Supplementary materials

The mechanism of action of 5-nitrothiophenes against *Mycobacterium tuberculosis*

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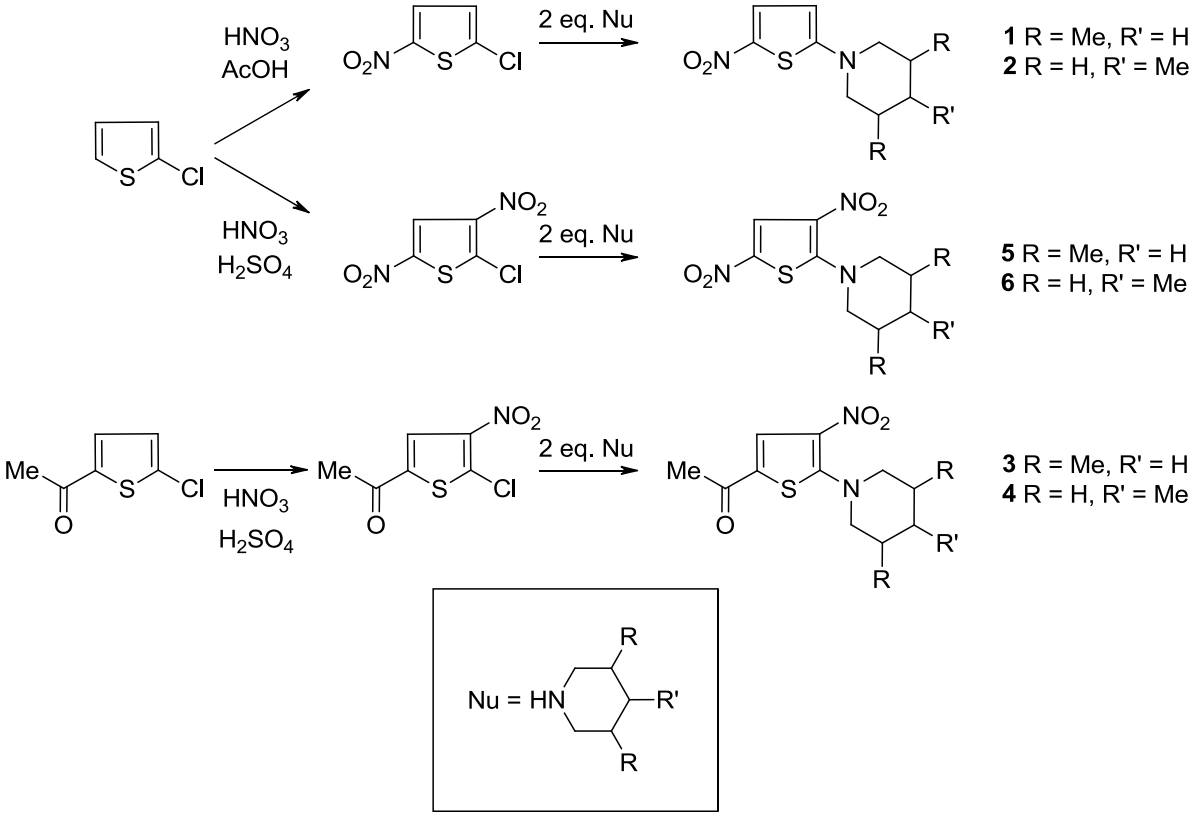
Synthesis of nitrothiophenes

Figure S1. Synthetic route for the synthesis of compounds **1-6**



Synthesis of compounds **1**, **2**, **5** and **6** was performed by sequential conversion of 2-chlorothiophene. Treatment of 2-chlorothiophene with nitric acid in acetic acid resulted in formation of 2-nitro-5-chlorothiophene while the same reaction performed in sulfuric acid generated 2,4-dinitro-5-chlorothiophene. These nitro-chlorothiophenes were treated with two equivalents of 4-methyl-piperidines or 3,5-dimethyl-piperidines in *N,N*-dimethylformamide. The reaction mixture was diluted with water and the resultant precipitate (product) collected by filtration. Compounds **3** and **4** were synthesized similarly starting from 2-acetyl-5-chlorothiophene. All compounds were purified by crystallization from ethanol. Analytical data are presented in Table S1 and the purity of all compounds was >96%.

Table S1. Nitrothiophene analytical data

Cmpd #	Yield, %	mp (^{o}C)	Real mass *	^{1}H NMR (DMSO-d_6), ppm
1	86	167-169	240	7.81 (1H, d, H), 5.73 (1H, d, H), 3.44 and 2.48 (2 m, 4H, N($\underline{CH_2}$)$_2$), 1.97 (2H, m, 2CH), 1.20 (2H, m, CH_2), 0.88 (6H, broad d, 2$\underline{CH_3}$)
2	72	105-108	226	7.73 (1H, d, H), 5.81 (1H, d, H), 3.21 (m, 4H, N($\underline{CH_2}$)$_2$), 1.53 (5H, broad m, CH_2-CH-CH_2), 0.95 (3H, s, CH_3)
3	81	71-75	282	8.08 (1H, s, H), 3.87 and 2.92 (2 m, 4H, N($\underline{CH_2}$)$_2$), 2.42 (3H, s, $COCH_3$), 1.95 (2H, m, 2CH), 1.22 (2H, m, CH_2), 0.90 (6H, broad d, 2$\underline{CH_3}$)
4	94	64-68	268	8.09 (1H, s, H), 3.63 (m, 4H, N($\underline{CH_2}$)$_2$), 2.41 (3H, s, $COCH_3$), 1.51 (5H, broad m, CH_2-CH-CH_2), 0.95 (3H, s, CH_3)
5	78	153-155	285	8.30 (1H, s, H), 3.87 and 2.91 (2 m, 4H, N($\underline{CH_2}$)$_2$), 1.92 (2H, m, 2CH), 1.15 (2H, m, CH_2), 0.89 (6H, broad d, 2$\underline{CH_3}$)
6	83	136-137	271	8.22 (1H, s, H), 3.68 (m, 4H, N($\underline{CH_2}$)$_2$), 1.58 (5H, broad m, CH_2-CH-CH_2), 0.96 (3H, s, CH_3)

* Determined using Finnigan SSQ-710