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Selective Hydrodefluorination of Hexafluoropropene to Industrially Relevant Hydrofluoroolefins

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Abstract. The selective hydrodefluorination of hexafluoropropene to HFO-1234ze and HFO-1234yf can be achieved by reaction with simple group 13 hydrides of the form $\text{EH}_3\bullet\text{L}$ ($\text{E} = \text{B}, \text{Al}$; $\text{L} = \text{SMe}_2, \text{NMe}_3$). The chemoselectivity varies depending on the nature of the group 13 element.

A combination of experiments and DFT calculations show that competitive nucleophilic vinylic substitution and addition-elimination mechanisms involving hydroborated intermediates lead to complementary selectivities.

Keywords: Hydrodefluorination; HFO-1234ze; HFO-1234yf; Alane; Hydroboration

Introduction

Synthetic refrigerants have improved our quality of life and contributed the year-on-year growth of the fluorocarbon industry.^[1] The most widespread synthetic refrigerants are volatile molecules of low molecular mass that contain at least one halogen atom. Refrigerants are applied in sealed compressor units in household refrigerators, climate control systems in cars or industrial air-conditioning units. Despite their immediate benefit to humanity, early generations of synthetic refrigerants and aerosols (CFCs and HFCs) have been a disaster for the environment. This led to legislation such as the Montreal Protocol restricting their use.^[2,3] The fluorocarbon industry has responded by beginning the manufacture, marketing and supply of hydrofluoroolefins (HFOs). HFOs have global warming potentials similar to CO_2 and do not deplete ozone. These volatile molecules are our most advanced refrigerants and hold promise as a long-term solution to a long-standing environmental problem.^[4]

The majority of known syntheses of industrially relevant HFOs rely on multistep processes involving partial chlorination of propane, halogen exchange to introduce the fluorine atom and a hydrodehalogenation step to obtain the olefin.^[5-7] An approach involving the hydrogenation and hydrodefluorination of HFP using a chromium-based heterogeneous catalyst has also been reported.^[8] Given that the majority of the patented industrial processes involve the redundant construction and destruction of a C–Cl bond along with toxic, corrosive and expensive materials, the

selective hydrodefluorination of hexafluoropropene (HFP) is an attractive route to a number of commercially relevant HFOs including HFO-1234ze and HFO-1234yf (Figure 1). HFP itself is bulk commodity used in the manufacture of poly(fluoro)olefins.

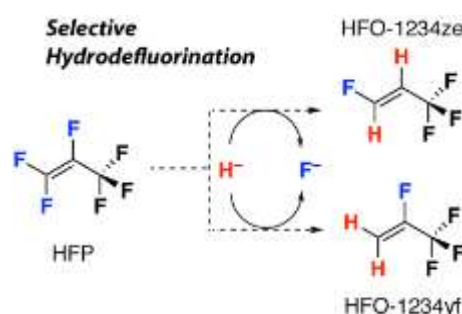


Figure 1. Selective hydrodefluorination of HFP as a route to HFOs.

The selective hydrodefluorination of HFP to form tetrafluoroolefins has limited precedent. A number of researchers have shown that boranes react with fluoroolefins via either catalysed or non-catalysed pathways that can involve the generation of mixtures from a combination of hydroboration and hydrodefluorination steps.^[9-13] Related alanes are also able to hydrodefluorinate these substrates. In 2018, it was reported that $\text{AlH}_3\bullet\text{NHC}$ ($\text{NHC} = \text{N-heterocyclic carbene}$) can selectively hydrodefluorinate HFP to form HFO-1234yf in 79% yield.^[14,15]

Herein, we detail the hydrodefluorination of HFP to commercially relevant HFO-1234ze and HFO-1234yf. The selectivity can be guided by careful choice of Lewis base and group 13 hydride ($\text{EH}_3\bullet\text{L}$; $\text{L} = \text{THF}$, SMe_2 , NMe_3 ; $\text{E} = \text{B}$, Al). We show that the tailored and expensive *N*-heterocyclic carbene ligand systems are actually unnecessary for selective reactions. While these reactions rely on the use of stoichiometric quantities of the main group reagents, the by-products ($\text{EF}_3\bullet\text{L}$) are industrially relevant materials in their own right, typically used as Lewis Acids.^[16,17] Through investigation of the mechanism we provide insight into the origin of selectivity and as such this work may act as a foundation for future (catalytic) routes from HFP to industrially relevant HFOs.

Results and Discussion

Hydrodefluorination of Hexafluoropropene:

Surprisingly there are no reports investigating the reaction of hexafluoropropene (HFP) with the simple borane adducts $\text{BH}_3\bullet\text{L}$ ($\text{L} = \text{THF}$, SMe_2 , NMe_3). Heating a sealed J Young NMR tube containing a 0.8 mM solution of $\text{BH}_3\bullet\text{SMe}_2$ in benzene- d_6 charged to 1 atm. of HFP at 100 °C forms isomers of 1,2,3,3,3-pentafluoropropene, *E*-2 and *Z*-2 after 24 h. Ultimately *E*-/*Z*-mixtures of 1,3,3,3-tetrafluoropropene (HFO-1234ze) are generated as the major product after heating for 5 d (Figure 2a).

