# A binary hydrogen bonding motif based on homochiral recognition: crystal structures and hydrogen bonding networks of *meso*-(*R*,*S*)-bis(trifluorolactate)s†

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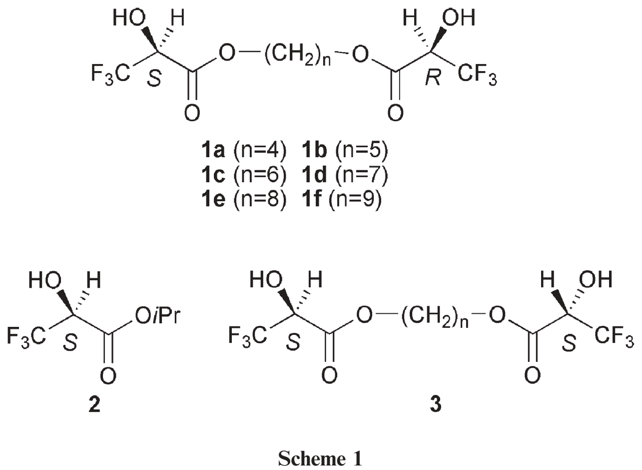
**A series of *meso*-compounds incorporating both enantiomers of a trifluorolactate constructed two-dimensional supramolecular sheets *via* homochiral hydrogen bonding chains as a binary hydrogen bonding motif.**

Binary hydrogen bond pairing such as A···T and G···C in a DNA double helix, plays an important role in the generation of supramolecular self-assembly and processing genetic information.[1] Development of a new binary hydrogen bonding motif may bring about not only a well-defined supramolecular architecture but also a processing method for molecular information in supramolecular chemistry.[2] The binary hydrogen bonding motifs of organic molecules incorporating two kinds or more of functional groups have been explored in the liquid and solid states.[3] Such molecules are designed to undergo self-assembly in a homolytic mode; however, control of selectivity between the homolytic and heterolytic modes is still a difficult problem due to structural interference between molecular functionalities and low energetic differences between the hydrogen bonding modes.[4]

On the other hand, homochiral recognition of a chiral molecule is a binary recognition process like a handshake, which is discrimination of the same and the opposite configuration. Homochiral recognition is usually mediated by stereoselective hydrogen bonding to result in two types of homochiral self-assembly, *R*···*R* and *S*···*S*. Although many examples have been reported of homochiral self-assembly from the corresponding racemic mixture,[5,6] no examples have been reported of application of the homochiral recognition event to a binary connecting motif for supramolecular architecture. A *meso*-compound incorporating both enantiomeric interaction moieties has the potential to follow two types of chirality-directed self-assembly[7]: homochiral (*R-S*···*S-R*···*R-S*···) and heterochiral (*R-S*···*R-S*···) self-assembly. It is a promising candidate for the demonstration of a binary hydrogen bonding motif. Although crystal structures involving homochiral hydrogen bonding of *meso*-compounds such as *meso*-hydrobenzoin derivatives have been reported to date,[8] these compounds seem to have low homochiral recognition ability and their molecular structure will be impossible to use in constructing a supramolecular architecture. Herein we report a binary hydrogen bonding motif based on homochiral recognition of polymethylene bridged (*R*,*S*)-*meso*-bis(trifluorolactate)s (**1**) (Scheme 1).

We have already discovered a homochiral recognition phenomenon of isopropyl trifluorolactate (**2**) in the liquid state. A simple distillation of **2** led to a disproportion of the enantiomeric excess between the distillate and the residue.[9] Because we considered that the phenomenon was due to stereoselective hydrogen bonding of **2**, the hydrogen bonding pattern of trifluorolactate in the solid state was investigated first. Crystallographic studies of (*S*)-**2** and (*S*,*S*)-double-headed trifluorolactates (**3**) revealed that one trifluorolactate moiety can interact with the neighboring moieties possessing the same chirality through infinite O–H···O–H, O–H···O(=C), and C–H···O(=C) hydrogen bonds.[10] However, this crystallographic information was not sufficient evidence for the homochiral recognition ability of trifluorolactate because the information was about only the enantiopure system. So, our next focus of interest was the homochiral recognition nature and supramolecular structure of *meso*-**1** as a model of racemic trifluorolactate.

