Tetrahedron 64 (2008) 5944–5948

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Alkylation of aryl 3-oxopropanedithioate and 3-amino-1-aryl-3-thioxo-1-propanones as an effective tool for the construction of differently substituted thiophenes and annulated thiophenes

Reichel Samuel, Prakash Chandran, S. Retnamma, K.A. Sasikala, N.K. Sreedevi, E.R. Anabha *,†, C.V. Asokan ‡

School of Chemical Sciences, Mahatma Gandhi University, Kottayam, Kerala, India

ARTICLE INFO

Article history:
Received 20 November 2007
Received in revised form 9 April 2008
Accepted 10 April 2008
Available online 12 April 2008

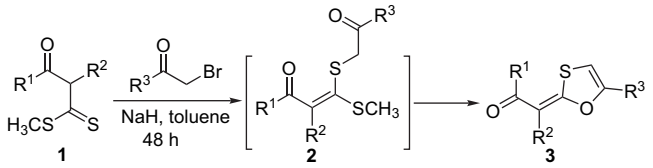
Keywords:
Alkylation
Aryl-3-oxopropanedithioate
β-Oxothioamides
1,3-Oxathiole
Thiophene

ABSTRACT

The alkylation of aryl 3-oxopropanedithioate with α-haloketones under different reaction conditions afforded substituted aryl[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanones and [3-aryl-5-(methylsulfanyl)-2-thienyl](phenyl)methanones. The same strategy was extended to 3-amino-1-aryl-3-thioxo-1-propanones to afford aryl[2-amino-4-phenyl-3-thienyl]methanones and ethyl 3-phenyl-5-piperidino-2-thiophene carboxylate.

1. Introduction

The synthesis of thiophenes and annulated thiophenes[1,2] are of special interest due to their potential use as pharmaceuticals,[3–5] conjugated polymers,[6,7] organic conductors,[8–10] semiconductors,[11,12] light emitting devices,[13] etc. A general strategy employing alkylation of an intermediate dimetaloketene dithioacetal is used for the synthesis of alkylthiothiophenes or thienothiophenes.[12,14–19] We envisioned that the difficulties involved in the selective sequential alkylations of the intermediate dimetaloketene dithioacetals could be circumvented by the use of β-oxodithiocarboxylates in the above reaction. Earlier report from this laboratory has described similar alkylation reactions of β-oxothioamides with α-haloketones for the synthesis of functionalized thiophenes.[20] In a recent preliminary report, we have explained the alkylations of aryl 3-oxopropanedithioates with α-haloketones such as phenacyl bromide and bromo acetone in the presence of sodium hydride in toluene yielding 1,3-oxathiole derivatives (Scheme 1).[21] Further investigations on the alkylations of aryl 3-oxopropanedithioates with α-haloketones yielding differently substituted thiophenes are explained in this paper.



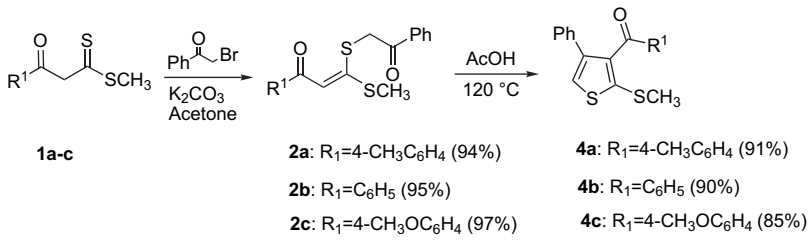
Scheme 1. Synthesis of 1-aryl-2-(5-alkyl/aryl-1,3-oxathiol-2-yliden)-1-ethanones **3**.

2. Results and discussion

In an earlier report, the formation of 1-aryl-2-(5-aryl-1,3-oxathiol-2-yliden)-1-ethanones **2** from aryl 3-oxopropanedithioates **1a–e**[21–25] is described by the cyclizations of intermediate ketene dithioacetals in the presence of sodium hydride.[21] We envisioned that the intermediate ketene dithioacetal **2** could be isolated from the reaction, conducting the alkylation in the presence of mild base like potassium carbonate. So the alkylation of 4-(methylphenyl) 3-oxopropanedithioate **1a** with phenacyl bromide was carried out in the presence of potassium carbonate in acetone at room temperature, yielding 1-(methylphenyl)-3-(methylsulfanyl)-3-{[oxo(phenyl)ethyl]sulfanyl}-2-propen-1-one **2a** in 94% yield. However, on

* Corresponding author. Fax: +91 481 2731009.
E-mail address: anabhaer@rediffmail.com (E.R. Anabha).
† Present address: Research Associate, Organic Chemistry Division, NIST (formerly RRL), Thiruvananthapuram. Tel.: +91 471 2515257; fax: +91 471 2491712.
‡ The work was carried out under the guidance of Dr. C. V. Asokan (Late), Reader, School of Chemical Sciences, Mahatma Gandhi University, Kottayam 686560, Kerala, India.

