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ORIGINAL ARTICLE

A facile one-pot synthesis of new functionalized pyrazolone-1,4-dithiafulvene hybrids

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Abstract

In this study, a one-pot reaction between β-keto esters or dialkyl acetylenedicarboxylates with hydrazines, carbon disulfide, and dialkyl acetylenedicarboxylates in the presence of triethylamine is reported. This reaction proceeded at room temperature and was completed within 6 h to produce functionalized pyrazolone-1,4-dithiafulvene hybrids in good yields.

Graphical abstract

Keywords 5-Pyrazolone · 1,4-Dithiafulvene · 1,3-Dithiole · Hybrid molecules · One-pot reaction

Introduction

Pyrazolones represent important structural motifs in heterocyclic chemistry and are found in many biologically active molecules used in the pharmaceutical and agrochemical industries. Pyrazolones show anti-tuberculosis [1], anti-viral [2], anti-hypertension [3], anti-oxidation [4], neuroprotection [5], anti-diabetic [6], anti-inflammatory [7], and anti-cancer [8] activities. They are also used as ligands [9] in complexes with catalytic activity. Some pyrazolones are used as wool, cotton, and silk dyes [10]. In addition, derivatives of sulfur heterocycles show significant biological and pharmaceutical activities [11]. 1,3-Dithiol-2-ylidenes derivatives have attracted much attention due to their excellent electron donation characteristics as a component in electronic materials [12, 13]. Also, sulfur-containing heterocycles such as 1,3-dithiole derivatives have been considered

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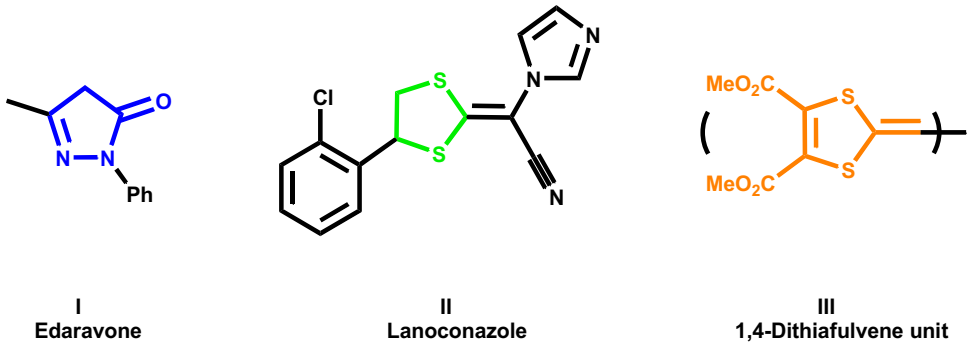


I
Edaravone

II
Lanoconazole

III
1,4-Dithiafulvene unit

Fig. 1 Structures of pyrazolone and sulfur-containing molecules applied in medicine (**I, II**) and 1,4-dithiafulvene unit (**III**) applied in the material industry

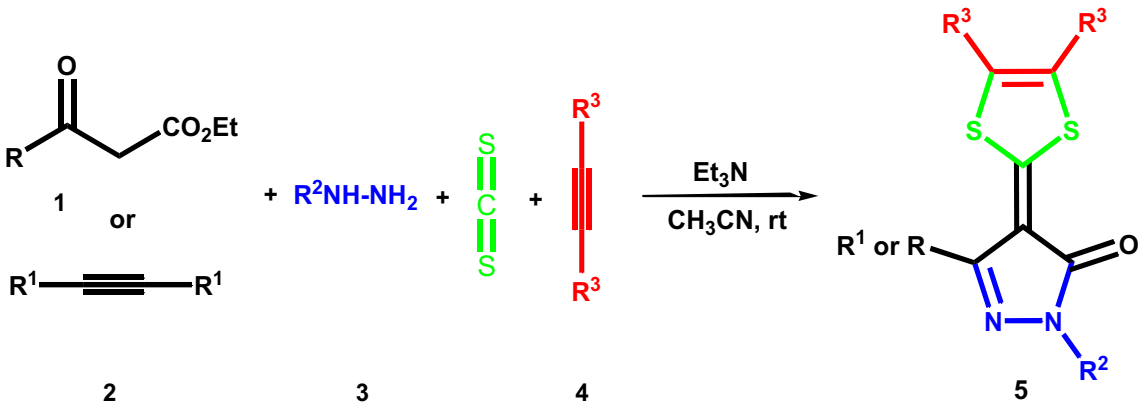
potential new substances due to their superconducting, optical, and electrical switching capabilities [14].

