Acceptor-Substituted Ferrocenium Salts as Strong, Single-Electron Oxidants: Synthesis, Electrochemistry, Theoretical Investigations, and Initial Synthetic Application

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Dedicated to the memory of Prof. Dr. Werner Schroth

Abstract: A series of mono- and 1,1'diheteroatom-substituted ferrocene derivatives as well as acylated ferrocenes was prepared efficiently by a unified strategy that consists of selective mono- and 1,1'-dilithiation reactions and subsequent coupling with carbon, phosphorus, sulfur and halogen electrophiles. Chemical oxidation of the ferrocene derivatives by benzoquinone, 2,3dichloro-5,6-dicyanobenzoquinone,

AgPF₆, or 2,2,6,6-tetramethyl-1-oxopiperidinium hexafluorophosphate provided the corresponding ferrocenium salts. The redox potentials of the synthesized ferrocenes were determined

Introduction

Ferrocene derivatives are extensively used in many areas of chemistry, such as catalysis, material science, and bioorganometallic chemistry.^[1] One of the reasons for their attractiveness is the fact that their redox state can be easily varied, which allows for a number of their applications in analytical and supramolecular chemistry.^[1] Ferrocenium salts have been used extensively as single-electron transfer (SET) reagents in organometallic and coordination chemistry to

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by cyclic voltammetry, and it was observed that all new ferrocenium salts have stronger oxidizing properties than standard ferrocenium hexafluorophosphate. An initial application of selected derivatives in an oxidative bicyclization revealed that they mediate the transformation under considerably milder conditions than ferrocenium hexafluorophosphate. Quantum chemical calculations of the reduction potentials of

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the substituted ferrocenium ions were carried out by using a standard thermodynamic cycle that involved the gasphase energetics and solvation energies of the contributing species. A remarkable agreement between theory and experiment was found: the mean average deviation amounted to only 0.030 V and the maximum deviation to 0.1 V. This enabled the analysis of various physical contributions to the computed reduction potentials of these ferrocene derivatives, thereby providing insight into their electronic structure and physicochemical properties.

switch the redox state of complexes.^[1,2] In contrast, applications of ferrocenium salts in organic chemistry are rare and mostly limited to easily accessible ferrocenium hexafluorophosphate A (Scheme 1).^[3,4] A promising, but not well-explored field are oxidative tandem reactions, in which starting molecules M are transformed to products P through multiple intermediates I of different redox state. High molecular complexity can be generated from very simple precursors in a single operation.^[3d,f,h] Few applications of A in the total synthesis of natural products exist.^[3a,b,5] Salt A is well suited to oxidize anionic intermediates to radicals, but has only limited capacity to oxidize radicals to carbocations.

In comparison to other metallic and non-metallic SET oxidants, ferrocenium salts are highly attractive, since their redox potential can be tuned easily by the introduction of substituents. Electron-donating substituents decrease their oxidation power, whereas acceptor substituents increase it, thus a wide potential area that ranges from very weak oxidants, such as the decamethylferrocenium ion, to very strong oxidants, such as the 1,1'-diacetylferrocenium ion, is accessible in principle.^[1,2] However, a major limitation that prevents the design of oxidative SET-mediated (tandem) transformations and other applications is the restricted availability of substituted and fine-tuned (with respect to their oxidation potential) ferrocenium salts. Generally,

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Scheme 1. Ferrocenium salts as oxidants: status and perspective.

mono- and 1,1'-disubstituted ferrocene derivatives have been prepared by reactions of lithiated ferrocenes with electrophiles, Friedel–Crafts reactions, or by means of ferrocenylmercury derivatives.^[1] However, most of these methods display only a limited substrate spectrum.

In this study, we describe the selective synthesis of a series of mono- and 1,1'-disubstituted ferrocene derivatives by a unified approach and reliable and convenient access to their ferrocenium salts **B** and **C**. The study focuses primarily on heteroatom-substituted ferrocenes, since they can be con-

pared ferrocenes and ferrocenium salts, a series of quantum chemical calculations was performed. Recent developments in computational chemistry including modern implicit solvation models, for example, the conductor-like screening model: real solvent (COSMO-RS),^[6] and accumulated experience^[7] nowadays enable us to make direct calculations of reduction potentials often with an accuracy better than 0.1 V ($\approx 10 \text{ kJ mol}^{-1}$ in the overall $\Delta G_{\text{ox/red}}$ value). Quantum chemical calculations thus represent an indispensable and complementary tool that not only reproduces the experimental data and makes qualified predictions for new ferrocenes, but also provides a genuine link between the electronic structure of the target molecules and their electrochemical properties.

Results and Discussion

Synthesis of mono- and 1,1'-disubstituted ferrocene derivatives: Two unified, generally applicable approaches based on ferrocene 1 were developed to cover the desired substituent spectrum in mono- and 1,1'-disubstituted ferrocenes 2 and 3, respectively. All monosubstituted ferrocene derivatives 2a-hwere synthesized in high yield and selectivity by adapting a procedure developed originally by Sanders and Mueller-Westerhoff,^[8a] which was later used by Leclercq et al. for the synthesis of diethyl ferrocenephosphonate (2d),^[8b] whereas a modified approach based on the one that was reported by Alley and Henderson for $3d^{[9]}$ was applied for the synthesis of all 1,1'-disubstituted ferrocenes (Table 1).

Thus, the reaction of 1 using the Schlosser–Lochmann base (*t*BuLi/KO*t*Bu) in THF at -78 °C followed by quench-

sidered the chemically most inert, whereas the very few known acylated ferrocenes, such as acetylferrocenes, are often not compatible with organometallic reaction conditions due to their acidity and electrophilicity. However, one mode of access to acylated ferrocenium salts that are less prone to deprotonation or nucleophilic attack is also presented. The applicability of selected ferrocenium salts B and C in an oxidative tandem cyclization, which does not proceed well with A under the very mild conditions, is reported. The reduced ferrocenes can be recovered, thus guaranteeing repeated use.

The oxidation power of salts **B** and **C** is determined by cyclic voltammetry. To gain deeper insight into the observed physicochemical properties of the preTable 1. Synthesis of mono and 1,1'-disubstituted ferrocenes ${\bf 2}$ and ${\bf 3}$ from ferrocene ${\bf 1}^{[a]}$

		E Condition A		ondition B	-E	
	5			Fe Cor	-E	
	2:	a-h	1	3a-h	_	
Entry	Condition	Electrophile	<i>t</i> [h]	E	2 [%] ^[b]	3 [%] ^[b]
1	Α	ClCO ₂ <i>i</i> Pr	2	-CO ₂ <i>i</i> Pr	a 80	a 3
2	В	ClCO ₂ <i>i</i> Pr	0.75	-CO ₂ <i>i</i> Pr	a 18	a 58
3	Α	ClCOPh	4	-COPh	b 86	b –
4	В	ClCOPh	2.5	-COPh	b 16	b 65
5	Α	ClPPh ₂	3	$-PPh_2$	c 75	c –
6	В	$ClPPh_2$	3	$-PPh_2$	c –	c 73
7	Α	$ClPO(OEt)_2$	4	$-PO(OEt)_2$	d 89	d –
8	В	$ClPO(OEt)_2$	3	-PO(OEt) ₂	d 22	d 60
9	Α	PhSSPh	2	-SPh	e 76	e –
10	$\mathbf{B}^{[c]}$	PhSSPh	68	-SPh	e –	e 70
11	Α	TsCl	2	-Cl	f 72	f 7
12	В	TsCl	2.5	-Cl	f 15	f 64 ^[d]
13	Α	BrCH ₂ CH ₂ Br	1	-Br	g 77 ^[e]	g –
14	В	$CBrCl_2CBrCl_2$	5	-Br	g –	g 89
15	Α	I_2	1	—I	h 71	h –
16	В	I_2	2.5	-I	h –	h 60

[a] Condition A: 2.0 equiv *t*BuLi, 0.12 equiv KO*t*Bu, THF, -78 °C to RT, then electrophile. Condition B: 2.2 equiv *n*BuLi, 2.4 equiv TMEDA, hexane, -78 °C to RT, then electrophile, THF, -78 °C to RT. [b] Isolated. [c] 2.0 equiv of each *n*BuLi and TMEDA. [d] Compounds **2f** and **3f** not separable; yield based on ¹H NMR spectroscopy. [e] Not separable from **1** by chromatography, separation by sublimation of **1**.