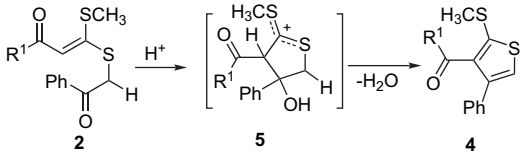
0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.04.036



Scheme 2. Synthesis of aryl[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanones **4**.

heating a solution of **2a** in dichloromethane, it underwent thermally induced cyclization affording (4-methylphenyl)[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanone **4a**. The reaction was applicable to other aryl 3-oxopropanedithioates **1a–c**. In order to improve the yield of the reaction the intermediate ketene dithioacetals **2a–c** were collected by filtration and a solution of **2** in acetic acid was heated at 120 °C. As expected **2a–c** were exclusively transformed into aryl[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanones **4a–c** (Scheme 2). However, these thermal cyclizations are limited to 3-oxopropanedithioates, having no substituents at the α-carbon atom.

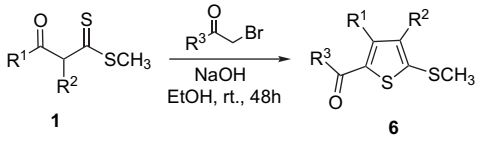
The mechanism of the reaction is explained by a thermally induced intramolecular cyclization of the intermediate ketene dithioacetal **2**. Due to the presence of vinylic alkylsulfanyl groups, the α-carbon atom of a ketene dithioacetal can act as a nucleophile under suitable reaction conditions. In an earlier report, we have described such a reactivity of aroyl ketene dithioacetals under Vilsmeier–Haack reaction conditions to afford 2-aroyl-3,3-bis(alkylsulfanyl)acrylaldehydes.[26] The addition of ketene dithioacetal moiety to the benzoyl group under thermal condition followed by the elimination of a water molecule from the intermediate **5** results in the formation of functionalized thiophenes **4** (Scheme 3).



Scheme 3. Mechanism for the formation of aryl[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanones **4** from 1-aryl-3-(methylsulfanyl)-3-{[oxo(phenyl)ethyl]sulfanyl}-2-propen-1-ones **2**.

Next, the intermediate ketene dithioacetal **2**, with an intention to cyclize them via an intramolecular aldol type reaction, yielding aryl[5-(methylsulfanyl)-3-phenyl-2-thienyl] methanones **6**, was treated with sodium hydroxide in ethanol for 48 h. The reactions of β-oxodithiocarboxylates with α-haloketones like phenacyl bromide or bromo acetone in the presence of sodium hydroxide in ethanol also resulted in alkylation followed by intramolecular aldol type reaction to afford aryl[5-(methylsulfanyl)-3-phenyl-2-thienyl] methanones **6a–e** (Scheme 4).

As a continuation to these studies, 3-morpholino-1-phenyl-3-thioxo-1-propanone **7a**, which was synthesized by refluxing methyl 3-oxo-3-phenylpropanedithioate **1a** with morpholine,[27] was alkylated with 2-bromo-1-(4-nitrophenyl)-1-ethanone in the presence of potassium carbonate in acetone at room temperature. The reaction was complete within an hour yielding a product mixture. The intermediate ketene-*N*,*S*-acetal being heat sensitive could not be separated from the reaction mixture by column chromatography. Considering the thermally induced cyclization reaction to afford functionalized thiophenes **5**, we decided to conduct the alkylation reaction in the presence of potassium carbonate in acetone at 60 °C. The reaction was complete



6a:R^1= 4-ClC_6H_4, R^2= H, R^3=Ph (67%)

6b:R^1= C_6H_5, R^2= H, R^3=Ph (71%)

6c:R^1, R^2=  , R^3=Ph (62%)

6d:R^1, R^2=  , R^3=Ph (78%)

6e:R^1= CH_3, R^2= H, R^3=Ph (76%)

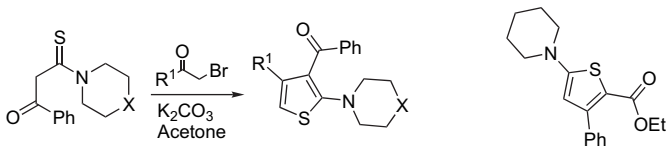
6f:R^1= C_6H_5, R^2= H, R^3=CH_3 (79%)

6g:R^1= 4-ClC_6H_4, R^2= H, R^3=CH_3 (70%)

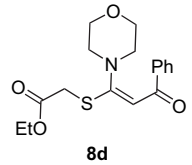
6h:R^1, R^2=  , R^3=CH_3 (84%)

Scheme 4. Synthesis of [3-aryl-5-(methylsulfanyl)-2-thienyl](phenyl)methanones **6a–e** and 1-[3-aryl-5-(methylsulfanyl)-2-thienyl]-1-ethanones **6f–h**.

