Thiophene decorated with Fischer carbene ligands†

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The activation of a section, or of all the carbons of thiophene by bromine in lithium–halogen exchange reactions, was implemented in a step-wise manner to facilitate the preparation of novel multiple Fischer carbene-bearing thiophene compounds.

Mononuclear complexes with two Fischer carbene ligands are far less studied than the corresponding alkoxy or amino monocarbene complexes.1 Carbon–carbon coupling reactions from reactive biscarbene intermediates facilitated by catalysts2 or from non-catalytic processes have been reported.3 The synthesis of mononuclear biscarbene chelate complexes are scarce4 and their potential in template reactions in organic chemistry has yet to be recognized.5 The classical Fischer method of carbene synthesis require organolithium reagents, metal carboxyls and a strong electrophile or alkylating agent.6 Hence, for arene substrates to form the backbone of a biscarbene chelate complex the creation of two adjacent carbanions is a necessity which can be synthetically challenging. Fischer reported the first example of such a biscarbene chelate by reacting 1,2-dilithiobenzene with chromium hexacarbonyl.6b The 1,2-dilithiation of benzene was troublesome and incorporated the formation of mercury polymers of benzene and a subsequent reaction with lithium metal.7 Reactions of 1,2-halobenzenes with butyllithium yielded polymeric material due to the reactivity of mixed lithium halogen intermediates. Heteroaromatic substrates such as thiophene (A, Fig. 1) and furan have two activated carbon atoms but these reside on positions 2 and 5.8 A common feature of metallations of furan and thiophene is the preference for the lithiations to occur at positions 2 and 5.

Fig. 1 Structures of thiophene and thiophene carbene complexes of tungsten.

Monolithiation in the 2 position of thiophene is readily achieved at -30 °C in THF by n-butyllithium.10b Harsh reaction conditions are required to effectively dilithiate thiophene in both the 2 and 5 positions with BuLi. Typically this reaction was performed in hexane in the presence of TMEDA at 60 °C and used in our laboratories to synthesize 2,5-binuclear biscarbene rods (B).11 Using 2,5-dibromothiophene as a precursor allows for dilithiation in much higher yields and at much lower temperatures in THF.12 A strategy to synthesize an unsymmetric biscarbene chelate would be to activate the 3 position to such an extent that lithiation occurs at this site before position 2 or 5. Blocking of position 5 by a methyl substituent and then attempting to dilithiate at positions 2 and 3 followed by the Fischer protocol did not afford biscarbene chelates and only mixtures of monocarbene complexes were isolated. A suitable precursor to achieve 2,3-dilithiation is to start with 3-bromothiophene. To retain the carbanion at position 3 and avoid lithium–hydrogen exchange with position 2 of thiophene a temperature between -60 °C to -90 °C was required. The addition of one equivalent of M(CO)5 (M = W, Cr) at this stage is important. The metal acylate intermediate that formed has a number of advantages. Firstly, the anionic charge is drawn away from the thiophene ring and is stabilized by electron delocalization over the O–C(acyl)–M fragment while positions 2 and 5 remained activated. Secondly, the acyl carbon is protected against possible nucleophilic attack from the second lithiated reagent which is added in the next step of the procedure. Anionic protection of an acyl carbon was first exploited by Aoki and co-workers in monocarbene syntheses,11 by Marianoa et al. in bithienyl biscarbene complexes14 and in our laboratories to synthesize mixed metal biscarbene complexes with thiophene, bithiophene and furan spacers.13 Thirdly, with position 3 secured as the site for the acyl substituent and because of the electron- withdrawing properties of this group on the thiophene ring, it exerts a higher activation of the 2 position leaving the 5 position unaffected. The second lithiation is accomplished by LDA6 at position 2 which leads to the attack on a second cis carbonyl ligand of the metal carbonyl moiety to give the metal diacetyl intermediate which, after subsequent alkylation with Et2OBF4,17 afforded the desired diethoxy-2,3-thienylcarbene complex (C) (Scheme 1) with a 5-membered metal biscarbene chelate ring.18 The major product C, a blue crystalline material was separated from a red fraction of monocarbene complexes and a yellow compound (ethoxy)butylcarbenepentacarbonylmetal(0) on silica by using

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hexane as eluent and recrystallized from dichloromethane–hexane mixtures.

Surrounding thiophene with two biscarbene chelates, i.e., four Fischer carbene ligands, was the next objective. The strategy which proved best was to activate all 4 carbons on thiophene by using tetrabromothiophene as a starting material instead of 3,4-dibromothiophene. In this instance positions 2 and 5 will be more activated compared to positions 3 and 4, but not so easy to control during a step-wise lithiation procedure. After the first dilithiation at sites 2 and 5 at sufficient low temperature to keep positions 3 and 4 least affected, two equivalents of W(CO)₆ were added. The diacyl ditungstenate formed predominately in positions 2 and 5 at sufficient low temperature to keep positions 3 and 4 least affected, two equivalents of W(CO)₆ were added. The diacyl ditungsten tetracarbene bischelate complex D was one of the products. Separation yielded as by-products a mixture consisting of a large number of monocarbene complexes, C and an oily red-brown polymeric residue which was discarded. The yield of D was not very high when 6–8 equivalents of BuLi was used, but could be improved and optimized to well above 30% by performing the reaction using 4–6 equivalents of butyllithium. A problem at the required low temperature was the poor solubility of W(CO)₆, which called for a larger volume of THF to be used and additions to be made over a much longer period of time.

