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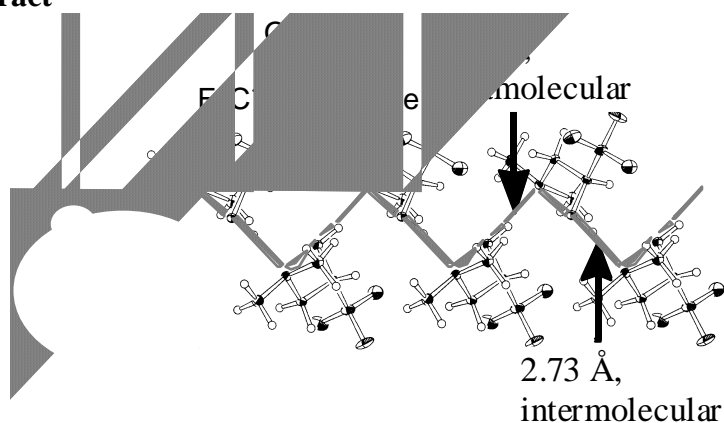
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Graphic Abstract



3-Dimethylamino-1,1,1-trifluoro-2-propanol constructs a hydrogen bonding chain built up with alternating intermolecular medium and intramolecular weak hydrogen bonds.

Intermolecular-medium and intramolecular-weak hydrogen bonding chains in the crystals of chiral trifluoromethylated amino alcohols

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Abstract

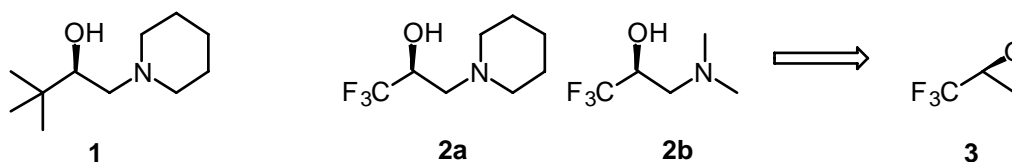
A structural feature of hydrogen bonding chains found in the crystals of trifluoromethylated amino alcohols is reported. Hydrogen bondings of 3-(*N,N*-dialkylamino)-1,1,1-trifluoro-2-propanols construct chiral spiral hydrogen bonding chains. Lone pairs on the nitrogen atoms of the amino alcohols participate in two hydrogen bondings. Detailed structural analysis of the hydrogen bonds of the 3-(*N,N*-dimethylamino)-1,1,1-trifluoro-2-propanol suggested that the chain built up with alternating intermolecular medium and intramolecular weak hydrogen bonds. The medium intermolecular hydrogen bond, which transfers a proton from the hydroxy group to the amino nitrogen, would make a tentative zwitterionic form of the molecule. Then, electrostatic attraction between the charges in the zwitterion centers induced a weak intramolecular hydrogen bond.

Keywords: Hydrogen bond; Weak hydrogen bond; Medium hydrogen bond; Hydrogen bonding chain; Trifluoromethylated amino alcohols; Chiral recognition; Structure of hydrogen bond

1. Introduction

The importance of optically pure amino alcohols as chiral ligands needs no restatement herein [1,2]. However, optical purification of the amino alcohols has still remained as a major problem which should be solved. For example, 1-piperidyl-3,3-dimethyl-2-butanol **1** is one of the best chiral ligands for Et₂Zn alkylation of benzaldehyde [3-6]. Compound **1** is liquid at room temperature. Thus, it cannot be purified optically by a simple recrystallization. A diastereomeric recrystallization or a chromatographic method is needed for its optical purification [7,8].

Meanwhile, both trifluoromethylated chiral ligands, **2a** and **2b**, prepared from highly available epoxide **3**, are needle crystals at room temperature. Thus, they are easily purified chemically as well as optically by simple recrystallization [9,10]. Therefore, these amino alcohols can be used as easily available optically pure chiral ligands. Recently, we have reported that the trifluoromethylated amino alcohol **2a** could be a good chiral ligand for enantioselective Et₂Zn alkylation [11] and **2b** could be one of the best chiral ligands for enantioselective Reformatsky reaction [12].



