Journal of the Iranian Chemical Society
https://doi.org/10.1007/s13738-019-01644-z

ORIGINAL PAPER

A catalyst-free 1,4-Michael-type reaction of in situ generated *ortho*-quinone methides (*o*-QMs) with dithiocarbamic acid salts in water

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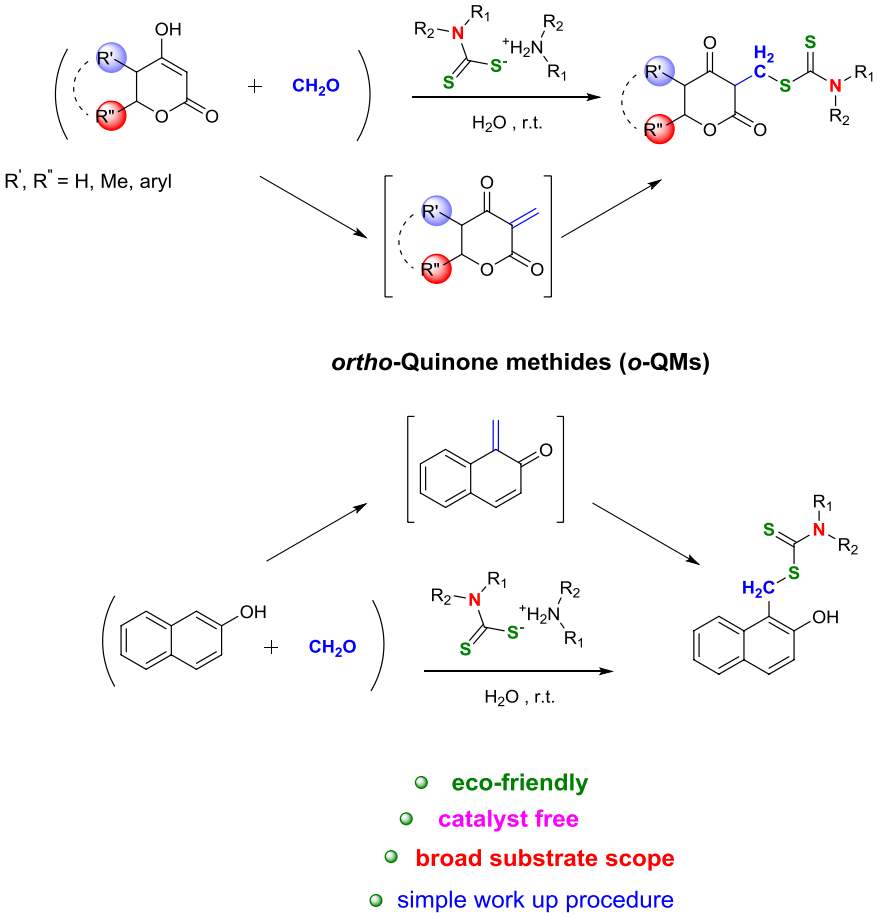
Received: 2 June 2018 / Accepted: 22 February 2019

Abstract

Abstract A catalyst-free conjugate addition of dithiocarbamic acid salts to in situ generated *ortho*-quinone methides (*o*-QMs) was investigated for the first time. Several dithiocarbamate derivatives of 4-hydroxycoumarine, 4-hydroxypyrone and 2-naphthol were synthesized in moderate-to-good yields in water at room temperature.

Graphical abstract



Catalyst-free addition of dithiocarbamic acid salts to in situ generated *o*-QMs in water at room temperature.

Extended author information available on the last page of the article

Published online: 08 April 2019

Keywords Catalyst-free · Chromanes · Dithiocarbamate · Green chemistry · *Ortho*-quinone methides

Introduction

ortho-Quinone methides (*o*-QMs) are valuable synthetic intermediates and are widely used in the synthesis of natural products, pharmaceuticals and biologically active molecules [1–3]. *o*-QMs are highly polarized and then quite reactive [4]. These reactive intermediates undergo 1,4-conjugate addition such as 1,4-Michael-type addition and aza-Michael reactions with nucleophiles [5, 6], as well as [4+2] cycloaddition reactions with various dienophiles [7, 8].

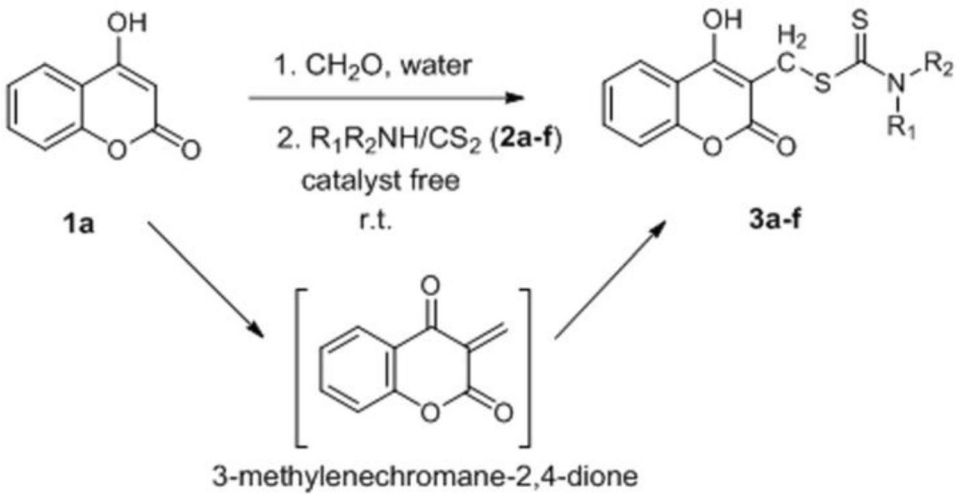
In recent years, many strategies have been established for in situ generation of *ortho*-quinone methides [9–15]. However, these methods have various limitations such as the use of oxidant, acidic or basic conditions, use of organic solvents, high temperatures, or photoirradiations, which limit the application of *o*-QMs in organic synthesis [16]. Accordingly, designing novel synthesis methodologies to access *ortho*-quinone methides in mild reaction conditions seems to be highly desirable. Herein, we wish to report a catalyst-free facile generation of *ortho*-quinone methides in water and their subsequent reaction with dithiocarbamic acid salts as nucleophiles.

