: C, 74.70; H, 4.91; N, 6.14.

2-Phenylbenzoxazole from α,α,α-trichlorotoluene and *o*-aminophenol: α,α,α-Trichlorotoluene (2.20 g, 0.0113 mol) and *o*-aminophenol (1.23 g, 0.0113 mol) were stirred in 60 g PPA. No acidic gas was detected at 50°C. The mixture was heated at 100 °C for 8 h and 120°C for 2 h. The crude product was purified by column chromatography (ethyl acetate) to afford 2-phenylbenzoxazole (1.3 g, 55%; mp 102-104°C; lit.[5] 102-104°C) and Compound **1** (0.60 g, 18%). Characterization of Compound **1** was previously reported.[16]

1,4-Bis(2-benzoxazole)benzene from 1,4-bis(α,α,α-trichloromethyl)benzene and *o*-aminophenol: 1,4-Bis(α,α,α-trichloromethyl)benzene (2.13 g, 6.81 mmol) and *o*-aminophenol (1.49 g, 13.6 mmol) were stirred in 60 g PPA. Hydrogen chloride was detected at 85°C. The reactor was heated at 100°C

for 2 h and 150°C for 4 h. The crude product was purified by sublimation to afford 1,4-bis(2-benzoxazole)benzene as a colorless solid (2.20 g, 94%). The compound decomposed before melting. The isolated product had identical ^1H NMR and mass spectra to those of a sample prepared from terephthalic acid and *o*-aminophenol in PPA.

2-Phenylbenzoxazole from α,α,α-trifluorotoluene and *o*-aminophenol: α,α,α-Trifluorotoluene (1.65 g, 0.0113 mol) and *o*-aminophenol (1.41 g, 0.0113 mol) were stirred in 60 g PPA. No acidic gas evolution was detected at 100°C. 2-Phenylbenzoxazole started to form at 120°C. The reactor was heated at 120°C for 24 h and 150°C for 10 h. The crude product was purified by column chromatography (ethyl acetate) to afford 2-phenylbenzoxazole (0.83 g, 35%, mp 102-104°C) and Compound **1** (0.84 g, 25%). Characterization of Compound **1** was previously reported.[16]

2-(4-Chlorophenyl)benzoxazole from 4-chlorobenzotrichloride and *o*-aminophenol: 4-Chlorobenzotrichloride (4.05 g, 17.6 mmol) and *o*-aminophenol (1.92 g, 17.6 mmol) were heated in 70 g of PPA at 100°C for 8 h and 120°C for 4 h. The crude product was purified by column chromatography (ethyl acetate) to afford 2-(4-chlorophenyl)benzoxazole as a white solid (2.42 g, 60%; mp 151°C; lit.[11] 148°C). IR (KBr) 1617 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, J = 8.5 Hz, 2H), 7.78-7.85 (m, 1H), 7.59-7.55 (m, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.38-7.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 152.3, 143.6, 139.3, 130.8, 130.4, 127.2, 126.9, 126.3, 121.7, 112.2; MS *m/z* (relative intensity) 231(33), 229(100). Anal. Calcd. for $C_{13}H_8ClNO$: C, 68.12; H, 3.49. Found: C, 68.40; H,

3.40. A compound with *m/z* (relative intensity) 369(66), 367(100), which suggested the possibility of 2-(4-chlorophenyl)-5(or 6)-(4-chlorobenzoyl)benzoxazole was detected by GC/MS.

