Defluorination of HFCs by a Magnesium Reagent

Daniel J. Sheldon[a] and Mark R. Crimmin*[a]

Department of Chemistry, Molecular Sciences Research Hub
Imperial College London, London, W12 0BZ (UK)
E-mail: m.crimmin@imperial.ac.uk

Abstract: *Reaction of a series of HFCs with a nucleophilic main group reagent containing a Mg–Mg bond results in defluorination to form the corresponding magnesium fluoride complex. In the case of 1,1,1,2-tetrafluoroethane (HFC-134a) generation of the fluoride occurs alongside selective formation of 1,1-difluoroethene. This is a highly unusual reactivity pattern for HFC-134a, which more commonly reacts by deprotonation and HF elimination. DFT calculations have been carried out to better understand the selectivity and compare the barriers for* sp^3 *C–F bond activation with* sp^3 *C–H bond activation in this system.*

Due to their unique chemical and physical properties hydrofluorocarbons (HFCs) have been widely used as 3rd generation refrigerants. The largest use HFC for this purpose is 1,1,1,2-tetrafluoroethane (HFC-134a). Perhaps as a result, HFC-134a has become most abundant fluorinated gas in the atmosphere. HFC-134a has a 100-year global warming potential (GWP_{100}) of 1530 and as such is contributing to climate change. Legislation is now in place to limit the use of HFCs globally.[1–5] The planned phase-down of HFCs is however a gradual process; developed countries have committed to phase-down by 85 % by 2036, with other countries committing to 80 % by the late 2040s.[6] Consequently, HFCs may continue to be emitted for a long time. There is a need to develop processes to repurpose HFCs, ideally with destruction and removal of the fluorine content of these molecules.

Reactions of 1,1,1,2-tetrafluoroethane nearly always involve pathways that result in the formal elimination of an equivalent of HF (Figure 1). Strong bases, organometallic reagents, or heterogeneous catalysts react with HFC-134a to form 1,1,2-trifluoroethene.[7–9] This chemoselectivity is driven by the strong sp^3 C–F bond strengths of both fluorinated sites, and the relative acidity of the adjacent sp^3 C–H bonds. In the case of reactions with organometallic compounds, *in situ* deprotonation of 1,1,2-trifluoroethane to form a trifluorovinyl moiety is common.[7–9] For example, it has been reported that the reaction of HFC-134a with 2 equiv. *n*-BuLi at –78 °C forms trifluorovinyllithium. This species, which decomposes if warmed to room temperature, can react at –78 °C with a wide range of electrophiles including metal halides, main group halides, CO_2, aldehydes and epoxides.[7,8,10–26] Other reports include the transfer of the trifluorovinyl group onto zinc chlorides for application in palladium-catalysed Negishi cross-coupling reactions.[19,27–31]

There is a distinct lack of examples of reactions of HFC-134a which involve solely sp^3 C–F bond activation. If such reactivity could be achieved, it might open new mechanistic pathways with complementary selectivity to established HF elimination processes. In this communication, we show that reaction of HFC-134 with a main group reagent containing a Mg–Mg bond leads to exclusive formation of 1,1-difluoroethene due to the formal 1,2-elimination of two F atoms from the substrate. This is a rare example of selective sp^3 C–F bond activation of this industrially important HFC.

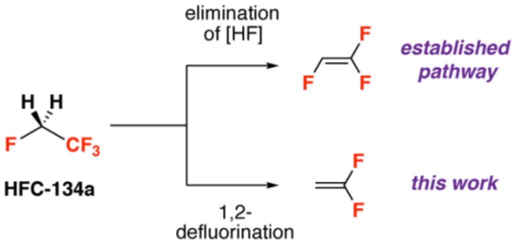
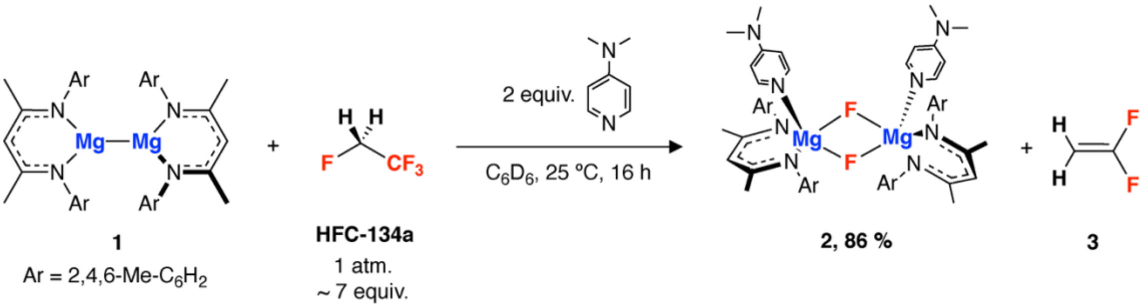


Figure 1. Established HF elimination pathway for HFC-134a and this work.