Organic dithiocarbamates are of significant importance as biologically active compounds [17], antibacterial [18, 19], antifungal [20] and potent anticancer agents [21], protecting groups in peptide synthesis [22], and linkers in solid phase organic synthesis [23]. Furthermore, they have found wide applications in the reversible addition–fragmentation chain transfer (RAFT) polymerization [24, 25], sulfur vulcanization in rubber manufacturing [26, 27] and in medicinal chemistry [28].

Dithiocarbamic acid salts are good nucleophils and react with different electrophiles such as epoxides [29], alkyl halides [30, 31], α,β-unsaturated carbonyl compounds [32], alkynes [33] and arylhalides [34, 35]. These compounds also undergo reaction with carbonyl compounds [36].

Functionalization of dithiocarbamates leads to molecular diversity and production of derivatives which may have interesting biological properties. For instance, a series of dithiocarbamates derived from fluconazole analogs were synthesized through incorporation of dithiocarbamate moiety with triazoles, showing enhanced antifungal activity of the resulting dithiocarbamates [37]. Kim and Lee have reported the synthesis of 3-[(*N,N*-disubstituted thiocarbonylthio) acetyl]coumarins and tested them for antifungal activity [38].

In continuation of our work on the synthesis of dithiocarbamates and investigations of their applications as intermediates in organic transformations [30–34, 39], herein, we reported the conjugate addition reaction of dithiocarbamic acid salts, as nucleophiles, to in situ generated *o*-QMs of bioactive heterocycles such as 4-hydroxycoumarine, 4-hydroxypyrones, and 2-naphthol in water under catalyst-free condition (Scheme 1). Surprisingly, to our knowledge, the trapping of *o*-QMs with dithiocarbamic acid salts as nucleophilic reagents has never been reported. Our studies are conceptually related to the works of Kumar et al. in which electron-rich arenes were employed as nucleophile in intermolecular Michael-type C–H hydroarylation of in situ generated *o*-QMs in water [40] and in glycerol [41].



Scheme 1 Addition of dithiocarbamates to in situ generated *ortho*-quinone methide

Results and discussion

We initiated our investigation by evaluating the one-pot, four-component reaction of in situ generated *o*-QM derived from 4-hydroxycoumarin and formaldehyde with pyrrolidine and carbon disulfide (CS_2) in water in the absence of any catalyst at room temperature. Under these conditions, the desired product **3a** was obtained in 20% yield. As an alternative synthetic strategy to overcome the low yield of the desired product, the dithiocarbamic acid salt of pyrrolidine was prepared in a separate vessel and was added to the solution of in situ generated *o*-QM in water at room temperature. It was found that the reaction was completed within 4 h and **3a** was obtained in 95% yield. The ^{1}H NMR spectra of **3a** show a characteristic peak at δ 4.70 ppm corresponding to the hydrogens of CH_2 attached to C-3 position of 4-hydroxycoumarin ring, whereas in the ^{13}C NMR spectra, the carbon of this CH_2 was appeared at δ 32.1 ppm. In addition, ^{13}C of dithiocarbamate moiety was assigned at δ 193.6 ppm in ^{13}C NMR spectra.

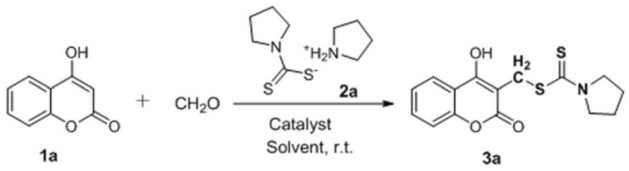
Comparative reactions were performed in other solvents to investigate the advantageous role of water as a solvent for this method. After screening different solvents such as ethanol, dichloromethane, toluene, tetrahydrofuran, and acetonitrile (Table 1, entries 1–6), it was found that the best solvent in terms of fast conversion, non-toxic, and quantified yield is water.

Attempts to obtain the desired product using a Bronsted acid such as boric acid, a heteropoly acid, or Lewis acids such as $ZnCl_2$ and $CuSO_4$ were not successful (Table 1, entries 7–10). Performing the reaction under reflux without any catalyst provided **3a** with considerably lower yield (Table 1, entry 11).

It is obvious that water is an inexpensive and environmentally benign green solvent for various chemical and biological reactions. In many cases using water as the reaction medium has high priority because of its unique reactivity and selectivity which is due to hydrophobic effects, that is different from those in organic solvents [42–44]. Hence, water was chosen for further investigations.

To evaluate the scope of this process, dithiocarbamic acid salts of various amines **a**–**f** were subsequently reacted with in situ generated *o*-QMs derived from the Knoevenagel condensation of 4-hydroxycoumarin and formaldehyde under the above-optimized reaction condition and the results are summarized in Table 2. In almost all cases studied, the reaction proceeded smoothly and was typically completed within 4–8 h at r.t. The products **3a**–**f** were obtained in good yields and their structures were assigned on the basis of ^{1}H and ^{13}C NMR spectral data. The proposed mechanism for 1,4-Michael-type addition of 4-hydroxycoumarin with dithiocarbamic acid salts is shown in Scheme 2.

Table 1 Optimization studies



Entry	Catalyst (20 mol%)	Solvent	Yield[a] **3a** (%)
1	Catalyst free	Water	95
2	Catalyst free	Ethanol	30
3	Catalyst free	DCM	10
4	Catalyst free	Toluene	10
5	Catalyst free	THF	20
6	Catalyst free	CH_3CN	20
7	Boric acid	Water	10
8[b]	HPA	Water	30
9	$ZnCl_2$	Water	Trace
10	$CuSO_4$	Water	Trace
11[c]	Catalyst free	Water	40
12[d]	Catalyst free	Water	92
13[e]	Catalyst free	Water	82

All reactions were carried out with 1 mmol of 4-hydroxycoumarin (1 equiv.), 2 mmol of formaldehyde (2 equiv.), 1.5 mmol of pyrrolidine dithiocarbamic acid salt (**2a**) (1.5 equiv.) and 10 mol% of catalyst in 2 mL of solvent at r.t. for 5 h

[a]Isolated yield

[b]Heteropoly acid ($H_3PW_{12}O_{40}$)

