

Solid Phase Synthesis of 4H-Pyrimido[2,1-b] Benzothiazol-4-ones from Resin-Bound Cyclic Malonic Ester

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Abstract: The solid phase synthesis of 4H-pyrimido[2,1-b] benzothiazol-4-ones has been reported.

Keywords: 4H-pyrimido[2,1-b]benzothiazol-4-ones, Meldrum's acid, solid phase synthesis.

There has been enormous interest in combinatorial and parallel synthesis in the last decade using solid phase methodology¹. With the successful synthesis of 4(1H)quinolones from resin-bound cyclic malonic ester², we attempted to carry out the solid phase synthesis of 4H-pyrimido[2, 1-b] benzothiazol-4-ones (**Scheme 1**). These compounds were successfully prepared *via* solution-phase synthesis by our group³ and others⁴. We used the 2-aminobenzothiazole or 2-amino-4-methyl-thiazole as doubly nucleophilic reagents. When the cyclic malonic ester resin **1** was converted to the resin **2**, the carbonyl peak in IR shifted to 1730 cm⁻¹ and 1670 cm⁻¹. Also a new peak appeared at 1615 cm⁻¹ (C=C) compared with resin **1**. The resin **2** was cleaved by thermal cyclization to form the heterocyclic compounds **3**. The yields and purities of **3** were listed in **Table 1**.

We treated the resin **3** (500 mg, 1.20 mmol/g) with triethyl orthoformate (5 mL) and 2-amino benzothiazole (6 mmol) to obtain the resin-bound amine methylene cyclic malonic ester **4**. Then the resin **4** was heated in oil-bath at 240°C for 20 minutes under N₂ atmosphere. The resin was washed with EtOH/acetone completely. The products generally do not require purification and show good purity (>95%) by ¹H NMR (**Table 1**).

This is also a novel traceless cleavage strategy to prepare 4H-pyrimido[2, 1-b] benzothiazol-4-ones. The resin **4** can be reused to prepare the resin **1**².

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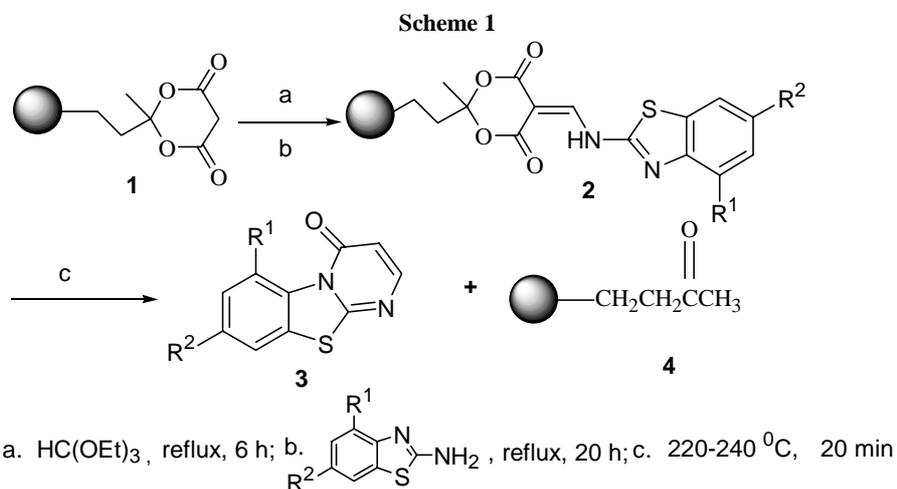


Table 2 Yields and purities of 4H-pyrimido[2,1-b] benzothiazol-4-ones 3a-f

Entry	Product	R ¹	R ²	Yield(%) ^a	Purity(%) ^b
1	3a	H	CH ₃ O	72	>95
2	3b	H	CH ₃	82	>95
3	3c	CH ₃	H	77	>95
4	3d	H	H	86	>95
5	3e	H	Cl	81	>95
6	3f	H	Br	77	>95

a. The crude yields are based on the loading of the cyclic malonic ester resin 11. b determined by ¹H NMR.

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