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Communication

Syntheses and Purification of the Versatile Synthons Iodoferrocene and 1,1'-Diiodoferrocene

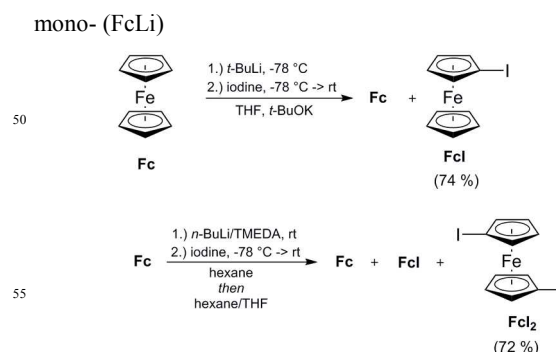
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This paper describes the improved synthesis and purification of iodoferrocene (FcI) and 1,1'-diiodoferrocene (FcI₂). FcI and FcI₂ were prepared by mono- and dilithiation of ferrocene followed by conversion into iodoferrocenes by reaction with iodine. Purification was accomplished by a simple sublimation/distillation procedure, affording FcI and FcI₂ in high yields (74 and 72%) and high purity (>99.9%). We determined the molecular structures of FcI and FcI₂ by X-ray single crystal diffraction.

The chemical, thermal and redox stability of the ferrocene is well known^{1,2} and therefore it has been incorporated in a variety of materials and devices including in molecular tunnel junctions^{3,4}, organic electronic devices⁵, thermotropic liquid crystals⁶, electrochromic materials⁷ and sensors of biomolecules⁸. Generally, the molecules can contain single ferrocene substituents, symmetrically or asymmetrically di- or poly substituted ferrocene moieties. Haloferrocenes such as iodoferrocene (FcI) and 1,1'-diiodoferrocene (FcI₂) are invaluable building blocks for the preparation of various of these materials. The iodo functionality is suitable for transition metal catalyzed cross-coupling reactions, such as, Ullmann^{9,10}, Stille¹¹, Negishi^{11,12}, Sonogashira^{13,14}-type reactions. Furthermore, it undergoes halogen lithium exchange reactions¹⁵, forms Grignard reagents upon reaction with magnesium¹⁶, Negishi reagents upon lithiation and subsequent reaction with zinc chloride¹⁷, can be transformed into other halogens as well as into an amine¹⁸. Due to the 1,1'-bifunctionality, FcI₂ is also suitable for the preparation of oligomers¹⁴ or polymers.^{19,20} High purity of the monomers is an important factor to obtain large molecular weights. Despite the fact that FcI and FcI₂ are important synthons, their commercial availability is lacking. The major reason is that it has been proved challenging to produce both compounds in high yields and purify the product mixtures via common methods. Several two or three step syntheses have been developed: iodoferrocenes have been prepared by mercuriation of ferrocene with mercury(II) acetate²¹, reaction of ferroceneboronic acid with N-iodo succinimide²² and lithiation of ferrocene, conversion into tri-*n*-butyltin derivatives and successive reaction with I₂.^{23,24,25} Lithiation of ferrocene and reaction with I₂ is the only method involving only one intermediate (FcLi species), which does not need to be isolated. These lithiation reactions afford mixtures of unreacted ferrocene,



Scheme 1 Syntheses of iodoferrocenes by reaction of ferrocenyl lithium species with iodine

and 1,1'-dilithiated species (FcLi₂) with FcLi as major product for the mono lithiation and FcLi₂ for the dilithiation, respectively.^{24,25,26,27} Upon reaction of FcLi with I₂, no amounts of FcI₂ are isolated^{28,29}. This is in contrast to the reaction with Bu₃SnCl, which produces noteworthy amounts of 1,1'-distannylated ferrocene.²⁴ Straightforward isolation of the title compounds was plagued by low to moderate yields and tedious work up procedures to separate from by-products. Main challenges were described to be ineffective methods for removal of tin-by products when using the pathway via tin intermediates or ineffective column chromatography to separate ferrocene, FcI and FcI₂.^{23,24,25} Starting from analytically pure FcLi³⁰ to minimize by-product formation does not bring much advantage as purification of the air sensitive and pyrophoric FcLi is challenging as well. Recently an oxidative purification method, which takes advantage of the different oxidation potentials of ferrocene, FcI and FcI₂, was reported.^{28,29} Washing of the product mixtures, obtained from reaction of lithioferrocenes with iodine, with aqueous FeCl₃ solution transferred the ferrocene, and also iodoferrocene for the case of the preparation of FcI₂, in form of ferrocenium salts in the aqueous phase and hence purifies the FcI or FcI₂. Reported yields for iodoferrocene (28 %²⁸ and 47 %²⁹) and 1,1'-diiodoferrocene (19 %²⁹) were moderate to low.

