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PBr_3-Mediated [5+1]Annulation of α-Alkenoyl-α-Carbamoyl Ketene-*S,S*-acetals: Access to Substituted Pyridine-2,6(*1H,3H*)-diones†

Liping Shi,[a] Qian Zhang,[b] Fengjiao Gan,[b] Rui Zhang,*[b] Yuanli Ding,[b] Chun Liu,[a] and Dewen Dong*[b]

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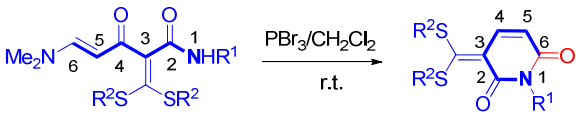

R^1: aryl, alkyl; R^2: alkyl; 13 examples; 75-87% yield

Facile and efficient synthesis of substituted pyridine-2,6(1*H*,3*H*)-diones *via* an intramolecular [5+1] annulation of readily available α-alkenoyl-α-carbamoyl ketene-*S,S*-acetals mediated by phosphorus bromide under very mild is developed.

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PBr_3-Mediated [5+1]Annulation of α-Alkenoyl-α-Carbamoyl Ketene-*S,S*-acetals: Access to Substituted Pyridine-2,6(*1H,3H*)-diones†

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A facile and efficient synthesis of substituted pyridine-2,6(1*H*,3*H*)-diones *via* an intramolecular [5+1] annulation of readily available α-alkenoyl-α-carbamoyl ketene-*S,S*-acetals mediated by phosphorus bromide (PBr_3) under very mild conditions is described.

Introduction

Cyclic imide and its derivatives have attracted considerable research interest since they are distributed in numerous natural products along with diverse useful bioactivities.[1-3] For example, acetiketal (RK-441S) was isolated from *Streptomyces pulveraceus* as a new antibiotic,[4] and AG-1 is an agent widely used for the treatment of breast cancer for postmenopausal patients (Figure 1).[5] In addition, the functionalized cyclic imides have been utilized as versatile intermediates in the synthesis of a wide variety of six-membered aza-heterocycles, and applied as disperse dyes in dyestuff industry as well.[6] To date, a variety of synthetic approaches have been well established to access to such cyclic imides and their analogues. The notable approaches involve the cyclization of dinitriles,[7] cyclization of monoamides with acids,[8] condensation of diacids with amines,[9] or [3+3]cycloaddition of α,β- unsaturated esters with acetamides.[10] Nevertheless, the development of efficient and convenient synthetic methods for such aza-heterocycles under milder conditions is still desirable.

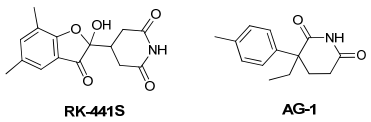
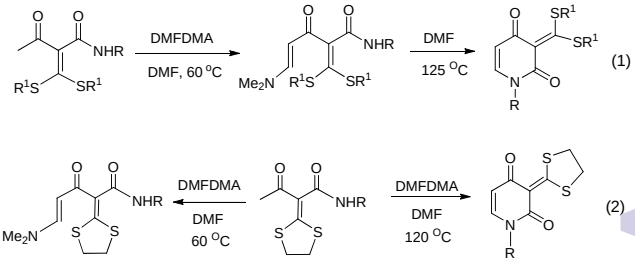


Figure 1

During the course of our studies on the chemistry of α-oxo ketene-*S,S*-acetals, we successfully developed novel strategies for the synthesis of highly valuable six-membered carbocycles[11] and heterocycles,[12] relying upon the utilization of α-alkenoyl ketene-*S,S*-acetals as a five carbon 1,5-dielectrophilic species in the formal [5+1] annulation with various nucleophiles. Also, we achieved facile and efficient synthesis of substituted pyridine-2,4(1*H*,3*H*)-diones *via* an intramolecular [5+1] annulations of α-aminopropenoyl ketene-*S,S*-acetals (Scheme 1).[13] In connection with our previous work and our continuing interest in the synthesis of functionalized heterocycles, we synthesized a series of α-dimethyl aminopropenoyl-α-carbamoyl ketene-*S,S*-acetals and examined their reaction behaviours under different conditions. As a result, we developed a facile one-pot synthesis of substituted pyridine-2,6(1*H*,3*H*)-diones from readily available α-alkenoyl-α-carbamoyl ketene-*S,S*-acetals mediated by phosphorus tribromide (PBr_3) in dichloromethane (DCM). Herein, we wish to report our results and proposed a mechanism involved in the reactions.