In this paper, a study on a structural feature of the unique hydrogen bonding systems of crystalline α -trifluoromethyl amino alcohols by X-ray crystallographic analysis is described. Two amino alcohols, 1,1,1-trifluoro-3-(*N*-piperidyl)-2-propanol **2a** (m.p. = 40 °C) [13,14,15], and 1,1,1-trifluoro-3-(*N,N*-dimethylamino)-2-propanol **2b** (m.p. = 41 °C) [13] were prepared by reported procedures. These compounds have higher melting points than those of the parent non-fluorinated compounds. (Both optically active (*N*-piperidyl)-2-propanol and 3-(*N,N*-dimethylamino)-2-propanol are liquid at ambient temperature.)

2. Results

Single crystal X-ray diffraction measurements and analyses of the amino alcohols, **2a** and **2b**, gave hydrogen bonding structures as shown in Figure 1 and 2, respectively. They constructed chiral spiral hydrogen bonding chains in their crystals.

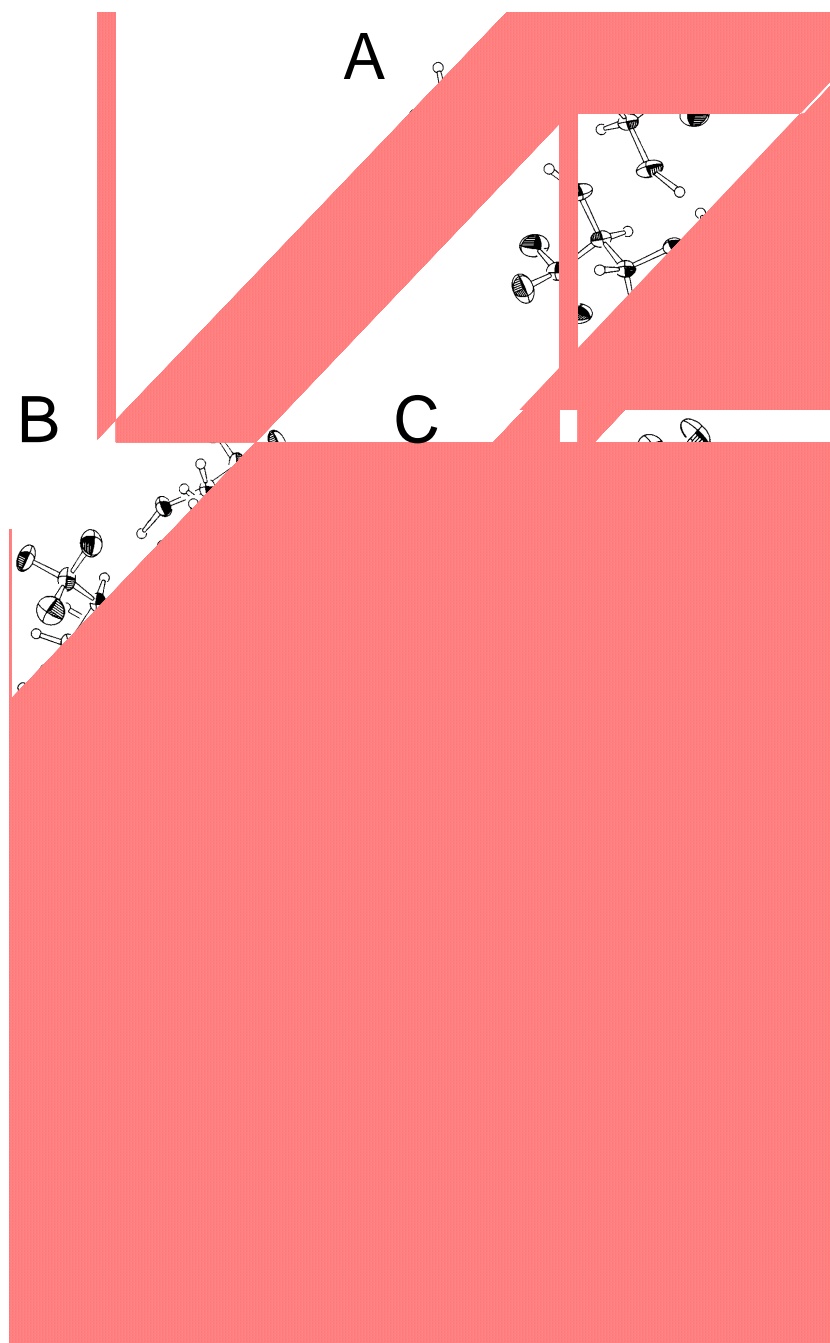


Figure 1. Crystal packing ORTEP view of 1,1,1-trifluoro-3-(*N*-piperidyl)-2-propanol **2a**. A: a view parallel to the spiral hydrogen bonding chains (*a* axis), B and C: views

perpendicular to the hydrogen bonding chain (b axis and c axis). Red lines are possible hydrogen bondings.