Herewith, we report a simple method to synthesize FcI and FcI₂ by reaction of lithioferrocenes with iodine and purify both by means of sublimation and distillation which allowed us to isolate FcI and FcI₂ in 74 and 72 % yields, respectively.

To prepare FcI, we mono-lithiated Fc with 2.5 eq. *t*-BuLi at -

78 °C and converted the FcLi to FcI by addition of solid iodine (Fig 1. path 1). In line with previously reported lithiations of ferrocene with 2 eq. *tert*-BuLi, we obtained mixtures of FcI and unreacted ferrocene. No amounts of FcI/FcI₂ could be isolated when carrying out the reaction at 0 °C. Purification (removal of the ferrocene from the mixture) was straightforwardly achieved by a simple sublimation under vacuum, using an air-cooled condenser. As ferrocene sublimes readily at 120 °C (0.1 mbar) and FcI not, analytically pure FcI is obtained by heating the crude mixture for 30 min under these conditions. The amount of unreacted ferrocene recovered by sublimation was only 3%.

Figure 1 shows the synthetic routes to prepare FcI₂ via 1,1'-dilithiation with *n*-BuLi in hexane with the presence of TMEDA following previously reported methods.^{23,26,29} We found that reaction with solid iodine to form FcI₂ did not proceed in pure hexane but diluting with THF (2 eq.) and cooling down to -78 °C yielded a mixture of FcI₂, FcI and unreacted ferrocene. We removed the ferrocene from this mixture by the same procedure as described above. The FcI could be easily removed by short-way vacuum distillation (Bp. 86-88 °C, 0.04 mbar), affording analytically pure FcI₂ (72%) as residue in the still pot.

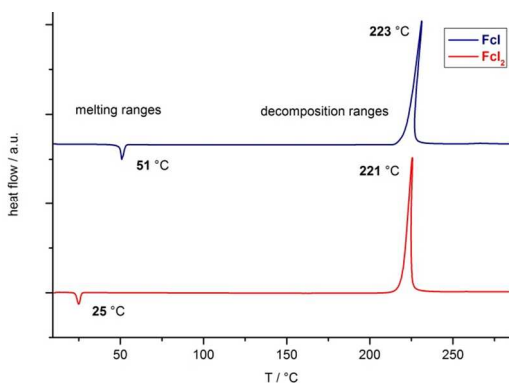


Fig. 1 DSC graphs of FcI and FcI₂, melting points were determined using two individual measurements. Reported values represent the minima of the curves.

The differential scanning calorimetry (DSC; Figure 1) graphs were recorded to determine the melting points of FcI and FcI₂ and their thermal stability; the melting points are 50-51 °C (lit. 44-45 °C)²¹ and 25-26 °C, respectively. FcI₂ was exclusively reported as dark oil at room temperature^{21,25,29}. These melting points are higher than previously reported and indicate that both FcI and FcI₂ are of high purity as impurities are the major reason for a melting point decrease. Indeed, GC-MS data show that the purities were both > 99.9 %. The DSC graphs also show that thermal decomposition of FcI and FcI₂ takes place at 223 °C for FcI and 221 °C for FcI₂. Hence no thermal decomposition takes place during distillation.

We show that it is possible to isolate the products by taking advantage of the different boiling/sublimation points of ferrocene, FcI, and FcI₂. Our method has the advantage over a recently reported method which used the differences in redox potentials of Fc/FcI (160 mV)/FcI₂ (290 mV), that it does not suffer from unwanted chemical side reactions such as reaction of the ferrocenium cations with water. The latter was investigated for several ferrocenes³¹ including halogenated ones³² and is well known for other 17-electron transition metal complexes.³³ The

lower yields of this method compared to ours could also originate in overlapping redox waves because the full width at half-maximum for a reversible one-electron process is 90.6 meV at 25 °C which is large compared to the difference in oxidation potentials of ferrocene, FcI, and FcI₂. Consequently, we assume that considerably large amounts of FcI and FcI₂ decompose during the washings with iron(III) chloride.

