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# Intermolecular Carbenoid Insertions: Reactions of 2-Substituted Thiophenes with Ethyl Diazoacetate in the Presence of Rhodium (II) Acetate.

Geoffrey K. Tranmer and Alfredo Capretta[1]*

*Department of Chemistry, Brock University, St. Catharines, Ontario, Canada L2S 3A1.*

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***Abstract:*** The reactions of ethyl diazoacetate with a series of 2-substituted thiophenes in the presence of catalytic rhodium (II) acetate were examined. In the cases of 2-methylthiophene and 2-(trimethylsilyl)thiophene, cyclopropane and thiopyran products predominated while thiophene-2-thiol and 2-(methylthio)thiophene gave rise to thiopyrans and ethyl 2-(2-thienylsulfanyl)acetate. No reaction was apparent when 2-pyrrolidinothiophene was used. 2-Alkoxythiophenes, however, allowed for the production of a series of ethyl 6-alkoxy-6-thioxo-2,4-hexadienoates. The mechanistic implications are discussed. 

*Keywords:* carbenoids; thiophenes; thiopyrans; cyclopropanation

The reactions of diazo compounds with furans under metal catalysis generally result in cyclopropanation followed by an apparent [4+2]-cycloreversion (which can either take place spontaneously, with heat or *via* the addition of acid) to yield polyene products. Novac and Sorm,[2] for example, observed that cyclopropanation of furan by ethyl diazoacetate under copper catalyzed conditions resulted in an unstable intermediate that upon ring opening yielded ethyl 6-oxo-2,4-hexadienoate. More recently, Wenkert[3] has made a complete study of the intermolecular carbenoid insertion of ethyl diazoacetate into furan in the presence of rhodium (II) acetate. Effectively, these insertions allow one to envision a furan as a masked unsaturated carbonyl synthon. This methodology has been applied to a number of total syntheses.[4] Reactions between thiophenes and diazocarbonyls have also been known for several years,[5] but unlike furanyl systems, thiophene reacts to give stable cyclopropanated products[6] or crystalline sulphur ylides.[7] To our knowledge, the only example of a [4+2]-cycloreversion in the thienyl series occurs during the rhodium acetate catalyzed decomposition of 1-diazo-3-(3-thienyl)-2-propanone.[8]

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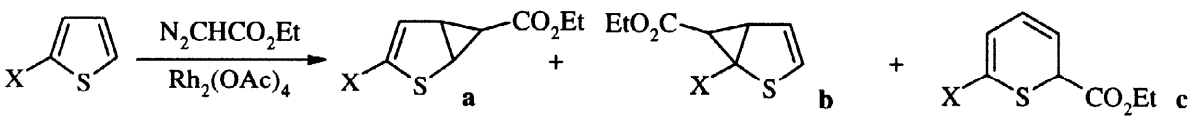
The propensity for cyclopropanated furans to undergo a net [4+2]-cycloreversion (*c.f.* cyclopropanated thiophenes) is likely a result of the greater bond strength of the aldehyde C=O bond generated compared to the thioaldehyde C=S bond. We envisioned, therefore, that the introduction of groups that can stabilize the thioacyl moiety (*i.e.* π- or σ-donors) should help promote the [4+2]-cycloreversion in the thienyl series. With this in mind, we looked at the reactions of various 2-substituted thiophenes with ethyl diazoacetate in the presence of rhodium(II) acetate.

The reactions were carried out by adding ethyl diazoacetate dropwise *via* a syringe pump over 16 hours to a solution of the 2-substituted thiophene and $Rh_2(OAc)_4$ in $CH_2Cl_2$. The products were then purified by preparative layer chromatography and characterized fully by NMR and MS. A sample of the crude reaction mixture was subjected to GC analysis and the product identities and distributions determined by comparison to pure samples isolated by PLC. The results obtained using 2-methylthiophene (**1**) and 2-

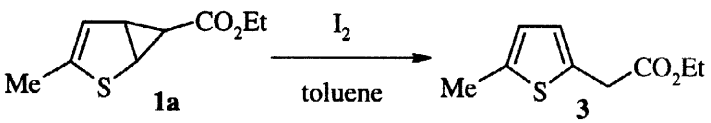
**Scheme 1**




| | | | | | | |
|---|---|---|---|---|---|---|
| **1**: X = $CH_3$ | total yield = 53% | 4 | : | 1 | : | 2 |
| **2**: X = TMS | total yield = 49% | 6 | : | not detected | : | 1 |

