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Syntheses of 2-arylbenzothiazoles from flash vacuum pyrolyses and photolyses of 2-methylthio-*N*-(arenylidene)anilines

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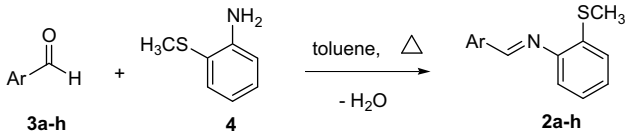
ABSTRACT

Flash vacuum pyrolyses and photolyses of 2-methylthio-*N*-(arenylidene)anilines **2a–h** are new and convenient methods for the syntheses of 2-arylbenzothiazoles **1a–h**.

2-Arylbenzothiazoles **1** have been known as important and useful compounds for pharmaceutical organic synthesis, as anticancer and Alzheimer's disease agents.[1–9] There have been numerous reports for the synthetic routes of these compounds, such as microwave assisted,[10,11] ionic liquid,[12] solid phase,[13] electrooxidation,[14] and the catalytic synthesis with Pd, Cu, Mn, Sc, etc.[15–21] Recently, we have prepared **1** from flash vacuum pyrolyses (FVP) and photolyses of 2-methylthio-*N*-(arenylidene)anilines **2**. We wish to report our results herein.

2-Methylthio-*N*-(arenylidene)anilines **2a–h** were prepared in quantitative yields from condensation of aryl aldehydes **3a–h** and *o*-(methylthio)aniline (**4**) (Scheme 1).[22] FVP of **2a–g** were performed using the pyrolysis set-up that has been previously described.[23] The tube furnace was maintained at temperatures ranging between 750 and 850 °C. A sample of **2** (100–200 mg) was placed into the sample chamber and the system was evacuated to ca. 1×10^{-2} Torr. The pyrolysis process was completed in 1 h. Pyrolysis at 800 °C and ca. 1×10^{-2} Torr appeared to be the optimum reaction conditions for our study. FVP of **2a–g** at temperatures lower than 800 °C would leave unreacted starting materials, whereas FVP of **2a–g** at temperatures higher than 850 °C would give lower yields of the desired products **1a–g**. FVP of **2a–e** gave 2-arylbenzothiazoles **1a–e** as the major products and benzothiazole (**5**) as the minor one (Table 1). However, FVP of **2f** and **2g**, in addition to the corresponding 2-arylbenzothiazoles **1f** and **1g**, and **5**, also gave by-products 2-indolylbenzothiazole (**6**) and phenanthridine (**7**), respectively. The yields for the pyrolysis products from FVP of **2a–g** are listed in Table 1. With the exception of **2d** and **2g** which gave low yields (<50%) of **1d** and **1g**, FVP of **2a–c** and **2e–f** gave moderate to good yields of the corresponding 2-arylbenzothiazoles.

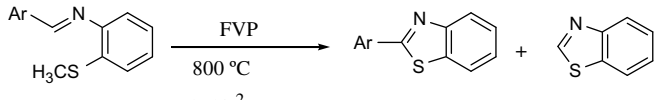
A mechanism to account for the formation of 2-arylbenzothiazoles **1a–g** from FVP of **2a–g** is proposed as shown in Scheme 2. Under the pyrolysis conditions, elimination of a methyl radical from **2** followed by cyclization of the resulting thiophenoxyl radical would lead to the final product **1**. Elimination of an aryl radical



a, Ar = phenyl; **b**, Ar = 2-furyl; **c**, Ar = 2-thienyl; **d**, Ar = 2-benzo[*b*]furyl; **e**, Ar = 2-benzo[*b*]thienyl; **f**, Ar = *2-(N*-methyl)indolyl; **g**, Ar = 2-chlorophenyl; **h**, Ar = 2,4-dimethoxyphenyl

Scheme 1.

Table 1
Pyrolysis products from FVP of 2-methylthio-*N*-(arenylidene)anilines **2a–g**



2a-g 1x10^{-2} Torr **1a-g** **5**

Substrate	Ar	Product[a,b] (yield, %)	
2a	Ph	**1a** (85)	**5** (6)
2b	2-Furyl	**1b** (73)	**5** (8)
2c	2-Thienyl	**1c** (69)	**5** (2)
2d	2-Benzo[*b*]furyl	**1d** (40)	**5** (2)
2e	2-Benzo[*b*]thienyl	**1e** (65)	**5** (7)
2f	2-(*N*-methyl)indolyl	**1f** (53)	**5** (5)
		6 (Ar = 2-indolyl, 23)	
2g	2-Chlorophenyl	**1g** (45)	**5** (15)
		Phenanthridine	(**7**, 10)

[a] The yields of products were measured by quantitative analysis of ^{1}H NMR analysis with dibromomethane as an integration standard.
[b] All products were characterized by their NMR and MS spectra.

