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Syntheses and coordination chemistry of thiosemicarbazone-based titanium complexes†

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Two routes leading to thiosemicarbazone-based complexes are reported with the view of developing ionic titanium complexes as cytotoxic metallodrugs. The reaction of bis(π-η^5:σ-η^1-pentafulvene)titanium complexes with most thiosemicarbazones gives κ^2N,S thiosemicarbazonido complexes *via* deprotonation of the acidic N–H bond by the pentafulvene ligand. The use of an *o*-cresyl TSCN revealed a κ^2N,O coordination mode by deprotonation of the O–H bond. The protonolysis of the remaining pentafulvene unit in these complexes with Brønsted acids and further functionalization with multiple bond substrates were attempted. The reaction of titanocene(III) triflate with TSCN reveals an unprecedented reactivity and leads to Ti(III) thiosemicarbazone complexes. The Ti(IV) complexes were characterized using NMR experiments and the nitrogen cores were identified *via* ^{1}H,^{15}N HMBC experiments by coupling with the adjacent aldimine proton or the methyl group of the thiosemicarbazone. These are the first structural examples of thiosemicarbazone-based titanium complexes obtained from single-crystal X-ray diffraction.

Introduction

Thiosemicarbazones (TSCN) are an important type of compound in both chemistry and medicine because of their role as ligands in coordination chemistry[1–4] and their pharmacological properties.[2–5] They count as Schiff bases and can be synthesized accordingly in a condensation reaction of a thiosemicarbazide with an aldehyde or a ketone.[6] In metal complexes, a series of different coordination modes have been observed, such as the κ^1S,[7,8] κ^2N,S[9] and κ^3N,S,X[10,11] (X = additional donor) coordination modes (Fig. 1, top), while also multimetallic bonding is possible.[7,11,12] The κ^2N,S coordination mode often resembles a five-membered ring system, where the N^α atom coordinates, which is considered more stable than the respective four-membered ring.[13] Although less common, there are also examples of the four-membered κ^2N^β,S coordination mode.[13,14] While TSCN complexes are present in catalysis,[15] their main purpose lie in the pharmacological and biological applications.[16,17] TSCN show antimicrobial,[18] antiviral[19] and, predominantly, antitumoral activities.[20] For instance, the TSCN Triapine is currently in medical trials as a potential antitumoral agent.[21] By metalation, the biological activities of TSCN increase significantly,[22] which is why much of recent research focuses on TSCN metal complexes.[17,23] As Cisplatin and its derivatives are the standout examples of antitumoral metal complexes,[24] many related studies were centered around

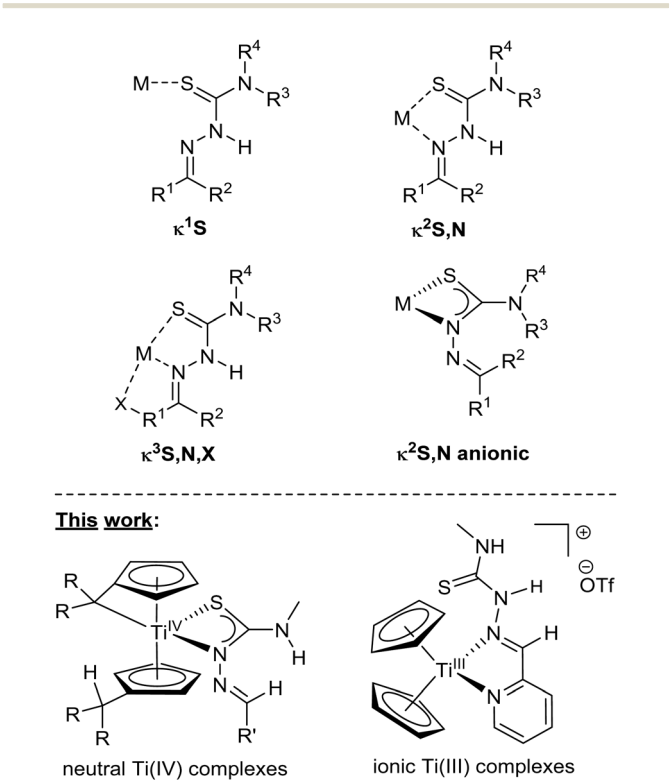

Fig. 1 Common coordination modes of TSCN complexes (top). Examples of TSCN-based Ti(IV) and Ti(III) complexes obtained in this work (bottom).

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† Electronic supplementary information (ESI) available: Crystallographic data, NMR, IR and EPR spectra. CCDC 2377765 (**Ti1a**), 2377767 (**Ti1c**), 2377764 (**Ti1d**), 2377768 (**Ti2b**) and 2377766 (**Ti3d**). For ESI and crystallographic data in CIF or other electronic format see DOI: **https://doi.org/10.1039/d4nj04061a**

heavier metals.[4,25] Titanium-based metal complexes also have shown promising results regarding cytotoxic properties,[26] but despite their promises, less attention has been paid to them and only a couple of works feature TSCN as ligands in neutral complexes.[27] In this work, we developed a facile route toward Ti(IV) TSCN complexes from bis(pentafulvene) complexes (Fig. 1, bottom left) and discussed the role of an additional donor in the ligand backbone.

Because of the multifaceted molecular bond activation[28] and functionalization[29,30] reactivity of bis(pentafulvene) complexes, they are excellent precursors for the creation of novel metallodrugs, while the adamantyl groups of one of the complexes is an interesting feature because of the biological properties of adamantane derivatives.[31] This work also features ^{15}N NMR values for the nitrogen cores within the TSCN and the first molecular structures of thiosemicarbazone-based titanium complexes obtained from single-crystal X-ray diffraction. First attempts have been made to obtain ionic complexes, either by protonation of mono(pentafulvene) titanium complexes or *via* ligand exchange of titanocene(III) triflate (Fig. 1, bottom right).[32]

Results and discussion

Reaction of TSCN with Bis(pentafulvene)titanium complexes

Thiosemicarbazones **a–d** were synthesized according to a general procedure *via* condensation of 4-methylthiosemicarbazide and the corresponding aldehyde.[33] While **a** has no additional donor site, **b–d** contain heterocycles such as thiophenyl (**b**) and pyridinyl (**c**) rests. Thiosemicarbazone **d** provides a donor site *via* the OH group of the *o*-cresyl rest and there is also potential for deprotonation of this group (Fig. 2). Our initial studies focused on thiosemicarbazones derived from thiosemicarbazide. Although this approach works in principle, the poor solubility of the TSCN in the commonly used solvents for bis(pentafulvene)titanium complexes (*n*-hexane, toluene, THF) led to incomplete reactions and therefore to an inferior purity of the obtained complexes. Therefore, we used TSCN based on 4-methylthiosemicarbazide because of the superior solubility, reactivity and higher purity of the obtained complexes.