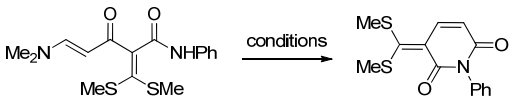
Scheme 1 Synthesis of Substituted Pyridine-2,4(1*H*,3*H*)-diones.[13]



Results and discussion

The substrates, α-aminopropenoyl-α-carbamoyl ketene-*S,S*-acetals **1** were prepared from α-acyl-α-carbamoyl ketene-*S,S*-acetals with *N,N*-dimethyl formamide dimethylacetal (DMFDMA) in high yields according to our published procedure.[13] Recently, we investigated the reaction behaviors of 2-arylamino-3-acetyl-5,6-dihydro-4*H*-pyrans and 1-carbamyl-1-oximyl cyclopropanes toward Vilsmeier reagent, *e.g.* $POCl_3$/DMF, and $POCl_3$ in DCM, respectively.[14] These obtained results suggested that $POCl_3$ showed different reaction behaviour when employed with or without DMF. Thus, in the present work, the reaction of 2-[bis(methylthio)methylene]-5-(dimethylamino)-3-oxo-*N*-phenyl pent-4-enamide **1a** and $POCl_3$ (1.0 equiv.) was first attempted in DCM at room temperature. The reaction could proceed as indicated by TLC result, and furnished a product after workup and purification by silica column chromatography, which was characterized as 3-[bis(methylthio)methylene]-1-phenylpyridine-2,6(1*H*,3*H*)-dione **2a** on the basis of its spectral and analytical data (Table 1, entry 1). It was observed that the variation of

Table 1 Screening of reaction conditions [a].



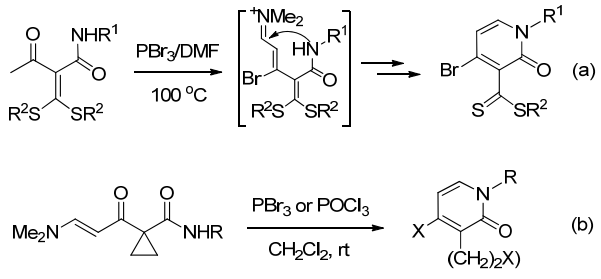
1a **2a**

Entry	Reagent (equiv.)	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1	$POCl_3$ (1.0)	DCM	r t	9.0	48
2	$POCl_3$ (1.2)	DCM	r t	7.0	52
3	$POCl_3$ (2.0)	DCM	r t	5.0	53
4	**PBr_3 (1.2)**	**DCM**	**r t**	**6.0**	**75**
5	PBr_3 (1.2)	DCM	0	6.0	nr[c]
6	PBr_3 (1.2)	DCM	45	3.5	67
7	PBr_3 (1.2)	toluene	r t	6.0	mixture
8	PBr_3 (1.2)	DMF	r t	6.0	nr

[a] Reagents and conditions: **1a** (1.0 mmol), solvent (15 mL); [b] Isolated yield; [c] No reaction.