[c]Refluxed

[d]At room temperature for 16 h

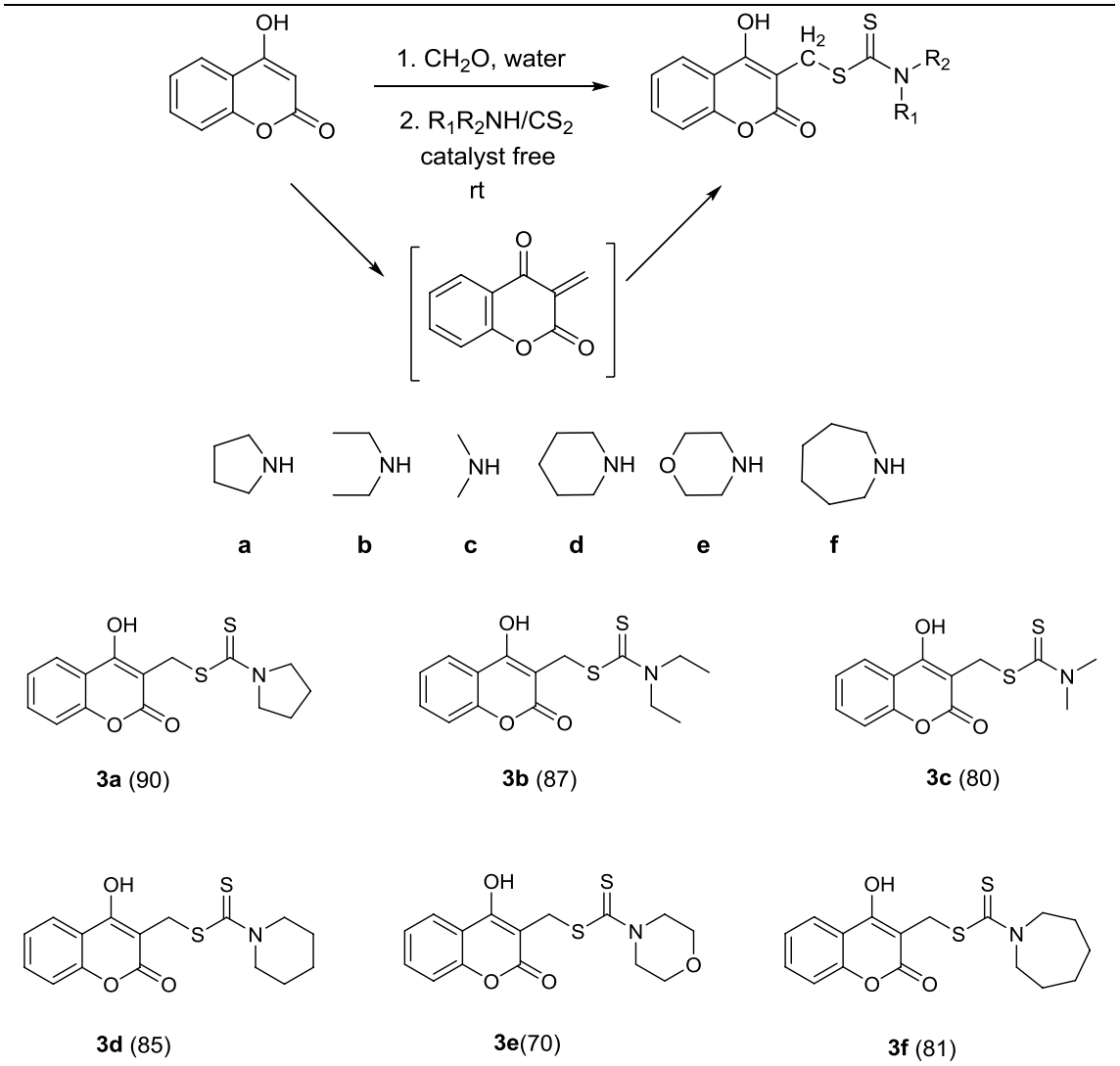
[e]1.0 equiv. of **2a** was used as the substrate

It should be noted that using dithiocarbamic acid salts of primary aliphatic amines (such as propyl amine, cyclohexyl amine and benzylamine) in this process led to formation of undesired dimer adduct **4a**, dicoumarol, as the major product (Scheme 3).

This process could easily be extended to other 4-hydroxy-2-pyrones as well. Thus, 4-hydroxy-6-methyl-2-pyrone was converted into corresponding *o*-QM in reaction with formaldehyde in water solution. Reaction of the in situ generated *o*-QM with various dithiocarbamic acid salts as nucleophile under the optimized reaction conditions furnished products **6a**–**f** in moderate-to-good overall yields (Table 3).

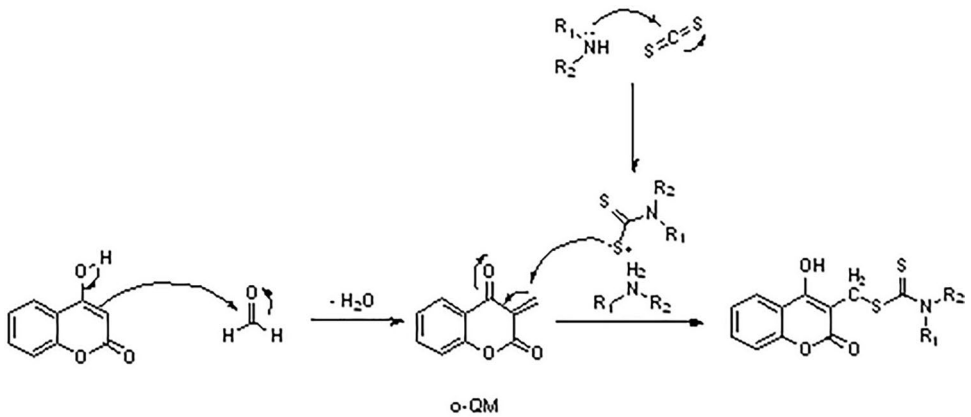
The excellent results obtained for 4-hydroxy-2-pyrones inspired us to pursue this strategy further and extent it to electron-rich naphthols which are also known to be good substrates for in situ generation of *o*-QMs [45]. Thus, reaction of 2-naphthol with formaldehyde in water generated highly reactive *o*-naphthoquinone methides (*o*-NQM), which

Table 2 Conjugate addition of various dithiocarbamic acid salts to *o*-QM of 4-hydroxycoumarin