We additionally report the crystal structure of FcI₂. Fig. 2 shows its molecular structure. Interestingly, the molecule crystallizes with 3 conformers in the asymmetric unit (Fig. 2). Cp rings of two conformers are in eclipsed positions with iodo substituents in 1,2' position for one conformer and 1,3' position for the other, respectively. For the third conformer, Cp rings are in staggered position with iodo substituents pointing in opposite directions (torsion angle I-C-Fe-I = 180.00°). All conformers are non-tilted (tilt angles 0°, 0.12° and 1.12°). C-I bond length vary from 2.084(3) to 2.094(3) Å. Also, we could characterize FcI crystallographically. Crystallization at -20 °C from pentane afforded its monoclinic modification. Crystallographic data is in agreement with the previously reported structure.³⁴

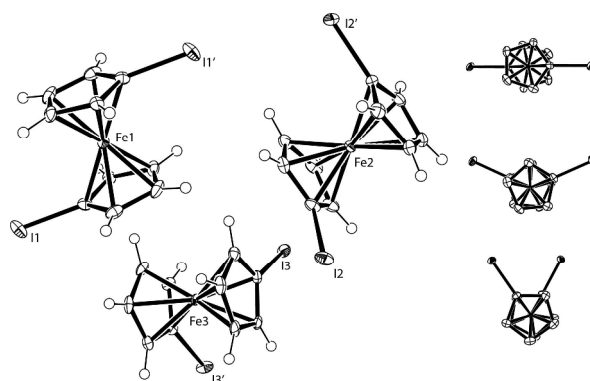


Fig. 2 ORTEP³⁵ diagram of the molecular structure of FcI₂ with 3 conformers in the asymmetric unit and top-view on the conformers (hydrogen atoms omitted for clarity), thermal ellipsoids with a probability of 50 %.

In summary, we describe two synthetic protocols suitable to prepare FcI and FcI₂ using readily available starting materials. The reaction mixtures contain ferrocene, FcI, and FcI₂, which can be separated virtually without any loss of product by taking advantage of the differences in sublimation and/or boiling points. The temperatures required for sublimation and vacuum distillation are well below the thermal decomposition temperature of ferrocene, FcI, and FcI₂. As our method does not require the use of other agents (e.g., oxidizing agents or toxic tin- or Hg-intermediates), we assume it to be so far the most economically and environmentally friendly one. Furthermore, our one-pot method is potentially suitable for up-scaling and affords both FcI and FcI₂ in high yields.

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Notes and references

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‡ Reactions were performed under argon atmosphere using standard Schlenk techniques. Hexane and THF were dried over sodium/benzophenone. N,N,N',N'-tetramethylethylenediamine (TMEDA) was distilled from sodium. Other compounds were used without further purification. We purchased ferrocene, *tert*-butyllithium (1.7 M in pentane), *n*-butyllithium (2.5 M in hexanes), TMEDA and iodine from Sigma-Aldrich. ¹H and ¹³C NMR spectra were recorded on a Bruker Avance 300 MHz (AV300) spectrometer using chloroform-*d* as solvent. X-ray single crystal diffraction was performed on a Bruker APEX diffractometer. Melting points and thermal stabilities were determined on a Mettler Toledo DSC 1 STARE system. APCI mass spectra and APCI high resolution mass spectra were recorded on a Bruker micrOTOF-QII mass spectrometer and GCMS spectra were recorded on an Agilent system.

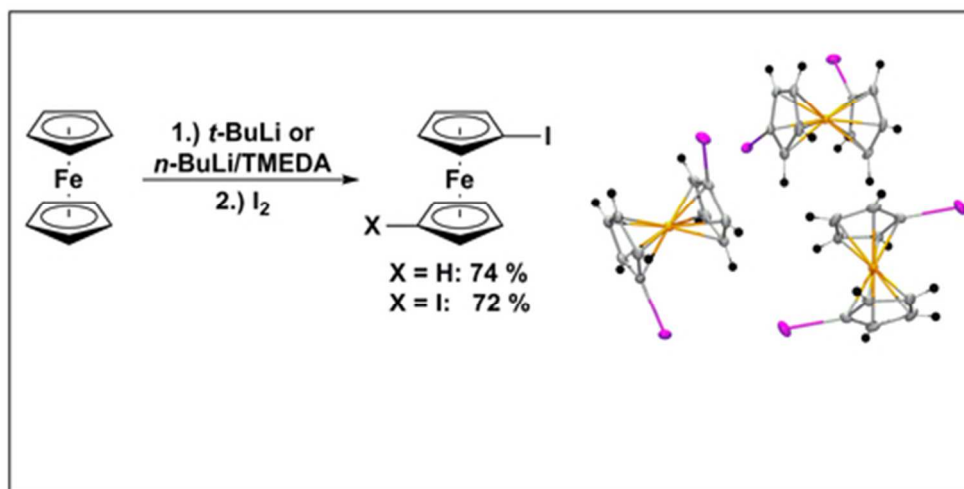
Crystal data for FeI₂: C₁₀H₈I₂Fe, *M* = 437.81, monoclinic, *a* = 14.002(1), *b* = 17.241(1), *c* = 14.647(2) Å, *U* = 3303.2(4) Å³, *T* = 173 K, space group C2/c (no.15), *Z* = 12, 3730 reflections measured, 3803 unique (*R*_{int} = 0.054) which were used in all calculations. The final *wR*(*F*₂) was 0.023 (all data). Single crystals were grown from pentane at -50 °C.