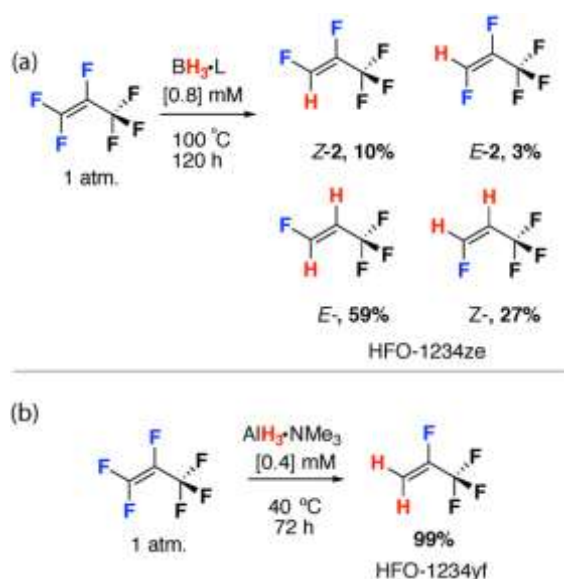


Figure 2. Hydrodefluorination of HFP with (a) $\text{BH}_3\bullet\text{L}$ and (b) $\text{AlH}_3\bullet\text{NMe}_3$.

The final product distribution represents an 86% yield of HFO-1234ze formed in a 2:1 ratio of *E*:*Z* isomers. The remaining mass balance has been characterised as *E*/*Z*-2 (13%) and trifluoropropene (<2%). The ratio of products proved dependent on the reaction scale, with preparative scale reactions albeit at the same absolute

concentration yielding a larger amount of pentafluoropropenes. The boron containing side-product contains diagnostic resonances in the ^{11}B and ^{19}F NMR spectra at $\delta_{\text{B}} = 3.2$ (s) ppm, $\delta_{\text{F}} = -136.67$ (br) ppm consistent with those reported for $\text{BF}_3\bullet\text{SMe}_2$.

In contrast, the reaction of HFP with $\text{AlH}_3\bullet\text{NMe}_3$ leads to the efficient and highly selective formation of 2,3,3,3-tetrafluoropropene (HFO-1234yf) under mild conditions in high yield and selectivity (1 atm. 40 °C, 72 h). Initial mixing of $\text{AlH}_3\bullet\text{NMe}_3$ with HFP in benzene- d_6 results in rapid formation of a colourless precipitate (assumed to be AlF_3) and high conversion to *E*-2 and *Z*-2, in ratio 2:1 as evidenced by ^1H NMR spectroscopy after 5 mins at 25 °C. Further HDF reactivity is observed even at ambient temperature, but warming the reaction to 40 °C gives optimum selectivity and rate, yielding HFO-1234yf as the major F-containing product (> 98%) after 72 h at 40 °C. Small quantities of 3,3,3-trifluoropropene (< 2%) are observed from over-reduction (Figure 2b).

Mechanisms of HDF: Several observations are consistent with the alane and borane reagents reacting by different pathways. The first of which is the ligand dependence of reactivity. Despite the strongly bound amine ligand, $\text{AlH}_3\bullet\text{NMe}_3$ reacts readily and with the same selectivity as the $\text{AlH}_3\bullet\text{NHC}$ system.^[14] In contrast, the borane system $\text{BH}_3\bullet\text{L}$ shows a strong ligand dependence with $\text{L} = \text{NMe}_3$ being ineffectual for HDF and $\text{L} = \text{THF}$ highly inefficient. The latter borane was used as a THF solution and it is likely that exogenous THF is acting as an inhibitor in the reaction. Only hydrocarbon solutions of $\text{BH}_3\bullet\text{L}$ ($\text{L} = \text{SMe}_2$, NMe_3) proved useful for HDF. The experiments are consistent with the borane reagents requiring a ligand dissociation step to react and the alane reagents not.

As part of detailed studies into the mechanism hydroboration with $\text{BH}_3\bullet\text{L}$, Brown and co-workers have concluded that the reaction can be considered a combination of a reversible ligand dissociation step to form BH_3 followed by extremely facile addition to the alkene.^[18,19] While solvent effects have historically been somewhat contentious in this field, the mechanism is now widely accepted. Brown and co-workers demonstrated that strong donor ligands, such as amines, decrease the rate of reaction.^[18]

The second observation which would be consistent with a switch in mechanism is the switch in selectivity which is observed in changing the reagent from $\text{AlH}_3\bullet\text{L}$ to $\text{BH}_3\bullet\text{L}$. The latter main group hydride gives a mixture of HFO-1234ze in low selectivity as the major product, while the former gives almost exclusively HFO-1234yf.

Alane Pathway (concerted $\text{S}_{\text{N}}\text{V}$): The hydrodefluorination of HFP with $\text{AlH}_3\bullet\text{NMe}_3$ was observed to proceed without the formation of defined reaction intermediates. No experimental evidence was obtained to suggest that hydroalumination of the

alkene occurs in the reaction mechanism. DFT calculations were used to probe the plausible pathways alongside a series of experiments investigating the formation and reactivity of reaction intermediates. Calculations were implemented in Gaussian09. A series of functionals (ω B97xD, M06L, M062x, B3PW91-GD3BJ) were investigated to confirm that the trends were reproducible across a number of methods. While *all* the computational approaches led to the same qualitative outcomes for every single mechanism and reaction step, data for the B3PW91 functional are presented herein.

In line with the lack of a significant effect of the ligand L on reactivity, HDF was calculated to proceed by a concerted S_NV pathway involving the 4-coordinate aluminium reagent (Figure 3a-c). Formation of *E*-2 is preferred over *Z*-2 with activation barriers of $\Delta G^\ddagger_{298K} = 24.8$ and 27.7 kcal mol⁻¹ respectively. *E*-2 and *Z*-2 can undergo a subsequent concerted HDF step with barriers of 28.3 and 28.2 kcal mol⁻¹ respectively, both yielding HFO-1234yf. The calculations are consistent with the experimental data and predict the observation of pentafluoropropenes *E*-2 and *Z*-2 as intermediates due to the more challenging second HDF step, the preferential formation of intermediate *E*-2, and ultimately the high selectivity for the formation of HFO-1234yf. Ligand dissociation from $AlH_3 \bullet NMe_3$ is calculated to be exergonic by 22 kcal mol⁻¹ and is not required for the cS_NV HDF pathway to operate. In fact, the lowest barriers for a direct HDF by the concerted pathway are already within a reasonable range of the ligand dissociation ΔG° before considering any bond making or breaking steps involving AlH_3 and the fluoroolefin.