(trimethylsilyl)thiophene (**2**) are summarized in Scheme 1. In these two cases, the prevalent product is the 4,5-cyclopropane (**a**). If products **a** and **b** are the result of direct cyclopropanation by a rhodium carbenoid (*vide infra*) then this would seem to indicate that steric factors play a larger role in determining the site of cyclopropanation than electronic ones. All the cyclopropanes isolated were found to have *exo* stereochemistry exclusively. The thiopyran products (**c**) are likely the result of ylide formation followed by Stevens rearrangement[9] although other routes to these products are possible (*vide infra*). It is interesting to note that no ylide product was isolated. The thermal stabilities of the cyclopropanes were studied by heating samples of **1a** and **2a** in toluene-d[8] in sealed NMR tubes to 150°C. In both cases, the cyclopropanes remained intact. Attempts to convert **1a** to a polyene product using Wenkert's method involving iodine[3] (Scheme 2) resulted in the exclusive production of ethyl 2-(5-methyl-2-thienyl)acetate **3**.

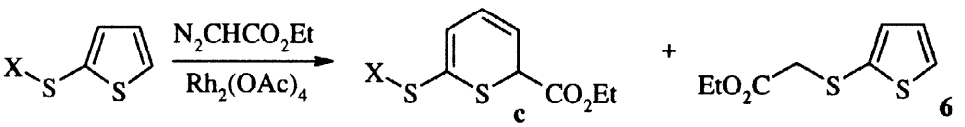
**Scheme 2**




The reactions involving thiophene-2-thiol (**4**) and 2-(methylthio)thiophene (**5**) were also carried out and the product distribution is summarized in Scheme 3. In these cases, carbenoid insertion into a CS bond can occur at either of two sites. Insertion at the aromatic sulfur results in an ylide which undergoes a Stevens rearrangement to give a thiopyran of the type **c**. However, insertion followed by hydrolysis of the ylide

formed at the exocyclic sulfur results in the formation of ethyl 2-(2-thienylsulfanyl)acetate **6**. Alternatively, the production of **6** in the case of thiophene-2-thiol (**4**) may also be the result of simple S-H insertion.

**Scheme 3**

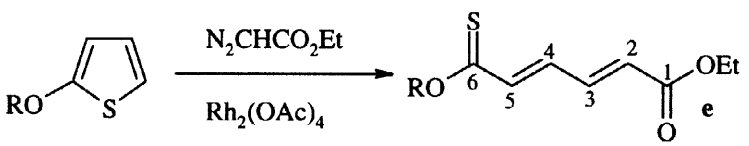



| | | | | |
|---|---|---|---|---|
| **4**: X = H | total yield = 31% | not detected | : | exclusively |
| **5**: X = $CH_3$ | total yield = 43% | 65 | : | 35 |

In order to examine the effect of an α-amino substituent on the insertion chemistry, 2-pyrrolidinothiophene was prepared following the protocol developed by Hartmann and Scheithauer[10] and treated with ethyl diazoacetate in the presence of $Rh_2(OAc)_4$. Unfortunately, chromatography revealed that no insertion chemistry had taken place after 48 hours.

The reaction of 2-methoxythiophene (**7**) with ethyl diazoacetate in the presence of $Rh_2(OAc)_4$, however, allowed for the production of ethyl 6-methoxy-6-thioxo-2,4-hexadienoate (**7e**) in 62% yield marking the first

**Scheme 4**



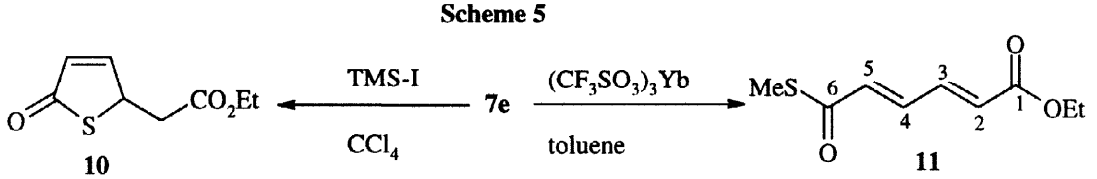

**7**: R = Me
**8**: R = Et
**9**: R = t-Bu

**7e**: R = Me (62%)
**8e**: R = Et (59%)
**9e**: R = t-Bu (58%)

example of a polyene product in the thienyl series. The compound exhibited the expected $^{13}$C-NMR, MS and HRMS. The $^1$H-NMR spectrum of the compound was somewhat more complicated than expected owing to second-order effects. Ultimately, the NMR assignments were secured by a combination of COSY and HETCOR experiments and the coupling pattern was simulated.[11] The vicinal coupling constants revealed that the geometry about each of the two double bonds was *trans*. Vibrational spectroscopy clearly indicated the presence of the C=S in **7e** with the expected bands seen in the IR (1229 $cm^{-1}$)[12] and Raman (1223 $cm^{-1}$)[13] spectra.