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ing with isopropyl chloroformate furnished isopropyl ferrocenecarboxylate (2a)^[10] in 80% yield accompanied by 3% of diisopropyl ferrocene-1,1'-dicarboxylate (3a; Table 1, entry 1). Benzoylferrocene (2b),^[11] (diphenylphosphanyl)ferrocene (2c),^[12] diethyl ferrocenephosphonate (2d),^[8] and (phenylthio)ferrocene $(2e)^{[13]}$ were also obtained in good yields (Table 1, entries 3, 5, 7, 9). The reaction of ferrocenyllithium with tosyl chloride did not afford the corresponding sulfonylferrocene, but provided a good yield of chloroferrocene (2 f; Table 1, entry 11).^[14,15] N-Chlorosuccinimide gave a poor yield in contrast. Bromoferrocene $(2g)^{[15]}$ and iodoferrocene (2h)^[15,16] were obtained by bromination using dibromoethane and iodination with iodine, respectively (Table 1, entries 13, 15).

By contrast, lithiation of **1** with nBuLi/N, N, N', N'tetramethylethylenediamine (TMEDA) at -78 to -40 °C furnished insoluble 1.1'-dilithioferrocene. which gave 3a by reaction with an excess amount of isopropyl chloroformate in 58% yield along with 18% of 2a (Table 1, entry 2). 1,1'-Dibenzoylferrocene (**3b**),^[11b] 1,1'-bis(diphenylphosphanyl)ferrocene (3c),^[17] tetraethyl ferrocene-1,1'-diphospho-(3d)^[9] and 1,1'-bis(phenylthio)ferrocene nate $(3e)^{[13e,18]}$ were similarly synthesized in moderate to

good yields (Table 1, entries 4, 6, 8, 10). The 1,1'-dihaloferrocenes 3 f-h were synthesized by quenching 1,1'-FcLi₂ with the corresponding electrophilic halogen sources as mentioned before in good vield (Table 1, entries 12, 14, 16), 1.1'-Dichloroferrocene (3 f) was purified for analytical purposes by repeated crystallization from methanol/water.

Benzylferrocene (2i) and 1,1'-dibenzylferrocene (3i) were obtained by reduction of benzoylferrocene (2b) and 1,1'-dibenzoylferrocene (3b), respectively, using the borane-dimethyl sulfide complex (Scheme 2).^[11a]



Scheme 2. Reduction of benzoylferrocenes 2b, 3b to benzylferrocenes 2i, 3i, respectively.

Oxidation of ferrocenylphosphanes and (phenylthio)ferrocenes: Mono- and 1,1'-disubstituted diphenylphosphanyl ferrocenes 2c and 3c were oxidized to the corresponding ferrocenyl phosphane oxides 2k and 3k by using 30% aqueous hydrogen peroxide in good yield (Scheme 3, Table 2, entries 1 and 2). The ferrocenyl sulfoxides 21 and 31 as well as the corresponding ferrocenyl sulfones 2m and 3m were obtained by oxidation of the phenylthioferrocenes 2e or 3e with meta-chloroperoxybenzoic acid (mCPBA) in very good yields (Table 2, entries 3-6).^[19]

Synthesis of ferrocenium salts: Ferrocenium hexafluorophosphate is commonly prepared from 1 by using concen-



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Scheme 3. Oxidation of phosphanyl and sulfenyl ferrocenes.

Table 2. Oxidation of (diphenylphosphanyl)ferrocene (2c), 1,1'-bis(diphenylphosphanyl)ferrocene (3c), (phenylthio)ferrocene (2e), and 1,1'-bis(phenylthio)ferrocene (3e).

Entry	Substrate	Oxidant [equiv]	Product [%]	
1	2 c	H_2O_2 (excess amount)	2k 82	
2	3c	H_2O_2 (excess amount)	3k 82	
3	2 e	mCPBA (1.2)	21 88	
4	2 e	mCPBA (3.0)	2m 84	
5	3e	mCPBA (2.4)	31 85	
6	3 e	mCPBA (5.0)	3m 82	

trated H₂SO₄ and KPF₆ in 84% yield as a dark blue powder.^[3g] These conditions are not applicable to other ferrocene derivatives, since they often lead to decomposition. Therefore, different oxidants were employed (Scheme 4, Table 3).



Scheme 4. Oxidation of ferrocenes 2 and 3 to ferrocenium salts 4 and 5.

The most generally applicable oxidants for these more electron-deficient ferrocenes proved to be benzoquinones 6a,b (Table 3, entries 1–5, 8–16). The stronger oxidant 2,3dichloro-5,6-dicyanobenzoquinone (DDQ; 6b) was more useful to oxidize 1,1'-diacceptor-substituted ferrocenes 3 (Table 3, entries 2 and 4). The strongest oxidizing ferrocenium salts 5 (R = SOPh, SO_2Ph , $POPh_2$, $PO(OEt)_2$) were also generated by using 6b as indicated by the formation of deep green or blue solutions in dichloromethane. They were, however, very sensitive to reduction to the starting ferrocenes 3 even by weak donor solvents such as diethyl ether. This precluded their isolation and characterization so far. Oxidation with AgPF₆ in dichloromethane was also efficient (Table 3,

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Table 3.	Synthesis	of	substituted	ferrocenium	hexaf	luorop	hosp	hates	4 an	ıd 5.
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	-		-	-					
Entry	2/3	R	Oxidant	Yield [%]	Entry	2/3	R	Oxidant	Yield [%]
1	2 a	CO ₂ <i>i</i> Pr	6a	4a 90	9	2 e	SPh	6 a	4e 91
2	3a	CO ₂ <i>i</i> Pr	6 b	5a 81	10	21	SOPh	6 a	41 70
3	2 b	COPh	6a	4b 82	11	2 m	SO_2Ph	6b	4m 72
4	3b	COPh	6 b	5b 76	12	2 f	Cl	6 a	4 f 70
5	2 k	POPh ₂	6a	4k 76	13	2 g	Br	6 a	4g 74
6	2 d	$PO(OEt)_2$	7	4d 66	14	3 g	Br	6 a	5g 72
7	2 d	$PO(OEt)_2$	$AgPF_6$	4d 64	15	2 h	Ι	6 a	4 h 80
8	2 d	$PO(OEt)_2$	6a	4d 97	16	3h	Ι	6 a	5 h 81

entry 7). It can also be used for the oxidation of other ferrocenes (not shown), but its price likely prohibits large-scale applications. Easily accessible oxoiminium hexafluorophosphate $7^{[20]}$ also proved to be an efficient oxidant for the ferrocenes (Table 3, entry 6). Most of the synthesized ferrocenium salts 4 and 5 are blue, blue-green, or green powders, which are stable in the solid state. They are stable and soluble in acetonitrile and dichloromethane, but slowly reduced back to 2 or 3, however, by alcoholic or ethereal solvents, DMF or DMSO.

Structural characterization of ferrocenes: The structures of most ferrocenes was confirmed by comparison of their NMR spectroscopic data.^[21] Those of ferrocenes **2a**, **3a**, **2m**, and **3m** were established by X-ray crystallography (Figures 1



Figure 1. X-ray crystal structure of isopropyl ferrocenecarboxylate (2a). The displacement ellipsoids are drawn at a 50% probability level.

to 4).^[22] The cyclopentadiene rings in 2a and 2m are in a synclinal arrangement (Figure 1, Figure 2). The ester group of 2a is almost coplanar to the cyclopentadiene ring and thus in full conjugation.

The difference between structures of 3a and 3m is more pronounced. A staggered arrangement of the cyclopentadienyl rings was found in 3a. The ester units in 3a are arranged in a *gauche* conformation, with both being conjugated to the cyclopentadiene rings (Figure 3). By contrast, the rings are almost synclinal in 3m, but an almost perfect antiperiplanar arrangement of the sulfonyl groups is favored in the solid state (Figure 4).



Figure 2. X-ray crystallographic view of ferrocenyl phenyl sulfone (**2m**). The displacement ellipsoids are drawn at a 50% probability level.

The equilibrium geometries of **2a**, **2m**, and **3m**, obtained by quantum chemical methods (all of the calculated equilibrium structures are deposited in the Supporting Information), are in excellent agreement with the solid-state structures. The comparison in **3a** revealed an interesting phenomenon: the conformer with the antiperiplanar arrangement of the ester groups was energetically marginally less stable in the gas phase (0.5–2.5 kcal mol⁻¹ depending on the basis set used; the lower value was obtained using the larger def2-TZVP basis set). However, the $\Delta(E_{ZPVE}-RT \ln Q)$ term ("gas-phase thermochemistry"; ZPVE=zero-point vibrational energy) and the difference in solvation energies reversed this order in the overall free-energy values, that is, the antiperiplanar conformation was more stable in solution by 1.0 and 0.5 kcal mol⁻¹ for the reduced and oxidized form,



Figure 3. X-ray crystallographic representation of ferrocene **3a**. The displacement ellipsoids are drawn at a 50% probability level. The molecule is positioned on a twofold axis of space group *Pbcn*; symmetry code (i): 2-x, y, 0.5-z.