2-(4-(2-Benzothiazolyl)phenyl)-benzoxazole: *o*-Aminothiophenol (1.25 g, 10 mmol), *o*-aminophenol (1.09 g, 10 mmol), α,α,α-trifluoro-*p*-toluic acid (1.90 g, 10 mmol), and 60 g PPA were stirred at 80°C overnight. A sample analyzed by GC showed the ratio of 2-(α,α,α-trifluoro-*p*-tolyl)benzothiazole (GC/MS: *m/z* = 279) to 2-(α,α,α-trifluoro-*p*-tolyl)benzoxazole (GC/MS: *m/z* = 263) to be 96 to 4. The reactor was further heated at 170°C overnight. Crude product was purified by sublimation to afford Compound **2** as a light yellow solid (3.1 g, 94%). The compound decomposed before melting. IR (KBr) 1617 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.32(ABq, J=8.6 Hz, Æ=39 Hz, 4H), 8.11(d, J=8.0 Hz, 1H), 7.93 (d, J=8.0 Hz, 1H), 7.81 (m, 1H), 7.61 (m, 1H), 7.55-7.37 (m, 4H); ^{13}C NMR (75 MHz, MSA) δ 172.0, 162.7, 149.8, 141.6; 132.3, 131.6, 131.5, 131.3, 131.1, 130.8, 130.1, 130.0, 129.5, 125.6, 124.7, 118.7, 116.7, 114.0; MS *m/z* (relative intensity) 328 (100). Anal. Calcd. for $C_{20}H_{12}N_2OS$: C, 73.17; H, 3.66; N, 8.54. Found: C, 73.26; H. 3.61; N, 8.52.

REFERENCES

1. Sturmer, D. M. In *Encyclopedia of Chemical Technology*, 4th ed.; Howe-Grant, M., Ed.; Wiley & Sons: New York, Vol. 8, **1993**, pp. 839-860.
2. McElhone, H. J. In *Encyclopedia of Chemical Technology*, 4th ed.; Howe-Grant, M., Ed.; Wiley & Sons: New York, Vol. 11, **1994**, pp. 227-241.

3. Wolfe, J. F. In *Encyclopedia of Polymer Science and Technology*, 3rd ed; Mark, H. F.; Kroschwitz, J. I. Eds. Wiley & Sons, New York, Vol. 11, **1988**, pp. 601-635.

4. Adams, W. W.; Eby, R. K.; McLemore, D. E., Eds. *The Materials Science and Engineering of Rigid-Rod Polymers*; Symposium Proceedings, Materials Research Society, Pittsburgh, Vol. 134, **1989**.

5. Hein, D.W.; Alheim, R.J.; Leavitt, J.J. *J. Am. Chem. Soc.* **1957**, *79*, 427.

6. Kanaoka, Y.; Hamada, T.; Yonemitsu, O. *Chem. Pharm. Bull.* **1970**, *18*, 587.

7. Boger, D. L. *J. Org. Chem.* **1978**, *43*, 2296.

8. [a] Perry, R. J.; Wilson, B. D.; Miller, R. J. *J. Org. Chem.* **1992**, *57*, 2883. [b] Perry, R. J.; Wilson, B. D. *Organometallics* **1994**, *13*, 3346.

9. Osuka, A.; Uno Y.; Horiuchi, H.; Suzuki, H. *Synthesis* **1984**, 145.

10. Boyd, G. V. In *Comprehensive Heterocyclic Chemistry*, Reactorts, K. T., Ed.; Pergamon: New York, Vol. 6, **1984**, p. 216.

11. Cohen, V. I. *J. Heterocycl. Chem.* **1979**, *16*, 13.

12. Yamamoto, K.; Watanabe, H. *Chemistry Letters*, **1982**, 1225.

13. Reinhardt, B. A. *Polymer Communications*, **1990**, *31*, 453.

14. Schrage, K. U.S. Patent 4,107,169, 1978. Trichloromethyl aromatics react with *o*-aminophenol and *o*-aminothiophenol in decalin or in the absence of any solvent to synthesize 2-arylbenzoxazoles and 2-arylbenzothiazoles in low yield.

15. [a] So, Y. H. U.S. Patent 5,235,023, August 1993 (*Chem. Abstr.*, **1995**, *123*, P199815f). [b] So, Y. H. *J. Poly. Sci.*, Part A: *Polymer Chemistry*, **1997**, *35*, 2143.

16. [a] So, Y. H.; Heeschen, J. P., Murlick, C. L. *Macromolecules* **1995**, *28*, 7289.

[b] So, Y. H.; Heeschen, *J. Org. Chem.* **1997**, *62*, 3552.

17. Kiparianov, A. I.; Ushenko, I. K.; Gershun, A. L., *J. Gen. Chem. USSR* (*Engl. Trans.*) **1944**, *14*, 865.

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