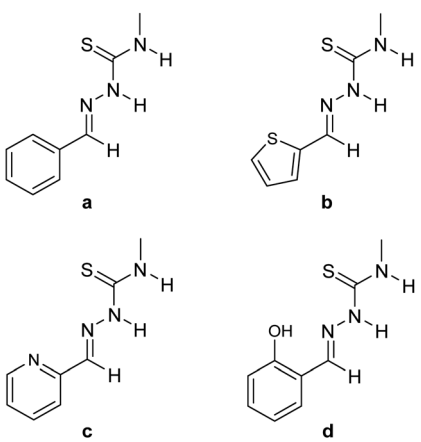
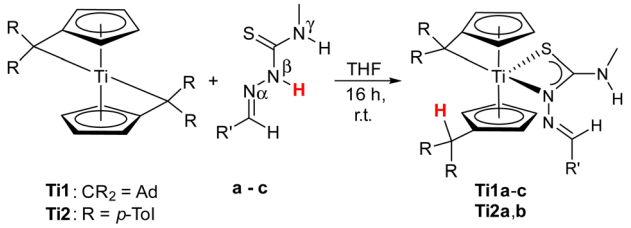


Fig. 2 Scope of thiosemicarbazone ligands **a–d** used in this work.



Scheme 1 Reaction of bis(π-η^5:σ-η^1-pentafulvene)titanium complexes **Ti1** and **Ti2** with thiosemicarbazones **a–c** to κ^{2}N$^\beta$,S-thiosemicarbazonate titanium complexes **Ti1a–c** and **Ti2a,b**.

Reactions of bis(π-η^5:σ-η^1-pentafulvene)titanium complexes **Ti1** and **Ti2** with the thiosemicarbazones **a–c** yielded the κ^{2}N,S-thiosemicarbazonate complexes **Ti1a–c** and **Ti2a,b** *via* deprotonation of the acidic N$^\beta$-proton by one pentafulvene unit (Scheme 1). The reaction of **Ti2** with **c** resulted in a mixture of products, which was not further characterized.

The products **Ti1a–c** and **Ti2a,b** were characterized by NMR spectroscopy and additionally, **Ti1a**, **Ti1c** and **Ti2b** by single-crystal X-ray diffraction (Fig. 3–5). Despite the multifunctionality of the thiosemicarbazone ligands, only the N$^\beta$-proton was deprotonated as evident by the eight different signals for the Cp-protons of the resulting complexes in the ^{1}H NMR spectra, corresponding to asymmetrical ring systems.[30] The ^{15}N NMR shifts of the nitrogen cores were determined *via* ^{1}H,^{15}N-HMBC experiments, with values between 207.0 and 213.3 ppm for the N$^\alpha$ atom, 341.3 and 354.6 ppm for the N$^\beta$ atom by coupling with the respective aldimine protons and values between 87.6 and 88.4 ppm for the N$^\gamma$ atom *via* coupling with the adjacent methyl group. The signal of the pyridinyl nitrogen core of **Ti1c** has a chemical shift of 316.8 ppm, which corresponds to a non-coordinating pyridine.[34] This was also revealed by the molecular structure obtained by single-crystal X-ray diffraction (Fig. 5).

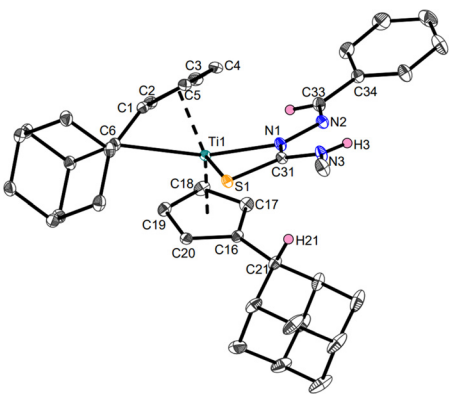


Fig. 3 Molecular structure of complex **Ti1a**. Displacement ellipsoids are drawn at the 50% probability level. Redundant H atoms (apart from H3, H21 and H33) have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Ti1–N1 2.1839(5), Ti1–S1 2.58107(19), Ti1–C6 2.744, N1–N2 1.3843(6), N2–C33 1.2906(7), N1–C31 1.3354(7), N3–C31 1.3409(7), S1–C31 1.7175(5), N1–Ti1–S1 63.823(13), N1–C31–S1 112.09(4), Ti1–N1–N2 139.81(4), C31–N1–N2 114.93(4), Ct1–Ti1–Ct2 136.7 (Ct1 = centroid of C1–C5; Ct2 = centroid of C16–C20).

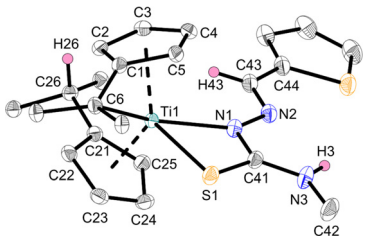


Fig. 4 Molecular structure of complex **Ti2b**. Displacement ellipsoids are drawn at the 50% probability level. Redundant H atoms (apart from H3, H26 and H43) have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Ti1–N1 2.1750(10), Ti1–S1 2.5798(4), Ti1–C6 2.7556, N1–C41 1.3338(15), S1–C41 1.7165(12), N3–C41 1.3423(15), C1–C6 1.4275(15), N1–N2 1.3785(13), N2–C43 1.2876(16), Ti1–C6–C1 53.570, S1–Ti1–N1 63.99(3), C41–N1–Ti1 104.32(7), C41–S1–Ti1 79.21(4), Ct1–Ti–Ct2 136.0 (Ct1 = centroid of C1–C5; Ct2 = centroid of C21–C25).

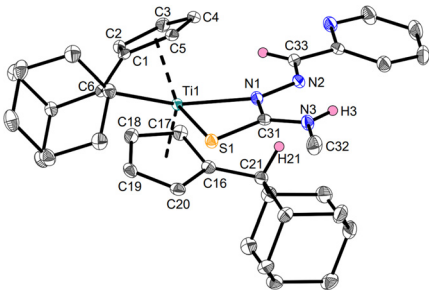


Fig. 5 Molecular structure of complex **Ti1c**. Displacement ellipsoids are drawn at the 50% probability level. Redundant H atoms (apart from H3, H26 and H43) have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Ti1–N1 2.2222(15), Ti1–S1 2.5823(5), Ti1–C6 2.7516(18), N1–N2 1.374(2), N2–C33 1.286(2), N1–C31 1.349(2), N3–C31 1.329(2), S1–C31 1.7118(18), N2–H21 2.383, N1–Ti1–S1 63.28(4), N1–C31–S1 111.56(13), Ti1–N1–N2 142.32(12), C31–N1–N2 113.55(14), Ct1–Ti1–Ct2 135.1 (Ct1 = centroid of C1–C5; Ct2 = centroid of C16–C20).