Figure 4. Structure of 3m in the crystal. The displacement ellipsoids are drawn at a 50% probability level.

Table 4. Results of the oxidative cyclizations of 8.

respectively. One has to admit, though, that these values are probably within the error bar of the methods. The calculated energy difference between the two forms translates to less than 0.02 V in the reduction potentials and should not significantly hamper the calculated values (vide infra). It does, however, suggest that the (free) energy differences of the major conformers of the studied ferrocenes are quite small.

An initial application of selected ferrocenium salts in a double oxidative cyclization: Oxidative tandem cyclizations of less reactive 2-(4-pentenyl)malonates, such as the 5,5-diphenyl derivative 8, proceed by using lithium bis(trimethyl-silyl)amide (LiHMDS) or lithium diisopropylamide (LDA) as a base and ferrocenium hexafluorophosphate A as the prototypical oxidant in good yield only at temperatures of 0° C or higher (Scheme 5, Table 4, entry 1).^[3g] Product 10



Scheme 5. Oxidative cyclization of diethyl 2-(5,5-diphenylpent-4-en-1-yl)-malonate (8). DME = 1,2-dimethoxyethane.

forms by transfer of an ethyl group from the bicyclic carbocationic intermediate, which leads to 9 to the enolate of substrate 8;^[3g] this is an indication of the slow oxidation of the latter. The use of BuLi as the base at -78 °C leads to an even more complex reaction and gives products 9, 11, and 12 as a partly separable mixture (Table 4, entry 2). This result can also be traced to a slow SET oxidation of the enolate of 8.

To improve the yield and selectivity, the oxidative cyclization of **8** was performed by using selected ferrocenium salts **4m**, **4a**, **5a**, and **5b** at -78 °C. Bicyclic lactone **9** was obtained in 48–77 % yield (Table 4, entries 3–6). No product **10** that resulted from the transfer of an ethyl group to the enolate of **8** was detected in any of the cyclizations, thus indicat-

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Entry	Base	Oxidant	9 [%]	10 [%]	11 [%]	12 [%]	8 [%] ^[a]	1, 2, or 3 [%] ^[b]			
1 ^[c]	LDA	А	62	20	2	-	2	66 ^[d]			
2	nBuLi	Α	28	-	24	13	22	58 ^[d]			
3	nBuLi	4 m	61	-	-	15	26	94			
4	LiHMDS	4a	48	-	-	-	3	93			
5	nBuLi	5a	53 ^[e]	-	-	12	31	64			
6	nBuLi	5 b	77	-	-	-	20	72 ^[f]			

[a] Recovered **8**. [b] Recovered **2** or **3**. [c] Conditions exactly as in Ref. [3g] at 0 °C. [d] The recovery of ferrocene was lower on account of incomplete oxidation. The remainder of the mass balance is unchanged **A**. [e] Product **9** and reduced ferrocene **3a** are not separable; yield based on the ¹H NMR spectrum. [f] Benzoylcyclopentadiene dimers isolated: 7%.

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ing two fast SET oxidation steps. However, in cyclizations in which BuLi was applied as the base, small amounts of acyclic products 12 that resulted from the addition of BuLi to 8 were formed (Table 4, entries 2, 3, 5). The yield and mass balance of the reaction was reduced to 48% when LiHMDS was used as the base, but lactone 9 remained the major product (Table 4, entry 4). The electrophilic carbonyl groups of the ferrocenium derivatives 4a, 5a, and 5b were not attacked by the nucleophilic enolate of 8, thus demonstrating the high facility of SET oxidation of both the enolate and the cyclized radical, although the recovered amount of the reduced ferrocene 5a was somewhat lower (Table 4, entry 5). In the reaction that used 5b, 7% of benzoylcyclopentadiene dimers were isolated that apparently resulted from some competing decomplexation under the reaction conditions (Table 4, entry 6).

Electrochemistry: The redox behavior of ferrocene derivatives **2a–m** and **3a–m** was studied by cyclic voltammetry in $0.1 \text{ M Bu}_4\text{NPF}_6$ solution in acetonitrile (Table 5). Ferrocene **1** was studied for comparison (Table 5, entry 1). Both cyclic voltammetry and impedance spectroscopy confirmed a reversible one-electron transfer reaction. For a given substituent atom, the anticipated direct relationship between the electron-withdrawing character of the substituents and its oxidation potential was observed. Therefore, upon going from benzylferrocene to isopropyl ferrocenecarboxylate, the oxidation increased in power from $E^0=0.463$ to 0.704 V(Table 5, entries 2–4). The phosphane oxide and phospho-

nate substituents led to a significant increase in the redox potential over the diphenylphosphanyl substituent (Table 5, entries 6 and 7 versus 5), although the effect of the phosphanoyl group on the redox potential is stronger than that of the phosphonate unit (Table 5, entry 6 versus 7). For sulfur substituents, the oxidation potential increases considerably as the degree of oxygenation increased (Table 5, entries 8-10). On the other hand, the redox potentials of the halogensubstituted ferrocenes are quite similar to each other (Table 5, entries 11-13). Incorporation of a second benzyl substituent has almost no effect on the redox potential (Table 5, entries 2 versus 14). The redox potential increases, however, with further acceptor substitution, though the effect of the second group is less pronounced (Table 5, entries 14-16). Similar trends to those for the monosubstituted derivatives 2c, 2k, 2d, or 2e, 2l, 2m were found for the corresponding diphosphorus and disulfur-substituted ferrocenes 3c, 3k, 3d, or 3e, 3l, 3m (Table 5, entries 17–19 and 20–22). The bis(phenylsulfonyl)ferrocenium ion is the strongest oxidant of the whole series (Table 5, entry 22). The introduction of a second halogen substituent increases the oxidation potential by only 0.1-0.17 V (Table 5, entries 23-25).

Theoretical investigation of acceptor-substituted 1- and 1,1'disubstituted ferrocenes and ferrocenium salts: Quantum chemical calculations of the reduction potentials by using the DFT method (Perdew–Burke–Ernzerhof (PBE) functional) and one of the presumably most accurate implicit solvation models, COSMO-RS, yielded values of the reduc-

	1	-		1	0 0	
Entry	Compound	$E_{\rm exp}^0$ [V]	$E_{ m calcd}^0$ [V]	IE [eV] ^[b]	$\Delta (E_{\rm ZPVE} - RT \ln Q)^{[c]} [eV]$	$\Delta\Delta G_{ m solv}^{[d]} [eV]$
1	1	0.480	0.525	6.75	-0.020	-1.709
2	2i (CH ₂ Ph)	0.463	-	-	_	-
3	2b (COPh)	0.693	0.712	6.69	-0.028	-1.454
4	2 a $(CO_2 i Pr)$	0.704	0.702	6.80	-0.025	-1.576
5	2c (PPh ₂)	0.560	0.502	6.26	-0.003	-1.259
6	$2 \mathbf{k} (POPh_2)$	0.713	0.700	6.57	-0.049	-1.318
7	2d (PO ₃ Et ₂)	0.695	0.708	6.65	-0.004	-1.436
8	2e (SPh)	0.610	0.567	6.40	0.003	-1.340
9	21 (SOPh)	0.783	0.735	6.75	-0.016	-1.495
10	$2 m (SO_2Ph)$	0.847	0.823	6.84	-0.008	-1.507
11	2 f (Cl)	0.624	0.633	6.82	-0.008	-1.679
12	2 g (Br)	0.630	0.668	6.83	-0.001	-1.657
13	2h (I)	0.635	0.640	6.77	-0.003	-1.626
14	$3i (CH_2Ph)_2$	0.458	0.501	6.38	0.012	-1.387
15	3b (COPh) ₂	0.917	0.952	6.77	-0.038	-1.274
16	$3a (CO_2 iPr)_2$	0.914	0.933	6.88	-0.024	-1.399
17	$3c (PPh_2)_2$	0.653	0.554	6.07	0.016	-1.036
18	$3\mathbf{k} (POPh_2)_2$	0.946	1.000	6.50	0.001	-1.001
19	3d $(PO_3Et_2)_2$	0.903	0.917	6.53	-0.017	-1.095
20	3e (SPh) ₂	0.681	0.671	6.28	0.050	-1.157
21	$31 (SOPh)_2$	0.983	0.994	6.79	-0.005	-1.290
22	$3 \mathrm{m} (\mathrm{SO}_2 \mathrm{Ph})_2$	1.190	1.165	6.94	-0.007	-1.266
23	3 f (Cl) ₂	0.771	0.765	6.92	0.003	-1.661
24	$3g(Br)_2$	0.797	0.828	6.93	0.016	-1.620
25	3h $(I)_{2}$	0.741	0.768	6.85	-0.009	-1.574

Table 5. Experimental and calculated reduction potentials of ferrocenes 2 and 3 with respect to the Ag/AgCl 1 M LiCl electrode.^[a]

[a] The electrode potential is 0.21 V versus standard hydrogen electrode.^[23] [b] In vacuo ionization energy: IE = E(oxidized) - E(reduced), calculated at the RI-PBE/def2-TZVP level. [c] The difference in the gas-phase chemical potential (including ZPVE corrections), $\Delta(E_{ZPVE} - RT \ln Q)$. [d] The difference in solvation energies: $\Delta\Delta G_{\text{solv}} = \Delta G_{\text{solv}}(\text{oxidized}) - \Delta G_{\text{solv}}(\text{reduced})$.