Various methods for preparing 1,3-dithiole derivatives have been published [15–19]. Among the dithiols, 1,4-dithiafulvenes bearing ester groups have attracted much attention as building blocks of electronic materials [20, 21]. The most common methods reported for the synthesis of 1,4-dithiafulvenes containing ester groups are the use of Wittig reaction between aldehydes or ketones with phosphonium salts [22–24]. These reactions are usually carried out at − 78 °C under argon atmosphere and in the presence of strong base such as butyl lithium. On the other hand, preparation of phosphonium salts also includes several steps [25]. In this study, we attempted to prepare 1,4-dithiafulvenes containing ester groups using ketene dithioacetal intermediates under easier conditions.

Ketene dithioacetals are used as efficient intermediates in the synthesis of 1,3-dithiol derivatives. Ketene dithioacetals can generate from the reaction between carbon nucleophile and carbon disulfide [26]. The reaction between ketene dithioacetals and dual electrophilic species such as dihaloalkanes [27, 28], or α-halo carbonyl compounds produce sulfur-containing heterocycles with two sulfur atoms [29, 30].

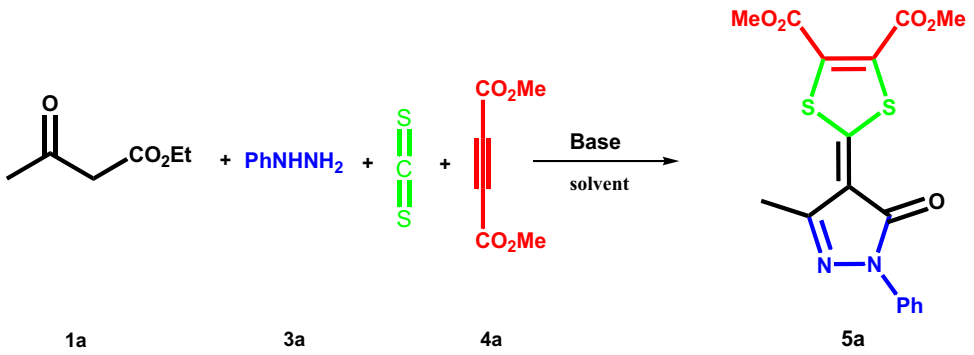
Laboratory studies show that the biological activities of bioactive molecules are usually recovered if two or more bioactive units are grouped in a single molecule [31]. Therefore, hybrid molecules of various heterocycles with pyrazolones contain more effective biological activities [32]. Edaravone (**I**) has practical medicinal effects on a variety of diseases, including cardiovascular diseases [33], and Lanoconazole (**II**) shows significant antifungal activity [34]. Besides that, the 1,4-dithiafulvene unit (**III**) has a strong electron-donating property [21–24, 35] and is frequently used as a donor unit in donor–acceptor systems (Fig. 1).

Due to potential of sulfur-containing heterocycles and pyrazolones as mentioned above, we became interested in the synthesis of hybrid molecules containing pyrazolones and 1,4-dithiafulvenes. Following our research on the one-pot synthesis of new heterocyclic compounds [36–39] herein, we report the facile one-pot synthesis of pyrazolone-1,4-dithiafulvene hybrids **5** from the reactions between *β*-keto esters **1** or dialkyl acetylenedicarboxylates **2** with hydrazines **3**, carbon disulfide, and dialkyl acetylenedicarboxylates **4** (Scheme 1).



Scheme 1 One-pot reaction for the synthesis of pyrazolone-1,4-dithiafulvene hybrids **5**

Table 1 Optimization of the reaction conditions for the synthesis of compound **5a**



1a 3a 4a 5a

Entry	Solvent	Base (mol%)	T(°C)	Time (h)	Yield% of **5a**[a]
1	H_2O	Et_3N (200)	r.t	24	25
2	H_2O	KOH (200)	r.t	12	N.R
3	H_2O	K_2CO_3 (200)	r.t	12	N.R
4	H_2O	Pyridine (200)	r.t	12	N.R
5	H_2O	DABCO (200)	r.t	12	Trace
6	EtOH	Et_3N (200)	r.t	24	25
7	CH_2Cl_2	Et_3N (200)	r.t	24	20
8	THF	Et_3N (200)	r.t	24	33
9	DMSO	Et_3N (200)	r.t	8	51
10	CH_3CN	Et_3N (200)	r.t	6	64
11	CH_3CN	Et_3N (200)	Reflux	6	40
12	CH_3CN	Et_3N (100)	r.t	6	35
13	CH_3CN	Et_3N (150)	r.t	8	55
14	CH_3CN	Et_3N (250)	r.t	6	64

