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# ONE-POT SYNTHESIS OF FUNCTIONALIZED 2-THIAZOLIDIN-4-ONES FROM THIOSEMICARBAZONE DERIVATIVES AND ACETYLENIC ESTERS IN WATER

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**Abstract**
Some derivatives of 2-thiazolidin-4-ones were synthesized from dialkyl acetylenedicarboxylates and thiosemicarbazone derivatives of chalchones in the presence of triphenylphosphine in water.

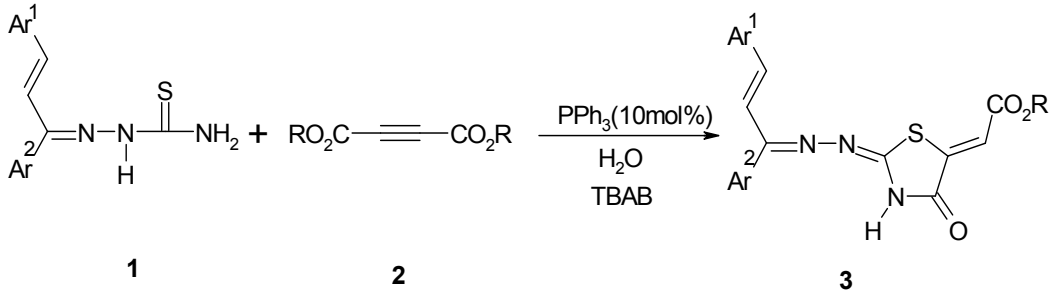
**Keywords:** 2-thiazolidin-4-one**,** dialkyl acetylenedicarboxylate**,** chalchone**,** thiosemicarbazone

## Introduction

Among the heterocyclic compounds, sulphur and nitrogen containing moieties have attracted maximum attention, as they are full of useful ramifications especially in the biological and industrial fields. Thiazole nucleus in particular is the centre of attraction in developing various essential moieties in pharmaceutical industries.
Functionalized 2-thiazolidin-4-ones are important heterocyclic compounds owing to their biological activities[i, ii], such as anti-tuberculosis[iii], anti-convulsant[iv], fungistatic[v].
In the past years, several methods have been reported for the preparation of thiazolidinone derivatives. For example, the reaction between thioamides and thiosemicarbazide derivatives with dialkyl acetylenedicarboxylates is known as a convenient and effective method to prepare 2-amino-5-methoxycarbonyl-thiazolidin-4-ones[vi, vii].

## Results and Discussion:

The reaction of thiosemicarbazone derivatives of chalcones **1** and dialkyl acetylene dicarboxylate **2** at reflux temperature in the presence of 10 mol% of triphenylphosphine ($Ph_3P$) and tetra butyl ammonium bromide (TBAB) in water as a solvent produced functionalized 2-thiazolidin-4-ones **3** in good yields (Scheme 1).

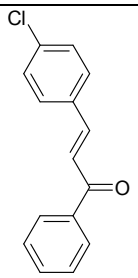
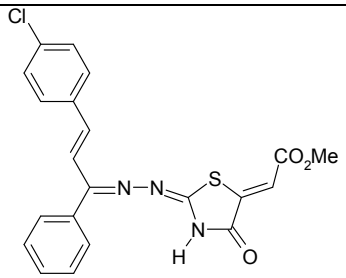
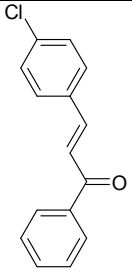
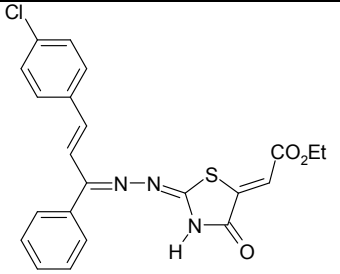
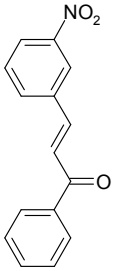
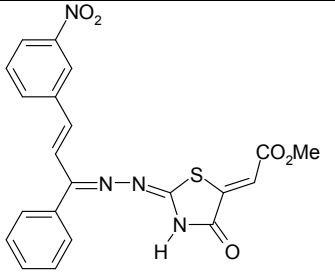