Further chemical manipulation of compound **7e** provided additional evidence for its formation and structure. Treatment of **7e** with an equivalent of trimethylsilyl iodide in carbon tetrachloride[14] allowed for

**Scheme 5**



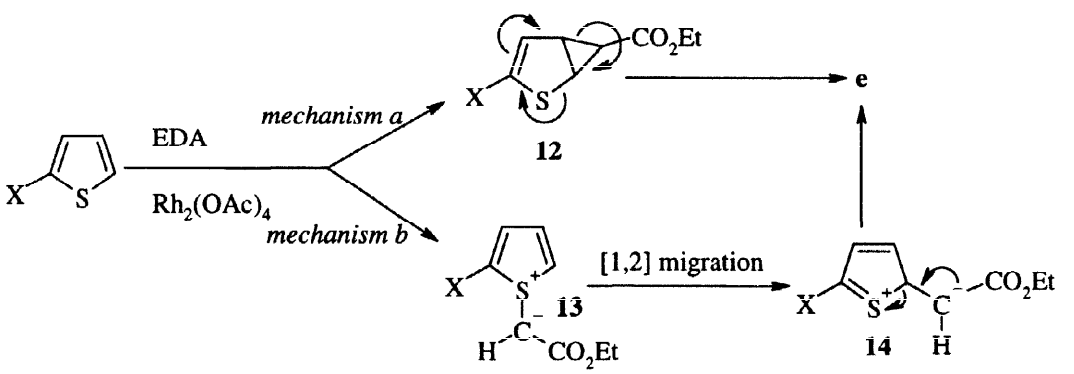

**10** **11**

cleavage of the thioester followed by intramolecular Michael addition to give the thiolactone **10** in 82% yield. Additionally, exposure of **7e** to ytterbium (III) triflate resulted in a Lewis acid catalyzed rearrangement of the thione ester to the thermodynamically more stable thiol ester **11** (in 72% yield).

Other α-alkoxy thiophenes were also shown to undergo this unraveling chemistry. 2-Ethoxythiophene (**8**) was converted to ethyl 6-ethoxy-6-thioxo-2,4-hexadienoate (**8e**) using the protocol described above (in 59% yield) while 2-*tert*-butoxythiophene (**9**) was transformed to ethyl 6-(*tert*-butoxy)-6-thioxo-2,4-hexadienoate (**9e**) (in 58% yield). The compounds were fully characterized by NMR and MS. It is interesting to point out that while the $^1$H-NMR spectrum for **8e** was similar to that of **7e** in that it exhibited second-order characteristics, the spectrum of **9e** was entirely first-order. Once again, an inspection of the vicinal coupling constants revealed that the geometry about the two double bonds was *trans* in both cases. This is somewhat surprising since one would expect *cis* geometry about C4=C5 based on the geometric constraints required for the initial unraveling of the thienyl moiety. The isomerization about these double bonds is likely a result of the highly polarized C=S ↔ C$^+$–S$^-$. Delocalization of the positive charge across the polyene system allows for a reduction in the bond order about C4=C5 double bond thereby facilitating isomerization to the more thermodynamically stable *trans* isomer.

Two mechanisms allow for a rationalization of polyene (**e**) production: one in which an initially formed cyclopropane (**12**) undergoes a [4+2]-cycloreversion (Scheme 6, *mechanism a*) in either a concerted (as shown)

**Scheme 6**




or step-wise fashion;[15] or *via* a mechanism which involves ylide (**13**) formation followed by [1,2]-migration to **14** and subsequent rearrangement (Scheme 6, *mechanism b*). Intermediates such as **14** have been proposed by Porter and Rzepa in their studies of thiopheniobis(alkoxycarbonyl)methanides although polyene production was not reported.[16] Given the thermal stabilities of the isolated cyclopropanes (**1a** and **2a**) and the inability to convert them to polyene products, *mechanism a* seems less likely. It may be argued, however, that the $CH_3$ and TMS substituents do not confer sufficient thermodynamic stability to an emerging C=S group. *Mechanism b*, on the other hand, has the advantage in that the intermediate (**14**) can collapse to give not only the polyene product (**e**) but also cyclopropanes (**a**) and thiopyrans (**c**) with the specific rearrangement of **14** depending on

the relative thermodynamic stabilities of the products. It is impossible, however, to determine without further study whether products **a** and **c** are the result of direct cyclopropanation or Stevens rearrangement or a consequence of *mechanism b*. Finally, the possibility exists that ***mechanism a*** might lead into *mechanism b* since cyclopropane **12** could fragment to a dipolar intermediate like **14**. Mechanistic and modeling studies are continuing.

