Journal of Organometallic Chemistry 778 (2015) 21-28

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Catalytic C-F activation via cationic group IV metallocenes

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ARTICLE INFO

Article history: Received 1 November 2014 Received in revised form 8 December 2014 Accepted 10 December 2014 Available online 16 December 2014

Keywords: C-F activation Metallocene Catalysis Friedel-Crafts

ABSTRACT

The catalytic cleavage of sp³ C–F bonds of 3,3,3-trifluoropropene (TFP) can be performed using cationic group IV metallocenes and an excess of triisobutylaluminum. The isobutyl adduct 1,1-difluoro-5-methyl-hex-1-ene (DFMH) as well as 3,3-(difluoroallyl)aromates (DFAArs) are formed in different ratios, depending on reaction conditions. The Friedel–Crafts type reaction of TFP and the aromatic solvent represents a new catalytic route toward DFAArs with different substituents (especially electron donors), such as alkyl groups. *In-situ* FTIR and ¹⁹F NMR spectroscopy were used to gain closer insight into the different defluorination reactions. The influence of the central metal, the ligand structure, the aromatic solvent and the concentration of the reactants was investigated and mechanistic conclusions were drawn.

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Introduction

Fluorinated organic molecules are widely spread in various fields such as polymers, refrigerants, pharmaceuticals, agrochemicals and many more [1,2]. Beneficial properties of most of these substances are based on extremely stable carbon–fluorine bonds, having homolytic dissociation energies up to (500 ± 50) kJ mol⁻¹ [3]. Synthesis of fluorinated organic molecules is a challenging task and can be achieved by introducing fluorinated groups as well as by selective fluorination or defluorination reactions [3–5]. Defluorination of easy to obtain, highly fluorinated molecules is a versatile pathway toward complex, partially fluorinated hydrocarbons [6]. Various strategies for the activation of C–F bonds have been developed and recent reviews give an excellent overview over the state of the art in this field [5–10].

Focusing on defluorination reactions, two major trends should be kept in mind concerning the stability of C–F bonds. Firstly, the higher the number of fluorine atoms attached to one C-unit, the shorter and stronger are all bonds to this C-species. This effect is more pronounced for sp³ than for sp² carbon atoms [11]. Secondly, sp² C–F bonds of aromatic and olefinic fluorocarbons are weaker than sp³ C–F bonds of the aliphatic analogs [12,13].

Lewis acids are known to be able to activate sp³ C–F bonds [7]. In general boron and aluminum containing Lewis acids, especially AlCl₃ and BBr₃ are capable of activating C–F bonds of alkyl fluorides

http://dx.doi.org/10.1016/j.jorganchem.2014.12.011 0022-328X/© 2014 Elsevier B.V. All rights reserved. toward the formation of the corresponding alkyl chloride or alkyl bromide, respectively. Thereby the C–F bond is cleaved *via* S_N1-type abstraction of fluoride by the Lewis acid. As a consecutive reaction, Friedel–Crafts alkylation of aromatic compounds is possible [4,6]. Terao et al. [14] enhanced this principle and developed a general method for the conversion of sp³ C–F bonds of alkyl fluorides to sp³ C-X (X = Cl, C, H, O, S, Se, Te, N) bonds using organoaluminum reagents of the composition R₂AlY (R = Et, ⁱBu; Y = Cl, Et, CH = CHⁿHex, C=C-ⁿHex, H, OPh, SPh, SePh, TePh, NEt₂). They were able to show that the reaction does not proceed *via* a S_N1 but *via* a S_N2 mechanism [14].

An example of catalytic hydrodefluorination of sp³ C–F bonds was reported by Ozerov et al. [15] An excess of triethylsilane was reacted with 1-fluoropentane in the presence of trityl tetrakis(pentafluorophenyl)borate or triethylsilyl tetrakis(pentafluorophenyl) borate to form pentane. Further investigations showed that the reaction can be performed with dialkylaluminum hydrides or trialkyl aluminum in a similar way, whereby trityl carboranes are used as long lived catalyst, which enable much higher turnover numbers (TONs) than the tetrakis(pentafluorophenyl)borates [16,17]. If the reaction is conducted in aromatic solvents or if aromatic substrates were used, Friedel–Crafts type alkylation products are formed as well. Similar results were reported by Müller et al. [18] and Rosenthal et al. [19], who performed catalytic hydrodefluorination reactions with silvlium borates and aluminum borates, respectively.

C–F bond activation by transition metal complexes *via* various mechanisms is a well established field although it is mainly limited to sp^2 C–F bonds [8]. Especially for group IV metal complexes







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several stoichiometric and also some catalytic strategies for sp² C–F bond activation are known [20–30]. Kiplinger and Richmond [28] reported that low valent Zr (II) or Ti (II) species, which are generated by treating Cp₂ZrCl₂ or Cp₂TiCl₂ with reducing agents (Al or Mg together with HgCl₂) can perform reductive defluorination *e.g.* of perfluorodecaline to octafluoronaphthalene. Furthermore the Zr systems can mediate hydrodefluorination reactions of fluorinated aromatic compounds *via* oxidative addition of the aromatic C–F bond followed by homolytic cleavage of Zr–C bond. Rearomatization takes place by radical hydrogen abstraction from the solvent THF [28,29]. Similar reactions were observed for Ti (II), Zr (II) and Hf (II) species generated by other strategies [9,24,30,31].

