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Non-Bonding 1,4-Sulphur–Oxygen Interaction Governs the Reactivity of α-Ketothioesters in Triphenylphosphine-Catalyzed Cyclization with Acetylenedicarboxylates

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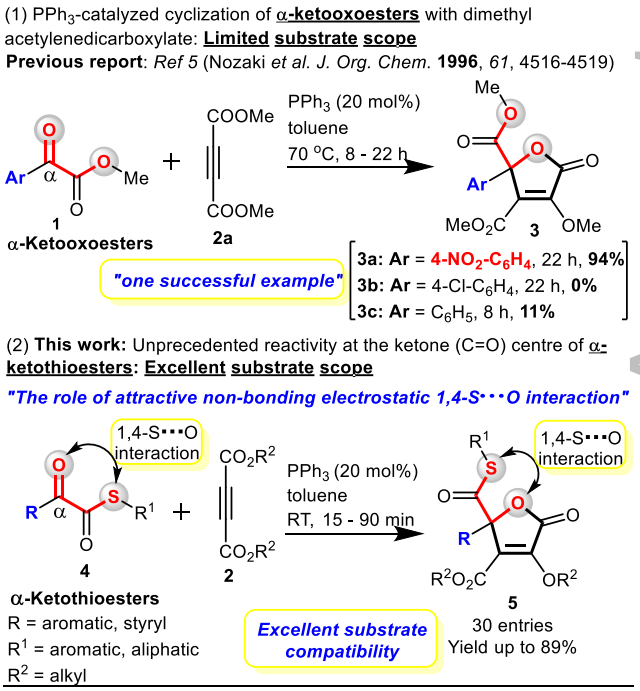
Abstract. α-Ketothioesters undergo triphenylphosphine (PPh_3)-catalyzed cyclization with acetylenedicarboxylate esters smoothly, in contrast to α-ketooxoesters which require more drastic conditions with the limited substrate scope. The reaction works well with a wide range of α-ketothioesters, delivering highly functionalized α,β-unsaturated γ-butyrolactones in moderate to excellent yields. The higher reactivity of the thioester derivatives is seemingly due to a favourable intramolecular non-bonding electrostatic 1,4-interaction involving C–S σ* orbital on the sulphur atom and the lone pair of electrons in the electron-donating oxygen atom. This is apparent from the X-ray crystallographically determined internuclear distance between the sulphur and ketone (C=O) oxygen atoms (2.71-2.85 Å), which is significantly less than the sum of their van der Waals radii (3.25-3.30 Å). The substitution on the S atom is oriented diametrically away from the ketone O atom to maximize the interaction between them. The trend is also seen in the 1,4-S···O contact between the S and furan O atoms (2.70 Å) in the γ-butyrolactone products.

Keywords: Cyclization; α-Ketothioesters; Nucleophilic addition; 1,4-S···O interaction; Zwitterion intermediate

Certain non-oxidized sulphur atoms in organic and bioorganic molecules can participate in attractive non-bonding 1,4-interactions with oxygen atoms, that are proving to be useful in governing important properties such as molecular conformation, and chemical as well as biochemical activity.[1] This effect is based on the σ-holes on sulphur atom that possess positive electrostatic potential and are available for interaction with lone pairs of electrons in the electron-donating oxygen atom.[2] These strong intramolecular electrostatic 1,4-S···O contacts ranging from 2.77-3.16 Å can be clearly observed in the X-ray crystal structures of many compounds, the distance being substantially less than the sum of the van der Waals radii (3.25-3.30 Å).[3] Computational studies have elucidated the origins of these stabilizing contacts, and this interaction has been widely demonstrated in model systems.[4] We herein show that such interaction is likely to account for the reactivity of the ketone carbon of α-ketothioesters in their cyclization reaction with acetylenedicarboxylates.

Nozaki and co-workers reported in 1996 a triphenylphosphine (PPh_3)-catalyzed cyclization of α-ketooxoesters **1** with dimethyl acetylenedicarboxylate **2a** in toluene at 70 °C to afford the highly functionalized α,β-unsaturated γ-butyrolactones **3** (Scheme 1).[5] They found that highly electron-deficient α-ketooxoester **1a** bearing a nitro group at the 4-position of the α-aromatic ring produced the desired product **3a** in excellent yield. Quite surprisingly, the corresponding electron-withdrawing 4-Cl-substituted derivative **1b** was recovered unchanged under the same reaction conditions, whereas use of the phenyl-substituted derivative **1c** did lead to product **3c**, but only in 11% yield. The authors presumed that the presence of a strong electron-withdrawing substituent



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Scheme 1. PPh_3-catalyzed cyclization of α-ketooxoesters **1** and α-ketothioesters **4** with acetylenedicarboxylate esters **2**.

