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Synthesis of ammonium S–S bond linked dipyridinedionates via four-component reactions of cyanoacetamide, aldehyde, amine and 1,3-thiazolidinedione

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ABSTRACT

An unprecedented and efficient synthetic protocol for polysubstituted ammonium S–S bond linked 2,6-pyridinedionates was developed via the novel four-component reactions of 1,3-thiazolidinedione, aromatic aldehydes, secondary amines and cyanoacetamide in acetonitrile. A feasible explanation is given based on the characteristic ring-open and recyclization properties of 1,3-thiazolidinedione.

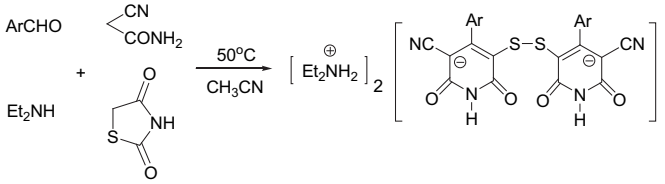
1. Introduction

Multicomponent reactions are one-pot processes in which several easily accessible components react to form a single product.[1–4] They offer significant advantages over conventional linear-type syntheses due to their flexible, convergent and atom efficient nature and have become an important area of research in organic, medicinal and combinatorial chemistry.[5–9] According to current synthetic requirements, effective and environmentally benign multicomponent procedures are particularly welcome.[9–12] Recently we have reported a novel four-component reaction of 1,3-thiazolidinedione, malononitrile, aromatic aldehydes and amines.[13] The reaction is very unique because the ring-opening/recyclization or spirocyclization process unexpectedly occurs at the ring of 1,3-thiazolidinedione with different kind of amines and reaction conditions. In continuation of our work on the development of useful synthetic methodologies and to examine the substrate scope and limitation of this novel domino reaction, in this text we wish to report the very interesting results of using cyanoacetamide in the multicomponent reaction.

2. Results and discussion

According to our previously established reaction condition,[13] a mixture of equal molecular ratio of benzaldehyde, cyanoacetamide, diethylamine and 1,3-thiazolidinedione in acetonitrile was heated at about 50 °C for 2 days. The resulting precipitates were collected and its structure was determined by ^{1}H NMR and MS spectra. We were very surprised to find that the diethylammonium salt of S–S bond linked 4-phenyl-5-cyano-pyridine-2,6-dinones **1a** was obtained in 40% yield. Similarly, various aromatic aldehydes were also tested under the same conditions and the corresponding diethylammonium salts (**1b**–**j**) were prepared in moderate yields (Table 1). The aromatic aldehydes with different kinds of substituted groups showed the similar reactivity. This

Table 1
The synthesis of diethylammonium S–S bond linked bis(dicyanopyridinedionates)



Entry	Compd	Amine	Ar	Yield (%)
1	**1a**	Et_2NH	C_6H_5	40
2	**1b**	Et_2NH	p-$CH_3C_6H_4$	43
3	**1c**	Et_2NH	p-$(CH_3)_2CHC_6H_4$	46
4	**1d**	Et_2NH	p-$(CH_3)_3CC_6H_5$	52
5	**1e**	Et_2NH	p-$CH_3OC_6H_4$	45
6	**1f**	Et_2NH	p-FC_6H_4	46
7	**1g**	Et_2NH	m-ClC_6H_4	52
8	**1h**	Et_2NH	p-ClC_6H_4	55
9	**1i**	Et_2NH	p-BrC_6H_4	50
10	**1j**	Et_2NH	m-$NO_2C_6H_4$	54

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surprising result is of value to us not only because we are interested in the design of the new multicomponent reaction, but also because we were unable to find examples of other methods allowing for such convenient synthesis in related literature. To the best of our knowledge, only one similar reaction is the Guareschi reaction, in which the three-component reaction of ketones, cyanoacetate and amines gave ammonium salt of 3,5-dicyano-4-phenyl-2,6-pyridinediones.[14,15]

The structures of ammonium salts **1a**–**j** were established by elemental analysis, ^{1}H and ^{13}C NMR, MS, IR spectra, and were further confirmed by single-crystal X-ray diffraction determination of two compounds **1f** (Fig. 1) and **1h**. In the ^{1}H NMR spectra of ammonium salt **1a** the two protons at diimides units shows a slight broad singlet at 10.23 ppm, and the two protons in diethylammonium cations display a broad peak at 8.23 ppm. From the crystal structure it can be concluded that the negative charge is located on the C-5 carbon atom bearing a cyano group. The pyridine-2,6-dione unit still exist in keto-form, not in enol form in solution and in solid state. The disulfide linkage in the products **1a**–**j** obviously indicated that 1,3-thiazolidinedione was taken part in the reaction and the whole reaction is a one-pot four-component reaction including diethylamine, aromatic aldehyde, cyanoacetamide and 1,3-thiazolidinedione.