However, not exclusively low valent group IV metal complexes can activate C–F bonds. Jones et al. [12,23,32–37] contributed comprehensive work on C–F activation by zirconocene and hafnocene dihydrides [12,23,32–37]. Depending on the substrate, various mechanisms were suggested involving the formation of Zr (III) radicals, Zr (II) species, or in case of fluorinated olefins insertion into Zr–H bonds followed either by β - or α -fluoride elimination [12,23,32–37]. For the stoichiometric reaction of bis(pentamethyl cyclopentadienyl)zirconium(IV) dihydride (Cp*₂ZrH₂) with 3,3,3trifluoropropene (TFP) both insertion regioisomers were observed at –90 °C and decomposed upon warming to –70 and –10 °C, respectively [12].

Although very stable metal-fluorine bonds are formed during the C-F activation, highly fluorophilic aluminum compounds enable the regeneration of both, neutral and cationic Zr (IV) hydrides from the corresponding fluorides [25,38]. Rosenthal et al. [25] published the first example for the hydrodefluorination of fluorinated pyridines catalyzed by neutral Zr (IV) hydrides. Crimmin et al. [20] extended this concept to non-heterocyclic fluoroarenes. Lentz et al. [22] published quite similar results for the hydrodefluorination of fluorinated olefins with Cp₂TiF₂ as a catalyst and silanes as fluorine trap. Ti (III) hydrides are stated to be the active species and the reaction is assumed to proceed both, via a σ bond metathesis mechanism as well as *via* a β -hydride insertion/ β fluoride elimination pathway. Radical mechanisms are assumed to be unlikely to occur [21]. Using TFP as a substrate even catalytic cleavage of sp³ C-F bonds was observed, albeit with low TOF (0.04 min^{-1}) and TON (43) values. Under the reaction conditions which were applied, the conversion of TFP is rather unselective and not only 1,1-difluoropropene, but also 1,1,1-trifluoropropane and 1fluoropropene were formed [21,22].

Whereas there are some reports on C-F bond activation by neutral group IV metallocene complexes, only few reports on the interaction of cationic metallocene complexes with fluorocarbons exist [39,40]. Cationic group IV metallocenes are well studied systems and find broad application especially in olefin polymerization reactions [41]. Attractive metal-fluorine interactions have been detected in crystal structures and low temperature ¹⁹F NMR studies [40,42,43]. Marks et al. [39] reported the decomposition of $[(CH_3)_2CpZrCH_3][B(C_6F_5)_4]$ in benzene solution after several weeks forming a fluorine bridged binuclear complex. Hessen et al. could prove the coordination of fluorobenzene to the cationic Ti(III) complex $[Cp_{2}^{*}Ti][B(C_{6}H_{5})_{4}]$, which weakens the C–F bond but does not cleave it [40]. In contrast to fluorobenzene, α, α, α -trifluorotoluene reacts rapidly with $[Cp_{2}^{*}Ti][B(C_{6}H_{5})_{4}]$ to form Cp*₂TiF₂ and 1,2-diphenyl-1,1,2,2-tetrafluoroethane as main products.

Formation of $Cp^*_2TiF_2$ was also observed for the corresponding complexes with borate counterions, which contain benzylic fluorine atoms, such as in $[Cp^*_2Ti][B(3,5-(CF_3)_2C_6H_3)_4]$.

Up to now, no attempts have been made to use cationic group IV metallocene complexes for selective defluorination of fluorocarbons, although there is a great potential.

Experimental section

General considerations

Unless otherwise stated, all manipulations were performed either under standard Schlenk conditions using dry argon or in an argon filled Glovebox (MBraun Unibox). Benzene was distilled over Na/benzophenone and stored over molecular sieves (4 Å). HPLC grade TCB was degassed and stored over molecular sieves (4 Å), toluene was obtained from an MBraun MB-SPS solvent purification system. Bis(cyclopentadienyl) zirconium(IV) dichloride (Cp₂ZrCl₂), bis(pentamethylcyclopentadienyl) zirconium(IV) dichloride $(Cp_2^*ZrCl_2)$, bis(cyclopentadienyl) hafnium(IV) dichloride (Cp_2HfCl_2) and 3,3,3-trifluoropropene (TFP) were purchased from ABCR, triisobutylaluminum (TIBA) was purchased from Aldrich and all were used without further purification. Trityl tetrakis(pentafluorophenyl) borate (borate) [2] and [1-(9-η⁵-fluorenyl)-2-(5,6-cyclopenta-2methyl-1- η^5 -indenyl)ethane]ZrCl₂ (C₁-ZrCl₂) [1] were prepared as described in literature. Solution NMR spectra were recorded on a Bruker AV-500CRYO or a Bruker AV-500 spectrometer. ¹H-, ¹³C-, and ¹⁹F NMR spectroscopic chemical shifts δ are reported in ppm relative to tetramethylsilane. $\delta({}^{1}H)$ is calibrated to the residual proton signal, δ ⁽¹³C) to the carbon signal of the deuterated solvent. δ ⁽¹⁹F) is calibrated to the signal of hexafluorobenzene (C_6F_6 , -164.9 ppm) or trichloro-fluoro-methane (CFCl₃, 0 ppm). GC–MS analysis was conducted using a Varian 3900 GC (Varian FactorFour VF-5 ms capillary column 0.25 mm Å ~ 30 m Å ~ 0,25 μm; injector temperature: 210 °C: carrier gas: He (1 ml/min): column temperature 80 °C (3 min) -> 250 °C (10 K/min) combined with a Varian Saturn 2100T system (EI: 70 eV; m/z: 20-650).