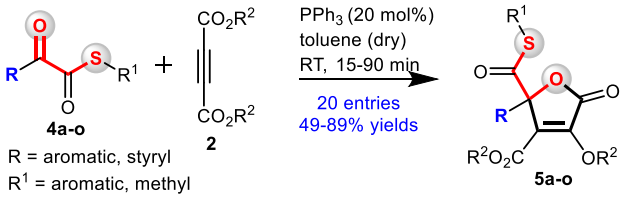
(4-NO_2-C_6H_4) is essential to facilitate the initial nucleophilic addition of a zwitterion intermediate to ketone carbon of **1**.

During the course of our continuing investigation on the reactivity of α-ketothioesters and its unsaturated analogues with various nucleophiles,[6] we observed that a similar zwitterion intermediate can be efficiently trapped by **4** as a dipolarophile, even at ambient temperature, and the reaction is compatible with a diverse range of substrates (Scheme 1). The sharply contrasting results concerning the difference in reactivity of the ketone moiety between the α-ketooxoesters **1** and α-ketothioesters **4** in the formation of γ-butyrolactones have prompted us to investigate the notable sulphur atom effects[7] of the latter in detail. We herein report our findings on the PPh_3-catalyzed cyclization of α-ketothioesters with acetylenedicarboxylate esters to yield the substituted γ-butyrolactones[8] **5**. It is nothworthy that although substantial progress has been made with the reaction of the zwitterion to various electron-deficient carbonyl compounds,[5,9] similar cyclization has not been reported with the corresponding α-ketothioesters[10] due to the lack of methods available to access them.

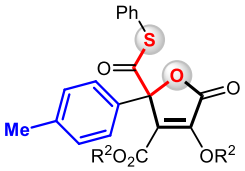
The requisite α-ketothioesters or its unsaturated analogues **4** were readily prepared in pure form following the previous reports.[6,11] When **4a** was treated with **2a** in presence of 20 mol % of PPh_3 in dry toluene at ambient temperature (25-30 °C), the desired γ-butyrolactone **5a** was isolated in 80% yield within 45 min; the initial light yellow solution slowly turned to an orange-coloured solution with the progress of the reaction (Table 1). But increasing the reaction temperature upto 70 °C proved counterproductive. It should be noted that a similar cyclization with the oxoester analogues needed reaction at 70 °C for 8-22 h (Scheme 1),[5] suggesting that the ketone carbon of **4** is more reactive than **1**. To improve the yield of **5a** further, different solvents were tried. But tetrahydrofuran, 1,4-dioxane, ethylacetate, methanol, or acetonitrile all proved unsuccessful.

We next assessed the substrate scope of this reaction with dialkyl (methyl, ethyl, *n*-propyl, and *n*-butyl) acetylenedicarboxylates **2** (Table 1). It was found that the α-ketothioesters containing electron-donating, electron-neutral, or electron-withdrawing substituents on the α-aromatic ring (**4a–i**) gave the expected products 5**a–i** in moderate to excellent yields. Substrates containing 2-naphthyl (**4j**) moiety at the α-position also furnished the expected product (**5j**). Further investigation demonstrated that methylthioesters (**4k-o**) containing substituted α-styryl moiety could also be converted to the corresponding products in moderate to good yields (**5k-o**). But the expected products **5fd** or **5ab** were not obtained when acetylenedicarboxylates bearing either *iso*-propyl (**2e**) or *tert*-butyl (**2f**) groups were either stirred at -20 to 0 °C or heated at ambient temperature (Table 1), possibly due to the poor nucleophilic character of the alkoxide anions ($^{i}PrO^{-}$ and $^{t}BuO^{-}$). Moreover, the generated alkoxides are strong bases, which may also lead to the undesired side reactions. Moreover,

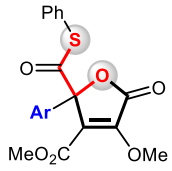
Table 1. Substrate scope for the synthesis of highly functionalized α,β-unsaturated γ-butyrolactones **5**.[a]



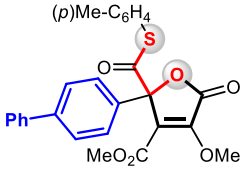
R = aromatic, styryl
R^1 = aromatic, methyl
R^2 = Methyl (**2a**), Ethyl (**2b**), *n*-Propyl (**2c**), *n*-Butyl (**2d**), *iso*-Propyl (**2e**), *tert*-Butyl (**2f**)



