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## Resin-bound Isothiocyanates and their Synthetic Equivalents as Intermediates for the Solid-Phase Synthesis of Substituted Thiophenes

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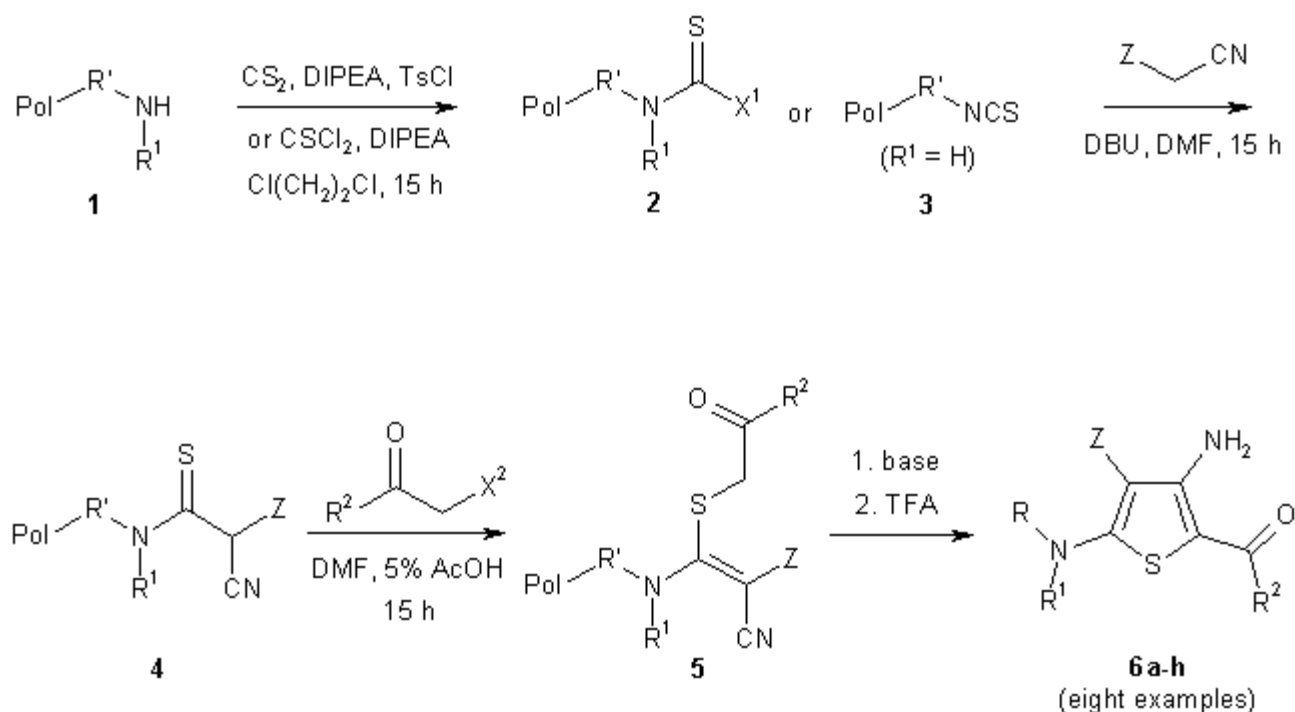
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**Abstract:** Highly reactive, polystyrene-bound thiocarbamoyl chlorides and isothiocyanates have been used as key intermediates in a new, robust solid-phase synthesis of substituted thiophenes.

**Keywords:** solid-phase synthesis, thiophenes, combinatorial chemistry.

The development of new synthetic methodology for the automated solid-phase synthesis of small heterocyclic compounds continues to be a major focus in chemical research. We recently reported a solid-phase protocol for the preparation of 3-aminothiophenes and 2-methylenethiazoles.[1] In this synthesis a resin-bound cyanoacetamide was reacted with isothiocyanates under basic conditions. The resulting thioamides were then alkylated at sulfur with aromatic haloketones to give methylenethiazoles. These could be directly cleaved from the support or cyclized to 3-aminothiophenes by treatment with DBU.[1] In order to further exploit this powerful synthetic sequence, we considered to utilize resin-bound, amine-derived isothiocyanates or their synthetic equivalents as key intermediates. This was achieved with very satisfactory results in the way sketched below.[2]



Pol: polystyrene with Wang linker; DIPEA: diisopropylethylamine; Ts: tosyl; X1: Cl, S-Ts; X2: Cl, Br; Z = electron withdrawing group; TFA: trifluoroacetic acid

[1] F. Zaragoza, Tetrahedron Lett. 1996, 37, 6213-6216.

[2] F. Zaragoza, J. Org. Chem. 1997, in press.

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## Comments

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