


Cite this: *RSC Adv.*, 2024, 14, 31517

Received 27th July 2024  
Accepted 10th September 2024

DOI: 10.1039/d4ra05449k

rsc.li/rsc-advances

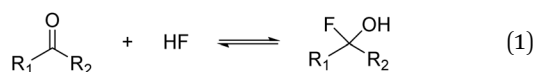
# Deoxyfluorination with superacids – synthesis and characterization of protonated $\alpha$ -fluorohydroxyacetic acid†

Alan Virmani,<sup>†</sup> Christoph Jessen, Alexander Nitzer and Andreas J. Kornath‡

$\alpha$ -Fluoroalcohols describe a rare and unstable class of compounds, accessible mainly by fluorination of highly electrophilic carbonyl compounds. In this work, we report the syntheses of  $\alpha$ -fluorohydroxyacetic acid (FHA) and its acyl fluoride (FHA-F) by reacting the dihydroxy species glyoxylic acid monohydrate (GAM) with SF<sub>4</sub>. Surprisingly, only one of the geminal hydroxy groups is substituted when excess SF<sub>4</sub> is employed. Implementing GAM with the binary superacid HF/AsF<sub>5</sub> also leads to a single yet quantitative deoxyfluorination at the diol group. The reaction pathways are discussed based on NMR experiments, the characterization was carried out using NMR and vibrational spectroscopy as well as single-crystal X-ray diffraction.

## Introduction

Organic compounds containing carbon atoms with more than one hydroxy group are known to be labile under regular conditions. According to the rule of Erlenmeyer, they undergo facile dehydration under the formation of the respective carbonyl compound. This also applies to alcohols with a geminal halogen atom, where the hydrogen halide is easily eliminated.<sup>1</sup> In the case of fluorinated compounds, only a few examples of  $\alpha$ -fluoroalcohols are known. Fluoromethanol CFH<sub>2</sub>OH, the simplest representative, was synthesized by Olah and Pavláth as early as 1953.<sup>2</sup> In 1977, Seppelt was able to generate the perfluorinated alcohol trifluoromethanol CF<sub>3</sub>OH by reacting CF<sub>3</sub>OCl with HCl. He operated at low temperatures to prevent the decomposition under the formation of COF<sub>2</sub> and HF, which is highly favored.<sup>3</sup> 30 years later, Christe *et al.* investigated this equilibrium.<sup>4</sup> The addition of HF or F<sup>−</sup> to a carbonyl group is a convenient way to access (per-)fluorinated alcohols, first shown by Andreades and England in 1961,<sup>5</sup> followed by others in recent studies.<sup>6,7</sup> The general equation is given below (eqn (1)).



However, the  $\alpha$ -fluoroalcohol is only stable when the electrophilicity of the carbonyl group is high enough, similar to the rule of Erlenmeyer.<sup>8</sup> The equilibrium of eqn (1) can be shifted to the right by transforming the alcohol into stable derivatives like acetals or oxonium ions.<sup>4,9,10</sup> The respective oxonium ions were generated by reacting the carbonyl compounds with the superacidic system HF/SbF<sub>5</sub> in anhydrous hydrogen fluoride (aHF). In this way, the perfluorinated oxonium ions of methanol, ethanol, *n*-propanol,<sup>10</sup> and isopropanol<sup>11</sup> have been synthesized.

An example of an exception to the rule of Erlenmeyer is glyoxylic acid (GA). The purchasable monohydrate form (GAM) does not imply co-crystallized but chemically bound water and is better described as dihydroxyacetic acid. Its reactivity toward highly acidic systems, in which it can be activated for electrophilic reactions, has been described by Prakash *et al.*<sup>12</sup> The high electrophilicity makes it an interesting target for generating  $\alpha$ -fluorohydroxy compounds with an additional functional group in the direct vicinity. To exploit this possibility or to determine if a difluorinated product is formed, we have implemented GAM with the deoxyfluorinating agent SF<sub>4</sub> as well as the superacidic medium HF/AsF<sub>5</sub>. We wish to report the results herein.

## Results and discussion

### Syntheses and properties

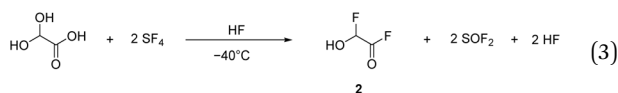
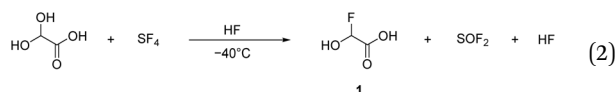
$\alpha$ -Fluorohydroxyacetic acid (FHA, 1) is synthesized by reacting glyoxylic acid monohydrate (GAM) with an equimolar amount of sulfur tetrafluoride (eqn (2)). For the synthesis of  $\alpha$ -fluorohydroxyacetyl fluoride (FHA-F, 2), a twofold amount of SF<sub>4</sub> is applied (eqn (3)). The formation of difluoroacetyl fluoride was not observed with an excess of SF<sub>4</sub>.

Ludwig-Maximilians-Universität München, Butenandtstraße 5-13 (D), D-81377 München, Germany

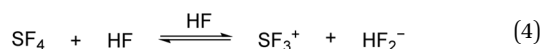
† Electronic supplementary information (ESI) available: For full details on vibrational spectroscopy, NMR spectroscopy, X-ray diffraction refinement, and computational details. CCDC 2173682. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d4ra05449k>

‡ Prof. Kornath passed away in March 2024.