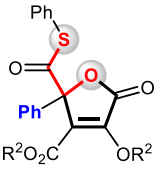
5a: R^2 = Me, 45 min, 80%
5aa: R^2 = Et, 45 min, 84%
5ab: R^2 = *tert*-Bu, 15 min, trace[b,c]



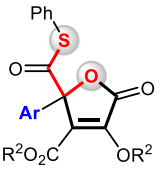
5b: **Ar** = 4-*iso*-butyl-C_6H_4, 45 min, 73%
5c: **Ar** = 4-OMe-C_6H_4, 90 min, 49%
5d: **Ar** = 3-OMe-C_6H_4, 60 min, 79%



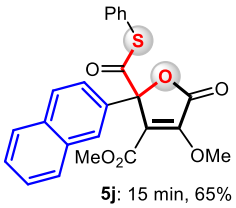
5e: 45 min, 69%



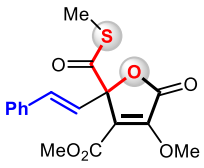
5f: R^2 = Me, 30 min, 63%
5fa: R^2 = Et, 35 min, 61%
5fb: R^2 = *n*-Pr, 20 min, 63%
5fc: R^2 = *n*-Bu, 20 min, 64%
5fd: R^2 = *iso*-Pr, 30 min, trace[b,c]



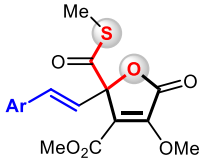
5g: **Ar** = 4-Br-C_6H_4, R^2 = Me, 15 min, 85%
5ga: **Ar** = 4-Br-C_6H_4, R^2 = Et, 15 min, 60%
5h: **Ar** = 4-F-C_6H_4, R^2 = Me, 15 min, 89%
5i: **Ar** = 4-Cl-C_6H_4, R^2 = Me, 15 min, 82%



5j: 15 min, 65%



5k: 40 min, 73%



5l: **Ar** = 4-Br-C_6H_4, 30 min, 55%[d]
5m: **Ar** = 4-OAc,3-OMe-C_6H_3, 45 min, 88%
5n: **Ar** = 3-Me-C_6H_4, 20 min, 57%
5o: **Ar** = 4-Me-C_6H_4, 20 min, 63%

[a] *Reaction conditions:* α-Ketothioesters or β,γ-unsaturated α-ketomethylthioesters **4** (0.05 g, 1 equiv), PPh_3 (20 mol%), and acetylenedicarboxylate esters **2** (1.2 equiv/mmol) in dry toluene (2.0 mL) at room temperature (25-30 °C); yields are of isolated products.
[b] With trace amount of desired product, inseparable mixtures of minor unidentified spots were observed.
[c] NMR indicates the presence of noticeable impurities.

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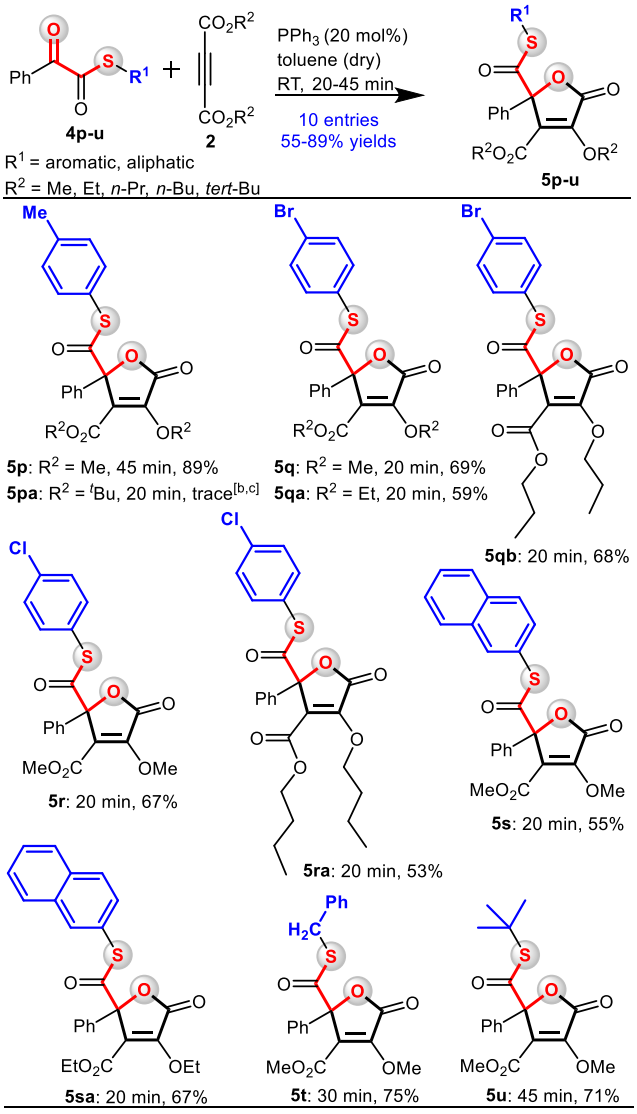
[d] **5l** contains trace amount of impurity not resolved by column chromatography.