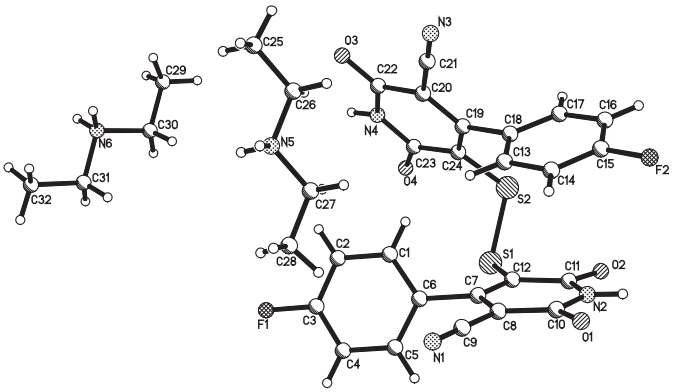
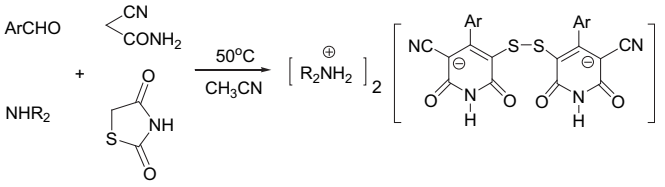


Figure 1. Molecular structure of diethylammonium salt **1f**.

Encouraged by the above results, the reactivity of other secondary amines was also tested in the reaction. When di(*i*-propyl)amine was used as the amine component in the reaction, the desired di(*i*-propyl) ammonium salts **2a**–**g** were also obtained in 42–56% yields (Table 2). On the other hand when piperidine was tested in reaction *p*-chloro, *p*-bromo and *m*-nitrobenzaldehydes also gave the dipiperidinium salts **2h**–**j** as main products. It should be pointed that the structure of the anion part of compounds **2a**–**j** is same as that of compounds **1a**–**j** and the only difference is the structure of the ammonium part. The structures of ammonium salts **2a**–**j** were also fully characterized by elemental analysis, ^{1}H and ^{13}C NMR, MS and IR spectra. The molecular structures of **2h** (Fig. 2) and **2i** were further determined by single-crystal X-ray diffraction determination. Thus our present protocol provides an efficient method for the synthesis of ammonium salts of S–S bond linked 4-phenyl-5-cyano-pyridine-2,6-dinones.

This four-component reaction proceeds very straightforwardly. To explain the formation of the ammonium salt via this one-pot four-component reaction, we proposed a plausible reaction mechanism, which is illustrated in Scheme 1. The first step is obviously the basic catalytic Knoevenagel condensation of cyanoacetamide with aromatic aldehyde to form arylidene cyanoacetamide (A). Then Michael addition of the carbanion of 1,3-thiazolidinedione to arylidene cyanoacetamide (A) to yield the adduct intermediate (B). In the third step the secondary amine attacks the carbonyl group of 1,3-thiazolidinedione to open its ring[13] and causes the formation of a mercapto diamide (C). Then the intermediate (C) converted to a glutarimde (D) by departure of a substituted urea. The species (D) was subsequently deprotonated by amine to form the carbanion (E), which was oxidized in air to give the intermediate (F). In the last step the thiol (F) was further oxidized in air to give the disulfide product **2**. It is well known that thiols and thiophenols can be easily oxidized in air to give the disulfide, which is an important aspect of protein chemistry. The formation of cyclic intermediate (E) could be explained from the very early reported Guareschi reaction of ketone, cyanoacetate and amine to form ammonium salt of 3,5-dicyano-4-phenyl-2,6-pyridinedione.[14,15] Polysubstituted 2-pyridiones could also be produced from the reactions of cyanoacetamide with α,β-unsaturated ketones or three-component reaction of cyanoacetamide with aldehydes and ketones.[16–18] In this proposed reaction mechanism 1,3-thiazolidinedione plays the determining factor. Its ring was opened by attack of amine and was recyclized by formation of a glutarimde structure, which is very different to the similar four-component reactions f 1,3-thiazolidinedione involving malononitrile and cyanoacetoacetate.[13]

Table 2
The synthesis of ammonium S–S bond linked bis(dicyanopyridinedionates)