Procedure for defluorination reactions

Defluorination reactions were performed using a React-FTIR/ MultiMax four-autoclave system (Mettler-Toledo). One of the 50 ml stainless steel reactors with a diamond window, a mechanical stirring and a heating device was dried and put under argon atmosphere prior to use. The reactor was heated to 40 °C and pressurized with 1.4 bar argon. Unless otherwise stated, all defluorination reactions were performed using benzene as aromatic solvent, 8 µmol of metallocene, 8 mmol of TIBA, 32 µmol of borate and a TFP partial pressure of 1.1 bar. The amount of aromatic solvent was adapted to yield a total volume of the reaction solution of 23 ml. If a metallocene dichloride was used, the cationic species was generated in-situ in two steps from neutral metallocene dichlorides. Firstly, the metallocene dichloride was placed in a 25 ml Schlenk tube and dissolved in the aromatic solvent (benzene, toluene or 1,2,4-trichlorobenzene). 200 equivalents of TIBA were added to give a total volume of 3 ml. The preactivation mixture was kept at 60 °C for 60 min. The preactivation solution was then transferred into the reactor, which was previously equipped with the corresponding amounts of aromatic solvent and TIBA. In a second step, 5 ml of a solution of borate and the aromatic solvent were added. This activation procedure is well known from olefin polymerization reactions using metallocene dichlorides as precatalysts [44].

The *in-situ* FTIR data collection was started and after three minutes of stirring at 40 °C and 500 rpm, TFP was added. The addition of TFP was controlled with an EL PRESS pressure meter controller unit (Bronkhorst High-Tech). Within seconds, the desired total pressure was reached. The reaction was stopped after 60 min by depressurizing the reactor. The reaction solution was immediately transferred to sealable glass vials and stored at -20 °C. Samples for ¹⁹F NMR spectroscopy were taken directly from the reaction solution and a sealed glass capillary filled with hexafluorobenzene in benzene-d8 (1 µL/ml) was added. For the ¹⁹F NMR spectra taken

directly from the reaction solutions, ¹⁹F NMR shifts were determined relative to the signal of hexafluorobenzene, which was referenced to -164.9 ppm. The ratio of product integrals to the hexafluorobenzene integral was used for quantification, whereby the observed concentration of hexafluorobenzene in the NMRsamples was previously determined by ¹⁹F NMR spectroscopy of a sample of α,α,α -trifluorotoluene in benzene (1 µL/ml) containing the same capillary.

Determination of max. rate, TON* and TOF values

Max. rates were determined from the maximum slope of the FTIR signal traces (1740–1760 cm⁻¹) and the sum of the yields of 3,3-(difluoroallyl)aromates (DFAAr), 1,1 difluoro-5-methyl-hex-1-ene (DFMH) and 1,1-difluoropropene (DFP) determined by ¹⁹F NMR spectroscopy. As even in absence of metallocene, certain amounts of DFAArs, DFMH and DFP are formed, for the calculation of corrected TON (TON*) and TOF values, FTIR traces were corrected by subtracting the FTIR trace of the corresponding metallocene free experiment.

3,3-(Difluoroallyl)benzene (DFAB)

The reaction solutions of several metallocene catalyzed reactions, which were performed in benzene were combined, carefully quenched with ice water and washed with 2 M hydrochloric acid. The organic layer was dried with MgSO₄ and distilled under reduced pressure. The sump containing mainly DFAB was purified by column chromatography in *n*-pentane. Removal of pentane under reduced pressure yielded DFAB as a colorless liquid. Analytical data is in accordance to literature [27].

¹H NMR, ¹³C NMR, ¹⁹F NMR, FT-IR, GC–MS.