within 30 min to afford [2-morpholino-4-(4-nitrophenyl)-3-thienyl](phenyl) methanone **9a** in 55% yield. The reaction was applicable to differently substituted 3-oxopropanethioamides (Scheme 5). However, the intermediate **8d** underwent an aldol type intramolecular cyclization reaction to afford ethyl 3-phenyl-5-piperidino-2-thiophene carboxylate **10a** in 60% yield. Their derivatives are used as P38 MAP kinase inhibitors in the treatment of inflammatory diseases.[28]



Scheme 5. Synthesis of aryl[2-amino-4-phenyl-3-thienyl]methanones **9a–c** and [5-amino-3-phenyl-2-thienyl](phenyl)methanone **10a**.



8d

In conclusion, we have demonstrated the alkylation of 3-oxopropanedithiocarboxylates and 3-oxopropanethioamides as an

effective tool for the construction of differently substituted thiophenes.

3. Experimental procedure

3.1. General

Melting points were uncorrected and were obtained on a Buchi-530 melting point apparatus. Infrared spectra were recorded with a Shimadzu IR 470 spectrometer and are given as cm^{-1}. ^1H NMR spectra were recorded in $CDCl_3$ on a Jeol GSX 400 (400 MHz) or a Bruker WM 300 (300 MHz) or Bruker WM 200 (200 MHz) spectrometer using TMS as internal standard and $CDCl_3$ as solvent. Coupling constants J are given in hertz. ^{13}C NMR spectra were recorded on a GSX 400 (100.00 MHz) or Brucker WM 300 (75.47 MHz) or Bruker WM 200 (22.64 MHz) spectrometer using $CDCl_3$ as solvent. Electron impact mass spectra (EIMS) were obtained on a Finnigen-Mat 312 instrument or a Schimadzu model GC–MS 5050 instrument. CHN analyses were done on an Elementar Vario EL III Carlo Erba 1108 instrument. All reagents were commercially available and were purified before use.

3.2. General procedure for the synthesis of 1-aryl-3-(methylsulfanyl)-3-{[oxo(phenyl)ethyl]sulfanyl}-2-propen-1-ones (2)

To a suspension of potassium carbonate (1.05 g, 5 mmol) in acetone (15 mL), 3-oxo-3-arylpropanedithiocarboxylate **1** (5 mmol) was added and the mixture was stirred for 5 min. To this reaction mixture, phenacyl bromide (0.96 g, 5 mmol) was added and further stirred at room temperature for 30 min. It was poured into ice-cold water; the solid separated was filtered and recrystallized from chloroform.

*3.2.1. 1-(4-Methylphenyl)-3-(methylsulfanyl)-3-{[oxo(phenyl)ethyl]sulfanyl}-2-propen-1-one (**2a**)*

Yield: 94%, white crystalline solid, mp: 110–112 °C. Anal. Calcd for $C_{19}H_{18}O_2S_2$: C, 66.63; H, 5.30. Found: C, 66.82; H, 5.32. IR (cm^{-1}) ν_{max} 1690, 1610, 1490, 1240, 756; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 4.40 (s, 2H, CH_2), 7.05 (s, 1H, vinylic), 7.12–7.32 (m, 2H, ArH), 7.45–7.58 (m, 2H, ArH), 7.60–7.72 (m, 1H, ArH), 7.8 (d, 2H, J=8 Hz, ArH), 8.00 (d, 2H, J=8 Hz, ArH); MS (EI): m/z (%) 324 (M^+-18, 36), 323 (40), 309 (5), 295 (47), 119 (80), 105 (100), 91 (72), 77 (94).

*3.2.2. 3-(Methylsulfanyl)-3-{[oxo(phenyl)ethyl]sulfanyl}-1-phenyl-2-propen-1-one (**2b**)*

Yield: 95%, white crystalline solid, mp: 108–110 °C. Anal. Calcd for $C_{18}H_{16}O_2S_2$: C, 65.82; H, 4.91. Found: C, 65.61; H, 4.94. IR (cm^{-1}) ν_{max} 1680, 1620, 1610, 1485, 1230, 1200, 750; ^1H NMR (200 MHz, $CDCl_3$) δ 2.53 (s, 3H, SCH_3), 4.44 (s, 2H, CH_2), 7.03 (s, 1H, vinylic), 7.30–7.72 (m, 6H, ArH), 7.87 (d, 2H, J=8 Hz, ArH), 7.99 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (22.64 MHz, $CDCl_3$) δ 15.4, 39.0, 111.2, 127.8, 128.5, 128.8, 129.0, 133.7, 138.9, 162.9, 185.8, 193.1; MS (EI): m/z (%) 310 (M^+-18, 100), 233 (35), 77 (17).

