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Per- and polyfluoroalkyl substances (PFAS)

In a light of recent ECHA PFAS restriction proposal, that includes literary all CF3-containing organic molecules, I like to highlight one very important fluorinated molecular class containing CF3O- moiety.

As mentioned in the current version of ECHAS PFAS Annex XV, this class of molecules are taken out of restriction proposal §1.1.1[1] due to:

"For the restriction proposal however one exception is introduced (see rationale given below). The exception concerns certain fully degradable PFASs subgroups that only contain some specific structural elements."

"A substance that only contains the following structural elements is excluded from the scope of the proposed restriction:
CF3-X or **X-CF2-X'**,
where **X = -OR** or -NRR' and
X' = methyl (-CH_3), methylene (-CH_2-), an aromatic group, a carbonyl group (-C(O)-), -OR'', -SR'' or –NR''R''';
and where R/R'/R''/R''' is a hydrogen (-H), methyl (-CH_3), methylene (-CH_2-), an aromatic group or a carbonyl group (-C(O)-)."

This substance class is especially important for already existing and upcoming Active Pharmaceutical Ingredients (API) and Active Agrochemical Ingredients (AI)[2], as CF3O- group in many cases can substitute CF3-C group, which is under concern to decompose in the nature liberating persistent Trifluoroacetic acid (TFA).

The Access to these valuable CF3O- APIs and AIs up to now is limited, due to lack of availability of industrial large scale reagents and processes[7], allowing introduction of CF3O- moiety. On the one hand so called HALEX process, converting CH3O- group to CF3O- group is environmentally questionable (high waste) and structurally limited. On the other hand well known reagents like "Togni Reagent", are not available on a scale and are highly expensive[3].

Recently one new reagent attracted attention from several research groups[3,4,5], that allows introduction of CF3O- moiety on various aromatic systems in a very elegant way, is shelf stable, cheap, and possible to produce on industrial scale out of industrially available bulk raw materials. This reagent is so called "Bis(trifluoromethyl)peroxide" – CF3OOCF3 (CAS: 927-84-4). In comparison to classical organic peroxides, that are explosive and highly dangerous, CF3OOCF3 is thermally stable, shock resistant[6], easy to handle (liquidified gas), and inert to moisture.

This promising molecule falls under current ECHA PFAS restriction proposal, and due to novelty it is not included in any derogation. Even in ECHA exception above, that includes CF3O- structural elements, CF3OOCF3 is not included, because X is defined as –OR, and –OR cannot be –OO-

I believe such a structural peroxide was not included in your exception, just because it is literally unknown and not obvious.

The decomposition path for this peroxide CF3OOCF3 according to not yet published results leads to full mineralization (CO2, HF), similar as stated in ECHA exception.

Therefore I call ECHA to amend the current PFAS restriction proposal in a way to exclude this highly valuable and future-proof reagent, allowing not only to further develop it, but also possibility to put it onto market in the near future. This will pave the way towards development of new PFAS free medicines and sustainable agrochemicals.

The possible amendment could be:

a) Including CF3OO- element

b) Defining R= oxygen (-O-)

Literature (attached):

1. https://echa.europa.eu/restrictions-under-consideration/-/substance-rev/72301/term
2. Successful trifluoromethoxy-containing pharmaceuticals and agrochemicals. Journal of Fluorine Chemistry, 257-258 (2022) 109978, https://doi.org/10.1016/j.jfluchem.2022.109978
3. Radical Trifluoromethoxylation of Arenes Triggered by a Visible-Light-Mediated N−O Bond Redox Fragmentation. Angew. Chem. Int. Ed., 2018, 57, 13784–13789. https://doi.org/10.1002/anie.201806296
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5. Co-thermolysis: a one-pot synthetic method for novel2-substituted-5-(trifluoromethoxy)thiophenes. Tetrahedron Letters, 51 (2010) 5242–5245. https://doi.org/10.1016/j.tetlet.2010.07.111
6. No Fear of Perfluorinated Peroxides: Syntheses and Solid-State Structures of Surprisingly Inert Perfluoroalkyl Peroxides. Angew. Chem. Int. Ed., 2019, 58, 3584 –3588. https://doi.org/10.1002/anie.201814417
7. Recent advances in new trifluoromethoxylation reagents. Sci. China Chem., May (2019) Vol.62 No.5. https://doi.org/10.1007/s11426-018-9402-x

Sincerely yours,
Janis Jaunzems
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