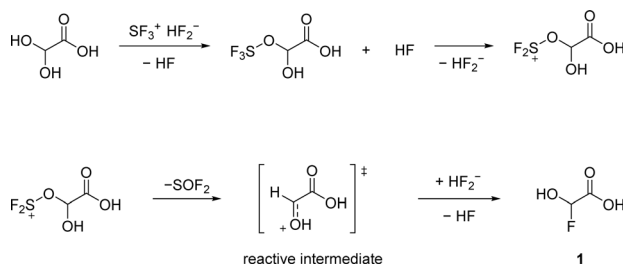
The mechanism of GAM in the system HF/SF<sub>4</sub> is proposed based on the literature-reported pathways of similar reactions.<sup>13–15</sup> In the first step, SF<sub>4</sub> dissociates in aHF according to eqn (4).



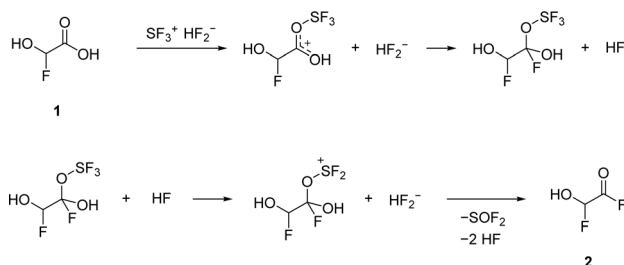
We confirm that the alcohol moiety is more nucleophilic than the carboxy group, which is why the first deoxyfluorination takes place there (Scheme 1). The reactive intermediate is a planar oxonium ion. Since the addition of a nucleophile in this mechanism is not stereoselective, a racemic mixture is expected.

The second deoxyfluorination of the carboxylic group proceeds in a similar fashion. However, in this case, the formation of a tetrahedral intermediate is likely, as it has been suggested in previous studies about the reactions of carbonyl compounds with HF/SF<sub>4</sub>.<sup>13,15</sup> The proposed mechanism is illustrated in Scheme 2.

Employing three or more equivalents of SF<sub>4</sub> did not result in a third deoxyfluorination of the last hydroxy group, hence in 2,2-



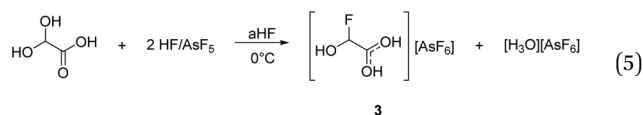
Scheme 1 Proposed reaction pathway of GAM with equimolar amounts of SF<sub>4</sub>.



Scheme 2 Proposed reaction pathway of the deoxyfluorination reaction at the carboxy group.

difluoroacetyl fluoride. Since the cationic intermediate would be a fluoro carbenium ion, it is presumably not sufficiently stabilized.

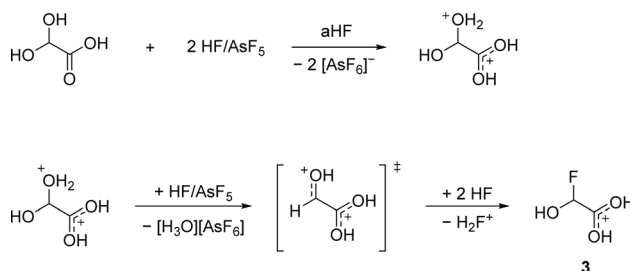
The deoxyfluorination agent SF<sub>4</sub> has been investigated in the past.<sup>13,15</sup> Interestingly, a similar reaction is observed for GAM reacting with superacids. Protonated α-fluorohydroxyacetic acid [FHA-1H]<sup>+</sup> is generated from GAM in the superacidic system HF/AsF<sub>5</sub>, resulting in [FHA-1H][AsF<sub>6</sub>] (3). The reaction is visualized in eqn (5).



According to eqn (5), a two-to-one ratio of AsF<sub>5</sub> to GAM would formally suffice to form [FHA-1H][AsF<sub>6</sub>]. However, full conversion takes place only when three equivalents of Lewis acid are applied. The carboxy group is more basic than the hydroxy groups due to better resonance stabilization, which is why it is likely protonated in the first step. The second protonation occurs at one of the hydroxy groups that subsequently is eliminated as H<sub>3</sub>O<sup>+</sup>. The formed substituted ethylene dication [C<sub>2</sub>(OH)<sub>3</sub>H]<sup>2+</sup> is superelectrophilic enough to add fluoride from the solvent aHF, similar to observations we made in a recent study.<sup>16</sup> 3 is found as a racemic mixture of the two enantiomers, strongly indicating an S<sub>N</sub>1 mechanism. The proposed mechanism is displayed in Scheme 3.

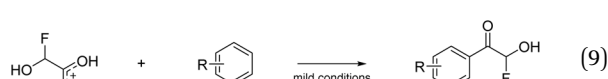
The necessity of three equivalents of Lewis acid to form 3 leads to the conclusion that a superelectrophilic carbocation is formed as the reactive intermediate.

Prakash *et al.*<sup>12</sup> showed that the carbonyl group (or dihydroxy group, respectively) of glyoxylic acid can be activated with strong acids in the presence of aromatic compounds for electrophilic reactions to synthesize diarylacetic acid derivatives (eqn (6)). α-Fluorohydroxyacetic acid may be useful similarly to generate aryl-fluoroacetyl acid derivatives (eqn (7)), while α-fluorohydroxyacetyl fluoride has the potential to be activated with Lewis acids at the C1-atom for Friedel-Crafts-acylations (eqn (8)). However, for this kind of reaction, the protonated species of α-fluorohydroxyacetic acid might be a better fit since the carboxy group is already activated and its [AsF<sub>6</sub>]<sup>−</sup> salt is relatively stable (eqn (9)).