Isolated yield

Scheme 2 Proposed mechanism for 1,4-Michael-type addition of 4-hydroxycoumarin with dithiocarbamic acid salts



Scheme 3 Reaction of benzyl amine dithiocarbamic acid salt with *o*-QM

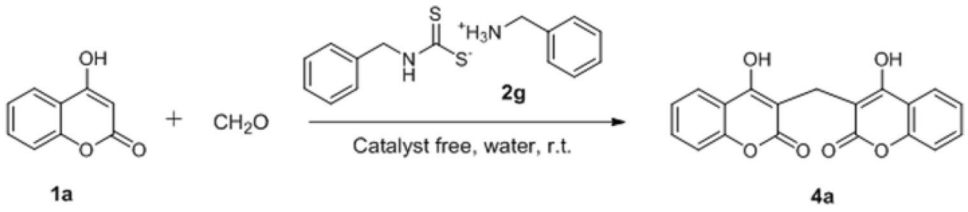
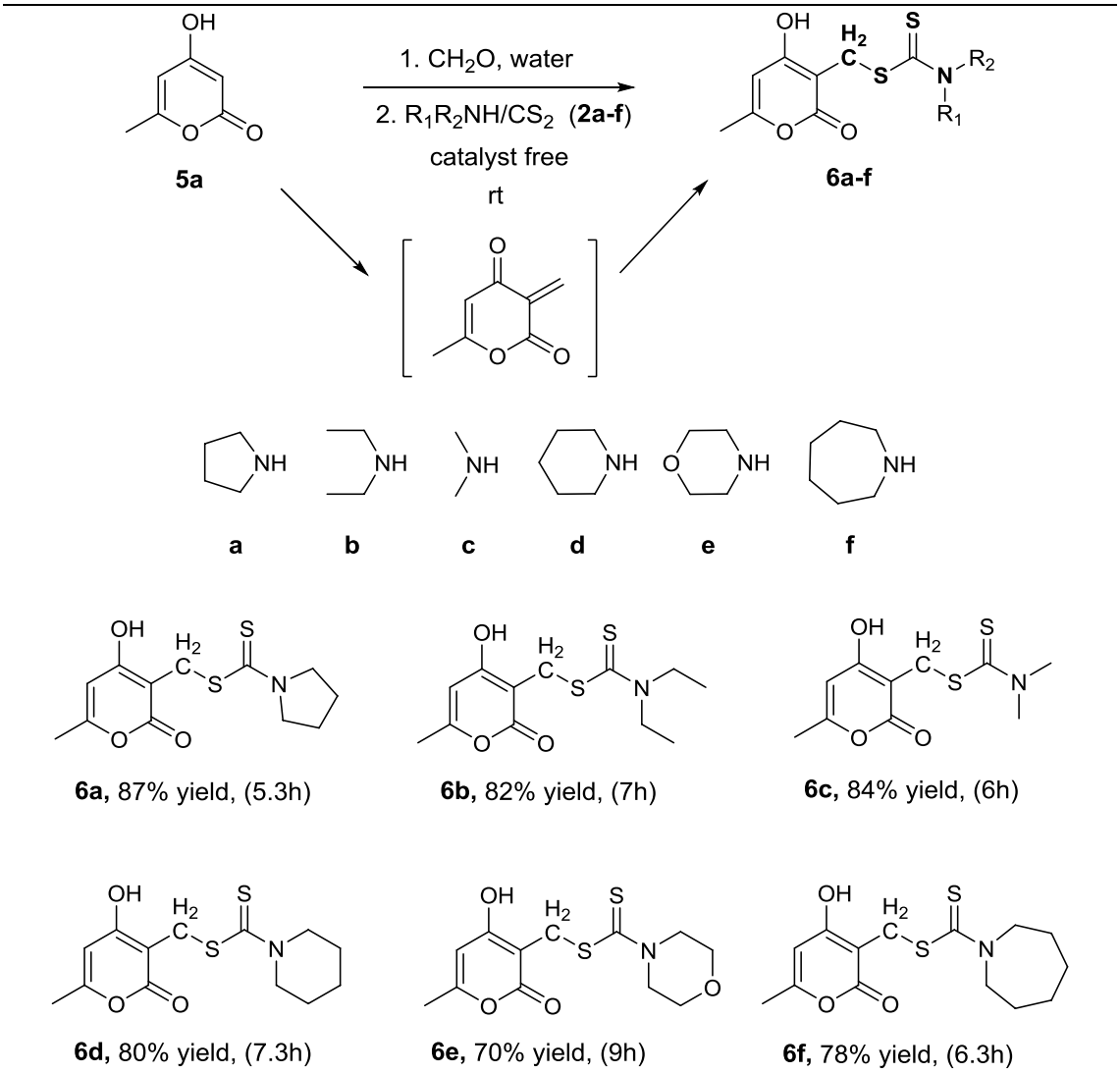


Table 3 Conjugate addition of various dithiocarbamic acid salts to *o*-QM of 4-hydroxy-6-methyl-2-pyrone