HFC-134a (1 bar, 25 °C, approx. 7 equiv.) was added to a degassed C_6D_6 solution of **1** and 4-dimethylaminopyridine (DMAP, 2 equiv.). The reaction mixture was agitated and left to proceed for 16 h at 25 °C, during which time the dark red solution turned yellow. ^1H and ^{19}F NMR spectroscopy of the resultant reaction mixture reveal the formation of **2** (86 % yield) and 1,1-difluoroethene (Scheme 1). **2** has been previously reported and characterised by our group, and shows a diagnostic resonance at δ −183.9 ppm in the ^{19}F NMR spectrum.[32] 1,1-Difluoroethene has a resonance at δ –81.8 ppm, in accordance with data in the literature.[33] Due to its volatility and partitioning between solution and reaction headspace, the amount of 1,1-difluoroethene was not quantified, subsequent onwards reactions however, support generation in reasonable yields (*vide infra*). Jones and co-workers have shown that this magnesium nucleophile used in this reaction, **1**,[34,35] displays enhanced reactivity on the addition of a Lewis base,[36,37] while we have recently demonstrated its use in the defluorination of PTFE.[32] Defluorination of HFC-134a with **1** can also occur in the absence of DMAP, but requires heating to 80 °C, and results in 30 % yield of an analogue of **2** which does not have DMAP coordinated.



Scheme 1. Defluorination of HFC-134a by a magnesium reagent (**1**) and DMAP.

To gain further insight into this unique reactivity, the mechanism of defluorination of HFC-134a was studied using computational techniques (DFT). Binding of DMAP to **1** was assumed to be fast and reversible under the reaction conditions, reinforced by observed fluxionality in ^{1}H NMR spectroscopic data for **1·DMAP** suggesting that the DMAP can move rapidly between Mg centres.[32,36,37]

The reaction is initiated by nucleophilic attack of **1·DMAP** at the sp^3 C–F bond of -CH$_2$F group of HFC-134a, *via* **TS-1** ($\Delta G^{\ddagger}_{298K}$ = 19.5 kcal mol^{-1}), to form **Int-1**. This reactivity mode for **1·DMAP** has been established previously in the defluorination of poly(tetrafluoroethene) (PTFE).[32] **TS-1** is asymmetric, the three-coordinate Mg centre of **1·DMAP** acts as a nucleophilic site, while the four-coordinate Mg centre acts as a fluoride acceptor. Calculated *NPA* charges in **1·DMAP** reveal the 3-coordinate Mg atom has a less positive charge (+0.84) compared to the four-coordinate Mg atom (+1.07), and hence nucleophilic attack originates from the three-coordinate Mg atom. It has been proposed by us and others that polarisation and stretching of the Mg–Mg bond in **1·DMAP** leads to enhanced reactivity compared to the symmetric species **1** or **1·DMAP$_2$**.[32,37] NBO calculations reveal a flow of charge consistent with a frontside nucleophilic attack by **1·DMAP** at the fluorine atom of HFC-134a as **TS-1** is traversed (See Supporting Information). **Int-1** undergoes fluoride elimination *via* **TS-2** ($\Delta G^{\ddagger}_{298K}$ = 6.6 kcal mol^{-1}) to form 1,1-difluoroethene, and reaction of the magnesium fluoride intermediate with a second equivalent of DMAP forms **2**. This second step effectively breaks one of the C–F bonds of the CF$_3$ group of HFC-134a completing the formal 1,2-defluorination (Figure 2). The overall reaction can be conceptualised in terms of a reduction of the HFC with **1** which converts 2 F + 2 e$^-$ → 2 F$^-$, ultimately generating the magnesium fluoride **2** and 1,1-difluoroethane.

