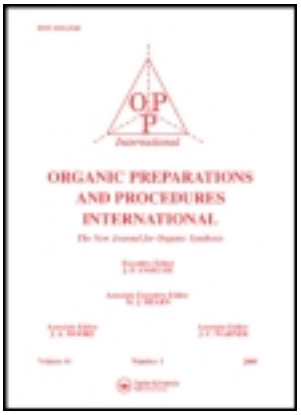

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Improved Preparation of 2,4-Thiazolidinedione

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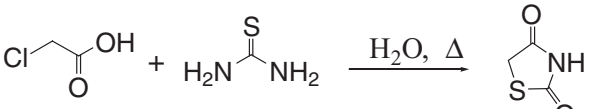
The widely utilized industrial product 2,4-thiazolidinedione (**3**) has been chosen as the starting material for our ongoing research on *rosiglitazone*,[1] which is a selective PPAR-γ receptor inhibitor for the treatment of type-II diabetes.[2] Based on the literature[3] and our own experience, we developed an efficient one-step method to obtain **3** using conc. hydrochloric acid.[4] This improved synthesis seemed to be much better than the previous methods,[3] all of which shared the disadvantage that the strongly acidic waste from the reaction and solvents from the recrystallization process have to be disposed of without harm to the environment.

In order to alleviate these problems, we decreased the amount of hydrochloric acid and our results show that the yield of **3** is still acceptable while the concentration of HCl has been decreased by more than one half (*Table 1*). This result encouraged us to do further research,[5] which resulted in a green and inexpensive method to prepare **3**. Herein, we report this economic and environmentally friendly synthesis of **3**, starting from chloroacetic acid (**1**) and thiourea (**2**) using water as the solvent for the preparation as well as the recrystallization process.



1 **2** **3**

Experimental Section

Melting points were taken on a WRS-1 digital melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet FI-IR 360 Spectrophotometer. ^{1}H NMR spectra were obtained on a Bruker AM 400 (400 MHz) spectrometer with TMS as an internal standard. Chemical shifts were reported in δ. Mass Spetra were measured on a HP5988A instrument

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Table 1
Concentration of HCl *versus* the yield

No.	1	2	3	4	5
C_{HCl} (%)	36	18	12	9	0
Yield (%)	84	83	67	78	79

by direct inlet at 70ev. All materials were obtained from commercial suppliers and used as received.

2,4-Thiazolinedione (3)

To a 100 mL three neck flask equipped with a thermometer, a stirrer and a condenser were added 2-chloroacetic acid (**1**, 18.9 g, 0.2 mol), thiourea (**2**, 15.2 g, 0.2 mol) and water (50 mL). This mixture was stirred at room temperature for at least 1 h, and then was heated to reflux. The process of the reaction was monitored by TLC (silica gel, Rf = 0.5, elution: chloroform-methanol: 20:1) until the reaction was complete (3 h). Then the solution was allowed to cool down gradually to room temperature while still being stirred. The large amount of pale yellow crystalline solid was collected, washed with small amount of water to give the crude product as pale yellow crystals, recrystallized from water (decolorized with active carbon) to give pure white crystals (**3**, 18.3 g, 79%), mp. 124–125°C, *lit*. 125–1126°C.[4]

IR(KBr): 3398, 2800, 1731, 1677 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.75(s, 2H, -CH_2); 9.9(s, 1H, -NH); MS(*m*/*z*,%): 118 (M^+). All the analytical data were agreed the literature data.[46]

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