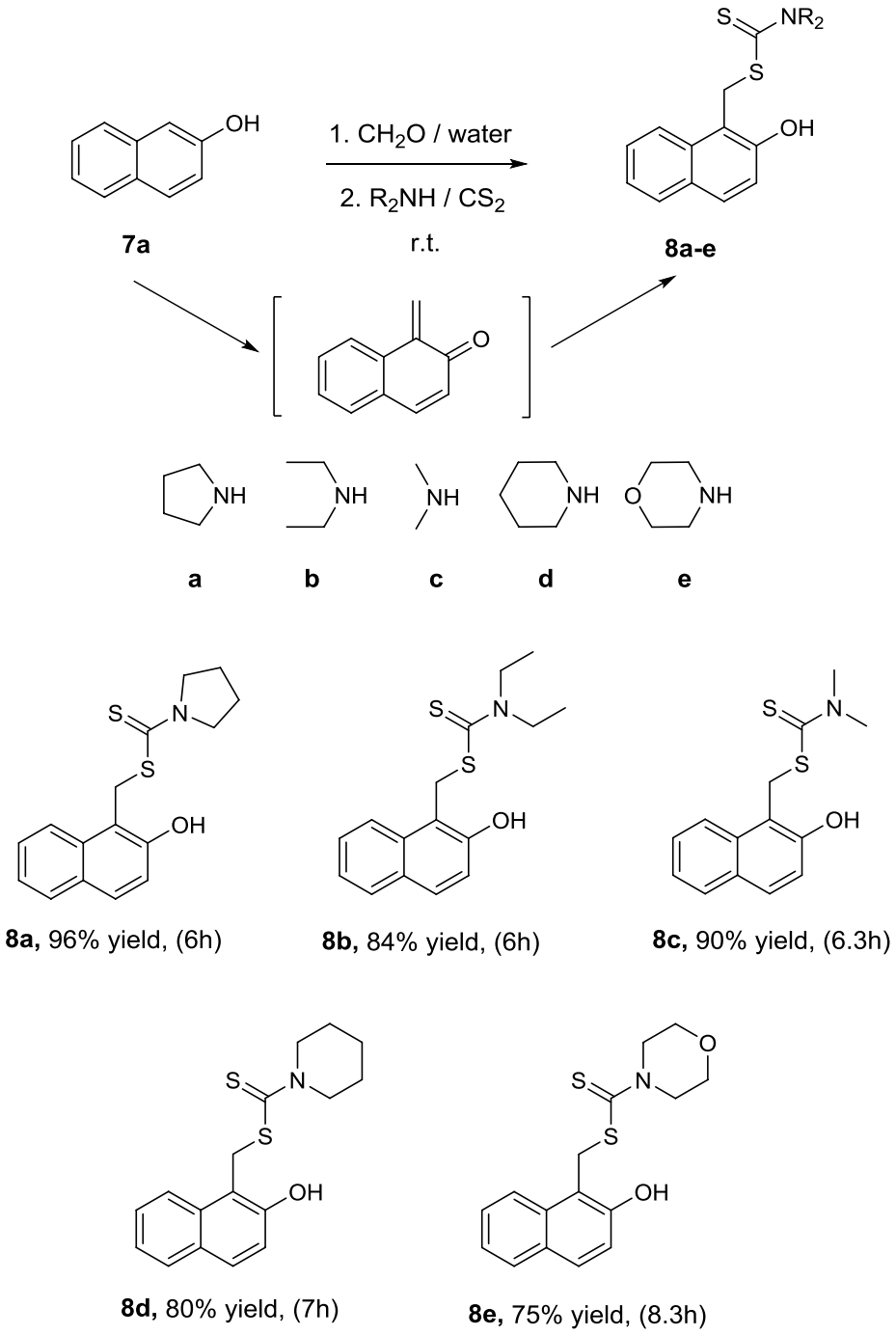


Isolated yield

could undergo facile conjugate addition with various dithiocarbamic acid salts. This reaction proceeded under ambient temperature in an aqueous solution and products **8a**–**e** were obtained in high overall yields (Table 4).

To demonstrate the practicality of this green process, we conducted the synthesis of (2-hydroxynaphthalen-1-yl) methyl pyrrolidine-1-carbodithioate (**8a**) on a gram scale. The conjugate addition reaction of pyrrolidine dithiocarbamic salt (**2a**) to in situ generated 2-naphthol *o*-QM (*o*-NQM) proceeded to completion within 6 h at room temperature in water as solvent and 1.43 g (96%) of product **8a** was obtained (Scheme 4).

Table 4 Conjugate addition of various dithiocarbamic acid salts to *o*-QM of 2-naphthol

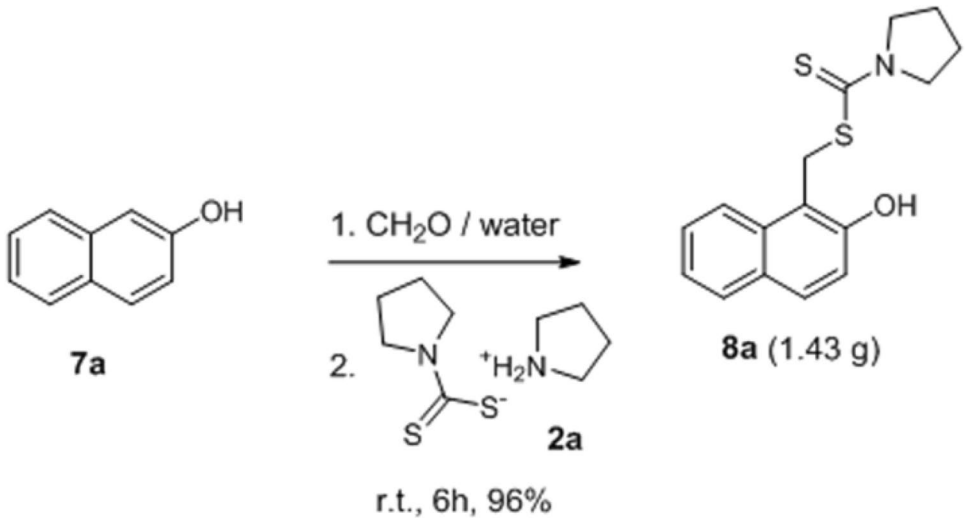


Isolated yield

Conclusions

In summary, the first conjugate additions of dithiocarbamic acid salts to *ortho*-quinone methides, generated by the Knoevenagel condensation, have been developed. An aqueous medium under catalyst-free condition at room temperature was used to synthesis these compounds. *Ortho*-quinone methides were in situ synthesized from formaldehyde with 4-hydroxycoumarin, 4-hydroxypyrone or 2-naphthol. Good yields (up to 96%) were achieved using stable *o*-QMs and a wide range of dithiocarbamic acid

Scheme 4 Synthesis of **8a** on a gram scale



salts. Furthermore, the products were isolated very easily by a simple filtration procedure.

Experimental section

General information

All reactions were carried out under an atmosphere of air. Melting points were determined in open capillary tubes with an electrothermal melting point apparatus and were uncorrected. FT-IR spectra were recorded on a Perkin-Elmer system 2000 FT-IR spectrometer. NMR spectra were recorded on a Bruker Avance DPX-300 and DPX-500 NMR spectrometer with TMS as the internal standard at room temperature. Chemical shifts (δ) are quoted in ppm and coupling constants (J) are measured in Hertz (Hz). All experiments were monitored by thin-layer chromatography (TLC) on precoated silica gel plates (Merck) and visualized under UV lamp at 254 nm for UV active materials. Elemental analysis was conducted with a Perkin-Elmer 2004 Series II CHN analyzer. Most reagents were obtained from commercial suppliers and used without further purification.

