

DOI: 10.1002/zaac.202200277

# Tricyanated Ferrocenes; Isolation, structure, electrochemistry and DFT calculations

Tobias Blockhaus,<sup>[a]</sup> Fabian L. Zott,<sup>[a]</sup> Peter M. Zehetmaier,<sup>[a]</sup> Christian Klein-Heßling,<sup>[a]</sup> and Karlheinz Sünkel<sup>\*[a]</sup>

Dedicated to Prof. Dr. Dr. h. c. Wolfgang Beck on the occasion of his 90th birthday

1,2,3- Tricyanoferrrocene and 1,3-dibromo-2,4,5-tricyanoferrrocene have been synthesized via metallation and usage of dimethylmalononitrile (DMMN) as cyanating agent. They are the first compounds where three nitrile functions could be introduced into the ferrocene skeleton. Further studies on the electrophilic cyanation of lithiated haloferrocenes  $[\text{Fe}(\text{C}_5\text{H}_m\text{X}_4\text{Li})(\text{C}_5\text{H}_5)]$  ( $\text{X}=\text{Cl}, \text{Br}; m=0-3$ ) show the formation of complex

mixtures of cyano-halo-ferrocenes  $[\text{Fe}(\text{C}_5\text{H}_m\text{X}_{5-m-n}(\text{CN})_n)(\text{C}_5\text{H}_5)]$  ( $m=0-3, n=0-3$ ) most likely induced by “halogen-dance” reactions. The molecular and crystal structures of  $[\text{Fe}(\text{C}_5\text{H}_2(\text{CN})_3)(\text{C}_5\text{H}_5)]$  and  $[\text{Fe}(\text{C}_5\text{Cl}_4\text{CN})(\text{C}_5\text{H}_5)]$  are discussed. Cyclic voltametric studies of both tricyanoferrrocenes show irreversible oxidations at very high potentials ( $E_{\text{onset}} \approx 845$  mV and 945 mV, respectively, vs  $\text{FCH}/\text{FCH}^+$ ).

## Introduction

The chemistry of nitrile compounds continues to be extensively explored, as can be concluded from the large number of recent review articles devoted to their synthesis.<sup>[1]</sup> This continuous interest is certainly due to the fact that nitriles not only themselves have widespread industrial applications, e.g. in pharmaceuticals,<sup>[2]</sup> but also can easily be transformed to numerous other functional groups, including nitrogen containing heterocycles.<sup>[3]</sup> For the coordination chemist, nitriles have proven as ligands with good leaving group abilities.<sup>[4]</sup> Ferrocene has been recognized as a “bioisosteric replacement for benzene”,<sup>[5]</sup> which is the reason for its successful application in medicinal chemistry.<sup>[6]</sup> It could be shown for example, that certain nitrile hydratase/ amidase enzymes can induce biotransformations on cyanoferrrocene  $[\text{Fe}(\text{C}_5\text{H}_4\text{CN})(\text{C}_5\text{H}_5)]$  (**1c**).<sup>[7]</sup> The antitubercular properties of a ferrocenyl thiadiazole, which was prepared via a condensation-cyclization reaction from **1c**,<sup>[8]</sup> and a ferrocenyl-isoquinolinone, which was also prepared from **1c**, were examined in a study directed towards tankyrase inhibitors.<sup>[9]</sup> Besides these limited medicinal studies, **1c** has mainly been used as ligand for metals like Cu, Ag, Rh or Pt.<sup>[10]</sup>

Cyanoferrrocene **1c**, first reported in 1957,<sup>[11]</sup> is a generally well-studied compound (156 references according to SciFinder<sup>®</sup>, accessed on January 10th, 2022), and many synthetic approaches have been reported, with many different starting materials, and yields between 5 and 90%.<sup>[9,11–20]</sup> In contrast to this, there are rather few reports on the three isomeric dicyanoferrrocenes (24 entries on 1,1'-, two entries on 1,2- and one on 1,3- dicyanoferrrocene) and none on ferrocenes with three or more cyano substituents. 1,2- Dicyanoferrrocene had been prepared from 1,2-diformylferrrocene either via the dioxime,<sup>[17b]</sup> or via treatment with  $\text{NH}_3/\text{I}_2$ .<sup>[15]</sup> An alternative approach started from 1,2-dibromoferrrocene, using a Pd-catalyzed cyanation with  $\text{Zn}(\text{CN})_2$ .<sup>[17a]</sup> The yields of dicyanoferrrocene were 71 %, 97 % and 16 %, respectively

Two old claims on “decacyanoferrrocene” could later be shown to be erroneous and the obtained compounds were found to be Fe nitrile-complexes.<sup>[21]</sup> Since we are working for quite a while on the coordination chemistry of tetra- and pentacyanocyclopentadienide and obtained so far only monomeric or polymeric N-coordinated complexes,<sup>[22]</sup> we found it worthwhile to look for synthetic pathways towards  $\pi$ -coordinated polycyanocyclopentadienyl complexes. Recently we reported the serendipitous synthesis of tricyanocymantrene.<sup>[23]</sup> Here we report on our studies towards the synthesis of polycyanoferrrocenes.

## Results and Discussion

### Synthetic Studies

Amazed by the near quantitative yield of 1,2-dicyanoferrrocene obtained with the  $\text{NH}_3/\text{I}_2$  method, we first considered a synthesis of tricyanoferrrocene via the known 1,2,3-triformylferrrocene.<sup>[24]</sup> Although we followed the synthetic pathway described in this publication, we failed to reproduce

[a] Dr. T. Blockhaus, MSc. F. L. Zott, Dr. P. M. Zehetmaier, Dr. C. Klein-Heßling, Prof. Dr. K. Sünkel  
Department Chemistry  
Ludwig Maximilians University Munich  
Butenandtstr. 5–13, 81377 Munich, Germany  
E-mail: [suenk@cup.uni-muenchen.de](mailto:suenk@cup.uni-muenchen.de)

Supporting information for this article is available on the WWW under <https://doi.org/10.1002/zaac.202200277>

© 2022 The Authors. Zeitschrift für anorganische und allgemeine Chemie published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution Non-Commercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

acceptable yields. While the formylations approximately matched the literature values, the dioxanyl functionalization and especially the removal of the 1,3-dioxanyl protection group couldn't be reproduced. Therefore, no attempts were made to transform the triformylferrocene to the tricyano compound (Supporting Info).