replacing the ester group of acetylenedicarboxylates **2** with aromatic ring (such as for diphenylacetylene) was found to be completely inactive under the standard reaction conditions (not shown), ostensibly owing to the lack of stability and subsequent reactivity of the in situ generated zwitterion. Efforts to address this limitation are presently ongoing in our laboratory.

We next sought to extend the scope of this reaction by changing the substituents on the sulphur atom. As indicated in Table 2, electron-donating (**4p**) or electron-withdrawing (**4q-r**) substituents in the aromatic ring, or naphthyl substituents (**4s**) were well-tolerated and produced the expected products in moderate to excellent yields (**5p-5sa**). Substrates bearing aliphatic thiols such as benzyl (**4t**) or *tert*-butyl (**4u**) groups were also found to react under these conditions, delivering the products in good yields (**5t-u**).

Table 2. Substrate scope for the sulphur moiety.[a]



[a] *Reaction conditions:* α-Ketothioesters **4** (0.05 g, 1 equiv), PPh_3 (20 mol%), and acetylenedicarboxylate esters **2** (1.2 equiv/mmol) in dry toluene (2.0 mL) at room temperature (25-30 °C); yields are of isolated products.
[b] With trace amount of desired product, inseparable mixtures of minor unidentified spots were observed.
[c] NMR contains noticeable peaks for impurities.

Based on the experimental results, α-ketothioesters **4** were found to be more reactive than oxoester analogous **1** toward zwitterion addition and subsequent cyclization. This difference in behavior may be due to the presence of an attractive non-bonding electrostatic 1,4-interaction in **4** involving low-lying C–S σ* orbital on the S atom and lone pairs of electrons in the ketone O atom, with the favourable contact influencing the electrophilicity of the ketone carbon of α-ketothioesters. In the single-crystal X-ray structure of the α-ketothioester **4g**, the *syn* preference of the ketone O and S atoms is noticeable with the distance between these two atoms measured at 2.71 Å (Figure 1),[12] substaintially less than the sum of the van der Waals radii. This finding is indicative of a favorable interaction between them. Such a stabilizing interaction between two electron-donating oxygen atoms is lacking in α-ketooxoesters **1**. Further support comes from the observation that the S-phenyl ring is oriented diametrically away from the ketone O atom. This arrangement would permit an optimal interaction between these two atoms. The powerful electron-withdrawing property associated with a thioester C(O)SR^1 moiety might also work for a productive interaction and subsequent reactivity of the ketone group in α-ketothioester. In related examples, similarly short 1,4-S···O distance of 2.74 Å in **4q** (Figure 2)[12] and **4r** (Figure 3),[12] *syn* direction for S and ketone O atoms, and the orientation of the S-aryl ring away from the ketone group had been observed.

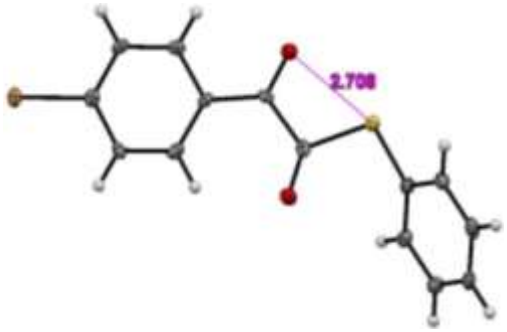


Figure 1. Single-crystal X-ray structure of **4g (CCDC 2041719)**, demonstrating the close contact between the ketone O and S atoms (2.71 Å).