The *meso*-compounds **1** were synthesized from (*R*)- and (*S*)-3,3,3-trifluorolactic acids and α,ω-alkanediols in two steps. Single crystals of **1** were prepared by slow evaporation of a hexane–ether solution of **1**. The crystal structures were determined by single crystal X-ray diffraction analysis. The crystal structure of **1f** ($n = 9$) is shown in Fig. 1 as a typical example of the series of **1**. As expected, the (*S*)-trifluorolactate moiety interacts with only (*S*)-moieties, and the (*R*)-moiety interacts with only (*R*)-moieties, to form homochiral hydrogen bonding chains along the $2_1$ axis. In short, the homochiral hydrogen bonding chains worked as a binary hydrogen bonding motif and the binary hydrogen bonding



**Scheme 1**

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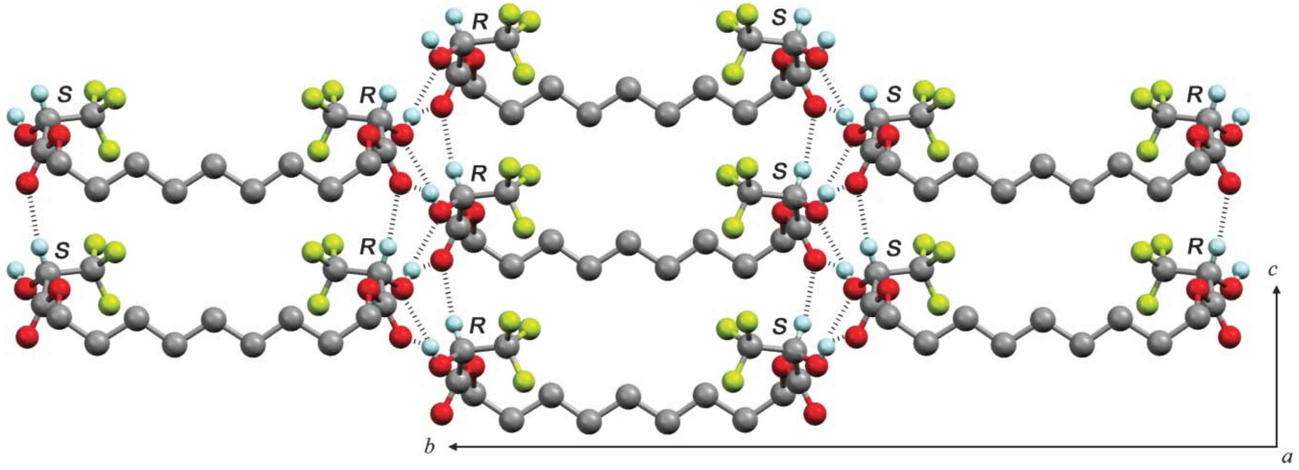

**Fig. 1** Crystal structure of **1f** viewed down *a* axis. Green, grey, red, and light blue spheres are fluorine, carbon, oxygen, and hydrogen, respectively. Hydrogen atoms of methylene chains and disordered solvent molecules in voids are omitted for clarity. Hash bonds are hydrogen bonds.

motif constructed an undulate two-dimensional supramolecular sheet. Crystals of other *meso*-**1** compounds showed similar supramolecular sheet structures through the binary hydrogen bonding motif (see ESI†). The intermolecular hydrogen bonding distances of compounds **1** are summarized in Table 1.

Moreover, a heterochiral hydrogen bonding chain of **1** could be observed. The crystal **1f** included crystallization solvents such as hexane and ether by $^1$H NMR and X-ray diffraction analysis, so compound **1f** was crystallized from bulky solvents (isooctane–THF) to give another single crystal **1f′** that included no guest molecules. Interestingly, the crystal **1f′** showed a different supramolecular sheet structure involving a heterochiral hydrogen bonding chain of (*R*)- and (*S*)-trifluorolactate moieties (Fig. 2). The hydrogen bonding distances of **1f′** were similar to those of **1f** (Table 1). A necessary difference between the two hydrogen bonding chains is the orientation of the $CF_3$ groups: the homochiral and heterochiral chains have antiparallel and parallel orientation of the $CF_3$ groups, respectively.

