SHORT PAPER

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Convenient synthesis of 5-(arylamino(alkylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-diones and 2-arylthio-4-quinolones

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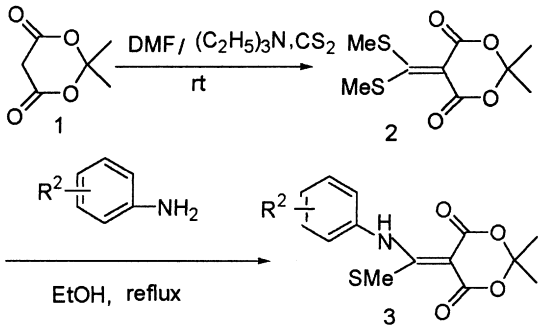
Meldrum's acid reacted with an aryl isothiocynate and alkyl halides to afford the 5-(arylamino(alkylthio)methylene)-5-methylthio-2,2-dimethyl-1,3-dioxane-4,6-diones and the compounds underwent thermal cyclization to give the 4-2-arylthio-4(1*H*)-quinolones

Keywords: 5-(arylamino(alkylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-diones, 2-anylthio-4(1*H*)-quinolones

Meldrum's acid, 2,2-dimethyl-1,3-dioxane-4,6-dione[1], appears to be an attractive reagent in organic synthesis,[1] and the derivative of Meldrum's acid, isopropylidene bis (methylthio)methylenemalonate **2** is a key intermediate for the preparation of a large number of the heterocyclic compounds. Various nucleophiles (amines, hydrazines, organometallic reagent) can displace one of the methylthio group and cyclisation of the intermediate can generally occur to afford heterocyclic compounds.[2,3] In our previous communications, 5-(arylaminoalkylidene)-5-methylthio-2,2-dimethyl-1,3-dioxane-4,6-diones **3** was prepared by condensation of Meldrum acid with the carbon disulfide under base catalysis, followed by the alkylation with methyl iodide to give the compound **2**,[4] then the compound **2** reacted with the arylamines to afford compound **3** (Scheme 1).[5] This method is limited by the lack of a convenient procedure and the yield is moderate.



Scheme 1

In this paper, we develop a new and more convenient method for the synthesis of 5-(arylamino(alkylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-diones **3** by one-pot reaction via the reaction of Meldrum's acid with aryl isothiocyanates (Scheme 2). Due to the acidity ($_pk_a$=4.97) of Meldrum's acid, we carry out the reaction using triethylamine as base to form the anion at room temperature. Then aryl isothiocyanates readily react with anion of Meldrum's acid in dry dimethylformamide at 40–45˚C for 5h, followed by alkylation with the alkyl halides at room temperature for 4h to produce 5-(arylamino(alkylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-diones in good yield. The results are listed in Table 1.

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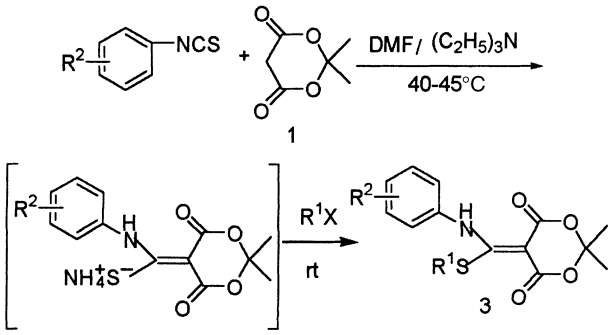
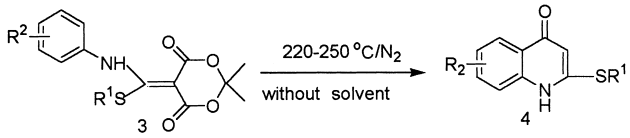
†This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 2

This method is superior to the previous report in which the product was obtained by a multistep reaction. As an example **3a**, we can obtain 90% yield by method of this paper, while, the reaction was carried out by our previous method, the overall yield is only 39.7%. It is obviously that the yields of multistep method were poorer than by one-pot method. The advantages of this method are the manipulative convenience, mild reaction condition and good yield.