Transition states involving hydride transfer to the internal position of HFP, *E*-2, or *Z*-2 are higher in

energy ($\Delta G^\ddagger_{298K} = 35 - 37$ kcal mol⁻¹) than those for the terminal position ($\Delta G^\ddagger_{298K} = 25 - 28$ kcal mol⁻¹) and are unlikely to be accessible at 40 °C (Figure 3d). Similarly, the generation of 1,1,1-trifluoropropene by a 3rd HDF step of HFO-1234yf at the internal site occurs by a high energy transition state ($\Delta G^\ddagger_{298K} = 36$ kcal mol⁻¹ see supporting information **TS-A8**). The relative barriers can be explained by considering the fluorinated substrates as Michael acceptors. HFP is known to undergo nucleophilic attack at the terminal position with a number of reactions occurring *trans* to the electron-withdrawing CF_3 group.^[20] In the cS_NV mechanism the CF_3 moiety acts as the electron-withdrawing group to activate the electrophile and the hydride takes the role of the nucleophile. Nucleophilic attack occurs at the terminal position due to a combination of inductive ($-F$ and $-CF_3$) and mesomeric effects ($-F$). These effects result in the polarisation of HFP in a manner consistent with a Michael acceptor, with the terminal carbon atom being considerably more electrophilic than the internal one. Comparing **TS-A1** and **TS-A3** (Figure 3e) it becomes clear that the most positively charged sp^2 carbon centre is that of the terminal position. Transfer of the hydride atom from Al to C occurs with transfer of charge to the alkene moiety. The aforementioned polarisation of HFP results in charge being best accommodated by the internal carbon atom and again favours attack at the terminal position. In **TS-1** nucleophilic attack occurs with H---C bond formation at the terminal carbon but charge transfer to the internal carbon as evidenced by a perturbation of the geometry of this carbon atom, from sp^2 toward sp^3 hybridisation (**TS-A1**, $\Theta = 111.1^\circ$).

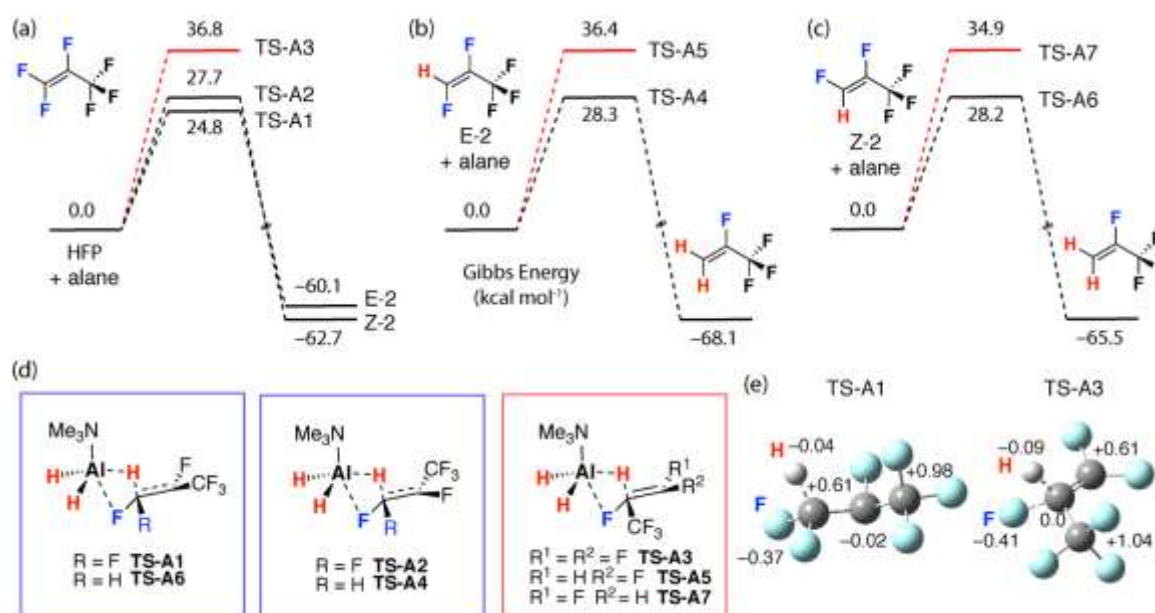


Figure 3. DFT calculations for $AlH_3 \bullet NMe_3$ with (a) HFP, (b) *E*-PFP and (c) *Z*-PFP. (d) Comparison of TS geometries. (e) Comparison of NPA charges in the anionic fluoroalkene fragments of **TS-A1** and **TS-A3**. **alane** = $AlH_3 \bullet NMe_3$ by-product $AlFH_2 \bullet NMe_3$ not shown.