The molecular structure of **Ti1c** shows a mono(pentafulvene)titanium complex with an anionic, four-membered κ^2N^β,S-thiosemicarbazonido ligand. The Ti1–N1 bond with 2.2222(15) Å corresponds to an elongated Ti–N single bond according to the sum of covalent radii (Σr_{cov}(Ti–N) = 2.07 Å),[35] while the Ti1–S1 bond (2.5823(5) Å) is an elongated Ti–S single bond (Σr_{cov}(Ti–S) = 2.39 Å).[35] This bonding situation is due to the negative charge of the thiosemicarbazonido ligand, which is shared across the N and S atoms. Therefore, both the N1–C31 bond (1.349(2) Å) and the S1–C31 bond (1.7118(18) Å) contain double bond character (Σr_{cov}(C–N) = 1.46 Å, Σr_{cov}(C=N) = 1.27 Å; Σr_{cov}(C–S) = 1.78 Å, Σr_{cov}(C=S) = 1.61 Å).[36] This structural feature is common for κ^2N^β,S-thiosemicarbazonido complexes.[13] The rather long Ti–C_{exo} bond of the remaining fulvene moiety (Ti1–C6 2.7516(18) Å) is significantly longer than that of the bis(pentafulvene)titanium complex **Ti1** (2.341(2) Å and 2.363(2) Å),[37] which is a common feature of functionalized mono(pentafulvene)titanium complexes.[30] The molecular structures of complexes **Ti1a** (Fig. 3) and **Ti2b** (Fig. 4) are similar and the heterocycles provide no additional coordination. The bond parameters and angles of all mono(pentafulvene)-thiosemicarbazonido titanium complexes are summarized in Table 1.

As previously reported for mono(pentafulvene)hydrazonido titanium complexes,[30] the lack of follow-up chemistry of **Ti1a–c** and **Ti2a,b** with multiple bond substrates and Brønsted acids can be explained by the formal 18-electron nature of the complexes.[38] Due to this restriction in reactivity, we were unable to further functionalize the complexes or to obtain the desired ionic complexes by protonolysis of the remaining pentafulvene moiety, which is necessary to avoid reactions with water and to improve water-solubility. Therefore, we attempted an intramolecular functionalization reaction by the introduction of an OH group in TSCN **d**. Previously, this approach led to a double deprotonation reaction to obtain a κ^3N,N,O complex.[30]

In this work, the reactions of bis(π-η^5:σ-η^1-pentafulvene) titanium complexes **Ti1** and **Ti2** with the thiosemicarbazone **d** led to the formation of a mixture of various products (ESI,† Fig. S10). One of the products was determined by single-crystal X-ray diffraction (Fig. 6), revealing a κ^2N,O titanium complex

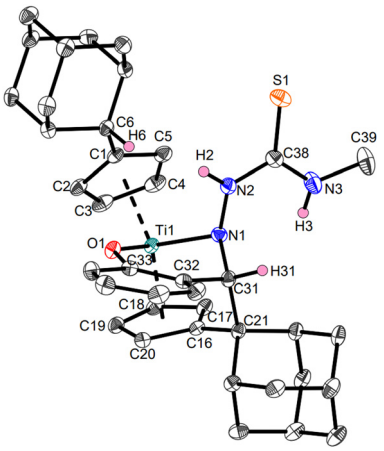
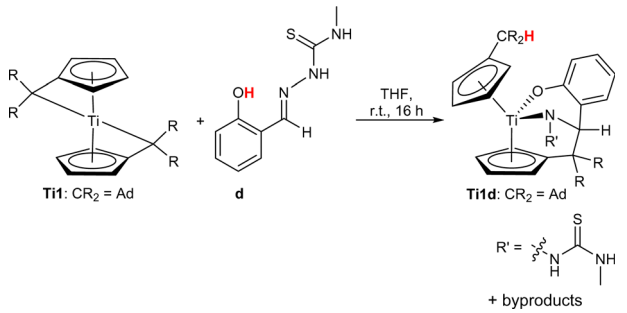


Fig. 6 Molecular structure of complex **Ti1d**. Displacement ellipsoids are drawn at the 50% probability level. Redundant H atoms and solvent molecules have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Ti1–N1 2.0437(12), Ti1–O1 1.9152(10), N1–N2 1.4100(17), N1–C31 1.4968(18), N2–C38 1.3458(19), O1–C33 1.3455(17), C33–C32 1.415(2), C32–C31 1.5313(19), C31–C21 1.573(2), O1–H6 2.68, C38–S1 1.6934(16), O1–Ti1–N1 88.09(5), N2–C38–S1 119.87(12), Ti1–N1–N2 120.00(9), C38–N1–N2 122.63(13), Ct1–Ti1–Ct2 132.4 (Ct1 = centroid of C1–C5; Ct2 = centroid of C16–C20).

Table 1 Selected bond parameters (bond lengths (Å) and angles (deg)) of complexes **Ti1a**, **Ti1c** and **Ti2b**

Complex	Ti1–N1	Ti1–S1	N1–C31/C41	S1–C31/C41	Ti1–C6	N1–Ti1–S1
Ti1a	2.1839(5)	2.58107(19)	1.3354(7)	1.7175(5)	2.744	63.823(13)
Ti1c	2.2222(15)	2.5823(5)	1.349(2)	1.7118(18)	2.7516(18)	63.28(4)
Ti2b	2.1750(10)	2.5798(4)	1.3338(15)	1.7165(12)	2.756	63.99(3)



Scheme 2 Reaction of bis(π-η^5:σ-η^1-pentafulvene)titanium complex **Ti1** with thiosemicarbazone **d** to κ^2N,O-thiosemicarbazonate titanium complex **Ti1d** and additional byproducts.

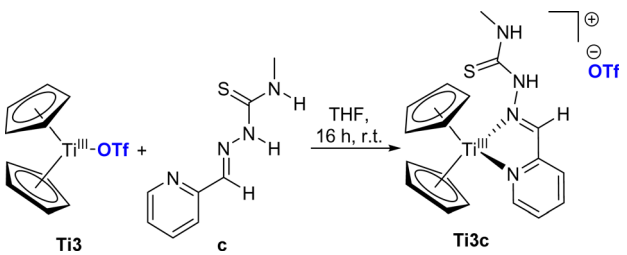
Ti1d similarly to that in a previous work.[30] Complex **Ti1d** is obtained *via* deprotonation of the acidic OH-proton by one pentafulvene unit and insertion of the C=N double bond into the Ti–C_{exo} bond of the second pentafulvene moiety alongside other byproducts (Scheme 2).