¹H NMR (500 MHz, CDCl₃, δ): 7.35–7.27 (m, 2H), 7.26–7.16 (m, 3H), 4.40 (dtd, J = 24.8, 8.0, 2.2 Hz, 1H), 3.33 (dt, J = 8.2, 1.8 Hz, 2H). ¹H NMR (500 MHz, C₆D₆, δ): 7.10–7.06 (m, 2H), 7.05–7.01 (m, 1H), 6.91–6.87 (m, 2H), 3.98 (dtd, J = 25.1, 8.0, 2.3 Hz, 1H), 2.93 (dt, J = 8.1, 1.7 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃, δ): 156.7 (dd, J = 287.6, 285.9 Hz), 139.6 (t, 2.3 Hz), 128.7, 128.2, 126.6, 77.8 (dd, 2.3, 2.2 Hz), 28.5 (d, 4.7 Hz). ¹⁹F NMR (471 MHz, C₆D₆, δ): -91.28 (dd, J = 46, 2 Hz), -94.33 (dtd, J = 45, 25, 2 Hz). GC–MS *m*/z (% relative intensity, ion): 155 (10, M), 154 (100, M), 134 (30, M–HF), 133 (46, M–HF). IR (thin film): ν_{max} 1749 cm⁻¹ (C=CF₂).

3,3-(Difluoroallyl)toluene (DFAT)

DFAT (mixture of isomers) was isolated in analogy to DFAB from the solution of the reaction with 8 μ mol of Cp₂ZrCl₂, 32 μ mol borate, 8 mmol TIBA and a TFP partial pressure of 1.1 bar in toluene. DFAT was obtained as a colorless liquid.

¹H NMR (500 MHz, C₆D₆, δ): 7.25–6.80 (m, 4H), 4.07–3.85 (m, 1H), 3.00–2.85 (m, 2H), 2.2–1.95 (m, 3H). ¹⁹F NMR (471 MHz, C₆D₆, δ): –91.3 (d, J = 46 Hz, 1F Isomer 1), –91.4 (d, J = 46 Hz, 1F Isomer 3), –91.5 (d, J = 46 Hz, 1F Isomer 2), –93.9 (ddt, J = 46, 25, 2 Hz, 1F Isomer 1), –94.3 to –94.5 (m, 1F Isomer 3), –94.5 (dd, J = 46, 25 Hz, 1F Isomer 2). ¹⁹F NMR (471 MHz, CDCl₃, δ): –88.8 (d, J = 46 Hz, 1F Isomer 2), –91.3 (ddt, J = 46, 25, 2 Hz, 1F Isomer 3), –89.0 (d, J = 46 Hz, 1F Isomer 2), –91.3 (ddt, J = 46, 25, 2 Hz, 1F Isomer 1), –91.8 (ddt, J = 46, 25, 2 Hz, 1F Isomer 3), –91.9 (ddt, J = 46, 25, 2 Hz, 1F Isomer 2). IR (thin film): v_{max} 1749 cm⁻¹ (C=CF₂). GC–MS *m*/z (% relative intensity, ion): 169 (11, M), 168 (100, M), 154 (5, M–CH₃), 153 (66, M–CH₃), 134 (6, M–CH₃–HF), 133 (59, M–CH₃ – HF).

1,1-Difluoro-5-methyl-hex-1-ene (DFMH)

The reaction solutions of several metallocene catalyzed reactions, which were performed in benzene were combined, carefully quenched with ice water and washed with 2 M hydrochloric acid. The organic layer was dried with MgSO₄ and distilled under reduced pressure. A fraction containing DFMH in benzene was obtained at 650 mbar and 55 °C.

¹H NMR (500 MHz, C₆D₆, δ): 3.81 (dtd, J = 25.8, 8.0, 2.5 Hz, 1H), 1.74 (q, J = 7.8 Hz, 2H), 1.31 (dh, J = 13.3, 6.6 Hz, 1H), 0.99 (q, J = 7.3 Hz, 2H), 0.76 (d, J = 6.6 Hz, 6H). ¹⁹F NMR (471 MHz, C₆D₆, δ): -91.9 (d, J = 50 Hz, 1F), -94.6 (ddt, J = 50, 26, 2 Hz, 1F). IR (thin film): v_{max} 1756 cm⁻¹ (C=CF₂). GC–MS *m*/z (% relative intensity, ion): 135 (5, M), 134 (31, M), 119 (11, -CH₃), 99 (10, -CH₃ – HF), 91 (15, -C₃H₇), 83 (16, -CHF₂), 77 (95, -C4H₉).

1,1-Difluoropropene (DFP)

DFP was identified by ¹⁹NMR spectroscopy using literature data [45].

Results and discussion

Metallocene catalyzed C-F activation of TFP

In contrast to most of the studies on the activation of C–F bonds with metallocene catalysts, we did not use neutral but cationic species with weakly coordinating counterions in the presence of an excess of trialkyl aluminum [46].

As depicted in Scheme 1, we observed that the defluorination reaction of TFP is much faster in the presence of preactivated group IV metallocene dichlorides (max. rate of 758 μ mol min⁻¹ for Cp₂ZrCl₂) compared to the reaction of TFP in a solution of TIBA and borate without metallocene (max. rate of 35 μ mol min⁻¹) or a solution of TIBA in benzene in absence of borate and metallocene (max. rate of 7.5 μ mol min⁻¹).

The addition of preactivated metallocene did not affect the reaction in absence of borate as no cation forming agent was present. This indicates that under the given conditions not neutral metallocene species but cationic metallocene complexes are the catalytically active species.