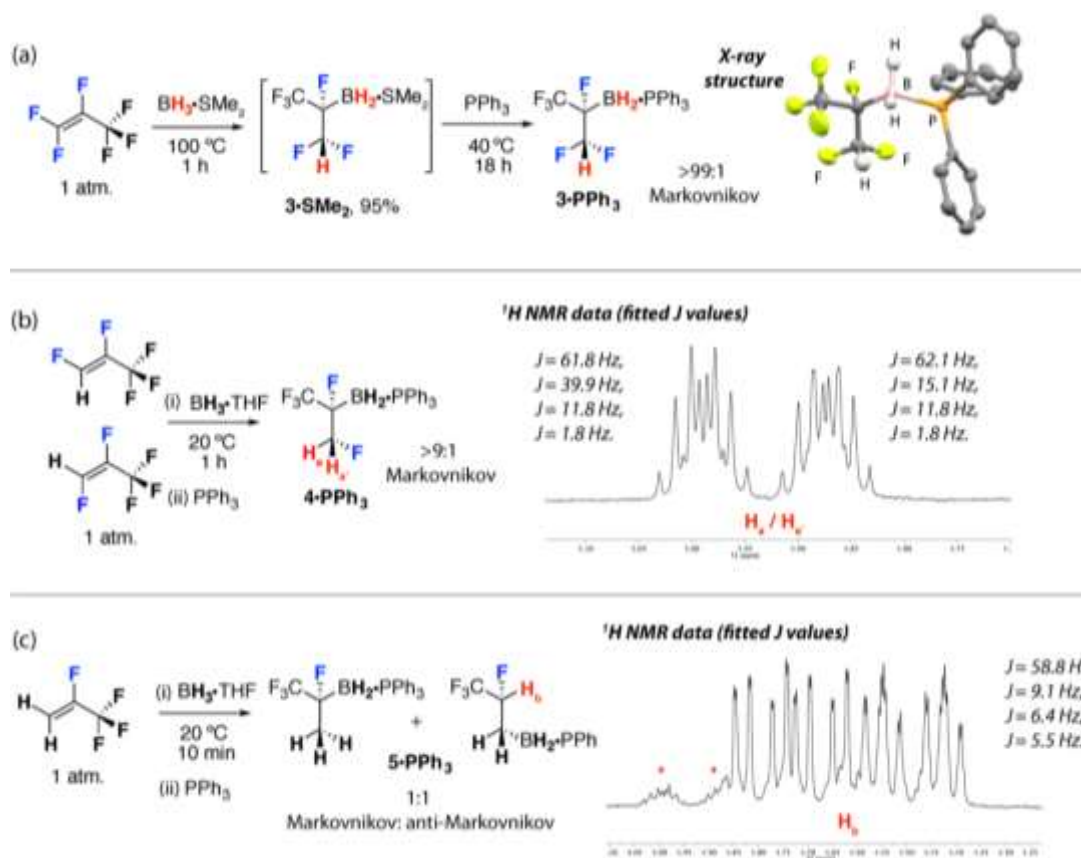


Figure 4. Reactions of $\text{BH}_3\bullet\text{L}$ with (a) HFP, (b) E/Z-2 and (c) HFO-1234yf. Along with selected data that support the assignment of the products and regioselectivity of hydroboration. J values from simulated spectra. Peaks marked with an * are the impurity $4\bullet\text{PPh}_3$ in samples of $5\bullet\text{PPh}_3$.

Hence, the HDF of HFP by a concerted $\text{S}_{\text{N}}\text{V}$ mechanism involving a metal hydride reagent occurs with a substrate bias for the formation of HFO-1234yf in high selectivity. This realisation may set the foundation for routes from HFP to HFO-1234yf by catalytic hydrodefluorination using hydrogen as a reductant and it is plausible that coordinatively saturated transition metal hydride complexes may behave in a similar manner to $\text{AlH}_3\bullet\text{NMe}_3$.

Borane Pathway (Addition-Elimination): The HDF of HFP by $\text{BH}_3\bullet\text{SMe}_2$ did not lead to HFO-1234yf but rather a mixture of E/Z-isomers of HFO-1234ze. This reaction required more forcing conditions (100 °C for 5 d *versus* 40 °C for 3 d) to reach high conversion and proceeds with a lower selectivity than observed for the alkane. Calculations show that the direct reaction of $\text{BH}_3\bullet\text{SMe}_2$ with HFP by a concerted $\text{S}_{\text{N}}\text{V}$ mechanism requires the formation prohibitively high energy transition states ($\Delta G^\ddagger_{298\text{K}} = 50 - 60 \text{ kcal mol}^{-1}$), effectively ruling out this pathway (see supporting information). In order to gain further insight into role of the borane in the HDF of HFP, and the potential for alkene hydroboration in the mechanism, a series of stoichiometric experiments were conducted. The 1:1 reaction of $\text{BH}_3\bullet\text{L}$ with HFP (L = NMe_3 , THF, SMe_2) led to the clean formation of hydroborated intermediates $3\bullet\text{L}$ (Figure 4). For both L = THF and

SMe_2 these reactions proceeded in high-yield allowing the *in-situ* generation of organoborane products as a single regioisomer. In contrast, for NMe_3 the reaction only proceeded in low conversion, consistent with the need for ligand dissociation prior to hydroboration and the formation of BH_3 as an intermediate. $3\bullet\text{SMe}_2$ was characterised by the appearance of a diagnostic resonance in the ^1H NMR spectrum corresponding to the $-\text{CF}_2\text{H}$ group at $\delta_{\text{H}} = 5.85$ (ddd, $^2J_{\text{HF}} = 56.1, 54.0 \text{ Hz}$, $^3J_{\text{HF}} = 8.5 \text{ Hz}$) ppm. The data are consistent with formation of a single regioisomer and Markovnikov addition of the borane to HFP. While this intermediate could not be isolated due to its volatility, reaction of $3\bullet\text{SMe}_2$ with PPh_3 at 40 °C in toluene for 18 h cleanly generated the phosphine adduct, $3\bullet\text{PPh}_3$, which can be isolated as a crystalline, colourless solid (Figure 4a). The crystal structure clearly shows the expected Markovnikov regioselectivity with no evidence for the formation of the anti-Markovnikov isomer in this instance (Figure 4a). The P–B distance of 1.950(5) Å in $3\bullet\text{PPh}_3$ is unremarkable and slightly elongated over $\text{BH}_3\bullet\text{PPh}_3$ (av. 1.917 Å).^[21]

