

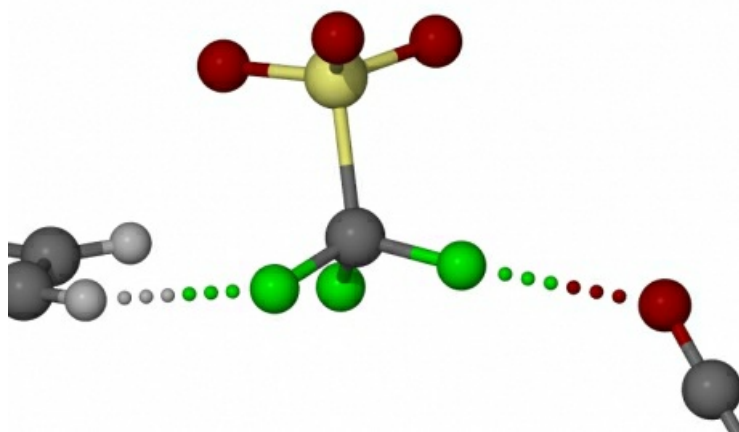
*Trifluoromethyl groups as halogen bond donors: the effect of group-polarizability*Catharine Esterhuysen¹¹Chemistry And Polymer Science, University Of Stellenbosch, Stellenbosch, South Africa
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The traditional picture of bonded fluorine as strongly δ^- suggests that it can only interact with electrophilic centers [1] and does not form halogen bonds,[2] however this view does not take polarization into account. In trifluoromethyl groups negative hyperconjugation (anomeric polarizability) results in two of the fluorine atoms becoming more polarizable and thus more able to form σ -holes.[3] The unique combination of the anomeric effect and the group-polarization process associated with it in trifluoromethyl groups allows the most negative molecular electrostatic potential (MEP) on the surface in contact with a nucleophile to become zero, so that the area of positive MEP on the backside of the carbon atom becomes dominant. The unusual group polarizability therefore results in the trifluoromethyl groups exhibiting amphiphilic behavior, i.e. acting not only as nucleophiles (as expected) but also as electrophiles and thus as halogen bond donors. A survey of experimental crystal structures obtained from the Cambridge Structural Database (CSD) and the Protein Databank (PDB) as well as MP2/aug-cc-pVDZ calculations on model systems demonstrate these interactions. In particular, a survey of structures in the CSD containing the trifluorotoluene moiety shows that the trifluoromethyl group forms more, and stronger, interactions with neighboring species than the F in fluorobenzene moieties, which does not experience anomeric polarization.

[1] Dunitz, J. D. (2004). *ChemBioChem*, 5, 614-621.

[2] Desiraju, G. R. & Parthasarathy, R. (1989). *J. Am. Chem. Soc.* 111, 8725-8726.

[3] Esterhuysen, C. et al. (2017). *ChemPhysChem*, 10.1002/cphc.201700027.



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