Scheme 3 Proposed mechanism of the synthesis of [FHA-1H]<sup>+</sup> from GAM.





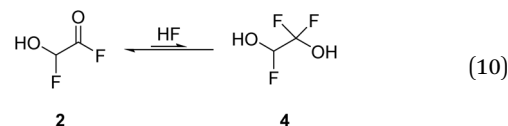
### NMR spectroscopy

The reactivity of glyoxylic acid monohydrate (GAM) in the systems HF/SF<sub>4</sub>, HF/AsF<sub>5</sub>, or solely aHF can be traced by <sup>1</sup>H, <sup>19</sup>F, and <sup>13</sup>C NMR spectroscopy. The samples were dissolved either in aHF or SO<sub>2</sub>, and acetone-*d*<sub>6</sub> was employed for external referencing. For more details of the experimental procedure, see the ESI† (Apparatus and Materials). The chemical shifts of **1**, **2**, and **3** are listed in Table 1. The respective solvent used for the measurements is given in the table footnote. A reference of GAM in D<sub>2</sub>O is displayed in Fig. S1 and S2.†

GAM has proven to be very reactive to HF. When dissolved in aHF, NMR spectra (Fig. S3–S5, ESI†) show a variety of fluorinated compounds. Doublets in both the <sup>1</sup>H (5.65 ppm, *J* = 61.2 Hz) and the <sup>13</sup>C NMR spectra (171.57 ppm, *J* = 32.6 Hz and 97.99 ppm, *J* = 225.2 Hz) are very similar to those assigned to **1**. This means that deoxyfluorination occurs in aHF, albeit uncontrolled. By first dissolving equimolar amounts of SF<sub>4</sub> (compared to GAM) in aHF and secondly adding GAM, **1** becomes the main product with an amount of roughly 74% (NMR spectra displayed in Fig. S6–S8, ESI†), as the doublet at 5.57 ppm is the most intensive one in the <sup>1</sup>H NMR spectrum. The <sup>19</sup>F signal at –130.38 ppm is assigned to the fluorine atom in FHA since the coupling constant is the same as for the <sup>1</sup>H

signal. The <sup>13</sup>C shift of the carboxy group is observed at 170.98 ppm, and the tetrahedral carbon shift at 96.95 ppm.

By employing two equivalents of SF<sub>4</sub>, **2** is the most abundant species. The NMR spectra recorded in aHF showed an equilibrium of **2** and its HF-adduct **4** (see eqn (10)). The spectra are displayed in Fig. S9–S11 in the ESI.†



The equilibrium is shifted to **2** by removing all volatile products at –78 °C, successively warming up the residue to 0 °C, and trapping the gas phase into a second vessel at –196 °C. The condensate was dissolved in SO<sub>2</sub>, and NMR spectra (Fig. S12–S14†) show **2** as the only organic compound, as shown by the intensive doublet at 7.00 ppm in the <sup>1</sup>H NMR spectrum. The <sup>13</sup>C signal of the acyl fluoride is observed at 154.33 ppm. The dd-splitting pattern shows the coupling to two fluorine atoms, just like the <sup>13</sup>C shift of the tetrahedral carbon at 92.59 ppm. In the <sup>19</sup>F NMR spectrum, these signals occur at –134.67, 23.63, and 22.97 ppm. Additional signals at 65.17 ppm and 64.48 ppm are assigned to residual SF<sub>4</sub> that has not been removed.<sup>17</sup>

A different approach to generating a derivative of α-fluorohydroxyacetic acid is the deoxyfluorination of GAM with superacids. By dissolving the Lewis acid in aHF in the first step, the superacidic medium is formed. Subsequently adding GAM to the solution led to a quantitative synthesis of [FHA-1H][AsF<sub>6</sub>] (**3**) (NMR spectra displayed in Fig. S15–S17, ESI†). The <sup>13</sup>C signal of the carboxy group (184.90 ppm) is shifted downfield compared to GAM and **1** due to the protonation in the superacidic system, similar to reported protonated carboxy groups.<sup>18</sup> The doublet at 97.00 ppm is assigned to the CHF(OH) group. The <sup>19</sup>F signal is observed at –128.88 ppm and the <sup>1</sup>H resonance at 5.61 ppm. The <sup>1</sup>H signal at 9.48 ppm confirms the formation of H<sub>3</sub>O<sup>+</sup>.<sup>19</sup>

### Vibrational spectroscopy

The synthesis of FHA-F and [FHA-1H][AsF<sub>6</sub>] is confirmed by vibrational spectroscopy. FHA-F (**2**) was generated by reacting GAM with a twofold amount of SF<sub>4</sub> in aHF. The solvent and other volatile products were removed *in vacuo* overnight at –78 °C

**Table 1** <sup>1</sup>H, <sup>19</sup>F, and <sup>13</sup>C chemical shifts [ppm] including coupling constants [Hz] of FHA (**1**), FHA-F (**2**), and [FHA-1H][AsF<sub>6</sub>] (**3**). Measured at –40 °C

	FHA <sup>a</sup>	FHA-F <sup>b</sup>	[FHA-1H][AsF <sub>6</sub> ] <sup>a</sup>
δ [ <sup>1</sup> H] (C–H)	5.57 (d), <i>J</i> = 54.4	7.00 (d) <i>J</i> = 51.2	5.61 (d) <i>J</i> = 56.9
δ [ <sup>1</sup> H] (H <sub>3</sub> O <sup>+</sup> )			9.48 (s)
δ [ <sup>19</sup> F] (C–F)	–130.38 (d) <i>J</i> = 54.4	–134.67 (d) <i>J</i> = 53.7	–128.88 (d) <i>J</i> = 53.9
δ [ <sup>19</sup> F] (COF)		23.63 (d) <i>J</i> = 16.3	
		22.97 (d) <i>J</i> = 14.1	
δ [ <sup>13</sup> C] (carboxylic)	170.98 (d) <i>J</i> = 32.7	154.33 (dd) <i>J</i> = 368.7, 34.8	184.90 (d) <i>J</i> = 34.0
δ [ <sup>13</sup> C] (tetrahedral)	96.95 (d) <i>J</i> = 225.1	92.59 (dd) <i>J</i> = 241.3, 82.4	97.00 (d) <i>J</i> = 227.1

<sup>a</sup> aHF as a solvent. <sup>b</sup> SO<sub>2</sub> as a solvent.