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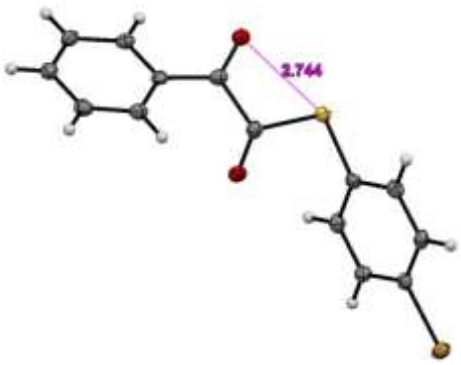

Figure 2. Single-crystal X-ray structure of **4q (CCDC 2041720)**, demonstrating the close contact between the ketone O and S atoms (2.74 Å).

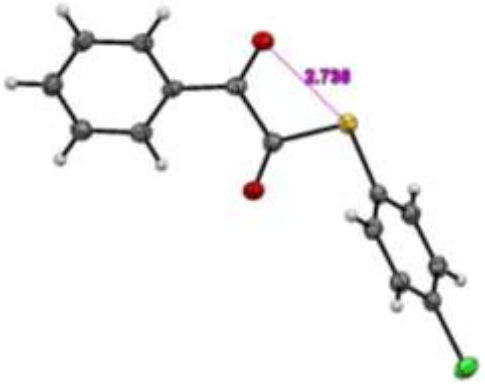

Figure 3. Single-crystal X-ray structure of **4r (CCDC 2041721)**, demonstrating the close contact between the ketone O and S atoms (2.74 Å).

A perusal of the X-ray crystallographic literature on α-ketothioesters also revealed the existence of attractive non-bonded electrostatic 1,4-S···O contact between the S and O atoms. The S···O distances of 2.80 Å, 2.85 Å, 2.75 Å, and 2.76 Å observed in single crystal structures such as for Ph-CH=CH(*E*)-C(=O)-C(=O)-SMe (**4k**),[11c,13-14] 4-CN-C_6H_4-CH=CH(*E*)-C(=O)-C(=O)-SMe,[13] $MeSO_2$-C_6H_4-C(=O)-C(=O)-SCH_2Ph,[14-15] and Ph-C(=O)-C(=O)-S-C_6H_4-*p*-Me (**4p**)[16] respectively are significantly less than the sum of the van der Waals radii of S and O atoms with the substituents on the sulphur atom oriented away from the ketone O atom.

Beside α-ketothioesters, the most striking observation with the single crystal X-ray crystal structure of the product γ-butyrolactone **5f** was that the S atom of the thioester moiety was proximal to the O-1 atom of the furan ring with contact distance of 2.70 Å (Figure 4),[12] indicative of an attractive electrostatic interaction between these atoms. This might also play a contributing role in influencing the stability of **5f** and subsequent reactivity of the substrates.

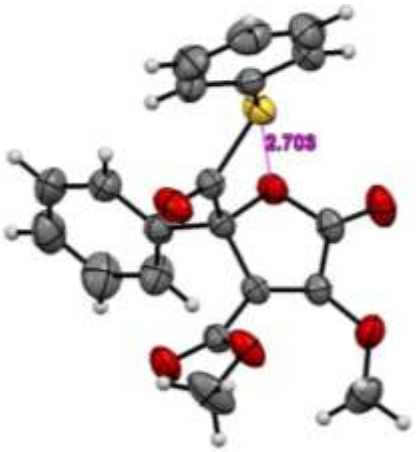

Figure 4. Single-crystal X-ray structure of **5f (CCDC 2041722)**, illustrating the close contact between the furan O and S atoms (2.70 Å).

For α-ketooxoesters, the *syn* preference of the ketone O and the pendent O atoms is also noticeable in the single-crystal X-ray structure of 3-NO_2-C_6H_4-C(=O)-C(=O)-OMe with the distance between these two oxygen atoms measured at 2.62 Å, which is significantly less than the sum of the van der Waals radii (3.04 Å).[17] Although the distance supports the favorable interaction, however, it is reasonable to assume that such a stabilizing interaction (like α-ketothioesters) is lacking in α-ketooxoesters **1** and also in the corresponding products **3** (Scheme 1), as the electron-rich oxygen atoms may experience electrostatic repulsion due to their electronegativity.[1] The electrophilicity of the ketone carbon of **1** may be dependent upon the substituents in the α-aromatic ring. Thus, the presence of a strongly electron-withdrawing nitro (NO_2) group is essential to facilitate the initial zwitterion addition to the ketone (C=O) carbon of 1.[5]