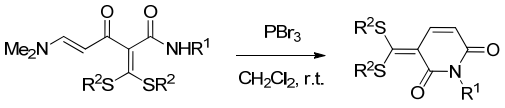
addition amount of $POCl_3$ had significant influence on the reaction time and yield of **2a** (Table 1, entries 2 and 3). When the reaction of **1a** was performed with PBr_3 (1.2 equiv) in DCM, **2a** could be obtained in 75% yield. The results suggested that PBr_3 was more effective than the previously investigated $POCl_3$ for the transformation of **1a** to **2a** (Table 1, entry 4). However, no reaction occurred when the reaction temperature was decreased to 0 °C (Table 1, entry 5). By increasing the reaction temperature to 45 °C, the reaction could be complete within 3.5 h as indicated by TLC along with 67 % yield of **2a** (Table 1, entry 6). Subjecting **1a** and PBr_3 (1.2 equiv) to toluene at room temperature, a complex mixture was formed, in which no main product could be isolated (Table 1, entry 7). It is should be mentioned that no reaction was observed when **1a** was treated with PBr_3 (1.2 equiv) in DMF at room temperature (Table 1, entry 8), whereas 4-bromo-pyridin-2(1*H*)-ones were obtained in Chen's work by subjecting *α*-acyl ketene-*S,S*-acetals to Vilsmeier conditions at 100 °C (Scheme 2a).[15] It should also be noted that 4-halo-pyridin-2(1*H*)-ones could be obtained by the reaction of 1-aminopropenoyl-1-carbamoyl cyclopropanes with $POCl_3$ or PBr_3 at room temperature (Scheme 2b).[16]

Scheme 2 Synthesis of 4-Halo-pyridin-2(1*H*)-ones.[15, 16]



Under the conditions as for **2a** in entry 4, Table 1, a series of reactions of *α*-alkenoyl ketene-*S,S*-acetals **1** were carried out, and some of the results are listed in Table 2. It was found that the *α*-aminopropenoyl-*α*-carbamoyl ketene-*S,S*-acetals **1b-f** bearing varied aryl groups or benzyl group R^1 could proceed efficiently to afford the corresponding pyridine-2,6(1*H*,3*H*)-diones **2b-f** in good to high yields (Table 2, entries 2-6). The versatility of this pyridine-2,6(1*H*,3*H*)-dione synthesis was further evaluated by performing **1g-l** bearing varied aryl groups or alkyl group R^1 and ethyl or benzyl groups R^2 under the identical conditions (entries 7-13). The structure of **2i** was further confirmed by X-ray single crystal analysis and its spectral and analytical data (Figure 2). The results shown above demonstrate the efficiency and synthetic value of the cyclization reaction of a variety of *α*-alkenoyl ketene-*S,S*-acetals **1**. It should be noted that the richness of the functionality of substituted pyridine-2,6(1*H*,3*H*)-diones **2** may render them versatile as synthons in further synthetic transformations, *e.g.* selective reduction of *C*-*C* double bond or carbonyl groups,[17] Michael addition,[18] and nucleophilic vinylic substitution (S_NV) reactions.[19]

Table 2 Synthesis of substituted pyridine-2,6(1*H*,3*H*)-diones **2** [a].



1 **2**

Entry	**1**	R^1	R^2	**2**	Yield(%)[b]
1	**1a**	Ph	Me	**2a**	75
2	**1b**	4-MeC_6H_4	Me	**2b**	83
3	**1c**	4-ClC_6H_4	Me	**2c**	80
4	**1d**	4-$MeOC_6H_4$	Me	**2d**	87
5	**1e**	2-$MeOC_6H_4$	Me	**2e**	76
6	**1f**	Bn	Me	**2f**	82
7	**1g**	Ph	Et	**2g**	86
8	**1h**	4-MeC_6H_4	Et	**2h**	85
9	**1i**	4-ClC_6H_4	Et	**2i**	79
10	**1j**	4-$MeOC_6H_4$	Et	**2j**	76
11	**1k**	Ph	Bn	**2k**	78
12	**1l**	4-MeC_6H_4	Bn	**2l**	84
13	**1m**	Me	Et	**2m**	77

[a] Reagents and conditions: **1a** (1.0 mmol), PBr_3 (1.2 equiv.), CH_2Cl_2 (15 mL), rt, 5.0-7.0 h; [b] Isolated yield.