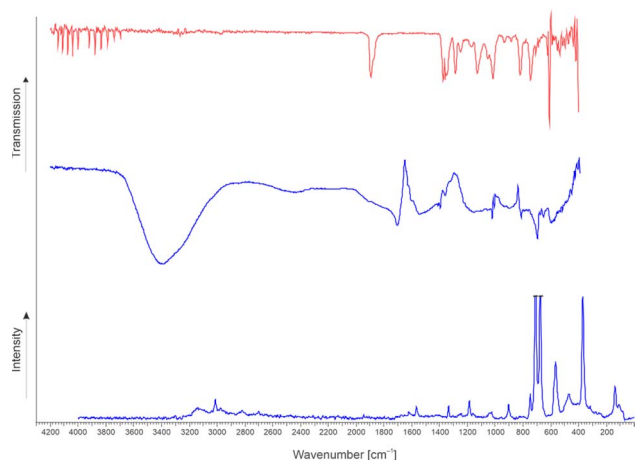


Fig. 1 The infrared spectrum of gaseous **2** at room temperature (top, red). Low-temperature infrared (middle) and Raman spectrum (bottom) of **3** (blue).

C. The sample was warmed up to 0 °C and an infrared spectrum of the gas phase was measured at room temperature. In the case of  $[\text{FHA-1H}]^+$ , the  $[\text{AsF}_6]^-$  salt (**3**) was synthesized by reacting GAM with  $\text{HF/AsF}_5$  in aHF and successively removing the solvent *in vacuo* at  $-78$  °C. Infrared and Raman spectroscopy of the colorless residue was performed at low temperatures (see ESI† for more details). The spectra are displayed in Fig. 1 and selected observed frequencies are listed in Table 2. Quantum chemical calculations of the respective compounds were performed to support the assignment of the vibrational frequencies. The detailed characterization of the compounds is found in the ESI.† FHA (**1**) could not be isolated from aHF, so an experimental frequency analysis was not feasible. However, the quantum chemically calculated frequencies and their assignment are listed in Table S3 in the ESI.†

The infrared spectrum of **2** shows rotational bands of remaining hydrogen fluoride between 3728 and 4143  $\text{cm}^{-1}$ , which was not completely removed after the reaction. The  $\nu(\text{C}=\text{O})$  vibration is observed at 1894  $\text{cm}^{-1}$ . This band is distinct for acyl fluorides<sup>20–22</sup> and is significantly blue-shifted compared to GAM (1742  $\text{cm}^{-1}$ ).<sup>23</sup> The stretching vibrations of the newly formed CF bonds occur at 1173 (acyl fluoride moiety) and 1016  $\text{cm}^{-1}$  (fluorohydroxy group). The intensive bands down

Table 2 Selected observed vibrational frequencies [ $\text{cm}^{-1}$ ] of **2** and **3**

FHA-F	$[\text{FHA-1H}][\text{AsF}_6]$		
Exp. IR <sup>a</sup>	Exp. IR <sup>a</sup>	Exp. Ra <sup>b</sup>	Assignment
1894 (m)	1705 (m) 1541 (m)	1567 (7)	$\nu(\text{CO}_a)$ $\nu(\text{CO}_a)$
1173 (m)			$\nu(\text{C}(\text{O})\text{F})$
1128 (m)	1151 (m)	1162 (3)	$\nu(\text{C}-\text{OH})$
1016 (m)	1022 (m)	1027 (4)	$\nu(\text{CF})$
822 (m)	897 (m)	903 (8)	$\nu(\text{CC})$

<sup>a</sup> Abbreviations: m = medium, a = acid. <sup>b</sup> Experimental Raman intensities are relative to a scale of 1 to 100.

from 708  $\text{cm}^{-1}$  are assigned to residual  $\text{SF}_4$ , which has been observed in the NMR study as well. A reference spectrum of  $\text{SF}_4$  is illustrated in Fig. S18 in the ESI.†

In the IR spectrum of **3**, a strong and broad band with a maximum at 3406  $\text{cm}^{-1}$  is found. This might be assigned to  $\text{H}_3\text{O}^+$ , however, it cannot be excluded that this band is attributed to the measurement method at low temperatures, where water can condense onto the specimen, superposing the OH and CH stretching vibrations. The protonation of the carboxy group can be traced by the  $\nu_{\text{as}}(\text{CO})$  band at 1705  $\text{cm}^{-1}$  (IR), which is red-shifted compared to  $\nu(\text{C}=\text{O})$  of GAM (1742  $\text{cm}^{-1}$ ).<sup>23</sup> The antisymmetric CO stretching mode of **3** occurs at 1541 (IR) and 1567  $\text{cm}^{-1}$  and is in return blue-shifted concerning  $\nu(\text{C}-\text{O})$  of GAM (1101  $\text{cm}^{-1}$ ). This convergence of the carboxylic vibrations is a direct result of protonation and has been described in several studies.<sup>24,25</sup> The stretching vibration of the newly formed CF bond is observed at 1022 (IR) and 1027  $\text{cm}^{-1}$  (Ra), similar to **2**.