We have recently started to look at the electrophilic cyanation of lithiated metallocenes with dimethylmalonodinitrile ("DMMN").<sup>[14]</sup> This reagent was introduced as cyanation reagent for carbanions in 2015,<sup>[25]</sup> and several synthetic modifications using nickel or rhodium catalysis have appeared since then.<sup>[26]</sup> We therefore decided to look at the electrophilic cyanation of lithiated ferrocenes with this reagent.

Lithiation of ferrocene with <sup>t</sup>BuLi/KO<sup>t</sup>Bu in THF followed by electrophilic quench with DMMN yielded apparently unreacted ferrocene (according to <sup>1</sup>H NMR ca. 35% recovery) and cyanoferrocene **1b** as main products (Scheme 1). After chromatographic work-up **1b** was isolated in 55% yield. An intermediate like **A** has been suggested before, as well as its decomposition to a nitrile or its hydrolysis to a ketone.<sup>[25]</sup> (For the numbering scheme, see Table S1 of the SI. Basically, in the general formula [Fe(C<sub>5</sub>H<sub>5</sub>){C<sub>5</sub>H<sub>m</sub>(CN)<sub>n</sub>X<sub>5-m-n</sub>}] the numerical of the compound name corresponds to 5-*m* for X=Br and 10-*m* for X=Cl, e.g. all compounds **1** and **6** have four hydrogens on the substituted ring, **2** and **7** have three and so on. The lettering in the name corresponds to the number *n* of cyano substituents: **a** has none, **b** has one, and so on.)

Next, we had a look at the reactivity of compound **1b**. Kinetic studies of H-D-exchange under acidic conditions had shown that **1b** was very unreactive.<sup>[27]</sup> Treatment of **1b** with TMPMgCl.LiCl followed by electrophilic quench had been reported to give several 1,2-disubstituted cyanoferrocenes, including 1,2-dicyanoferrocene **2c**-1,2.<sup>[17a,28]</sup>

Therefore, we used **1b** as starting material and DMMN or tetrabromoethane as electrophiles. We tried out sterically hindered lithium bases under different conditions. The amount of lithium base or lithiation time didn't show any clear trend, the main impact resulted from the lithiation temperature; above -35 °C the nucleophilic attack of the nitrile function and other side reactions became increasingly important. Below -50 °C merely the starting material **1b** could be recovered (Table S6 of the Supporting Information). While with LDA the amount of

recovered starting material decreased with increasing temperature, no cyanoferrocenes could be identified. This might be the consequence of the work-up procedures, which included a silica gel filtration of the reaction mixture. Thus, an ionic product like **A** or a trimerization product of **1c**, as has been observed with other nitriles and BuLi or LDA,<sup>[29]</sup> might remain in the silica, when THF is the solvent. With LiTMP as base, we could reproducibly obtain mixtures of apparently unreacted **1b** with 1,2-dicyanoferrocene **2c** and 1,2,3-tricyanoferrocene **3d** (Scheme 2), together with varying amounts of unidentified side products.

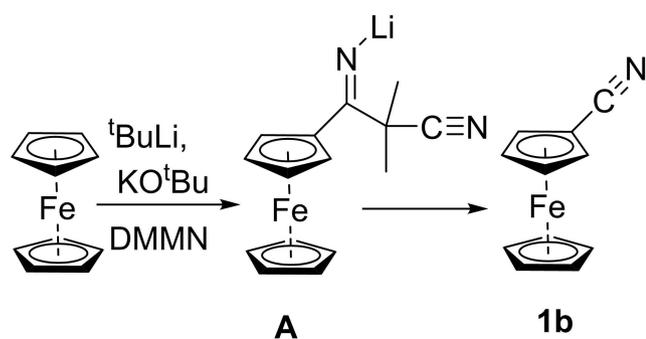
The highest obtained yields were 23% for 1,2-dicyanoferrocene **2c** and 6–8% for the 1,2,3-tricyanoferrocene **3d**.

Using **2c** and **3d** as starting materials for further cyanations led only to decomposition.

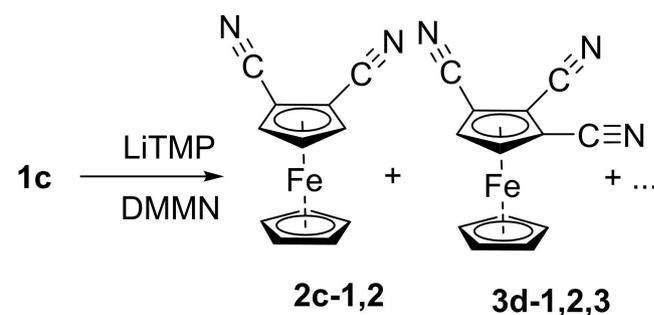
Compound **3d** was characterized by <sup>1</sup>H, <sup>13</sup>C NMR and IR spectra as well as by HRMS and also yielded crystals that were suitable for an X-ray diffraction study. **2c** has been reported before (see also above).<sup>[15,20]</sup>

From our experience with cymantrene chemistry we knew, that pentabromocyclopentadienyl complexes are also good starting materials for the perfunctionalization of a cyclopentadienyl ring.<sup>[30]</sup> The reactivity of 1,2,3,4,5-pentabromoferrocene (**5a**) has apparently not yet been studied. We therefore decided to look also at a possible electrophilic cyanation of **5a**.