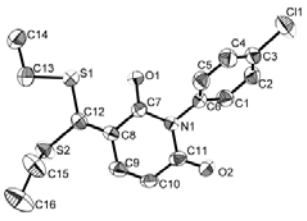
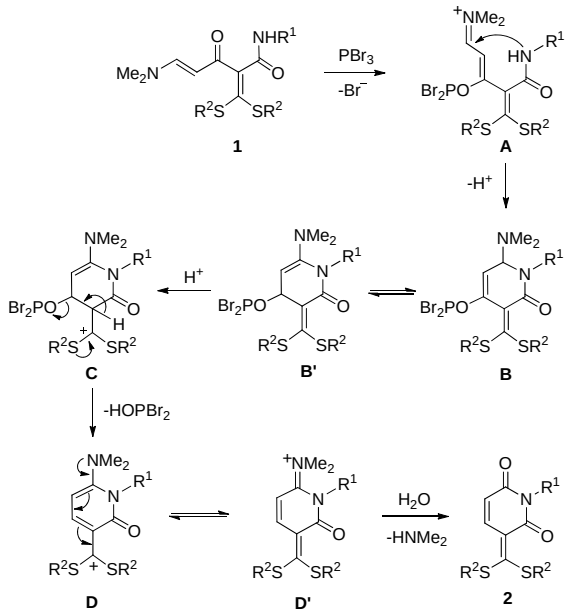


Figure 2 ORTEP drawing of **2i.**



Scheme 3 Plausible mechanism for the reaction of α-alkenoyl-α-carbamoyl ketene-*S,S*-acetal **1** with PBr_3.

On the basis of the above experimental results together with some literatures, a mechanism for the synthesis of pyridine-2,6(1*H*,3*H*)-dione **2** is proposed as depicted in Scheme 3. In the presence of PBr_3, α-aminopropenoyl-α-carbamoyl ketene-*S,S*-acetal **1** is transformed into iminium ion intermediate **A**, which undergoes an intramolecular cyclization to afford intermediate **B** and its tautomer **B'**.[20,21] The protonation of the *C*-*C* double bond of **B'** gives carbocation **C**,[15] followed by elimination of $HOPBr_2$ to form carbocation **D** and its tautomer iminium ion **D'**. The latter is hydrolyzed to the final product pyridine-2,6(1*H*,3*H*)-dione **2** during the workup process under acidic conditions.[14b, 21]

Conclusions

In summary, an efficient synthesis of substituted pyridine-2,6(1*H*,3*H*)-diones *via* an intramolecular [5+1] annulation of readily available α-alkenoyl-α-carbamoyl ketene-*S,S*-acetals **1** mediated by phosphorus bromide (PBr_3) is developed. This protocol is associated with readily available starting materials, mild conditions, high yields, a wide range of substrate scope, and rich functionalities and important synthetic potential of the products.

Experimental

General

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^1H NMR spectra and ^{13}C NMR spectra were obtained at 25 °C at 300 MHz (or 400 MHz) and 100 MHz, respectively, on a Bruker AV300 (or AV 400) spectrometer using $CDCl_3$ (otherwise indicated) as solvent and TMS as internal standard. Mass spectra were recorded on a Bruker autoflex III(smartbeam MALDI-TOF) mass spectrometer. IR spectra (KBr) were recorded on a Shimadzu FTIR-8400S spectrophotometer in the range of 400-4000 cm^{-1}.

Typical procedure for the synthesis of 2 (2a as an examples)

To a solution of **1a** (336 mg, 1.0 mmol) in CH_2Cl_2 (15 mL) was added PBr_3 (325 mg, 1.2 mmol) at 0 °C. Then the reaction mixture was allowed to warm to room temperature and stirred for 6.0 h. After the reaction was completed, the resulting mixture was poured into saturated aqueous NaCl (100 mL), which was extracted with dichloromethane (3×30 mL). The organic extracts were washed with water, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification was carried out by flash silica gel chromatography using petroleum ether: ethyl acetate (9:1, v/v) as eluent to give product **2a** (218 mg, 75%).