### Crystal structure of $[\text{FHA-1H}][\text{AsF}_6]$

Single crystals of **3** were obtained by dissolving the colorless powder in aHF at  $-55$  °C. Colorless needles suitable for single-crystal X-ray diffraction grew as racemic twins within three days. In the following, the S-enantiomer is discussed. **3** crystallizes in the orthorhombic space group  $P2_12_12_1$  with four formula units per unit cell. The asymmetric unit is displayed in Fig. 2. Table 3 contains selected geometric parameters.

The C1–C2 bond of 1.515(5) Å is similar to the starting material glyoxylic acid monohydrate (GAM, 1.522(3) Å),<sup>26</sup> yet slightly longer than a regular  $\text{Csp}^3\text{--Csp}^2$  single bond (1.502 Å) in carboxylic acids.<sup>27</sup> The C1–O1 (1.258(4) Å) and C1–O2 (1.272(4) Å) bond distances are approximately the same, as has been observed in a variety of protonated carboxylic acids.<sup>24,25,28</sup> The C2–O3 bond (1.355(5) Å) is significantly shorter than the two C–OH bonds in GAM (1.400(4) and 1.404(3) Å) and even more significant than a regular C–O single bond in primary alcohols (1.426 Å).<sup>27</sup> The newly formed C2–F1 of 1.376(5) Å, on the other hand, is longer than a regular C–F bond with an electron-withdrawing group in the geminal position (1.349 Å).<sup>27</sup> The nature of this bond relation will be discussed below in the Theoretical Study.

The O1–C1–O2 angle of 120.6(3)° is significantly smaller than in GAM (125.1(2)°)<sup>26</sup> as a result of the protonated carboxy group. Subsequently, the O1–C1–C2 is widened from 111.9(2)°

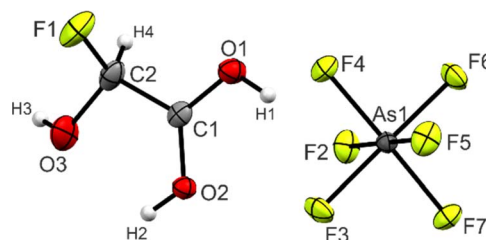


Fig. 2 Projection of the asymmetric unit of **3** (50% probability displacement ellipsoids, hydrogen atoms displayed as spheres of arbitrary radius).





**Table 3** Selected geometric parameters of **3**. Symmetry codes:  $i = x, 1 + y, z$ ;  $ii = 1.5 - x, 2 - y, 0.5 + z$ 

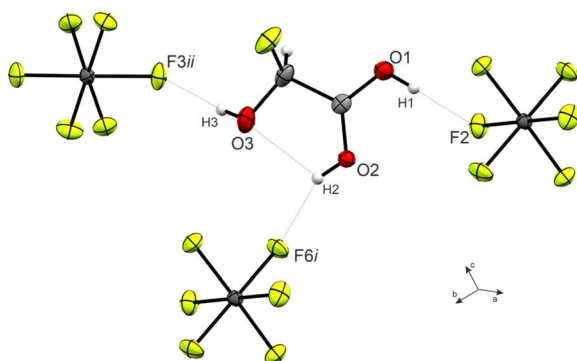
Bond lengths [Å]		Intermolecular interactions D(–H)⋯A [Å]	
C1–O1	1.258(4)	O1(–H1)⋯F2	2.579(4)
C1–O2	1.272(4)	O2(–H2)⋯O3	2.587(4)
C1–C2	1.515(5)	O2(–H2)⋯F6 <i>i</i>	2.669(3)
C2–O3	1.355(5)	O3(–H3)⋯F3 <i>ii</i>	2.826(4)
C2–F1	1.376(5)	C1⋯F7	2.733(5)
Bond angles [deg]		Dihedral angles [deg]	
O1–C1–O2	120.6(3)	O3–C2–C1–O1	179.5(4)
O1–C1–C2	117.4(3)	F1–C2–C1–O1	–61.2(5)
O2–C1–C2	122.0(3)	O3–C2–C1–O2	–1.0(6)
O3–C2–C1	106.6(3)	F1–C2–C1–O2	118.3(4)
F1–C2–C1	106.1(4)		
O3–C2–F1	111.9(4)		

in **GAM** to 117.4(3)° in **3**, while the remaining bond angles remain approximately unchanged. Regarding the torsion angles, the O3–C2–C1–O2 dihedral is reduced from 9.9(9)° to –1.0(6)°. This is due to an intramolecular hydrogen bond O2(–H2)⋯O3 with a distance of 2.587(4) Å that is formed upon protonation. The cation exhibits three additional, moderately strong hydrogen bonds<sup>29</sup> (Fig. 3) to form layers in the *bc*-plane (O1(–H1)⋯F2, O2(–H2)⋯F6*i*, and O3(–H3)⋯F3*ii*). These layers are connected along the *a*-axis by nearly perpendicular C1⋯F7 interactions with a distance of 2.733(5) Å (Fig. S21, ESI†), which is about 14% within the sum of the van-der-Waals radii (3.17 Å).<sup>30</sup>

The bond distances of the anion range between 1.698(3) and 1.754(2) Å. As–F bonds involved in donor–acceptor interactions (As1–F2, As1–F6, and As1–F6*i*) are slightly longer than the others, resulting in a distorted octahedral structure. These values have been observed for [AsF<sub>6</sub>]<sup>–</sup> anions in literature.<sup>28,31,32</sup>

### Theoretical Study

For **FHA** (**1**), **FHA-F** (**2**), and the free [FHA-1H]<sup>+</sup> cation, quantum chemical calculations were performed. The gas-phase

