SHORT PAPER

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Microwave assisted Willgerodt-Kindler reaction of styrenes[†]

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Styrenes are efficiently transformed to thioamides *via* the Willgerodt-Kindler reaction under microwave irradiation.

The classical Willgerodt reaction involves heating an aryl alkyl ketone with ammonium polysulfide in a sealed vessel and results in formation of a thioamide with the same number of carbon atoms.[1,2] Reaction times of several hours are common and high pressure is caused by H_2S formation. The operational pressure difficulties could be eliminated by the Kindler modification of the reaction, *i.e.* performing the reaction in a primary or secondary amine at atmospheric pressure under reflux.[3] The reaction times are still of the order of hours. Morpholine, a cheap and readily available secondary amine, is found to be most suitable. The Willgerodt reaction and the modified Kindler form has been extended from the original alkyl aryl ketone to many functional groups such as aldehydes, unsaturated hydrocarbons, amines, imines, epoxides and alcohols.[1] Recently, we and others showed the efficiency of microwave dielectric heating and especially the focused monomode system for the Willgerodt–Kindler reaction of aldehydes and ketones in dry media, compare to conventional heating.[4] In continuation of our increased interest in microwave promoted organic reactions,[5] we now report the microwave assisted Willgerodt-Kindler reaction of styrenes, which, to the best of our knowledge has not been studied previously. In the classical Willgerodt-Kindler reaction of styrenes harsh reaction conditions (high temperature about 160ºC and long reflux times around 4–6 hours) are required.[6] We found that this reaction could be performed in about 8 minutes under microwave irradiation. The reaction conditions were optimized by examination of different parameters such as time of irradiation and the ratio of sulfur to morpholine and styrene. After performing several experiments the optimum molar ratio of styrene: sulfur: morpholine was found to be 1:2.5:2. In a typical procedure, styrene (0.01 mol), sulfur (0.25 mol) and morpholine (0.02 mol) were mixed in a Teflon flask (~20 ml) and irradiated for about 8 minutes. After conventional work-up, the thiomorpholide was isolated in good yields. Table 1 shows our results. Phenylacetylene gave better yield than the parent styrene (Table 1 entry 6). Comparing our results with those reported by conventional heating reveals the advantage of microwave irradiation especially the focused monomode system, which we have developed in our laboratory.[7] Interestingly, the thioamides obtained could be hydrolysed with excellent yields (> 85%) to their corresponding carboxylic acids in 15% NaOH solution under microwave irradiation in one minute. The spectroscopic data of the carboxylic acids were compared to those of authentic samples.[4a] In conclusion, we have developed a simple, rapid and convenient method for the transformation of styrenes to thioamides *via* Willgerodt–Kindler reaction under microwave irradiation.

Experimental

Starting materials (styrenes) were either commercially available or prepared from corresponding aryl methyl ketone in two steps by modified known methods.[9] ^{1}H NMR spectra were recorded on a Bruker FT-80 AC spectrometer. Mass spectra were obtained on a Fisson 800 Trio GC–MS with an ionizing voltage of 70 eV. IR spectra were performed on a Mattson 1000 spectrometer. Melting points were determined on a Mettler FPS and are uncorrected.

General procedure for Willgerodt-Kindler reaction of styrenes: A mixture of styrene (0.01 mol), sulfur (0.025 mol) and morpholine (0.02 mol) in a Teflon flask (~20 ml) was subjected to microwave irradiation for given time (Table 1). The cooled reaction mixture was taken up in chloroform, after filtration was washed successively with water and dilute hydrochloric acid to remove the excess of morpholine. The solvent was removed under vacuum and the residue was recrystallized from aqueous methanol or ethanol.

Spectroscopic data for compound 3*:* m.p. 104–106°C (lit. 105–105°C); [8f] IR (KBr) u_{max}/cm^{-1} 2869, 2853, 1500, 1435, 1261, 1192, 1115, 1038, 969; ^{1}H NMR (80 MHz, $CDCl_3$) d_{ppm} 7 (bs, 4H), 4.1 (m, 4H), 3.37 (m, 4H), 3.2 (m, 2H), 2.15 (s, 3H); MS (70 eV) *m/z* (rel. int. %) 235 (M^+, 87), 202 (26), 148 (43), 130 (100), 112 (21), 105 (63), 86 (66), 77 (23).

General procedure for hydrolysis of thiomorpholides: Thiomorpholide (0.01 mol) was mixed with ~5 ml of NaOH (15%) in a Teflon flask (~20 ml) and exposed to microwave irradiation for 1 minute. After cooling, the reaction mixture was made acidic with HCl (10%), the crude acid was filtered and recrystallised from acetic acid and/or a mixture of ethanol and water.

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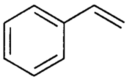
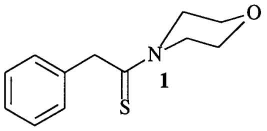
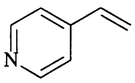
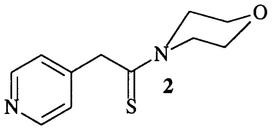
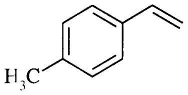
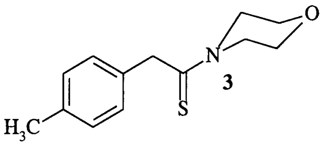
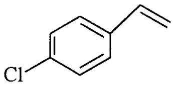
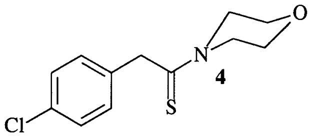
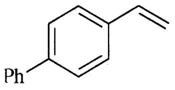
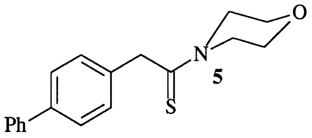
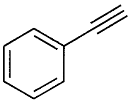
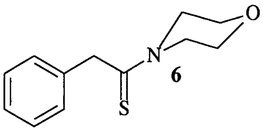
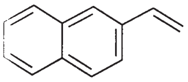
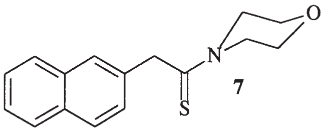
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Willgerodt–Kindler reaction of styrenes under microwave heating

Entry	Substrate	Product[c]	% Yield[a] time (min.)	m.p.(°C) Found	Literature
1		 1	63 (8)[b]	77–79	79–80
2		 2	75 (7)	103–105	104–105.5
3		 3	59 (12)	104–106	105–106
4		 4	68 (10)	94–97	96–97
5		 5	74 (10)	141–144	142–143
6		 6	72 (8)	77–19	79–80
7		 7	82 (10	98–102	102–108

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[a] All yields refer to isolated products. [b] Ref. 8a (52% yield after 6.5h reflux). [c] All products were characterized by m.p., IR, 1H NMR, and their physical data were similar to those reported in the literature.[8]