*3.2.3. 1-(4-Methoxyphenyl)-3-(methylsulfanyl)-3-{[oxo-(phenyl)ethyl]sulfanyl}-2-propen-1-one (**2c**)*

Yield: 97%, white crystalline solid, mp: 101–102 °C. Anal. Calcd for $C_{19}H_{18}O_3S_2$: C, 63.66; H, 5.06. Found: C, 63.85; H, 5.09. IR (cm^{-1}) ν_{max} 1680, 1600, 1470, 1230, 790; ^1H NMR (300 MHz, $CDCl_3$) δ 2.54 (s, 3H, SCH_3), 3.87 (s, 3H, OCH_3), 4.48 (s, 2H, CH_2), 6.64–7.26 (m, 6H, vinylic and ArH), 7.48–7.58 (m, 2H, ArH), 7.85–7.90 (m, 1H, ArH), 7.98–7.99 (m, 1H, ArH); MS (EI): m/z (%) 340 (M^+-18, 13), 339 (16), 311 (10), 135 (45), 105 (46), 77 (56).

3.3. General procedure for the synthesis of (aryl)[2-(methylsulfanyl)-4-phenyl-3-thienyl] methanones (4)

The appropriate 1-aryl-3-(methylsulfanyl)-3-{[oxo(phenyl)-ethyl]sulfanyl}-2-propen-1-ones **3a–c** (5 mmol) were taken in 20 mL glacial acetic acid and refluxed at 120 °C for 2 h. The reaction mixture was cooled, poured into ice-cold water and extracted using dichloromethane. The organic layer was dried over anhydrous sodium sulfate and the solvent was removed under vacuum. The residue was passed through a silica gel column using hexane and ethylacetate (20:1) as eluent. The solid products obtained were recrystallized from methanol.

*3.3.1. (4-Methylphenyl)[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanone (**4a**)*

Yield: 91%, yellow crystalline solid, mp: 163–164 °C. Anal. Calcd for $C_{19}H_{16}O_2S$: C, 70.33; H, 4.97. Found: C, 70.60; H, 4.99. IR (cm^{-1}) ν_{max} 1620, 1490, 1440, 1390, 990; ^1H NMR (200 MHz, $CDCl_3$) δ 2.25 (s, 3H, CH_3), 2.65 (s, 3H, SCH_3), 6.8–7.7 (m, 10H, C-5 and ArH); ^{13}C NMR (22.64 MHz, $CDCl_3$) δ 18.7, 20.1, 126.7, 128.1, 128.5, 128.8, 131.1, 131.8, 135.4, 136.7, 137.1, 145.3, 146.7, 187.6; MS (EI): m/z (%) 324 (M^+, 13), 248 (7.4), 227 (100), 212 (97.5), 173 (13.4), 136 (15.9).

*3.3.2. [2-(Methylsulfanyl)-4-phenyl-3-thienyl](phenyl) methanone (**4b**)*

Yield: 90%, yellow crystalline solid, mp: 77–78 °C. Anal. Calcd for $C_{18}H_{14}OS_2$: C, 69.64; H, 4.55. Found: C, 69.89; H, 4.56. IR (cm^{-1}) ν_{max} 1620, 1520, 1400, 1285, 715; ^1H NMR (300 MHz, $CDCl_3$) δ 2.63 (s, 3H, SCH_3), 7.03 (s, 1H, C-5), 7.11–7.15 (m, 5H, ArH), 7.25–7.29 (m, 2H, ArH), 7.53–7.56 (m, 3H, ArH); ^{13}C NMR (22.64 MHz, $CDCl_3$) δ 18.9, 127, 127.3, 127.8, 128.5, 128.8, 131.27, 134.6, 136.9, 145.7, 146.9, 188.2; MS (EI): m/z (%) 310 (M^+, 100), 234 (14.2), 233 (28.5), 158 (17.6), 105 (38.8).

*3.3.3. (4-Methoxyphenyl)[2-(methylsulfanyl)-4-phenyl-3-thienyl]methanone (**4c**)*

Yield: 85%, yellow crystalline solid, mp: 80–82 °C. Anal. Calcd for $C_{19}H_{16}O_2S_2$: C, 67.03; H, 4.74. Found: C, 67.31; H, 4.76. IR (cm^{-1}) ν_{max} 2916, 2843.07, 1608.45, 1498.94, 1395.6, 1280.14, 1243.56, 1170.63, 1036.88, 866.54, 824.02; ^1H NMR (300 MHz, $CDCl_3$) δ 2.54 (s, 3H, SCH_3), 3.72 (s, 3H, OCH_3), 6.55 (d, 2H, J=9 Hz, ArH), 6.91 (t, 1H, C-5), 7.00 (d, 2H, J=8 Hz, ArH), 7.07 (t, 2H, J=8 Hz, ArH), 7.33 (t, 1H, J=9 Hz, ArH), 7.47 (d, 2H, J=9 Hz, ArH); ^{13}C NMR (22.64 MHz, $CDCl_3$) δ 19.2, 54.8, 113.2, 127.5, 129.2, 130.2, 131.6, 131.8, 135.5, 137.5, 145.8, 146.9, 159.0, 163.2, 188.4; MS (EI): m/z (%) 340 (M^+, 66), 263 (23), 216 (12), 173 (8), 145 (11), 105 (58), 77 (100).