FeI: A Schlenk flask was charged with 6.00 g (32.2 mmol) ferrocene, 0.45 g (3.7 mmol) of potassium *tert*-butoxide and 300 ml THF. The solution was cooled to -78 °C and 2.5 equivalents (47 ml, 1.7 M in pentane) of *tert*-butyllithium were added dropwise while stirring. After stirring for 0.5 h at -78 °C an orange precipitate had formed. Stirring was continued for another 1.5 h. Solid iodine (20.46 g (81 mmol)) was added to the suspension. Stirring was continued at -78 °C for an additional 15 min before the mixture was allowed to warm up to room temperature. The reaction mixture was washed with 200 ml saturated sodium thiosulfate solution, 200 ml hexane was added and the organic phase was collected. The aqueous phase was washed once with 100 ml hexane. Combined organic extracts were concentrated using rotary evaporator. The resulting dark oil was taken up in little hexane and filtered through a pad of silica (5 x 4 cm) using hexane as an eluent. After removal of the solvents *in vacuo*, the crude product containing FeI with minor amounts of ferrocene as impurity was heated for 30 min in a round bottom flask, equipped with an air cooled glass condenser to 120 °C (0.1 mbar), to remove unreacted ferrocene via sublimation. After cooling down, the residue crystallized upon standing at room temperature to yield analytically pure FeI (7.41 g, 23.7 mmol, 74 %). δ_{H} = 4.41 (AA', Cp, 2 H), 4.19 (s, Cp, 5 H), 4.15 (BB', Cp, 2 H). δ_{C} = 74.40 (subst. Cp), 70.10 (unsubst. Cp), 68.78 (subst. Cp), 39.71 (ipso-C). HRMS (APCI): calcd: 311.9098, found: 311.9084. GC-MS: *m/z* 312 (*M*⁺). mp: 49-50 °C.

FeI₂: A 1 l Schlenk flask was charged at room temperature with 5.0 g (26.9 mmol) ferrocene, 10 ml (67.2 mmol, 2.5 eq.) TMEDA, 26.8 ml (67.2 mmol, 2.5 eq.) *n*-butyllithium and 180 ml hexane. The orange solution was stirred at room temperature for 16 hours after which a thick pale orange precipitation had formed. The suspension was cooled down to -78 °C and 400 ml THF were added slowly using a dropping funnel. Solid iodine (15.0 g, 59.1 mmol, 2.2 eq.) was added and the mixture was kept at -78 °C for an additional 15 min after which it was allowed to warm up slowly to room temperature. Stirring was continued for an additional 2 h at room temperature. The reaction mixture was washed with 200 ml Na₂S₂O₃-solution, the organic phase was separated and dried over Na₂SO₄ after which the solvents were removed using a rotary evaporator. The resulting dark oil was taken up in little hexane and flash-filtered through a plug of silica. Solvent removal afforded 9.4 g of a crude oil, containing FeI₂ accompanied by minor amounts of ferrocene and FeI. Ferrocene was removed by sublimation at 120 °C at 0.1 mbar using an air-cooled condenser. FeI₂ and FeI remained in the still pot. After no more ferrocene was visibly condensing, the condenser was removed and the flask was attached to a short-way distillation set-up. The temperature was increased to 150 °C and about 0.5 g of the distillate was collected, it contained all FeI accompanied by FeI₂. The still pot contained 8.5 g (19.4 mol) of pure FeI₂ in form of a dark oil, which crystallized upon standing (72 %). Recrystallization from pentane at -50 °C afforded the product in form of light brown needles. δ_{H} = 4.33 (AA', Cp, 4 H), 4.13 (BB', Cp, 4 H). δ_{C} =

77.51 (Cp), 72.23 (Cp), 40.32 (ipso-C) ppm. HRMS (APCI): calcd: 437.8065, found: 437.8044. GC-MS: *m/z* 438 (*M*⁺). mp: 25-26 °C.

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