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tion potentials that are in excellent agreement with the experimental results (Table 5). The mean unsigned deviation (MUD) is approximately 0.03 V, which is well below the anticipated error bar of theoretical methods (≈ 0.1 V). It can be concluded that the agreement is almost quantitative, thus suggesting a high predictive potential of theoretical calculations for this series of compounds. On the contrary, the correlation between the calculated ionization energies (IE) and the experimental reduction potentials is only qualitative. This qualitative agreement, though, is in line with the expected change of oxidative power induced by the ferrocene substituents as discussed above. Essentially, the reduction potential is dependent on two terms, IE and $\Delta\Delta G_{solv}$ whereas the effects of zero-point vibrational energy and entropic contributions are only marginal (< 0.05 V). The importance of both IE and $\Delta\Delta G_{solv}$ can be demonstrated for compounds 2f and 3k with IE values of 6.82 and 6.50 eV, respectively. The difference in the solvation energies of their oxidized and reduced species corresponds, however, to 0.678 eV and reverses the order of their reduction potentials. It is therefore a delicate balance between the two quantities that determines the oxidative power of the ferrocenes. The observation of a dramatic influence of solvation therefore precludes any semiquantitative analysis on the basis of molecular orbital pictures (such as the stabilization of HOMO/ LUMO orbitals) to be generally applicable to a series of chemically distinct species. On the other hand, within a given series of similar substituents, the trends in their reduction potentials are already included in their ionization energies, which is in line with the qualitative discussion in the previous section. In other words, the contribution that arises from the difference in solvation energies of the reduced and oxidized species remains approximately constant for similar substituents.

The analysis of the resulting wave functions of the oxidized complexes revealed-not unexpectedly-that the unpaired electron resides mostly on the iron atom. However, variations can be observed for ferrocenium ions that possess lone pairs at the heteroatom substituents. The bis(phosphanyl)ferrocenium ion 5c carries significant spin density at one of the phosphorus atoms according to a Mulliken population analysis (Figure 5), whereas it is negligible in the corresponding bis(phenylthio)ferrocenium ion 5e (Figure 6).

Conclusion

A series of mono- and 1,1'-disubstituted ferrocene derivatives and their ferrocenium salts was prepared. The new ferrocenium salts 4 and 5 are stronger oxidants than parent ferrocenium hexafluorophosphate. The redox potentials of the prepared acceptor-substituted ferrocene derivatives were determined by using cyclic voltammetry. 1,1'-Disubstituted ferrocenes with electron-withdrawing groups (SO₂Ph, SOPh, PO(OEt)₂, POPh₂, COPh, and CO₂*i*Pr) have higher oxidation potentials than their monosubstituted counterparts. Halogen, thioether, and phosphane derivatives have

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Figure 5. Electron spin density in bis(diphenylphosphanyl)ferrocenium ion (5c) as obtained by density functional theory calculations using a Mulliken population analysis.



Figure 6. Electron spin density in bis(phenylthio)ferrocenium ion (5e) as obtained by the density functional theory calculations using a Mulliken population analysis.

medium potentials in the series. Selected mono- and 1,1'-acceptor-substituted ferrocenium salts were advantageously applied to an oxidative tandem cyclization under very mild conditions, which ferrocenium hexafluorophosphate A is not able to promote well.

It is demonstrated that the synthetic effort can be assisted by computational methods. The electrochemical properties of ferrocenes were reliably and almost quantitatively reproduced, and computations can be therefore easily used in the predictive design of new ferrocenium salts with fine-tuned oxidative power. The results clearly show the delicate balance between the solvation energies of the oxidized and reduced species and their ionization energies. Therefore, any

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www.chemeurj.org These are not the final page numbers! **77** quantitative predictions for ferrocenes with different types of substituents based solely on in vacuo computational data will lead to erroneous results. The theoretical treatment significantly extends the understanding of the electrochemistry of substituted ferrocenes. In addition to that, the quantum chemical calculations provide insights into the electronic structure of ferrocenium salts, such as their spin densities and the contribution of ligand-centered radical cations. With tunable oxidation potentials, these ferrocenium salts can be expected to find wide applications in chemoselective oxidative reactions in organic chemistry. The investigation of the reactivity of these ferrocenium salts as SET oxidants in organic chemistry is underway in these laboratories. Moreover, they will be certainly useful in organometallic and inorganic chemistry. Applications in material chemistry as dopants and as units in electron-transfer active materials can also be foreseen.

Experimental Section

For the general experimental methods, see the Supporting Information. Monosubstituted ferrocenes 2 (general procedure): KOtBu (72 mg, 0.65 mmol) was added to a solution of ferrocene (1.0 g, 5.38 mmol) in THF (10 mL) at room temperature. The solution was cooled to -78°C and tBuLi (6.32 mL, 10.76 mmol, 1.7 M in pentane) was added dropwise. The reaction mixture was stirred at -78°C for 1 h. The electrophile (see at the individual compounds and in the Supporting Information) was added to the orange solution at -78 °C. The solution was slowly warmed to room temperature until the reaction was complete as indicated by TLC. The reaction was quenched after the given time by the addition of water (Table 1). The reaction mixture was diluted by an organic solvent (Table 1, CH₂Cl₂ for entries 1, 3, 5, 7, 9, 11, 15, and diethyl ether for entry 13). The layers were separated and the aqueous layer was extracted three times. The combined organic fractions were dried over Na2SO4 and evaporated. The crude product 2 was purified by flash column chromatography. Compounds $2\mathbf{b}$,^[11] $2\mathbf{c}$,^[12] and $\mathbf{2e}$ ^[13] are known and their analytical data are in full agreement with those reported in the cited references. Compounds $2d^{[8]}$ and $2f-h^{[14-16]}$ were previously partially characterized; their full data are provided in the Supporting Information.

Isopropyl ferrocenecarboxylate (2a): Prepared with ClCO₂*i*Pr (10.75 mL, 10.76 mmol, 1.0 м solution in toluene). Flash chromatography hexane gradient to hexane/EtOAc: 4:1. Yield: 1.17 g (80%) as an orange solid. M.p. 31 °C; *R*_f (hexane/EtOAc: 9:1) = 0.60; ¹H NMR (400 MHz): *δ* = 5.17 (sept, *J* = 6.3 Hz, 1H; CO₂*CH*(CH₃)₂), 4.80 (t, *J* = 1.9 Hz, 2H; *Hα*), 4.37 (t, *J* = 1.9 Hz, 2H; *Hβ*), 4.19 (s, 5H; Cp*H*), 1.33 ppm (d, *J* = 6.2 Hz, 6H; CO₂CH(*CH*₃)₂); ¹³C NMR (100 MHz): *δ* = 171.2 (s; CO₂CH(CH₃)₂), 72.1 (s; *ipsoC*_{Cp}), 71.2 (d; Cβ), 70.2 (d; Cα), 69.8 (d; CpC), 67.4 (d; CO₂CH-(CH₃)₂), 22.2 ppm (q; CO₂CH(CH₃)₂); II: *ν* = 2978, 2934, 1703, 1656, 1458, 1374, 1273, 1141, 1104, 1024, 1001, 932, 820, 774 cm⁻¹; UV/Vis (CH₃CN): *λ*_{max} (log *ε*) = 445 (2.31), 335 (2.50), 307 (2.97), 260 (3.53), 221 nm (sh) (3.7); MS (EI): *m/z* (%): 272/270 (32/5) [*M*⁺], 230/228 (100/4) [*M*⁺ −*H*₂C=-CHCH₃]; HRMS (EI): *m/z* calcd for C₁₄H₁₆⁶FeO₂: 272.0500; found: 272.0501; elemental analysis calcd (%) for C₁₄H₁₆FeO₂ (272.12): C 61.79, H 5.93; found: C 61.71, H 5.99.