Reaction of $\text{BH}_3\bullet\text{THF}$ with a mixture of E/Z-2 (generated from the partial reduction of HFP by $\text{AlH}_3\bullet\text{NMe}_3$ followed by vacuum transfer to remove the involatile inorganic side-products) also resulted in hydroboration generating $4\bullet\text{THF}$ which could be

trapped as **4•PPh₃**. The major product is again that of Markovnikov addition. **4•PPh₃** is characterised by a distinct multiplet at $\delta_{\text{H}} \sim 4.50$ ppm which could be modelled as the two diastereotopic ¹H environments of the $-\text{C}(\text{F})\text{CFH}_2$ group considered as an ABMX spin system insulated from the $-\text{CF}_3$ and B-containing moieties (Figure 4b). Equally diagnostic was the triplet resonance at $\delta_{\text{F}} = -220.55$ (t, $^2J_{\text{F-H}} = 50.4$ Hz) ppm in the ¹⁹F NMR which collapsed to a singlet on proton decoupling. Despite **4•PPh₃** being the major product, it is not generated cleanly, in part this is due to the difficulty in the selective reduction of HFP to *E/Z*-**2**, which in our hands contains small amounts of HFP and HFO-1234yf. The analysis is further complicated by the realisation that *E*-**2** and *Z*-**2** would give rise to two possible diastereomers of the anti-Markovnikov isomer of **4•PPh₃**. Based on total integration of quantitative ¹⁹F{¹H} NMR experiments it can be determined that Markovnikov **4•PPh₃** forms in at least 81 % yield giving a minimum selectivity of 4:1 for the major product. The true selectivity for the Markovnikov isomer is likely much higher.

Commercial samples of HFO-1234yf react with BH₃•THF to form an approximate 1:1 mixture of Markovnikov and anti-Markovnikov products **5•PPh₃**, following trapping with PPh₃. In this instance, the analysis is simplified due to the lower fluorine content of the substrate, along with its availability in high purity. Markovnikov **5•PPh₃** is characterised by a diagnostic doublet for the $-\text{CH}_3$ group $\delta_{\text{H}} = 1.58$ (d, $^3J_{\text{F-H}} = 23.8$ Hz) ppm, while the anti-Markovnikov isomer shows a distinct resonance at $\delta_{\text{H}} = 4.49$ ppm which is assigned to the terminal proton of the $-\text{CH}_2\text{CHFCF}_3$ moiety with appropriate coupling (Figure 4c). The assignments have been confirmed by ¹⁹F, ¹⁹F{¹H}, ¹H-¹H and ¹H-¹⁹F NMR spectroscopy. In the case of the anti-Markovnikov product of **5•PPh₃** the data are further supported by a known germanium analogue Et₃GeCH₂CHFCF₃ formed from the hydrogermylation of HFO-1234yf under catalytic conditions.^[22]

In combination, these reactions show that, while the hydroboration of HFP proceeds in high-selectivity, the regioselectivity is sensitive to the fluorine content of the olefin. Hence, although *E*-**2** and *Z*-**2** give predominantly Markovnikov products, HFO-1234yf reacts unselectively with both modes of addition of BH₃ to the olefin observed. Substituent effects on the regioselectivity of alkene hydroboration are well understood.^[23-25] Expanding on the work of Stone,^[13,26] Brown and co-workers have demonstrated previously that trifluoropropene reacts with HBX₂ (X = Cl, Br, H) to give primarily Markovnikov substitution products with the selectivity being sensitive to the number of halogen ligands on the borane and ranging from 7:1 to >9:1.^[12] Similarly, vinyl chloride has been proposed to react with BH₃ by Markovnikov addition.^[27] As with the cS_NV pathway, selectivity is dictated by a combination of inductive ($-\text{F}$ and $-\text{CF}_3$) and mesomeric effects ($-\text{F}$). The halogen containing

groups primarily lead to stabilisation of the negative charge at the adjacent carbon centre in the transition state for hydroboration, and hence Markovnikov selectivity. For HFO-1234yf it would seem that the influence of the electron-withdrawing substituents is counter-balanced by the mesomeric effect of the sp²C-F moiety favouring the anti-Markovnikov addition and connection of the boron to a carbon atom that bears no fluorine atoms.

Accurate computation modelling of hydroboration pathways with BH₃ by DFT calculations is surprisingly complex. Due to the extremely low energy local barrier for the hydroboration step, Singleton and others have commented that the approximations of transition state theory may not hold.^[28-30] Precise determination of the regioselectivity of the addition of boranes to even simple alkenes requires the consideration of reaction dynamics and modelling of reaction trajectories in place of more standard computational approaches.^[31-33] As such, we are reluctant to use DFT calculations to model the complete reaction mechanism of the HDF of HFP with BH₃. The complexity described above is further confounded by the realisation that a mixture of reagents that may be involved in the HDF step, viz BH₃, BH₂F and BHF₂ which may perform the hydroboration step with different selectivities.^[12] The concentrations of the latter boron fluorides are expected to increase at higher conversion. Furthermore, bimolecular pathways involving the reaction of hydroborated intermediates with a further equiv. of borane cannot be excluded at this point.

What is clear from the experiments is that both Markovnikov and anti-Markovnikov products are accessible under the reaction conditions, with the selectivity for the major Markovnikov isomer decreasing with decreasing fluorine content of the olefin. Heating solutions of **3•SMe₂** in C₆D₆ led to slow HDF. Similarly, both **4•THF** and **5•THF** are competent reaction intermediates giving rise to HDF products. In the latter case it is notable that both Markovnikov and anti-Markovnikov isomers are consumed in the reaction to form predominantly 3,3,3-trifluoropropene.