1	**2a**	$(i\text{-Pr})_2NH$	C_6H_5	42
2	**2b**	$(i\text{-Pr})_2NH$	$p\text{-}(CH_3)_2CHC_6H_4$	46
3	**2c**	$(i\text{-Pr})_2NH$	$p\text{-}CH_3OC_6H_4$	50
4	**2d**	$(i\text{-Pr})_2NH$	$m\text{-}ClC_6H_4$	55
5	**2e**	$(i\text{-Pr})_2NH$	$p\text{-}ClC_6H_4$	48
6	**2f**	$(i\text{-Pr})_2NH$	$p\text{-}BrC_6H_4$	56
7	**2g**	$(i\text{-Pr})_2NH$	$m\text{-}NO_2C_6H_4$	55
8	**2h**	$(CH_2)_5NH$	$p\text{-}ClC_6H_4$	45
9	**2i**	$(CH_2)_5NH$	$p\text{-}BrC_6H_4$	43
10	**2j**	$(CH_2)_5NH$	$m\text{-}NO_2C_6H_4$	45

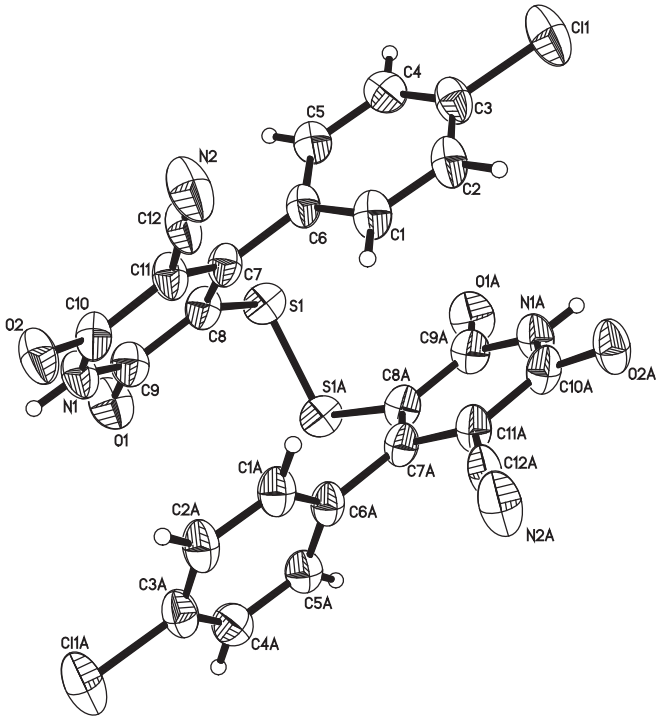
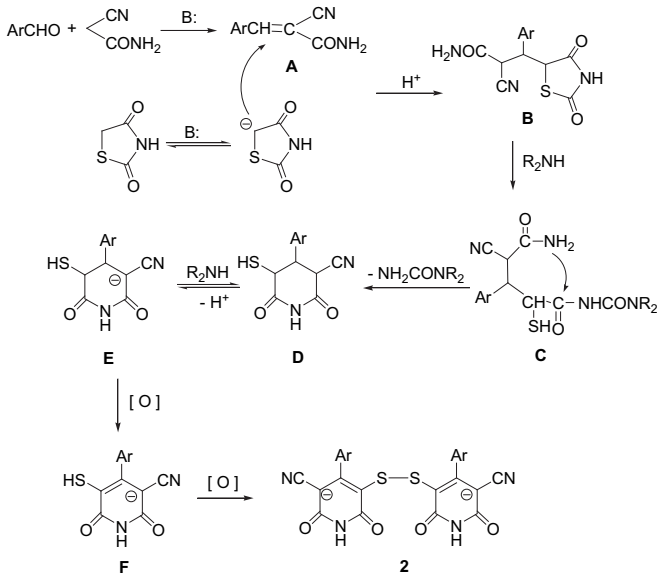


Figure 2. Molecular structure of ammonium salt **2h** (cations are omitted for clarity).



Scheme 1. Proposed mechanism for the four-component reaction.

3. Conclusion

In summary we have developed a four-component reactions of cyanoacetamide, aromatic aldehydes, 1,3-thiazolidinedione and secondary amines leading to the novel ammonium salts of S–S bond linked bis(2,6-pyridinedionates) in an efficient manner. In this reaction 1,3-thiazolidinedione shows very interesting reactivity. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

4. Experimental section

4.1. General procedure for the synthesis of S–S bond linked diethylammonium 2,6-pyridinedionate by four-component reaction of 1,3-thiazolidinedione, aldehyde, cyanoacetamide and diethylamine

A mixture of aromatic aldehyde (4.0 mmol), cyanoacetamide (4.0 mmol, 0.336 g) and diethylamine (4.0 mmol, 0.293 g) in acetonitrile (5.0 mL) was stirred at room temperature until the TLC analysis of aldehyde has been disappeared. Then 1,3-thiazolidinedione (4.0 mmol, 0.468 g) was added and the reaction was stirred at 40–50 °C for additional 48 h. The resulting precipitate was collected by filtration and washed with some acetonitrile to give the pure product.