Disubstituted ferrocenes 3 (general procedure): TMEDA (1.95 mL, 12.9 mmol) and *n*BuLi (7.39 mL, 11.84 mmol, 1.6 m in hexane) were added dropwise to a stirred solution of $(C_5H_5)_2$ Fe (1.0 g, 5.38 mmol) in hexane (10 mL) under a dry N₂ atmosphere at room temperature. The solution was stirred at room temperature overnight. The orange slurry was allowed to settle and the hexane layer was removed with a syringe. The remaining orange powder was washed with dry hexane (5 mL) and dissolved in dry THF (10 mL). The electrophile (see at the individual compounds and in the Supporting Information) was added to the orange

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solution at -78 °C. The solution was slowly warmed to room temperature until the reaction was complete as indicated by TLC. The reaction was quenched after the given time by the addition of water (Table 1). The reaction mixture was diluted with an organic solvent (Table 1, EtOAc for entry 2, and CH₂Cl₂ for entries 4, 6, 8, 10, 12, 14, 16, 18). The layers were separated and the aqueous was extracted thoroughly. The combined organic fractions were dried over Na₂SO₄ and evaporated to give the crude product **3**, which was purified by flash column chromatography. Compounds **3b**,^[11] **3c**,^[17] **3d**,^[9] **3e**,^[13e,18] **3g**,^[14] and **3h**^[24] are known and their analytical data correspond to those in the cited references.

Diisopropyl 1,1'-ferrocenedicarboxylate (3a): Prepared with ClCO₂*i*Pr (21.49 mL, 21.50 mmol, 1.0 м solution in toluene). Flash chromatography hexane gradient to hexane/EtOAc: 19:1. Yield: 1.11 g (58%) as a reddish-orange solid. M.p. 51 °C; R_t (hexane/EtOAc 9:1)=0.48; ¹H NMR (400 MHz): δ =5.16 (sept, J=6.3 Hz, 2H; CO₂CH(CH₃)₂), 4.79 (t, J= 2.0 Hz, 4H; $H\alpha$), 4.37 (t, J=1.9 Hz, 4H; $H\beta$), 1.34 ppm (d, J=6.3 Hz, 12H; CO₂CH(CH₃)₂); ¹³C NMR (100 MHz): δ =170.1 (s; CO₂CH(CH₃)₂), 73.6 (s; *ipsoC*_{Cp}), 73.0 (d; Cβ), 71.5 (d; Cα), 67.8 (d; CO₂CH(CH₃)₂), 22.2 ppm (q; CO₂CH(CH₃)₂); IR: $\bar{\nu}$ =2978, 1706, 1459, 1373, 1273, 1144, 1104, 1027, 932, 830, 775 cm⁻¹; UV/Vis (CH₃CN): λ_{max} (log ε)=451 (2.45), 350 (2.53), 300 (sh) (3.10), 258 (3.55), 225 nm (sh) (3.39); MS (EI): *m/z* (%): 358/356 (40/1) [*M*⁺], 274/272 (100/2) [*M*⁺-2 CH₂=CH₂CH₃]; HRMS (EI): *m/z* calcd for C₁₈H₂₂FeO₄ (358.21): C 60.35, H 6.19, Fe 15.59; found: C 60.51, H 6.35, Fe 15.50.

(Diphenylphosphanoyl)ferrocenes 2k, 3k (general procedure): A solution of 30% aqueous H₂O₂ (5 mL for 2c, or 10 mL for 3c) was added to a solution of 2c (1.0 g, 2.70 mmol) or 3c (1.0 g, 1.80 mmol) in CH₂Cl₂ (30 mL). The reaction mixture was stirred at room temperature for 2 h. The layers were separated and the aqueous was extracted with CH₂Cl₂, dried over Na₂SO₄, and evaporated. The crude products 2k or 3k were purified by flash column chromatography. Compound 2k is known and its analytical data correspond to those reported.^[25]

Sulfinyl and sulfonyl ferrocenes 21, 31, and 2m, 3m (general procedure): Ferrocene 2e (1.0 g, 3.40 mmol) or 3e (1.0 g, 2.48 mmol) was dissolved in dry CH₂Cl₂ (20 mL). After cooling the reaction mixture to 0°C, *m*CPBA (amounts provided for the individual compounds) in CH₂Cl₂ (10 mL) was added at 0°C. The reaction mixture was stirred at room temperature for 1 h and quenched by addition of water. The layers were separated and the aqueous was extracted with CH₂Cl₂. The combined organic fractions were dried over Na₂SO₄ and evaporated to give crude products 21, 31, 2m, or 3m, which were purified by flash column chromatography. Compounds $2l^{1/3c,d]}$ and $2m^{1/9,21]}$ are known and their analytical data correspond to those found in the literature.

meso/DL-1,1'-Bis(phenylsulfinyl)ferrocene (31): Prepared with mCPBA (1.28 g, 7.0 mmol). Flash chromatography hexane/EtOAc (9:1) gradient to CH₂Cl₂/*i*PrOH: 10:1. Yield: 0.90 g (84%) as an unassigned 1.2:1 meso/ DL mixture as a yellow solid. M.p. 164–166 °C; $R_{\rm f}$ (EtOAc)=0.53; ¹H NMR (400 MHz): $\delta = 7.61$ (m, 4H; $o - H_{Ar}^*$), 7.59 (m, 4H; $o - H_{Ar}$), 7.45–7.43 (m, 12H; m- H_{Ar}^* , p- H_{Ar}^* , m- H_{Ar} , p- H_{Ar}), 4.80 (m, 1H; $H\alpha$), 4.78 (m, 1H; $H\alpha^*$), 4.72 (m, 1H; $H\alpha'^*$), 4.70 (m, 1H; $H\alpha'$), 4.66 (m, 1H; *H*β), 4.65 (m, 2H; *H*β*, *H*β'*), 4.58 ppm (m, 1H; *H*β'); ¹³C NMR (100 MHz): $\delta = 146.1$ (s; $ipsoC_{Ar}^*$), 146.0 (s; $ipsoC_{Ar}$), 130.9 (d; $p-C_{Ar}^*$), 130.8 (d; p- C_{Ar}), 129.2 (d; m- C_{Ar} , m- C_{Ar} *), 124.2 (d; o- C_{Ar}), 124.1 (d; o- C_{Ar}^{*}), 96.8 (s; *ipsoC*_{Cp}, *ipsoC*_{Cp}*), 72.2 (d; C β), 72.0 (d; C β *), 71.9 (d; $C\beta'^{*}$), 71.8 (d; $C\beta'$), 70.2 (d; $C\alpha$), 69.9 (d; $C\alpha^{*}$), 66.4 (d; $C\alpha'^{*}$), 66.3 ppm (d; $C\alpha'$); IR: $\tilde{\nu} = 3085$, 1674, 1476, 1443, 1415, 1306, 1164, 1106, 1044, 828, 750 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε) = 436 (2.42), 282 (sh) (3.57), 248 nm (3.61); MS (ESI): m/z (%): 459/457/455 (11/90/5) [M+Na⁺], 437/ 435/433 (12/100/7) [M+H⁺]; elemental analysis calcd (%) for C22H18FeO2S2 (434.35): C 60.83, H 4.18; found: C 60.93, H 4.26.