[a]Isolated yield

Results and discussion

Synthesis and optimization of reaction conditions

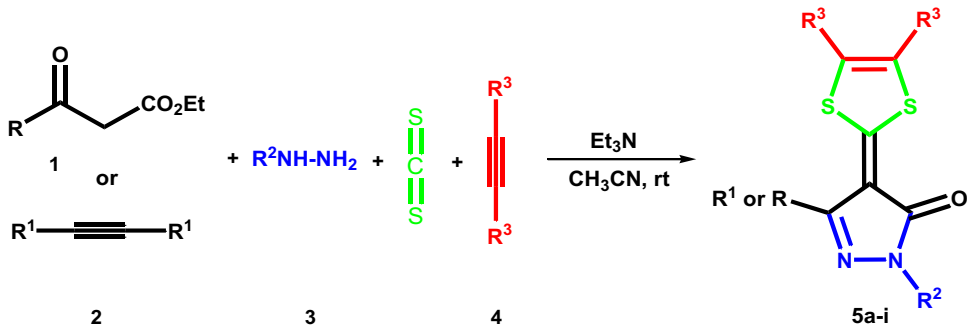
The one-pot reaction between ethyl acetoacetate **1a**, phenyl hydrazine **3a**, carbon disulfide, and dimethylacetylenedicarboxylate **4a** was selected as a model reaction to produce pyrazolone-1,4-dithiafulvene hybrid **5a** (Table 1). At first, the reaction was carried out in the water in the presence of two equimolar of Et_3N at room temperature. The progress of the reaction was monitored by TLC. After compilation of the reaction, product **5a** was separate as orange powder by filtration. The reaction yield was 25%. To optimize the reaction conditions, the reaction was carried out in the presence of various bases and solvents, and the results are collected in Table 1. As illustrated in Table 1, the reaction was not done in the presence of KOH, K_2CO_3, and pyridine in water, and the reaction yield in the presence of 1,4-diazabicyclo[2.2.2] octane (DABCO) was negligible (Table 1, entries 1–5). Therefore, the Et_3N was selected as the appropriate base for this reaction. The use of CH_2Cl_2 and EtOH as the solvent could not increase the reaction yield (Table 1, entries 6, 7). When the reaction was performed in THF or DMSO, the reaction yield increased, but the increase of reaction yield in acetonitrile was more significant (Table 1, entries 8–10). Further studies investigating the effect of temperature on the reaction yield showed that when the reaction was carried out in refluxing acetonitrile, the reaction yield was reduced because of the generation of complex by-products (Table 1, entry 11). Therefore, it is found that room temperature is the optimum temperature for the synthesis of pyrazolone-1,4-dithiafulvene hybrid **5a**. In addition, the study of the effect of the amount of base on the reaction yield showed that the two equimolar of the base is the optimum amount of base for this reaction (Table 1, entries 10, 12–14).

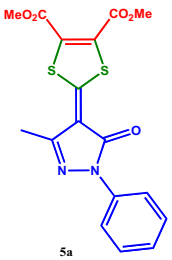
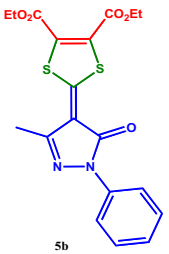
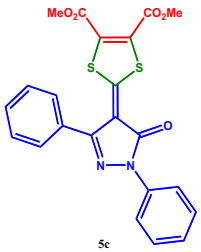
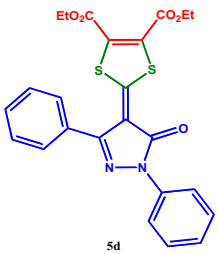
In this reaction, no detectable by-products were formed. In addition to the desired product, small amounts of acetonitrile-soluble dark materials were formed which were separated from the main product by filtration. To evaluate the scalability of the reaction, the model reaction was performed at double and quadruple scale in optimal conditions and no significant change in the reaction yield was observed.

Characterization of products

The structure of **5a** was confirmed by FT-IR, ^{1}H NMR, ^{13}C NMR, Mass, and elemental analysis data. In the IR spectra of **5a**, the peaks related to the stretching vibration of the ester carbonyl groups and S-C bonds appear in 1735 and 755 cm^{-1}, respectively. In the ^{1}H NMR spectrum of **5a**, methyl protons of pyrazolone moiety appear at $\delta = 2.46$ ppm. Two methyl groups of ester moieties appear at $\delta = 3.95$ and 3.96 ppm. The aromatic protons of **5a**

