*Acta Chemica Scandinavica, 1993: 47: 1214–1220*
*Printed in Belgium – all rights reserved*


ACTA
CHEMICA SCANDINAVICA
*ISSN 0904-213X*

# Potentially Aromatic Thiophenium Ylides. V.[1] Reactions of Ethoxycarbonyl- (and Methoxycarbonyl)-2-(2-thienyl)phenylcarbene

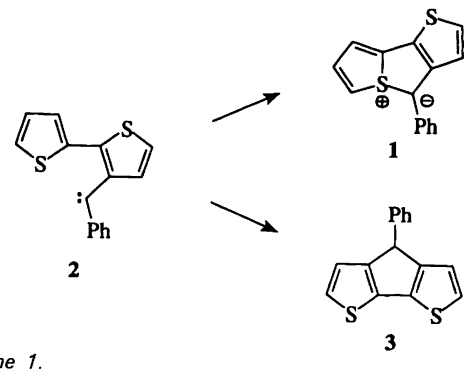
Magne Solbakken and Jan Skramstad

Department of Chemistry, University of Oslo, P.O. Box 1033 Blindern, N-0315 Oslo, Norway

Solbakken, M. and Skramstad, J., 1993. Potentially Aromatic Thiophenium Ylides. V. Reactions of Ethoxycarbonyl- (and Methoxycarbonyl)-2-(2-thienyl)phenylcarbene. – Acta Chem. Scand. 47: 1214–1220. © Acta Chemica Scandinavica 1993.

In an attempt to make thiophenium ylides in which the ylide bond is part of a five-membered ring annulated to the *a*-side of the thiophene moiety, two alkoxycarbonyl substituted 2-(2-thienyl)phenylcarbenes have been made, with and without chlorine substituents in the remaining thiophene positions. With rhodium acetate as a catalyst the carbene without chlorines cyclized to the 3-position of the thiophene to give a fluorene analogue, whereas no cyclization was detected when the 3-position was blocked.

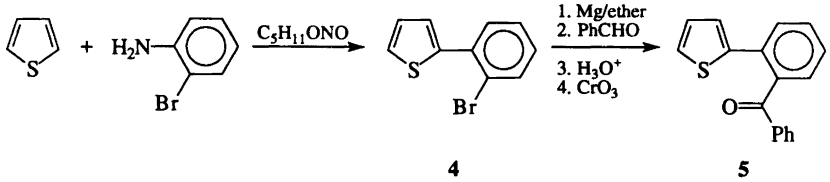
Some years ago we reported unsuccessful attempts to generate the unknown thieno[1,2-*a*]thiophene **1** by cyclization of the carbene **2** onto sulfur.[2] Instead the fluorene analogue **3** was formed (Scheme 1). As an extension of this work we wanted to investigate the effect of electron attracting groups in the phenyl substituent and here we report our results.




*Scheme 1.*

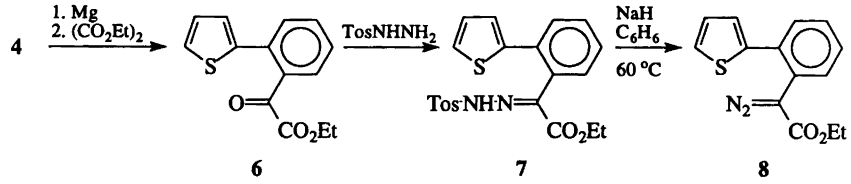
To facilitate synthesis of the biaryl moiety the disubstituted thiophene ring was replaced by a benzene ring, thus a key intermediate in the synthesis was the ketone **5** (Scheme 2). The bromide **4** was prepared in 68 % yield in a dry Gomberg reaction from 2-bromoaniline and thiophene using 3-methylbutyl nitrite.[3] The Grignard reagent of **4** was reacted with benzaldehyde to give the alcohol which, in turn, was oxidized to the corresponding ketone **5**. However, attempts to convert **5** into the tosylhydrazone (carbene precursor) failed, in contrast with the bithienyl case where this reaction worked well.[2] These ketones are rather sterically hindered, and small changes in bond lengths and valence angles may have a profound effect on their reactivity. Since this strategy was unsuccessful in the unsubstituted case no attemps were made to modify the system with electron-attracting substituents in the phenyl ring.

The outcome of the cyclization reaction in Scheme 1 may be ascribed to the formation of the triplet state of the carbene,[4] instead of the singlet state assumed to be required.[5] In order to obtain the right multiplicity of the carbene we decided to introduce an ester group at the carbene carbon.[5,6] An ester group in this position should also provide enhanced stability to the expected ylide structure. For synthetic reasons the disubstituted thiophene ring in **2** was replaced by a benzene ring. Hence, we wanted to synthesize the diazo ester **8** as a carbene precursor in cyclization reactions. Our plan is outlined in Scheme 3.




