

## ULTRASOUND-ACCELERATED SYNTHESIS OF FERROCENE-CONTAINING PYRIMIDINE DERIVATIVES

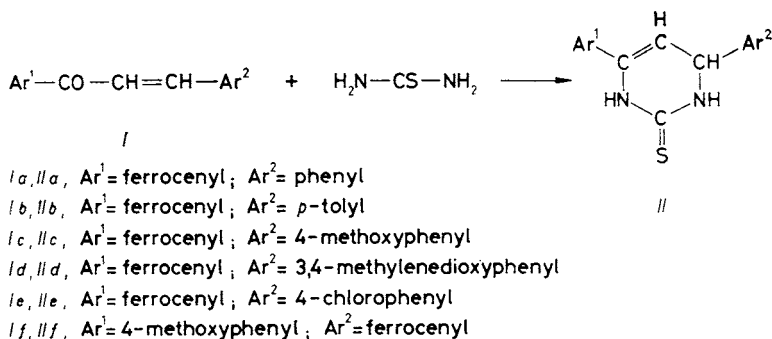
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The base-catalyzed addition of thiourea to ferrocene analogues of chalcones is faster and more selective when the reaction mixture is sonicated than when merely heated. 4-Aryl-6-ferrocenyl- and 6-aryl-4-ferrocenyl-3,4-dihydropyrimidine-2(1*H*)-thiones were isolated in 58–79% yields.

The synthesis and reactivity of various heterocyclic ferrocene derivatives, in which the heterocyclic ring is bonded or annelated to the ferrocene cyclopentadienyl ring, have so far received little attention. The aim of our present work has been to investigate the possible synthesis of ferrocene-containing pyrimidine derivatives by addition of thiourea to arylferrocenylpropenones (Scheme 1).



SCHEME 1

Our first experiments were carried out under conditions analogous to those described by Al-Hajjar and co-workers<sup>1</sup>. Heating the reaction components to 60–70°C for 3–5 h afforded a mixture which could not be separated because chromatography on silica gel or alumina was accompanied by decomposition of some products. Since it is known that ultrasound accelerates many heterogeneous as well as homogeneous reactions<sup>2</sup>, we tried sonication also in this synthesis. We have found that with sonication the desired products are obtained in 58–79% yields; thanks to their

insolubility they precipitated from the reaction mixture whereas the starting compounds and side products remained in solution.

Ethanol proved to be the solvent of choice and sodium ethoxide was found to be the best catalyst. Reactions performed with sodium hydroxide as catalyst afforded only minor quantities of the desired products. Experiments carried out without any catalyst in ethanol, or with potassium carbonate or sodium hydroxide as catalysts in the presence of 18-crown-6 as a co-catalyst in dioxane, gave no desired products. Attempts to add thiourea to 3-thienyl- or 3-furyl-1-ferrocenylpropenone, or urea or phenylthiourea to cinnamoylferrocene, were unsuccessful.

In the reaction of thiourea with *m*- or *p*-nitrocinnamoylferrocene, sonication as well as mere heating gave a mixture of products which could not be purified and identified.

The addition of thiourea to 1,3-diphenylpropenone was not markedly affected by ultrasound, being complete after 30 min with or without sonication. This can be explained by the much higher (two orders of magnitude) reactivity of 1,3-diphenylpropenone than its ferrocene analogue, *i.e.* 1-ferrocenyl-3-phenylpropenone (cinnamoylferrocene), towards nucleophiles<sup>3</sup>.

TABLE I  
Physical constants, yields and analytical data for 4,6-diaryl-3,4-dihydropyrimidine-2(1*H*)-thiones

Compound	Formula Mol. w.	M.p., °C	Reaction time, h Yield, %	Calculated/found			
				% C	% H	% N	% Fe
<i>Ila</i>	C <sub>20</sub> H <sub>18</sub> FeN <sub>2</sub> S 374.3	196–199	3.5	64.18	4.85	7.48	14.92
			79	63.90	4.76	7.27	14.86
<i>Ilb</i>	C <sub>21</sub> H <sub>20</sub> FeN <sub>2</sub> S 388.3	205–209	4.0	64.96	5.19	7.21	14.38
			58	65.04	5.21	7.22	14.63
<i>Ilc</i>	C <sub>21</sub> H <sub>20</sub> FeN <sub>2</sub> OS 404.3	198–202	10.0	62.38	4.99	6.93	13.81
			77	62.38	4.86	6.88	13.86
<i>Ild</i>	C <sub>21</sub> H <sub>18</sub> FeN <sub>2</sub> O <sub>2</sub> S 418.3	224–226	11.0	60.30	4.34	6.70	13.35
			79	60.22	4.42	6.71	13.18
<i>Ile</i>	C <sub>20</sub> H <sub>17</sub> ClFeN <sub>2</sub> S 408.7	196–203	7.0	58.77	4.19	6.85	13.66
			76	58.51	4.18	6.73	13.52
<i>Ilf</i>	C <sub>21</sub> H <sub>20</sub> FeN <sub>2</sub> OS 404.3	197–201	10.0	62.38	4.99	6.93	13.81
			75	61.82	4.89	6.49	13.62

## EXPERIMENTAL

The starting arylferrocenylpropenones were prepared by base-catalysed condensation of substituted benzaldehydes with acetylferrocene, or of *p*-methoxyacetophenone with ferrocenecarbaldehyde, according to ref.<sup>4</sup>.