The two carbene carbon atoms of a chelate ring attached to thiophene in C and D are distinctly different. In a test reaction (Scheme 2), ammonia was bubbled through an ether solution of the chromium analogue of (C) (C’) for 15 min. Aminolysis occurred instantly, but only at the carbene carbon remote from the sulfur atom, to give E. We ascribe this to the role of the sulfur in the heteroarene and to a better stabilization pathway through π-delocalization from the conjugated thiophene double bonds to the carbene carbon next to sulfur (Fig. 2). By contrast, both carbene carbons were aminolysed in a similar reaction of the symmetrical thiophene analogue, [Cr{1.2-C(OEt)C₆H₄C(OEt)}(CO)₄] studied by Fischer and coworkers.

Support for the carbene carbons being in different electronic environments is confirmed by the NMR spectral data. In the 'H NMR spectrum the ethoxy substituents show two separate sets of signals for C [δ: 4.76 (CH₃), 1.61 (CH₂), 4.74 (CH₃), 1.60 (CH₂)], C’ [δ: 4.77 (CH₃), 1.64 (CH₃), 4.73 (CH₃), 1.63 (CH₂)] and for D [δ: 4.90 (CH₃), 1.59 (CH₃), 4.86 (CH₃), 1.57 (CH₂)]. In the ¹³C NMR spectra two different resonances for the carbene carbon atoms are observed for C [δ: 313.9 and 283.3], C’ [δ: 321.0 and 312.3] and D [δ: 317.8 and 283.7].

In the solid state structure of D’ (Fig. 3) there are differences in the W–C(carbene) distances within both chelates with W1–C5 = 2.134(10) and W1–C6 = 2.189(11) Å, and with W2–C15 = 2.134(10) and W2–C16 = 2.186(11) Å. However, this could also be the result of strain caused by the two chelate rings with their ethoxy substituents. Owing to the intervening sulfur atom, the ethoxy substituents on that side of the thiophene ring are not crowded but for the carbones bonded to the two adjacent ring carbons, C22 and C23, the ethoxy substituents are very crowded with a close O6...O16 distance of 2.81(1) Å. Thus these oxygen atoms cannot lie approximately coplanar with the thiophene ring – as evinced by a non-bonded O6...C22–C23...O16 torsion angle of 90°.

![Scheme 1](image1.png)  
**Scheme 1** Synthesis of C from 3-bromothiophene. (i) BuLi/THF/-90 °C, (ii) W(CO)₆, (iii) LDA/THF/-78 °C, (iv) Et₃OBF₄/DCM/-30 °C.

![Scheme 2](image2.png)  
**Scheme 2** Aminolysis reaction of C’.

![Image 3](image3.png)  
**Fig. 2** Thiophene ring electron delocalization in C showing discrimination between the two carbene sites.

![Image 4](image4.png)  
**Fig. 3** ORTEP/Pov-Ray drawing of D’ showing the atom numbering scheme. ADP ellipsoids are shown at the 50% probability level. Selected bond distances (Å) and bond angles (°): W1–C5 2.134(10); W2–C15 2.134(12); W1–C6 2.189(11); W2–C16 2.186(11); C5–O5 1.290(12); C15–O15 1.330(14); C6–O6 1.310(13); C16–O16 1.312(12); C5–C21 1.474(14); C15–C24 1.451(16); C6–C22 1.469(15); C16–C23 1.498(14); C5–W1–C6 77.5(13); C15–W2–C16 77.6(13); C1–W1–C2 84.3(5); C11–W2–C12 83.9(6); C3–W1–C4 177.0(5); C13–W2–C14 178.1(5); W1–C5–C21 113.1(7); W2–C15–C24 112.8(8); W1–C5–O5 138.6(7); W2–C15–O15 139.5(8); O5–C5–C21 108.3(9); O15–C15–C24 107.6(10); W1–C6–C22 114.2(7); W2–C16–C23 114.4(7); W1–C6–O6 135.2(8); W2–C16–O16 136.3(8).
which have electronically equivalent carbene carbon atoms. Modifications unlike the 1,2-symmetrical benzene biscarbene chelates carbene ligands in a chelate ring holds potential for unique mod-
carbon–carbon bond formations. Discrimination between the two 
exploited and holds promise for many unique applications. Areas 
chelates with a shared heteroarene substituent must still be 
0.03(3), C15 0.05(2), C16 0.21(2), O15 0.13(2) and O16 0.47(2).

In conclusion, the synthesis and chemistry of multicarbene 
clusters with randomly oriented carbene ligands in a chelate ring holds potential for unique applications. Areas 
chelates with a shared heteroarene substituent must still be 
0.03(3), C15 0.05(2), C16 0.21(2), O15 0.13(2) and O16 0.47(2).

Notes and references

‡ Crystal data for D: C20H14O2S2, M = 359.2, triclinic, a = 7.0967(17) Å, b = 12.537(3) Å, c = 17.225(4) Å, α = 101.650(4)°, β = 100.894(4)°, γ = 95.156(4)°, V = 1460.8(8) Å³, T = 293(2) K, space group P̅1, Z = 2, μ(Mo-Kα) = 7.997 mm⁻¹, 6527 reflections measured, 4941 

independent reflections (Rint = 0.0266). The final R values were: R1 = 0.0513 (I > 2σ(I)), wR2(F²) = 0.1180 (I > 2σ(I)), R2 = 0.0783 (all data), wR2(F²) = 0.1329 (all data).

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