General procedure for the synthesis of 3a–f:

In a 25 mL round bottom flask equipped with a magnetic stir bar, 4-hydroxycoumarin (1 mmol), formaldehyde (2 mmol), and water (2 mL) were added. The reaction mixture was stirred at room temperature for 30 min. Then, the prepared dithiocarbamic acid salt [in a separate vessel with the reaction of an amine (1.5 mmol) and CS_2 (3 mmol)] was added. The reaction mixture was further stirred at room temperature for an appropriate time and the progress of the reaction was monitored by TLC. After completion of the reaction, the solid product was filtered off and recrystallized from ethanol. The purified product was obtained as a white solid.

General procedure for the synthesis of 6a–f:

4-Hydroxy-6-methyl-2-pyrone (1 mmol), formaldehyde (2 mmol), and water (2 mL) were taken in a 25 mL round bottom flask equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 30 min. After that, the prepared dithiocarbamic acid salt [in a separate vessel with the reaction of an amine (1.5 mmol) and CS_2 (3 mmol)] was added. The reaction mixture was further stirred at room temperature for an appropriate time and its progress was monitored by TLC. After completion of the reaction, the solid product was filtered off and recrystallized from ethanol. The purified product was obtained as a pale brown solid.

General procedure for the synthesis of 8a–e

In a 25 mL round bottom flask equipped with a magnetic stir bar, 2-naphthol (1 mmol), formaldehyde (2 mmol), and water (2 mL) were added. The reaction mixture was stirred at room temperature for 1 h. Then, the prepared dithiocarbamic acid salt [in a separate vessel with the reaction of an amine (1.5 mmol) and CS_2 (3 mmol)] was added. The reaction mixture was further stirred at room temperature for an appropriate time and TLC was used to monitor the reaction progress. After completion of the reaction, the solid product was filtered off and recrystallized from ethanol. The purified product was obtained as an off-white solid.

(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl pyrrolidine-1-carbodithioate (3a) White solid; yield: 95%; m.p. 179–181 °C, IR (KBr, cm^{-1}) ν_{max} 3383, 2957, 2873, 2701, 2544, 1704, 1628, 1540, 1465, 1441, 1275,

1219, 1147, 1102, 1052, 1004, 954, 903, 864, 763; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.50 (s, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.26 (m, 2H), 4.70 (s, 2H), 3.95 (t, J = 6.4 Hz, 2H), 3.64 (t, J = 6.4 Hz, 2H), 2.04 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 193.6, 163.7, 161.9, 152.6, 132.1, 124.0, 123.9, 116.3, 116.1, 102.5, 55.9, 51.3, 32.1, 25.9, 24.2. Anal. calcd for $C_{15}H_{15}NO_3S_2$: C, 56.05; H 4.70, N 4.36. Found: C 55.83, H 4.79, N 4.33.

(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl dimethylcarbamodithioate (3b) White solid; yield 93%; m.p. 185–189 °C, IR (KBr, cm^{-1}) ν_{max} 3217, 2928, 1675, 1625, 1498, 1454, 1616, 1393, 1254, 1212, 1165, 1132, 1106, 1061, 984, 950, 934, 769; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.36 (br, 1H), 7.89 (d, J = 7.1 Hz, 1H), 7.53 (dt, J = 1.18, J = 7.1 Hz, 1H), 7.28 (m, 2H), 4.74 (s, 2H), 3.61 (s, 3H), 3.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 192.6, 175.7, 165.8, 154.1, 131.5, 124.3, 123.1, 121.2, 116.5, 88.8, 56.2, 42.7. Anal. calcd for $C_{13}H_{13}NO_3S_2$: C 52.85, H 4.43, N 4.74. Found: C 52.77, H 4.52, N 4.72.

(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl diethylcarbamodithioate (3c) White solid; yield: 89%; m.p. 170–173 °C, IR (KBr, cm^{-1}) ν_{max} 3735, 2980, 2695, 2496, 1696, 1625, 1526, 1455, 1270, 1222, 1143, 1102, 1049, 977, 954, 902, 767 ; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.51 (s, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.28 (m, 2H), 4.74 (s, 2H), 4.06 (q, J = 6.7 Hz, 2H), 3.77 (q, J = 6.7 Hz, 2H), 1.31 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 196.8, 163.8, 162.1, 152.7, 132.2, 124.1, 123.9, 116.3, 116.2, 102.5, 50.9, 47.6, 32.9, 12.1, 11.5. Anal. calcd for $C_{15}H_{17}NO_3S_2$: C 55.71, H 5.30, N 4.33. Found: C 55.63, H 5.41, N 4.31.

(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl piperidine-1-carbodithioate (3d) White solid; yield 90%; m.p. 180–181 °C, IR (KBr, cm^{-1}) ν_{max} 3340, 2998, 2863, 1701, 1628, 1469, 1429, 1273, 1127, 1100, 1004, 921, 830; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.20 (s, 1H), 7.85 (d, J = 7.3 Hz, 1H), 7.47 (t, J = 7.3 Hz, 1H), 7.26 (m, 2H), 4.56 (s, 2H), 4.18 (t, J = 6.3 Hz, 2H), 3.88 (t, J = 6.3 Hz, 2H), 1.30–1.51 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 193.2, 163.3, 162, 152.7, 132.3, 124.1, 123.8, 116.4, 116.1, 102.6, 53.2, 51.6, 32.8, 26.4, 25.8, 24.6. Anal. calcd for $C_{16}H_{17}NO_3S_2$: C 57.28, H 5.11, N 4.17. Found: C 57.19, H 5.23, N 4.16.

(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl morpholine-4-carbodithioate (3e) White solid; yield 79%; m.p. 128–130 ◦C, IR (KBr, cm^{-1}) ν_{max} 3055, 1638, 1600, 1537, 1445, 1407, 1225, 1075, 952, 753; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.21 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.54 (m, 1H), 7.29 (m, 2H), 4.78 (s, 1H), 4.38 (t, J = 6.5 Hz, 2H), 3.96 (t, J = 6.5 Hz, 2H), 3.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 198.9, 163.7, 162.0, 152.7, 132.3, 124.1, 124.0, 116.4, 116.0, 102.3, 66.3, 65.8, 52.8, 50.9, 32.7. Anal. calcd for $C_{15}H_{15}NO_4S_2$: C 53.39, H 4.47, N 4.15. Found: C 53.31, H 4.59, N 4.12.