Although the byproducts could not be determined unequivocally, they are most likely precursors of **Ti1d** – either by single protonolysis or by single insertion, a complex similar to **Ti1a**, **Ti1c** and **Ti2b**, or the desired κ^3N,N,O follow-up product. While the mixture cannot be converted into a singular product by heating and changes in the reaction conditions only slightly impact the outcome, the formation of this complex demonstrates an unusual TSCN reactivity pattern.

The molecular structure of **Ti1d** reveals a slightly shortened Ti–N bond (2.0437(12) Å) and a shortened Ti–O bond (1.9152(10) Å) when compared with the sum of covalent radii (Σr_{cov}(Ti–N) = 2.07 Å, Σr_{cov}(Ti–O) = 1.99 Å).[35] These structural features are similar to a suchlike, reported κ^2N,O titanium complex (Ti–N: 2.0073(6) Å, Ti–O: 1.9332(6) Å).[30]

Reaction of TSCN with titanocene(III) triflate

As we were unable to produce ionic complexes using the first route, we attempted to obtain ionic complexes using titanocene(III) triflate (**Ti3**) as the starting material. Because treatment of **Ti3** with bidentate ligands yields ionic triflate complexes by displacement of the coordinating triflato ligand,[32] the multidentate TSCN appear to be excellent ligands for this reaction. While no reaction occurred with TSCN **a** and **b**, the reaction of **Ti3** with **c** resulted in the formation of the formal κ^2N,N titanium(III) complex **Ti3c** (Scheme 3). Because of the poor crystallization properties of



Scheme 3 Reaction of titanocene triflate **Ti3** with TSCN **c** to κ^2N,N titanium(III) triflate complex **Ti3c**.

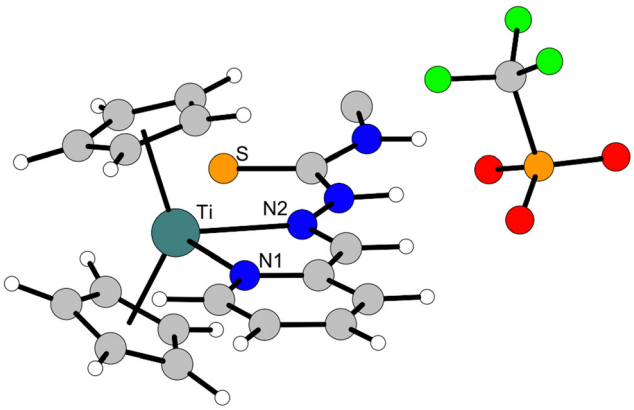


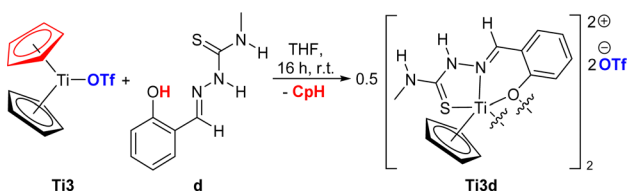
Fig. 7 Ground state optimized geometry of complex **Ti3c**, calculated in gas phase at the B3LYP/Def2-TZVP level of theory. Selected bond lengths (Å): Ti–N1 2.26, Ti–N2 2.39, Ti–S 3.71.

Ti3c, we could not obtain suitable crystals for single-crystal X-ray diffraction, therefore, we calculated the molecular structure of **Ti3c** (Fig. 7).

Although a κ^3N,N,S coordination mode seems reasonable, the respective complex is not a minimum on the potential energy surface; instead, the κ^2N,N coordination mode was revealed, as indicated by the long Ti–S distance (3.71 Å) which does not correlate to a Ti–S bond (Fig. 4). This is most likely due to the higher stability of the formal 17 electron κ^2N,N complex compared with the formal 19 electron κ^3N,N,S complex. A similar κ^2N,N complex (titanocene(III) 2-pyridinecarboxaldehyde phenylhydrazone) has also been reported previously,[32] while there are also several other examples of Ti(III) κ^2N,N complexes.[39] The formation of a Ti(III) complex is supported by EPR spectrosopy, showing a typical signal that correlates to a Ti(III) species (ESI,† Fig. S24, g = 1.980).[32,40]

In a quite different manner, the reaction of **Ti3** with TSCN **d** produces a dinuclear, dicationic κ^3O,N,S titanium complex **Ti3d** *via* protonolysis of one cyclopentadienyl ligand by the acidic OH group of the *o*-cresyl rest, whereas the former coordinating triflato ligands are displaced by the TSCN and now act as counter ions (Scheme 4). The protonolysis of a cyclopentadienyl ligand of **Ti3** is a novel reactivity that has not been reported so far and most likely ocurred due to the acidity of the OH group of TSCN **d** along with the chelating effect of the tridentate ligand and the oxophilicity of titanium complexes.[32]

The structure of **Ti3d** was revealed by single-crystal X-ray diffraction (Fig. 8), while the elemental analysis support the elemental composition of the obtained solid and verify



Scheme 4 Reaction of titanocene triflate **Ti3** with TSCN **d** to dinuclear Ti(III) thiosemicarbazonido triflate complex **Ti3d**.

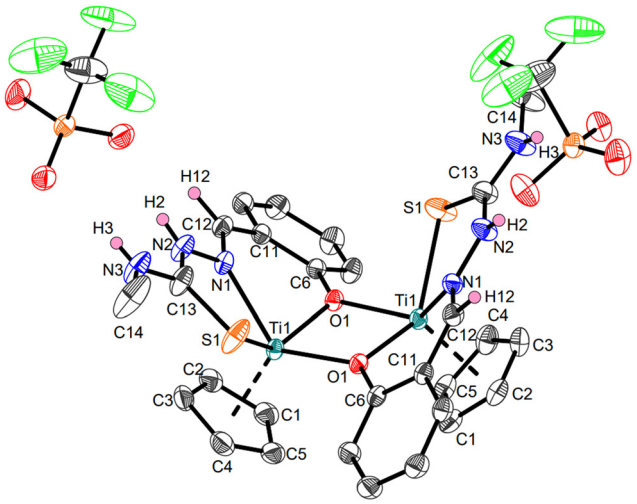


Fig. 8 Crystal structure of complex **Ti3d**. Displacement ellipsoids are drawn at the 50% probability level. Redundant H (apart from H2, H3 and H12) atoms and have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Ti1–O1 2.0482(15), Ti1–O#1 2.0639(14), Ti1–N1 2.1810(18), Ti1–S1 2.4774(7), O1–C6 1.360(2), N1–N2 1.374(3), N3–C13 1.319(3), N2–C13 1.342(3), N1–C12 1.295(3), S1–C13 1.705(2), O1–Ti1–O#1 77.83(6), Ti1–O1–Ti#1 102.09(6), N1–Ti1–O1 81.00(6), S1–Ti1–O#1 84.33(4), N1–Ti1–S1 76.95(5), N2–C13–S1 120.41(17), Ti1–N1–N2 119.66(14), C13–N2–N1 119.91(19).