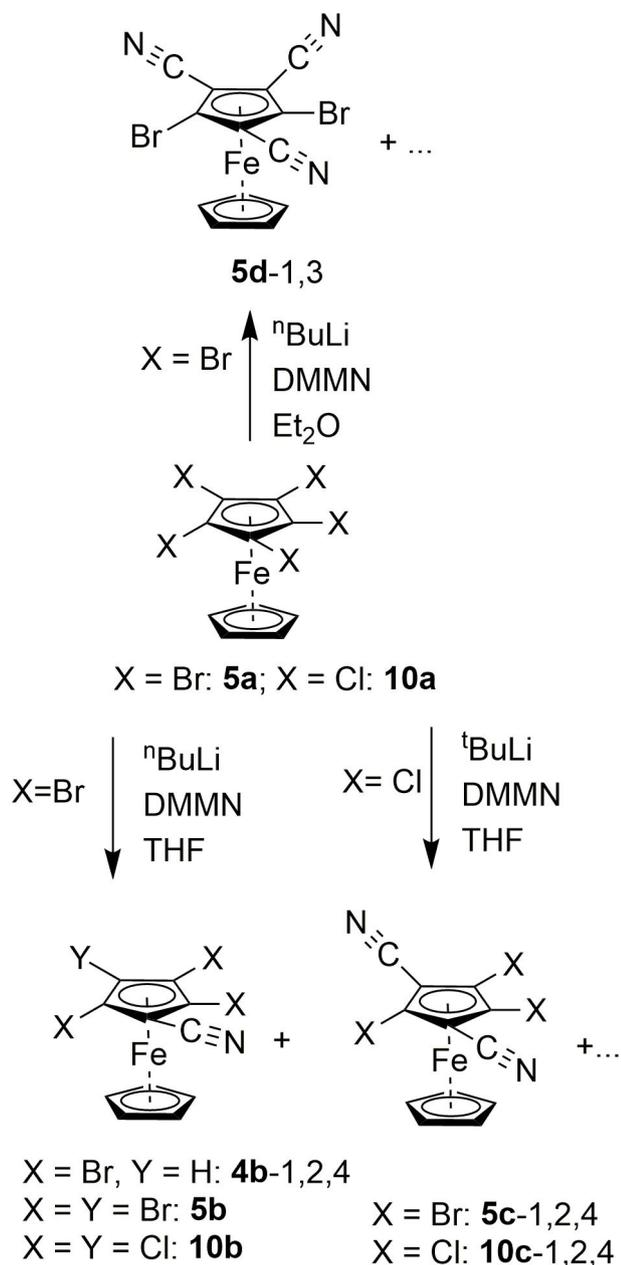
In the cymantrene system, treatment of [Mn(C<sub>5</sub>Br<sub>5</sub>)(CO)<sub>3</sub>] with one or two equivalents of <sup>n</sup>BuLi at -78 °C leads selectively to the mono- or 1,3-di-substituted products. For the sake of comparison, we treated **5a** at -78 °C in Et<sub>2</sub>O with 2.0 eq. <sup>n</sup>BuLi followed by hydrolysis with MeOH and obtained a 91% yield of 1,2,4-tribromoferrocene **3a**-1,2,4. The reaction of **5a** with 1.0 eq. <sup>n</sup>BuLi and DMMN in Et<sub>2</sub>O or THF at -78 °C, followed by slow warming-up to r.t. within 16 h, afforded complex mixtures of several bromo- and bromo-cyano-ferrocenes [Fe{C<sub>5</sub>H<sub>m</sub>Br<sub>5-m</sub>(CN)<sub>n</sub>}(C<sub>5</sub>H<sub>5</sub>)]. 1,3-Dibromo-2,4,5-tricyanoferrocene (**5d**) could be isolated from the reaction in Et<sub>2</sub>O, while **4b**, **5b** and **5c** could be isolated from the reaction in THF (Scheme 3 and Table S3, entries 5 and 6, in the SI). The <sup>1</sup>H-NMR and MS data did not allow specification of the regiochemistry of compound **5d**, however, the structure solutions obtained with some low-quality crystals suggested the stereochemistry shown in Scheme 3. Further support for the suggested stereochemistry



Scheme 1. Electrophilic cyanation of lithiated ferrocene.



Scheme 2. Reaction of monocyanoferrocene **1c** with LiTMP and DMMN.



**Scheme 3.** Reactions of the pentahaloferrocenes **5a** and **10a** with BuLi and DMMN.

comes from our earlier observation, that pentabromocycman-trene and butyl lithium usually react to 1,3-disubstituted and 1,2,4-trisubstituted products.<sup>[29]</sup>

We also had a look at the reactions of bromoferrocenes **1a-4a** with 1.5 equivalents of LiTMP and DMMN. Quite astonishingly, despite the low excess of base in nearly all cases a mixture of tri-, tetra- and pentasubstituted mixed bromocyanoferrocenes was obtained, including the tricyanoferrocene **5d** (see Table S3, entries 1–4, of the Supporting Information). Quite astonishingly, in the product mixture obtained from **1a** also dimethylsuccinonitrile could be identified (NMR, MS and X-ray structure).

Next, we studied the reaction of pentachloroferrocene **10a** with  $t\text{BuLi}$  and DMMN (Scheme 3). We obtained again a complex product mixture, from which the mono- and dicyano complexes **10b** and **10c** could be identified together with all chloroferrocenes. The specific outcome of this and some other reactions of lithiated chloroferrocenes with DMMN are summarized in Table S4 of the SI.

All compounds in Schemes 2 and 3 could be characterized by NMR and/ or mass spectrometry (see Tables S2 - S5 of the Supporting Information). We obtained crystals of compounds **5b**, **5d**, **10b**, but only the ones from **10b** were of sufficient quality for publication (for preliminary views of the molecular structures of **5b** and **5d** see Figures S1 – S2 of the Supporting Information). No attempt was made to optimize yields of individual compounds.

The formation of dimethylsuccinonitrile hints to an alternative radical pathway in the cyanation with DMMN. The “parent”  $\text{Fc-CMe}_2\text{CN}$  has been reported as the product of a radical reaction of ferrocene with azodiisobutyronitrile.<sup>[31]</sup>

The complex product mixtures that were obtained whenever a bromine or chlorine substituent was involved are a clear indication for the operation of “halogen-dance” reactions.<sup>[32]</sup> While they are quite common for bromo- and iodoferrocenes, they make the isolation of pure compounds in acceptable yields very difficult (however, recently “halogen dance” reactions have successfully been used for stereospecific synthesis of multi-substituted ferrocenes.<sup>[33]</sup>).

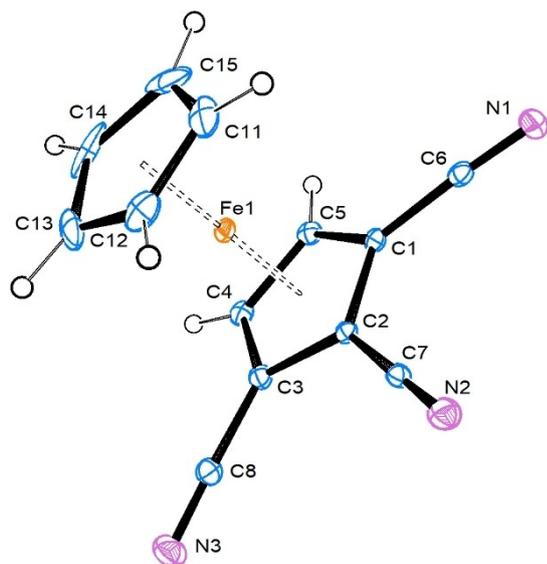
### Crystallography

It was very difficult to obtain suitable crystals of compound **3d**. Most crystals suffered from severe twinning, which made meaningful structure solutions impossible. Even the crystal finally used for the structure discussed here showed twinning and had to be refined with a modified dataset (“HKLF5”). It should be mentioned here, that also the crystal structure determination of the known compound **2c** suffered from twinning.<sup>[17b]</sup> Compound **3d** crystallizes in the monoclinic space group  $P2_1/n$ . The asymmetric unit is displayed in Figure 1.

