BEHAVIOR OF THE ACTIVE ALDEHYDE GENERATED FROM THIAMINE AND ITS DERIVATIVES

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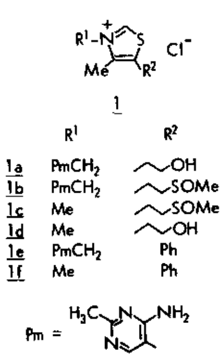
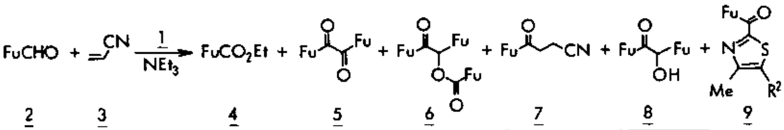
Methylsulfinylmethylthiamine (MSIT, 1b) was prepared as a sulfur derivative of thiamine (1a) and its chemical reactivity was investigated.[1] As an extension of this work, we studied the reactivity of the active aldehyde produced by the reaction of 1 or its related compounds with base (NEt_3) in EtOH or MeCN in the presence of aldehyde (2-furaldehyde, 2) and Michael acceptor (acrylonitrile, 3). The results are shown in Scheme I.

Scheme I





Run	Solv.	1	Cond.[a]	Yield (%)[b] 4	5	6	7	8	9
1	EtOH	1a	↑↓, 2 h		3			23	10
2	EtOH	1b	↑↓, 2 h		5			21	
3	MeCN	1b	rt, 24 h[c]						
4	MeCN	1c	↑↓, 4 h			28	14		
5	MeCN	1d	↑↓, 4 h			17	28		
6	EtOH	1c	↑↓, 2 h	13	2	2	30	13	
7	EtOH	1d	↑↓, 2 h	3			46	6	
8	EtOH	1e	↑↓, 2 h				5	10	8
9	EtOH	1f	↑↓, 2 h	10			48		

[a] Molar ratio of the reactants 2:3:1=5:6:1. [b] Based on 2. [c] Slow reaction.

Reaction in EtOH was faster than in MeCN. Ester 6 was obtained only in MeCN with thiazolium salts 1c,d. Substituent R^1 of 1 had an marked effect on the reactivity of the active aldehyde. Thiamine derivatives (1a,b) underwent only acyloin condensation yielding 5 and 8 with almost no isolation of ester 4 in EtOH. Acylthiazole was produced in about 50% yield based on 1, which was formed via base induced fragmentation of the active aldehyde. On the other hand, with thiazolium salts bearing N-Me group, reaction in EtOH gave predominantly Michael-Stetter product (7) and acyloin product (8) was a minor product, while in MeCN, 1c,d,f catalyzed the both reactions giving a mixture of 7 and 6 (instead of 8). Furthermore, the reaction using 1c,d,f was always accompanied by the formation of ester 4 or 6, which indicated the alcoholysis of the active aldehyde.

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(1) K.Hirai, T.Ishiba, H.Sugimoto, T.Takahashi, and K.Inazu, Chem. Pharm. Bull., 26, 3675 (1978).