Compound **1a**: Yellow solid, 40%, mp 232–234 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.03 (s, 2H, NH), 8.23 (br s, 4H, NH_2^+), 7.19 (br s, 6H, ArH), 6.90 (br s, 4H, ArH), 2.92–2.91 (m, 8H, CH_2), 1.15 (br s, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.1, 164.0, 162.0, 139.2, 130.0, 129.8, 129.2, 128.0, 127.0, 126.9, 120.4, 101.7, 80.0, 41.4, 11.0; IR (KBr) ν: 3468, 3394, 3063, 2981, 2792, 2499, 2206, 1613, 1486, 1456, 1400, 1367, 1260, 1221, 1201, 1164, 1075, 1029, 919, 881, 842, 780, 762 cm^{-1}; MS (m/z): 242.86 [(M−2$C_4H_{12}N$)$^+$/2] 100%. Anal. Calcd for $C_{32}H_{36}N_6O_4S_2$: C 60.74, H 5.73, N 13.28; found: C 60.55, H 5.98, N 12.86.

Compound **1b**: Yellow solid, 43%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.04 (s, 2H, NH), 8.09 (br s, 4H, NH_2^+), 7.00 (d, J=7.8 Hz, 4H, ArH), 6.79 (d, J=7.8 Hz, 4H, ArH), 2.91 (q, J=7.2 Hz, 8H, CH_2), 2.30 (s, 6H, CH_3), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.2, 164.1, 162.0, 136.2, 136.0, 128.0, 127.6, 120.5, 101.8, 80.1, 41.4, 20.9, 11.0; IR (KBr) ν: 3419, 2982, 2940, 2780, 2522, 2197, 1648, 1592, 1496, 1450, 1398, 1374, 1309, 1222, 1209, 1183, 1163, 1080, 1021, 885, 844, 813, 786 cm^{-1}; MS (m/z): 257.01 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{34}H_{40}N_6O_4S_2$: C 61.79, H 6.10, N 12.72; found: C 61.56, H 6.34, N 12.47.

Compound **1c**: Yellow solid, 46%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.06 (s, 2H, NH), 8.19 (br s, 4H, NH_2^+), 7.05 (d, J=7.2 Hz, 4H, ArH), 6.80 (d, J=7.2 Hz, 4H, ArH), 2.92 (q, J=7.2 Hz, 8H, CH_2), 2.88–2.83 (m, 2H, CH), 1.21 (d, J=7.2 Hz, 12H, CH_3), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.3, 164.2, 162.4, 146.7, 136.5, 128.0, 124.8, 120.4, 101.9, 80.4, 41.4, 33.1, 23.8, 11.0; IR (KBr) ν: 3097, 2963, 2868, 2782, 2472, 2418, 2206, 1590, 1486, 1392, 1267, 1223, 1204, 1155, 1107, 1069, 1021, 889, 853, 815, 797, 779, 752 cm^{-1}; MS (m/z): 284.75 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{38}H_{48}N_6O_4S_2$: C 63.66, H 6.75, N 11.72; found: C 63.27, H 6.80, N 11.54.

Compound **1d**: Yellow solid, 52%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 9.99 (s, 2H, NH), 8.13 (br s, 4H, NH_2^+), 7.20 (d, J=7.2 Hz, 4H, ArH), 6.81 (br s, 4H, ArH), 2.92 (q, J=7.2 Hz, 8H, CH_2), 1.28 (s, 18H, CH_3), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.4, 164.1, 163.5, 162.5, 161.7, 151.6, 149.0, 136.2, 127.8, 127.7, 124.9, 123.6, 120.4, 118.9, 101.9, 81.5, 80.4, 41.4, 34.1, 31.2, 31.1, 31.0, 11.0; IR (KBr) ν: 3428, 3101, 2961, 2785, 2465, 2413, 2207, 1590, 1486, 1388, 1304, 1222, 1156, 1094, 1069, 1054, 1022, 891, 852, 815, 795, 779 cm^{-1}; MS (m/z): 298.77 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{40}H_{52}N_6O_4S_2$: C 64.49, H 7.04, N 11.28; found: C 64.33, H 6.75, N 11.47.