The C–N bond lengths are nearly identical and also with the bond length reported for the structure of **2c** (see Table 1). The C–CN bonds are close to linear, as usual. The substituted cyclopentadienyl ring is slightly distorted towards a “butadienyl” form (C1–C5 1.427(3)/ C1–C2 1.440(3)/ C2–C3 1.442(3)/ C3–C4 1.428(3)/ C4–C5 1.416(3) Å). Both rings are planar (r.m.s. deviations 0.0028 Å and 0.0019 Å) for the substituted and unsubstituted ring, respectively, with the iron atom significantly closer (by 0.021(1) Å) to the former. All nitrile groups are bent away from the iron atom out of the ring plane, with the largest deviation observed for the middle cyano group.

Compound **10b** crystallized in the monoclinic space group  $P2_1/m$  with half a molecule in the asymmetric unit, i.e., the iron atom, the CCN group and one CH group are situated on a mirror plane (Figure 2).

Both rings are planar (r.m.s. deviations 0.0039 and 0.0007 Å for the substituted and unsubstituted ring, respectively), with



**Figure 1.** Molecular structure of **3d**. Thermal ellipsoids at 30% probability level.

the iron atom significantly (by 0.040(2) Å) closer to the substituted ring. The C–Cl bond lengths are identical (1.705(4) and 1.704(4) Å) and correspond to the usually observed values. All substituents are bent away to the distal side of the ring (C11 by 0.119(1) Å, C12 by 0.075(1) Å), with the largest shift observed for the nitrile nitrogen (0.201(8) Å). In contrast to the structure of **3d**, there are no bond alternations in both rings. The unusually short C–N bond in combination with the significant deviation from linearity of the CCN group might be an artifact due to the crystallographically enforced placement of this group on the mirror plane.

We also performed a Hirshfeld Analysis for the analysis of non-covalent interactions in the crystal.<sup>[34]</sup> Details of this analysis and a short discussion can be found in the Supporting Information.

## Electrochemistry

The electrochemistry of cyanoferrocenes was investigated by cyclic voltammetry in previous publications. Half-wave potentials (relative to the FcH/FcH<sup>+</sup> couple) for monocyanoferrrocene at 436 mV (1.0 mmol/L in CH<sub>2</sub>Cl<sub>2</sub> with 0.1 mmol/L NBu<sub>4</sub>B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub> as supporting electrolyte, scan rate 100 mV/s)<sup>[10d]</sup> and for the dicyanoferrrocene compound at either 767 mV (concentration not given, in CH<sub>2</sub>Cl<sub>2</sub> with 0.1 mmol/L NBu<sub>4</sub>PF<sub>6</sub> as supporting electrolyte, scan rate 100 mV/s)<sup>[12a]</sup> or 860 mV (1.0 mmol/L in CH<sub>2</sub>Cl<sub>2</sub> with 0.1 mmol/L NBu<sub>4</sub>B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub> as supporting electrolyte, scan rate 100 mV/s)<sup>[17b]</sup> were reported.

For both cases the oxidations are to be classified as reversible one-electron transfers. Generally, for functionalized ferrocenes a linear relation between the Hammett parameter  $\sigma_p$  (CN: 0.66) of the substituent and the redox potential  $E_{1/2}$  at the iron center exists.<sup>[35]</sup>

Cyclovoltammetric measurements were performed of compounds **3d** and **5d**. For both compounds, the oxidation waves can be classified as irreversible one-electron processes (Figure 3). While for reversible one-electron processes and also for the majority of quasi-reversible processes the  $E_{1/2} = E(0)$  approximation provides in practice reliable values, the “onset” – although not as clearly defined as the half-wave potential – is more suitable for irreversible processes, and also gives better results in bandgap calculations.<sup>[36]</sup>

The onsets of the oxidation peaks are found for **3d** and **5d** at  $E_{1/2} = 845$  mV and 945 mV, respectively (relative to FcH/FcH<sup>+</sup>).

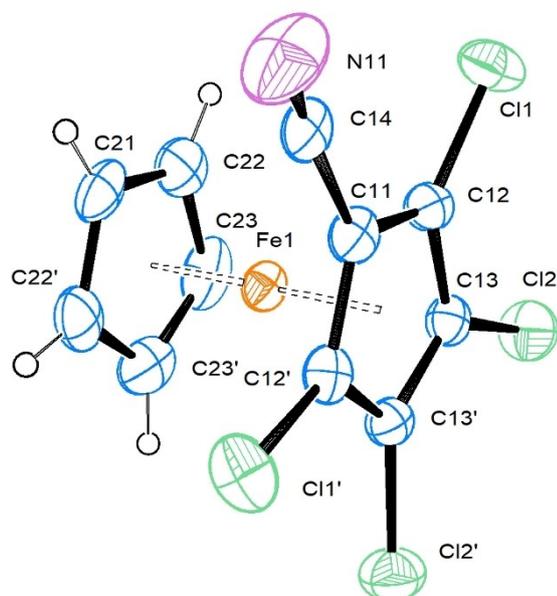
For compound **5d** also the reduction wave was examined, which appeared also to be irreversible (Figure S6). The onset of the reduction wave was found at –1.38 V (vs FcH/FcH<sup>+</sup>), corresponding to a HOMO-LUMO gap of 2.325 eV.