4 5

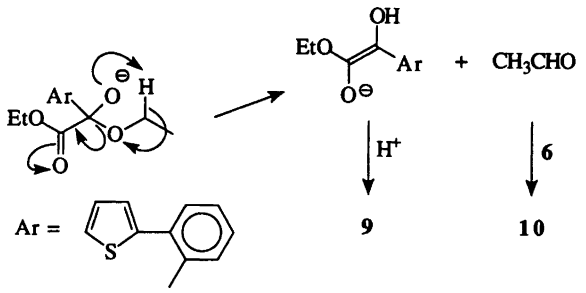
*Scheme 2.*




*Scheme 3.*

The Grignard reagent of **4** was added to an excess of diethyl oxalate at low temperature. In addition to the desired keto ester **6**, obtained in only 15% yield, 2-phenylthiophene (22%), the hydroxy ester **9** (21%) and the aldol product **10** (3%) were also isolated.

The reason for the disappointingly low yield of **6** is probably that the Grignard reagent is rather sterically hindered.[7] The α-hydroxy ester **9** is probably produced by elimination of acetaldehyde from the initially formed adduct between the Grignard reagent and diethyl oxalate. Although acetaldehyde was not actually detected, the formation of aldol **10** is evidence of its formation (Scheme 4). The considerable amount of 2-phenylthiophene isolated from the reaction also reflects the low reactivity of the system.




*Scheme 4.*

The keto ester **6** was converted into the corresponding tosyl hydrazone **7** by reaction with tosylhydrazine in methanol. The key intermediate **8** was then obtained by reaction with sodium hydride followed by careful thermal cleavage in dry benzene, thus preventing further decomposition to the carbene.

*Carbene reactions.* The diazo ester **8** was decomposed to the corresponding carbene (or carbenoid) under thermal, photochemical and catalytic conditions and in a variety of solvents. In all cases substantial amounts of polymeric material were formed. The best result was obtained with rhodium acetate as the catalyst in dry benzene, when

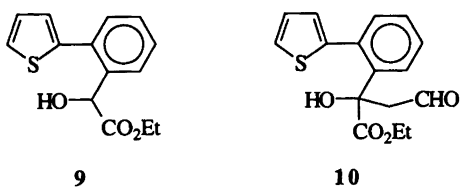



*Fig. 1.*

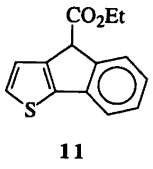
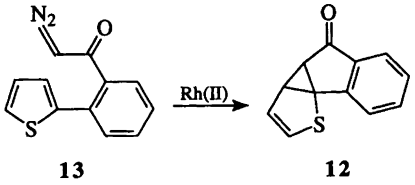



*Fig. 2.*

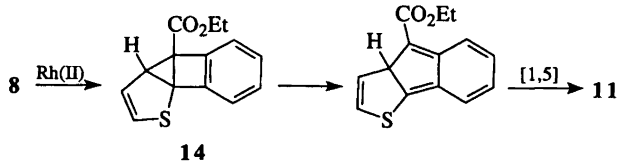
the fluorene analogue ethyl indeno[1,2-*b*]thiophene-4-carboxylate (**11**) was isolated in 53% yield.

Several explanations are possible for the formation of **11**. Formally, this is a C–H insertion product and a direct insertion cannot be completely ruled out. This is, however, less likely since rhodium-catalysed decomposition of diazo esters normally give cyclopropanation and not C–H insertion both with benzene and with thiophene.[8,9] In addition, the very strained cyclopropane **12** has been isolated by rhodium-catalysed decomposition of the diazo ketone **13** (Scheme 5).[3]



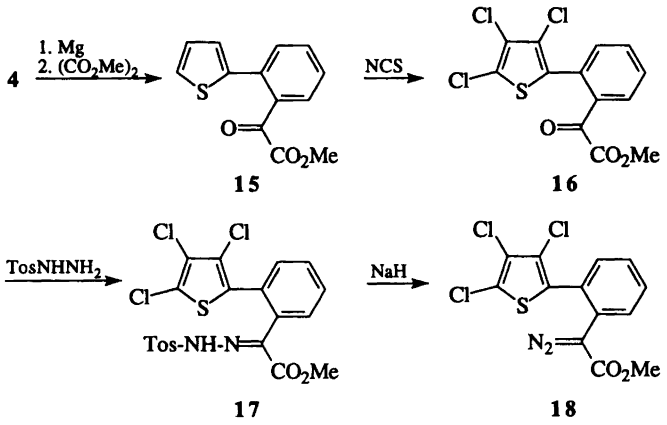

*Scheme 5.*

In accordance with this we suggest that **11** is formed by a ring-opening of the initially formed, highly strained, cyclopropane **14** (cf. the thermally forbidden disrotatory ring opening of bicyclo[2.1.0]pent-2-ene to cyclopentadiene[10]). The subsequent rearomatization by a [1.5]-hydrogen shift to give **11** should be a very fast process (Scheme 6).




