SYNTHESIS AND REACTIONS OF THIOPHENE ANALOGS OF CHALCONE

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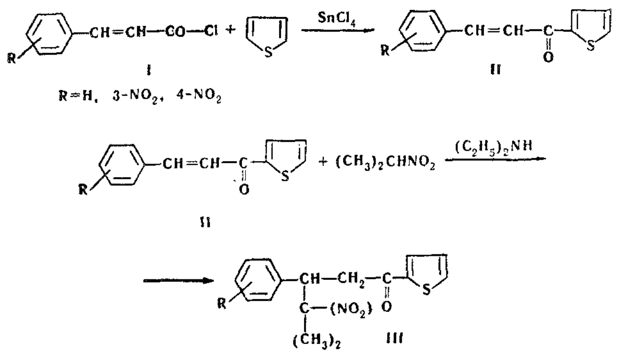
A method of synthesizing thiophene analogs of chalcone is described. It is based on condensation of chlorides of α, β-unsaturated acids with thiophene in the presence of an equimolecular amount of $SnCl_4$ in benzene or toluene solution. Addition of 2-nitropropane at the active double bond of the thiophene analogs of chalcone gives γ-nitroketones.

α,β-Unsaturated ketones containing benzene and thiophene rings, are prepared by various methods. Crotonaldehyde-type condensation [1,2] of 2-acetothienone, thiophene-2-aldehyde, and 2-thienylacrolein with benzaldehyde, acetophenone, and their homologs, in the presence of acid or alkaline catalysts finds extensive application. They can be obtained by condensing aryl-β-chlorovinyl ketones with thiophene and its homologs [3]. Also known is a method of preparing these compounds by the Friedel-Crafts reaction, involving condensing chlorides of α,β-unsaturated acids with thiophene [4] in the presence of anhydrous aluminum chloride catalyst, in dimethylsulfate or carbon disulfide solution. However this reaction is attended by extensive complications [1] (resinification, isomerization, etc), so that the yields of end products are low.

The present paper gives data regarding the synthesis of thiophene analogs of chalcone [5] (II), by condensing chlorides of α,β-acids (I) with thiophene in the presence of (acting as a condensing agent) equimolecular amounts of anhydrous stannic chloride, dissolved in dry benzene, toluene, or xylene, at temperatures close to 0° (in the range −10° to +10°). Reaction of thiophene analogs of chalcone with 2-nitro propane in the presence of diethylamine gives good yields of the corresponding γ-nitro ketones (III).



EXPERIMENTAL

α-Thienylstyryl ketone. 7.8 g (0.03 mole) $SnCl_4$ was added dropwise, with good stirring and cooling (ice-salt), to 5 g (0.03 mole) cinnamyl chloride and 2.52 g (0.03 mole) thiophene in 100 ml dry toluene or benzene. The mixture was stirred for half an hour, then 50 ml ether and 50 ml water added. The organic layer was separated off, washed with 5% Na_2CO_3 solution until all the tin was removed, then dried over $CaCl_2$. The solvent was distilled off, and the residue crystallized on cooling. Yellowish needles, mp 80° (ex petrol ether). The literature [6] gives mp 80° (ex petrol ether). Yield 5.5 g (86%).

2-Methyl-2-nitro-3-phenyl-5-(α-thienyl)pentan-5-one. Prepared by heating a mixture of 0.3 g (0.0014 mole) α-thienylstyryl ketone, 0.2 g (0.0022 mole) 2-nitropropane, and 0.1 ml Et_2NH on a steam bath for 2.5 hr. After distilling off the excess 2-nitropropane and Et_2NH, addition of 0.5 ml EtOH caused the substance to crystallize; white needles, mp 110–111° (ex EtOH). Yield 0.31 g (90%). Found: C 63.25; 62.98; H 5.47; 5.40; S 10.22; 10.16; N 4.53; 4.60%, calculated for $C_{16}H_{17}NO_3S$: C 63.36; H 5.61; S 10.56; N 4.62%.

3-(α-Thienyl)-1-(m-nitrophenyl)prop-1-en-3-one. Prepared from 5 g (0.023 mole) p-nitrocinnamyl chloride, 1.93 g (0.023 mole) thiophene, and 6 g (0.023 mole) $SnCl_4$ in 50 ml dry toluene. Colorless crystals mp 145° (ex EtOH). Yield 4.1 g (67%). Found: C 60.38; 60.50; H 3.44; 3.65; S 12.00; 12.26; N 5.78%, calculated for $C_{13}H_9NO_3S$: C 60.23; H 3.47; S 12.35; N 5.40%.

3-(α-Thienyl)-1-(p-nitrophenyl)prop-1-en-3-one. Prepared from 10 g p-nitrocinnamyl chloride, 3.86 g (0.046 mole) thiophene, and 12 g (0.046 mole) $SnCl_4$ in 100 ml toluene. Colorless crystals mp 220° (ex benzene), yield 8.8 g (72%), the literature [1] gives mp 220°.

2-Methyl-2-nitro-3-(p-nitrophenyl)-5-(α-thienyl)pentan-5-one. Prepared from 0.3 g (0.001 mole) 3-(α-thienyl)-1-(p-nitrophenyl)prop-1-en-3-one, 0.2 g (0.002 mole) 2-nitropropane, and 0.2 ml Et_2NH. White crystals, mp 151° (ex EtOH), yield 0.34 g (85%). Found: C 55.48; 55.13; H 4.65; 4.58; S 8.57; 8.52%, calculated for: $C_{16}H_{16}N_2O_5S$: C 55.17; H 4.89; S 9.19%.

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