3.4. General procedure for the synthesis of [3-aryl-5-(methylsulfanyl)-2-thienyl](phenyl)methanones (6a–e) and 1-[3-aryl-5-(methylsulfanyl)-2-thienyl]-1-ethanones (6f–h)

To a well stirred suspension of sodium hydroxide (0.8 g, 20 mmol) in ethanol (15 mL), the dithiocarboxylate **1** (5 mmol) was added and stirred for 15 min. To this mixture, appropriate α-haloketone (5 mmol) was added and was stirred at room temperature for 48 h. It was then poured into ice-cold water (50 mL) and the precipitated solid was filtered, dissolved in chloroform (25 mL), dried over anhydrous sodium sulfate and concentrated to get the crude product. The functionalized thiophenes thus obtained were purified by recrystallization from hexane–ethylacetate (5:1).

*3.4.1. [3-(4-Chlorophenyl)-5-(methylsulfanyl)-2-thienyl](phenyl)methanone (**6a**)*

Yield: 67%, yellow crystalline solid, mp: 82–83 °C. Anal. Calcd for $C_{18}H_{13}ClOS_2$: C, 62.69; H, 3.80; Cl, 10.28. Found: C, 62.88; H, 3.83; Cl, 10.31. IR (cm^{-1}) ν_{max} 2887, 2356, 1713, 1613, 1545, 1476, 1383, 1264,

1076, 946 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=2.62 (s, 3H, SCH_3), 6.96 (s, 1H, H-4), 7.07–7.14 (m, 5H, ArH), 7.29 (d, 2H, J=9 Hz, ArH), 7.55 (d, 2H, J=9 Hz, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ=19.6, 104.8, 127.9, 128.2, 129.5, 129.6, 130.4, 132.2, 133.86, 133.9, 136.7, 137.7, 137.7, 146.1, 146.6, 188.3; MS (EI): m/z (%) 346 (M^++2, 21), 344 (M^+, 48), 267 (22), 232 (10), 105 (50), 77 (100).

*3.4.2. [5-(Methylsulfanyl)-3-phenyl-2-thienyl](phenyl)-methanone (**6b**)*

Yield: 71%, yellow crystalline solid, mp: 89–90 °C. Anal. Calcd for $C_{18}H_{14}OS_2$: C, 69.64; H, 4.55. Found: C, 69.91; H, 4.52. IR (cm^{-1}) ν_{max} 1620, 1563, 1526, 1395, 1264, 1170, 1095, 1064, 1015 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.64 (s, 3H, SCH_3), 7.03 (s, 1H, H-4), 7.11–7.14 (m, 6H, ArH), 7.27(br s, 2H, ArH), 7.54 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 19.7, 127.5, 127.7, 127.8, 128.0, 129.2, 129.6, 131.9, 135.42, 136.8, 137.7, 146.2, 147.4, 188.7; MS (EI): m/z (%) 310 (M^+, 90), 263 (12), 233 (40), 190 (13), 158 (24), 146 (19), 114 (18), 105 (59), 77 (100).

*3.4.3. [3-(Methylsulfanyl)-4,5-dihydronaphtho[1,2-c]thiophen-1-yl](phenyl)methanone (**6c**)*

Yield: 62%, yellow crystalline solid, mp: 78–79 °C. Anal. Calcd for $C_{20}H_{16}OS_2$: C, 71.39; H, 4.79. Found: C, 71.65; H 4.81. IR (cm^{-1}) ν_{max} 2916, 1641, 1593, 1423 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (s, 3H, SCH_3), 2.8 (t, 2H, J=7.2 Hz, CH_2), 2.92 (t, 2H, J=7.2 Hz, CH_2), 6.86–7.80 (m, 9H, ArH); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 19.96, 24.41, 30.16, 96.19, 105.49, 127.98, 128.12, 128.22, 129.99, 137.64, 141.67, 189.23; MS (EI): m/z (%) 336 (M^+, 55), 259 (29), 216 (20), 105 (60), 77 (100).