*Scheme 6.*

*Blocking the reactive positions with chlorines.* The above results indicated that introducing a substituent in the 3-position of the thiophene should have a profound effect on the outcome of the reaction, not only by excluding an insertion reaction, but also by increasing the possibility of cyclization onto the sulfur atom. It is also suggested that



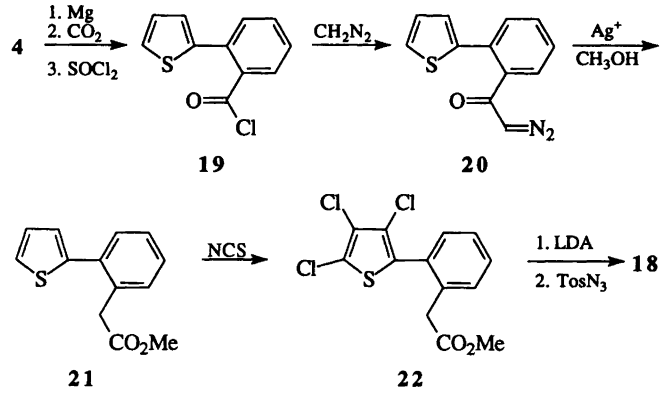
Scheme 7.

chlorines have a stabilizing effect on thiophenium ylides.[10] In a first approach we decided, for synthetic reasons, to replace all the remaining hydrogens in the thiophene ring with chlorines. The key intermediate, the trichlorinated diazo ester **18**, was synthesized by two different methods. In the first approach (Scheme 7) the Grignard reagent of **4** was reacted with dimethyl oxalate to produce the methyl ester **15**. Also in this case a substantial amount of the hydroxy ester was formed. Although the reaction mixture was treated with pyridinium chlorochromate, the maximum yield of the keto ester **15** was only 24%. Trichlorination of the thiophene ring was achieved with *N*-chlorosuccinimide. The keto ester **16** was converted into the tosylhydrazone **17** and subsequently to the diazo ester **18**.

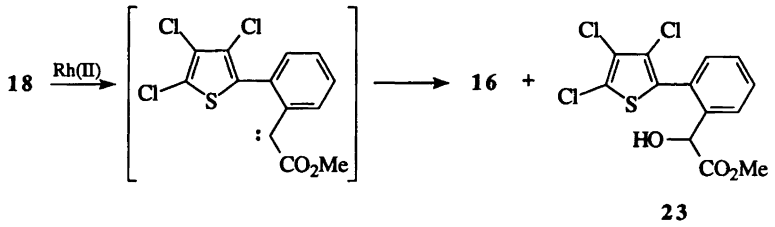
The outcome of the chlorination reactions is worthy of comment. It is not obvious why trichlorination of the thiophene ring of **15** should take place while the phenyl ring remains unsubstituted. However, in the case of 2-(2-methylphenyl)thiophene we had previously obtained a good yield of the product which was fully chlorinated in the thiophene ring, despite the fact that the phenyl ring in that case contained an activating substituent. This chlorination pattern was confirmed by X-ray crystallography.[11] This fact augured well for the outcome of the chlorination of **15**, where the phenyl ring is deactivated. However, while trichlorination of 2-(2-methylphenyl)thiophene was performed in acetic acid at 80°C (10 h), the reaction rate of **15** in acetic acid was considerably lower and only monochlorination was achieved. When the temperature was increased, acetylation took place. Various other solvents were tried, and the best result was obtained with nitrobenzene at 120°C (3 days) where **16** was produced in an isolated yield of 49%.

In the alternative approach (Scheme 8) the bromide **4** was converted into the corresponding acid chloride **19** by conventional functional group chemistry. Further reaction with diazomethane produced the diazo ketone **20**, which, in turn, gave a quantitative yield of the methyl ester **21** by a silver-catalysed Wolff rearrangement. In contrast with **15**, trichlorination of **21** was achieved in acetic acid at 75°C (2 days) to afford **22** in 63% isolated yield. Attempts to activate the ester **22** for a diazo transfer reaction (triethylamine–tosylazide), by introducing a formyl group in the α-position, were unsuccessful. Instead the stronger base lithium diisopropylamide was used directly on the monoactivated ester **22** to produce the diazo ester **18** in 62% yield.

*Decomposition of the diazo ester* **18**. The diazo ester **18** was decomposed using rhodium acetate in benzene solution. Besides polymeric material two products were iden-



Scheme 8.




*Scheme 9.*

tified, the keto ester **16** and the corresponding alcohol **23** (Scheme 9). The formation of these products can be explained by reaction of the carbene with dissolved oxygen and with water, respectively, and care was taken to remove oxygen and water by standard methods. Although formation of the ketone could be completely suppressed, formation of the alcohol could not be prevented even after elaborate drying of the solvent and the reactants.