Compound **1e**: Yellow solid, 45%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.09 (s, 2H, NH), 8.15 (br s, 4H, NH_2^+), 6.85 (d, J=7.8 Hz, 4H, ArH), 6.75 (d, J=7.8 Hz, 4H, ArH), 3.76 (s, 6H, OCH_3), 2.91 (q, J=7.2 Hz, 8H, CH_2), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.2, 164.1, 161.9, 158.2, 131.3, 129.3, 120.5, 113.5, 112.4, 102.0, 80.5, 54.8, 41.5, 11.0; IR (KBr) ν: 3428, 3073, 2988, 2942, 2784, 2515, 2426, 2207, 1587, 1516, 1486, 1408, 1392, 1371, 1325, 1294, 1248, 1225, 1203, 1174, 1110, 1095, 1065, 1048, 1028, 936, 910, 888, 865, 849, 823, 805, 778 cm^{-1}; MS (m/z): 272.56 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{34}H_{40}N_6O_6S_2$: C 58.94, H 5.82, N 12.13; found: C 58.63, H 6.21, N 12.45.

Compound **1f**: Yellow solid, 46%, mp 244–246 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.11 (s, 2H, NH), 7.98 (br s, 4H, NH_2^+), 6.99–6.98 (m, 4H, ArH), 6.93–6.92 (m, 4H, ArH), 2.90 (q, J=7.2 Hz, 8H, CH_2), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.0, 163.8, 162.0, 160.9, 160.4, 135.4, 130.0, 129.9, 120.3, 114.0, 113.8, 101.8, 80.0, 41.4, 11.0; IR (KBr) ν: 2989, 2788, 2509, 2203, 1598, 1490, 1454, 1390, 1223, 1159, 1094, 1016, 887, 850, 815, 778 cm^{-1}; MS (m/z): 260.57 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{32}H_{34}F_2N_6O_4S_2$: C 57.47, H 5.12, N 12.57; found: C 57.28, H 5.50, N 12.45.

Compound **1g**: Yellow solid, 52%, mp 214–216 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.10 (s, 2H, NH), 8.06 (br s, 4H, NH_2^+), 7.30 (d, J=7.8 Hz, 2H, ArH), 7.21 (br s, 2H, ArH), 6.93–6.85 (m, 4H, ArH), 2.91 (q, J=7.2 Hz, 8H, CH_2), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.0, 163.3, 160.5, 160.4, 160.3, 141.1, 132.8, 132.0, 131.9, 130.3, 129.0, 128.0, 127.9, 127.5, 127.0, 126.7, 126.4, 120.2, 118.4, 101.5, 81.7, 80.0, 79.1, 41.4, 11.0; IR (KBr) ν: 2989, 2790, 2518, 2209, 1599, 1484, 1458, 1389, 1202, 1160, 1080, 883, 828, 785, 773 cm^{-1}; MS (m/z): 276.60 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{32}H_{34}Cl_2N_6O_4S_2$: C 54.77, H 4.88, N 11.98; found: C 54.69, H 5.21, N 11.63.

Compound **1h**: Yellow solid, 55%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.21 (s, 2H, NH), 8.15 (br s, 4H, NH_2^+), 7.25 (d, J=6.6 Hz, 4H, ArH), 6.91 (d, J=6.6 Hz, 4H, ArH), 2.92 (q, J=7.2 Hz, 8H, CH_2), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.0, 163.8, 160.6, 137.9, 131.9, 129.8, 127.2, 120.2, 101.5, 79.7, 41.4, 11.0; IR (KBr) ν: 3428, 3075, 2988, 2944, 2785, 2514, 2424, 2205, 1647, 1518, 1486, 1411, 1389, 1371, 1224, 1203, 1179, 1160, 1094, 1048, 1017, 946, 910, 885, 864, 849, 810, 778 cm^{-1}; MS (m/z): 276.64 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{32}H_{34}Cl_2N_6O_4S_2$: C 54.77, H 4.88, N 11.98; found: C 54.45, H 5.10, N 11.75.

Compound **1i**: Yellow solid, 50%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.18 (s, 2H, NH), 8.18 (br s, 4H, NH_2^+), 7.37 (d, J=4.2 Hz, 4H, ArH), 6.83 (d, J=4.8 Hz, 4H, ArH), 2.92 (q, J=7.2 Hz, 8H, CH_2), 1.15 (t, J=7.2 Hz, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.0, 163.8, 160.6, 138.2, 130.1, 120.6, 120.1, 101.4, 79.7, 41.5, 11.0; IR (KBr) ν: 3069, 2987, 2943, 2784, 2515, 2426, 2204, 1647, 1588, 1485, 1411, 1389, 1371, 1226, 1202, 1160, 1097, 1071, 1049, 1013, 947, 908, 883, 865, 848, 808, 778 cm^{-1}; MS (m/z): 321.14 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{32}H_{34}Br_2N_6O_4S_2$: C 48.61, H 4.33, N 10.63; found: C 48.34, H 4.80, N 10.27.