The mechanism proposed based on DFT calculations is perhaps intuitive. The fluorophilicity of **1** likely results in selective sp^3 C–F bond activation over sp^3 C–H bond activation, while the trends in bonds strengths would favour reaction at the isolated sp^3 C–F bond.[38] Alternative mechanisms were calculated and found to lead to transition states that were less energetically accessible than **TS-1**. Deprotonation of the sp^3 C–H bond of HFC-134a with **1·DMAP** was calculated to occur via **TS-3** with $\Delta G^{\ddagger}_{298K}$ = 27.1 kcal mol^{-1}. Nucleophilic attack at a fluorine atom of the CF_3 group of HFC-134a was calculated to occur via **TS-4**, $\Delta G^{\ddagger}_{298K}$ = 26.5 kcal mol^{-1}.

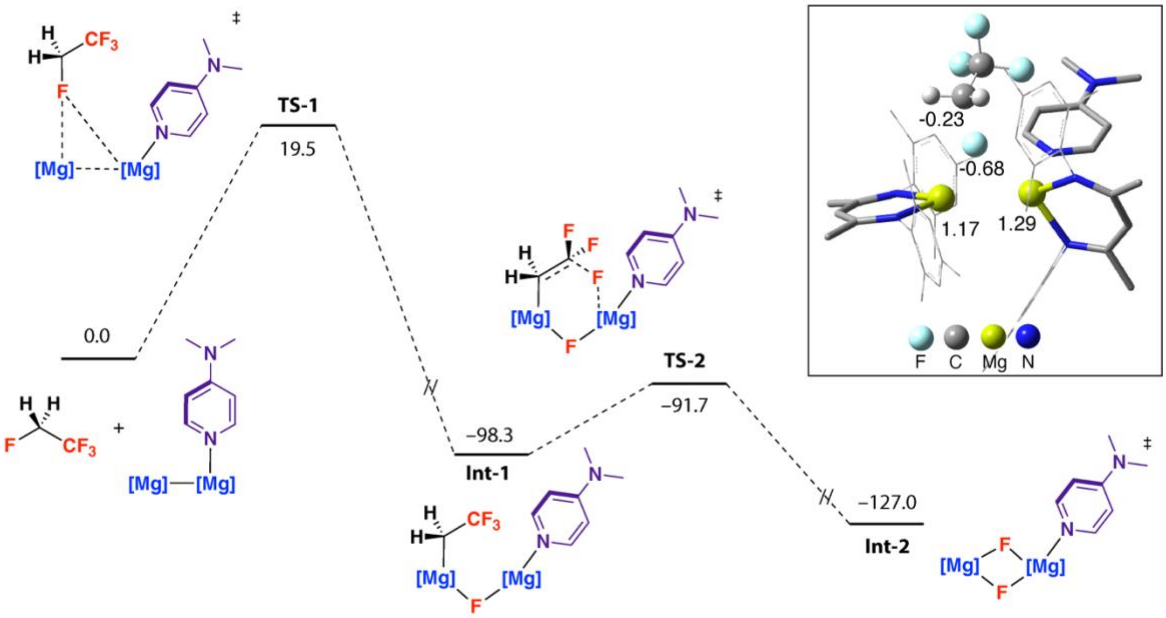


Figure 2. Calculated reaction pathway for defluorination of HFC-134a by **1** + DMAP. Gibbs energies in kcal mol^{-1}. G09: B3PW91-GD3BJ / 6-311+G* (CH,N,F) / SDDAll (Mg). Inset, representation of **TS-1** annotated with *NPA* charges on key atomic sites.