Porter has shown that ylide formation in chlorinated thiophenes may be reversible; 2,5-dichlorothiophenium bis(methoxycarbonyl)methanide can act as a source of bis(methoxycarbonyl)carbene when treated with rhodium acetate.[12] An explanation in our case may be that the ylide is actually formed but exists in equilibrium with the carbene, and that the alcohol **23** is produced by reaction with water during work-up. We were, however, unable to trap the ylide or the carbene by reaction with activated aldehydes or olefins.

## Conclusions

The reactions described above did not lead to stable cyclopenta[*a*]thiophenes. We have indications, but no proof, that cyclization onto the sulfur atom occurs. Possibly, annulation of a five-membered ring to the *a*-side of the thiophene ring is energetically less likely for steric and/or electronic reasons when the sulfur atom is part of an ylide structure. In the stable thiophenium methanides studied by Porter *et al.*[13] the sulfur atom has a pyramidal geometry, the angle between the ring plane and the ylide bond being ca. 50°. Annulation of a larger ring is therefore interesting. This will be the subject of a forthcoming report.

## Experimental

The $^1$H NMR data were recorded at 60, 200, 300 and 400 MHz on Varian 60 A and Jeol-PMX 60, Bruker CPX-200 and Varian Gemini-200, Varian XL-300 and Bruker WM-400 spectrometers, respectively. The $^{13}$C NMR data were recorded at operating frequencies of 15, 22.5, 50, 75 and 100 MHz on Jeol JNM-FX 60, Jeol FX 90 Q, Bruker CPX-200 and Varian Gemini-200, Varian XL-300 and Bruker WM-400 spectrometers. IR spectra were measured as films, solutions or KBr discs with a Perkin-Elmer 1310 spectrometer. The mass spectra were obtained on a VG Micromass 7070 F and on a Hewlett Packard 5990a GC–MS instrument. The melting points, determined with a Reichert Thermopan melting point microscope, are uncorrected.

*2-(2-Thienyl)benzophenone* (**5**). The reaction was run under nitrogen. The Grignard reagent was prepared in dry THF (20 ml) at 60°C from 2-(2-bromophenyl)-thiophene[3] (**4**) (4.0 g, 17 mmol) and magnesium (0.45 g, 19 mmol). The solution was cooled to 30°C and a solution of benzaldehyde (2.0 g, 19 mmol) in dry THF (10 ml) was added. The reaction mixture was stirred for 30 min and then hydrolysed with aqueous ammonium chloride. The THF was evaporated off and the product was taken up in ether. The ethereal solution was washed with water, dried ($MgSO_4$) and evaporated. The residue was dissolved in acetone (50 ml) and 8 M chromic acid (Jones' reagent) was added dropwise until the red colour persisted. The acetone was evaporated off and the product was taken up in ether. The ethereal solution was washed with water and sodium bicarbonate solution, dried ($MgSO_4$) and evaporated. The product was purified by column chromatography (silica; hexane–ethyl acetate 15:2) followed by crystallization from ethanol–water. Yield 1.5 g (33%), m.p. 61–62°C. $^1$H NMR (60 MHz, $CCl_4$): δ 6.8–7.7 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 264 (100, *M*), 236 (9), 235 (21), 187 (60), 115(45), 105 (59), 77 (58). IR (KBr): 1680 $m^{-3}$.

*Ethyl oxo[2-(2-thienyl)phenyl]acetate* (**6**). The reaction was run under nitrogen. To an ice-cooled solution of diethyl oxalate (8.0 g, 55 mmol) in dry THF (30 ml) was added, with vigorous stirring, a THF solution of the Grignard reagent of 2-(2-bromophenyl)thiophene[3] (**4**) (8.0 g, 34 mmol). The reaction mixture was thereafter stirred at 25°C for 10 min and then hydrolysed with dilute hydrochloric acid. The solvent was evaporated off and the product was taken up in ether. The ether solution was dried ($MgSO_4$) and evaporated. The crude product was distilled through a short Vigreux column to give 2-phenylthiophene (b.p. 116–117°C/8 mmHg, 1.2 g, 7.6 mmol) and a fraction (b.p. 160/0.04 mmHg) containing **6**, **9** and **10** which were separated by column chromatography (silica; hexane–ethyl acetate 4:1). The yield of the oxo ester **6** was 1.3 g (5.0 mmol, 15%). $^1$H NMR (60 MHz, $CCl_4$): δ 1.1 (3 H, t, $CH_3$), 3.8 (2 H, q, $CH_2$), 6.7–7.7 (7 H, m, ArH). $^{13}$C NMR (22.5 MHz, $CDCl_3$): 13.8, 62.2, 127.66, 127.74, 128.1, 129.5, 130.2, 132.6, 135.1, 135.3, 141.1, 162.0, 189.2. MS [IP 70 eV; *m/z*

(% rel. int.)]: 260 (5, *M*), 187 (100), 159 (9), 158 (6), 115 (44). IR (film): 1740, 1700 $cm^{-1}$.