Table 2 One-pot synthesis of pyrazolone-1,4-dithiafulvene hybrids **5a–i**



Entry	R /or R^1	R^2	R^3	Product	Yield (%)[a]
1	Me	Ph	CO_2Me	 5a	64
2	Me	Ph	CO_2Et	 5b	57
3	Ph	Ph	CO_2Me	 5c	53
4	Ph	Ph	CO_2Et	 5d	63

showed two triplets at $\delta = 7.16$ ppm ($^3J_{HH} = 8.4$ Hz) and $\delta = 7.40$ ppm ($^3J_{HH} = 8.2$ Hz), and a doublet at $\delta = 7.99$ ppm ($^3J_{HH} = 8.5$ Hz). In addition, in the ^{13}C NMR spectra of **5a**, two ester CO signals overlapped at 160.4 ppm, and the ^{13}C NMR spectra of **5a** revealed 14 distinct signals, indicating that the hypothesized structure is correct. The mass spectrum of compound **5a** showed the molecular ion peak at 390 m/*z*, which was expected (See experimental section).

To confirm the generalizability of the reaction, compounds **5a-i** were synthesized through the one-pot reaction between *β*-keto esters **1** or acetylenic esters **2**, with hydrazines **3**, CS_2, and dialkyl acetylenedicarboxylates **4** in the presence of Et_3N in CH_3CN. The reactions proceeded well, and the products **5b-i** were obtained with a good yield within 6 h (See Table 2).

The proposed mechanism for this reaction is depicted in Scheme 2. Initially, the pyrazolone derivatives **I** were generated from the reaction of *β*-keto esters **1** or acetylenic esters **2**, with hydrazine derivatives **3** [40, 41]. Subsequently, the tautomeric intermediates **II** and **III** were obtained by adding the in situ generated pyrazolone derivative **I** to CS_2 in the presence of Et_3N [42]. Following the Michel addition of sulfur anion of **II** or **III** to triple bound of acetylenic esters **4**, resulting in the production of intermediate **IV**. Cyclization of intermediate **IV** through the second Michel addition, resulting in intermediate **V** [43]. Finally, intermediate **V** is then oxidized in the presence of air to produce product **5** spontaneously (Scheme 2).

To investigate the effect of atmospheric oxygen on the formation of the product **5a**, the model reaction was performed under an argon atmosphere. In this case, TLC analysis showed that product **5a** was not formed. This shows that atmospheric oxygen acts as an oxidant in this reaction.

Conclusion

In conclusion, we successfully presented a mild, facile, and one-pot method for the synthesis of new pyrazolone-1,4-dithiafulvene hybrids by using readily available starting materials through a one-pot reaction between *β*-keto esters or dialkyl acetylenedicarboxylates with hydrazines, carbon disulfide, and dialkyl acetylenedicarboxylates in good yields. A screening of the reaction conditions demonstrated that, performing this reaction at room temperature and in acetonitrile in the presence of two equivalents of triethylamine as a base, are the best ones. The good yields and the ease of workup procedure make it an appealing, practical, and acceptable one-pot method for producing functionalized pyrazolone-1,4-dithiafulvene hybrids.

Experimental section

General information

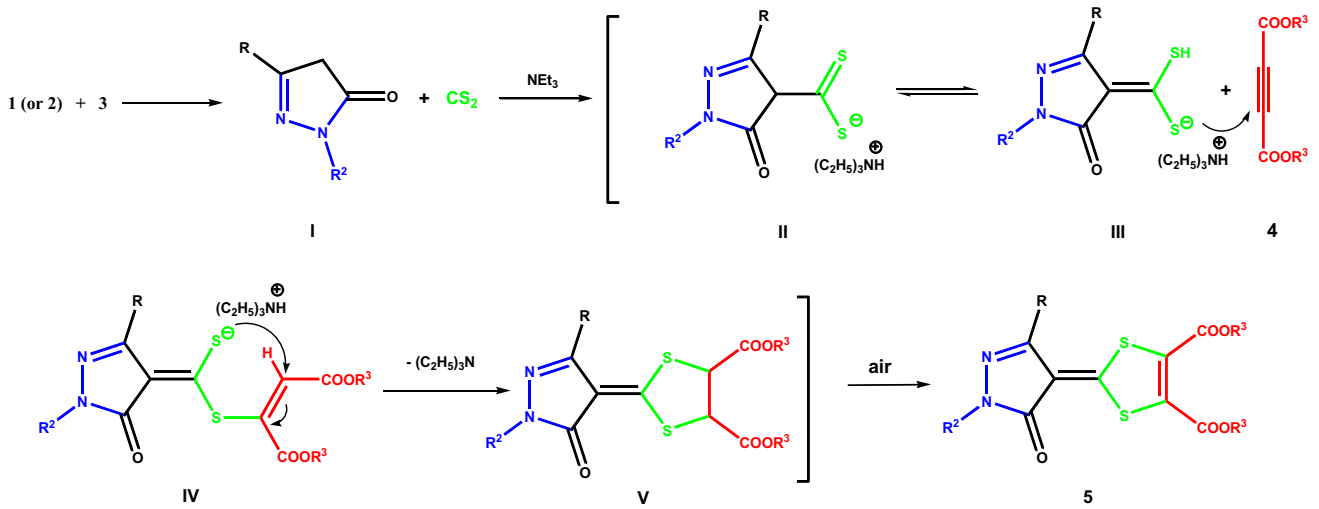
Dialkyl acetylendicarboxylate, hydrazines, carbon disulfide, *β*-keto esters, and all solvents were obtained from Merck (Germany) and were used without further purification. R_F values refer to thin-layer chromatography (TLC) performed on silica gel 60 F_{254} aluminum-backed silica plates (Merck). Melting points were measured with a Stuart SMP-3 apparatus. IR spectra of products were measured with an FTIR Perkin Elmer RXI. NMR spectra were reported on a Varian Inova 500 MHz (500 MHz for ^{1}H and 125 MHz for ^{13}C) with $CDCl_3$ as the solvent. Chemical shifts are given in ppm (δ) relative to internal TMS, and coupling constants (J) are reported in Hertz (Hz). Mass spectra were recorded with an Agilent 5977A Series MSD spectrometer operating at an ionization potential of 70 eV.