We are currently looking at the effect of different diazocarbonyl compounds on the chemistry shown and the applicability of the polyenes (**e**) as substrates for Michael addition chemistry.

## Experimental.

Starting materials were purchased from Aldrich Chemical Co. or Lancaster and used without further purification. 2-*tert*-butoxythiophene[17] and 2-ethoxythiophene[18] were prepared by the protocols cited. Ethyl diazoacetate was prepared using the procedure described by Rabjohn.[19] $^1$H- and $^{13}$C-NMR spectra were recorded on a Bruker Avance DPX-300 Digital FT spectrometer (at 300.13 MHz) with chloroform-d as the solvent and internal reference unless otherwise noted. Low resolution mass spectra (MS) and high resolution mass spectra (HRMS) were obtained on Concept 1S double focusing mass spectrometer interfaced to a Kratos DART acquisition system and a SUN Spectrostation 10 workstation using XMACH3 software. Ions were generated using electron impact (EI). IR spectra were obtained on a ATI Mattson Research FTIR Spectrometer using ATI Mattson WinFIRST software. Raman spectra were obtained on a Jobin Yvon/ISA Mole S-3000 spectrometer using a Spectra Physics Stabilite 2016 argon ion laser. Gas chromatography was performed on a HP 5890A gas chromatograph which used a flame-ionization detector and HP ChemStation software.

## General Synthetic Procedure.

To a solution of substituted thiophene (4.00 mmol) and rhodium(II) acetate (approximately 2 mg) in dichloromethane (10 mL) was added ethyl diazoacetate (0.1305 g, 1.14 mmol) in dichloromethane (10 mL) via a syringe pump at a rate of 0.5 mL/hr. After 16 hours, a small sample of the reaction mixture (100 μL) was taken and analyzed by GC. The solvent from the remainder of the reaction mixture was evaporated under a reduced pressure and the residue purified using preparative layer chromatography.[20]

## Ethyl *exo*-3-methyl-2-thiabicyclo[3.1.0]hex-3-ene-6-carboxylate (1a).

The compound showed: $R_f$=0.16 (33% dichloromethane in hexane); $^1$H NMR ($CDCl_3$, 300 MHz); δ 1.24 (3H triplet + 1H singlet, $CH_2CH_3$ + $CHCO$), 1.91 (s, 3H, $CH_3C$), 2.91 (m, 1H, *J=3, 4, 8* Hz, SCHCH), 3.41 (dd, 1H, *J=3, 8* Hz, SCHCH), 4.10 (q, 2H, $CH_2CH_3$), 5.49 (d, 1H, *J=4* Hz, S-C($CH_3$)CH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ 14.22 ($CH_2CH_3$), 15.52 ($CH_3C$), 25.55 (SCHCH), 34.91 (SCHCH), 39.32 (CHCO), 60.67 ($CH_2CH_3$), 118.41 (S-C($CH_3$)CH), 140.69 (S-C($CH_3$)), 173.76 (C=O); MS [EI+] m/z (RI%); 184 $[M]^+$ (8), 155 $[M-CH_2CH_3]^+$ (6), 111 $[M-CO_2CH_2CH_3]^+$ (100); HRMS for $C_9H_{12}O_2S$: calculated 184.0558; observed 184.0559.

**Ethyl *exo*-1-methyl-2-thiabicyclo[3.1.0]hex-3-ene-6-carboxylate (1b).**

The compound showed: $R_f$=0.14 (33% dichloromethane in **hexane**); $^1$H NMR ($CDCl_3$, 300 MHz); δ 1.25 (t, 3H, $CH_2CH_3$), 1.40 (d, 1H, *J=4* Hz, CHCO), 1.74 (s, 3H, $CH_3C$), 2.83 (t, 1H, *J=4* Hz, S-C($CH_3$)CH), 4.16 (q, 2H, $CH_2CH_3$), 5.83 (dd, 1H, *J=6, 4* Hz, SCHCH), 6.13 (d, 1H, *J=6* Hz, SCHCH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ 14.32 ($CH_2CH_3$), 16.36 ($CH_3C$), 30.46 (S-C($CH_3$)CH), 42.63 (CHCO), 44.23 (S-C($CH_3$)), 60.73 ($CH_2CH_3$), 123.64 (SCHCH), 127.13 (SCHCH), 173.07 (C=O); MS [EI+] m/z (RI%); 184 $[M]^+$ (22), 155 $[M-CH_2CH_3]^+$ (7), 111 $[M-CO_2CH_2CH_3]^+$ (100); HRMS for $C_9H_{12}O_2S$: calculated 184.0558; observed 184.0552.