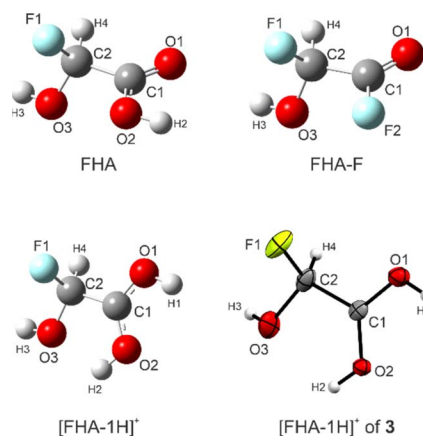
**Fig. 3** Hydrogen bonds in the crystal packing of **3** (50% probability displacement ellipsoids, hydrogen atoms displayed as spheres of arbitrary radius).**Table 4** Calculated bond distances [Å] of **FHA**, **FHA-F**, and [FHA-1H]<sup>+</sup> compared to the experimental values of **3** obtained from the X-ray structure analysis

	<b>FHA</b> <sup>a</sup>	<b>FHA-F</b> <sup>a</sup>	[FHA-1H] <sup>+</sup> <sup>a</sup>	X-ray ( <b>3</b> )
C1–O1	1.201	1.180	1.268	1.258(4)
C1–O2/F2	1.338	1.342	1.268	1.272(4)
C1–C2	1.532	1.529	1.538	1.515(5)
C2–O3	1.376	1.373	1.368	1.355(5)
C2–F1	1.392	1.389	1.367	1.376(5)

<sup>a</sup> Calculated on the B3LYP/aug-cc-pVTZ level of theory.

structures were optimized and the vibrational frequencies were computed on the B3LYP/aug-cc-pVTZ level of theory. In the case of the cation, a direct comparison to the experimental X-ray values is possible. The bond lengths are listed in Table 4. The calculated structures are illustrated together with the cation of **3** in Fig. 4. The labeling of the atoms is based on the crystal structure analysis for consistency.

The C–O bond distances of the protonated carboxy group are in fair agreement with the experimental values. For **FHA**, the values are consistent with comparable carboxylic acids like **GAM** or difluoroacetic acid.<sup>26,33</sup> The C=O bond length of **FHA-F** is the shortest among the investigated, yet it is in agreement with structural analyses of gaseous acyl fluorides reported in the literature, as well as the C(O)F bond.<sup>34,35</sup> The C2–O3 distances of all calculated structures (1.368–1.376 Å) are similar, while the X-ray data of **3** is a little shorter. However, all these values are shorter than a regular C–O single bond in primary alcohols (1.426 Å).<sup>27</sup> The calculated C2–F1 bond lengths of **FHA** and **FHA-F** are longer than in the case of [FHA-1H]<sup>+</sup>. The bond distances of  $\alpha$ -fluoroalcohols compared to regular C–F and C–OH bonds have been discussed in a study by Krossing *et al.* Accordingly, the elongation of the C–F bond is suspected to be a result of lone-pair conjugation of the oxygen atom into the antibonding  $\sigma^*(\text{C–F})$  orbital, subsequently shortening the C–OH bond.<sup>7</sup> This is in agreement with our DFT results. We performed NBO

**Fig. 4** Optimized gas-phase structures of **FHA**, **FHA-F**, [FHA-1H]<sup>+</sup>, and the cation [FHA-1H]<sup>+</sup> of **3**. Calculated on the B3LYP/aug-cc-pVTZ level of theory.

**Table 5** The stabilization energy by the non-bonding lone-pairs ( $n$ ) of the O3 and the F1 atom. NBO calculations on the MP2/aug-cc-pVTZ level of theory<sup>a</sup>

	$n(\text{O3}) \rightarrow \sigma^*(\text{C2-F1})$	$n(\text{F1}) \rightarrow \sigma^*(\text{C1-C2})$
FHA	109.3 kJ mol <sup>-1</sup>	16.8 kJ mol <sup>-1</sup>
FHA-F	111.5 kJ mol <sup>-1</sup>	19.3 kJ mol <sup>-1</sup>
[FHA-1H] <sup>+</sup>	105.7 kJ mol <sup>-1</sup>	29.0 kJ mol <sup>-1</sup>

<sup>a</sup> Calculated on the MP2/aug-cc-pVTZ level of theory.

calculations of all three investigated compounds (MP2/aug-cc-pVTZ level of theory) to assess this effect. The stabilization energies according to the second-order perturbation theory analyses of these interactions are summarized in Table 5.

The interactions of the oxygen lone-pair with the  $\sigma^*(\text{C-F})$  orbital are similar among the investigated compounds, explaining the shortening of the C–OH bond. The C–F distance of the neutral compounds FHA and FHA-F is subsequently elongated. In the case of the protonated species, the calculated C–F bond length rather coincides with a regular distance. Since the protonation has no significant influence on the described interaction, there must be another that strengthens the C–F bond. This is found to be the donation of a fluorine lone-pair into the  $\sigma^*(\text{C-C})$  orbital. The stabilization energy of this interaction in [FHA-1H]<sup>+</sup> is calculated to be 12.2 kJ mol<sup>-1</sup> higher than in FHA. This also explains why the C–C bond of the protonated species is the longest. However, the calculation estimates it longer than the experimental X-ray data shows. Similarly, the C–C bonds of FHA (1.532 Å) and FHA-F (1.529 Å) are longer than expected when compared to the corresponding bonds in difluoroacetic acid and difluoroacetyl fluoride.<sup>35</sup> This indicates that solid-state effects might have an additional influence on the bond distances.