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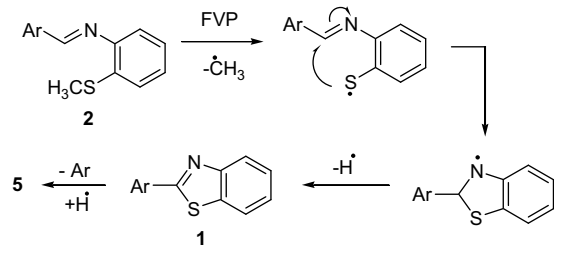
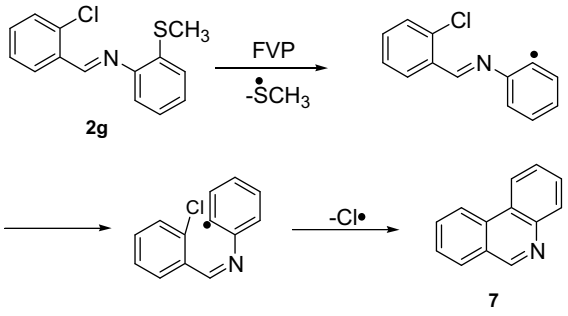
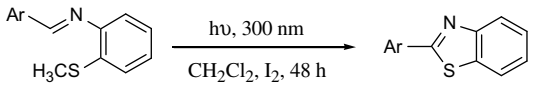


Scheme 2.



Scheme 3.

Table 2
Products from photolysis of 2-methylthio-*N*-(arenylidene)anilines **2a–f**



2a-g **1a-g**

Substrate	Product[a,b] (yield, %)
2a	**1a** (92)
2b	**1b** (83)
2c	**1c** (82)
2d	**1d** (89)
2e	**1e** (80)
2f	**1f** (85)
2g	**1g** (98)

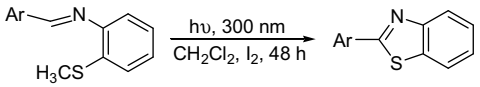
[a] The yields of products were measured by quantitative analysis of ^{1}H NMR analysis with dibromomethane as an integration standard.
[b] All products were characterized by their NMR and MS spectra.

from **1** then gave minor product, benzothiazole (**5**). By the same token elimination of a methyl radical from **1f** would give **6**.

The mechanism for the formation of **7** from FVP of **2g** is proposed as shown in Scheme 3.

For the purpose of comparison, syntheses of 2-arylbenzothiazoles by the photolysis method have also been studied. 2-Methylthio-*N*-(arenylidene)anilines **2a–g** (1×10^{-4} M in CH_2Cl_2, and with ca. 5 mol % of iodine as catalyst) were irradiated (300 nm) in a Rayonet apparatus for 48 h. Compounds **2a–g** were all converted into the corresponding 2-arylbenzothiazoles **1a–g** with high yields and no side-products. A radical process as shown in Scheme 2 for the FVP method can also be used to account for the formation of **1a–g** from the photolysis method. The yields for the photolysis products from **2a–g** are listed in Table 2. It is apparent that photolysis method is a better synthetic mean for the synthesis of 2-arylbenzothiazoles **1** than the pyrolysis method. Furthermore, the photolysis method is comparable to the commonly used methods employing 2-aminobenzenethiol as the precursor.[11,12,16]

Application of the photolysis method was then employed for the synthesis of 2-(2,4-dimethoxyphenyl)benzothiazole (**1h**). In contrast to the Suzuki coupling approach which failed to prepare **1h**,[15] photolysis of 2-methylthio-*N*-(2,4-dimethoxybenzylidene)aniline (**2h**), under similar reaction conditions, gave **1h** in 88% yield.



2h **1h** (88%)

In summary, FVP and photolysis of 2-methylthio-*N*-(arenylidene)anilines **2a–h** are new methods to synthesize 2-arylbenzothiazoles **1a–h**. However, for the compounds under study, the photolysis method gives higher yields and cleaner products, as compared to the FVP method. We are currently extending our study to the other heterocyclic systems.

Acknowledgement

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