Based on earlier reports,[5,9] a plausible reaction mechanism is proposed in Scheme 2. We presume that in presence of acetylenedicarboxylate ester **2**, PPh_3 would initially generate a zwitterionic intermediate **I**, which can add to the highly reactive ketone carbon (C=O) of α-ketothioester **4** to produce the intermediate **II**. It is reasonable to expect that strongly electrophilic carbonyl carbon accelerates the nucleophilic addition of **I** due to the presence of an attractive non-bonding electrostatic 1,4-S···O interaction. Intermediate **II** undergoes cyclization with concomitant elimination of the alkoxide anion to generate the intermediate **III** bearing a phosphonium cation at C-4, which may be replaced by the in situ generated alkoxide anion to yield γ-butyrolactones **5**, and regenerate the catalyst PPh_3 to continue the catalytic cycle.[18]

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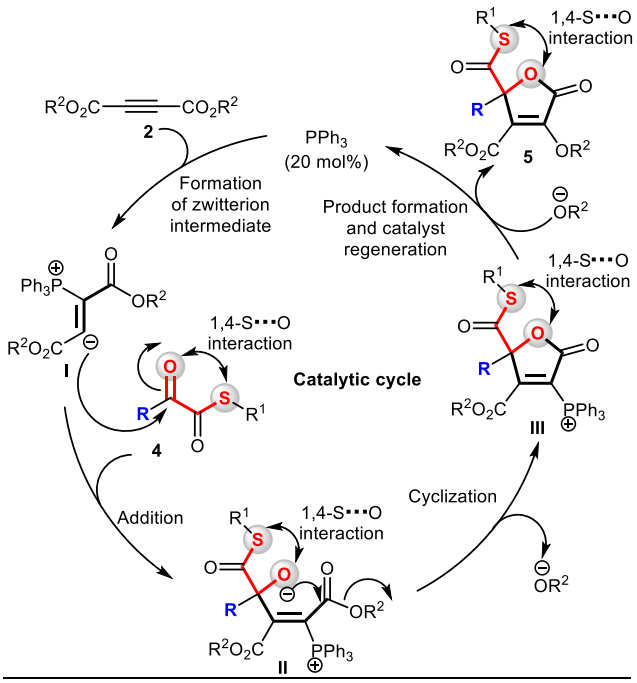
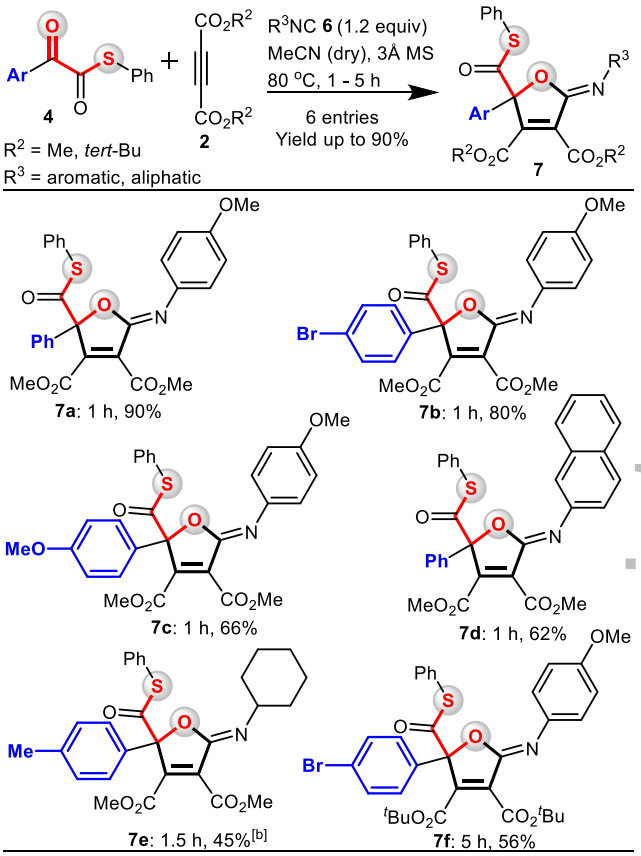


Scheme 2. Proposed mechanism for the formation of **5** from **4**.

To further demonstrate non-bonded 1,4-S···O interaction-supported reactivity of the α-ketothioesters, we treated **4** with aromatic isocyanide **6** and dialkyl acetylenedicarboxylate **2** in acetonitrile solvent at 80 °C, and isolated the corresponding highly substituted α,β-unsaturated γ-iminolactones **7a-d** in moderate to excellent yields (Table 3). Isocyanide containing an aliphatic group (cyclohexyl) was transformed into the corresponding product **7e** under slightly modified conditions (THF instead of MeCN) at room temperature. An acetylenedicarboxylate ester bearing a *tert*-butyl group also furnished the expected product **7f** in moderate yield. Based on earlier reports, the reaction is believed to proceed via zwitterionic intermediate from the reaction of dialkyl acetylenedicarboxylate **2** and isocyanide **6** followed by the addition to the ketone carbon of **4** and subsequent cyclization to yield **7**.[19]