the purity of **Ti3d**. The paramagnetic nature of **Ti3d** is supported by EPR spectrosopy, displaying a similar signal compared with **Ti3c**, corralating to a Ti(III) species (ESI,† Fig. S25, g = 1.977).[32,40]

Similar to the κ^2N,S-thiosemicarbazonate titanium complexes **Ti1a**, **Ti1c** and **Ti2b**, the Ti–N and Ti–S bonds are best described as elongated single bonds. The Ti–O bonds are also elongated single bonds (Σr_{cov}(Ti–O) = 1.99 Å)[35] as they are shared across two titanium cores. The triflate anions exhibit hydrogen bonds by interaction of the oxygen atoms with the NH groups of the TSCN (H2···O4 2.01(3) Å, H3···O3 2.20(4) Å). This effect was also observed with other ionic titanium triflate complexes.[32]

While this series of complexes is not suitable for further biological studies, this work provides great insight into the coordination chemistry of thiosemicarbazones within titanium complexes.

Conclusions

In this work, we employed two synthetic strategies to obtain Ti(IV) and Ti(III) complexes with bis(pentafulvene)titanium complexes and titanocene(III) triflate as starting materials. While most thiosemicarbazones (TSCN) were deprotonated in N-position by one pentafulvene unit and form κ^2N,S complexes, the OH group of the *o*-cresyl TSCN was deprotonated, revealing a κ^2N,O titanium complex. The Ti(IV) complexes were characterized by NMR spectroscopy and the ^{15}N NMR values were obtained for each nitrogen core *via* two-dimensional ^{1}H,^{15}N NMR experiments. Reaction of the pyridinyl TSCN with titanocene(III) triflate yielded a κ^2N,N titanium complex *via* ligand exchange, displacing the former coordinating triflato ligand and forming an ionic complex. Reaction with the *o*-cresyl TSCN displayed a novel reactivity of titanocene(III) triflate, as the cyclopentadienyl ligand underwent protonolysis, subsequently forming a dinuclear, dicationic κ^3O,N,S titanium complex. Herein, the multifaceted coordination chemistry of TSCN was demonstrated and the first structural examples of thiosemicarbazone-based titanium complexes obtained by single-crystal X-ray diffraction are described. Future work will focus on more applicable TSCN-based titanium complexes because none of these complexes are suitable for biological studies.

Experimental section

All reactions were carried out under a dry nitrogen or argon atmosphere using standard Schlenk and glove box techniques. Solvents were dried according to standard procedures over Na/K alloy with benzophenone as indicator and subsequently distilled and stored under a nitrogen atmosphere. The pentafulvene complexes,[37] titanocene(III) triflate[32] and TSCN[33] were prepared according to general methods and published procedures. NMR spectra were recorded on a Bruker AVANCE III 500 spectrometer (^{1}H 500 MHz). IR spectra were recorded on a Bruker Tensor 27 spectrometer using an attenuated total reflection (ATR) method. Elemental analyses were carried out on a Euro EA 3000 Elemental Analyzer. Melting points were determined using a "Mel-Temp" from Laboratory Devices, Cambridge, or a Mettler Toledo MP30. Further exact details of crystallographic data and NMR, IR, EPR spectra are given in the ESI.†

Synthesis of Ti1a

Bis(adamantylidenefulvene)titanium complex **Ti1** (300 mg, 0.675 mmol) and benzaldehyde *N*-methylthiosemicarbazone **a** (130 mg, 0.675 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red solution. The solvent was removed under reduced pressure and the residue was washed with 10 mL of *n*-hexane. All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a dark red solid. Red crystals suitable for single crystal X-ray diffraction analysis precipitated from a slowly evaporating solution of **Ti1a** in C_6D_6 after several days. Yield: 0.330 g, 0.517 mmol, 75%. ^{1}H NMR (500 MHz, C_6D_6, 305 K): δ = 1.44–2.45 (m, 27 H, Ad–H), 2.64 (d, 3 H, J = 5.0 Hz, N–CH_3), 2.74–2.82 (m, 2 H, Ad–H), 4.15–4.18 (m, 1 H, Cp–H), 4.94–4.97 (m, 1 H, Cp–H), 4.98–5.01 (m, 1 H, Cp–H), 5.13–5.17 (m, 1 H, Cp–H), 5.39–5.43 (m, 1 H, Cp–H), 5.45–5.49 (m, 1 H, Cp–H), 5.79–5.83 (m, 1 H, Cp–H), 6.13–6.17 (m, 1 H, Cp–H), 6.67 (q, 1 H, J = 5.0 Hz, N–H), 7.11–7.14 (m, 1 H, Ph–H), 7.19–7.24 (m, 2 H, Ph–H), 7.32 (s, 1 H, aldimine–H), 7.58–7.62 (m, 1 H, Ph–H) ppm. ^{13}C{^{1}H} NMR (125 MHz, C_6D_6, 305 K): δ = 28.4 (Ad–CH), 28.6 (CH_3), 28.7 (Ad–CH), 28.8 (Ad–CH), 29.7 (Ad–CH), 32.8 (Ad–CH_2), 32.9 (Ad–CH_2), 33.0 (Ad–CH), 33.3 (Ad–CH), 36.3 (Ad–CH),

36.4 (Ad–CH), 37.8 (Ad–CH_2), 38.1 (Ad–CH_2), 38.4 (Ad–CH_2), 38.5 (Ad–CH_2), 39.4 (Ad–CH_2), 39.5 (Ad–CH_2), 44.8 (Ad–CH), 44.9 (Ad–CH_2), 45.2 (Ad–CH_2), 97.8 (Cp–CH), 99.6 (Cp–CH), 101.5 (Cp–CH), 102.2 (Cp–CH), 103.7 (Cp–CH), 105.1 (Cp–CH), 105.5 (Cp–CH), 118.2 (C_{exo}–C_q), 123.3 (Cp–CH), 127.3 (2 × Ph–CH), 129.0 (2 × Ph–CH), 129.1 (Ph–CH), 130.0 (C_{ipso}–C_q), 132.9 (C_{ipso}–C_q), 136.5 (Ph–C_q), 143.2 (aldimine–CH), 181.6 (N–C_q–N) ppm. ^{15}N NMR (51 MHz, C_6D_6, 305 K): δ = 87.6 (H–N–CH_3), 211.7 (C═N–N), 346.0 (C═N–N) ppm. IR (ATR): $\tilde{\nu}$ = 3387, 3059, 3023, 2899, 2844, 2651, 2361, 2101, 1594, 1568, 1531, 1465, 1446, 1429, 1377, 1332, 1297, 1260, 1212, 1168, 1094, 1081, 1061, 1028, 946, 899, 853, 792, 754, 729, 691, 654, 618, 565, 509, 464 cm^{-1}. Mp. 109–114 °C (dec.). EA: calcd for $C_{39}H_{47}N_3STi$: C 73.45, H 7.43, N 6.59. Found: C 73.59, H 7.58, N 6.14.