## DFT calculations

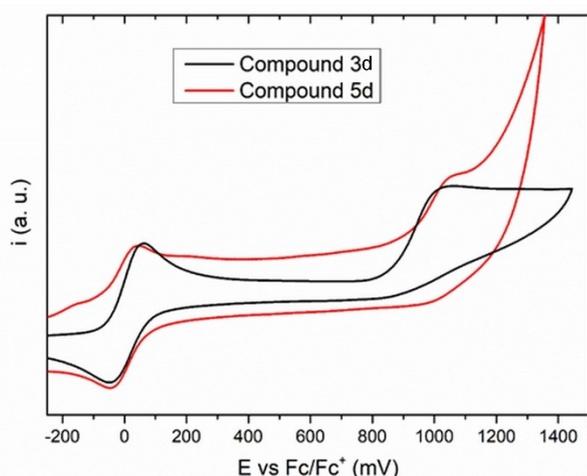
In order to investigate the electrochemical process more closely the frontier orbitals were examined. Geometry optimization as well as frequency calculations were performed using the Gaussian 09 suite at the (U)B3LYP–D3/Def2TZVP and (U)B3LYP(D3)/Def2TZVP level of theory with the implicit continuum solvation model (SMD) in acetonitrile. This method has

**Table 1.** Bond parameters of **3d** and **10b** in comparison with **1b** and **2c**.

	<b>3d</b>	<b>10b</b>	<b>1b</b> <sup>[21]</sup>	<b>2c</b> <sup>[17b]</sup>
Fe–CT <sub>sub</sub>	1.635(1)	1.622(2)	1.642(1)	1.645(1)
Fe–CT <sub>H</sub>	1.656(1)	1.662(2)	1.649(1)	1.655(1)
(C–C) <sub>sub</sub>	1.416(3)–1.442(3)	1.421(5)–1.428(5)	1.409(4)–1.435(4)	1.412(4)–1.448(3)
(C–C) <sub>H</sub>	1.386(5)–1.425(5)	1.396(9)–1.404(8)	1.399(5)–1.410(5)	1.415(3)–1.430(4)
C–N	1.143(3) 1.147(3) 1.147(3)	1.004(9)	1.139(3)	1.143(3)
C–CN	176.2(2) 179.6(2) 177.2(2)	172.8(7)	179.4(3)	178.4(3)



**Figure 2.** Molecular Structure of **10b**. Thermal ellipsoids at the 30% probability level.

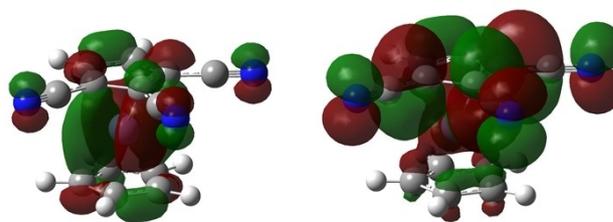


**Figure 3.** Cyclic voltammograms of **3d** and **5d** (0.1 M); ferrocene (0.1 M) as internal standard, electrolyte  $\text{NEt}_4\text{PF}_6$  (0.1 M); work-/counter electrode: Pt; reference: Ag.

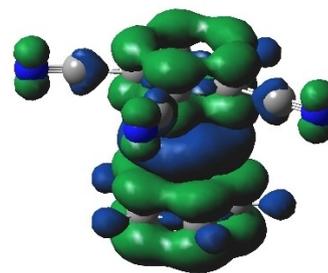
been found accurate in benchmark experiments for the ferrocenium/ferrocene system.<sup>[37]</sup>

In case of **3d** the nitrile functions contribute substantially to the HOMO extension increasing the probability that an oxidation occurs here (Figure 4) leading to a lower potential than the theoretically predicted one. This also would explain why for compound **5d** no further increase of the oxidation potential due to the bromine substituents is observed.

Quite interestingly, similar to the calculations made for the  $[\text{Fe}(\text{C}_5(\text{SR})_5)(\text{C}_5\text{H}_5)]$  systems,<sup>[27]</sup> a spin density calculation for  $[\mathbf{3d}]^+$  shows only a small contribution of the ring substituents to the spin density (Figure 5).



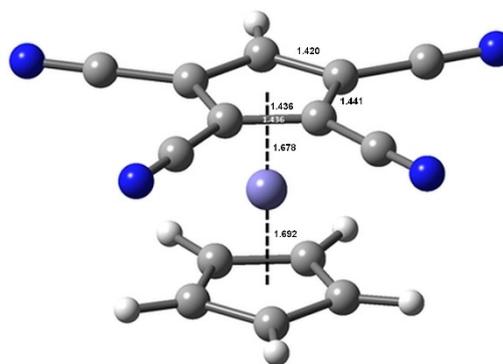
**Figure 4.** HOMO (left)/LUMO (right)-Plot of compound **3d** on the B3LYP/Def2SVP level of theory.



**Figure 5.** Spin density plot of compound  $[\mathbf{3d}]^+$ .

For the sake of comparison calculations of the energy differences between the cationic and neutral species for all the compounds  $[\text{Fe}(\text{C}_5\text{H}_{5-n}(\text{CN})_n)(\text{C}_5\text{H}_5)]$  ( $n=0-3$ ) were performed. For the tricyanated compound a theoretical value of 930 mV was obtained which fits nicely with the experimentally observed oxidation around 900 mV (see above and Table S7 of the Supporting Information).

We also performed calculations on the same level of theory for several other ferrocenes with a substituted Cp ring bearing different numbers of cyano groups and their constitution isomers. For the yet unknown compound 1,2,3,4-tetracyanoferrocene **4e**, the tendency towards longer bonds between substituted carbons atoms is found similar to compound **3d** (Figure 6). However, although we could obtain some spectro-



**Figure 6.** Tetracyanoferrocene with important bonds and distances displayed (B3LYP(D3)/Def2TZVP level of theory).

scopic hints on the formation of **4e**, we were not able to isolate it.

## Conclusion

Our experiments showed that dimethylmalononitrile is a rather slowly reacting electrophile. In combination with substrates that are able to undergo “halogen dance reactions” like bromoferrocenes and -under certain circumstances- chloroferrocenes, this leads to the formation of complex product mixtures with a low degree of reproducibility. However, it was possible for the first time to prepare compounds with three nitrile moieties on one ring of the metallocene scaffold, albeit in low yields. The compounds were characterized by NMR and mass spectroscopic as well as electrochemical experiments. They show one of the highest redox potentials for ferrocenes with oxidative electron transfer probably occurring at the nitrile functions.