Ethyl hydroxy[2-(2-thienyl)phenyl]acetate (**9**) (1.9 g, 7.2 mmol): $^1H$ NMR (60 MHz, $CCl_4$): δ 1.2 (3 H, t, $CH_3$), 3.3 (1 H, br s, removed with $D_2O$, OH), 4.2 (2 H, q, $CH_2$), 5.2 [1 H, s, CH(OH)], 6.8–7.3 (7 H, m, ArH). $^{13}C$ NMR (22.5 MHz, $CDCl_3$): δ 13.9, 62.0, 69.9, 126.1, 127.15, 127.23, 127.9, 128.2, 128.4, 131.3, 134.5, 137.2, 141.1, 173.9. IR (film): 3600–3200, 1730 $cm^{-1}$.

Ethyl 2-hydroxy-4-oxo-2-[2-(2-thienyl)phenyl]butanoate (**10**) (0.27 g, 0.89 mmol): $^1H$ NMR (300 MHz, $CDCl_3$): δ 1.18 (3 H, t, $CH_3$), 3.07 (1 H, dd, H3A), 3.13 (1 H, dd, H3B), 4.0 (1 H, br s, OH), 3.95–4.11 (2 H, m, $CH_2O$), 7.0–7.6 (7 H, m, ArH), 9.72 (1 H, dd, H4); coupling constants (Hz): $J_{3A,3B}$ 16.6, $J_{3A,4}$ 2.4, $J_{3B,4}$ 1.9. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 14.0, 51.2, 62.6, 74.2, 125.8, 126.4, 126.6, 127.9, 128.6, 128.8, 133.3, 134.0, 140.0, 141.3, 173.4, 200.5. MS [IP 70 eV; *m/z* (% rel. int.)]: 304 (21, *M*), 287 (6), 269 (70), 260 (1), 243 (12), 231 (6), 213 (13), 187 (100), 159 (7), 115 (16). IR (film): 3600–3200, 1730, 1710 $cm^{-1}$. The total yield of isolated products was 61%.

*Ethyl oxo[2-(2-thienyl)phenyl]acetate tosylhydrazone* (**7**). A solution of ethyl oxo[2-(2-thienyl)phenyl]acetate (**6**) (2.4 g, 9.2 mmol) and tosyl hydrazine (1.8 g, 9.7 mmol) in methanol (25 ml) was refluxed for 30 min. The reaction mixture was cooled, the solvent was evaporated off, and the product was crystallized from ether. Yield 2.7 g (68%), m.p. 168–170°C. $^1H$ NMR (60 MHz, DMSO-$d_6$): δ 1.9 (3 H, t, $CH_2CH_3$), 2.4 (3 H, s, $ArCH_3$), 3.9 (2 H, q, $CH_2$), 6.2–7.8 (11 H, m, ArH), 11.4 (1 H, br s, NH). IR (KBr): 3160, 1720 $cm^{-1}$.

*Ethyl diazo[2-(2-thienyl)phenyl]acetate* (**8**). The reaction was run under nitrogen. To a solution of ethyl oxo[2-(2-thienyl)phenyl]acetate tosylhydrazone (**7**) (1.0 g, 2.3 mmol) in dry benzene (100 ml) was added sodium hydride (60 mg, 2.5 mmol). After the gas evolution had ceased, the reaction mixture was refluxed for 45 min and then cooled. The solution was filtered, washed with water, dried ($Na_2SO_4$) and concentrated to give a yellow oil. Yield 0.53 g (83%). IR (benzene): 2086, 1728 $cm^{-1}$.

*Ethyl indeno[1,2-b]thiophene-4-carboxylate* (**11**). The reaction was run under nitrogen. Rhodium(II) acetate (1.0 mg) was added to a solution of ethyl diazo-[2-(2-thienyl)phenyl]acetate (**8**) (0.15 g, 0.55 mmol) in dry, oxygen-free benzene (20 ml). The solution was stirred at room temperature until the IR spectrum of the reaction mixture showed no diazo absorption (4 days). The solution was concentrated to yield an oil which was subjected to preparative thin layer chromatography (silica; hexane–ethyl acetate 5:1). Yield 80 mg (55%), m.p. 48–50°C. $^1H$ NMR (60 MHz, $CCl_4$): δ 1.2 (3 H, t, $CH_3$), 4.1 (2 H, q, $CH_2$), 4.5 (1 H, s, H 4), 6.9–7.5 (6 H, m, ArH). $^{13}C$ NMR (22.5 MHz, $CDCl_3$): δ 14.2, 50.9, 61.4, 119.0, 123.2, 125.5, 125.7, 127.5, 128.1, 138.3, 143.5, 143.9, 144.9, 169.8. MS [IP 70 eV; *m/z* (% rel. int.)]: 244 (34, *M*), 171 (100), 127 (8), 126 (3). IR (KBr): 1740 $cm^{-1}$.