Two fluorinated main products, 3,3-(difluoroallyl)benzene (DFAB) and 1,1-difluoro-5-methyl-hex-1-ene (DFMH) were identified by NMR and GC–MS analyses. 1,1-Difluoropropene (DFP) was formed as a minor product. All three of these products have a characteristic IR absorption band between 1740 and 1760 cm⁻¹ corresponding to a $F_2C = CHR$ ($R = CH_2-C_6H_5$, CH₃,



Scheme 1. Formation of DFAB and DFMH from TFP (partial pressure 1.1 bar with a) TIBA, b) TIBA and borate, c) TIBA, borate and Cp₂ZrCl₂.



Fig. 1. Yields of DFAB and DFMH for defluorination reactions of TFP determined by ¹⁹F NMR spectroscopy. Reactions were performed without metallocene using TIBA ("TIBA"), TIBA and borate ("borate"), and with TIBA, borate and 8 μmol of either Cp₂TiCl₂, Cp₂HfCl₂, or Cp₂ZrCl₂, respectively ("Cp₂TiCl₂", "Cp₂HfCl₂", and "Cp₂ZrCl₂").

CH₂–CH₂–CH(CH₃)₃) double bond stretching vibration. Due to the lack of further intense and characteristic IR-bands it is not possible to differentiate between these three compounds in *in-situ* FTIR spectra. Therefore, ¹⁹F NMR spectroscopy was applied for the determination of product yields, product ratios and TONs, while *in-situ* FTIR signal traces (1740–1760 cm⁻¹) reflect the reaction progress toward DFAB, DFMH, and DFP and were used to calculate max. rates and max. TOFs.

TON is defined as number of TFP molecules that are converted into DFAB, DFMH or DFP by one molecule of metallocene in the investigated time span (57 min). As mentioned above, significant amounts of DFAB, DFMH and DFP are produced even in absence of metallocene in the reaction mixture (see "borate" in Fig. 1 Fig. 2). Therefore, for the calculation of corrected TON values (TON*) we subtracted the total yield of DFMH, DFAB and DFP of the metallocene free experiment from the corresponding value of the metallocene catalyzed reaction.

The max. TOF is defined to be the max. number of turnovers per minute per molecule of metallocene. For the calculation of max. TOF values, the FTIR signal trace (1740–1760 cm⁻¹) of the metallocene free experiment is subtracted from the FTIR signal traces of the corresponding metallocene catalyzed reactions. Product yields obtained from ¹⁹F NMR spectroscopy were used to calculate the max. TOFs from the max. slopes of these corrected FTIR signal traces.

In order to investigate effects of the catalyst composition, metallocene dichlorides with Ti, Zr and Hf as central metal and different ligand structures were tested. As there are multiple reactions taking



Fig. 2. FTIR signal traces $(1740-1760 \text{ cm}^{-1})$ of DFAB, DFMH and DFP for TFP defluorination reactions with TIBA, borate, and 8 µmol of either Cp₂ZrCl₂, Cp₂HfCl₂, or Cp₂TiCl₂ ("Cp₂ZrCl₂", "Cp₂HfCl₂", and "Cp₂TiCl₂"), control experiments without metallocene using TIBA and borate ("borate"), or only TIBA ("TIBA"), respectively.

place at the same time, we performed several sets of experiments whereby reaction parameters, such as concentration of TIBA, TFP, borate and metallocene, as well as the type of solvent were varied in order to gain insight into the different reaction pathways.

Influence of the central metal

Defluorination reactions of TFP were performed using TIBA ("TIBA"). TIBA and borate ("borate") (max. rate: 35 μ mol min⁻¹). and TIBA, borate and 8 µmol of either Cp₂TiCl₂, Cp₂ZrCl₂, or Cp₂HfCl₂ in the presence of TIBA and borate ("Cp₂TiCl₂", "Cp₂ZrCl₂", and "Cp₂HfCl₂") (see Figs. 1 and 2). Both, Cp₂ZrCl₂ (max. rate: 758 μ mol min⁻¹; max. TOF: 80 min⁻¹; TON*: 117) and Cp₂HfCl₂ (max. rate 750 μ mol min⁻¹; max. TOF: 78 min⁻¹, TON*: 95) strongly accelerate the defluorination reaction during the first minutes after TFP addition compared to the metallocene free control experiment (borate). Cp_2TiCl_2 (max. rate: 300 min⁻¹; max. TOF: 26 min⁻¹; TON*: 25) enhances the reaction as well, although the effect is much weaker. ¹⁹F NMR product analysis (Fig. 1) reveals that the addition of Cp₂ZrCl₂, Cp₂HfCl₂, and Cp₂TiCl₂ increase the formation of DFAB by 242%, 191%, and 23% respectively, compared to the metallocene free control experiment. Meanwhile, the production of DFMH barely changes.

The higher catalytic activities found for the zirconocene and the hafnocene complex compared to the corresponding titanocene complex are in accordance with higher catalytic activities being found for zirconocene and hafnocene complexes in well studied metallocene catalyzed olefin polymerization reactions [1,44,47]. The lower activity, which is observed for titanocenes is mostly contributed to their tendency toward reduction of Ti (IV).