Quinolones are important compounds. The 5-(arylamino(alkylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-diones can be cyclised by heating to give 2-alkylthio-4(1*H*)-quinolones (Scheme 3). The results are listed in Table 2.



Scheme 3

Table 1 5-(arylamino(alkylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-diones **3**

Product	R^2	R^1	Yield/%*
3a	C_6H_5	CH_3	90
3b	*p*-$CH_3C_6H_4$	CH_3	85
3c	*o*-$CH_3C_6H_4$	CH_3	80
3d	*p*-$CH_3OC_6H_4$	CH_3	81
3e	*p*-ClC_6H_4	CH_3	86
3f	*p*-BrC_6H_4	CH_3	89
3g	C_6H_5	CH_2Ph	88
3h	*p*-ClC_6H_4	CH_2Ph	84

*Isolated and purified yield.

Table 2 2-Alkylthio-4(1*H*)-quinolones

Product	R^2	R^1	Yield/%*
4a	H	SCH_3	81
4b	6-Br	SCH_3	73
4c	6-CH_3	SCH_3	86
4d	6-CH_3O	SCH_3	60
4e	8-CH_3	SCH_3	62
4f	6-Cl	SCH_3	71
4g	H	SCH_2Ph	75
4h	6-Cl	SCH_2Ph	70

*Isolated and purified yields.

In summary, we have developed a simple and convenient method for the synthesis of 5-(aryl(aminoalkylthio)methylene)-2,2-dimethyl-1,3-dixane-4,6-dione in excellent yields and applicated the compounds to synthesize the 2-alkylthio-4-quinoneons by thermal cyclization.

Experimental

^{1}H NMR spectra were recorded on a Bruker 400MHz instrument spectrometer using $CDCl_3$ or DMSO-D_6 as the solvent with TMS as an internal standard. Chemical shifts (δ) are reported in ppm and coupling constants *J* is given in Hz. IR spectra were recorded using KBr disks with a Bruker Vector-22 infrared spectrometer. Mass spectra were obtained on an HP 5989A spectrometer. Meeting points were uncorrected.

Typical procedure for the preparation of **(3)**: To a solution of Meldrum's acid (1.5g, 10mmol) in dry DMF (10ml), triethylamine (2g, 20mmol) was added and stirred for 30min at room temperature. Then phenyl isothiocyanate (1.35g, 10mmol) was added to the solution and stirred for 5h at 40–45°C. The mixture was cooled in an ice-bath and methyl iodide (0.75ml, 10mmol) was added. The mixture was stirred for 4h at room temperature, ice water was added to precipitate out the solid product, which was recrystallised from tetrahydrofuran petroleum ether to give pure product. Yield: 2.58g (90%).

Typical procedure for 2-Alkylthio-4-quinolones **(4)**: Compound **3a** (1.46g, 5mmol) was heated without solvent at 250–260°C for about 10-15min while a current of nitrogen is passed through the reaction mixture, After cooling, the product was purified by recystallisation from dimethyformamide/water. Yield: 0.77g (81%).

3a: m.p. 152–153°C (lit [5] 153°C) ^{1}H NMR ($CDCl_3$) δ=1.77 (s, 6H), 2.27 (s, 3H), 7.45–7.26 (m, 5H); 12.72 (s, 1H); MS *m/z* (relative intensity) M (293, 235, 188, 144); IR (KBr): ν_{max} (cm^{-1}) (1722, 1642, 1539).

3b: m.p. 145–146°C (lit [5] 145°C) ^{1}H NMR ($CDCl_3$) δ=1.76 (s, 6H); 2.30 (s, 3H); 2.39 (s, 3H); 7.27 (d, 2H, *J*=8.12Hz), 7.20 (d, 2H, *J*=8.24 Hz), 12.71 (s, 1H); MS *m/z* (relative intensity) M (307, 249, 202, 158); IR (KBr): ν_{max} (cm^{-1}) (1711, 1656, 1550).

3c: m.p. 96–98°C (dec) ^{1}H NMR ($CDCl_3$) δ= 1.77 (s, 6H); 2.26 (s, 3H); 2.32 (s, 3H); 7.31–7.27 (m, 4H); 12.56 (s, 1H); Elemental analyses. Calcd for $C_{15}H_{17}NSO_4$ C 58.61%, H 5.57%, N 4.56%, Found C 58.72%, H 5.74%, N 4.45%, MS *m/z* (relative intensity) M (307, 249, 202); IR (KBr): ν_{max} (cm^{-1}) (1711, 1656, 1550).