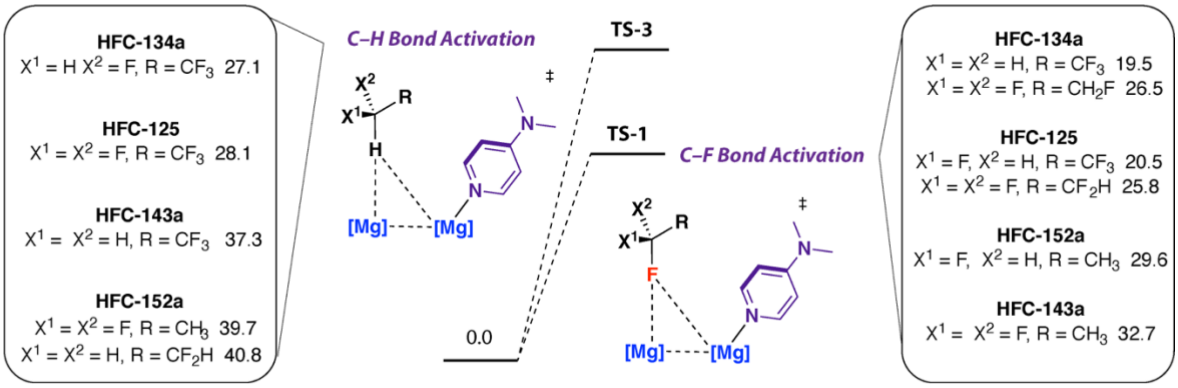
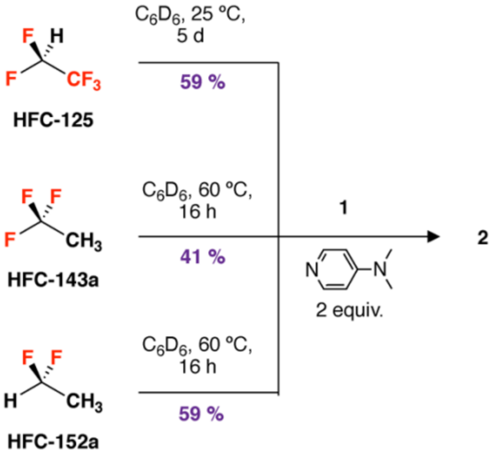


Figure 3. Calculated barriers for C–F and C–H activation of HFCs with **1** + **DMAP**. Gibbs energies in kcal mol^{-1}. G09: B3PW91-GD3BJ / 6-311+G* (CH,N,F) / SDDAll (Mg).

Consideration of selectivity in the possible bond breaking events for HFC-134a raises the question as to how small changes to structure might affect the reaction outcome. A range of hydrofluoroethanes including 1,1,1-trifluoroethane (HFC-143a, GWP_{100} = 5810), 1,1-difluoroethane (HFC-143a, GWP_{100} = 164) and 1,1,1,2,2-pentafluoroethane (HFC-125, GWP_{100} = 3740) are widely available and used in the refrigeration sector.[9,39] Along with HFC-134a this series of substrates, represents a group with systematic changes in number and position of fluorine atoms.

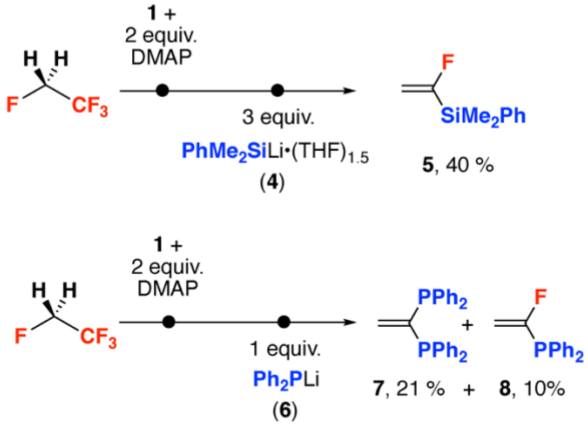
The computational model was extended to examine the activation barriers for sp^3 C–F activation and sp^3 C–H activation of this range of HFCs. Several trends are consistent across the series: (i) in general activation barriers increase with lower fluorine content of the substrate, (ii) in cases where multiple C–F bonds are present there is preference for CFH_2 > CF_3 and CF_2H > CF_3 groups and (iii) sp^3 C–F activation is consistently a more facile process than sp^3 C–H bond activation (Figure 3). For example, the activation barriers for sp^3 C–F bond activation (**TS-1**) increase in the order 1,1,1,2,2-pentafluoroethane (HFC-125, $\Delta G^{\ddagger}_{298K}$ = 20.5, 25.8 kcal mol^{-1}), 1,1,1-trifluoroethane (HFC-143a, $\Delta G^{\ddagger}_{298K}$ = 29.6 kcal mol^{-1}), 1,1-difluoroethane (HFC152a, $\Delta G^{\ddagger}_{298K}$ = 32.7 kcal mol^{-1}). For 1,1,1,2,2-pentafluoroethane, there are two possible isomeric transition states for C–F bond activation, with attack of **1·DMAP** occurring at either the CF_2H or CF_3 bond of the substrate, the lowest energy pathway involves defluorination of the difluoromethyl site. The activation barriers for sp^3 C–H bond activation (**TS-3**) were all found to be 5 – 10 kcal mol^{-1} higher in energy than those for sp^3 C–F bond activation for these substrates. The calculations suggest that these HFCs should also undergo chemoselective defluorination under accessible conditions with **1** + DMAP, however as most do not contain the correct substitution pattern to achieve a 1,2-defluorination, i.e. via **TS-1**, it is not immediately clear if fluoroalkenes will be generated as products.