## Experimental Section

### General Remarks

All reactions were carried out under an argon atmosphere using standard Schlenk techniques and dry solvents. Solvents and solutions were degassed by three freeze-pump-thaw cycles. Chromatography was performed on silica gel (Merck, 40–63  $\mu\text{m}$ ). Eluents petroleum ether (PE), diethyl ether ( $\text{Et}_2\text{O}$ ), ethyl acetate (EA) and dichloromethane (DCM) were of technical grade and were distilled before use. NMR spectra were recorded in ( $\text{CD}_3$ )<sub>2</sub>CO or  $\text{CDCl}_3$ ; chemical shifts are referenced to  $\text{CHCl}_3$  ( $^1\text{H}$ : 7.26 ppm) and  $\text{CDCl}_3$  ( $^{13}\text{C}$ : 77.0 ppm). For the assignment of peaks, the following abbreviations are used: s=singlet. High-resolution mass spectra were recorded on an ESI-QqaoTOF MS system. Dimethylmalononitrile (DMMN), 2,2,6,6-Tetramethylpiperidine (TMPH),  $n$ -BuLi (1.6 M/2.5 M in hexane);  $^t\text{BuLi}$  (1.7 M in pentane) as well as ferrocene and ferrocene carbonitrile were purchased from Sigma Aldrich.

Here only the synthetic procedures for the two tricyanoferrocenes are described. A complete description of all experiments discussed in this paper can be found in the Supporting Information

### Preparation of 1,2,3-Tricyanoferrocene (**3d**)

A solution of LiTMP was prepared from 2.5 M  $^t\text{BuLi}$  solution (0.84 mL, 2.13 mmol) and TMPH (0.33 mL, 2.13 mmol) in THF (20 mL). This was treated at  $-45^\circ\text{C}$  with a solution of **1c** (300 mg, 1.42 mmol) in THF (5 mL) with stirring for 5 hours. Then the reaction mixture was cooled to  $-100^\circ\text{C}$  and treated with DMMN (201 mg, 2.14 mmol). After gradual warming up to room temperature in the course of 16 hours, the mixture was filtered through a plug of silica and evaporated to dryness.  $^1\text{H-NMR}$  spectroscopic examination of the residue showed an 86:8:6 mixture of apparently unreacted **1b**, **2c** and **3d** (Figure S31, top half). Chromatography on silica using a 9:1 mixture of petroleum ether and  $\text{Et}_2\text{O}$  eluted **1b** (136 mg, 0.64 mmol, 45% recovery). Further elution with pure  $\text{Et}_2\text{O}$  yielded first **2c** (77 mg, 0.33 mmol, 23% yield), then a mixture of mainly **2c** and **3d** (in approximate 1:2 ratio). NMR examination (Figure S31, bottom half) showed also the presence of some unknown compounds, one of which might be **4e** (signals at  $\delta$  5.50 and

5.00 ppm), while MS showed besides the signals of **3d** three unknown species (labelled as A, B and X, Figure S67). The  $m/z$  value of signal A corresponds to the calculated value for **4e** (calc. 286.0), while the mass of B corresponds to a “dimer” [( $\text{NCH}_4\text{C}_5\text{Fe}(\text{C}_5\text{H}_4\text{CN})$ )] (calc. 420.0). A second chromatography of the 3<sup>rd</sup> fraction followed by recrystallization of the latter from petroleum ether gave nearly pure **3d** (29 mg, ca. 0.11 mmol, ca. 7%, NMR purity ca 95%, see Figures S36 and S37).

$^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 5.09 (s, 2H), 4.78 (s, 5H). (Figure S36)

$^1\text{H-NMR}$  (400 MHz, ( $\text{CD}_3$ )<sub>2</sub>CO)  $\delta$  = 5.56 (s, 2H), 4.88 (s, 5H)

$^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 114.6, 113.7, 76.4, 75.7, 59.1, 59.0 (Figure S37)

$^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, ( $\text{CD}_3$ )<sub>2</sub>CO):  $\delta$  = 116.58, 115.76, 115.12, 77.45, 77.03 (C5H5), 59.6, 59.5.

IR (ATR,  $\text{cm}^{-1}$ ):  $\nu_{\text{C-N}}$  = 2230.

HRMS (EI):  $m/z$  = 260.9984; calc. for  $\text{C}_{13}\text{H}_7\text{FeN}_3$ : 260.9984.

EA: found: C 59.83; H 2.60, N 16.38. calc: 59.81; H 2.70; N 16.10%.

### Preparation of 1,3-Dibromo-2,4,5-tricyanoferrocene (**5d**)

Under an argon atmosphere using standard Schlenk techniques **5a** (220 mg, 0.38 mmol) was dissolved in 12 ml  $\text{Et}_2\text{O}$  and cooled to  $-78^\circ\text{C}$ . While maintaining the temperature a solution of  $^t\text{BuLi}$  (0.24 mL, 1.6 M in hexane, 0.38 mmol) was added dropwise. The reaction mixture was stirred for 30 min and DMMN (37 mg, 0.38 mmol) was added. The solution was stirred for 1 h at  $-78^\circ\text{C}$ . Subsequently the mixture was allowed to reach room temperature within 16 h. After removal of the solvent under reduced pressure, the crude product (120 mg) was first examined by NMR (see Figure S21). This showed an approximate 16 mol-% content in **5d** (corresponding to an NMR yield of ca. 11%). After extraction with pentane, the residue was placed on top of a silica gel chromatography column. Four fractions were eluted with  $\text{Et}_2\text{O}$ . From the third and 4th fraction **5d** could be isolated as dark orange solid (combined yield 14 mg, ca. 33  $\mu\text{mol}$ , 9%; for more details see Supporting Information, Table S3, Entry 6).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 4.82 ppm (Figure S40).

IR (ATR,  $\text{cm}^{-1}$ ):  $\nu_{\text{C-N}}$  = 2238

HRMS (EI):  $m/z$  = 418.8174, calc. for  $\text{C}_{13}\text{H}_5\text{Br}_2\text{FeN}_3$ : 418.8179

### Crystallography

Crystals of compounds **3d** and **10b** were measured on a BRUKER D8 venture diffractometer. Structures were solved using SHELXT and refined with SHELXL 2018/3, both implemented in the WINGX program package.<sup>38</sup> Experimental details of the structure solutions are collected in Table S15. CCDC-2155106 and 2155107 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), by emailing [data\\_request@ccdc.cam.ac.uk](mailto:data_request@ccdc.cam.ac.uk), or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033

## Supplementary Data

Additional data (tables, ORTEP plots, DFT results including cartesian coordinates, explicit experimental details for all

described reactions, copies of NMR and mass spectra) are contained in the Supplementary Information.

