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Melt Reaction Method for the Synthesis of 2-Arylbenzotiazoles

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Abstract

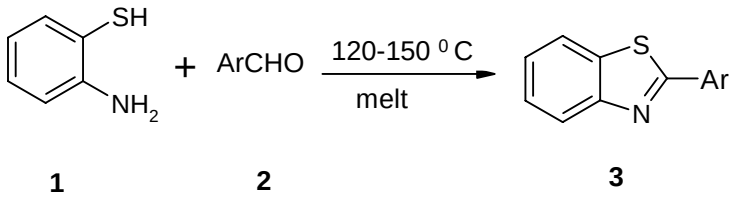
A variety of 2-arylbenzothiazoles were prepared by the melt reaction of 2-aminothiophenol and aryl aldehydes under oxygen atmosphere. No further oxidative reagent is needed.

Introduction

In recent years the privileged structure concept has emerged as a fruitful approach for the discovery of novel biologically active molecules. Privileged structures, with their inherent affinity for diverse biological receptors, represent an ideal source of core scaffolds and capping fragments for the design and synthesis of combinatorial libraries targeted at various receptors on a reasonable time scale.[1] Arylbenzothiazoles bearing a substituent at C-2 are of great interest, as this structural framework has proved to be an important class of bicyclic privileged substructures owing to their potent utility as imaging agents for β-amyloid, as chemiluminescent agents, antitumor agents, calcium channel antagonists, antituberculotics, antiparasitics and also as photo sensitizers.[2–7]
There are many methods for the synthesis of 2-arylbenzothiazoles. The most common direct method is the condensation of an *o*-aminothiophenol with the substituted aromatic aldeydes[8] and carboxylic acids or its derivatives in polyphosphoric acid (PPA),[9] polyphosphate ester,[10] or a mixture of methane sulfonic acid and phosphorous pentoxide.[11] Some of these methods have been used successfully for the preparation of 2-arylbenzothiazoles, however, most of them suffer from drawbacks, namely high thermal conditions, long reaction times and the use of an acidic or basic catalysts and toxic metallic compounds that result in waste streams.
In wake of health and economic awareness, it is desirable to device a safe and metal free method with minimum disposable wastes. Melt reactions have recently gained popularity because of cleaner conditions and ease of manipulation.
In this paper we wish to report a facile, environmental friendly and clean synthesis of 2-substituted benzothiazoles under solvent-free melt reactions. We have carried out the reaction of aromatic or hetero aromatic aldehydes with *o*-aminothiophenol without any catalyst under melt reaction conditions.

Results and Discussions

The melt reaction of 1.0 mmol of 2-aminothiophenol (**1**) with 1.0 mmol of an aryl aldehyde (**2**) in a round bottom flask and under ambient atmosphere affords the corresponding 2-aryl benzothiazoles (**3**) with good yield in 60-90 minutes. The reaction mixture was heated in an ordinary oven.
Adopting the above method, various aryl aldehydes reacted with 2-aminothiophenol to produce the corresponding 2-arylbenzothiazoles (Scheme 1, Table 1).



1 **2** **3**

Scheme 1. Synthesis of 2-aryl benzothiazoles

This method is suitable for heterocyclic aldehydes (**2e, 2f**) as well as aromatic aldehydes. In some cases no further purification is needed. Melting point of the crude reaction products correlate well with the literature values.[12]
The results are summarized in Table 1. As shown in the table, the 2- arylbenzothiazoles were obtained in good to high yields independent of substituents on the aryl rings. The method is also applicable for the reaction of aromatic heterocyclic compounds with *o*-aminothiophenol affording the corresponding 2-heteroarylbenzothiazoles in good to high yields (Entries **2e**, **2f**).

Conclusion

Melt reaction is a very efficient method for the synthesis of 2-aryl/heteroaryl benzothiazoles. The method is very simple, efficient and environmentally friendly as it does not use any auxiliary or solvent.

Acknowledgment

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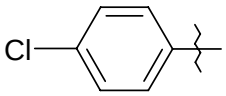
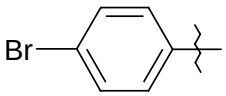
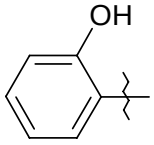
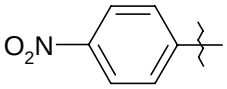
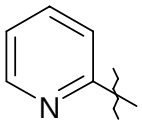
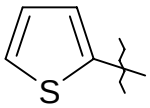
Experimental Section

A mixture of 1.0 eq of 2-aminothiophenole (**1**) and 1.0 eq of aldehyde (**2**) was heated in an evacuated flask in an ordinary oven or in an oil bath for 30-90 minutes to afford the crude product (**3**). The progress of the reaction was monitored by TLC and FT-IR. Further purification was recrystallization from 96% ethanol, if necessary.

Table 1. Direct synthesis of 2-aryl benzothiazoles

Aldehydes	Ar	Temp. (°C)	Time (min)	m.p. (°C)	Yield (%)
2a		125	60	115-118	85
2b		125	60	132-133	97
2c		150	90	130-132	85
2d		125	60	224-228	81
2e		150	60	135-136	97
2f		150	90	90-92	78

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