Reaction of 1,1,1,2,2-pentafluoroethane with **1** + **DMAP** at 25 °C in C_6D_6 for 5 days led to the formation of **2** in a 59 % yield. Reaction of **1** + **DMAP** with 1,1-difluoroethane in C_6D_6 occurred slowly at 25 ºC, but was complete within 16h at 60 °C t forming **2** in 41 % yield. **1** + **DMAP** also reacts with 1,1,1-trifluoroethane in C_6D_6 to form **2** after 16 h at 60 °C. The elevated temperatures required for these reactions are consistent with the trends in calculated activation energies. In the case of both 1,1-difluoroethane and 1,1,1-trifluoroethane, we could not identify the organic products of these reactions, the implication is that without fluorine substitution at both carbon atoms of the ethane the 1,2-elimination pathway may be switched off. In these cases, sp^3 C–F bond activation would generate intermediate organomagnesium complexes likely to decompose through α-elimination pathways forming **2** along with unstable carbene fragments. A minor fluoroalkene containing product could be identified from the reaction of 1,1,1,2,2-pentafluoroethane with **1** and DMAP, identified as α,β,β-trifluorostyrene-d_5, formed in a 5-10 % yield (based on 1 equivalent of **1**). α,β,β-Trifluorostyrene-d_5 likely derives from a defluorinative coupling of the HFC and the benzene-d_6 reaction solvent. While the pathway for its formation remains unclear, generation of a fluoroethene intermediate cannot be ruled out at this stage.



Scheme 2. Defluorination of HFC-125, HFC-143a, HFC-152a by **1** + DMAP.

In terms of further utilisation of the products from the defluorination of HFCs, we have previously shown that **2** can act as a nucleophilic source of fluoride, capably of fluorinating a small array of highly activated electrophiles.[32] In the case of HFC-134a, the volatile product 1,1-difluoroethene could be separated from **2** by vacuum transfer, allowing further derivatisation by nucleophilic substitution. 1,1-Difluoroethene was defluorosilylation upon reaction with the lithium silanide **4** to form the organosilicon compound **5** in 40% (NMR yield, over two steps based on **1** as the limiting reagent). **5**, a known compound, was characterised by a diagnostic resonance in the ^{19}F NMR spectroum at $\delta = -103.0$ ppm.[40] Related defluorosilylation reactions of fluoroalkenes including difluoroethene have been previously reported.[41-43] 1,1-Difluoroethene also reacts lithium diphenylphosphide (**6**) to form a mixture of double and single addition products **7** and **8** respectively in an approximate 2:1 ratio in 31 % (NMR yield, over two steps based on **1** as the limiting reagent). The phosphine derivatives **7** and **8** have previously been proposed as novel precursors for coordination chemistry. [44-45] While the yields for both these derivatisation processes are only modest, it is important to note they represent an unoptimised two-step process direct from HFC-134a.



Scheme 3. Two-step derivatisation of HFC-134a via 1,2-defluorination and nucleophilic substitution. Yields determined by ^{19}F or ^{31}P NMR spectroscopy.

In summary, we report the defluroination of a range of HFC refrigerants using a magnesium reagent. In the case of 1,1,1,2-tetrafluoroethene (HFC-134a), the largest commercial HFC, a highly unusual pathway for 1,2-defluorination to form 1,1-difluoroethene was observed. This pathway complements established reaction patterns which nearly always result in formation of 1,1,2-trifluoroethene through elimination of an equivalent of HF. DFT calculations have been used to compare the chemoselectivity in these systems. sp^3 C–F bond activation universally occurs with lower barriers than sp^3 C–H bond activation, likely due to participation of fluorophilic magnesium sites in the key transition state for bond breaking. The development of mechanistic understanding in reactions that defluorinated HFCs has the potential to underpin future approaches to repurpose these potent greenhouse gases.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material (ESI) of this article available at https://doi.org/10.1002/anie.xxx,which contains the experimental procedures, details of calculations and charac-terization data (PDF) along with coordinates for DFT calculations(xyz).