Analytical data of 2

3-[Bis(methylthio)methylene]-1-phenylpyridine-2,6(1*H*,3*H*)-dione (2a)

Yellow solid; mp 149-150 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.54 (s, 3 H), 2.67 (s, 3H), 6.24 (d, J = 10.0 Hz, 1 H), 7.18-7.21 (m, 2 H), 7.47-7.49 (m, 3 H), 8.07 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 164.6, 162.9, 138.6, 135.2, 129.2, 128.6, 128.4, 123.2, 116.3, 21.6, 19.8. IR (KBr, cm^{-1}) 3446, 2918, 1677, 1639, 1592, 1491, 1452, 1411, 1178, 782. Anal. Calcd for $C_{14}H_{13}NO_2S_2$: C, 57.71; H, 4.50; N, 4.81. Found: C, 57.48; H, 4.43; N, 4.87

3-[Bis(methylthio)methylene]-1-*p*-tolylpyridine-2,6(1*H*,3*H*)-dione (2b)

Yellow solid; mp 142-143 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3 H), 2.52 (s, 3H), 2.66 (s, 3H), 6.24 (d, J = 10.0 Hz, 1 H), 7.06 (d, J = 8.0 Hz,, 2 H), 7.28 (d, J = 8.0 Hz, 2 H), 8.05 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 164.7, 163.0, 138.5, 138.3, 132.4, 130.0, 128.2, 123.1, 116.3, 21.6, 21.2, 19.8. IR (KBr, cm^{-1}) 3446, 2919, 1686, 1637, 1513, 1449, 1408, 1187, 841. Calcd for $C_{15}H_{15}NO_2S_2$: C, 58.99; H, 4.95; N, 4.59. Found: C, 58.68; H, 5.06; N, 4.50.

3-[Bis(methylthio)methylene]-1-(4-chlorophenyl)pyridine-2,6(1*H*,3*H*)-dione (2c)

Yellow solid; mp 137-139 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.54 (s, 3 H), 2.68 (s, 3 H), 6.22 (d, J = 10.2 Hz, 1 H), 7.12-7.15 (m, 2 H), 7.43-7.53 (m, 2 H), 8.06 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 164.5, 162.7, 138.9, 134.4, 133.7, 130.0, 129.5, 122.8, 116.0, 21.7, 19.9. IR (KBr, cm^{-1}) 3421, 2956, 1685, 1645, 1603, 1505, 1469, 1453, 1186, 839. Anal. Calcd for $C_{14}H_{12}ClNO_2S_2$: C, 51.61; H, 3.71; N, 4.30. Found: C, 51.81; H, 3.79; N, 4.18.

3-[Bis(methylthio)methylene]-1-(4-methoxyphenyl)pyridine-2,6(1*H*,3*H*)-dione (2d)

Yellow solid; mp 166-168°C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.53 (s, 3 H), 2.67 (s, 3 H), 3.83 (s, 3H), 6.23 (d, J = 10.2 Hz, 1 H), 7.00 (d, J = 8.7, 2 H), 7.11 (d, J = 8.7, 2 H), 8.05 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 164.8, 163.1, 159.3, 138.5, 129.4, 127.6, 123.2, 116.3, 114.6, 55.4, 21.6, 19.8. Anal. Calcd for $C_{15}H_{15}NO_3S_2$: C, 56.05; H, 4.70; N, 4.36. Found: C, 56.33; H, 4.82; N, 4.45.

3-[Bis(methylthio)methylene]-1-(2-methoxyphenyl)pyridine-2,6(1*H*,3*H*)-dione (2e)

Yellow solid; mp 142-143°C.^1H NMR (300 MHz, $CDCl_3$): δ 2.52 (s, 3 H), 2.65 (s, 3 H), 3.76 (s, 3 H), 6.22 (d, J = 10.2 Hz, 1 H

7.01-7.07 (m, 2 H), 7.12-7.15 (m, 1 H), 7.37-7.42 (m, 1 H), 8.06 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 164.3, 162.5, 154.9, 138.6, 130.0, 129.9, 124.0, 123.3, 120.9, 116.4, 111.9, 55.7, 21.5, 19.8. IR (KBr, cm^{-1}) 3446, 1683, 1642, 1600, 1500, 1451, 1410, 1192, 759. Anal. Calcd for $C_{15}H_{15}NO_3S_2$: C, 56.05; H, 4.70; N, 4.36. Found: C, 56.31; H, 4.56; N, 4.29.