1,1'-Bis(phenylsulfonyl)ferrocene (3m): Prepared with *m*CPBA (2.13 g, 12.40 mmol). Crystallized from CH₂Cl₂. Yield: 0.95 g (82%) as orange crystals. M.p. 286 °C (decomp); *R*_f (EtOAc)=0.85; ¹H NMR (400 MHz): δ =7.85 (m, 4H; *o*-*H*_{Ar}), 7.55 (m, 2H; *p*-*H*_{Ar}), 7.47 (m, 4H; *m*-*H*_{Ar}), 4.93 (t, *J*=2.0 Hz, 4H; *H*α), 4.89 ppm (t, *J*=2.0 Hz, 4H; *H*β); ¹³C NMR (100 MHz): δ =142.4 (s; *ipsoC*_{Ar}), 133.2 (d; *p*-*C*_{Ar}), 129.3 (d; *m*-*C*_{Ar}), 127.0 (d; *o*-*C*_{Ar}), 92.4 (s; *ipsoC*_{Cp}), 74.6 (d; *C*β), 71.6 ppm (d; *C*α); IR:

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$$\begin{split} & \bar{\nu}\!=\!3096,\,1446,\,1316,\,1306,\,1144,\,1085,\,829,\,756~\mathrm{cm}^{-1};\,\mathrm{UV/Vis}~(\mathrm{CH}_2\mathrm{Cl}_2):\\ & \lambda_{\mathrm{max}}~(\log \varepsilon)\!=\!437~(2.54),\,306~(3.37),\,280~(\mathrm{sh})~(3.56),\,246~\mathrm{nm}~(3.60);~\mathrm{MS}~(\mathrm{EI}):~m/z~(\%):~491/489/487~(12/100/6)~[M\!+\!\mathrm{Na}^+],\,469/467/465~(10/68/3)\\ & [M\!+\!\mathrm{H}^+];~\mathrm{elemental}~\mathrm{analysis}~\mathrm{calcd}~(\%)~\mathrm{for}~\mathrm{C}_{22}\mathrm{H}_{18}\mathrm{FeO_4S_2}~(466.35):~\mathrm{C}~56.66,\,\mathrm{H}~3.89;~\mathrm{found}:\mathrm{C}~56.54,\,\mathrm{H}~3.74. \end{split}$$

Ferrocenium hexafluorophosphates 4a, 4b, 4d–h, 4k–m, and 5a, 5b, 5g, 5h: Benzoquinone or DDQ (0.5 mmol) (see Table 3) was added to ferrocenes 2a, 2b, 2d–h, 2k–m, or 3a, 3b, 3g, 3h (1.0 mmol) in diethyl ether (20 mL) at room temperature. The reaction mixture was stirred for 10 min. Then HPF₆ (65 wt % solution in H₂O, 2.0 mmol) was added at 0°C. A greenish blue solid was formed, which was filtered through a sintered glass funnel and washed with ice cold ether until the ether solution became colorless to give products 4a, 4b, 4d–h, 4k–m, or 5a, 5b, 5g, 5h. The analytical data of representative compounds 4a, 4b, 4g, 4h, 4m, and 5a, 5b, 5g, 5h are presented below. The full analytical characterization of all prepared compounds can be found in the Supporting Information.

(Isopropyloxycarbonyl)ferrocenium hexafluorophosphate (4a): Yield: 1.37 g (90%) as a blue solid. M.p. 131–132 °C (melting with decomp); IR: $\bar{\nu}$ =3010, 1716, 1284, 1109, 824, 556 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε) = 628 (2.31), 360 (3.17), 282 (sh) (3.94), 259 (4.06), 236 nm (sh) (3.95); MS (ESI): m/z (%): 272/270 (48/5) $[M^+-PF_6]$, 231/229 (82/7) $[M+H^+$ $-PF_6-H_2C=CHCH_3]$, 230/228 (82/7) $[M^+-PF_6]$, 231/229 (82/7) $[M+H^+$ (100/12); HRMS (ESI): m/z calcd for C₁₄H₁₆⁵⁶FeO₂+: 272.0494; found: 272.0493; elemental analysis calcd (%) for C₁₄H₁₆ $_6$ FeO₂P (417.08): C 40.32, H 3.87, F 27.33, Fe 13.39; found: C 40.25, H 3.81, F 27.04, Fe 13.68.

Benzoylferrocenium hexafluorophosphate (4b): Yield: 1.22 g (82 %) as a green solid. M.p. 118–120 °C (melting with decomp); IR: $\tilde{\nu}$ =3120, 1661, 1597, 1280, 834, 557 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε) = 635 (2.56), 290 (sh) (4.07), 258 nm (4.29); MS (ESI): m/z (%): 313/311 (27/2) [*M*+Na⁺ -PF₆], 290/288 (100/20) [*M*⁺-PF₆]; HRMS (ESI): m/z calcd for C₁₇H₁₄⁵⁶FeO⁺: 290.0389; found: 290.0387; elemental analysis calcd (%) for C₁₇H₁₄F₆FeOP (435.10): C 46.93, H 3.24, Fe 12.83, P 7.12; found: C 46.99, H 3.25, Fe 13.17, P 7.39.

Bromoferrocenium hexafluorophosphate (4g): Yield: 1.14 g (74%) as a green solid. M.p. 233–235 °C (decomp); IR: $\tilde{\nu}$ =3121, 1420, 826, 731, 556 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε)=684 (2.31), 565 (2.12), 272 (sh) (4.18), 263 nm (4.19); MS (ESI): *m/z* (%): 266/264/262 (85/100/5) [*M*⁺ -PF₆], 186/184 (66/6) [*M*+H⁺-PF₆-Br]; HRMS (ESI): *m/z* calcd for C₁₀H₉⁷⁹Br⁵⁶Fe⁺: 263.9232; found: 263.9231; elemental analysis calcd (%) for C₁₀H₉BrF₆FeP (409.89): C 29.30, H 2.21, Br 19.49, F 27.81, Fe 13.62, P 7.56; found: C 29.45, H 2.10, Br 19.56, F 27.89, Fe 13.38, P 7.42.

Iodoferrocenium hexafluorophosphate (4h): Yield: 1.17 g (80%) as a blue solid. M.p. 233–235 °C (melting with decomp); IR: $\tilde{\nu}$ =3116, 1413, 829, 557 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε)=718 (2.68), 278 (sh) (3.97), 259 nm (4.03). MS (ESI): *m/z* (%): 312/310 (100/6) [*M*⁺−PF₆]. HRMS (ESI): *m/z* calcd for C₁₀H₉I⁵⁶Fe⁺: 311.9093; found: 311.9092; elemental analysis calcd (%) for C₁₀H₉F₆IFeP (456.89): C 26.29, H 1.99, I 27.78, Fe 12.22, P 6.78; found: C 26.28, H 2.00, I 27.40, Fe 12.64, P 7.25.

(Phenylsulfonyl)ferrocenium hexafluorophosphate (4m): Yield: 1.03 g (72%) as a green solid. M.p. 118–120°C; IR: $\bar{\nu}$ =3108, 1447, 1304, 1141, 840, 724, 558 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε)=635 (2.39), 287 (sh) (4.35), 259 (4.51), 230 nm (4.47); MS (EI): m/z (%): 328/326/324 (8/100/18) [M^+ -PF₆]; HRMS (ESI): m/z calcd for C₁₆H₁₄⁵⁶FeO₂³²S⁺: 326.0064; found: 326.0060; elemental analysis calcd (%) for C₁₆H₁₄F₆FeO₂PS (471.16): C 40.79, H 3.00, Fe 11.85, S 6.81; found: C 40.27, H 3.01, Fe 12.21, S 7.21.

1,1'-Bis(isopropyloxycarbonyl)ferrocenium hexafluorophosphate (5a): Yield: 1.14 g (81%) as a blue solid. M.p. 90–92 °C (melting with decomp); IR: $\tilde{\nu}$ =2987, 1722, 1471, 1376, 1280, 1107, 829, 557 cm⁻¹; UV/ Vis (CH₂Cl₂): λ_{max} (log ε) = 641 (2.41), 287 (sh) (3.84), 262 (4.00), 229 nm (4.08); MS (ESI): m/z (%): 381/379 (100/10) [M+Na⁺-PF₆]; HRMS (ESI): m/z calcd for C₁₈H₂₂⁵⁶FeO₄Na⁺: 381.0760; found: 381.0759; elemental analysis calcd (%) for C₁₈H₂₂F₆FeO₄P (503.17): C 42.97, H 4.41, F 22.65, Fe 11.10, P 6.16; found: C 42.47, H 4.33, F 22.28, Fe 11.13, P 6.18. **1,1'-Dibenzoylferrocenium hexafluorophosphate (5b)**: Yield: 1.03 g (76%) as a green solid. M.p. 99–101 °C (melting with decomp); IR: $\tilde{\nu}$ = 3116, 1653, 1596, 1314, 826, 556 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε) = 655 (2.54), 290 (sh) (4.26), 259 nm (4.46); MS (ESI): m/z (%): 417 (100) [M+Na⁺-PF₆]; HRMS (ESI): m/z calcd for C₂₄H₁₈⁵⁶FeO₂Na⁺: 417.0548; found: 417.0548; elemental analysis calcd (%) for C₂₄H₁₈F₆FeO₂P (539.21): C 53.46, H 3.36, F 21.14, Fe 10.36, P 5.74; found C 53.86, H 3.37, F 20.86, Fe 10.41, P 5.68.