Influence of the ligand structure

Different zirconocene dichlorides were used as precatalysts in order to investigate effects of the ligand structure on the defluorination reaction (see Fig. 3).

The comparison of L_2ZrCl_2 (L = Cp, Cp^{*}) shows that pentamethylcyclopentadienyl (Cp^{*}) ligands lead to a lower catalytic activity (max. rate 196 µmol min⁻¹; max. TOF 13 min⁻¹), during the first minutes of the reaction compared to the cyclopentadienyl-system (Cp₂ZrCl₂) (max. rate 758 µmol min⁻¹; max. TOF 80 min⁻¹) (see Fig. 4). This can be contributed to a higher sterical demand of the Cp^{*}. The well studied ethylene-bridged, C₁-symmetric metallocene [1-(9- η^5 -fluorenyl)-2-(5,6-cyclopenta-2-methyl-1- η^5 -indenyl)

ethane]ZrCl₂ (C₁–ZrCl₂) gives a lower catalytic activity (max. rate 121 μ mol min⁻¹; max. TOF 13 min⁻¹) and a longer catalytic lifetime than Cp₂ZrCl₂ [44,48] Figs. 5,6.



Fig. 3. FTIR signal traces $(1740-1760 \text{ cm}^{-1})$ of DFAB, DFMH and DFP for TFP defluorination reactions with TIBA, borate and either Cp₂ZrCl₂, C₁–ZrCl₂, or Cp^{*}₂ZrCl₂, respectively ("Cp₂ZrCl₂", "C₁–ZrCl₂", and "Cp^{*}₂ZrCl₂") and the control experiment without metallocene using TIBA and borate (borate).



Fig. 4. Long term measurement of the FTIR signal traces (1740–1760 cm⁻¹) of DFAB, DFMH and DFP for TFP defluorination reactions with Cp*₂ZrCl₂, Cp₂ZrCl₂ and reference experiment without any metallocene ("borate").



Fig. 5. Sum of the yields of DFAAr, DFMH and DFP for TFP defluorination reactions with TIBA, borate and Cp_2ZrCl_2 in benzene, toluene and TCB calculated from FTIR signal traces (1740–1760 cm⁻¹) and ¹⁹F NMR spectra.



Fig. 6. Yields of DFAArs (DFAB, DFAT and DFATCB) and DFMH for defluorination reactions of TFP with TIBA, borate and Cp_2ZrCl_2 in TCB, benzene and toluene determined by ¹⁹F NMR spectroscopy (DFATCB < 150 μ mol).

In contrast to the Cp system, the Cp* system stays catalytically active even after more than one hour (TOF of 1.2 min⁻¹ after 50 min). The deactivation of the catalytically active species is suppressed by the sterically demanding methyl groups in Cp*₂ZrCl₂. This result shows that long catalyst lifetimes are possible for the catalytic defluorination of TFP with cationic metallocenes if the ligand system is properly substituted.

Influence of the solvent

Three aromatic solvents: benzene, toluene, and 1,2,4-trichlorobenzene (TCB) were tested under similar conditions using Cp₂ZrCl₂ as metallocene precatalyst.

In-situ FTIR studies and ¹⁹F NMR analyses reveal that the conversion of TFP strongly depends on the aromatic solvent. In case of



Scheme 2. Reaction of benzene (a), toluene (b) or other aromatic substances (c) with TFP in the presence of TIBA, borate, and Cp_2ZrCl_2 .

toluene and TCB not DFAB, but isomers of the corresponding 3,3-(difluoroallyl)aromates (DFAArs) 3,3-(difluoroallyl)-toluene (DFAT) and 3,3-(difluoroallyl)-trichlorobenzene (DFATCB) are expected. While DFAT could be isolated, DFATCB was not identified unambiguously. The comparison of the experiments conducted in benzene and toluene indicates that higher DFAAr yields are reached for more electron rich aromates. The fact that no, or only low amounts of DFATCB are formed also supports this conclusion, although steric effects might also play a role in case of TCB. In order to prove that the catalytically active species is not decomposed rapidly in TCB, 1hexene was added to the reaction solution. 1-hexene is known to be oligomerized by cationic metallocenes generated from Cp₂ZrCl₂ [26]. Consumption of 1-Hexene was observed, as the FTIR absorbance of the C=C bending vibration at 910 cm⁻¹ decreased with time. While the yields of DFAArs vary strongly, the yields of DFMH are less affected by the solvent.

We could not only show that the rate of the formation of DFAArs depends on the electron density in the π -system of the aromatic solvent but also established a new catalytic route toward DFAArs with different substituents, especially electron donors, such as alkyl groups (see Scheme 2). These might be of interest *e.g.* for pharmaceutical applications [49].

