α-Hydroxybenzylation and Benzylidenation of the Methyl Group in 2-Methyl-1,3-benzoxazole and 2-Methyl-1,3-benzothiazole

V. Dryanska, Chr. Ivanov

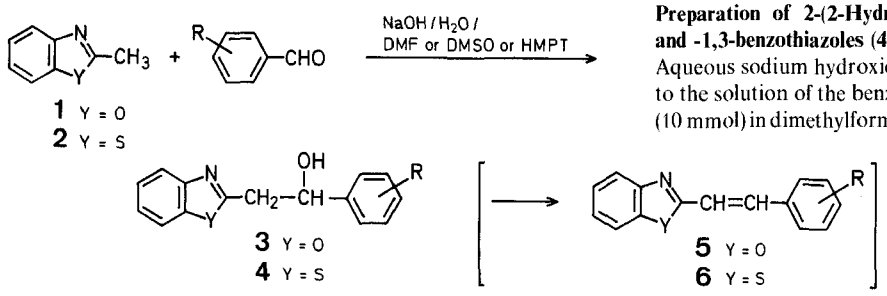
Department of Chemistry, University of Sofia, Sofia 26, Bulgaria

In the presence of basic[1, 2] or acidic[1, 3] catalysts, 2-methyl-1,3-benzoxazole (**1**) and 2-methyl-1,3-benzothiazole (**2**) react with aromatic aldehydes to give the corresponding 2-styryl derivatives (**5** and **6**). So far, the reaction has been stopped at the aldol stage (**3**, **4**) only by performing it in liquid ammonia in the presence of lithium amide[4]. We have now found that the alcohols **3**, **4** can be easily obtained by carrying out the reaction in dimethylformamide, dimethyl sulfoxide, or hexamethylphosphortriamide (HMPT) in the presence of catalytic amounts of aqueous sodium hydroxide.

The reaction was studied under different conditions. The best results were obtained at room temperature using 4 ml DMSO or HMPT, respectively, or 10 ml DMF per 10 mmol of **1** or **2**. When larger quantities of solvent were used mixtures of the alcohols (**3**, **4**) and their dehydration products (**5**, **6**) or only the latter were formed. This fact indicates that the final reaction product is strongly dependent on the solubility of the alcohol initially formed.

Attempts to carry out the same reaction in ether, ethanol or dioxane failed.

The direct synthesis of 2-styryl-1,3-benzoxazoles (**5**) and 2-styryl-1,3-benzothiazoles (**6**) from **1** or **2**, respectively, and benzaldehydes is best accomplished in dimethyl sulfoxide as solvent in the presence of excess aqueous sodium hydroxide. We have found that under these conditions the condensation is complete within a few hours. This method for the preparation of **5** and **6** appears to be more convenient than the known methods using zinc chloride[1], potassium methoxide[1], boric acid[3], or sodium amide[2] as condensing agents. Attempts to carry out the reaction in ether or ethanol failed.



Preparation of 2-(2-Hydroxy-2-phenylethyl)-1,3-benzoxazoles (3) and -1,3-benzothiazoles (4); General Procedure:

Aqueous sodium hydroxide (4% solution, 1 ml, 1 mmol) is added to the solution of the benzazole (**1**, **2**; 10 mmol) and the aldehyde (10 mmol) in dimethylformamide (10 ml), dimethyl sulfoxide (4 ml),

Table. 2-(2-Hydroxy-2-phenylethyl)-1,3-benzoxazoles (**3**), 2-(2-Hydroxy-2-phenylethyl)-1,3-benzothiazoles (**4**), 2-Styryl-1,3-benzoxazoles (**5**), and 2-Styryl-1,3-benzothiazoles (**6**) from Benzazoles (**1**, **2**) and Benzaldehydes by Claisen Addition or direct Condensation, respectively

	Y	R	Compound	Reaction Solvent	Reaction Time [h]	Yield [%]	m.p.	Brutto formula[a]	Compound	Yield [%] 2 h/24 h reaction time	m.p.	Lit. m.p.	Lit.
a	O	H	**3**	DMSO	24	60	160–161°		**5**	45/58	81–82°	82°	6
b	O	2-Cl	**3**	HMPT	24	11	133–134°	$C_{15}H_{12}ClNO_2$ (273.6)	**5**	62/64	106–107°	106–107°	3
c	O	4-Cl	**3**	DMSO	24	67	172–174°	$C_{15}H_{12}ClNO_2$ (273.6)	**5**	54/62	148–150°	144–145°	2
d	O	2-CH_3	**3**	DMSO	24	14	114–116°	$C_{16}H_{15}NO_2$ (253.3)	**5**	38/57	49–51°	49–51°	3
e	O	4-CH_3	**3**	DMF	2	17	133–134°		**5**	50/53	130–132°	131–132°	2
f	O	4-OCH_3	**3**	DMF	2	7	150–152°	$C_{16}H_{15}NO_3$ (269.3)	**5**	72/78	136–137°	136–137°	2
g	O	4-$N(CH_3)_2$							**5**	14/43	174–176°	170–172°	2
a	S	H	**4**	DMSO	24	65	155–156°		**6**	84/98	111–112°	112°	1
b	S	2-Cl	**4**	DMSO	24	12	167–168°	$C_{15}H_{12}ClNOS$ (289.8)	**6**	66/92	100–101°	100–101°	3
c	S	4-Cl	**4**	DMF	2	20	165–166°	$C_{15}H_{12}ClNOS$ (289.8)	**6**	81/86	176–178°	176–178°	3
d	S	2-CH_3	**4**	DMF	2	25	128–130°	$C_{16}H_{15}NOS$ (269.4)	**6**	26/84	62–63°	62–63°	3
e	S	4-CH_3	**4**	DMF	2	20	131–132°		**6**	56/56[b]	140–142°	142–143°	4
f	S	4-OCH_3	**4**	HMPT	24	63	166–167°	$C_{16}H_{15}NO_2S$ (285.4)	**6**	96/99	144–145°	144–145°	1
g	S	4-$N(CH_3)_2$							**6**	46/71	202–204°	206–208°	5

[a] Satisfactory elemental analyses and I.R. spectra were obtained for all compounds.
[b] Yield of crude product: 96%.

or hexamethylphosphoric triamide (4 ml). The mixture is allowed to stand at room temperature for 2–24 h. Water (100 ml) is then added, the resultant precipitate isolated by filtration, and recrystallized from ethanol.

Preparation of 2-Styryl-1,3-benzoxazoles (5) and -1,3-benzothiazoles (6); General Procedure:
Aqueous sodium hydroxide (50% solution, 3 ml, 37.5 mmol) is added to the solution of the benzazole (**1**, **2**; 10 mmol) and the aldehyde (10 mmol) in dimethyl sulfoxide (10 ml). The mixture is allowed to stand at room temperature for 2–24 h. Then, water (100 ml) is added, the crystalline product is isolated by filtration, washed with water, and recrystallized from ethanol.

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