## Conclusions

For the first time,  $\alpha$ -fluorohydroxyacetic acid (FHA), its acyl fluoride (FHA-F), and its protonated species ([FHA-1H]<sup>+</sup>) are described. The syntheses of FHA and FHA-F are achieved by reacting glyoxylic acid monohydrate (GAM) with HF/SF<sub>4</sub>. By applying the binary superacid HF/AsF<sub>5</sub>, [FHA-1H][AsF<sub>6</sub>] is the only organic compound, allowing a complete characterization by NMR, vibrational spectroscopy, and single-crystal X-ray diffraction. The superacidic deoxyfluorination only occurs when three equivalents of Lewis acid are used, implying that the superelectrophile [C<sub>2</sub>(OH)<sub>3</sub>H]<sup>2+</sup> is formed intermediately. NBO calculations reveal a complex relation between the C–F and the C–OH bond of the fluorohydroxy group. The use of superacids in aHF could enable convenient access to fluorinated compounds with a high electrophilicity and give deoxyfluorination reagents a new appeal.

## Data availability

The data supporting this article have been included as part of the ESI.† For full details on vibrational spectroscopy, NMR

spectroscopy, X-ray diffraction refinement, and computational details see the ESI.† Crystallographic data for [CH(OH)FC(OH)<sub>2</sub>][AsF<sub>6</sub>] has been deposited at the CCDC under the accession number 2173682 and can be obtained from <http://www.ccdc.cam.ac.uk>.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

Financial support of this work by the Ludwig-Maximilian University Munich (LMU), by the Deutsche Forschungsgemeinschaft (DFG), and F-Select GmbH is gratefully acknowledged. Special thanks to Prof. Dr Konstantin Karaghiosoff for his help in the publication process after Prof. Kornath's passing.

## Notes and references

- W. A. Sheppard and C. M. Sharts, *Organic Fluorine Chemistry*, Benjamin, New York, 1969.
- G. A. Olah and A. Pavláth, Synthesis of Organic Fluorine Compounds III. The Preparation of Fluoromethanol, *Acta Chim. Acad. Sci. Hung.*, 1953, **3**, 203–207.
- K. Seppelt, Trifluoromethanol, CF<sub>3</sub>OH, *Angew. Chem. Int. Ed. Engl.*, 1977, **16**, 322–323.
- K. O. Christe, J. Hegge, B. Hoge and R. Haiges, Convenient access to trifluoromethanol, *Angew. Chem. Int. Ed. Engl.*, 2007, **46**, 6155–6158.
- S. Andreades and D. C. England,  $\alpha$ -HALOALCOHOLS, *J. Am. Chem. Soc.*, 1961, **83**, 4670–4671.
- A. F. Baxter, J. Schaab, K. O. Christe and R. Haiges, Perfluoroalcohols: The Preparation and Crystal Structures of Heptafluorocyclobutanol and Hexafluorocyclobutane-1,1-diol, *Angew. Chem. Int. Ed. Engl.*, 2018, **57**, 8174–8177.
- J. Schaab, M. Schwab, D. Kratzert, J. Schwabedissen, H.-G. Stammer, N. W. Mitzel and I. Krossing, The perfluorinated alcohols  $\text{c-C}_6\text{F}_{11}\text{OH}$ ,  $\text{c-C}_6\text{F}_{10-1,1}(\text{OH})_2$  and  $\text{c-C}_6\text{F}_{10-1}(\text{CF}_3)\text{OH}$ , *Chem. Commun.*, 2018, **54**, 9294–9297.
- L. F. Fieser and M. Fieser, *Organische Chemie*, Verlag Chemie, Weinheim/Bergstrasse, 1st edn, 1972.
- G. A. Olah and G. D. Mateescu, Organic fluorine compounds. XXXII. Protonated fluoromethyl alcohol, *J. Am. Chem. Soc.*, 1971, **93**, 781–782.
- A. F. Baxter, J. Schaab, J. Hegge, T. Saal, M. Vasilu, D. A. Dixon, R. Haiges and K. O. Christe,  $\alpha$ -Fluoroalcohols: Synthesis and Characterization of Perfluorinated Methanol, Ethanol and n-Propanol, and their Oxonium Salts, *Chemistry*, 2018, **24**, 16737–16742.
- R. Minkwitz and S. Reinemann, Darstellung, spektroskopische Charakterisierung und Kristallstruktur von  $(\text{CF}_3)_2\text{C}(\text{F})\text{OH}_2^+ \text{Sb}_2\text{F}_{11}^-$ , *Z. Anorg. Allg. Chem.*, 1999, **625**, 121–125.
- G. S. Prakash, F. Paknia, A. Kulkarni, A. Narayanan, F. Wang, G. Rasul, T. Mathew and G. A. Olah, Taming of superacids:



- PVP-triflic acid as an effective solid triflic acid equivalent for Friedel–Crafts hydroxyalkylation and acylation, *J. Fluorine Chem.*, 2015, **171**, 102–112.
- 13 W. R. Hasek, W. C. Smith and V. A. Engelhardt, The Chemistry of Sulfur Tetrafluoride. II. The Fluorination of Organic Carbonyl Compounds 1, *J. Am. Chem. Soc.*, 1960, **82**, 543–551.
  - 14 J. Kollonitsch, S. Marburg and L. Perkins, Selective Fluorination of Hydroxy Amines and Hydroxy Amino Acids with Sulfur Tetrafluoride in Liquid Hydrogen Fluoride, *J. Org. Chem.*, 1975, **40**, 3808–3809.
  - 15 D. G. Martin and F. Kagan, The Reaction of Sulfur Tetrafluoride with Steroids, *J. Org. Chem.*, 1962, **27**, 3164–3168.
  - 16 A. Virmani, C. Jessen and A. J. Kornath, Synthesis and Structure of the Small Superelectrophile  $C_2(OH)_2Me_2^{2+}$ , *Chem.–Eur. J.*, 2024, **30**, e202400354.
  - 17 T. V. Oommen, B. Gotthardt and T. R. Hooper, Reactions of lower fluorides of sulfur with hydrogen sulfide, *Inorg. Chem.*, 1971, **10**, 1632–1635.
  - 18 A. Nitzer, M. Regnat, C. Jessen and A. J. Kornath, Third Time is a Charm – Protonating Tricarboxybenzenes, *Eur. J. Org. Chem.*, 2022, **2022**(5), e202101488.
  - 19 K. O. Christe, C. J. Schack and R. D. Wilson, Novel onium salts. Synthesis and characterization of oxonium hexafluoroantimonate ( $OH_3^+SbF_6^-$ ) and oxonium hexafluoroarsenate ( $OH_3^+AsF_6^-$ ), *Inorg. Chem.*, 1975, **14**, 2224–2230.
  - 20 J. R. Durig, G. A. Guirgis and T. A. Mohamed, Infrared and raman spectra, conformational stability, normal coordinate analysis, *ab initio* calculations, and vibrational assignment of difluoroacetyl fluoride, *J. Mol. Struct.*, 1998, **444**, 165–182.
  - 21 J. R. Durig, W. Zhao, D. Lewis and T. S. Little, Conformational stability, barriers to internal rotation, vibrational assignment, and *ab initio* calculations of chloroacetyl fluoride, *J. Chem. Phys.*, 1988, **89**, 1285–1296.
  - 22 J. R. Durig, M. M. Bergana and H. V. Phan, Raman and infrared spectra, conformational stability, barriers to internal rotation, *ab initio* calculations and vibrational assignment of dichloroacetyl fluoride, *J. Raman Spectrosc.*, 1991, **22**, 141–154.
  - 23 K. L. Plath, J. L. Axson, G. C. Nelson, K. Takahashi, R. T. Skodje and V. Vaidaa, Gas-phase vibrational spectra of glyoxylic acid and its gem diol monohydrate. Implications for atmospheric chemistry, *React. Kinet. Catal. Lett.*, 2009, **96**, 209–224.
  - 24 C. Jessen and A. J. Kornath, Syntheses and Structures of Protonated Acetylenedicarboxylic Acid, *Eur. J. Inorg. Chem.*, 2022, **2022**, DOI: [10.1002/ejic.202100965](https://doi.org/10.1002/ejic.202100965).
  - 25 A. Virmani, M. Pfeiffer, C. Jessen, Y. Morgenstern and A. J. Kornath, Protonation of Pyruvic Acid – Synthesis of a plain Superelectrophile, *Z. Anorg. Allg. Chem.*, 2022, **648**(14), e202200005.
  - 26 T. Lis, Structure of dihydroxyacetic acid (glyoxylic acid monohydrate),  $C_2H_4O_4$ , *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1983, **39**, 1082–1084.
  - 27 F. H. Allen, D. G. Watson, L. Brammer, A. G. Orpen and R. Taylor, in *International Tables for Crystallography*, ed. E. Prince, H. Fuess, T. Hahn, H. Wondratschek, U. Müller, U. Shmueli, A. Authier, V. Kopský, D. B. Litvin, M. G. Rossmann, E. Arnold, S. Hall and B. McMahon, International Union of Crystallography, Chester, England, 2006, pp. 790–811.
  - 28 M. Schickinger, T. Saal, F. Zischka, J. Axhausen, K. Stierstorfer, Y. Morgenstern and A. J. Kornath, The Tetrahydroxydicarbenium Cation  $[(HO)_2CC(OH)_2]^{2+}$ , *ChemistrySelect*, 2018, **3**, 12396–12404.
  - 29 G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford Univ. Press, New York, 1997.
  - 30 A. Bondi, V. van der Waals and J. Radii, *Phys. Chem.*, 1964, **68**, 441–451.
  - 31 R. Minkwitz, F. Neikes and U. Lohmann, Protonated Trithiocarbonic Acid – Synthesis, Spectroscopic Characterization and the Crystal Structure of  $C(SH)_3^+AsF_6^-$ , *Eur. J. Inorg. Chem.*, 2002, **2002**, 27–30.
  - 32 D. Mootz and M. Wiebcke, Fluorides and fluoro acids. 10. Crystal structures of acid hydrates and oxonium salts. 23. Crystal structure of the low-temperature form of oxonium hexafluoroarsenate(V), *Inorg. Chem.*, 1986, **25**, 3095–3097.
  - 33 J. M. J. M. Bijen and J. L. Derissen, On the molecular structure of difluoroacetic acid as investigated by means of gas electron diffraction, *J. Mol. Struct.*, 1975, **27**, 233–240.
  - 34 Y. Berrueta Martínez, C. G. Reuter, Y. V. Vishnevskiy, Y. B. Bava, A. L. Picone, R. M. Romano, H.-G. Stämmler, B. Neumann, N. W. Mitzel and C. O. Della Védova, Structural Analysis of Perfluoropropanoyl Fluoride in the Gas, Liquid, and Solid Phases, *J. Phys. Chem. A*, 2016, **120**, 2420–2430.
  - 35 B. P. van Eijck, P. Brandts and J. P. M. Maas, Microwave spectra and molecular structures of rotational isomers of fluoroacetic acid and fluoroacetyl fluoride, *J. Mol. Struct.*, 1978, **44**, 1–13.