## Acknowledgements

We thank Prof. Dr. T.M. Klapötke for providing the NMR facilities, Prof. Dr. T. Bein for providing the cyclovoltammetry equipment, and Dr. P. Mayer for performing the X-ray data collection and Prof. Dr. H. Zipse for providing the computational capacities. Open Access funding enabled and organized by Projekt DEAL.

## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

**Keywords:** Haloferrocenes · Cyanoferrocenes · Electrophilic Cyanation · Crystal Structure

- [1] a) S. Pimparkar, A. Koodan, S. Maiti, N. S. Ahmed, M. M. Mostafa, D. Maiti, *Chem. Commun.* **2021**, 57, 2210–2232; b) M. Neetha, C. M. A. Afsina, T. Aneja, G. Anilkumar, *RSC Adv.* **2020**, 10, 33683–33699; c) M. S. Ahmad, I. N. Pulidindi, C. Li, *New J. Chem.* **2020**, 44, 17177–17197; d) G. Yan, Y. Zhang, J. Wang, *Adv. Synth. Catal.* **2017**, 359, 4068–4105.
- [2] a) A. Kleemann, J. Engel, B. Kutscher, D. Reichert, *Pharmaceutical Substances: Synthesis, Patents, Applications*, 4th edn., Georg Thieme Verlag, Stuttgart, **2001**; b) F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk, B. C. Shook, *J. Med. Chem.* **2010**, 53, 7902–7917; c) Y. Wang, Y. Du, N. Huang, *Future Med. Chem.* **2018**, 10, 2713–2727; d) P. Ertl, E. Altmann, J. M. McKenna, *J. Med. Chem.* **2020**, 63, 8408–8418.
- [3] a) Z. Rappoport, *The Chemistry of the Nitrile Group*, Interscience Publishers, London, **1970**; b) R. C. Larock, in *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*, Wiley-VCH, Weinheim, **1989**; c) E. Ikarashi, K. Sakamoto, T. Yoshimura, J. Matsuo, *Tetrahedron Lett.* **2019**, 60, 13–15; d) Q. Bian, C. Wu, J. Yuan, Z. Shi, T. Ding, Y. Huang, H. Xu, Y. Xu, *J. Org. Chem.* **2020**, 85, 4058–4066; e) M. Beuvin, M. Manneveau, S. Diab, B. Picard, M. Sanselme, S. R. Piettre, J. Legros, I. Chataigner, *Tetrahedron Lett.* **2018**, 59, 4487–4491.
- [4] S. F. Rach, F. E. Kühn, *Chem. Rev.* **2009**, 109, 2061–2080.
- [5] For the general concept of „Bioisosterism“, see: G. A. Patani, E. J. LaVoie, *Chem. Rev.* **1996**, 96, 3147–3176; for its connection to ferrocene chemistry, see: V. Ganesh, V. S. Sudhir, T. Kundu, S. Chandrasekaran, *Chem. Asian J.* **2011**, 6, 2670–2694.
- [6] a) B. Sharma, V. Kumar, *J. Med. Chem.* **2021**, 64, 23, 16865–16921; b) F. A. Larik, A. Saeed, T. A. Fattah, U. Muqadar, P. A. Channar, *Appl. Organomet. Chem.* **2017**, 31, e3664.
- [7] N. D'Antona, R. Morrone, G. Nicolosi, S. Pedotti, *RSC Adv.* **2013**, 3, 11456–11458.
- [8] C. Quintana, A. H. Klahn, V. Artigas, M. Fuentealba, C. Biot, I. Halloum, I. Kremer, R. Arancibia, *Inorg. Chem. Commun.* **2015**, 55, 48–50.
- [9] H. A. Paine, A. Nathubhai, E. C. Y. Woon, P. T. Sunderland, P. J. Wood, M. F. Mahon, M. D. Lloyd, A. S. Thompson, T. Haikarainen, M. Narwal, L. Lehtiö, M. D. Threadgill, *Bioorg. Med. Chem.* **2015**, 23, 5891–5908.
- [10] a) F. Strehler, A. Hildebrandt, M. Korb, H. Lang, *Z. Anorg. Allg. Chem.* **2013**, 639, 1214–1219; b) F. Strehler, T. Rüffer, J. Noll, D. Schaarschmidt, A. Hildebrandt, H. Lang, *Z. Naturforsch. B* **2018**, 73, 759; c) P. Vosahlo, P. Harmach, I. Cisarova, P. Stepnicka, *J. Organomet. Chem.* **2021**, 953, 122065; d) F. Strehler, A. Hildebrandt, M. Korb, T. Rüffer, H. Lang, *Organometallics* **2014**, 33, 4279–4289.
- [11] P. J. Graham, R. V. Lindsey, G. W. Parshall, M. L. Peterson, G. M. Whitman, *J. Am. Chem. Soc.* **1957**, 79, 3416–3420.
- [12] a) L. A. Wilkinson, T. T. C. Yue, E. Massey, A. J. P. White, N. J. Long, *Dalton Trans.* **2019**, 48, 72–78; b) X.-D. An, S. Yu, *Org. Lett.* **2015**, 17, 5064–5067.
- [13] a) G. D. Broadhead, J. M. Osgerby, P. L. Pauson, *J. Chem. Soc.* **1958**, 650–656; b) J. L. Zhang, C. E. Dong, Y. G. Zhi, L. F. Zhang, *Chin. Chem. Lett.* **2000**, 11, 107–108; c) A. Kivrak, M. Zora, *J. Organomet. Chem.* **2007**, 692, 2346–2349; d) M. K. Singh, M. K. Lakshman, *J. Org. Chem.* **2009**, 74, 3079–3084; e) H. Meng, S. Gao, M. Luo, X. Zeng, *Eur. J. Org. Chem.* **2019**, 4617–4623.
- [14] N. A. Nesmeyanov, O. A. Reutov, *Dokl. Akad. Nauk SSSR* **1958**, 120, 1267–1270.
- [15] M. Sato, T. Ito, I. Motoyama, K. Watanabe, H. Hata, *Bull. Chem. Soc. Jpn.* **1969**, 42, 1976–1981.
- [16] A. Wrona, M. Palusiak, J. Zakrzewski, *J. Organomet. Chem.* **2008**, 693, 263–268.
- [17] a) D.-P. Medina, J. Fernandez-Ariza, M. S. Rodriguez-Morgade, T. Torres, *J. Porphyrins Phthalocyanines* **2020**, 24, 786–793; b) M. A. Abdulmalic, S. W. Lehigh, H. Lang, T. Rüffer, *Can. J. Chem.* **2016**, 94, 547–551.
- [18] V. N. Nemykin, A. Y. Maximov, A. Y. Kuposov, *Organometallics* **2007**, 26, 3138–3148.
- [19] C. C. Lee, C. I. Azogu, P. C. Zhang, R. G. Sutherland, *J. Organomet. Chem.* **1981**, 220, 181–186.
- [20] I. N. Nekrasov, L. P. Yur'eva, *Russ. J. Electrochem.* **2000**, 36, 299–307.
- [21] T. Blockhaus, K. Sünkel, *Acta Crystallogr.* **2022**, C78, 94–100.
- [22] See for example: a) P. R. Nimax, N. Rotthowe, F. Zoller, T. Blockhaus, F. Wagner, D. Fattakhova, K. Sünkel, *Dalton Trans.* **2021**, 50, 17643–17652; b) T. Blockhaus, K. Sünkel, *Z. Anorg. Allg. Chem.* **2021**, 647, 1849–1854; c) P. R. Nimax, F. Zoller, T. Blockhaus, T. Küblböck, D. Fattakhova-Rohlfing, K. Sünkel, *New J. Chem.* **2020**, 44, 72–78.
- [23] C. Klein-Heßling, T. Blockhaus, K. Sünkel, *J. Organomet. Chem.* **2021**, 943, 121833.
- [24] W. Steffen, M. Laskoski, G. Collins, U. H. F. Bunz, *J. Organomet. Chem.* **2001**, 630, 132–138.
- [25] J. T. Reeves, C. A. Malapit, F. C. Buono, K. P. Sidhu, M. A. Marsini, C. A. Sader, K. R. Fandrick, C. A. Busacca, C. H. Senanayake, *J. Am. Chem. Soc.* **2015**, 137, 9481–9488.
- [26] a) H. Li, S. Zhang, X. Yu, X. Feng, Y. Yamamoto, M. Bao, *Chem. Commun.* **2019**, 55, 1209–1212; b) L. R. Mills, J. M. Graham, P. Patel, S. A. L. Rousseaux, *J. Am. Chem. Soc.* **2019**, 141, 19257–19262.
- [27] M. Sabatini, M. A. Franco, R. Psaro, *Inorg. Chim. Acta* **1980**, 42, 267–270.
- [28] A. H. Stoll, P. Mayer, P. Knochel, *Organometallics* **2007**, 26, 6694–6697.
- [29] a) A. R. Sanger, *Inorg. Nucl. Chem. Lett.* **1973**, 9, 351; b) D. R. Armstrong, W. Clegg, M. MacGregor, R. E. Mulvey, P. A. O'Neil, *J. Chem. Soc. Chem. Commun.* **1993**, 608–610.