Two potential mechanisms explain the observed intermediates and the selectivity for HFO-1234ze in the HDF of HFP. Both involve addition-elimination and BH₃ as a reaction intermediate. A reaction sequence involving, Markovnikov addition / β -fluoride elimination followed by anti-Markovnikov addition / β -fluoride elimination would yield mixtures of *E/Z*-**2** and *E/Z*-HFO-1234ze with limited preference for the *E*- or *Z*-isomer as observed experimentally (Figure 5 – Pathway 1).

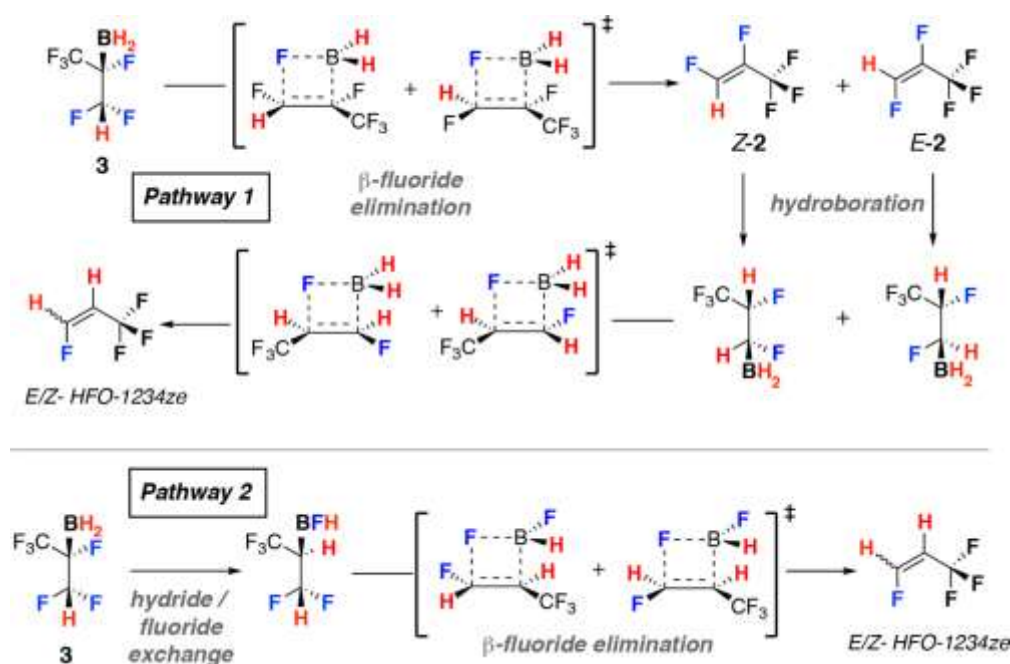


Figure 5. Plausible addition-elimination reaction mechanisms originating from hydroborated intermediate **3**.

Alternatively, Markovnikov hydroboration of HFP with BH_3 to generate **3** followed by intramolecular hydride / fluoride exchange and subsequent β -fluoride elimination would yield mixtures of *E/Z*-HFO-1234ze directly (Figure 5 – Pathway 2). While unusual, this type of intramolecular rearrangement has been proposed before.^[27]

In order to probe the viability of these steps the local energy barriers for the β -fluoride elimination and hydride / fluoride exchange reactions were calculated by DFT (B3PW91 functional). Although the resulting data are of limited value in assessing the complete reaction sequence, they do provide some insight into whether these steps are accessible under the reaction conditions. β -Fluoride eliminations steps from either Markovnikov or anti-Markovnikov hydroborated intermediates **3** and **4** proceed with local Gibbs activation energies of $\Delta G_{298\text{K}}^\ddagger = 15 - 25 \text{ kcal mol}^{-1}$. The hydride / fluoride exchange mechanism originates from intermediate **2** which is formed exclusively as a single regioisomer based on the experimental data. The local Gibbs activation energy for the exchange transition state is $\Delta G_{298\text{K}}^\ddagger = 32.3 \text{ kcal mol}^{-1}$. This transition state involves a concerted migration of the hydride from boron-to-carbon and the fluoride from carbon-to-boron and develops cationic character on the carbon centre adjacent to boron.

Based on the calculations neither Pathway 1 nor Pathway 2 can be discounted at this stage. While it is possible that both may be operating under the reaction conditions (days at 100°C) as Pathway 2 does not yield *E/Z*-2 as intermediates it is unlikely to be the only mechanism in action. Experimentally *E/Z*-2 mixtures were found to form Markovnikov hydroboration products with high selectivity, however the formation

of a 1:1 mixture of regioisomers for HFO-1234yf shows that the selectivity in these reactions is finely tuned. It is plausible that the substituted boranes BH_2F and BHF_2 react with higher selectivity for anti-Markovnikov addition favouring Pathway 1. Alternatively, the hydroboration step may be reversible and selectivity determined by the β -fluoride elimination step.

Conclusion

In summary, we report a new synthetic route to HFO-1234yf and HFO-1234ze that exploits the selective hydrodefluorination of hexafluoropropene. This method uses a bulk chemical commodity and does not rely on sequential chlorination and dichlorination sequences. Using main group hydrides of the form $\text{EH}_3\cdot\text{L}$ ($\text{E} = \text{B}$, $\text{L} = \text{SMe}_2$; $\text{E} = \text{Al}$, $\text{L} = \text{NMe}_3$) leads to complementary chemoselectivity in the hydrodefluorination sequence. With the borane reagent yielding a ~ 2:1 mixture of *E*- and *Z*-isomers of HFO-1234ze and the alane almost exclusively HFO-1234yf. The reaction by-products are boron and aluminium fluorides, compounds of commercial interest in their own right.