1,1'-Dibromoferrocenium hexafluorophosphate (5g): Yield: 1.02 g (72%) as greenish blue solid. M.p. 177–179°C (decomp); IR: $\tilde{\nu}$ =3121, 1416, 827, 557 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε)=716 (2.35), 400 (2.94), 282 nm (3.98); MS (ESI): *m/z* (%): 346/344/342/340 (55/100/75/5) [*M*⁺ -PF₆], 300/298/296 (13/12/1), 256/254/252 (11/18/1); HRMS (ESI): *m/z* calcd for C₁₀H₈⁷⁹Br₂⁵⁶Fe⁺: 341.8337; found: 341.8339; elemental analysis calcd (%) for C₁₀H₈Br₂F₆FeP (488.79): C 24.57, H 1.65; found: C 24.65, H 1.59.

1,1'-Diiodoferrocenium hexafluorophosphate (5h): Yield: 1.07 g (81%) as a blue solid. M.p. 133–135 °C (melting with decomp); IR: $\tilde{\nu}$ =3116, 1409, 826, 556 cm⁻¹; UV/Vis (CH₂Cl₂): λ_{max} (log ε) = 725 (2.47), 410 (3.23), 320 (sh) (3.73), 287 (sh) (3.93), 259 (3.92), 236 nm (sh) (3.86); MS (ESI): *m*/*z* (%): 438/436 (100/15) [*M*+-PF₆], 312/310 (55/5) [*M*+H⁺-PF₆-I]; HRMS (ESI): *m*/*z* calcd for C₁₀H₈F₆I₂FeP (582.79): C 20.61, H 1.38, Fe 9.58; found: C 20.81, H 1.43, Fe 9.94.

Oxidative cyclization of diethyl 2-(5,5-diphenylpent-4-en-1-yl)malonate 8 (general procedure): nBuLi (0.17 mL, 0.27 mmol, 1.6 M in hexane) was added dropwise to a stirred solution of 8 (0.100 g, 0.26 mmol) in 1,2-dimethoxyethane (10 mL) under a dry N2 atmosphere at -78 °C. The reaction mixture was stirred at -78°C for 15 min. The ferrocenium hexafluorophosphates A, 4m, 5a, or 5b (0.65 mmol, 2.5 equiv) were added in one portion with vigorous stirring at -78 °C. TLC indicated complete conversion after completion of the addition. The reaction was quenched after 15 min by the addition of a few drops of water. The solution was diluted with ether and filtered through a pad of silica gel. The solvent was evaporated under reduced pressure, the nonhomogeneous residue was preadsorbed on silica gel, and purified by flash column chromatography (hexane, gradient to hexane/EtOAc 9:1, 9 eluted last). The analytical data of 9 and 10 are in agreement with those published.^[3g] The analytical data of compounds 11 and 12 are found in the Supporting Information. Computational methods: The quantum chemical calculations were performed using the TURBOMOLE 6.3 program. The geometry optimizations were carried out at the DFT level, using the PBE functional.[26] The DFT (PBE) calculations were expedited by expanding the Coulomb integrals in an auxiliary basis set, the resolution-of-identity (RI-J) approximation.[27] For the geometry optimization, the def2-SVP basis set was employed on all of the atoms,^[28] whereas the def2-TZVP basis set was used for the final single-point calculations to obtain presumably accurate molecular energies.[29]

The solvation effects were taken into account by using the COSMO-RS method^[6,30] using TURBOMOLE 6.3 for the COSMO calculation^[31] with $\varepsilon_r = \infty$ (ideal screening) and the COSMO*therm*^[32] program for the subsequent COSMO-RS calculation. The recommended protocol involving the Becke–Perdew (B-P) functional^[33] for the in vacuo and the $\varepsilon_r = \infty$ calculations together with the def-TZVP basis set was used.

The Gibbs free energy was then calculated as the sum of the following contributions [Eq. (1)]:

$$G = E_{\rm el} + G_{\rm solv} + E_{\rm ZPVE} - RT \ln(q_{\rm trans}q_{\rm rot}q_{\rm vib}) \tag{1}$$

in which $E_{\rm el}$ is the in vacuo energy of the system (at the RI-PBE/def2-TZVP//RI-PBE/def2-SVP level) and $G_{\rm solv}$ is the solvation free energy (calculated using the RI-BP/def-TZVP(COSMO-RS, $\varepsilon = 1, \ \varepsilon = \infty$) method as described above). $E_{\rm ZPVE}$ is the zero-point energy, and $-RT\ln(q_{\rm trans}q_{\rm rot}q_{\rm vib})$ accounts for thermal corrections to the enthalpy and entropic terms. $E_{\rm ZPVE}$ and $-RT\ln(q_{\rm trans}q_{\rm rot}q_{\rm vib})$ were obtained from a frequency calculation by using the same method and software as for the geometry optimization (RI-PBE/def2-SVP level), 298 K, and 1 atm using the ideal-gas approximation.

The reduction potentials were then calculated according to Equation (2):

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$$E^{0} [V] = 27.21 (G_{ox} [a.u.] - G_{red} [a.u.]) - E^{0}_{abs} (NHE) [V]$$
(2)

in which $G_{\rm ox}$ and $G_{\rm red}$ are the free energies calculated according to Equation (1) and $E_{\rm abs}^0(\rm NHE)$ is the absolute potential of the normal hydrogen electrode (NHE). In the literature, the values for $E_{\rm abs}^0(\rm NHE)$ range between 4.24 and 4.5 V;^[34] the most recent value of $E_{\rm abs}^0(\rm NHE)=4.281$ V was advocated by Isse and Gennaro.^[35] Solely for the sake of convenience, the value of $E_{\rm abs}^0(\rm NHE)=4.291$ V was used, which yielded the best agreement between the calculated and experimental data, that is, the mean signed error (MSE) equal to zero. In Table 5, the calculated data are also referenced to the Ag|AgCl 1 M LiCl electrode, that is, 0.21 V was subtracted from $E_{\rm calcd}^{0}$.^[23]

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- For reviews, see: a) Ferrocenes: Ligands, Materials and Biomolecules (Ed.: P. Stepnicka), Wiley, Hoboken, 2008; b) Ferrocenes (Eds.: A. Togni, T. Hayashi), Wiley-VCH, Weinheim, 1995; c) A. Togni, N. Bieler, U. Burckhardt, C. Köllner, G. Pioda, R. Schneider, A. Schnyder, Pure Appl. Chem. 1999, 71, 1531; d) R. Gómez Arrayás, J. Adrio, J. C. Carretero, Angew. Chem. 2006, 118, 7836; Angew. Chem. Int. Ed. 2006, 45, 7674; e) N. J. Long, Angew. Chem. 1995, 107, 37; Angew. Chem. Int. Ed. Engl. 1995, 34, 21; Angew. Chem. 1995, 107, 37; f) D. R. van Staveren, N. Metzler-Nolte, Chem. Rev. 2004, 104, 5931.
- [2] N. G. Connelly, W. E. Geiger, Chem. Rev. 1996, 96, 877.
- [3] a) U. Jahn, E. Dinca, J. Org. Chem. 2010, 75, 4480; b) U. Jahn, E. Dinca, Chem. Eur. J. 2009, 15, 58; c) U. Jahn, F. Kafka, R. Pohl, P. G. Jones, Tetrahedron 2009, 65, 10917; d) U. Jahn, P. Hartmann, E. Kaasalainen, Org. Lett. 2004, 6, 257; e) U. Jahn, P. Hartmann, I. Dix, P. G. Jones, Eur. J. Org. Chem. 2002, 718; f) U. Jahn, Chem. Commun. 2001, 1600; g) U. Jahn, P. Hartmann, I. Dix, P. G. Jones, Eur. J. Org. Chem. 2001, 3333; h) U. Jahn, M. Müller, S. Aussieker, J. Am. Chem. Soc. 2000, 122, 5212; i) U. Jahn, J. Org. Chem. 1998, 63, 7130.
- [4] a) E. S. Krygowski, K. Murphy-Benenato, M. D. Shair, Angew. Chem. 2008, 120, 1704; Angew. Chem. Int. Ed. 2008, 47, 1680; Angew. Chem. 2008, 120, 1704; b) J. M. Richter, B. W. Whitefield, T. J. Maimone, D. W. Lin, M. P. Castroviejo, P. S. Baran, J. Am. Chem. Soc. 2007, 129, 12857; c) J. P. Goddard, C. Gomez, F. Brebion, S. Beauviere, L. Fensterbank, M. Malacria, Chem. Commun. 2007, 2929; d) M. P. Sibi, M. Hasegawa, J. Am. Chem. Soc. 2007, 129, 4124; e) F. C. Pigge, J. J. Coniglio, N. P. Rath, J. Org. Chem. 2004, 69, 1161; f) P. Q. Nguyen, H.-J. Schäfer, Org. Lett. 2001, 3, 2993; g) T. Langer, M. Illich, G. Helmchen, Synlett 1996, 1137.
- [5] a) H. G. Lee, J. Y. Ahn, A. S. Lee, M. D. Shair, *Chem. Eur. J.* 2010, 16, 13058 and cited ref; b) J. Xu, E. J. E. Caro-Diaz, L. Trzoss, E. A. Theodorakis, *J. Am. Chem. Soc.* 2012, 134, 5072–5075.
- [6] A. Klamt, V. Jonas, T. Buerger, J. C. W. Lohrenz, J. Phys. Chem. A 1998, 102, 5074.
- [7] a) P. Winget, C. J. Cramer, D. G. Truhlar, *Theor. Chem. Acc.* 2004, *112*, 217; b) M. Srnec, J. Chalupský, M. Fojta, L. Zendlová, L. Havran, M. Hocek, M. Kývala, L. Rulíšek, *J. Am. Chem. Soc.* 2008, *130*, 10947; c) C. K. Chua, M. Pumera, L. Rulíšek, *J. Phys. Chem. C*, 2012, *116*, 4243–4251; d) M. Namazian, C. Y. Lin, M. L. Coote, *J. Chem. Theory Comput.* 2010, *6*, 2721.
- [8] a) R. Sanders, U. T. Mueller-Westerhoff, J. Organomet. Chem. 1996, 512, 219; b) O. Oms, F. Maurel, F. Carre, J. Le Bideau, A. Vioux, D. Leclercq, J. Organomet. Chem. 2004, 689, 2654.