(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl azepane-1-carbodithioate (3f) White solid; yield 85%; m.p. 180–183 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.50 (br, 1H), 7.92 (d, J = 7.2 Hz, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.29 (m, 2H), 4.76 (s, 1H), 4.23 (t, J = 6.0 Hz, 2H), 3.92 (t, J = 6.0 Hz, 2H), 1.90 (m, 4H), 1.60 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.8, 163.9, 162.5, 152.9, 132.0, 124.3, 124.0, 116.7, 116.4, 102.9, 56.4, 53.4, 32.5, 28.3, 27.4, 27.0, 26.8. Anal. calcd for $C_{17}H_{19}NO_3S_2$: C 58.42, H 5.48, N 4.01. Found: C 58.33, H 5.56, N 3.98.

(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl pyrrolidine-1-carbodithioate (6a) Pale brown solid; yield: 87%; m.p. 155–157 °C, IR (KBr, cm^{-1}) ν_{max} 3388, 2965, 2867, 2635, 1660, 1629, 1558, 1424, 1327, 1254, 1108, 1009, 953, 915, 869; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 10.7 (br, 1H), 5.83 (s,1H), 4.52 (s, 2H), 3.93 (t, J = 6.5 Hz, 2H), 3.62 (t, J = 6.5 Hz, 2H), 2.18 (s, 3H), 2.08 (t, J = 6.7 Hz, 2H), 1.99 (t, J = 6.7 Hz, 2H);^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 193.9, 166.9, 165.5, 161.2, 101.4, 99.7, 55.8, 51.2, 31.8, 25.9, 24.3, 19.7. Anal. calcd for $C_{12}H_{15}NO_3S_2$: C 50.51, H 5.30, N 4.91. Found: C 50.39, H 5.39, N 4.90.

(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl diethylcarbamodithioate (6b) Pale brown solid; yield 82%; m.p. 147–149 °C, IR (KBr, cm^{-1}) ν_{max} 3408, 2970, 2869, 2624, 1632, 1564, 1438, 1331, 1261, 1100, 959, 919, 836, 767; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.2 (s, 1H), 5.80 (s, 1H), 4.55 (s, 2H), 4.04 (q, J = 6.7 Hz, 2H), 3.71 (q, J = 6.7 Hz, 2H), 2.19 (s, 3H), 1.26–1.99 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 193.9, 166.5, 165.2, 160.9, 101.0, 99.5, 47.9, 46.7, 31.8, 19.7, 13.0, 12.1. Anal. calcd for $C_{12}H_{17}NO_3S_2$: C 50.15, H 5.96, N 4.87. Found: C 50.06, H 6.05, N 4.86.

(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl dimethylcarbamodithioate (6c) Pale brown solid; yield: 84%; m.p. 160–162 °C, IR (KBr, cm^{-1}) ν_{max} 3419, 3009, 2955, 1673, 1529, 1471, 1446, 1375, 1289, 1246, 1213, 1160, 1111, 1038, 972, 944, 894, 787; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.5 (s, 1H), 5.95 (s, 1H), 4.40 (s, 2H), 3.54 (s, 3H), 3.34 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 193.4, 166.5, 164.9, 161.3, 101.3, 99.9, 56.5, 33.5, 19.5. Anal. calcd for $C_{10}H_{13}NO_3S_2$: C 46.30, H 5.05, N 5.40. Found: C 46.21, H 5.16, N 5.37.

(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl piperidine-1-carbodithioate (6d) Pale brown solid; yield 80%; m.p. 151–156 °C, IR (KBr, cm^{-1}) ν_{max} 3329, 3015, 2859, 1653, 1546, 1474, 1449, 1380, 1297, 1245, 1219, 1171, 1117, 972, 839, 740; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.8 (br, 1H), 5.89 (s, 1H), 4.49 (s, 2H), 4.13 (t, J = 6.6 Hz, 2H), 3.84 (t, J = 6.6 Hz, 2H), 2.20 (s, 3H), 1.23–1.28 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 192.5, 164.9, 164.2, 160.1, 101.1, 99.7, 52.7, 51.3, 31.8, 26.2, 25.5, 24.4, 19.4. Anal. calcd for $C_{13}H_{17}NO_3S_2$: C 52.15, H 5.71, N 4.68. Found: C 52.03, H 5.82, N 4.65.

(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl morpholine-4-carbodithioate (6e) Pale brown solid; yield 70%; m.p. 130–133 °C, IR (KBr, cm^{-1}) ν_{max} 3291, 3015, 1653, 1589, 1509, 1476, 1350, 1297, 1234, 1208, 1125, 1104, 979, 820, 715; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.20 (br, 1H), 5.85 (s, 1H), 4.63 (s, 2H), 4.35 (t, J = 6.4 Hz, 2H), 4.10 (t, J = 6.4 Hz, 2H), 3.63 (m, 4H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 199.1, 166.8, 164.9, 161.0, 101.2, 99.7, 66.2, 65.4, 52.4, 50.5, 32.3, 19.9. Anal. calcd for $C_{12}H_{15}NO_4S_2$: C 47.82, H 5.02, N 4.65. Found: C 47.75, H 5.12, N 4.62.

(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl azepane-1-carbodithioate (6f) Pale brown solid; yield 78%; m.p. 153–155 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.70 (br, 1H), 5.80 (s, 1H), 4.53 (s, 2H), 4.20 (t, J = 6.1 Hz, 2H), 3.90 (t, J = 6.1 Hz, 2H), 2.17 (s, 3H), 1.85 (m, 4H), 1.54 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.7, 167.8, 165.3, 161.6, 101.7, 101.3, 56.2, 52.1, 30.5, 28.2, 27.8, 26.9, 26.5, 19.5. Anal. calcd for $C_{14}H_{19}NO_3S_2$: C 53.64, H 6.12, N 4.47. Found: C 53.51, H 6.19, N 4.45.