1-Benzyl-3-[bis(methylthio)methylene]pyridine-2,6(1*H*,3*H*)-dione (2f)

Yellow solid: mp 98-100 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.53 (s, 3 H), 2.72 (s, 3 H), 5.21(s, 2 H), 6.21 (d, J = 10.4 Hz, 1 H), 7.28-7.30 (m, 1 H), 7.32-7.36 (m, 2 H),7.52 (d, J = 7.6 Hz, 2 H), 8.01 (d, J = 10.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$):δ172.2, 163.6, 161.6, 137.0, 136.3, 127.9, 127.2, 126.2, 122.3, 115.2, 41.9, 20.6, 18.7; Anal. Calcd for $C_{15}H_{15}NO_2S_2$: C, 58.99; H, 4.95; N, 4.59; Found: C, 58.76; H, 4.99; N, 4.72. MS (MALDI): calcd for $C_{15}H_{16}NO_2S_2$ $[M+H]^+$ 306.1, found 306.1

3-[Bis(ethylthio)methylene]-1-phenylpyridine-2,6(1*H*,3*H*)-dione (2g)

Yellow solid; mp 119-120 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32-1.39 (m, 6 H), 2.96-3.03 (m, 2 H), 3.18-3.26 (m, 2 H), 6.23 (d, J = 10.2 Hz, 1 H), 7.18-7.21 (m, 1 H), 7.38-7.51 (m, 4 H), 8.09 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 164.6, 163.0, 138.8, 135.2, 129.2, 128.6, 126.3, 123.9, 116.3, 34.1, 30.8, 14.8, 13.9. IR (KBr, cm^{-1}) 3442, 2924, 1686, 1641, 1593, 1493, 1453, 1413, 1190, 698. Anal. Calcd for $C_{16}H_{17}NO_2S_2$: C, 60.16; H, 5.36; N, 4.38. Found: C, 60.35; H, 5.28; N, 4.50.

3-[Bis(ethylthio)methylene]-1-*p*-tolylpyridine-2,6(1*H*,3*H*)-dione (2h)

Yellow solid; mp 115-117 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27-1.37 (m, 6 H), 2.39 (s, 3H), 2.96-2.99 (m, 2 H), 3.19-3.22 (m, 2 H), 6.22 (d, J = 10.0 Hz, 1 H), 7.06-7.08 (m, 2 H), 7.26-7.29 (m, 2H), 8.08 (d, J = 10.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 164.7, 163.0, 138.7, 138.2, 132.4, 129.9, 128.2, 123.8, 116.2, 34.0, 30.7, 21.2, 14.7, 13.8. Anal. Calcd for $C_{17}H_{19}NO_2S_2$: C, 61.23; H, 5.74; N, 4.20. Found: C, 61.48; H, 5.88; N, 4.31.

3-[Bis(ethylthio)methylene]-1-(4-chlorophenyl)pyridine-2,6(1*H*,3*H*)-dione (2i)

Yellow solid; mp 122-123 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32-1.39 (m, 6 H), 2.96-3.04 (m, 2 H), 3.19-3.24 (m, 2 H), 6.21 (d, J = 10.2 Hz, 1 H), 7.13 (d, J = 8.4 Hz, 2 H), 7.43 (J = 8.4 Hz, 2 H), 8.09 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 164.4, 162.8, 139.0, 134.3, 133.7, 130.1, 129.4, 123.5, 115.9, 34.1, 30.9, 14.8, 13.9. IR (KBr, cm^{-1}) 3443, 1679, 1647, 1598, 1493, 1454, 1407, 1190, 783, 695. Anal. Calcd for $C_{16}H_{16}ClNO_2S_2$: C, 54.30; H, 4.56; N, 3.96. Found: C, 53.94; H, 4.45; N, 4.09.