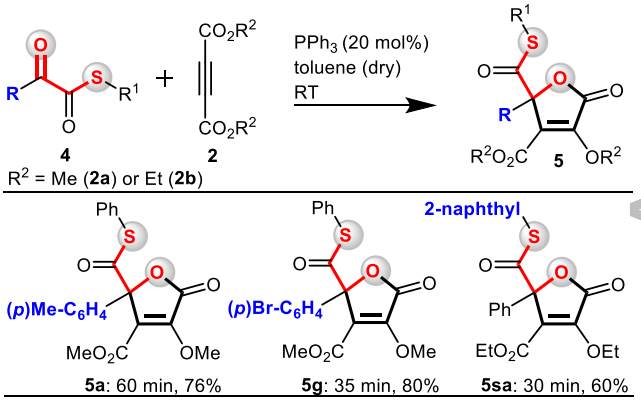
Table 3. Synthesis of highly functionalized α,β-unsaturated γ-iminolactones **7** from **4**.[a]



[a] *Reaction conditions:* α-Ketothioesters **4** (0.05 g, 1 equiv), dialkyl acetylenedicarboxylate **2** (1.2 equiv/mmol), and aromatic or alkyl isocyanide **6** (1.2 equiv/mmol) in dry MeCN (2.0 mL) at 80 °C; yields are of isolated products.
[b] THF as solvent instead of MeCN under ambient temperature (25 – 30 °C).

The versatility of the developed procedure was highlighted by scaling up the reaction to 0.5 g batch of α-ketothioesters **4** under optimized reaction conditions

Table 4. Scale-up batches.[a]



[a] α-Ketothioesters **4a**, **4g**, or **4s** (0.5 g, 1 equiv), PPh_3 (20 mol%), and acetylenedicarboxylate esters **2a** or **2b** (1.2 equiv) in dry toluene (14.0 mL) at room temperature (25-30 °C); yields are of isolated products. For detailed procedure, see the Supporting Information.

to isolate **5a**, **5g**, and **5sa** without any significant diminution in the yields (Table 4).

In conclusion, we have demonstrated the reaction of α-ketothioesters with zwitterion intermediate generated from catalytic PPh_3 and acetylenedicarboxylate esters to obtain highly substituted γ-butyrolactones in moderate to excellent yields. An α-ketothioester was found to be more reactive than the analogous α-ketooxoester for this transformation. This difference in behavior may be due to the presence of an attractive non-bonding electrostatic 1,4-interaction in α-ketothioester involving low-lying C–S σ* orbital on sulphur atom and the lone pairs of electrons in ketone oxygen atom (C=O). Such a stabilizing interaction is lacking in the corresponding α-ketooxoesters, as electron-rich oxygen atoms may not form particularly favorable contact with each other due to their electronegativity. The remarkably short 1,4-S···O distances observed in the single-crystal X-ray structures of the α-ketothioesters (2.71-2.85 Å) or its product γ-butyrolactone (2.70 Å) support the favorable interaction between the S and O atoms. Further evidence for the existence of a productive S···O interaction in α-ketothioesters is the observation that the substitution on the S atom is oriented diametrically away from the ketone O atom, which also maximizes the non-bonded interaction between them. To further demonstrate non-bonded 1,4-S···O interaction-supported reactivity of the α-ketothioesters, the synthesis of α,β-unsaturated γ-iminolactones has been reported. Computational studies concerning the relative reactivities of the O- and S-analogues will be reported in due course.

Experimental Section

General Procedure and Representative Examples

General Procedure for the Synthesis of 5. To a well-stirred solution of α-ketothioesters or its unsaturated analogues **4** (0.05 g, 1 equiv) in dry toluene (2.0 mL) under an argon atmosphere at room temperature (25-30 °C), triphenylphosphine (PPh_3, 20 mol%) was added. Acetylenedicarboxylate ester **2** (1.2 equiv/mmol) was then added drop-wise via syringe. The resulting reaction mixture was stirred at the same temperature employing time as mentioned. After completion of the reaction (TLC), saturated NH_4Cl solution was added, and the mixture was extracted with dichloromethane (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified by silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **5**.