General procedure for the synthesis of products (5a-i), exemplified by 5a

A mixture of ethyl acetoacetate (1 mmol) with phenyl hydrazine (1 mmol) and Et_3N (2 mmol) in CH_3CN (5 mL) was stirred for 2 h at room temperature. After that, carbon disulfide (1.2 mmol) was added, and the mixture was stirred for 30 min. Then, dropwise additions of DMAD (1 mmol) were made, and the mixture was stirred for 6 h. Following that, the solvent was removed under reduced pressure, and the residue was washed with water to yield the pure product. The product was recrystallized in ethanol to achieve higher purity samples.

Dimethyl 2-(3-methyl-5-oxo-1-phenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5a)

Orange powder; yield: 0.25 g (64%); m.p. 200–201 °C. TLC $R_F = 0.65$ (ethyl acetate/*n*-hexane = 3:7), IR (KBr, υ, cm^{-1}): 1737 (CO_2Me), 1526 (C=CS_2), 1252 (C−O), 754 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 390 (M^+, 100), 331 (40), 257 (27), 207 (17), 91 (17). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.46$ (s, 3H, N=CCH_3), 3.95 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.16 (t, 1H, $^3J_{HH} = 7.4$ Hz, CH_{para}), 7.4 (t, 2H, $^3J_{HH} = 7.2$ Hz, CH_{meta}), 7.99 (d, 2H, $^3J_{HH} = 8.5$ Hz, CH_{ortho}) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): $\delta = 16.6$ (N=C–CH_3), 54.1 and 54.2



Scheme 2 The proposed mechanism for the synthesis of pyrazolone-1,4-dithiafulvene hybrids **5**

($2OCH_3$), 112.9 ($C{=}CS_2$), 118.7 ($2CH_{ortho}$), 124.8 (CH_{para}), 129.0 ($2CH_{meta}$), 131.2 and 137.5 ($2{=}C{-}CO_2CH_3$), 138.7 (C_{ipso}), 144.4 (C=N), 158.9 (S–C–S), 159.5 (N–C=O), 160.4 ($2CO_2CH_3$) ppm.

Diethyl 2-(3-methyl-5-oxo-1-phenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5b)

Orange powder; yield: 0.24 g (57%); m.p. 198–199 °C. TLC $R_F = 0.55$ (ethyl acetate/*n*-hexane = 3:7), IR (KBr, υ, cm^{-1}): 1735 (CO_2Et), 1524 ($C{=}CS_2$), 1238 (C−O), 755 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 418 (M^+, 100), 345 (12), 215 (25), 185 (14), 91 (27), 28 (16). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.40$ (t, 6H, $^3J_{HH} = 7.1$ Hz, $2CO_2CH_2CH_3$), 2.48 (s, 3H, $N{=}CCH_3$), 4.41 (q, 4H, $^3J_{HH} = 7.1$ Hz, $2CO_2CH_2CH_3$), 7.17 (t, 1H, $^3J_{HH} = 7.3$ Hz, CH_{para}), 7.40 (t, 2H, $^3J_{HH} = 7.4$ Hz, $2CH_{meta}$), 7.99 (d, 2H, $^3J_{HH} = 8.0$ Hz, $2CH_{ortho}$) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): $\delta = 14.1$ ($2OCH_2CH_3$), 16.6 ($N{=}C{-}CH_3$), 63.8 ($2OCH_2$), 112.7 ($C{=}CS_2$), 118.6 ($2CH_{ortho}$), 124.8 (CH_{para}), 129.0 ($2CH_{meta}$), 131.4 and 137.5 ($2{=}C{-}CO_2CH_3$), 138.7 (C_{ipso}), 144.5 (C=N), 158.5 (S–C–S), 158.6 (N–C=O), 159.1 ($2CO_2CH_2CH_3$) ppm.