A series of *meso*-trifluorolactates **1** have maintained the homochiral hydrogen bonding motif in the crystal with systematic modification of the molecular structure. This result suggests that the crystal structure of **1** is directed by the one-dimensional hydrogen bonding chain. Formation of the homochiral hydrogen bond is preferable, but a limitation in the binary hydrogen bonding motif was found. In the case of compound **1f**, both the homochiral and heterochiral hydrogen bonding networks were observed by a change of the crystallization conditions. The supramolecular isomerism may arise from three factors: (1) guest-selective inclusion ability of **1f**, (2) conformational flexibility of **1f**, and (3) lower chiral discrimination energy of trifluorolactate than crystal packing energy. Previously, the chiral discrimination energy was estimated to be *ca.* 1.1 kcal mol$^{-1}$;[9] the estimation for the liquid state is consistent with the present result of the solid state. Therefore, the limitation for the binary hydrogen bonding motif will become obvious in the case of a crystal structure containing guest accessible cavities. In addition, binary recognition processes *via* zero-dimensional (1:1) interactions for DNA-bases and infinite one-dimensional interactions for **1** contrasted sharply. From the viewpoint of the dimensional number, it is conceivable that the binary hydrogen bonding motif of trifluorolactate is suitable for controlling one-dimensional molecular alignment in a well-defined supramolecular architecture rather than the memorizing and processing of molecular information based on the chirality.

**Table 1** Intermolecular hydrogen bonding distances *D* in Å for crystals **1a–1f′**

| | $D_{\text{O–H}\cdots\text{O–H}}$ | $D_{\text{O–H}\cdots\text{O=C}}$ | $D_{\text{C–H}\cdots\text{O=C}}$ |
|---|---|---|---|
| **1a** | 2.769(1) | 3.154(2) | 3.244(2) |
| **1b** | 2.740(8) | 2.951(7) | 3.20(1) |
| | 2.802(8) | 3.050(8) | 3.26(1) |
| **1c** | 2.839(1) | 2.863(1) | 3.246(2) |
| **1d** | 2.861(3) | 2.839(4) | 3.240(5) |
| **1e** | 2.823(5) | 2.813(5) | 3.282(6) |
| | 2.938(5) | 2.923(5) | 3.376(6) |
| **1f** | 2.821(2) | 2.886(2) | 3.208(2) |
| **1f′** | 2.830(1) | 2.933(2) | 3.260(2) |
| | 2.840(2) | 2.941(1) | 3.277(2) |

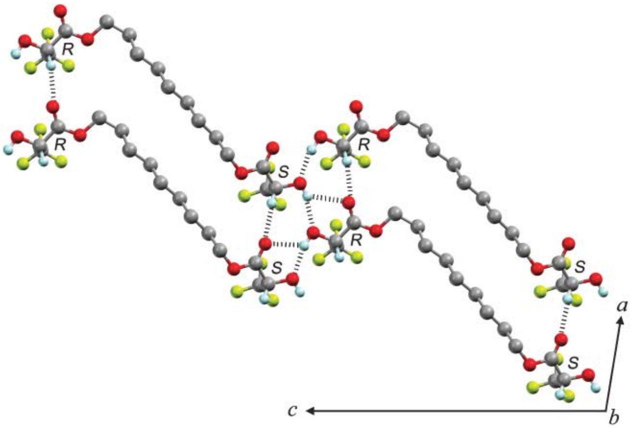

**Fig. 2** Crystal structure of **1f′** viewed down *b* axis. Green, grey, red, and light blue spheres are fluorine, carbon, oxygen, and hydrogen, respectively. Hydrogen atoms of methylene chains are omitted for clarity. Hash bonds are hydrogen bonds.

Recently, a racemic mandelate which formed a homochiral hydrogen bonding chain to give the crystal of a racemic compound was reported.[11] Although all α-hydroxy esters have the potential to form a molecular handshake,[12] the trifluorolactate has some advantages as a *supramolecular synthon*[13] among all α-hydroxy esters: (1) reinforcement of the hydrogen bond by the electron-withdrawing (EWG) effect of the $CF_3$ group,[14] (2) formation of C–H⋯O hydrogen bonds by the EWG effect and the compact size of the $CF_3$ group, and (3) enhancement of the homochiral preference by the multiple hydrogen bonding interaction.