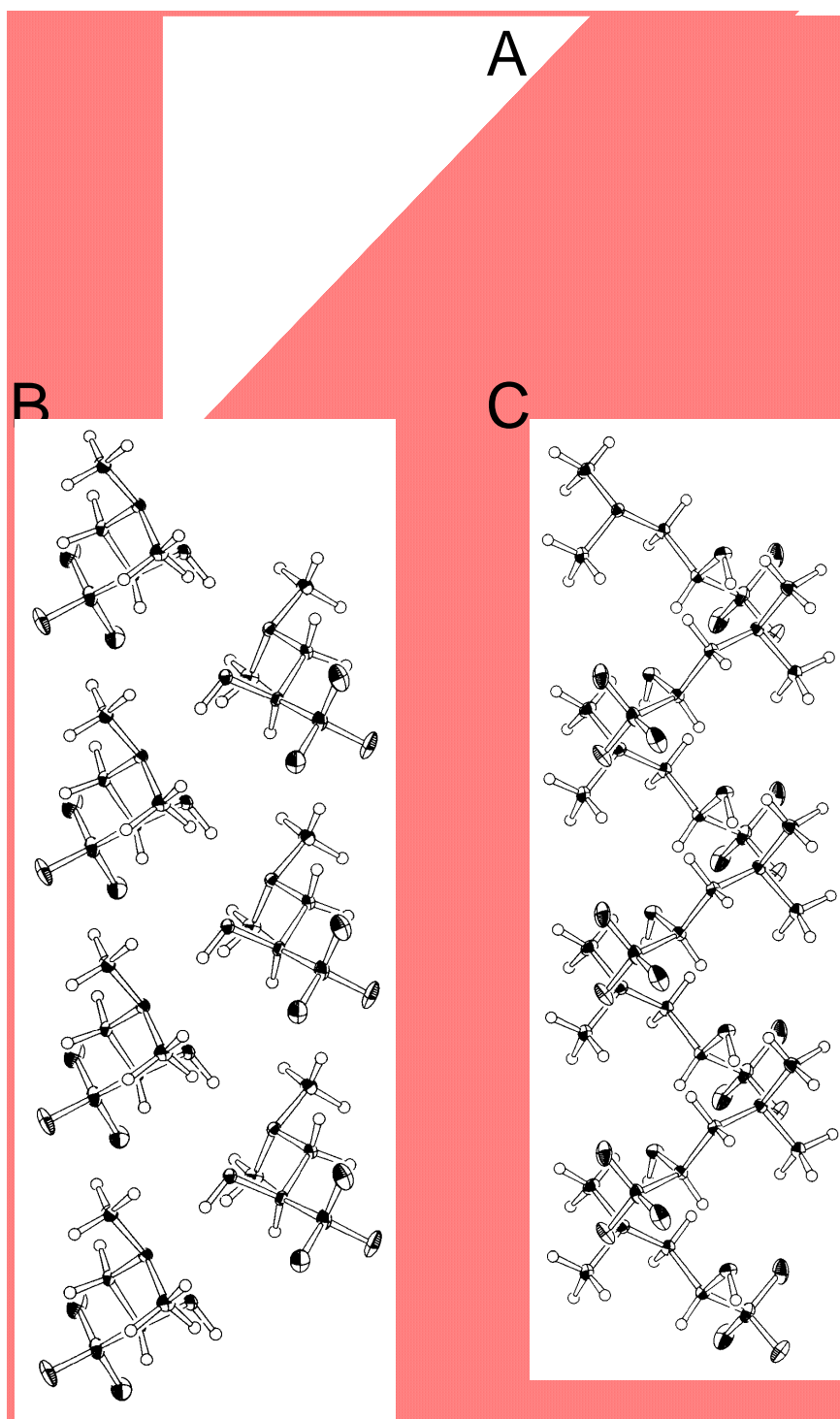


Figure 2. Crystal packing ORTEP view of 1,1,1-trifluoro-3-(*N,N*-dimethylamino)-2-propanol **2b**. A: a view parallel to the spiral hydrogen bonding chains (*a* axis), B and

C: views perpendicular to the hydrogen bonding chain (b axis and c axis). Red lines are possible hydrogen bondings.

Hydrogen bonding systems of **2a** and **2b** constructed infinite chiral helical chains. All the oxygen and the nitrogen atoms were the center of two hydrogen bonds, one intramolecular and one intermolecular. The distance between oxygen and nitrogen of the intramolecular hydrogen bonding was 3.028(4) Å and that of the intermolecular was 2.778(4) Å for amino alcohol **2a**, and 2.943(1) Å and 2.734(1) Å for amino alcohol **2b**. Noteworthy, the nitrogens of the amino alcohols **2a** and **2b** participate in two hydrogen bonds, even though they have only one lone pair. Moreover, the hydrogen bonding chains have only one proton per two hydrogen bonds. These hydrogen bonding systems seemed to be typical single-proton, multi-center hydrogen bondings, at a glance [16].