*Comment.* Decomposition experiments with the diazo ester **8** were performed by different methods: thermally, photochemically (high-pressure mercury lamp at temperatures below 0°C) and catalytically [rhodium(II) acetate at different temperatures], and in a wide variety of solvents. In all these cases mainly polymeric material was formed.

*Methyl oxo[2-(2-thienyl)phenyl]acetate* (**15**). The experimental procedure was as described for the preparation of **6**, using the Grignard reagent of 2-(2-bromophenyl)-thiophene[3] (**4**) (12 g, 50 mmol), dimethyl oxalate (6.5 g, 55 mmol) and dry THF (40 ml). The crude product consisted of the oxo- and hydroxy-ester in the ratio 2.5:1 (NMR, GLC).

The crude product was dissolved in dry dichloromethane (20 ml), pyridinium chlorochromate (5.0 g, 23 mmol) was added, and the reaction mixture was refluxed for 10 h and then cooled. Ether (25 ml) was added, the reaction mixture was filtered through silica and the solvents were evaporated off. The oxo ester was purified by distillation. Yield 3.2 g (24%), b.p. 140–142°C/0.01 mmHg. $^1H$ NMR (200 MHz, $CDCl_3$): δ 3.45 (3 H, s, $CH_3$), 6.89 (1 H, dd, Th-H3), 7.02 (1 H, dd, Th-4), 7.39–7.62 (4 H, m, Th-H5, Ph-H3,4,5), 7.76 (1 H, m, Ph-H6); coupling constants (Hz) in the thiophene ring: $J_{34}$ 3.5, $J_{35}$ 1.2, $J_{45}$ 5.1. $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 52.9, 128.1, 128.5, 128.7, 130.2, 130.7, 130.8, 133.4, 135.5, 138.8, 141.6, 163.0, 189.5. MS [IP 70 eV; *m/z* (% rel. int.)]: 246 (8, *M*), 187 (100), 159 (12), 158 (8), 115 (67). IR (film): 1740, 1690 $cm^{-1}$.

*Methyl oxo[2-(3,4,5-trichloro-2-thienyl)phenyl]acetate* (**16**). Methyl oxo[2-(2-thienyl)phenyl]acetate (**15**) (1.0 g, 4.1 mmol) and *N*-chlorosuccinimide (2.0 g, 15 mmol) were dissolved in nitrobenzene (10 ml) and the reaction mixture was stirred at 120°C for 3 days. The solution was cooled and diluted with $CCl_4$ (40 ml), and precipitated material was filtered off and washed with $CCl_4$. After evaporation of the solvents, the crude product was distilled in a Kugelrohr apparatus (240°C/0.01 mmHg). Yield 0.70 g (49%), yellow–white oil which solidified in the refrigerator. $^1H$ NMR (400 MHz, $CDCl_3$): δ 3.71 (3 H, s, $CH_3$), 7.43 (1 H, dd, H3), 7.62 (1 H, td, H5), 7.69 (1 H, td, H4), 7.90 (1 H, dd, H6); coupling constants (Hz): $J_{34}$ 7.6, $J_{35}$ 1.0, $J_{45}$ 7.6, $J_{46}$ 1.3, $J_{56}$ 7.7. $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 53.2, 123.7, 126.1, 130.4, 131.1, 131.4, 131.5, 131.7, 132.3, 133.9, 135.5, 163.5, 187.4. MS [IP 70 eV; *m/z* (% rel. int.)]: 348 (2, 3 Cl, *M*), 313 (67, 2 Cl), 289 (97, 3 Cl), 254 (37, 2 Cl), 226 (58, 2 Cl), 217 (11, 3 Cl). IR ($CCl_4$): 1735, 1600 $cm^{-1}$.

*Methyl oxo[2-(3,4,5-trichloro-2-thienyl)phenyl]acetate tosylhydrazone* (**17**). A solution of methyl oxo[2-

(3,4,5-trichloro-2-thienyl)phenyl]acetate (**16**) (67 mg, 0.27 mmol) and tosylhydrazine (56 mg, 0.30 mmol) in methanol (5 ml) was refluxed for 24 h. The solution was cooled, the methanol was evaporated off and the residue was crystallized from ether. Yield 85 mg (61%), m.p. 169–172°C. $^1$H NMR (60 MHz, acetone-$d_6$): δ 2.5 (3 H, s, Ts-$CH_3$), 3.7 (3 H, .s, $CH_3O$), 7.3–7.9 (8 H, s, Ar-H).

*Methyl diazo[2-(3,4,5-trichloro-2-thienyl)phenyl]acetate* (**18**) *(Scheme 7)*. Methyl oxo[2-(3,4,5-trichloro-2-thienyl)-phenyl]acetate tosylhydrazone (**17**) (52 mg, 0.1 mmol) was dissolved in dry benzene (5 ml) and sodium hydride (2.4 mg, 1 mmol) was added. The reaction mixture was stirred at room temperature for 10 min and subsequently refluxed for 15 min. After work-up with water the crude product was purified by column chromatography (silica; hexane–ethyl acetate 3:1). Yield 25 mg (69%), yellow oil. $^1$H NMR (60 MHz, acetone-$d_6$): δ 3.75 (3 H, s, $CH_3$), 7.4–7.8 (4 H, m, Ph). IR (benzene): 2086, 1728 $cm^{-1}$.