Synthesis of Ti1b

Bis(adamantylidenefulvene)titanium complex **Ti1** (300 mg, 0.675 mmol) and 2-thiophenecarboxaldehyde *N*-methylthiosemicarbazone **b** (135 mg, 0.675 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red solution. The solvent was removed under reduced pressure and the residue was washed with 10 mL of *n*-hexane. All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a dark red solid. Yield: 0.376 g, 0.584 mmol, 87%. ^{1}H NMR (500 MHz, C_6D_6, 305 K): δ = 1.45–2.41 (m, 27 H, Ad–H), 2.51 (d, 3 H, J = 5.0 Hz, N–CH_3), 2.70–2.79 (m, 2 H, Ad–H), 4.11–4.15 (m, 1 H, Cp–H), 4.88–4.92 (m, 1 H, Cp–H), 4.96–5.01 (m, 1 H, Cp–H), 5.09–5.14 (m, 1 H, Cp–H), 5.37–5.40 (m, 1 H, Cp–H), 5.44–5.48 (m, 1 H, Cp–H), 5.77–5.82 (m, 1 H, Cp–H), 6.09–6.13 (m, 1 H, Cp–H), 6.62 (q, 1 H, J = 5.0 Hz, N–H), 6.75–6.78 (m, 1 H, Ar–H), 6.82–6.85 (m, 1 H, Ar–H), 6.95–6.98 (m, 1 H, Ar–H), 7.49 (s, 1 H, aldimine–H) ppm. ^{13}C{^{1}H} NMR (125 MHz, C_6D_6, 305 K): δ = 28.4 (Ad–CH), 28.6 (Ad–CH), 28.6 (CH_3), 28.6 (Ad–CH), 29.7 (Ad–CH), 32.8 (Ad–CH_2), 32.9 (Ad–CH_2), 33.0 (Ad–CH), 33.2 (Ad–CH), 36.2 (Ad–CH), 36.4 (Ad–CH), 37.8 (Ad–CH_2), 38.1 (Ad–CH_2), 38.4 (Ad–CH_2), 38.5 (Ad–CH_2), 39.4 (Ad–CH_2), 39.5 (Ad–CH_2), 44.8 (Ad–CH), 44.9 (Ad–CH_2), 45.2 (Ad–CH_2), 97.7 (Cp–CH), 99.5 (Cp–CH), 101.5 (Cp–CH), 102.0 (Cp–CH), 103.9 (Cp–CH), 105.2 (Cp–CH), 105.5 (Cp–CH), 118.2 (C_{exo}–C_q), 123.2 (Cp–CH), 126.4 (Ar–CH), 128.6 (Ar–CH), 129.3 (Ar–CH), 129.9 (C_{ipso}–C_q), 133.1 (C_{ipso}–C_q), 137.3 (aldimine–CH), 142.0 (Ar–C_q), 181.2 (N–C_q–N) ppm. ^{15}N NMR (51 MHz, C_6D_6, 305 K): δ = 88.4 (H–N–CH_3), 211.0 (C═N–N), 342.0 (C═N–N) ppm. IR (ATR): $\tilde{\nu}$ = 3386, 3099, 3022, 2899, 2845, 2667, 2360, 2341, 2108, 1579, 1536, 1465, 1447, 1429, 1371, 1351, 1331, 1289, 1259, 1212, 1166, 1096, 1071, 1041, 974, 947, 924, 857, 792, 754, 729, 695, 666, 654, 567, 504, 464 cm^{-1}. Mp. 114–121 °C (dec.). EA: calcd for $C_{37}H_{45}N_3S_2Ti$: C 69.03, H 7.05, N 6.53. Found: C 68.73, H 7.26, N 6.16.

Synthesis of Ti1c

Bis(adamantylidenefulvene)titanium complex **Ti1** (300 mg, 0.675 mmol) and 2-pyridinecarboxaldehyde *N*-methylthiosemicarbazone **c** (131 mg, 0.675 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red solution. The solvent was removed under reduced pressure and the residue was washed with 10 mL of *n*-hexane. All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a dark red solid. Orange crystals suitable for single crystal X-ray diffraction analysis precipitated from a slowly evaporating solution of **Ti1c** in C_6D_6 after several days. Yield: 0.379 g, 0.593 mmol, 88%. ^{1}H NMR (500 MHz, C_6D_6, 305 K): δ = 1.42–2.49 (m, 27 H, Ad–H), 2.64 (d, 3 H, J = 5.0 Hz, N–CH_3), 2.70–2.83 (m, 2 H, Ad–H), 4.05–4.08 (m, 1 H, Cp–H), 4.81–4.84 (m, 1 H, Cp–H), 5.05–5.08 (m, 1 H, Cp–H), 5.10–5.13 (m, 1 H, Cp–H), 5.34–5.37 (m, 1 H, Cp–H), 5.53–5.57 (m, 1 H, Cp–H), 5.85–5.88 (m, 1 H, Cp–H), 6.14–6.17 (m, 1 H, Cp–H), 6.64–6.68 (m, 1 H, Ar–H), 6.70 (q, 1 H, J = 5.0 Hz, N–H), 7.12–7.15 (m, 1 H, Ar–H), 7.62 (s, 1 H, aldimine–H), 7.72–7.75 (m, 1 H, Ar–H), 8.48–8.52 (m, 1 H, Ar–H) ppm. ^{13}C{^{1}H} NMR (125 MHz, C_6D_6, 305 K): δ = 28.4 (Ad–CH), 28.7 (CH_3), 28.8 (Ad–CH), 29.7 (Ad–CH), 32.0 (Ad–CH), 32.9 (2 × Ad–CH_2), 32.9 (Ad–CH), 33.3 (Ad–CH), 36.2 (Ad–CH), 36.3 (Ad–CH), 37.8 (Ad–CH_2), 38.1 (Ad–CH_2), 38.5 (2 × Ad–CH_2), 39.5 (Ad–CH_2), 39.5 (Ad–CH_2), 44.8 (Ad–CH), 44.9 (Ad–CH_2), 45.1 (Ad–CH_2), 98.3 (Cp–CH), 100.2 (Cp–CH), 101.8 (Cp–CH), 102.6 (Cp–CH), 103.4 (Cp–CH), 104.9 (Cp–CH), 105.3 (Cp–CH), 118.2 (C_{exo}–C_q), 119.4 (Ar–CH), 122.8 (Ar–CH), 123.1 (Cp–CH), 129.3 (Ar–C_q), 130.4 (C_{ipso}–C_q), 132.7 (C_{ipso}–C_q), 135.7 (Ar–CH), 144.3 (aldimine–CH), 150.0 (Ar–CH), 182.7 (N–C_q–N) ppm. ^{15}N NMR (51 MHz, C_6D_6, 305 K): δ = 88.4 (H–N–CH_3), 213.3 (C═N–N), 317.1 (pyridine–N), 354.6 (C═N–N) ppm. IR (ATR): $\tilde{\nu}$ = 3390, 2899, 2844, 2358, 2164, 2111, 1579, 1561, 1526, 1465, 1447, 1430, 1370, 1331, 1276, 1260, 1212, 1146, 1096, 1071, 1032, 992, 945, 931, 853, 795, 775, 730, 694, 670, 657, 618, 582, 565, 519, 464 cm^{-1}. Mp. 91–96 °C (dec.). EA: calcd for $C_{38}H_{46}N_4STi$: C 71.46, H 7.26, N 8.77. Found: C 71.23, H 7.38, N 8.70.