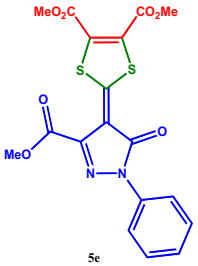
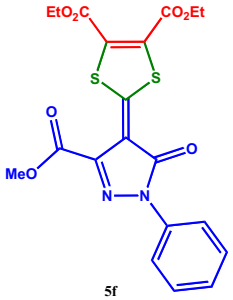
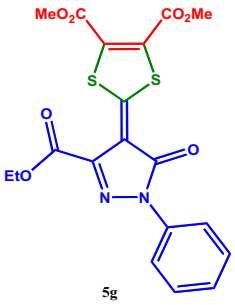
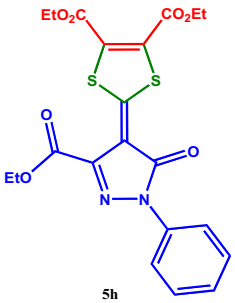
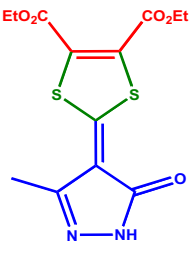
Dimethyl 2-(5-oxo-1,3-diphenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5c)

Orange powder; yield: 0.24 g (53%); m.p. 207–209 °C. TLC $R_F = 0.6$ (ethyl acetate/*n*-hexane = 3:7), IR (KBr, υ, cm^{-1}): 1738 (CO_2Me), 1501 ($C{=}CS_2$), 1258 (C−O), 756 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 394 (M^+-CO_2Me, 100), 366 (11), 335 (12), 281 (13), 261 (17), 207 (28), 145 (39), 91 (13). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.87$ (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 7.20 (t, 1H, $^3J_{HH} = 7.3$ Hz, CH_{para}), 7.42 (t, 2H, $^3J_{HH} = 7.8$ Hz, $2CH_{meta}$), 7.54–7.60 (m, 5H, 5CH-Ar), 8.07 (d, 2H, $^3J_{HH} = 8.2$ Hz, $2CH_{ortho}$) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): $\delta = 53.7$ and 53.8 ($2OCH_3$), 111.1 ($C{=}CS_2$), 118.8 ($2CH_{ortho}$), 124.9 (CH_{para}), 128.7 ($4CH_{meta}$), 129.1 ($2CH_{ortho}$), 130.1 (CH_{para}), 131.4 ($=C{-}CO_2CH_3$), 132.4 (C_{ipso}), 135.9 ($=C{-}CO_2CH_3$), 138.4 (C_{ipso}), 147.2 (C=N), 159.0 (S–C–S), 159.2 (N–C=O), 162.0 and 162.1 ($2CO_2CH_3$) ppm.

Diethyl 2-(5-oxo-1,3-diphenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5d)

Orange powder; yield: 0.3 g (63%); m.p. 184–185 °C. TLC $R_F = 0.55$ (ethyl acetate/*n*-hexane = 3:7), IR (KBr, υ, cm^{-1}): 1729 (CO_2Et), 1494 ($C{=}CS_2$), 1244 (C−O), 756 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 480 (M^+, 100), 407 (20), 310 (5), 277 (32), 247 (16), 145 (40), 91 (36). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.32$ (t, 3H, $^3J_{HH} = 7.1$ Hz, $CO_2CH_2CH_3$), 1.39 (t, 3H, $^3J_{HH} = 7.0$ Hz, $CO_2CH_2CH_3$), 4.33 (q, 2H, $^3J_{HH} = 7.1$ Hz, OCH_2), 4.39 (q, 2H, $^3J_{HH} = 7.0$ Hz, OCH_2), 7.20 (t, 1H, $^3J_{HH} = 7.3$ Hz, CH_{para}), 7.42 (t, 2H, $^3J_{HH} = 7.8$ Hz, $2CH_{meta}$), 7.55–7.61 (m, 5H, 5CH-Ar), 8.08 (d, 2H, $^3J_{HH} = 8.2$ Hz, $2CH_{ortho}$) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): $\delta = 14.0$ and 14.1 ($2OCH_2CH_3$), 63.4 and 63.5 ($2OCH_2$), 111.2 ($C{=}CS_2$), 119.0 ($2CH_{ortho}$), 125.1 (CH_{para}), 129.0 ($4CH_{meta}$), 129.3 ($2CH_{ortho}$), 130.3 (CH_{para}), 131.7 ($=C{-}CO_2CH_3$), 133.0 (C_{ipso}), 136.1 ($=C{-}CO_2CH_3$), 138.7 (C_{ipso}), 147.4 (C=N), 158.9 (S–C–S), 159.2 (N–C=O), 162.4 and 162.8 ($2CO_2CH_3$) ppm.