3d: m.p. 146–147°C (lit [5] 146°C) ^{1}H NMR ($CDCl_3$) δ=1.76 (s, 6H); 2.32 (s, 3H); 3.84 (s, 3H); 7.26 (d, 2H, *J*=8.84 Hz), 6.96 (d, 2H, *J*=8.88 Hz), 12.63 (s, 1H); MS *m/z* (relative intensity) M (323, 265, 218, 174); IR (KBr): ν_{max} (cm^{-1}) (1712, 1659, 1551)

3e: m.p. 143–144°C (lit [5] 143°C) ^{1}H NMR ($CDCl_3$) δ= 1.77 (s, 6H); 2.32 (s, 3H); 7.43 (d, 2H, *J*=8.64 Hz), 7.27 (d, 2H, *J*=8.68 Hz), 12.73 (s, 1H); MS *m/z* (relative intensity) M (327, 269, 222, 178); IR (KBr): ν_{max} (cm^{-1}) (1723, 1658, 1585)

3f: m.p. 143–145°C (lit [5] 143°C) ^{1}H NMR ($CDCl_3$) δ= 1.77 (s, 6H); 2.30 (s, 3H); 7.48 (d, 2H, *J*=8.61 Hz), 7.26 (d, 2H, *J*=8.60 Hz), 12.73 (s, 1H); MS *m/z* (relative intensity) M (372, 314, 267, 223); IR (KBr): ν_{max} (cm^{-1}) (1720, 1660, 1582)

3g: m.p. 154–156°C (dec) ^{1}H NMR ($CDCl_3$) δ=1.71 (s, 6H), 4.00 (s, 2H), 6.86 (m, 2H), 6.99 (m, 2H), 7.28(m, 2H), 7.42 (d, 2H, *J*=8.78Hz), 7.46 (m, 2H), 11.89 (s, 1H). Elemental analyses. Calcd for $C_{20}H_{19}NSO_4$, C 65.02%, H 5.18%, N 3.79% Found C 65.19%, H 5.03%, N 3.49%, MS *m/z* (relative intensity) M (369, 293, 188, 144, 91, 77) (100), 77 (58). IR (KBr): ν_{max} (cm^{-1}) (1702, 1669, 1588)

3h: m.p. 142–144°C (dec) ^{1}H NMR ($CDCl_3$) δ=1.77 (s, 6H), 4.10 (s, 2H), 6.86 (m, 2H), 6.99 (m, 2H), 7.28(d, 2H, *J*=8.70Hz), 7.42 (d, 2H, *J*=8.66Hz), 7.46 (m, 1H), 11.89 (s, 1H). Elemental analyses. Calcd for $C_{20}H_{18}NSO_4Cl$, C 59.48%, H, 4.49%, N 3.47% Found C 59.35%, H, 4.49%, N 3.32%, MS *m/z* (relative intensity) M (403, 347, 300, 256, 77), IR (KBr): ν_{max} (cm^{-1}) (1697, 1659, 1588)

4a: m.p. 221–222°C (lit [5] 221–222°C) ^{1}H NMR (DMSO-d_6) δ= 2.57 (s, 3H), 5.97 (s, 1H), 7.27 (m, 1H), 7.43–7.4 (m, 1H), 7.61 (m, 1H), 8.00-8.02 (d, 1H, *J*=7.72Hz), 11.84 (s, 1H). IR (KBr): MS *m/z* (relative intensity) 191 (M^+, 100), 145(25), 105(15). ν_{max} (cm^{-1}) 3280, 1640, 1585,

4b: m.p. 273–276°C (lit [5] 273–276°C) ^{1}H NMR (DMSO-d_6) δ= 2.58 (s, 3H), 5.97 (s, 1H), 7.39 (d, 1H, *J*=9.21 Hz), 7.77 (dd, 1H, J_1=9.31 Hz, J_2=2.62 Hz), 8.04 (d, 1H, *J*=2.7 Hz), 11.99 (s, 1H), MS *m/z* (relative intensity) 269 (M^+, 100), 271 (M^++2, 97), 225 (40), 183 (26), 116 (22), 88 (28). IR (KBr): ν_{max} (cm^{-1}) 3280, 1640, 1580

