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SYNTHESIS OF 2-SUBSTITUTED 3-METHYLBENZOTHIAZOLINES BY THE REACTION OF 3-METHYLBENZOTHIAZOLIUM IODIDE WITH GRIGNARD REAGENTS

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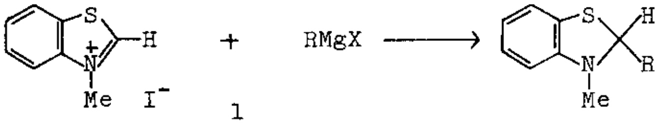
2-Substituted 3-methylbenzothiazolines (2) were prepared by the reaction of 3-methylbenzothiazolium iodide (1) with Grignard reagents in high yields.

Benzothiazolines have been synthesized by condensation of o-aminothiophenol with carbonyl compounds.[1] We report here versatile synthesis of 2-substituted 3-methylbenzothiazolines by the reaction of easily obtainable 3-methylbenzothiazolium iodide (1) with Grignard reagents.



1

2

A typical example is shown below (Method B): An ethereal solution (50 ml) of phenylmagnesium bromide prepared from bromobenzene (24.0 mmol) and magnesium turnings (24.4 mmol) was filtered through a teflon tube fitted with glass wool and added to a suspension of **1** (19.9 mmol) in benzene (40 ml) and ether (30 ml) at -40 °C under nitrogen with stirring. The temperature was allowed to rise to -20 °C and kept there, during which almost all the reaction ended. Then stirring was continued until the temperature of the solution came up to room temperature. The solution was treated as usual, and after evaporation of the solvent, the residue was recrystallized from ethanol-n-hexane (1:1) to give 3-methyl-2-phenylbenzothiazoline (**2c**, 14.3 mmol, 72%, mp 113.0-115.0 °C).

The results are shown in Table 1. If the reaction is carried out in the presence of excess magnesium at room temperature (Method A), considerable amount of red tarry material is produced and separation of pure products becomes laborious. Therefore, it is recommended to carry out the reaction in the absence of excess magnesium and at low temperature (ca. -20 °C) (Method B).

In the preparation of **2e**, bis-3-methyl-2,3-dihydrobenzothiazol-2-yl was obtained in about 20% yield as a by-product (Method A). This was deemed to be due to reduction of **1** by excess magnesium and magnesium halide under the reaction condition. Therefore, Method B should be generally used to

Table 1 The Yield of 2-Substituted 3-Methylbenzothiazolines (2) and Their NMR Data (δ from TMS in $CDCl_3$)

2	RX	Method	Yield (%)	mp [°C] or bp (°C/mmHg)	δ N-Me	δ and J^4 2-C-H		
a)	p-$MeOC_6H_4Br$	A	34	[106.5-108.5]	2.58	5.94 (s)		
b)	p-MeC_6H_4Br	A	66	[85.7-88.7]	2.64	5.99 (s)		
		B	68					
c)	PhBr	A	60	[113-115]	2.59	5.96 (s)		
		B	72					
d)	p-ClC_6H_4Br	A	55	[76.8-78.9]	2.65	5.99 (s)		
e)	MeI	A	35	(68-69/0.16)	2.57	4.96 (q)	J_{H-Me}	6.0
		B	67					
f)	n-BuCl	A	42	(97-98/0.20)	2.80	5.01 (q)	J_{AB}	5.1
							J_{AC}	6.3
g)	$PhCH_2Cl$	A	88	(152-154/0.20)	2.61	5.07 (q)	J_{AB}	4.8
							J_{AC}	9.0
h)	p-ClC_6H_4Cl	B	88	[74.4-76.5]	2.84	5.12 (q)	J_{AB}	4.5
							J_{AC}	8.7

give better yields of the products (2).

In the cases of benzylmagnesium chlorides, products were obtained in high yields irrespective of the presence or the absence of excess magnesium.

Based on the knowledge that the thiazolium salt (1) gives the corresponding carbene by base induced elimination,[2] this preparative method of 2 with Grignard reagents is unique and versatile for its facile procedure and high yields, although there has been one such example offered by French chemists.[3]

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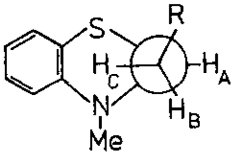
4 

The conformation of 2f-2h on the 2-C can be shown as depicted. J_{AB} and J_{AC} correspond to the coupling constants of protons as shown in the figure.

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