**Ethyl 6-methyl-2*H*-2-thiopyrancarboxylate (1c).**

The compound showed: $R_f$ = 0.12 (33% dichloromethane in hexane); $^1$H NMR ($CDCl_3$, 300 MHz); δ 1.27 (t, 3H, $CH_2CH_3$), 2.00 (s, 3H, $CH_3C$), 4.16 (m, 3H, $CH_2CH_3$ + CHCO), 5.52 (dd, 1H, *J=6, 10* Hz , SCHCH), 5.93 (d, 1H, *J=6* Hz, S-C($CH_3$)CH), 6.11 (dd, 1H, *J=6, 10* Hz, SCHCHCH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ 14.09 ($CH_2CH_3$), 22.66 ($CH_3C$), 41.36 (CHCO), 60.77 ($CH_2CH_3$), 111.68 (SCHCH), 117.34 (SCHCHCH), 127.27 (S-C($CH_3$)CH), 131.84 ($CH_3C$), 170.35 (C=O); MS [EI+] m/z (RI%); 184 $[M]^+$ (12), 155 $[M-CH_2CH_3]^+$ (9), 111 $[M-CO_2CH_2CH_3]^+$ (100), 112 (9); HRMS for $C_9H_{12}O_2S$: calculated 184.0558; observed 184.0546.

**Ethyl *exo*-3-(trimethylsilyl)-2-thiabicyclo[3.1.0]hex-3-ene-6-carboxylate (2a).**

The compound showed: $R_f$=0.45 (10% diethyl ether in hexane); $^1$H NMR ($CDCl_3$, 300 MHz); δ 0.15 (s, 9H, $(CH_3)_3Si$), 1.02 (t, 1H, *J=3*, CHCO), 1.26 (t, 3H, $CH_2CH_3$), 3.10 (m, 1H, *J=3, 3, 7* Hz, SCHCH), 3.54 (dd, 1H, *J=3, 7* Hz, SCHCH), 4.19 (q, 2H, $CH_2CH_3$), 5.97 (d, 1H, *J=3* Hz, S-C(TMS)CH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ -1.23 ($(CH_3)_3Si$), 14.28 ($CH_2CH_3$), 24.59 (SCHCH), 36.15 (SCHCH), 42.78 (CHCO), 60.81 ($CH_2CH_3$), 130.32 (S-C(TMS)CH), 144.26 (C-$(CH_3)_3Si$), 174.14 (C=O); MS [EI+] m/z (RI%); 242 $[M]^+$ (4), 227 $[M-CH_3]^+$ (4), 169 $[M-CO_2CH_2CH_3]^+$ (100), 170 (15); HRMS for $C_{11}H_{18}O_2SSi$: calculated 242.0797; observed 242.0797.

**Ethyl 6-(trimethylsilyl)-2*H*-2-thiopyrancarboxylate (2c).**

The compound showed: $R_f$=0.42 (10% diethyl ether in hexane); $^1$H NMR ($CDCl_3$, 300 MHz); δ 0.29 (s, 9H, $(CH_3)_3Si$), 1.28 (t, 3H, $CH_2CH_3$), 4.08 (d, 1H, *J=6* Hz, CHCO), 4.18 (q, 2H, $CH_2CH_3$), 5.65 (dd, 1H, *J=6, 10* Hz, SCHCH), 6.16 (dd, 1H, *J=6, 10* Hz, SCHCHCH), 6.34 (d, 1H, *J=6* Hz, S-C(TMS)CH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ -0.08 ($(CH_3)_3Si$), 14.19 ($CH_2CH_3$), 38.79 (CHCO), 61.68 ($CH_2CH_3$), 114.24 (SCHCHCH), 126.70 (SCHCH), 128.11 (S-C(TMS)CH), 135.48 (C-$(CH_3)_3Si$), 171.24 (C=O); MS [EI+] m/z (RI%); 242 $[M]^+$

(28), 227 [M-$CH_3$]$^+$ (88), 169 [M-$CO_2CH_2CH_3$]$^+$ (100), 170 (16); HRMS for $C_{11}H_{18}O_2SSi$: calculated 242.0797; observed 242.0803.