*2-(2-Thienyl)benzoyl chloride* (**19**). The reaction was run under nitrogen. The Grignard reagent of 2-(2-bromophenyl)thiophene[3] (**4**) (20.3 g, 85.0 mmol), prepared in dry THF, was poured onto dry ice covered with dry THF. The reaction mixture was hydrolysed with dilute sulfuric acid. The product was extracted with ether and the organic phase was washed several times with water. The product was extracted into a basic water phase, the water solution was washed with ether and then acidified. The precipitated material was dissolved in ether and the solution was dried ($MgSO_4$), filtered and evaporated to give 2-(2-thienyl)benzoic acid (14.7 g, 85%) as an oil which was crystallized from hexane–ethyl acetate, m.p. 95–97°C. $^1$H NMR (200 MHz, $CDCl_3$): δ7.1 (2 H, m), 7.3–7.6 (4 H, m), 7.9 [1 H, m(d), Ph-H6], 9.1 (1 H, br s, OH). $^{13}$C NMR (50 MHz, $CDCl_3$): δ 126.6, 127.3, 127.8, 128.3, 130.7, 131.0, 132.3, 132.4, 135.6, 142.1, 174.0.

A solution of 2-(2-thienyl)benzoic acid (14.0 g, 68.5 mmol) in thionyl chloride (40 ml) was stirred at room temperature for 3 h. The excess of thionyl chloride was evaporated off and the product was purified by distillation. Yield 11.0 g (72%), b.p. 119–122°C/0.4 mmHg. MS [IP 70 eV: *m/z* (% rel. int.)]: 222/224 (5/2, *M*), 187 (57), 186 (100), 159 (9), 158 (33). IR (film): 1770 $cm^{-1}$.

*α-Diazo-2-(2-thienyl)acetophenone* (**20**). 2-(2-Thienyl)-benzoyl chloride (7.1 g, 32 mmol), dissolved in dry ether (15 ml), was added to an ice-cooled solution of diazomethane (35 mmol) and triethylamine (3.4 g, 34 mmol) in dry ether (30 ml). The reaction mixture was left to stand overnight. Precipitated material was filtered off, the ethereal solution was concentrated to half the volume, and the product was crystallized from this solution at −20°C. Yield 5.2 g (71%), m.p. 100–102°C (decomp.). IR (KBr): 2080, 1580 $cm^{-1}$.

*Methyl [2-(2-thienyl)phenyl]acetate* (**21**). A freshly prepared catalyst solution [silver acetate (75 mg, 0.4 mmol), triethylamine (1.0 ml), methanol (0.5 ml)] was slowly added to a solution of α-diazo-2-(2-thienyl)acetophenone (**20**) (2.0 g, 8.6 mmol) in absolute methanol (25 ml) at 40°C. The reaction mixture was stirred for 5 min, filtered and evaporated. Work-up with ether–water afforded the product as an analytically pure yellow–white oil. Yield 1.9 g (93%). $^1$H NMR (200 MHz, $CDCl_3$): δ 3.66 (3 H, s, $CH_3$), 3.75 (2 H, s, $CH_2$), 7.0–7.1 (2 H, m, ArH), 7.3–7.5 (5 H, m, ArH). $^{13}$C NMR (50 MHz, $CDCl_3$): δ 39.4, 52.3, 126.3, 127.5, 127.7, 127.8, 128.7, 131.3, 131.8, 133.3, 135.3, 142.5, 172.8. MS [IP 70 eV; *m/z* (% rel. int.)]: 232 (61, *M*), 200 (11), 173 (100), 172 (54), 171 (40), 129 (49), 128 (34), 127 (21), 115 (15), 59 (18). IR (film): 1730 (br) $cm^{-1}$.

*Methyl [2-(3,4,5-trichloro-2-thienyl)phenyl]acetate* (**22**). A solution of methyl [2-(2-thienyl)phenyl]acetate (**21**) (1.86 g, 8.00 mmol) and *N*-chlorosuccinimide (4.0 g, 38 mmol) in glacial acetic acid was stirred at 75°C for 2 days. The reaction mixture was diluted with hexane (50 ml) and cooled to −20°C. Precipitated material was filtered off and the filtrate was washed with sodium carbonate solution, dried ($MgSO_4$) and concentrated. Repeated flash chromatography (silica; toluene, then hexane–ethyl acetate 3:1) afforded the product as a yellow–white oil. Yield 1.70 g (63%). $^1$H NMR (300 MHz, acetone-$d_6$): δ 3.57 (3 H, s, $CH_3$), 3.69 (2 H, s, $CH_2$), 7.35–7.53 (4 H, m, Ph). $^{13}$C NMR (75 MHz, acetone-$d_6$): δ 39.1, 52.1, 122.4, 123.4, 124.9, 128.3, 129.7, 131.0, 132.0, 132.4, 134.2, 135.9, 171.5. MS [IP 70 eV; *m/z* (% rel. int.)]: 334 (53, 3 Cl, *M*), 299 (33, 2 Cl), 275 (20, 3 Cl), 240 (100, 2 Cl), 239 (58, 3 Cl), 59 (15). IR ($CCl_4$): 1760 $cm^{-1}$.