Exploration of the plausible reaction mechanisms by experiments and DFT calculations suggests that the complementary selectivities may have a mechanistic origin. For the alane, a concerted $\text{S}_{\text{N}}\text{V}$ mechanism occurs with high substrate bias for H/F-exchange at the terminal position of HFP. For the borane, ligand dissociation followed by an addition elimination sequence proceeds with selectivity for H/F-exchange at the terminal and internal positions of HFP.

Our findings lay out an experimental and mechanistic template for the synthesis of modern refrigerants by a selective hydrodefluorination approach.

Experimental Section

General Procedure for HDF with a Borane: $\text{Me}_2\text{S}\cdot\text{BH}_3$ (0.4 mmol) dissolved in C_6D_6 (0.5 ml) in a J-Young NMR tube and was degassed by the freeze-pump-thaw method. Hexafluoropropene (1 atm, 2 ml, ca. 0.08 mmol) was allowed to fill the tube and the reaction mixture was heated to 100 °C for 96 h. The hydrodefluorination products were characterised *in situ* and by vacuum transfer of the volatile species to a clean NMR tube. Integrations were carried out against an internal standard of 1-fluorohexane and showed 59% E-HFO-1234ze, 27% Z-HFO-1234ze along with 10% Z-2 and 3% E-2. NMR data are provided in the supporting information.

General Procedure for HDF with an Alane: $\text{Me}_3\text{N}\cdot\text{AlH}_3$ (0.2 mmol) dissolved in C_6D_6 (0.5 ml) in a J-Young NMR tube and was degassed by the freeze-pump-thaw method. Hexafluoropropene (1 atm, 2 ml, ca. 0.08 mmol) was allowed to fill in the flask and the reaction mixture was heated to 40 °C for 72 h. The hydrodefluorination product (HFO-1234yf) was characterised *in situ* and by vacuum transfer of the volatile species to a clean NMR tube. Integrations were carried out against an internal standard of durenene and showed >98% yield.

HFO-1234yf (2,3,3,3-tetrafluoropropene) ^1H NMR (C_6D_6 , 400 MHz, 298 K): δ_{H} 4.45 (1H, dd, $^3J_{\text{HF}} = 13.2$ Hz, $^2J_{\text{HH}} = 4.9$ Hz, CH_2), 4.32 (1H, ddd, $^3J_{\text{HF}} = 14.8$ Hz, $^2J_{\text{HH}} = 4.8$ Hz, $^4J_{\text{HF}} = 1.6$ Hz, CH_2). ^{19}F NMR (C_6D_6 , 376 MHz, 298 K): δ_{F} -73.34 (m, CF_3), -124.33 (q, $^3J_{\text{FF}} = 10.3$ Hz, CF).

Synthesis of 3a: $\text{Me}_2\text{S}\cdot\text{BH}_3$ (48 μl , 0.5 mmol) dissolved in toluene (5 ml) was degassed by the freeze-pump-thaw method. Hexafluoropropene (1 atm, 15 ml, 0.6 mmol) was allowed to fill in the flask and the reaction mixture was heated to 100 °C for 1 h. PPh_3 (131 mg, 0.5 mmol) was added and the reaction was heated to 40 °C for 16 h. Removal of the volatiles under reduced pressure and trituration with pentane yielded the title complex as a colourless solid (133 mg, 63% yield). Dissolution in Et_2O and storage at -30 °C gave colourless crystals suitable for X-ray diffraction analysis. CCDC-1866058 contains 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.

^1H NMR (C_6D_6 , 400 MHz, 298 K): δ_{H} 7.55 (6H, m, CH-Ph), 6.93 (9H, m, CH-Ph), 5.86 (1H, t d, $^2J_{\text{HF}} = 55.0$ Hz, $^3J_{\text{HF}} = 8.7$ Hz, CF_2H), 2.71 (2H, br, BH_2).

^{13}C NMR (C_6D_6 , 100 MHz, 298 K): δ_{C} 134.2 (d, $^1J_{\text{CP}} = 19.8$ Hz, C-Ph), 133.9 (d, $^3J_{\text{CP}} = 9.1$ Hz, CH-Ph), 131.6 (CH-Ph), 128.9 (d, $^2J_{\text{CP}} = 10.6$ Hz, CH-Ph), 126.1 (m, CF_3), 114.6 (t d, $^1J_{\text{CF}} = 246.2$ Hz, $^2J_{\text{CF}} = 29.1$ Hz, CF_2H), 96.4 (br, CF).

^{11}B NMR (C_6D_6 , 128 MHz, 298 K): δ_{B} -28.3 (br d, $^1J_{\text{BP}} = 78.6$ Hz, BH_2).

^{19}F NMR (C_6D_6 , 376 MHz, 298 K): δ_{F} -74.43 (d, $^3J_{\text{FF}} = 7.3$ Hz, CF_3), -127.16 (dd, $^2J_{\text{FF}} = 295.3$ Hz, $^2J_{\text{FH}} = 55.3$ Hz, CF_2H), -128.17 (dd, $^2J_{\text{FF}} = 295.3$ Hz, $^2J_{\text{FH}} = 56.5$ Hz, CF_2H), -191.87 (m, CF).

^{31}P NMR (C_6D_6 , 162 MHz, 298 K): δ_{P} 14.68 (br d, $^1J_{\text{BP}} = 76.6$ Hz).

Elemental Analysis: found %C 59.30, %H 4.38; calc. %C 59.19, %H 4.26.