Attempted synthesis of Ti1d

Bis(adamantylidenefulvene)titanium complex **Ti1** (200 mg, 0.450 mmol) and salicylaldehyde *N*-methylthiosemicarbazone **d** (94 mg, 0.450 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red brown solution. The solvent was removed under reduced pressure and the residue was washed with 10 mL of *n*-hexane. All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield a red brown solid. Orange crystals suitable for single crystal X-ray diffraction analysis precipitated from a saturated solution of the product mixture in toluene at −20 °C after several days. Further characterization is ommited as this reaction resulted in a mixture of products which was not further characterized.

Synthesis of Ti2a

Bis(di-*para*-tolylfulvene)titanium complex **Ti2** (300 mg, 0.531 mmol) and benzaldehyde *N*-methylthiosemicarbazone **a** (103 mg, 0.531 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red solution. The solvent was removed under reduced pressure and the residue was washed with 10 mL of

n-hexane. All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a dark red solid. Yield: 0.283 g, 0.373 mmol, 70%. ^{1}H NMR (500 MHz, C_6D_6, 305 K): δ = 1.99 (s, 3 H, *p*-Tol–CH_3), 2.08 (s, 3 H, *p*-Tol–CH_3), 2.12 (s, 6 H, 2 × *p*-Tol–CH_3), 2.49 (d, 3 H, J = 4.9 Hz, N–CH_3), 4.80–4.83 (m, 1 H, Cp–H), 5.02–5.05 (m, 1 H, Cp–H), 5.10–5.13 (m, 1 H, Cp–H), 5.16–5.18 (m, 1 H, Cp–H), 5.19 (s, 1 H, C_{exo}–H), 5.64–5.69 (m, 2 H, 2 × Cp–H), 5.73–5.76 (m, 1 H, Cp–H), 5.90–5.93 (m, 1 H, Cp–H), 6.58 (q, 1 H, J = 4.9 Hz, N–H), 6.79–6.82 (m, 3 H, Ar–H), 6.99 (s, 1 H, aldimine–H), 6.99–7.15 (m, 10 H, Ar–H), 7.35–7.39 (m, 4 H, Ar–H), 7.45–7.48 (m, 2 H, Ar–H), 7.50–7.55 (m, 2 H, Ar–H) ppm. ^{13}C{^{1}H} NMR (125 MHz, C_6D_6, 305 K): δ = 20.9 (2 × *p*-Tol–CH_3), 21.0 (2 × *p*-Tol–CH_3), 28.5 (N–CH_3), 53.1 (C_{exo}H), 99.0 (Cp–CH), 100.3 (Cp–CH), 104.7 (Cp–CH), 107.2 (Cp–CH), 108.5 (Cp–CH), 108.7 (Cp–CH), 110.0 (Cp–CH), 120.9 (C_{exo}–C_q), 123.6 (Cp–CH), 127.4 (2 × Ar–CH), 127.5 (Ar–C_q), 128.6 (Ar–C_q), 128.7 (2 × Ar–CH), 128.8 (2 × Ar–CH), 129.0 (2 × Ar–CH), 129.0 (Ar–CH), 129.1 (2 × Ar–CH), 129.2 (2 × Ar–CH), 129.3 (2 × Ar–CH), 129.5 (2 × Ar–CH), 129.6 (2 × Ar–CH), 129.9 (C_{ipso}–C_q), 130.8 (2 × Ar–CH), 135.4 (2 × Ar–C_q), 135.9 (2 × Ar–C_q), 136.2 (Ar–C_q), 140.7 (2 × Ar–C_q), 142.9 (aldimine–CH), 143.2 (C_{ipso}–C_q), 143.2 (2 × Ar–C_q), 178.1 (N–C_q–N) ppm. ^{15}N NMR (51 MHz, C_6D_6, 305 K): δ = 87.6 (H–N–CH_3), 207.8 (C═N–N), 345.2 (C═N–N) ppm. IR (ATR): $\tilde{\nu}$ = 3399, 3020, 2919, 2862, 2360, 1594, 1568, 1531, 1508, 1467, 1447, 1431, 1379, 1332, 1301, 1261, 1220, 1188, 1160, 1085, 1066, 1042, 1020, 946, 886, 795, 765, 759, 730, 694, 656, 619, 593, 575, 563, 544, 510, 458, 465 cm^{-1}. Mp. 184–187 °C (dec.). EA: calcd for $C_{49}H_{47}N_3STi$: C 77.66, H 6.25, N 5.54. Found: C 77.66, H 6.42, N 5.28.