*Methyl diazo[2-(3,4,5-trichloro-2-thienyl)phenyl]acetate* (**18**) *(Scheme 8)*. The reaction was run under nitrogen. Butyllithium (1.4 M solution in hexane, 1.0 ml, 1.4 mmol) was added to a solution of diisopropylamine (0.30 g, 3.0 mmol) in dry THF (0.5 ml) at 0°C. Methyl [2-(3,4,5-trichloro-2-thienyl)phenyl]acetate (**22**) (0.45 g, 1.3 mmol), dissolved in dry THF (2 ml), was added, and the reaction mixture was stirred for 10 min before a solution of tosyl azide (0.28 g, 1.4 mmol) in dry THF (1 ml) was added. The ice–water bath was removed and the temperature was slowly raised to 40°C. The reaction mixture was stirred at this temperature for 3 h and then cooled. Ether–hexane (1:1) (15 ml) was added, precipitated material was filtered off and the solution was washed with water, dried and concentrated. Flash chromatography (silica; toluene) afforded the product as a yellow oil. Yield 0.29 g (62%). For the spectroscopic data, see above.

*Decomposition of the diazo ketone.* A solution of methyl diazo[2-(3,4,5-trichloro-2-thienyl)phenyl]acetate (**18**) (85.mg, 0.24 mmol) and rhodium(II) acetate (1.0 mg) in benzene (20 ml) was stirred under nitrogen until the IR

spectrum showed no diazo absorption, and was then concentrated. The two main products which were formed, in addition to the substantial amount of polymeric material, were identified by TLC, HPLC and GC–MS as the keto ester **16** and methyl hydroxy [2-(3,4,5-trichloro-2-thienyl)phenyl]acetate (**23**). MS (EI, IP 70 eV) of **23**: *m/z* 350 (13; 3 Cl, *M*), 314 (6; 2 Cl), 291 (33; 3 Cl), 283 (10; 2 Cl), 256 (17; 2 Cl), 255 (100; 2 Cl). When oxygen was removed from the solvent by helium bubbling followed by distillation from sodium–benzophenone and repeated crystallizations, only the hydroxy ester was formed.

## References


1. Previous paper in this series: Storflor, H. and Skramstad, J. *Acta Chem. Scand., Ser. B 40* (1986) 303.
2. Skramstad, J. and Storflor, H. *Acta Chem. Scand., Ser. B 38* (1984) 533.
3. Storflor, H. and Skramstad, J. *Acta Chem. Scand., Ser. B 40* (1986) 178.
4. Moss, R. A. and Jones, M., Jr. *Carbenes*, Wiley, New York 1975, Vol. 2, Chap. 5.
5. (a) Ando, W., Yagihara, T., Tozune, S., Imai, I., Suzuki, J., Toyama, T., Nakaido, S. and Migita, T. *J. Org. Chem. 37* (1972) 1721; (b) Alonso, M. E. and Gomez, M. *Tetrahedron Lett.* (1979) 2763.
6. Gillespie, R. J., Murray-Rust, J., Murray-Rust, P. and Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* (1978) 83.
7. (a) Lapkin, I. I. and Lyubimova, A. V. *Zh. Obshch. Khim. 18* (1948) 701; *Chem. Abstr. 43* (1949) 188a; (b) Lapkin, I. I., Shklyaeva, M. G., Koryakina, G. A. and Vinokurova, O. N. *Zh. Obshch. Khim. 17* (1947) 1332; *Chem. Abstr. 42* (1948) 4978a. (c) Lapkin, I. I. and Karavanov, N. A. *Zh. Obshch. Khim. 30* (1960) 1638; *Chem. Abstr. 55* (1961) 1422e.
8. Maas, G. In: *Methoden der organischen Chemie (Houben-Weyl), Band E19b*, Thieme, Stuttgart 1989, p. 1116.
9. Gillispie, R. J. and Porter, A. E. A. *J. Chem. Soc., Perkin Trans 1* (1979) 2624.
11. Meth-Cohn, O. and van Vuuren, G. *J. Chem. Soc., Chem. Commun.* (1984) 190.
12. Skramstad, J., Solbakken, M. and Nordenson, S. *Unpublished results.*
13. (a) Cuffe, J., Gillespie, R. J. and Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* (1978) 641; (b) Gillispie, R. J., Murray-Rust, J., Murray-Rust, P. and Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* (1979) 366.


Received April 7, 1993.