In conclusion, we have found that the hydrogen bond of chiral trifluorolactates could work as a new type of binary supramolecular connecting motif based on homochiral recognition. This finding is a simple example of a molecular handshake that can be utilized for the design and creation of homochiral supramolecular architectures.‡

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## Notes and references

‡ Single crystal X-ray diffraction data were collected on a Rigaku R-AXIS IV diffractometer using Mo-Kα radiation [$\lambda = 0.7107$ Å]: **1a**) $C_{10}H_{12}F_6O_6$, $M = 342.19$, monoclinic, $P2_1/c$ (no. 14), $a = 7.1113(8)$, $b = 5.0864(3)$, $c = 18.142(2)$ Å, $\beta = 98.398(2)^\circ$, $U = 649.17(10)$ Å$^3$, $T = 120$ K, $Z = 2$, $\mu = 0.193$ mm$^{-1}$, 2819 reflections measured, 1487 unique ($R_{int} = 0.022$), w$R_2(F^2) = 0.116$ (all 1247 data); **1b**) $C_{11}H_{14}F_6O_6$, $M = 356.22$, orthorhombic, $Pna2_1$ (no. 33), $a = 15.40(1)$, $b = 18.79(2)$, $c = 5.045(3)$ Å, $U = 1460(6)$ Å$^3$, $T = 120$ K, $Z = 4$, $\mu = 0.175$ mm$^{-1}$, 6719 reflections measured, 2218 unique ($R_{int} = 0.073$), w$R_2(F^2) = 0.132$ (all 2218 data); **1c**) $C_{12}H_{16}F_6O_6$, $M = 370.24$, monoclinic, $C2/c$ (no. 15), $a = 19.891(2)$, $b = 5.1138(2)$, $c = 15.605(1)$ Å, $\beta = 100.918(1)^\circ$, $U = 1558.6(2)$ Å$^3$, $T = 120$ K, $Z = 4$, $\mu = 0.167$ mm$^{-1}$, 5843 reflections measured, 1679 unique ($R_{int} = 0.012$), w$R_2(F^2) = 0.127$ (all 1371 data); **1d**) $C_{13}H_{18}F_6O_6$, $M = 384.27$, orthorhombic, $Pnma$ (no. 62), $a = 15.613(3)$, $b = 21.793(4)$, $c = 5.0901(5)$ Å, $U = 1731(1)$ Å$^3$, $T = 120$ K, $Z = 4$, $\mu = 0.153$ mm$^{-1}$, 10363 reflections measured, 1888 unique ($R_{int} = 0.037$), w$R_2(F^2) = 0.140$ (all 1541 data); **1e**) $C_{14}H_{20}F_6O_6$, $M = 398.30$, triclinic, $P\bar{1}$ (no. 2), $a = 5.120(1)$, $b = 10.895(3)$, $c = 17.165(4)$ Å, $\alpha = 72.489(8)$, $\beta = 89.58(2)$, $\gamma = 85.41(2)^\circ$, $U = 910.0(4)$ Å$^3$, $T = 120$ K, $Z = 2$, $\mu = 0.149$ mm$^{-1}$, 4258 reflections measured, 2601 unique ($R_{int} = 0.03$), w$R_2(F^2) = 0.269$ (all 2601 data); **1f**) $C_{15}H_{22}F_6O_6(C_6H_{14})_n$, $M = 498.50$, orthorhombic, $Pnma$ (no. 62), $a = 15.7479(5)$, $b = 27.135(1)$, $c = 5.0309(1)$ Å, $U = 2149.8(5)$ Å$^3$, $T = 100$ K, $Z = 4$, $\mu = 0.14$ mm$^{-1}$, 4499 reflections measured, 1900 unique ($R_{int} = 0.013$), w$R_2(F^2) = 0.117$ (all 1900 data); **1f′**) $C_{15}H_{22}F_6O_6$, $M = 412.32$, monoclinic, $P2_1/c$ (no. 14), $a = 5.3266(7)$, $b = 20.331(5)$, $c = 16.967(4)$ Å, $\beta = 94.52(1)^\circ$, $U = 1831.8(7)$ Å$^3$, $T = 115$ K, $Z = 4$, $\mu = 0.075$ mm$^{-1}$, 6940 reflections measured, 4035 unique ($R_{int} = 0.020$), w$R_2(F^2) = 0.156$ (all 3330 data). CCDC numbers: (**1a**) CCDC 246911, (**1b**) CCDC 246912, (**1c**) CCDC 246913, (**1d**) CCDC 246914, (**1e**) CCDC 246915, (**1f**) CCDC 246916, (**1f′**) CCDC 264877. See http://dx.doi.org/10.1039/b504676a for crystallographic data in CIF or other electronic format.

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