Acknowledgements

We are grateful to the ERC for generous funding (Fluorocycle: 101001071) and Imperial College London and the EPSRC for DTP studentship funding (DJS). We thank Apollo Scientific for donation of HFCs.

Keywords: HFCs • Defluorination • Magnesium • F-gas • Mechanism

References

[1] F. Polonara, L. J. . Kuijpers, R. . Peixoto, *Int. J. Heat Technol.* **2017**, *35*, S1–S8.

[2] A. J. Manning, A. L. Redington, D. Say, S. O'Doherty, D. Young, P. G. Simmonds, M. K. Vollmer, J. Mühle, J. Arduini, G. Spain, et al., *Atmos. Chem. Phys.* **2021**, *21*, 12739–12755.

[3] H. Flerlage, G. J. M. Velders, J. de Boer, *Chemosphere* **2021**, *283*, 131208.

[4] G. J. M. Velders, J. S. Daniel, S. A. Montzka, I. Vimont, M. Rigby, P. B. Krummel, J. Muhle, S. O'Doherty, R. G. Prinn, R. F. Weiss, et al., *Atmos. Chem. Phys.* **2022**, *22*, 6087–6101.

[5] J. M. Calm, *Int. J. Refrig.* **2008**, *31*, 1123–1133.

[6] E. A. Heath, *Int. Leg. Mater.* **2017**, *56*, 193–205.

[7] J. Burdon, P. L. Coe, I. B. Haslock, R. L. Powell, *Chem. Commun.* **1996**, 49–50.

[8] K. K. Banger, A. K. Brisdon, A. Gupta, *Chem. Commun.* **1997**, 139–140.

[9] D. J. Sheldon, M. R. Crimmin, *Chem. Soc. Rev.* **2022**, *51*, 4977–4995.

[10] S. Duric, B. M. Schmidt, N. M. Ninnemann, D. Lentz, C. C. Tzschucke, *Chem. Eur. J.* **2012**, *18*, 437–441.

[11] K. K. Banger, A. K. Brisdon, *J. Organomet. Chem.* **1999**, *582*, 301–309.

[12] A. K. Brisdon, I. R. Crossley, R. G. Pritchard, G. Sadiq, *J. Organomet. Chem.* **2007**, *692*, 2125–2130.

[13] N. A. Barnes, A. K. Brisdon, W. I. Cross, J. G. Fay, J. A. Greenall, R. G. Pritchard, J. Sherrington, *J. Organomet. Chem.* **2000**, *616*, 96–105.

[14] P. L. Coe, J. Burdon, I. B. Haslock, *J. Fluor. Chem.* **2000**, *102*, 43–50.

[15] J. Burdon, P. L. Coe, I. B. Haslock, R. L. Powell, *J. Fluor. Chem.* **1997**, *85*, 151–153.

[16] K. K. Banger, R. P. Banham, A. K. Brisdon, W. I. Cross, G. Damant, S. Parsons, R. G. Pritchard, A. Sousa-Pedrares, *J. Chem. Soc. Dalt. Trans.* **1999**, 427–434.

[17] J. E. Phelps, S. B. Frawley, R. G. Peters, *Heteroat. Chem.* **2009**, *20*, 393–397.

[18] K. Wu, Q.-Y. Chen, *Tetrahedron* **2002**, *58*, 4077–4084.

[19] J. Burdon, P. L. Coe, I. B. Haslock, R. L. Powell, *J. Fluor. Chem.* **1999**, *99*, 127–131.

[20] K. Nickisch, W. Elger, J. Cessac, N. Kesavaram, B. Das, R. Garfield, S.-Q. Shi, O. Amelkina, R. Meister, *Steroids* **2013**, *78*, 255–267.

[21] N. A. Barnes, A. K. Brisdon, F. R. W. Brown, W. I. Cross, I. R. Crossley, C. Fish, J. V Morey, R. G. Pritchard, L. Sekhri, *New J. Chem.* **2004**, *28*, 828–837.