Melting points were determined on a Kofler block and are uncorrected. <sup>1</sup>H NMR spectra were taken on a Tesla BS 487 (80 MHz) spectrometer in deuteriochloroform or hexadeuterio-dimethyl sulfoxide with tetramethylsilane and hexamethyldisiloxane as the respective internal standards. Ultrasound was generated by a 4 litre ultrasonic cleaning bath Tesla UG 160/320 TA (25 KHz, 160 W).

Preparation of 4-Aryl-6-ferrocenyl- and 6-Aryl-4-ferrocenyl-  
-3,4-dihydropyrimidine-2(1*H*)-thiones (*Ila*—*Ilf*)

Thiourea (0.76 g; 10 mmol) and the arylferrocenylpropenone (2 mmol) were added to a solution of sodium ethoxide prepared from sodium (0.46 g; 20 mmol) and anhydrous ethanol (60 ml). The flask with the reaction mixture was immersed into an ultrasonic cleaning bath filled with water and the reaction was monitored by thin-layer chromatography. The bath temperature rose

TABLE II  
Proton magnetic resonance data for 4,6-diaryl-3,4-dihydropyrimidine-2(1*H*)-thiones

Compound	CH <sub>3</sub> ; CH <sub>2</sub>	C <sub>5</sub> H <sub>5</sub> H <sub>β</sub> H <sub>α</sub>	=CH—CH—	Ar
<i>Ila</i>	—	4.10 (bs, 5 H) 4.22 (t, 2 H) 4.73 (t, 2 H)	4.90 (d, 1 H) 5.25 (d, 1 H)	7.31 (bs, 5 H)
<i>Ilb</i>	2.26 (s, 3 H)	4.12 (bs, 5 H) 4.22 (t, 2 H) 4.73 (t, 2 H)	4.86 (d, 1 H) 5.17 (d, 1 H)	7.16 (bs, 4 H)
<i>Ilc</i>	3.69 (s, 3 H)	4.12 (bs, 5 H) 4.21 (t, 2 H) 4.73 (t, 2 H)	4.81 (d, 1 H) 5.18 (d, 1 H)	6.89 (d, 2 H) 7.18 (d, 2 H)
<i>Ild</i>	5.94 (rs, 2 H)	4.11 (bs, 5 H) 4.21 (t, 2 H) 4.72 (t, 2 H)	4.81 (d, 1 H) 5.18 (d, 1 H)	6.80 (bs, 3 H)
<i>Ile</i>	—	4.11 (bs, 5 H) 4.22 (t, 2 H) 4.74 (t, 2 H)	4.95 (d, 1 H) 5.22 (d, 1 H)	7.35 (m, 4 H)
<i>Ilf</i>	3.71 (s, 3 H)	4.0—4.30 (m, 9 H)	4.79 (d, 1 H) 5.28 (d, 1 H)	6.93 (d, 2 H) 7.45 (d, 2 H)

to 50°C during 0.5 h and then was constant throughout the whole reaction period. Sonication was stopped when the concentration of the starting material no more decreased.

The reaction mixture was concentrated on a rotatory evaporator *in vacuo* (maximum bath temperature 40°C) to 40 ml and set aside in the dark at room temperature. After standing for 24 h, the product was collected on a filter, washed with dilute ethanol and water, and crystallized from a dimethylformamide–water mixture at temperatures not exceeding 50°C. The experimental results are summarized in Table I, <sup>1</sup>H NMR spectra of the products are given in Table II.

The mother liquor after filtration of the reaction mixture was poured into water and the organic material was taken up in dichloromethane. After drying over sodium sulfate and filtration, the solvent was distilled off and the residue chromatographed on a column of silica gel, using a mixture of benzene–ethyl acetate (95 : 5 to 85 : 15) as eluant. Five bands were observed of which one corresponded to the starting compound and another to the principal product. The remaining minor components were not sufficiently pure to allow identification.

#### Attempted Addition of Thiourea to Cinnamoylferrocene

Thiourea (0.3 g; 4 mmol) and cinnamoylferrocene (3 mmol) were added to a solution of sodium ethoxide prepared from sodium (0.2 g; 9 mmol) and anhydrous ethanol (25 ml). After refluxing for 3–5 h, the solvent was removed on a rotatory evaporator. The residue was washed with water, dried and chromatographed on a column of silica gel in benzene–ethyl acetate (95 : 5 to 85 : 15). Of the seven bands observed, the third gave 3–10% of the starting cinnamoylferrocene, the fourth 10–15% of the main product. Small amounts of the orange or dark-violet compounds, obtained from the other bands, were not pure enough to allow identification.

#### REFERENCES

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