*3.4.4. [3-(Methylsulfanyl)-4,5,6,7-tetrahydro-2-benzothiophen-1-yl](phenyl)methanone (**6d**)*

Yield: 78%, yellow crystalline solid, mp: 69–70 °C. Anal. Calcd for $C_{16}H_{16}OS_2$: C, 66.63; H, 5.59. Found: C, 66.68; H 5.60. IR (cm^{-1}) ν_{max} 1620, 1565, 1505, 1405, 1380, 1320 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.7–1.85 (m, 4H, CH_2), 2.55 (s, 3H, SCH_3), 2.60 (t, 2H, J=7 Hz, CH_2), 3.0 (t, 2H, J=7 Hz, CH_2), 7.45 (t, 2H, J=8 Hz, ArH), 7.54 (t, 1H, J=8 Hz, ArH), 7.77 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 18.56, 22.35, 22.67, 25.30, 28.23, 128.17, 128.49, 131.51, 132.36, 138.82, 140.66, 142.22, 148.33, 187.99; MS (EI): m/z (%) 288 (M^+, 100), 240 (39), 211 (8), 106 (51), 77 (47).

*3.4.5. [3-Methyl-5-(methylsulfanyl)-2-thienyl](phenyl)-methanone (**6e**)*

Yield: 76%, dark brown oil. Anal. Calcd for $C_{13}H_{12}OS_2$: C, 62.87; H, 4.87. Found: C, 62.94; H 4.89. IR (cm^{-1}) ν_{max} 1620, 1570, 1515, 1440, 1395, 1330, 1310, 1270, 1180, 1140, 1080, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 6.83 (s, 1H, H-4), 7.46 (t, 2H, J=8 Hz, ArH), 7.54 (t, 1H, J=8 Hz, ArH), 7.78 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 16.83, 19.23, 128.12, 128.49, 128.70, 131.75, 134.22, 139.95, 146.64, 146.70, 188.20; MS (EI): m/z (%) 248 (M^+, 100), 200 (43), 171 (39), 128 (6), 105 (27), 77 (42).

*3.4.6. 1-[5-(Methylsulfanyl)-3-phenyl-2-thienyl]-1-ethanone (**6f**)*

Yield: 79%, yellow crystalline solid, mp: 86–87 °C. Anal. Calcd for $C_{13}H_{12}OS_2$: C, 62.87; H, 4.87. Found: C, 62.93; H, 4.90. IR (cm^{-1}) ν_{max} 1630, 1540, 1400, 1270 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H, CH_3), 2.56 (s, 3H, SCH_3), 6.79 (s, 1H, H-4), 7.31 (m, 5H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 19.08, 29.11, 128.70, 129.90, 130.02, 130.37, 134.59, 134.67, 138.65, 146.07, 147.72, 190.33; MS (EI): m/z (%) 248 (M^+, 80), 233 (100), 218 (5), 190 (14), 158 (20).

*3.4.7. 1-[3-(4-Chlorophenyl)-5-(methylsulfanyl)-2-thienyl]-1-ethanone (**6g**)*

Yield: 70%, yellow crystalline solid, mp: 70–72 °C. Anal. Calcd for $C_{13}H_{11}ClOS_2$: C, 55.21; H, 3.92, Cl, 12.54. Found: C, 55.32; H 3.94; Cl, 12.59. IR (cm^{-1}) ν_{max} 1620, 1520, 1480, 1360, 1260, 1080 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.1 (s, 3H, CH_3), 2.6 (s, 3H, SCH_3), 6.81 (s, 1H, H-4), 7.29 (d, 2H, J=9 Hz, ArH), 7.42 (d, 2H, J=9 Hz, ArH); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 18.96, 29.00, 128.57, 129.74, 130.26, 134.47, 138.49, 145.95, 147.60, 190.16; MS (EI): m/z (%) 286 (M^++2, 29), 284 (M^+, 74), 269 (100), 234 (32.1), 182 (7.6), 146 (8.6).

*3.4.8. [3-(Methylsulfanyl)-4,5,6,7-tetrahydro-2-benzothiophen-1-yl]-1-ethanone (**6h**)*

Yield: 84%, yellow crystalline solid, mp: 74–76 °C. Anal. Calcd for $C_{11}H_{14}OS_2$: C, 58.37; H, 6.23. Found: C, 58.40; H 6.22. IR (cm^{-1}); ν_{max} 1640, 1510, 1410, 1380, 1350, 1315, 1260, 1160, 1140, 980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.74–1.80 (m, 4H, CH_2), 2.46 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 2.56 (br s, 2H, CH_2), 3.0 (br s, 2H, CH_2); ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 18.6, 22.35, 22.72, 25.55, 28.07, 29.43, 134.37, 139.19, 140.07, 146.43, 189.35; MS (EI): m/z (%) 226 (M^+, 14), 225 (94), 210 (100), 182 (15), 167 (12).

3.5. General procedure for the synthesis of 4-aryl-2-dialkylamino-3-thienyl(phenyl) methanone 9 and ethyl 3-phenyl-5-piperidino-2-thiophene carboxylate 10

The appropriate β-oxothioamides **7** (2 mmol), prepared by refluxing phenyl 3-oxopropanedithioate with secondary amines,[8] were stirred with anhydrous potassium carbonate (3 g, 20 mmol) in dry acetone (30 mL) at reflux temperature for 10 min. The reaction mixture was cooled and α-haloketone (2 mmol) was added; then refluxed for 30 min. In order to remove potassium carbonate, the reaction mixture was filtered through a small column and the filtrate was evaporated to get the crude product, which was further purified by column chromatography using hexane–ethylacetate (9:1) as the eluent.