**Ethyl 2-(5-methyl-2-thienyl)acetate (3).**

Ethyl *exo*-3-methyl-2-thiabicyclo[3.1.0]hex-3-ene-6-carboxylate (**1a**) (35 mg, 0.188 mmol) was dissolved in toluene (1 mL) and treated with iodine (5 mg). The mixture was allowed to stir for 18 hours at which time the solvent was evaporated under a reduced pressure and the residue chromatographed on a preparative layer silica gel plate using 33% hexanes in dichloromethane as the eluent. Ethyl 2-(5-methyl-2-thienyl)acetate (3) was obtained as an oil in 69% yield (24 mg, 0.130 mmol). The compound showed: $R_f$=0.16 (33% dichloromethane in hexanes); $^1$H NMR ($CDCl_3$, 300 MHz); δ 1.27 (t, 3H, $CH_2CH_3$), 2.44 (s, 3H, C-$CH_3$), 3.74 (s, 1H, $CH_2CO$), 4.17 (q, 2H, $CH_2CH_3$), 6.59 (d, 1H, *J=3* Hz, S-C($CH_3$)-CH-CH), 6.70 (d, 1H, *J=3* Hz, S-C($CH_3$)-CH-CH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ 14.19 ($CH_2CH_3$), 15.26 (C-$CH_3$), 35.72 ($CH_2CO$), 61.12 ($CH_2CH_3$), 124.76 (S-C($CH_3$)-CH-CH), 126.56 (S-C($CH_3$)-CH-CH), 132.78 (C-$CH_2$), 139.49 (C-$CH_3$), 170.69 (C=O); MS [EI+] m/z (RI%); 184 [M]$^+$ (24), 111 [M-$CO_2CH_2CH_3$]$^+$ (100), 112 (8); HRMS for $C_9H_{12}O_2S$: calculated 184.0558; observed 184.0565.

**Ethyl 6-(methylsulfanyl)-2*H*-2-thiopyran carboxylate (5c).**

The compound showed: $R_f$=0.58 (25% diethyl ether in hexane); $^1$H NMR ($CDCl_3$, 300 MHz); δ 1.29 (t, 3H, $CH_2CH_3$), 2.42 (s, 3H, $SCH_3$), 4.24 (q, 2H, $CH_2CH_3$), 4.20 (d, *J=6* Hz, CHCO), 5.63 (dd, 1H, *J=6, 3* Hz, SCHCH), 6.14 (dd, 1H, *J=6, 3* Hz, SCHCHCH), 6.24 (d, 1H, *J=6* Hz, S-C(SMe)CH); $^{13}$C NMR ($CDCl_3$, 75 MHz); δ 14.05 ($CH_2CH_3$), 18.70 ($SCH_3$), 42.95 (CHCO), 61.93 ($CH_2CH_3$), 113.51 (SCHCHCH), 119.33 (SCHCH), 127.23 (S-C(SMe)CH), 137.03 (C-(SMe)), 165.09 (C=O); MS [EI+] m/z (RI%); 216 [M]$^+$ (13), 143 [M-$CO_2CH_2CH_3$]$^+$ (100), 45 [$OCH_2CH_3$]$^+$ (43), 71 [SCHCHCH]$^+$ (29); HRMS for $C_9H_{12}O_2S_2$: calculated 216.0279; observed 216.0281.

**Ethyl 2-(2-thienylsulfanyl)acetate (6).**

The compound showed: $R_f$=0.55 (25% diethyl ether in hexane); $^1$H NMR ($CDCl_3$, 300 MHz); δ 1.24 (t, 3H, $CH_2CH_3$), 3.48 (s, 2H, $SCH_2CO_2Et$), 4.16 (q, 2H, $CH_2CH_3$), 6.98 (dd, 1H, *J=3, 5* Hz, SCHCH), 7.17 (d, 1H, *J=3* Hz, SCHCH), 7.38 (d, 1H, *J=5* Hz, (S-C(SR)CH) $^{13}$C NMR ($CDCl_3$, 75 MHz); δ 14.05 ($CH_2CH_3$), 40.93 ($SCH_2CO_2Et$), 61.46 ($CO_2CH_2CH_3$), 127.55 (S-C(SR)CH), 127.67 (S-C(SR)CH), 130.46 (SCHCH), 135.04 (SCHCH), 169.30 (C=O); MS [EI+] m/z (RI%); 202 [M]$^+$ (89), 129 [M-$CO_2CH_2CH_3$]$^+$ (100), 45 [$OCH_2CH_3$]$^+$ (91), 71 [SCHCHCH]$^+$ (55); HRMS for $C_8H_{10}O_2S_2$: calculated 202.0122; observed 202.0122.