(2-Hydroxynaphthalen-1-yl)methyl pyrrolidine-1-carbodithioate (8a) Off-white solid; yield 96%; m.p. 136–138 °C, IR (KBr, cm^{-1}) ν_{max} 3276, 2987, 2860, 1631, 1603, 1513, 1492, 1450, 1352, 1239, 1157, 1002, 919, 862, 835, 743; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.50 (br, 1H), 7.79 (m, 2H), 7.26–7.31 (m, 3H), 7.25 (d, J = 7.9 Hz, 1H), 5.21 (s, 2H), 4.00 (t, J = 6.6 Hz, 2H), 3.64 (t, J = 6.6 Hz, 2H), 1.91–2.12 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 197.5, 154.7, 135.1, 130.2, 129.8, 128.8, 122.9, 122.1, 119.7, 114.8, 54.9, 50.6, 33.3, 26.5, 24.6. Anal. calcd for $C_{16}H_{17}NOS_2$: C 63.33, H 5.65, N 4.62. Found: C 63.20, H 5.72, N 4.61.

(2-Hydroxynaphthalen-1-yl)methyl diethylcarbamodithioate (8b) Off-white solid; yield 84%; m.p. 130–132 °C, IR (KBr, cm^{-1}) ν_{max} 3281, 3056, 2975, 2930, 1626, 1581, 1492, 1452, 1422, 1223, 1202, 1143, 1122, 1062, 973, 914, 862, 811, 747; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.25 (s, 1H),7.81 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.53 (dt, J = 1.0, J = 8.1 Hz, 1H), 7.36 (dt, J = 1.0, J = 8.1 Hz, 1H), 7.16 (d, J = 8.9 Hz, 1H), 5.19 (s, 2H), 4.09 (q, J = 7.09 Hz, 2H), 3.76 (q, J = 7.09 Hz, 2H), 1.28 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.5, 152.7, 132.7, 129.5, 128.7, 128.4, 122.7, 121.8, 119.1, 114.2, 46.9, 33.1, 11.9, 11.1. Anal. calcd for $C_{16}H_{19}NOS_2$: C 62.91, H 6.25, N 4.59. Found: C 62.83, H 6.34, N 4.57.

(2-Hydroxynaphthalen-1-yl)methyl diethylcarbamodithioate (8b) Off-white solid; yield 84%; m.p. 130–132 °C, IR (KBr, cm^{-1}) ν_{max} 3281, 3056, 2975, 2930, 1626, 1581, 1492, 1452, 1422, 1223, 1202, 1143, 1122, 1062, 973, 914, 862, 811, 747; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.25 (s, 1H),7.81 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.53 (dt, J = 1.0, J = 8.1 Hz, 1H), 7.36 (dt, J = 1.0, J = 8.1 Hz, 1H), 7.16 (d, J = 8.9 Hz, 1H), 5.19 (s, 2H), 4.09 (q, J = 7.09 Hz, 2H), 3.76 (q, J = 7.09 Hz, 2H), 1.28 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.5, 152.7, 132.7, 129.5, 128.7, 128.4, 122.7, 121.8, 119.1, 114.2, 46.9, 33.1, 11.9, 11.1. Anal. calcd for $C_{16}H_{19}NOS_2$: C 62.91, H 6.25, N 4.59. Found: C 62.83, H 6.34, N 4.57.

(2-Hydroxynaphthalen-1-yl)methyl dimethylcarbamodithioate (8c) Off-white solid; yield 90%; m.p. 145–148 °C, IR (KBr, cm^{-1}) ν_{max} 3172, 2869, 1652, 1603, 1589, 1426, 1380, 1209, 1119, 921, 817, 775; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.55 (s, 1H), 7.85 (m, 2H), 7.32–7.45 (m, 3H), 7.32 (d, J = 7.1 Hz, 1H), 5.19 (s, 2H), 3.57 (s, 3H), 3.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 192.8, 153.9, 135.2, 130.3, 128.9, 128.5, 122.7, 122.1, 119.3, 114.5, 56.5, 34.2. Anal. calcd for $C_{14}H_{15}NOS_2$: C 60.63, H 5.43, N 5.05. Found: C 60.51, H 5.51, N 5.02.

(2-Hydroxynaphthalen-1-yl)methyl piperidine-1-carbodithioate (8d) Off-white solid; yield 80%; m.p. 137–139 °C, IR (KBr, cm^{-1}) ν_{max} 3301, 3117, 2986, 1617, 1589, 1486, 1459, 1422, 1223, 1219, 1143, 1131, 832, 715; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.55 (s, 1H), 7.85 (m, 2H), 7.32–7.45 (m, 3H), 7.32 (d, J = 7.1 Hz, 1H), 5.21 (s, 2H), 4.12 (t, J = 6.0 Hz, 2H), 3.52 (t, J = 6.0 Hz, 2H), 1.62 (m, 6H);^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.5, 154.5, 135.0, 130.4, 129.7, 128.4, 122.7, 122.0, 119.9, 114.5, 52.9, 51.6, 33.6, 26.5, 25.0, 24.8. Anal. calcd for $C_{17}H_{19}NOS_2$: C 64.32, H 6.02, N 4.41. Found: C 64.27, H 6.12, N 4.39.

(2-Hydroxynaphthalen-1-yl)methyl morpholine-4-carbodithioate (8e) Off-white solid; yield 75%; m.p. 123–125 °C, IR (KBr, cm^{-1}) ν_{max} 3321, 3079, 2968, 1603, 1543, 1465, 1474, 1441,1216, 1158, 1112, 950, 853, 749; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.10 (br, 1H), 7.72–7.84 (m, 2H), 7.68 (d, J = 8.8 Hz, 1H), 7.45 (m, 1H), 7.29 (m, 1H), 7.10 (d, J = 8.8 Hz, 1H), 5.20 (s, 2H), 4.16 (m, 4H), 3.91 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 197.1, 153.0, 134.7, 130.4, 128.9, 128.5, 123.9, 122.5, 121.3, 115.8, 67.1, 66.0,

53.6, 51.4, 33.5. Anal. calcd for $C_{16}H_{17}NO_2S_2$: C 60.17, H 5.35, N 4.38. Found: C 60.04, H 5.64, N 4.37.

Acknowledgements The authors wish to express their gratitude to Research Council of Standard Research Institute for the support of this work.

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