*3.5.1. [2-Morpholino-4-(4-nitrophenyl)-3-thienyl](phenyl) methanone (**9a**)*

Yield: 55%, yellow crystalline solid, mp: 170–172 °C. Anal. Calcd for $C_{21}H_{18}N_2O_4S$: C, 63.94; H, 4.60; N, 7.10. Found: C, 64.11; H, 4.62; N, 7.15. IR (cm^{-1}) ν_{max} 1640, 1510, 1449, 1410, 1372, 1341, 1264, 1201, 1142, 1109, 1027, 986, 937, 901, 852, 738; ^1H (300 MHz, $CDCl_3$) δ 2.99 (t, 4H, J=6 Hz, NCH_2), 3.45 (t, 4H, J=5 Hz, OCH_2), 6.93 (s, 1H, C-5), 7.35–7.44 (m, 4H, ArH), 7.5–7.58 (t, 1H, J=8 Hz, ArH), 7.82 (d, 2H, ArH), 8.07 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.6, 66.6, 94.2, 105, 116, 126.5, 128.2, 1287, 129, 133.7, 138.3, 140.3, 147.1, 162, 193; MS (EI): m/z (%) 394 (M^+, 7), 364 (8), 149 (12), 105 (21), 91 (32), 71 (61), 57 (100).

*3.5.2. [2-Morpholino-4-phenyl-3-thienyl](phenyl) methanone (**9b**)*

Yield: 60%, yellow crystalline solid, mp: 128–130 °C. Anal. Calcd for $C_{21}H_{19}NO_2S$: C, 72.18; H, 5.48; N, 4.01. Found: C, 72.31; H, 5.51; N, 4.02. IR (cm^{-1}) ν_{max} 1590, 1466, 1368, 1299, 1115, 915, 872, 755, 631; ^1H NMR (300 MHz, $CDCl_3$) δ 3.32 (t, 4H, J=6 Hz, NCH_2), 3.85 (t, 4H, J=5 Hz, OCH_2), 6.16 (s, 1H, C-5), 6.95–7.19 (m, 8H, ArH), 7.39 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.8, 66.3, 108.8, 123.5, 127.7, 127.9, 128.1, 129.5, 129.4, 131.4, 136.9, 139.6, 150.3, 164.2, 189.0; MS (EI): m/z (%) 349 (M^+, 100), 348 (41), 290 (17), 272 (15), 77 (12).

*3.5.3. Phenyl(4-phenyl-2-piperidino-3-thienyl) methanone (**9c**)*

Yield: 67%, yellow crystalline solid, mp: 108–110 °C. Anal. Calcd for $C_{22}H_{21}NOS$: C, 76.04; H, 6.09; N, 4.03. Found: C, 76.29; H, 6.12; N, 4.05. IR (cm^{-1}) ν_{max} 1657, 1595, 1528, 1498, 1446, 1384, 1263, 1199, 1168, 1116, 1070, 1025, 980, 922, 850; ^1H (300 MHz, $CDCl_3$) δ 1.23–1.37 (m, 6H, CH_2), 3.2 (t, 4H, J=5.5 Hz, NCH_2), 6.75 (s, 1H, C-5), 7.18–7.39 (m, 5H, ArH), 7.36 (t, 2H, J=8 Hz, ArH), 7.48 (t, 1H, J=8 Hz, ArH), 7.86 (d, 2H, J=8 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 21.5, 56, 113, 125.7, 127.4, 128.2, 128.4, 128.5, 128.7, 129.9, 130.2, 133.0, 137.0,

138.4, 142.0, 162.9, 194.5; MS (EI): *m*/*z* (%) 347 (M^+, 36), 330 (41), 187 (16), 134 (14), 115 (31), 105 (49), 91 (25), 77 (100).

*3.5.4. Ethyl 3-phenyl-5-piperidino-2-thiophene carboxylate (**10a**)*

Yield: 60%, yellow crystalline solid, mp: 132–134 °C. Anal. Calcd for $C_{18}H_{21}NO_2S$: C, 68.54; H, 6.71; N, 4.44. Found: C, 68.81; H, 6.75; N, 4.42. IR (cm^{-1}) ν_{max} 1654, 1466, 1380, 1288, 1121, 900, 851, 806, 755, 632; ^1H NMR (300 MHz, $CDCl_3$) δ 1.1 (t, 3H, J=7 Hz, CH_3), 1.42–1.58 (m, 6H, CH_2), 3.2 (t, 4H, J=5.5 Hz, NCH_2), 4.2 (q, 2H, J=7 Hz, OCH_2), 5.99 (s, 1H, C-5), 7.3–7.5 (m, 5H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.68, 23.99, 25.34, 51.1, 60.4, 108.2, 110, 127.9, 128, 129.4, 137, 150.8, 162.7, 162.9; MS (EI): *m*/*z* (%) 315 (M^+, 58), 287 (13), 270 (14), 243 (100), 128 (22), 115 (51), 81 (9), 69 (61).