Table 2 (continued)

Entry	R /or R^1	R^2	R^3	Product	Yield (%)[a]
5	CO_2Me	Ph	CO_2Me	 5e	51
6	CO_2Me	Ph	CO_2Et	 5f	54
7	CO_2Et	Ph	CO_2Me	 5g	50
8	CO_2Et	Ph	CO_2Et	 5h	51
9	Me	H	CO_2Et	 5i	52

[a]Isolated yields after recrystallization

Dimethyl 2-(3-(methoxycarbonyl)-5-oxo-1-phenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5e)

Yellow powder; yield: 0.22 g (51%); m.p. 246–248 °C. TLC R_F = 0.55 (ethyl acetate/*n*-hexane = 4:6), IR (KBr, υ, cm^{-1}): 1753 and 1712 (CO_2Me), 1487 (C=CS_2), 1226 (C−O), 764 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 434 (M^+, 100), 406 (12), 375 (11), 347 (21), 315 (15), 273 (11), 77 (19). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.97 (s, 6H, 2OCH_3), 4.03 (s, 3H, OCH_3), 7.27 (t, 1H, $^3J_{HH}$ = 7.0 Hz, CH_{para}), 7.45 (t, 2H, $^3J_{HH}$ = 7.0 Hz, CH_{meta}), 8.02 (d, 2H, $^3J_{HH}$ = 8.0 Hz, CH_{ortho}) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): δ = 53.0, 54.0, and 54.1 (3OCH_3), 108.7 (C=CS_2), 120.2 (2CH_{ortho}), 126.4 (CH_{para}), 129.1 (2CH_{meta}), 135.3 (=C–CO_2CH_3), 135.5 (C_{ipso}), 137.1 (=C–CO_2CH_3), 138.0 (C=N), 159.3 (S–C–S), 159.4 (N–C=O), 162.7 (2CO_2CH_3), 167.6 (CO_2CH_3) ppm.

Diethyl 2-(3-(methoxycarbonyl)-5-oxo-1-phenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5f)

Orange powder; yield: 0.25 g (54%); m.p. 165–167 °C. TLC R_F = 0.5 (ethyl acetate/*n*-hexane = 4:6), IR (KBr, υ, cm^{-1}): 1731 (CO_2Et), 1491 (C=CS_2), 1241 (C−O), 757 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 390 (M^+-CO_2Et, 74), 281 (42), 253 (13), 207 (100), 133 (10), 77 (14). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.39 (t, 6H, $^3J_{HH}$ = 7.1 Hz, 2$CO_2CH_2CH_3$), 4.03 (s, 3H, OCH_3), 4.43 (q, 4H, $^3J_{HH}$ = 7.1 Hz, 2OCH_2), 7.20 (t, 1H, $^3J_{HH}$ = 7.3 Hz, CH_{para}), 7.44 (t, 2H, $^3J_{HH}$ = 7.3 Hz, 2CH_{meta}), 8.01 (d, 2H, $^3J_{HH}$ = 8.6 Hz, 2CH_{ortho}) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): δ = 14.1 (2OCH_2CH_3), 53.0 (OCH_3), 63.7 and 63.8 (2OCH_2), 108.5 (C=CS_2), 120.3 (2CH_{ortho}), 126.4 (CH_{para}), 129.1 (2CH_{meta}), 135.3 (=C–CO_2CH_3), 135.9 (C_{ipso}), 137.0 (=C–CO_2CH_3), 138.0 (C=N), 159.1 (S–C–S), 162.3 (N–C=O), 162.7 (2CO_2CH_3), 167.9 (CO_2CH_3) ppm.