Reaction of TFP with TIBA in absence of borate and metallocene

Trialkyl aluminum reagents are known to react with fluoroalkanes by activating sp³ C–F bonds and forming sp³ C–C bonds instead [14]. In accordance to literature, we observed a reaction of TFP with the trialkylaluminum compound TIBA in benzene as solvent [14]. The conversion of TFP was extremely low compared to experiments conducted in the presence of borate or metallocene and borate. DFAB, DFP and DFMH are formed, whereby DFMH is the main product.

Depending on the concentration of TIBA in the reaction mixture, the product ratios changed (Fig. 7). With increasing TIBA concentration, the yield of DFMH rises while the amount of DFAB does not change significantly. Variation of the TFP partial pressure resulted in no significant change in the product composition (Fig. 8).

Reliable kinetic measurements could not be performed due to very low yields. However, the data indicate that the reaction toward DFMH is of first order with respect to TIBA.

In absence of borate and metallocene, DFMH is formed by the reaction of TIBA with TFP (see Scheme 3). Insertion reactions of olefins into Al–C bonds in so called Aufbau reactions are known for



Fig. 7. Yields of DFAB and DFMH for defluorination reactions of TFP in absence of borate and metallocene at different TIBA concentrations.



Fig. 8. Yields of DFAB and DFMH for defluorination reactions of TFP with TIBA in absence of borate and metallocene at different TFP partial pressures.



Fig. 9. Yields of DFAB and DFMH for defluorination reactions of TFP with TIBA, borate at different C_1 – $ZrCl_2$ concentrations.



Fig. 10. Double logarithmic plot of the corrected max. rates (max. rate*) [µmol/min] versus the C₁–ZrCl₂ concentrations [µmol/ml] for TFP defluorination reactions conducted with 2, 4 and 8 µmol C₁–ZrCl₂.



Scheme 3. Proposed mechanism for the formation of DFMH in one reaction step *via* a six membered transition state (TS) (counterclockwise) or in a sequence of two reaction steps *via* an insertion elimination mechanism (clockwise).

many years and usually take place at elevated temperatures and high olefin concentrations [50]. The electron withdrawing $-CF_3$ substituent is expected to change the selectivity of this insertion reation from 1,2-, which is usually preferred for α -olefins to 2,1insertion [12,47,50,51]. A consecutive β -fluoride elimination leads to DFMH and fluoro diisobutylaluminum (ⁱBu₂AlF). In contrast, the reaction *via* a six membered transition state (TS) leads to the reaction products in a one step reaction.

As shown in Fig. 7, the formation of DFAB is not enhanced at higher TIBA concentrations. We assume the formation of DFAB to take place *via* a cationic mechanism (Scheme 4) even in absence of a cation forming agent, such as borate. In a first step, the reaction of TIBA with TFP leads to the formation of anionic ⁱBu₃AlF⁻ and cationic $C_3H_3F_2^+$. This carbocation subsequently reacts either with the aromatic solvent benzene to form DFAB in a Friedel—Crafts type reaction or with TIBA to form DFMH. The formation of DFP is most likely caused by DIBAL-H impurities [52]. All three reaction



Scheme 4. Proposed mechanisms for the formation of DFAB, DFMH and DFP via a difluoroallyl cation.

pathways lead to the formation of a diisobutylaluminium cation (${}^{i}Bu_{2}Al^{+}$), which can react with TFP to form another C₃H₃F₂⁺ carbocation and ${}^{i}Bu_{2}AlF$. Thus, the reaction cycle of this chain reaction is closed [15,16].

Reaction of TFP with TIBA in the presence of borate

In accordance to literature, we found the reaction of TIBA and TFP in the presence of borate to give higher yields of DFAB and DFMH compared to borate free reactions, whereby DFAB is produced as the main product (Figs. 7 and 11) [15–17]. The higher yields of DFMH compared to borate free experiments give another hint that DFMH is not exclusively formed by the reaction of TIBA and TFP (Scheme 3) but also *via* a mechanism involving cationic species similar to the one depicted in Scheme 4. Upon addition of borate, the yield in DFAB is increased by a factor of 18 (22.83 μ mol -> 408.5 μ mol) compared to a factor of only 3.6 (62.87 μ mol -> 225.8 μ mol) for DFMH. This strongly indicates that DFMH is formed *via* two different mechanisms, whereby only one of them involves a cationic species. This cationic mechanism only plays a minor role in absence of borate, but becomes dominant if borate is present.



Fig. 11. Yields of DFAB and DFMH for defluorination reactions of TFP with TIBA and borate at different TFP partial pressures a) in the presence and b) in absence of C_1 -ZrCl₂.

Reaction of TFP with TIBA in the presence of borate and metallocene

For the following experiments $[1-(9-\eta^5-fluorenyl)-2-(5,6-cyclopenta-2-methyl-1-\eta^5-indenyl)ethane]ZrCl_2$ (C₁–ZrCl₂) was used as metallocene compound because of its moderate catalytic activity and life time.

Influence of the metallocene concentration

If catalytic amounts of preactivated C_1 –ZrCl₂ are added to the reaction mixture, the defluorination reaction is accelerated compared to the control experiment with TIBA and borate. Experiments with different amounts of C_1 –ZrCl₂ (4 µmol, 8 µmol and 16 µmol) were performed under similar reaction conditions (see Fig. 9).