- [30] a) K. Sünkel, J. Hofmann, *Organometallics* **1992**, *11*, 3923–3925; b) K. Sünkel, J. Hofmann, *Chem. Ber.* **1993**, *126*, 1791–1795; c) K. Sünkel, C. Stramm, S. Soheili, *Dalton Trans.* **1999**, 4299–4302.
- [31] A. L. J. Beckwith, R. J. Leydon, *Tetrahedron Lett.* **1963**, 385–388.
- [32] a) A. Zirakzadeh, A. Herlein, M. A. Groß, K. Mereiter, Y. Wang, W. Weissensteiner, *Organometallics* **2015**, *34*, 3820–3832; b) T. Blockhaus, S. Bernhartzeder, W. Kempinger, C. Klein-Heßling, S. Weigand, K. Sünkel, *Eur. J. Org. Chem.* **2020**, *42*, 6576–6587; c) M. Korb, H. Lang, *Eur. J. Inorg. Chem.* **2022**, e202100946.
- [33] a) M. Tazi, W. Erb, Y. S. Halauko, O. A. Ivashkovich, V. E. Matulis, T. Roisnel, V. Dorcet, F. Mongin, *Organometallics* **2017**, *36*, 4770–4778; b) M. Tazi, M. Hadidi, W. Erb, Y. S. Halauko, O. A. Ivashkevich, V. E. Matulis, T. Roisnel, V. Dorcet, G. Bentabed-Ababsa, F. Mongin, *Organometallics* **2018**, *37*, 2207–2211; c) M. Wen, W. Erb, F. Mongin, Y. S. Halauko, O. A. Ivashkevich, V. E. Matulis, T. Roisnel, V. Dorcet, *Organometallics* **2021**, *40*, 1129–1147; d) I. R. Butler, *Organometallics* **2021**, *40*, 3240–3244.
- [34] P. R. Spackman, M. J. Turner, J. J. McKinnon, S. K. Wolff, D. J. Grimwood, D. Jayatilaka, M. A. Spackman, *J. Appl. Crystallogr.* **2021**, *54*, 1006–1011.
- [35] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165.
- [36] a) E. M. Espinoza, J. A. Clark, J. Soliman, J. B. Derr, M. Morales, *J. Electrochem. Soc.* **2019**, *166*, H3175–H3187; b) W. Alhalasah, R. Holze, *J. Solid State Electrochem.* **2007**, *11*, 1605–1612; c) L. Micaroni, F. Nart, I. Hümmelgen, *J. Solid State Electrochem.* **2002**, *7*, 55–59.
- [37] a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; b) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; c) S. Grimme, *J. Comput. Chem.* **2006**, *27*, 1787–1799; d) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.
- [38] Crystallographic programs used: a) WINGX: L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837–838; b) MERCURY: C. F. Macrae, P. R. Edgington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, M. Towler, J. van der Streek, *J. Appl. Crystallogr.* **2006**, *39*, 453–457; c) ORTEP3 for Windows: L. J. Farrugia, *J. Appl. Crystallogr.* **1997**, *30*, 565; d) PLATON: A. L. Spek, *J. Appl. Crystallogr.* **2003**, *36*, 7–13; e) SHELX: G. M. Sheldrick, *Acta Crystallogr.* **2015**, *A71*, 3–8; G. M. Sheldrick, *Acta Crystallogr.* **2015**, *C71*, 3–8.

---

Manuscript received: August 15, 2022

Revised manuscript received: September 13, 2022

Accepted manuscript online: September 29, 2022