Crystal data for **2i**: $C_{16}H_{16}ClNO_2S_2$, colourless crystal, M = 352.9, Monoclinic, P2(1)/n, a = 12.739(5) Å, b = 5.382(2) Å, c = 24.848(10) Å, α = 90.00 º, β = 103.362(6) º, γ = 90.00 º, V = 1657.3(11) Å3, Z = 4, T = 273(2), F000 = 736.0, R1 = 0.0636, wR2 = 0.1423. CCDC deposition number: 1058034. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

3-[Bis(ethylthio)methylene]-1-(4-methoxyphenyl)pyridine-2,6(1*H*,3*H*)-dione (2j)

Yellow solid; mp 118-120 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31-1.38 (m, 6 H), 2.95-3.02 (m, 2 H), 3.18-3.25 (m, 2 H), 3.83(s, 3 H), 6.22 (d, J = 10.2 Hz, 1 H), 6.98 (d, J = 9.0 Hz, 2 H), 7.09 (d, J = 9.0 Hz, 2 H), 8.07 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 164.9, 163.2, 159.3, 138.7, 129.5, 127.7, 123.9, 116.3, 114.6, 55.4, 34.0, 30.7, 14.8, 13.9. IR (KBr, cm^{-1}) 3441, 1693, 1647, 1454, 1412, 1190, 674. Anal. Calcd for $C_{17}H_{19}NO_3S_2$: C, 58.43; H, 5.48; N, 4.01. Found: C, 58.77; H, 5.57; N, 4.10.

3-[Bis(benzylthio)methylene)-1-phenylpyridine-2,6(1*H*,3*H*)-dione (2k)

Yellow solid; mp 165-166 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 4.05 (s, 2 H), 4.29 (s, 2 H), 6.09 (d, J = 10.2 Hz, 1 H), 7.15-7.49 (m, 15 H), 7.81 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 164.4, 163.0, 138.5, 135.6, 135.1, 135.0, 129.4, 129.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 127.7, 124.6, 116.6, 43.9, 41.4. IR (KBr, cm^{-1}): 3445, 2923, 2853, 1658, 1557, 1540, 1487, 1350, 1260, 748. Anal. Calcd for $C_{26}H_{21}NO_2S_2$: C, 70.40; H, 4.77; N, 3.16. Found: C, 70.69; H, 4.70; N, 3.07.

3-[Bis(benzylthio)methylene]-1-(*p*-tolyl)pyridine-2,6(1*H*,3*H*)-dione (2l)

Yellow solid; mp 166-168 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 (s, 3 H), 4.04 (s, 2 H), 4.29 (s, 2 H), 6.09 (d, J = 10.2 Hz, 1 H), 7.03 (d, J = 7.8 Hz, 2 H), 7.22-7.32 (m, 12 H), 7.79 (d, J = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 164.5, 163.1, 138.4, 135.7, 135.2, 132.3, 130.0, 129.4, 128.9, 128.8, 128.7, 128.3, 128.2, 127.7, 124.6, 116.6, 43.9, 41.1, 21.2. IR (KBr, cm^{-1}) 3446, 2935, 1692, 1644, 1600, 1511, 1493, 1454, 1191, 820. Anal. Calcd for $C_{27}H_{23}NO_2S_2$: C, 70.87; H, 5.07; N, 3.06. Found: C, 70.66; H, 5.13; N, 2.98.

3-[Bis(ethylthio)methylene]-1-methylpyridine-2,6(1*H*,3*H*)-dione (2m)

Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (t, J = 7.5 Hz, 3 H), 1.37 (t, J = 7.5 Hz, 3 H), 2.93 (q, J = 7.5 Hz, 2 H), 3.22 (q, J = 7.5 Hz, 2 H), 3.33 (s, 3H), 6.12 (d, J = 10.2 Hz, 1 H), 7.97 (d, J = 10.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 14.6, 26.2, 30.6, 33.9, 116.0, 124.0, 137.8, 163.1, 164.8, 170.5; Anal. Calcd for $C_{11}H_{15}NO_2S_2$: C, 51.33; H, 5.87; N, 5.44. Found: C, 51.60; H, 5.72; N, 5.37. MS (MALDI): calcd for $C_{11}H_{16}NO_2S_2$ $[M+H]^+$ 258.1, found 258.1.

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