Methyl 4-methoxy-2-(3-methoxyphenyl)-5-oxo-2-((phenylthio)carbonyl)-2,5-dihydrofuran-3-carboxylate 5d: Prepared according to the general procedure discussed above: time = 60 min; R_f = 0.3; eluent, EtOAc/*n*-hexane (19%); colourless gum (0.060 g, 79%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.44 (s, 5 H), 7.33 (t, J = 7.8 Hz, 1 H), 7.06 (d, J = 8.4 Hz, 1 H), 7.04 (t, J = 2.4 Hz, 1 H), 6.96 (dd, J = 8.4, 2.4 Hz, 1 H), 4.25 (s, 3 H), 3.82 (s, 3 H), 3.76 ppm (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 193.8, 164.5, 161.6, 159.5, 147.8, 135.1, 134.7 (2 CH), 130.0, 129.6, 129.5 (2 CH), 126.4, 123.0, 119.4, 115.0, 113.3, 89.8, 60.0, 55.4, 52.6 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1786, 1718, 1654, 1451, 1410, 1114, 1021 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{21}H_{18}O_7SNa$ [M + Na]$^+$: 437.0671; found: 437.0664.

General Procedure for the Synthesis of 7. To a well-stirred solution of α-ketothioesters **4** (0.05 g, 1 equiv) in dry acetonitrile (2.0 mL) and 3Å MS under an argon atmosphere, aromatic and aliphatic isocyanide R^3NC (**6**, 1.2 equiv) was added. Dialkyl acetylenedicarboxylate **2** (1.2 equiv/mmol) was successively added drop-wise via syringe. The resulting reaction mixture was heated under reflux (80 °C) employing time as mentioned. After completion of the reaction (TLC), saturated NH_4Cl solution was added, and the mixture was extracted with dichloromethane (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified by silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **7**.

Dimethyl (*Z*)-5-((4-methoxyphenyl)imino)-2-phenyl-2-((phenylthio)carbonyl)-2,5-dihydrofuran-3,4-dicarboxylate 7a: Prepared according to the general procedure discussed above: time: 1 h; R_f = 0.3; eluent, EtOAc/*n*-hexane (15%); colourless gum (0.096 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, J = 9.0 Hz, 2 H), 7.40 - 7.51 (m, 10 H), 6.91 (d, J = 9.0 Hz, 2 H), 3.98 (s, 3 H), 3.82 (s, 3 H), 3.73 ppm (s, 3 H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 193.9, 161.5, 160.6, 158.1, 151.5, 143.7, 137.0, 136.1, 134.8 (2 CH), 133.8, 130.0, 129.7, 129.4 (2 CH), 128.6 (2 CH), 127.0 (2 CH), 126.6 (2 CH), 126.2, 113.9 (2 CH), 96.8, 55.4, 53.3, 52.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1739, 1684, 1504, 1442, 1353, 1287, 1241, 1042, 1003, 836, 746 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{24}NO_7S$ [M + H]$^+$: 518.1273; found: 518.1271 and *m/z* calcd for $C_{28}H_{23}NO_7SNa$ [M + Na]$^+$: 540.1093; found: 540.1088.

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[12] CCDC 2041719 (**4g**), 2041720 (**4q**), 2041721 (**4r**), 2041722 (**5f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam. ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

[13] See the Supporting Information for the single-crystal X-ray structures of Ph-CH=CH(*E*)-C(=O)-C(=O)-SMe and 4-CN-C_6H_4-CH=CH(*E*)-C(=O)-C(=O)-SMe, illustrating the close contact between the ketone O and S atoms.

[14] CCDC accession numbers for α-ketothioesters Ph-CH=CH(*E*)-C(=O)-C(=O)-SMe (**4k**) and $MeSO_2$-C_6H_4-C(=O)-C(=O)-SCH_2Ph are 960814 and 1895971, respectively, data taken from the Cambridge Crystallographic Database (CSD).

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[18] One of the reviewers suggested another plausible mechanism via the attack of PPh_3 to the ketone centre of α-ketothioesters to generate the corresponding zwitterionic intermediate, which undergoes subsequent cyclization with acetylenedicarboxylates **2** to yield γ-butyrolactones **5**. However, we believe that the zwitterion is less stable than that of the generated from acetylenedicarboxylates **2** and PPh_3 (intermediate **I**, Scheme 2), probably due to the lack of resonance structures, steric effects at the tertiary centre, and also from the HSAB principle (the ketone carbon being a hard electrophile and the phosphorus as a soft nucleophile).

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COMMUNICATION

Non-Bonding 1,4-Sulphur–Oxygen Interaction Governs the Reactivity of α-Ketothioesters in Triphenylphosphine-Catalyzed Cyclization with Acetylenedicarboxylates

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