[22] K. K. Banger, A. K. Brisdon, C. J. Herbert, H. A. Ghaba, I. S. Tidmarsh, *J. Fluor. Chem.* **2009**, *130*, 1117–1129.

[23] G. DiMartino, M. B. Hursthouse, M. E. Light, J. M. Percy, N. S. Spencer, M. Tolley, *Org. Biomol. Chem.* **2003**, *1*, 4423–4434.

[24] D. J. Brauer, G. Pawelke, *J. Organomet. Chem.* **2000**, *604*, 43–51.

[25] K. Wu, Q.-Y. Chen, *J. Fluor. Chem.* **2003**, *122*, 171–174.

[26] T. Okano, M. Chokai, M. Hiraishi, M. Yoshizawa, T. Kusukawa, M. Fujita, *Tetrahedron* **2004**, *60*, 4031–4035.

[27] A. Raghavanpillai, D. J. Burton, *J. Org. Chem.* **2004**, *69*, 7083–7091.

[28] K. Fuchibe, K. Shigeno, N. Zhao, H. Aihara, R. Akisaka, T. Morikawa, T. Fujita, K. Yamakawa, T. Shimada, J. Ichikawa, *J. Fluor. Chem.* **2017**, *203*, 173–184.

[29] R. Anilkumar, D. J. Burton, *Tetrahedron Lett.* **2002**, *43*, 2731–2733.

[30] H. Miyauchi, N. Kondo, N. Nagasaki, Substituted bis(trifluorovinylbenzene) compound, **2020**, US Pat., US2020017429.

[31] P. V. Ramachandran, G. V. Reddy, *J. Fluor. Chem.* **2008**, *129*, 443–446.

[32] D. J. Sheldon, J. M. Parr, M. R. Crimmin, *J. Am. Chem. Soc.* **2023**, *145*, 10486–10490.

[33] N. O. Andrella, N. Xu, B. M. Gabidullin, C. Ehm, R. T. Baker, *J. Am. Chem. Soc.* **2019**, *141*, 11506–11521.

[34] S. P. Green, C. Jones, A. Stasch, *Science* **2007**, *318*, 1754–1757.

[35] C. Jones, *Nat. Rev. Chem.* **2017**, *1*, 59.

[36] K. Yuvaraj, I. Douair, A. Paparo, L. Maron, C. Jones, *J. Am. Chem. Soc.* **2019**, *141*, 8764–8768.

[37] K. Yuvaraj, I. Douair, D. D. L. Jones, L. Maron, C. Jones, *Chem. Sci.* **2020**, *11*, 3516–3522.

[38] D. O'Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308–319.

[39] V. Masson-Delmotte, P. Zhai, A. Pirani, S. L. Connors, C. Péan, S. Berger, N. Caud, Y. Chen, L. Goldfarb, M. I. Gomis, et al., *Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*, Cambridge University Press, Oxford, UK, **2021**.

[40] H. Sakaguchi, M. Ohashi, S. Ogoshi, *Angew. Chem., Int. Ed.* **2018**, *57*, 328–332.

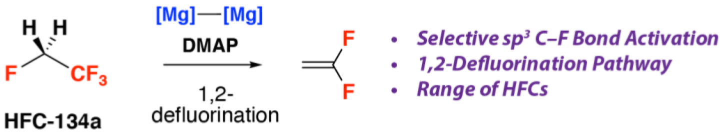
[41] G. Coates, H. Y. Tan, C. Kalff, A. J. P. White, M. R. Crimmin, *Angew. Chem., Int. Ed.* **2019**, *58*, 12514–12518.

[42] T. Hanamoto, S. Harada, K. Shindo, M. Kondo, *Chem. Commun.* **1999**, 2397–2398.

[43] Unreacted HFC-134a is also present in this reaction mixture, and if left for 16 hours some deprotonation by **4** is observed, leading to a more complicated product mixture.

[44] M. Ohashi, H. Saijo, M. Shibata, S. Ogoshi, *European J. Org. Chem.* **2013**, *2013*, 443–447.

[45] T. Hanamoto, Y. Kiguchi, K. Shindo, M. Matsuoka, M. Kondo, *Chem. Commun.* **1999**, 151–152.



The reaction of HFC-134 with a main group reagent containing a Mg–Mg bond leads to exclusive formation of 1,1-difluoroethene due to the formal 1,2-elimination of two F atoms from the substrate