Compound **1j**: Yellow solid, 54%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.17−10.07 (m, 2H, NH), 8.16 (br s, 7H, NH_2^+, ArH), 7.82 (br s, 1H, ArH), 7.49 (br s, 2H, ArH), 7.34 (br s, 2H, ArH), 2.93 (br s, 8H, CH_2), 1.15 (br s, 12H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 163.8, 163.7, 159.4, 146.7, 146.6, 140.5, 140.4, 134.3, 128.9, 128.7, 123.2, 123.0, 122.2, 122.1, 120.1, 120.0, 101.2, 101.1, 79.7, 41.4, 11.0; IR (KBr) ν: 3422, 3081, 2992, 2792, 2516, 2197, 1598, 1529, 1454, 1409, 1372, 1350, 1279, 1222, 1162, 1096, 1074, 1051, 1000, 892, 846, 811 cm^{-1}; MS (m/z): 287.75 [(M−2$C_4H_{12}N$)$^+$/2]100%. Anal. Calcd for $C_{32}H_{34}N_8O_8S_2$: C 53.17, H 4.74, N 15.50; found: C 52.86, H 5.15, N 15.27.

4.2. General procedure for the synthesis of S–S bond linked 2,6-pyridinedionate by four-component reaction of 1,3-thiazolidinedione, aldehyde, cyanoacetamide and amine

A mixture of aromatic aldehyde (4.0 mmol), cyanoacetamide (4.0 mmol, 0.336 g) and amine (4.0 mmol) in acetonitrile (5.0 mL) was stirred at room temperature until the TLC analysis of aldehyde has been disappeared. Then 1,3-thiazolidinedione (4.0 mmol, 0.468 g) was added and the reaction was stirred at 40–50 °C for additional 48 h. The resulting precipitate was collected by filtration and washed with some acetonitrile to give the pure product.

Compound **2a**: Yellow solid, 42%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 7.25−7.19 (m, 6H, ArH), 6.90 (d, J=6.6 Hz, 4H, ArH), 3.36−3.32 (m, 4H, CH), 1.20 (d, J=6.6 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.1, 163.7, 161.8, 139.1, 127.9, 127.0, 126.9, 120.4, 102.1, 79.6, 46.2, 18.7; IR (KBr) ν: 3359, 3086, 2199, 1721, 1644, 1615, 1528, 1491, 1448, 1390, 1347, 1291, 1215, 1156, 1134, 1113, 1076, 868, 797, 776 cm^{-1}; MS (m/z): 242.97 [(M−2$C_6H_{16}N$)/2]$^+$ 14%, 485.66 (M−2$C_6H_{16}N$)$^+$ 100%. Anal. Calcd for $C_{36}H_{44}N_6O_4S_2$: C 62.76, H 6.44, N 12.20; found: C 62.31, H 6.80, N 11.76.

Compound **2b**: Yellow solid, 46%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 7.25−7.19 (m, 6H, ArH), 6.90 (d, J=6.6 Hz, 4H, ArH), 3.36−3.32 (m, 4H, CH), 1.20 (d, J=6.6 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.1, 163.8, 147.7, 146.7, 136.6, 135.5, 128.7, 128.0, 125.2, 124.8, 120.6, 102.3, 99.8, 80.9, 79.9, 46.2, 33.0, 23.8, 18.6; IR (KBr) ν: 3466, 3107, 2964, 2867, 2795, 2212, 1741, 1613, 1510, 1479, 1404, 1298, 1248, 1222, 1148, 1097, 1055, 1017, 896, 833, 807, 783 cm^{-1}; MS (m/z): 285.63 [(M−2$C_6H_{16}N$)/2]$^+$ 13%, 569.72 (M−2$C_6H_{16}N$)$^+$ 100%. Anal. Calcd for $C_{42}H_{56}N_6O_4S_2$: C 65.25, H 7.30, N 10.87; found: C 64.97, H 5.76, N 10.39.