Dimethyl 2-(3-(ethoxycarbonyl)-5-oxo-1-phenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5 g)

Yellow powder; yield: 0.22 g (50%); m.p. 223–224 °C. TLC R_F = 0.5 (ethyl acetate/*n*-hexane = 4:6), IR (KBr, υ, cm^{-1}): 1717 (CO_2Me), 1491 (C=CS_2), 1227 (C−O), 759 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 448 (M^+, 100), 347 (23), 284 (12), 257 (25), 207 (23), 77 (17). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.49 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 3.97 and 3.98 (2 s, 6H, 2OCH_3), 4.51 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 7.26 (Overlapped with solvent peak, 1H, CH_{para}), 7.45 (t, 2H, $^3J_{HH}$ = 8.6 Hz, 2CH_{meta}), 8.03 (d, 2H, $^3J_{HH}$ = 8.6 Hz, 2CH_{ortho}) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): δ = 14.4 (OCH_2CH_3), 54.0 and 54.1 (2OCH_3), 62.4 (OCH_2), 109.1 (C=CS_2), 120.3 (2CH_{ortho}), 126.4 (CH_{para}), 129.1 (2CH_{meta}), 135.5 (=C–CO_2CH_3), 135.7 (C_{ipso}), 137.0 (=C–CO_2CH_3), 138.0 (C=N), 159.4 (S–C–S), 159.5 (N–C=O), 162.4 and 162.5 (2CO_2CH_3 and $CO_2C_2H_5$) ppm.

Diethyl 2-(3-(ethoxycarbonyl)-5-oxo-1-phenyl-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5 h)

Yellow powder; yield: 0.24 g (51%); m.p. 158–159 °C. TLC R_F = 0.65 (ethyl acetate/*n*-hexane = 4:6), IR (KBr, υ, cm^{-1}): 1725 (CO_2Et), 1494 (C=CS_2), 1254 (C−O), 756 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 404 (M^+-CO_2Et, 58), 312 (100), 281 (18), 212 (24), 207 (45), 110 (11), 77 (7). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (t, 3H, $^3J_{HH}$ = 6.9 Hz, OCH_2CH_3), 1.41 (t, 3H, $^3J_{HH}$ = 6.9 Hz, OCH_2CH_3), 1.49 (t, 3H, $^3J_{HH}$ = 7.1 Hz, OCH_2CH_3), 4.40–4.45 (m, 4H, 2OCH_2), 4.51 (q, 2H, $^3J_{HH}$ = 7.1 Hz, OCH_2), 7.26 (Overlapped with solvent peak, 1H, CH_{para}), 7.44 (t, 2H, $^3J_{HH}$ = 8.2 Hz, 2CH_{meta}), 8.03 (d, 2H, $^3J_{HH}$ = 8.1 Hz, 2CH_{ortho}) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): δ = 14.1 (2OCH_2CH_3), 14.4 (OCH_2CH_3), 62.3, 63.6, and 63.7 (3OCH_2), 108.6 (C=CS_2), 120.3 (2CH_{ortho}), 126.3 (CH_{para}), 129.1 (2CH_{meta}), 135.7 (=C–CO_2CH_3), 135.9 (C_{ipso}), 136.9 (=C–CO_2CH_3), 138.1 (C=N), 159.0 (S–C–S), 159.1 (N–C=O), 162.4 (2$CO_2C_2H_5$), 167.8 ($CO_2C_2H_5$) ppm.

Diethyl 2-(3-methyl-5-oxo-1*H*-pyrazol-4(5*H*)-ylidene)-1,3-dithiole-4,5-dicarboxylate (5i)

Orange powder; yield: 0.18 g (52%); m.p. 187–190 °C. TLC R_F = 0.5 (ethyl acetate/*n*-hexane = 6:4), IR (KBr, υ, cm^{-1}): 3462 (N–H), 1742 and 1736 (CO_2Et), 1507 (C=CS_2), 1287 (C−O), 767 (S−C) cm^{-1}. MS (EI): *m/z* (%) = 342 (M^+, 100), 297 (5), 269 (9), 242 (35), 185 (16), 140 (29), 83(16). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35–1.37 (m, 6H, 2OCH_2CH_3), 2.35 (s, 3H, CH_3), 4.37–4.39 (m, 4H, 2OCH_2CH_3), 9.67 (s, 1H, NH) ppm. ^{13}C NMR (125.59 MHz, $CDCl_3$): δ = 14.0 and 14.1 (2OCH_2CH_3), 16.6 (N=C–CH_3), 63.6 and 63.7 (2OCH_2), 111.5 (C=CS_2), 131.0 and 137.4 (2=C–CO_2CH_3), 144.9 (C=N), 158.6 (S–C–S), 159.2 (N–C=O), 160.6 and 165.5 (2$CO_2C_2H_5$) ppm.

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Declarations

Conflict of interest No potential conflict of interest was reported by the authors.

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