4c: m.p. 224–227°C (lit [5] 224–227°C) ^{1}H NMR (DMSO-d_6) δ= 2.33 (s, 3H), 2.57 (s, 3H), 5.95 (s, 1H), 7.42 (m, 2H), 7.93 (s, 1H), 11.8.0 (s, 1H). MS *m/z* (relative intensity) 205 (M^+, 100), 159 (22), 86 (45), 77 (12). IR (KBr): ν_{max} (cm^{-1}) 3280, 1641, 1580.

4d: m.p. 230–232°C (lit [5] 230–232°C) ^{1}H NMR (DMSO-d_6) δ=2.58 (s, 3H), 3.84 (s, 3H), 5.94 (s, 1H), 7.24 (dd, 1H, J_1=9.63 Hz, J_2=4.32Hz), 7.44 (d, 1H, *J*=4.24Hz), 7.59 (d,1H, *J*=9.52 Hz), 11.81 (s, 1H). MS *m/z* (relative intensity) 221 (M^+, 100), 188 (19), 145 (26), 77(15). IR (KBr): ν_{max} (cm^{-1}) 3240, 1640, 1580

4e: m.p. 192–193°C dec) ^{1}H NMR (DMSO-d_6) δ=2.04 (s, 3H), 2.57 (s, 3H), 6.50 (s, 1H), 7.19–7.98 (m, 3H), 10.90 (s, 1H). Elemental analyses. Calcd for $C_{11}H_{11}NSO$, C 64.36%, H, 5.40%, N 6.82% Found C 64.66%, H, 5.28%, N 7.01%, MS *m/z* (relative intensity) 205 (M^+, 100), 159 (22), 86 (45), 77 (12). IR (KBr): ν_{max} (cm^{-1}) 3280, 1640, 1572

4f: m.p. 255–257°C (lit [5] 255–257°C) ^{1}H NMR (DMSO-d_6) δ= 2.55 (s, 3H), 5.94 (s, 1H), 7.36–7.41 (d, 1H, *J*=8.88Hz), 7.43 (dd, 1H, J_1=8.91Hz, J_2=2.73Hz), 7.45 (d, 1H, *J*=2.68Hz), 11.78 (s, 1H). MS *m/z* (relative intensity) 225 (M^+, 100), 179 (46), 139 (34), 123 (19), IR (KBr): ν_{max} (cm^{-1}) 3265, 1643, 1580

4g: m.p. 197–199°C (dec) ^{1}H NMR (DMSO-d_6) δ=4.33 (s, 2H), 6.28 (s, 1H), 7.20–7.52 (m, 3H), 7.54–7.77(d, 2H, *J*=8.68), 7.80–8.05 (m, 4H) 11.80 (s, 1H). Elemental analyses. Calcd for $C_{16}H_{13}NSO$, C 71.88%, H, 4.90%, N 5.24% Found C 71.71%, H, 5.09%, N 5.20% MS *m/z* (relative intensity) 267(M^+, 37), 234 (24), 190 (8), 91 (100), 77 (15). IR (KBr): ν_{max} (cm^{-1}) 3331, 1630, 1577

4h: m.p. 226–228°C (dec) ^{1}H NMR (DMSO-d_6) δ= 4.31 (s, 2H), 6.30 (s, 1H), 7.20 (d, 1H, *J*=9.33 Hz), 7.52(dd, 1H, J_1=9.42 Hz, J_2=2.56 Hz), 7.55–7.87 (m, 5H), 7.91 (d, 1H, *J*=2.47 Hz), 11.68 (s, 1H). Elemental analyses. Calcd for $C_{16}H_{12}NSOCl$, C 63.68%, H, 4.01%, N 4.64% Found C 63.80%, H, 3.89%, N 4.61% MS *m/z* (relative intensity) 301 (M^+, 21), 268 (18), 224 (7), 91 (100), 77 (15). IR (KBr): ν_{max} (cm^{-1}) 3280, 1638, 1567.

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