The analysis of the reaction products reveals that mainly the reaction toward DFAB is accelerated by the addition of metallocene, while the amount of DFMH does not change significantly.

In analogy to the max. TOF values, so called "corrected max. rates" (max. rate*) were determined from *in-situ* FTIR and ¹⁹F NMR data. For the determination of max. rate*s, the FTIR signal trace (1740–1760 cm⁻¹) of the metallocene free experiment is subtracted from the FTIR signal traces of the corresponding metallocene catalyzed reactions prior to the determination of the maximum slope. This correction of the data is necessary to omit the share of

defluorination reactions, which are not attributed to metallocene catalysis.

The data presented in Fig. 10 indicates that the reaction toward DFAB is approximately of first order with respect to the metallocene.

Influence of the TFP partial pressure

A set of experiments at varying TFP pressures in the presence and absence of metallocene C_1 – $ZrCl_2$ was performed. The comparison of these results indicates that under the given conditions the metallocene catalyzed reaction (*e.g.* the difference between metallocene containing and metallocene free reactions) is independent of the TFP pressure.

Influence of the TIBA concentration

In order to investigate the influence of the TIBA concentration on the product composition, experiments were conducted using variable TIBA concentrations (see Fig. 12). As expected from the data obtained for the reaction in absence of borate and metallocene (see Fig. 7) the production of DFMH increases with increasing TIBA concentrations. However, to our surprise, less DFAB was produced at higher TIBA concentrations. This leads us to the conclusion that high TIBA concentrations lead to a faster decomposition of the catalytically active, cationic metallocene species.



Fig. 12. Yields of DFAB and DFMH for defluorination reactions of TFP with different amounts of TIBA in the presence of borate and C_1 – $ZrCl_2$.

Reaction mechanism for the metallocene catalyzed formation of DFAB

Based on our experimental data we suggest the following mechanism for the metallocene-catalyzed defluorination of TFP to form the Friedel–Crafts adduct DFAB (see Scheme 5).

The cationic metallocene species is stabilized by the weakly coordinating borate anion. The coordination of TFP to the metal center is assumed to take place both, via the π -system of the C=C double bond, as well as via agostic interaction of one of the fluorine atoms and the metal center. We assume the fluorine atom to be coordinated in the central equatorial site and the double bond, as well as the isobutyl group to be coordinated in the lateral sites. Therefore, the spatial separation of the isobutyl group and the C1atom of the olefin inhibit an intramolecular insertion reaction, which would be followed by a β -fluoride elimination to give DFMH. This coordination activates the terminal sp² carbon atom toward the electrophilic attack of aromates, which simultaneously leads to the formation of a metal-carbon bond. The resulting carbocationic intermediate [L₂M ⁱBu DFAB]⁺ can react in two manners, which both lead to the formation of DFAB, [L₂MⁱBuF], ⁱBuAl⁺ and 2methylpropane. Firstly, it can undergo a β -fluorine elimination to



Scheme 5. Proposed mechanism for the formation of DFAB by catalytic defluorination of TFP with cationic metallocenes.

yield the monofluorinated metallocene [L₂MⁱBuF] and the 6-(3,3,3trifluoropropyl)cyclohexadienylium cation. This cation consequently reacts with TIBA to form DFAB, ⁱBu₂Al⁺, and 2methylpropane. As a second option, [L₂M ⁱBu DFAB]⁺ can first react with TIBA to give ⁱBu₂Al⁺, 2-methylpropane, and a neutral metallocene complex, which then undergoes β -fluorine elimination to yield the monofluorinated metallocene [L2MiBuF], and DFAB. The catalytic cycle is closed by the reaction of ⁱBu₂Al⁺ with the monofluorinated metallocene, which recovers the cationic metallocene species [L₂MⁱBu⁺]. Experiments with different aromatic solvents such as toluene and TCB support the suggested mechanism, as the reaction toward the corresponding Friedel-Crafts adduct proceeds faster the more electron rich the aromatic system is.

Conclusion

In the presence of an excess of trialkylaluminum, cationic group IV metallocenes catalytically activate sp³ C–F bonds, which enables their cleavage and the simultaneous formation of C-C bonds leading to DFMH and 3,3-(difluoroallyl)aromates (DFAArs) such as DFAB and DFAT. This opens a new synthetic route toward a broad variety of DFAArs. The product ratio strongly depends on the reaction conditions, as different reaction pathways are involved. Based on the experimental results we suggest a mechanism in which TFP is coordinated to a cationic metallocene species. This coordination activates TFP toward the attack of relatively weak nucleophiles such as aromatic solvents. Cationic metallocene is regenerated in-situ and thus TON*s of up to 117 with a max. TOF of 80 min⁻¹ were achieved in case of the highly active metallocene Cp₂ZrCl₂. Systems with highly substituted Cp^{*}-Ligands show high catalytic life times of more than 6 h, whereby the maximum catalytic activity is comparatively low.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http:// dx.doi.org/10.1016/j.jorganchem.2014.12.011.

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