**Ethyl (2*E*, 4*E*)-6-methoxy-6-thioxo-2,4-hexadienoate (7e).**

The compound showed: $R_f$=0.38 (66% dichloromethane in hexane); $^1$H-NMR ($CDCl_3$; 300 MHz; see Scheme 4 for numbering) δ 1.27 (t, 3H, $CH_2CH_3$), 4.13 (s, 3H, $OCH_3$); 4.21 (q, 2H, $CH_2CH_3$), 6.21 (m, 1H, *J(H2,H3)=15.20* Hz, H2), 6.67 (m, 1H, *J(H4,H5)=14.16* Hz, H5) 7.25 (m, 1H, *J(H2,H3)=15.20* and *J(H3,H4)=11.10* Hz, H3), 7.26 (dd, 1H, *J(H3,H4)=11.10* and *J(H4,H5)=14.16* Hz, H4); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 14.10 ($CO_2CH_2CH_3$), 58.71 ($OCH_3$), 60.70 ($CO_2CH_2CH_3$), 128.56 (C2), 136.56 (C5), 137.44 (C3), 141.80 (C4), 165.83 (*C*=O), 209.38 (*C*=S); MS [EI] m/z (RI%); 200 $[M]^+$ (18), 171 $[M\text{-}CH_2CH_3]^+$ (8), 127 $[M\text{-}CO_2CH_2CH_3]^+$ (100), 128 (8); HRMS for $C_9H_{12}O_3S$: calculated 200.0507; observed 200.0515.

**Ethyl (2*E*, 4*E*)-6-ethoxy-6-thioxo-2,4-hexadienoate (8e).**

The compound showed: $R_f$=0.50 (10% ethyl acetate in hexane); $^1$H-NMR ($CDCl_3$; 300 MHz; see Scheme 4 for numbering) δ 1.30 (t, 3H, $CO_2CH_2CH_3$), 1.44 (t, 3H, $CSOCH_2CH_3$), 4.22 (q, 2H, $CO_2CH_2CH_3$), 4.57 (q, 2H, $CSOCH_2CH_3$), 6.25 (m, 1H, *J(H2,H3)=14.96* Hz, H2), 6.69 (m, 1H, *J(H4,H5)=14.52* Hz, H5), 7.30 (m, 1H, *J(H2,H3)=14.96* and *J(H3,H4)=11.05* Hz, H3), 7.34 (m, 1H, *J(H3,H4)=11.05* and *J(H4,H5)=14.52* Hz, H4); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 13.68 ($CO_2CH_2CH_3$), 14.20 ($CSOCH_2CH_3$), 60.78 ($CO_2CH_2CH_3$), 68.14 ($CSOCH_2CH_3$), 128.54 (C2), 136.29 (C5), 138.00 (C3), 141.49 (C4), 165.98 (*C*=O), 208.92 (*C*=S); MS [EI] m/z (RI%); 214 $[M]^+$ (34), 185 $[M\text{-}CH_2CH_3]^+$ (5), 141 $[M\text{-}CO_2CH_2CH_3]^+$ (100), 125 [M-$CSOCH_2CH_3$] (33); HRMS for $C_{10}H_{14}O_3S$: calculated 214.0664; observed 214.0666.

**Ethyl (2*E*, 4*E*)-6-(*tert*-butoxy)-6-thioxo-2,4-hexadienoate (9e).**

The compound showed: $R_f$=0.61 (20% ethyl acetate in hexane); $^1$H-NMR ($CDCl_3$; 300 MHz; see Scheme 4 for numbering) δ 1.30 (t, 3H, $CH_2CH_3$), 1.62 (s, 9H, $C(CH_3)_3$); 4.20 (q, 2H, $CH_2CH_3$), 6.21 (d, 1H, *J(H2,H3)=15.16* Hz, H2), 6.53 (d, 1H, *J(H4,H5)=14.72* Hz, H5), 7.08 (dd, 1H, *J(H2,H3)=15.16* and *J(H3,H4)=11.65* Hz, H3), 7.26 (dd, 1H, *J(H3,H4)=11.65* and *J(H4,H5)=14.72* Hz, H4); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 14.20 ($CO_2CH_2CH_3$), 28.081 ($C(CH_3)_3$), 60.65 ($CO_2CH_2CH_3$), 87.39 ($C(CH_3)_3$), 127.94 (C2), 134.20 (C5), 140.96 (C3), 141.87 (C4), 166.03 (*C*=O), 207.24 (*C*=S); MS [EI] m/z (RI%); 242 $[M]^+$ (12), 153 [M-$C(CH_3)_3S]^+$ (33), 169 $[M\text{-}CO_2CH_2CH_3]^+$ (5), 57 $[C(CH_3)_3]^+$ (100); HRMS for $C_{12}H_{18}O_3S$: calculated 242.0977; observed 242.0978.