Synthesis of Ti2b

Bis(di-*para*-tolylfulvene)titanium complex **Ti2** (300 mg, 0.531 mmol) and 2-thiophenecarboxaldehyde *N*-methylthiosemicarbazone **b** (106 mg, 0.531 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red solution. The solvent was removed under reduced pressure and the residue was washed with 10 mL of *n*-hexane. All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a dark red solid. Red crystals suitable for single crystal X-ray diffraction analysis precipitated from a slowly evaporating solution of **Ti2b** in C_6D_6 after several days. Yield: 0.323 g, 0.423 mmol, 80%. ^{1}H NMR (500 MHz, C_6D_6, 305 K): δ = 2.01 (s, 3 H, *p*-Tol–CH_3), 2.06 (s, 3 H, *p*-Tol–CH_3), 2.12 (s, 3 H, *p*-Tol–CH_3), 2.14 (s, 3 H, *p*-Tol–CH_3), 2.36 (d, 3 H, J = 4.9 Hz, N–CH_3), 4.76–4.79 (m, 1 H, Cp–H), 5.00–5.03 (m, 1 H, Cp–H), 5.07–5.10 (m, 1 H, Cp–H), 5.14 (s, 1 H, C_{exo}–H), 5.18–5.21 (m, 1 H, Cp–H), 5.61–5.64 (m, 1 H, Cp–H), 5.67–5.70 (m, 1 H, Cp–H), 5.71–5.74 (m, 1 H, Cp–H), 5.89–5.92 (m, 1 H, Cp–H), 6.56 (q, 1 H, J = 4.9 Hz, N–H), 6.70–6.72 (m, 2 H, Ar–H), 6.78–6.87 (m, 5 H, Ar–H), 6.99–7.03 (m, 4 H, Ar–H), 7.04–7.07 (m, 2 H, Ar–H), 7.13 (s, 1 H, aldimine–H), 7.34–7.39 (m, 2 H, Ar–H), 7.43–7.45 (m, 2 H, Ar–H), 7.47–7.52 (m, 2 H, Ar–H) ppm. ^{13}C{^{1}H} NMR (125 MHz, C_6D_6, 305 K): δ = 20.9 (2 × *p*-Tol–CH_3), 21.1 (2 × *p*-Tol–CH_3), 28.7 (N–CH_3), 53.1 (C_{exo}H), 99.1 (Cp–CH), 100.4 (Cp–CH), 104.4 (Cp–CH), 107.3 (Cp–CH), 108.5 (Cp–CH), 108.6 (Cp–CH), 109.9 (Cp–CH), 121.0 (C_{exo}–C_q), 123.5 (Cp–CH), 126.3 (Ar–CH), 127.4 (2 × Ar–CH), 127.5 (Ar–C_q), 128.6 (Ar–C_q), 128.7 (Ar–CH), 128.8 (2 × Ar–CH), 128.9 (2 × Ar–CH), 129.1 (2 × Ar–CH), 129.2 (2 × Ar–CH), 129.3 (Ar–CH), 129.6 (2 × Ar–CH), 129.6 (2 × Ar–CH), 129.8 (C_{ipso}–C_q), 130.7 (2 × Ar–CH), 135.4 (2 × Ar–C_q), 135.9 (2 × Ar–C_q), 137.1 (Ar–C_q), 141.7 (2 × Ar–C_q), 143.0 (aldimine–CH), 143.3 (C_{ipso}–C_q), 177.7 (N–C_q–N) ppm. ^{15}N NMR (51 MHz, C_6D_6, 305 K): δ = 87.6 (H–N–CH_3), 207.0 (C═N–N), 341.3 (C═N–N) ppm. IR (ATR): $\tilde{\nu}$ = 3395, 3020, 2916, 2358, 1579, 1536, 1507, 1467, 1448, 1430, 1372, 1332, 1289, 1232, 1214, 1180, 1159, 1112, 1082, 1042, 1020, 930, 885, 858, 828, 806, 793, 767, 755, 730, 710, 697, 654, 593, 576, 563, 544, 506, 486, 464 cm^{-1}. Mp. 182–186 °C (dec.). EA: calcd for $C_{47}H_{45}N_3S_2Ti$: C 73.90, H 5.94, N 5.50. Found: C 74.09, H 5.84, N 5.57.

Synthesis of Ti3c

Titanocene(III)triflate **Ti3** (100 mg, 0.306 mmol) and 2-pyridinecarboxaldehyde *N*-methylthiosemicarbazone **c** (59.4 mg, 0.306 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a dark red solution. The solvent was removed under reduced pressure and the residue was washed with *n*-hexane (3 × 10 mL). All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a red solid. Yield: 121 mg, 0.232 mmol, 76%. IR (ATR): $\tilde{\nu}$ = 3283, 3120, 2944, 1587, 1526, 1469, 1435, 1325, 1236, 1212, 1164, 1109, 1083, 1019, 998, 929, 814, 778, 766, 726, 676, 629, 592, 516, 467, 412 cm^{-1}. Mp. 166 °C (dec.). EPR: g = 1.980. EA: calcd for $C_{19}H_{20}F_3N_4S_2O_3Ti$: C 43.77, H 3.87, N 10.75. Found: C 43.73, H 3.91, N 10.44.

Synthesis of Ti3d

Titanocene(III)triflate **Ti3** (100 mg, 0.306 mmol) and salicylaldehyde *N*-methylthiosemicarbazone **d** (64 mg, 0.306 mmol) were dissolved in 10 ml of dry THF. The reaction mixture was stirred for 16 h at room temperature to give a yellow solution. The solvent was removed under reduced pressure and the residue was washed with *n*-hexane (3 × 10 mL). All volatile components were removed under reduced pressure and the residue was dried under vacuum to yield the product as a brown solid. Yield: 121 mg, 0.232 mmol, 76%. IR (ATR): $\tilde{\nu}$ = 3241, 3051, 2942, 1602, 1560, 1480, 1468, 1440, 1401, 1360, 1339, 1272, 1243, 1223, 1157, 1026, 964, 917, 816, 794, 764, 731, 696, 626, 591, 576, 544, 516, 456, 405 cm^{-1}. Mp. 195 °C (dec.). EPR: g = 1.977. EA: calcd for $C_{15}H_{15}F_3N_3S_2O_4Ti$: C 38.31, H 3.21, N 8.93. Found: C 38.85, H 3.64, N 9.10.

Author contributions

Conceptualization, methodology, synthesis, characterization, writing – original draft preparation, writing – review and editing: K. S., synthesis, characterization: M. C., X-ray crystallography: M. S., supervision, funding acquisition, writing – review and editing: R. B.

Data availability

CCDC 2377765 (**Ti1a**), 2377767 (**Ti1c**), 2377764 (**Ti1d**), 2377768 (**Ti2b**), 2377766 (**Ti3d**) contain supplementary crystallographic data for this paper. The data supporting this article have been included as part of the ESI.†

Conflicts of interest

The authors declare no competing financial interest.

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