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Declaration of Interest

Aspects of this work are the subject of UK patent application number 1810647.6 filed 28th June 2018 in collaboration with Imperial Innovations. A version of this manuscript was filed on the preprint server ChemRxiv.^[34]

References

- [1] G. J. M. Velders, A. R. Ravishankara, M. K. Miller, M. J. Molina, J. Alcamo, J. S. Daniel, D. W. Fahey, S. A. Montzka, S. Reimann, *Science* **2012**, 335, 922–923.
- [2] International Actions – The Montreal Protocol on Substances that Deplete the Ozone Layer, <https://www.epa.gov/ozone-layer-protection/international-actions-montreal-protocol-substances-deplete-ozone-layer>. (accessed 5th Feb. 2019)
- [3] Eu legislation to control F-gases, https://www.ec.europa.eu/clima/policies/f-gas/legislation_en. (accessed 5th Feb. 2019)
- [4] Honeywell Blowing Agents, <https://www.fluorineproducts-honeywell.com/blowingagents/regulation>. (accessed 5th Feb. 2019)
- [5] H. K. Nair, R. R. Singh, A. J. Poss, D. Nalewajek, US Pat. 8889924B2, 2012; Honeywell International, Inc.
- [6] H. S. Tung, H. K. Nair, S. S. M. Mukhopadhyay, M. Van der Puy, WO Pat.2005108332A1, 2004, Honeywell International, Inc.
- [7] S. A. Cottrell, H. S. Tung, Y. C. Wang, G. Cerri, US Pat. 9255046B2, 2003, Honeywell International, Inc.
- [8] S. Lim, M. S. Kim, J.-W. Choi, H. Kim, B. S. Ahn, S. D. Lee, H. Lee, C. S. Kim, D. J. Suh, J.-M. Ha, K. H. Song, *Catal. Today* **2017**, 293–294, 42–48.
- [9] T. Braun, M. A. Salomon, K. Altenhöner, M. Telteuws, S. Hinze, *Angew. Chem. Int. Ed.*, **2009**, 48, 1818–1822.
- [10] T. Braun, F. Wehmeier, K. Altenhöner, *Angew. Chem. Int. Ed.*, **2007**, 46, 5321–5324.
- [11] P. V. Ramachandran, M. P. Jennings, H. C. Brown, *Org. Lett.* **1999**, 1, 1399–1402.
- [12] H. C. Brown, G.-M. Chen, M. P. Jennings, P. V. Ramachandran, *Angew. Chem. Int. Ed.* **1999**, 38, 2052–2054.
- [13] J. R. Phillips, F. G. A. Stone, *J. Chem. Soc.* **1962**, 94–97.
- [14] H. Schneider, A. Hock, A. D. Jaeger, D. Lentz, U. Radius, *Eur. J. Inorg. Chem.* **2018**, 4031–4043.
- [15] A. D. Jaeger, C. Ehm, D. Lentz, *Chem. Eur. J.* **2018**, 24, 6769–6777.
- [16] R. J. Brotherton, C. J. Weber, C. R. Guibert, L. J. L., in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2000**, 6, pp. 237–255.

- [17] J. Aigueperse, P. Mollard, D. Devilliers, M. Chemla, R. Faron, R. Romano, J. P. Cuer, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2000**, 15, pp. 397-441.
- [18] H. C. Brown, J. Chandrasekharan, *J. Am. Chem. Soc.* **1984**, 106, 1863–1865.
- [19] K. K. Wang, H. C. Brown, *J. Am. Chem. Soc.* **1982**, 104, 7148–7155.
- [20] J. Walkowiak, H. Koroniak, in *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons, Ltd. **2009**, pp. 1–5.
- [21] J. C. Huffman, W. A. Skupinski, K. G. Caulton, *Cryst. Struct. Commun.* **1982**, 11, 1435.
- [22] G. Meißner, K. Kretschmar, T. Braun, E. Kemnitz, *Angew. Chem. Int. Ed.* **2017**, 56, 16338–16341.
- [23] H. C. Brown, G. Zweifel, *J. Am. Chem. Soc.* **1960**, 82, 4708–4712.
- [24] G. D. Graham, S. C. Freilich, W. N. Lipscomb, *J. Am. Chem. Soc.* **1981**, 103, 2546–2552.
- [25] H. C. Brown, A. W. Moerikofer, *J. Am. Chem. Soc.* **1963**, 85, 2063–2065.
- [26] B. Bartocha, W. A. G. Graham, F. G. A. Stone, *J. Inorg. Nucl. Chem.* **1958**, 6, 119–129.
- [27] D. J. Pasto, R. Snyder Sr., *J. Org. Chem.* **1966**, 31, 2773–2777.
- [28] J. O. Bailey, D. A. Singleton, *J. Am. Chem. Soc.* **2017**, 139, 15710–15723.
- [29] Y. Oyola, D. A. Singleton, *J. Am. Chem. Soc.* **2009**, 131, 3130–3131.
- [30] D. R. Glowacki, C. H. Liang, S. P. Marsden, J. N. Harvey, M. J. Pilling, *J. Am. Chem. Soc.* **2010**, 132, 13621–13623.
- [31] D. J. S. Sandbeck, C. M. Kuntz, C. Luu, R. A. Mondor, J. G. Ottaviano, A. V. Rayer, K. Z. Sumon, A. L. East, *J. Phys. Chem. A* **2014**, 118, 11768–11779.
- [32] X. Wang, Y. Li, Y.-D. Wu, M. N. Paddon-Row, N. G. Rondan, K. N. Houk, *J. Org. Chem.* **1990**, 55, 2601–2609.
- [33] M. J. S. Dewar, M. L. McKee, *Inorg. Chem.* **2002**, 41, 1075–1082.
- [34] N. A. Phillips, A. J. P. White, M. R. Crimmin, *ChemRxiv*, **2019**, DOI:10.26434/chemrxiv.7699970.v1.

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