**Ethyl 2-(5-oxo-2,5-dihydro-2-thiophenyl)acetate (10).**

Ethyl (2*E*, 4*E*)-6-methoxy-6-thioxo-2,4-hexadienoate (139 mg, 0.69 mmol) was dissolved in $CCl_4$ (2 mL) and placed under an argon atmosphere. Iodotrimethylsilane (0.096 mL, 135 mg, 0.675 mmol) was introduced and the reaction mixture heated in a water bath at 45°C for 22 hours. Distilled water (1.5 mL) was added and the mixture stirred vigorously for 45 minutes. The two fractions were then separated and the

aqueous layer was extracted with $CCl_4$ (2 x 1 mL) and the combined organic layers were then concentrated and purified via PLC. The reaction yielded ethyl 2-(5-oxo-2,5-dihydro-2-thiophenyl)acetate **10** (103 mg ,0.554 mmol, 82% yield) as a clear, pale-yellow oil. The compound showed: $R_f$=0.39 (50% dichloromethane in hexane); $^1$H-NMR ($CDCl_3$; 300 MHz) δ 1.25 (t, 3H, $CH_2CH_3$), 2.73 (dd, 1H, *J=9, 8* Hz, SCHCH*H*$CO_2$Et), 2.88 (dd, 1H, *J=10, 7* Hz, SCHC*H*HCO$_2$Et), 4.17 (q, 2H, $CH_2CH_3$), 4.78 (m, 1H, SC*H*CHHCO$_2$Et), 6.29 (dd, 1H, *J=2, 4* Hz, OSCCH=C*H*CHR), 7.46 (dd, 1H, *J=3, 3* Hz, OSCC*H*=CHCHR); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 14.12 ($CO_2CH_2CH_3$), 38.80 (SCH*C*H$_2$CO$_2$Et), 49.25 (S*C*HCH$_2$CO$_2$Et), 61.36 ($CO_2CH_2CH_3$), 133.10 (OSC*C*H=CHCHR), 156.82 (OSCCH=*C*HCHR), 170.08 (*C*=O), 199.01 (O=*C*S); MS [EI] m/z (RI%); 186 $[M]^+$ (49), 158 (10), 140 (21), 112 (100); HRMS for $C_8H_{10}O_3S$: calculated 186.0351; observed 186.0353.

**Ethyl (2*E*, 4*E*)-6-(methylsulfanyl)-6-oxo-2,4-hexadienoate (11).**

Ethyl (2*E*, 4*E*)-6-methoxy-6-thioxo-2,4-hexadienoate (365 mg, 0.182 mmol) in toluene (7 mL) was treated with $Yb(CF_3SO_3)_3$ (95.4 mg, 0.154 mmol). The reaction mixture was stirred vigorously for 30 minutes and then refluxed for 4 hours, at which time the reflux was stopped and the vessel was allowed to stir overnight. The reaction mixture was concentrated under a reduced pressure and the residue purified by PLC. Ethyl (2*E*, 4*E*)-6-(methylsulfanyl)-6-oxo-2,4-hexadienoate (11) was isolated as a clear yellow oil in 72% yield (26.2 mg, 0.131 mmol). The compound showed: $R_f$=0.37 (66% dichloromethane in hexane); $^1$H-NMR ($CDCl_3$; 300 MHz; see Scheme 5 for numbering) δ 1.35 (t, 3H, $CH_2CH_3$), 2.43 (s, 3H, $SCH_3$); 4.25 (q, 2H, $CH_2CH_3$), 6.25 (m, 1H, *J(H2,H3)=15.70* Hz, H2), 6.46 (m, 1H, *J(H4,H5)=14.16* Hz, H5), 7.26 (m, 1H, *J(H2,H3)=15.70* and *J(H3,H4)=11.80* Hz, H3), 7.30 (m, 1H, *J(H3,H4)=11.80* and *J(H4,H5)=14.16* Hz, H4); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 11.68 (S*C*H$_3$), 14.19 ($CO_2CH_2CH_3$), 60.87 ($CO_2CH_2CH_3$), 129.48 (C2), 134.06 (C5), 136.28 (C3), 140.62 (C4), 165.75 (*C*=O), 189.69 (O=*C*SCH$_3$); MS [EI] m/z (RI%); 200 $[M]^+$ (8), 153 $[M\text{-}SCH_3]^+$ (100), 127 $[M\text{-}CO_2CH_2CH_3]^+$ (16), 125 $[M\text{-}COSCH_3]^+$ (10); HRMS for $C_9H_{12}O_3S$: calculated 200.0507; observed 200.0512.

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