Compound **2c**: Yellow solid, 50%, mp 239−240 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 6.85 (d, J=8.4 Hz, 4H, ArH), 6.75 (d, J=7.8 Hz, 4H, ArH), 3.77 (s, 6H, OCH_3), 3.36−3.32 (m, 4H, CH), 1.20 (d, J=6.6 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.1, 163.8, 161.6, 158.2, 131.4, 129.3, 120.6, 113.5, 112.3, 102.4, 81.7, 80.0, 54.8, 46.2, 18.6; IR (KBr) ν: 3422, 3092, 2941, 2777, 2206, 1590, 1515, 1488, 1399, 1293, 1247, 1175, 1102, 1028, 911, 848, 808, 779 cm^{-1}; MS (m/z): 272.79 [(M−2$C_6H_{16}N$)/2]$^+$ 28%, 545.63 (M−2$C_6H_{16}N$)$^+$ 100%. Anal. Calcd for $C_{38}H_{48}N_6O_6S_2$: C 60.94, H 6.46, N 11.22; found: C 60.85, H 6.88, N 10.73.

Compound **2d**: Yellow solid, 55%, mp 240−241 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 7.31 (d, J=7.8 Hz, 2H, ArH), 7.24−7.21 (m, 2H, ArH), 6.93−6.85 (m, 4H, ArH), 3.77−3.33 (m, 4H, CH), 1.20 (d, J=6.6 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 163.9, 163.6, 141.1, 131.8, 129.0, 128.0, 127.9, 127.0, 120.2, 101.8, 79.7, 46.2, 18.6; IR (KBr) ν: 3421, 3092, 2982, 2776, 2203, 1604, 1479, 1456, 1397, 1222, 1200, 1148, 1085, 914, 831, 784 cm^{-1}; MS (m/z): 278.41 [(M−2$C_6H_{16}N$)/2]$^+$ 24%, 553.78 (M−2$C_6H_{16}N$)$^+$ 100%. Anal. Calcd for $C_{36}H_{42}Cl_2N_6O_6S_2$: C 57.06, H 5.59, N 11.09; found: C 56.72, H 5.96, N 10.76.

Compound **2e**: Yellow solid, 48%, mp 244−245 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.08 (s, 2H, NH), 8.03 (br s, 4H, NH_2^+), 7.24 (br s, 4H, ArH), 6.91 (br s, 4H, ArH), 3.35 (m, 4H, CH_2), 1.19 (d, J=6.0 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 163.9, 163.4, 138.1, 131.7, 129.8, 127.1, 120.5, 101.6, 79.2, 46.3, 18.8; IR (KBr) ν: 3421, 3096, 2983, 2777, 2202, 1603, 1486, 1452, 1395, 1196, 1147, 1091, 1014, 882, 850, 810, 778 cm^{-1}; MS (m/z): 278.01 [(M−2$C_6H_{16}N$)/2]$^+$ 14%, 555.58 (M−2$C_6H_{16}N$)$^+$ 100%. Anal. Calcd for $C_{36}H_{42}Cl_2N_6O_6S_2$: C 57.06, H 5.59, N 11.09; found: C 56.95, H 5.77, N 10.54.

Compound **2f**: Yellow solid, 56%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.14 (s, 2H, NH), 8.07 (br s, 4H, NH_2^+), 7.37 (d, J=6.0 Hz, 4H, ArH), 6.84 (d, J=7.2 Hz, 4H, ArH), 3.36−3.34(m, 4H, CH), 1.19 (d, J=6.0 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 163.9, 163.6, 160.3, 138.4, 131.0, 130.7, 130.0, 120.5, 120.3, 101.6, 79.4, 46.3, 18.8; IR (KBr) ν: 3421, 3085, 2980, 2779, 2200, 1610, 1576, 1485, 1454, 1407, 1302, 1222, 1146, 1090, 1011, 946, 882, 846, 810, 777 cm^{-1}; MS (m/z): 322.30 [(M−2$C_6H_{16}N$)/2]$^+$ 35%, 324.04 {[(M−2$C_6H_{16}N$)/2]+2}$^+$ 26%, 643.52 (M−2$C_6H_{16}N$)$^+$ 91%, 645.56 (M−2$C_6H_{16}N$+2)$^+$ 100%. Anal. Calcd for $C_{36}H_{42}Br_2N_6O_6S_2$: C 51.07, H 5.00, N 9.93; found: C 50.66, H 5.47, N 9.62.