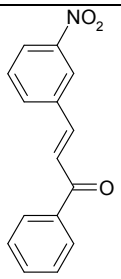
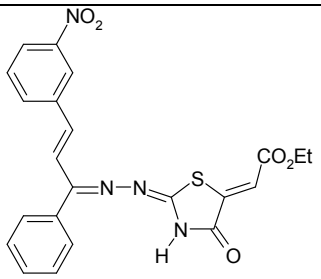
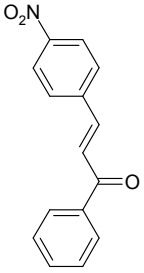
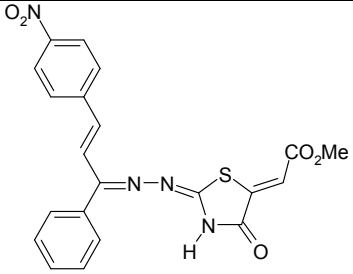
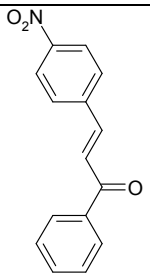
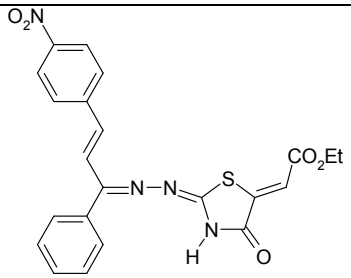

**1** **2** **3**

**Scheme 1**.

To establish the scope and generality of the process therefore a series of thiosemicarbazone derivatives were used under the optimized reaction conditions.
In all cases good yields of the 2-thiazolidin-4-one derivatives were obtained. The results are summarized in table 1.

**Table1.** Yields of 2-thiazolidin-4-ones

| Product **3** | Chalcone | Product structure | Yield (%) |
|---|---|---|---|
| a |  |  | 85 |
| b |  |  | 80 |
| c |  |  | 88 |

| | | | |
|---|---|---|---|
| d |  |  | 77 |
| e |  |  | 85 |
| f |  |  | 80 |

**Experimental section:**
All chemical compounds were purchased from Merck chemical company and used without further purification. All products are known and identified by comparison of their spectral data and physical properties with those of the authentic samples. Melting points were recorded on an Electrothermal-9100 apparatus and are uncorrected. NMR spectra were recorded on a BRUKER DRX-500 AVANCE NMR spectrometer using DMSO-$d_6$ as solvent.

**Genaral procedure for the preparation of 2-thiazolidin-4-ones:**
A mixture of thiosemicarbazone **1** (1 mmol), acetylenic ester **2** (1 mmol), $PPh_3$ (0.1 mmol) and TBAB (1 mmol) were mixed in 10 mL of water and refluxed for 2h.
The resulting precipitate after filtering was recrystalized from ethanol.

**Compound 3a:** Mp. 210-211$^o$C, IR (KBr):817, 1203, 1331, 1597, 1680, 1731, 3173 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$) δ (ppm): 3.83 (3H, s, $OCH_3$), 6.56 (1H, d , J =16.0 Hz, CH), 6.67 (1H, s, CH), 7.28-7.30 (2H, m, Ar-H), 7.37 (1H, d, J = 16.4 Hz, CH), 7.42 (2H, d, J = 8.40 Hz, Ar-H), 7.47-7.52 (3H, m, Ar-H), 7.66 (2H, d, J =8.40 Hz), 12.83 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$) δ (ppm): 52.91, 114.82, 128.70, 129.13, 129.16, 129.29, 129.70, 130.12, 134.11, 134.92, 134.96, 138.53, 143.25, 160.22, 165.94, 165.97, 166.34.