- [9] S. R. Alley, W. Henderson, J. Organomet. Chem. 2001, 637–639, 216.
- [10] For applications of 2a, see: a) H. Naka, M. Uchiyama, Y. Matsumoto, A. E. H. Wheatley, M. McPartlin, J. V. Morey, Y. Kondo, J. Am. Chem. Soc. 2007, 129, 1921; b) G. Diehl, A. Liesener, U. Karst, Analyst 2001, 126, 288.
- [11] Alternative preparation: a) M. A. Carroll, A. J. P. White, D. A. Widdowson, D. J. Williams, *J. Chem. Soc. Perkin Trans.* 1 2000, 1551;
 b) M. Rausch, M. Vogel, H. Rosenberg, *J. Org. Chem.* 1957, 22, 903;
 c) N. Weliky, E. S. Gould, *J. Am. Chem. Soc.* 1957, 79, 2742.
- [12] Alternative preparation: a) G. P. Sollott, H. E. Mertwoy, S. Portnoy, J. L. Snead, *J. Org. Chem.* **1963**, *28*, 1090; b) A. K. Diallo, J. Ruiz, D. Astruc, *Org. Lett.* **2009**, *11*, 2635.
- [13] Alternative preparation: a) M. D. Rausch, J. Org. Chem. 1961, 26, 3579; b) C. Pichon, B. Odell, J. M. Brown, Chem. Commun. 2004, 598; c) P. Diter, S. Taudien, O. Samuel, H. B. Kagan, J. Org. Chem. 1994, 59, 370; d) P. Diter, S. Taudien, O. Samuel, H. B. Kagan, Tetrahedron: Asymmetry 1994, 5, 549; e) J. A. Adeleke, Y.-W. Chen, L.-K. Liu, Organometallics 1992, 11, 2543.
- [14] Similar results were obtained with TsBr: T.-Y. Dong, L.-L. Lai, J. Organomet. Chem. 1996, 509, 131.
- [15] For alternative preparations, see: a) A. S. Romanov, J. M. Mulroy, V. N. Khrustalev, M. Y. Antipin, T. V. Timofeev, *Acta Crystallogr. C* 2009, 65, m426; b) R. W. Fish, M. Rosenblum, *J. Org. Chem.* 1965, 30, 1253.
- [16] For alternative preparation, see: a) J. C. Goeltz, C. P. Kubiak, Organometallics 2011, 30, 3908; b) G. Laus, K. Wurst, W. Stolz, H. Schottenberger, Z. Kristallogr. New Cryst. Struct. 2005, 220, 229; c) I. R. Butler, S. B. Wilkes, S. J. McDonald, L. J. Hobson, A. Taralp, C. P. Wilde, Polyhedron 1993, 12, 129.
- [17] For a related preparation, see: a) J. J. Bishop, A. Davison, M. L. Katcher, D. W. Lichtenberg, R. E. Merrill, J. C. Smart, *J. Organomet. Chem.* 1971, *27*, 241. For electrochemical oxidations of dppf, see: b) G. Pilloni, B. Longato, B. Corain, *J. Organomet. Chem.* 1991, *420*, 57; c) D. Brett, B. D. Swartz, C. Nataro, *Organometallics* 2005, *24*, 2447.
- [18] Alternative preparation: B. McCulloch, D. L. Ward, J. D. Woollins, C. H. Brubaker Jr., Organometallics 1985, 4, 1425.
- [19] Alternative preparation and electrochemical investigation of 2k-m:
 A. Gref, P. Diter, D. Guillaneux, H. B. Kagan, *New J. Chem.* 1997, 21, 1353.
- [20] Prepared by using HPF₆ in analogy to: M. Shibuya, M. Tomizawa, Y. Iwabuchi, J. Org. Chem. 2008, 73, 4750.
- [21] T. E. Pickett, C. J. Richards, Tetrahedron Lett. 1999, 40, 5251.
- [22] CCDC-877550 (2a), CCDC-877552 (3a), CCDC-877551 (2m), and CCDC-877549 (3m) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [23] a) R. Sokolová, I. Degano, M. Hromadová, J. Bulíčková, M. Gál, M. Valášek, *Collect. Czech. Chem. Commun.* 2010, 75, 1097. For an overview, see: b) D. J. G. Ives, G. J. Janz, *Reference Electrodes*, Academic Press, New York, 1961.
- [24] M. D. Rausch, D. J. Ciappenelli, J. Organomet. Chem. 1967, 10, 127.
- [25] M. Sawamura, A. Yamauchi, T. Takegawa, Y. Ito, J. Chem. Soc. Chem. Commun. 1991, 874.
- [26] J. P. Perdew, K. Burke, M. Ernzerhof, Phys. Rev. Lett. 1996, 77, 3865.
- [27] K. Eichkorn, O. Treutler, H. Öhm, M. Häser, R. Ahlrichs, Chem. Phys. Lett. 1995, 240, 283.
- [28] F. Weigend, R. Ahlrichs, Phys. Chem. Chem. Phys. 2005, 7, 3297.
- [29] A. Schäfer, C. Huber, R. Ahlrichs, J. Chem. Phys. 1994, 100, 5829.
- [30] A. Klamt, J. Phys. Chem. 1995, 99, 2224.
- [31] a) A. Klamt, G. Schuurmann, J. Chem. Soc. Perkin Trans. 2 1993, 799; b) A. Schäfer, A. Klamt, D. Sattel, J. C. W. Lohrenz, F. Eckert, Phys. Chem. Chem. Phys. 2000, 2, 2187.
- [32] COSMOtherm, version C2.1, release 01.10. COSMOlogic GmbH & Co KG, Leverkusen, Germany.

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- [33] a) A. D. Becke, Phys. Rev. A 1988, 38, 3098; b) S. H. Vosko, L. Wilk, M. Nusair, Can. J. Phys. 1980, 58, 1200; c) J. P. Perdew, Phys. Rev. B **1986**, *33*, 8822.
- [34] a) J. Llano, L. A. Eriksson, Phys. Chem. Chem. Phys. 2004, 6, 4707; b) S. Trasatti, Pure Appl. Chem. 1986, 58, 955; c) C. P. Kelly, C. J. Cramer, D. G. Truhlar, J. Phys. Chem. B 2007, 111, 408.

[35] A. A. Isse, A. Gennaro, J. Phys. Chem. B 2010, 114, 7894.

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Ferrocenium Salts -

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Acceptor-Substituted Ferrocenium Salts as Strong, Single-Electron Oxidants: Synthesis, Electrochemistry, Theoretical Investigations, and Initial Synthetic Application



Expanding the range: A combined synthetic, electrochemical, and theoretical approach lays the foundation for the application of new ferrocenium salts with fine-tuned oxidative power, as exemplified by a double oxidative cyclization to bicyclic lactones under very mild conditions (see scheme).