Compound **2g**: Yellow solid, 55%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 8.17 (d, J=7.8 Hz, 2H, ArH), 7.82 (s, 1H, ArH), 7.51 (s, 2H, ArH), 7.35 (s, 2H, ArH), 3.37−3.33(m, 4H, CH), 1.20 (d, J=6.0 Hz, 24H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 163.9, 163.8, 163.7, 163.6, 163.5, 159.7, 159.3, 146.7, 146.6, 140.5, 140.4, 135.1, 135.0, 134.3, 134.2, 134.1, 128.9, 128.8, 123.2, 123.0, 122.2, 122.1, 120.0, 119.9, 101.4, 79.6, 46.2, 18.6; IR (KBr) ν: 3427, 3106, 2968, 2200, 1612, 1584, 1528, 1505, 1460, 1400, 1349, 1306, 1225, 1151, 1098, 898, 840, 805, 717 cm^{-1}; MS (m/z): 575.82 (M−2$C_6H_{16}N$)$^+$ 100%. Anal. Calcd for $C_{36}H_{42}N_8O_8S_2$: C 55.51, H 5.44, N 14.39; found: C 55.27, H 5.86, N 13.85.

Compound **2h**: Yellow solid, 45%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.15 (s, 2H, NH), 8.31 (br s, 4H, NH_2^+), 7.25 (s, 4H, ArH), 6.90 (s, 4H, ArH), 3.00 (s, 8H, CH_2), 1.64 (s, 8H, CH_2), 1.54 (s, 4H, CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.0, 163.9, 137.9, 131.9, 129.8, 127.2, 120.1, 101.4, 101.3, 80.0, 43.8, 22.2, 21.6; IR (KBr) ν: 3391, 2946, 1861, 2199, 1595, 1483, 1453, 1402, 1307, 1272, 1220, 1089, 1029, 1014, 946, 920, 882, 849, 814, 776 cm^{-1}; MS (m/z): 276.73 [(M−2$C_5H_{12}N$)/2]$^+$ 100%, 278.53 [(M−2$C_5H_{12}N$)/2+2]$^+$ 38%. Anal. Calcd for $C_{34}H_{34}Cl_2N_6O_4S_2$: C 56.27, H 4.72, N 11.58; found: C 56.20, H 5.24, N 11.44.

Compound **2i**: Yellow solid, 43%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.20 (br s, 2H, NH), 8.26 (br s, 4H, NH_2^+), 7.38 (s, 4H, ArH), 6.83 (d, J=6.6 Hz, 4H, ArH), 3.01 (t, J=5.4 Hz, 8H, CH_2), 1.65−1.62 (m, 8H, CH_2), 1.55 (br s, 4H, CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 164.0, 160.7, 138.2, 130.1, 120.6, 120.1, 101.3, 79.9, 43.9, 22.1, 21.6; IR (KBr) ν: 3418, 2952, 2198, 1603, 1484, 1406, 1307, 1221, 1069, 1030, 1011, 881, 848, 808, 776 cm^{-1}; MS(m/z): 321.32 [(M−2$C_5H_{12}N$)/2]$^+$ 100%, 323.56 [(M−2$C_5H_{12}N$)/2+2]$^+$ 59%. Anal. Calcd for $C_{34}H_{34}Br_2N_6O_4S_2$: C 50.13, H 4.21, N 10.32; found: C 49.76, H 4.66, N 9.88.

Compound **2j**: Yellow solid, 45%, mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.16 (br s, 2H, NH), 8.16 (d, J=7.2 Hz, 2H, ArH), 7.82 (s, 1H, ArH), 7.63 (br s, 1H, ArH), 7.50 (s, 2H, ArH), 7.34 (s, 2H, ArH), 3.01−3.00 (m, 8H, CH_2), 1.66−1.62 (m, 8H, CH_2), 1.56−1.53 (m, 4H, CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 163.0, 162.9, 158.9, 158.5, 145.7, 145.6, 139.2, 139.1, 133.3, 128.0, 127.8, 122.1, 122.0, 121.9, 121.3, 121.2, 118.8, 118.7, 100.3, 100.2, 78.8, 44.8, 42.8, 21.0, 20.5; IR (KBr) ν: 3425, 3090, 2960, 2865, 2199, 1609, 1525, 1454, 1403, 1352, 1306, 1278, 1224, 1203, 1160,

1098, 1030, 947, 901, 867, 843, 809, 776 cm^{-1}; MS (m/z): 287.81 $[(M-2C_5H_{12}N)/2]^+$ 100%. Anal. Calcd for $C_{34}H_{34}N_8O_8S_2$: C 54.68, H 4.59, N 15.00; found: C 54.35, H 4.83, N 14.72.

5. Supporting information

Crystallographic data (**1f**: CCDC 753686; **1h**: CCDC 754768; **2h**: CCDC 753687; **2i**: CCDC 753688) have been deposited at the Cambridge Crystallographic Database Centre.

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