**Compound 3b:** Mp. 162-164$^o$C, IR (KBr): 3148, 1710, 169, 1597, 1316, 1191, 813 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$) δ (ppm): 1.29 (3H, t, J = 6.80 Hz, $CH_3$), 4.27 (2H, q, J = 7.20 Hz, $OCH_2$), 6.56 (1H, d , J =16.4 Hz, CH), 6.63 (1H, s, CH), 7.28-7.30 (2H, m, Ar-H), 7.36 (1H, d, J = 16.4 Hz,

CH), 7.42 (2H, d, J = 8.0 Hz, Ar-H), 7.44-7.62 (3H, m, Ar-H), 7.66 (2H, d, J = 8.4 Hz), 12.83 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$) δ (ppm): 14.53, 61.76, 114.98, 128.69, 129.14, 129.29, 129.46, 129.48, 129.51, 130.16, 134.08, 134.95, 134.39, 134.98, 143.34, 165.79, 165.92, 166.19.

**Compound 3c:** Mp. 200-201$^{o}$C, IR (KBr): 3208, 2950, 1726, 1696, 1598, 1530, 1432, 1322 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$) δ (ppm): 3.81 (3H, s, $OCH_3$), 6.67 (1H, s, CH), 6.75 (1H, d, J =16.0 Hz, CH), 7.31-7.51 (5H, m, Ar-H), 7.54 (1H, d, J = 16.4 Hz, CH), 7.66-8.17 (3H, m, Ar-H), 8.43 (1H, s), 12.87 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$) δ (ppm): 52.92, 114.92, 122.67, 123.82, 128.72, 129.21, 129.23, 130.69, 132.07, 133.07, 134.68, 137.47, 137.92, 143.18, 148.77, 160.77, 165.65, 165.95, 166.32.

**Compound 3d:** Mp. 215-217$^{o}$C, IR (KBr): 3125, 1710, 1697, 1527, 1324, 1197 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$) δ (ppm): 1.29 (3H, t, J = 7.20 Hz, $CH_3$), 4.28 (2H, q, J = 7.20 Hz, $OCH_2$), 6.64 (1H, s, CH), 6.75 (1H, d , J =16.4 Hz, CH), 7.30-7.57 (6H, m, Ar-H), 7.66 (1H, d, J = 16.0 Hz, CH), 8.42 (1H, s), 12.86 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$) δ (ppm): 14.51, 61.79, 112.88, 122.63, 123.80, 128.71, 129.21, 129.52, 130.68, 132.06, 133.71, 134.68, 137.38, 137.91, 143.08, 148.74, 160.90, 165.55, 165.88, 165.95.

**Compound 3e:** Mp. 222-226$^{o}$C, IR (KBr): 3210, 2960, 1730, 1692, 1598, 1530, 1432, 1322 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$) δ (ppm): 3.80 (3H, s, $OCH_3$), 6.68 (1H, s, CH), 7.31-7.51-7.66 (5H, m, Ar-H), 7.77 (1H, d, J = 8.2 Hz, CH), 8.02 (2H, d, J = 8.2 Hz, Ar-H), 12.87 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$) δ (ppm): 53.00, 114.90, 122.07, 123.80, 128.82, 129.21, 129.23, 130.69, 132.07, 133.07, 134.68, 137.47, 138.92, 143.18, 149.77, 160.77, 165.65, 165.95, 166.32.

**Compound 3f:** Mp. 240-245$^{o}$C, IR (KBr): 3105, 1710, 1697, 1527, 1324, 1197 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$) δ (ppm): 1.28 (3H, t, J = 7.20 Hz, $CH_3$), 4.26 (2H, q, J = 7.20 Hz, $OCH_2$), 6.66 (1H, s, CH), 7.30-7.57 (5H, m, Ar-H), 7.79 (1H, d, J = 8.1 Hz, CH), 8.02 (2H, d, J = 8.1 Hz, Ar-H), 12.88 (1H, s, NH). $^{13}$C NMR (DMSO-$d_6$) δ (ppm): 14.50, 61.69, 113.80, 122.63, 123.80, 128.71, 129.21, 129.52, 130.68, 132.06, 133.71, 134.68, 137.38, 137.91, 143.08, 149.74, 160.90, 165.55, 165.88, 165.90.

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