Acknowledgements

R.S. thanks UGC, P.C. thanks Prof. Wim Dehaen and Prof. Erick van der Eycken, KU, Leuven and E.R.A. thanks the CSIR, New Delhi for the award of research fellowships. We thank the Directors of CDRI Lucknow and the Department of Chemistry, Madurai Kamaraj University for providing spectral and analytical data.

References and notes

1. Bohlmann, F.; Zdero, C. *Thiophenes and its Derivatives*; Gronowitz, S., Ed.; John Wiley and Sons: New York, NY, 1985; Part 1, pp 261–323.
2. Gronowitz, S. *Thiophenes and its Derivatives*; Gronowitz, S., Ed.; John Wiley and Sons: New York, NY, 1985; Part 1, pp 42–59.
3. Pinto, I. L.; Jarvest, R. L.; Serafinowska, H. T. *Tetrahedron Lett.* **2000**, *41*, 1597.
4. Luker, T. J.; Beaton, H. G.; Whiting, M.; Kete, A.; Cheshire, D. R. *Tetrahedron Lett.* **2000**, *41*, 7731.
5. Holmes, J. M.; Lee, G. C. M.; Wijino, M.; Weinkam, R.; Wheeler, L. A.; Garst, M. E. *J. Med. Chem.* **1994**, *37*, 1646.
6. Roncali, J. *Chem. Rev.* **1997**, *97*, 173.
7. Schopf, G.; Kossemehl, G. *Adv. Polym. Sci.* **1997**, *129*, 1.
8. Kiani, M. S.; Mitchell, G. R. *Synth. Met.* **1992**, *46*, 293.
9. Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99.
10. Wolf, J. J.; Wortmann, R. *Adv. Phys. Org. Chem.* **1999**, *32*, 121.
11. Morrison, J. J.; Murray, M. M.; Li, X. C.; Holmes, A. B.; Morratti, S. C.; Friend, R. H.; Sirringhaus, H. *Synth. Met.* **1999**, *102*, 987.
12. Li, X. C.; Sirringhaus, H.; Garrier, F.; Holmes, A. B.; Morratti, S. C.; Feeder, N.; Clegg, W.; Teat, S. J.; Friend, R. H. *J. Am. Chem. Soc.* **1998**, *120*, 2206.
13. Greenham, N. C.; Morratti, S. C.; Bradley, D. D. C.; Friend, R. H.; Holmes, A. B. *Nature (London)* **1993**, *365*, 628.
14. Lee, S. B.; Hong, J.-I. *Tetrahedron Lett.* **1995**, *36*, 8439.
15. Mashraqui, S. H.; Hariharasubrahmanian, H.; Kumar, S. *Synthesis* **1999**, 2030.
16. Prim, D.; Joseph, D.; Kirsch, G. *Liebigs. Ann. Chem.* **1996**, 239.
17. Prim, D.; Kirsch, G. *Synth. Commun.* **1995**, 2449.
18. Augustine, M.; Rudorf, W. D.; Schimdt, U. *Tetrahedron* **1976**, *32*, 3055.
19. Dalgard, L.; Jensen, L.; Lawesson, S. O. *Tetrahedron* **1974**, *39*, 93.
20. Suma, S.; Ushakumari, N. K.; Asokan, C. V. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1997**, *131*, 161.
21. Samuel, R.; Asokan, C. V.; Chandran, P.; Suma, S.; Retnamma, S.; Anabha, E. R. *Tetrahedron Lett.* **2007**, *48*, 8376.
22. Voss, J. Synthesis of Thiolesters and Thiolactones. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1990; Vol. 6, p 435.
23. Nair, S. K.; Samuel, R.; Asokan, C. V. *Synthesis* **2001**, 573.
24. Ramdas, S. R.; Srinivasan, P. S.; Ramachandran, J.; Sastry, V. V. S. K. *Synthesis* **1983**, 605.
25. Singh, G.; Bhattacharjee, S. S.; Ila, H.; Junjappa, H. *Synthesis* **1982**, 693.
26. Anabha, E. R.; Asokan, C. V. *Synthesis* **2006**, 151.
27. Viswakarma, J. N.; Apparao, S.; Ila, H.; Junjappa, H. *Ind. J. Chem.* **1985**, *24B*, 466.
28. Gill, A. L.; Woodhead, S.; Carr, M. *Chem. Abstr.* **2004**, *141*, 366122h (PCT Int. Appl. WO 89,929, 2004).