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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 catalysts[2] or from non-catalytic processes have been reported.[3] The synthesis of mononuclear biscarbene chelate complexes are scarce[4] 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 carbonyls 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.[4b] 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. Heteroarene 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.

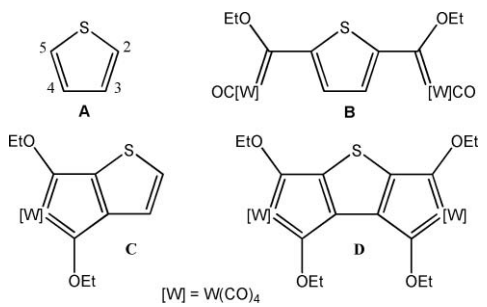

Fig. 1 Structures of thiophene and thiophene carbene complexes of tungsten.

The relative kinetic acidities between the protons in the 2 and 3 position was determined by H/D exchange experiments and shows the 2 proton to be 500 times more acidic than the 3 proton.[9] The degree of activation of adjacent carbons 2 and 3 towards direct deprotonation with butyllithium differ too much to allow for sequential lithiation and an alternative strategy is required to synthesize biscarbene chelates.

Monolithiation in the 2 position of thiophene is readily achieved at −30 °C in THF by *n*-butyllithium.[10] Harsher 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 $M(CO)_6$ (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,[13] by Marioana *et al.* in bithienyl biscarbene complexes[14] and in our laboratories to synthesize mixed metal biscarbene complexes with thiophene, bithiophene and furan spacers.[15] 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 LDA[16] at position 2 which leads to the attack on a second *cis* carbonyl ligand of the metal carbonyl moiety to give the metal diacyl intermediate which, after subsequent alkylation with Et_3OBF_4,[17] afforded the desired diethoxy-2,3-thienylenecarbene 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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† Electronic supplementary information (ESI) available: Synthesis and characterization of **C**, **C′**, **D** and **E**. CCDC reference number 769120. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0dt00301h

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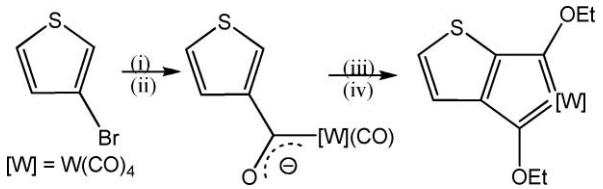


Scheme 1 Synthesis of **C** from 3-bromothiophene. (i) BuLi/THF/−90 °C, (ii) $W(CO)_6$, (iii) LDA/THF/−78 °C, (iv) Et_3OBF_4/DCM/−30 °C.

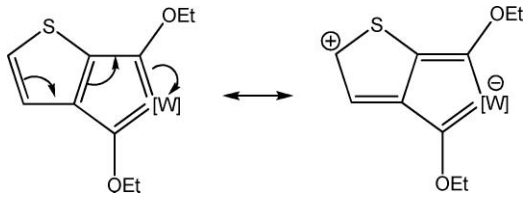
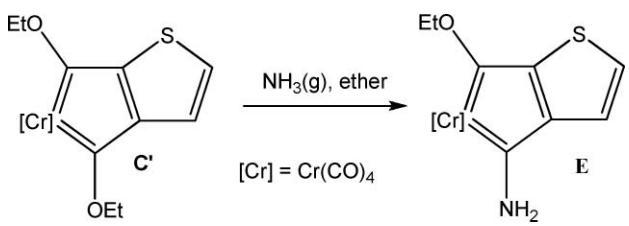


Fig. 2 Thiophene ring electron delocalization in **C** showing discrimination between the two carbene sites.

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 and, as above, the acyl carbons were protected by charge delocalization from metal to oxygen in the two substituents. Lithiation of the remaining two sites followed by the *in situ* reaction with two further carbonyl ligands of the tungsten carbonyl moieties afforded, after alkylation of all acylate species with Et_3OBF_4, the novel ditungsten tetracarbene bischelate complex **D** as 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[18] 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 benzene analogue, $[Cr\{1,2\text{-}C(OEt)C_6H_4C(OEt)\}(CO)_4]$ studied by Fischer and coworkers.[19]



Scheme 2 Aminolysis reaction of **C′**.

Support for the carbene carbons being in different electronic environments is confirmed by the NMR spectral data. In the ^1H NMR spectrum the ethoxy substituents show two separate sets of signals for **C** [δ: 4.76 (CH_2), 1.61 (CH_3) and 4.74 (CH_2), 1.60 (CH_3)], **C′** [δ: 4.77 (CH_2), 1.64 (CH_3) and 4.73 (CH_2), 1.63 (CH_3)] and for **D** [δ: 4.90 (CH_2), 1.59 (CH_3) and 4.86 (CH_2), 1.57 (CH_3)]. In the ^{13}C 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(12) 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 carbenes 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

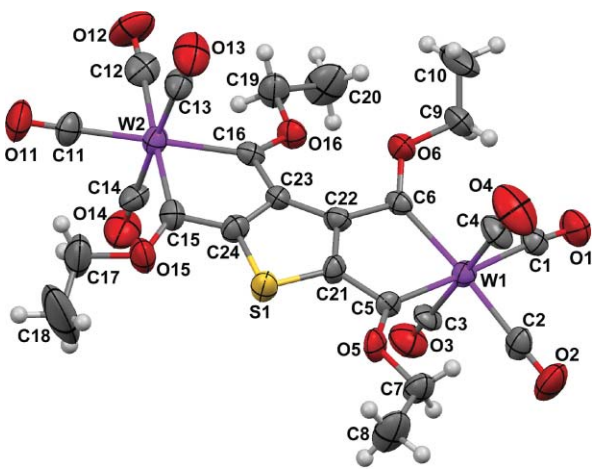


Fig. 3 ORTEP[20]/POV-Ray[21] drawing of **D**‡ showing the atom numbering scheme. ADP elipsoids are shown at the 50% probability level. Selected bond distances (Å) and bond angles (°): W1–C5 2.134(10); W2–C15 2.134(12); W1–C6 2.189(11); W2–C16 2.186(11); C5–O5 1.290(12); C15–O15 1.330(14); C6–O6 1.310(13); 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(4); C15–W2–C16 77.8(4); 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); O6–C6–C22 110.6(9); O16–C16–C23 109.3(9).

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26.8(8)°. In contrast the corresponding O5 ··· C21 ··· C24 ··· O15 torsion angle is −3(2)°. These distortions also induce deviations from planarity of the chelate rings as indicated by the following deviations from the mean plane through the thiophene ring: W1 0.41(3), C5 0.16(2), C6 −0.15(2), O5 0.09(2), O6 −0.62(2), W2 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 chelates with a shared heteroarene substituent must still be exploited and holds promise for many unique applications. Areas to be investigated are arene and carbene modification reactions, multicentered metathesis reactions, template reactions and novel carbon–carbon bond formations. Discrimination between the two carbene ligands in a chelate ring holds potential for unique modifications unlike the 1,2-symmetrical benzene biscarbene chelates which have electronically equivalent carbene carbon atoms.[19]

Notes and references

‡ Crystal data for **D**: $C_{24}H_{20}O_{12}SW_2$, M = 900.16, 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(6) Å^3, T = 293(2) K, space group $P\bar{1}$, Z = 2, μ(Mo-Kα) = 7.997 mm^{-1}, 6527 reflections measured, 4941 independent reflections (R_{int} = 0.0266). The final R values were: R_1 0.0513 ($I > 2\sigma(I)$), w$R(F^2)$ 0.1180 ($I > 2\sigma(I)$), R_1 0.0783 (all data), w$R(F^2)$ 0.1329 (all data).

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