3. Discussion

The remarkable progress in elucidating hydrogen bonding structures and energies in these two decades has spread the scope of the hydrogen bondings and caused confusion in its limitation and classification. Nowadays, an electrostatic attraction without covalent orbital interaction (e.g. C-H... π interaction) has also been called "a weak hydrogen bond [17,18]." An X-ray diffraction analysis is a key technique to discriminate "medium hydrogen bond" (conventional hydrogen bond) and "weak hydrogen bonds" (electrostatic attraction) [18].

Detailed structure of the hydrogen bonds of **2b** is shown in Figure 3. The distance between the proton-donor and the acceptor atoms of the intermolecular hydrogen bond was 2.734 Å and that of the intramolecular was 2.943 Å. Thus, the former intermolecular hydrogen bond would be a "medium" hydrogen bond with transfer of proton, while that of the intramolecular straddled the divide between "medium" and "weak" hydrogen bonds [17,18].

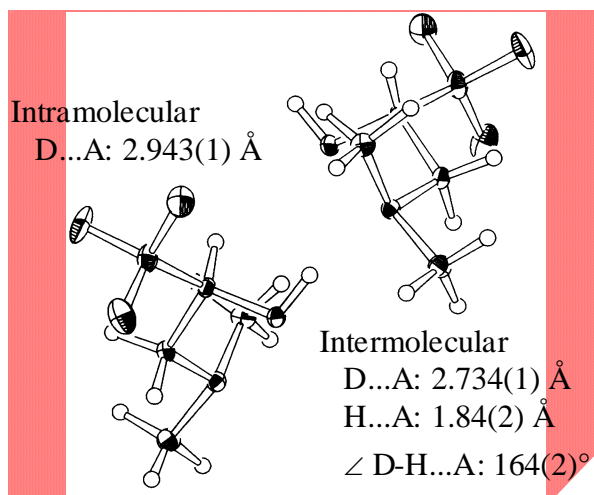
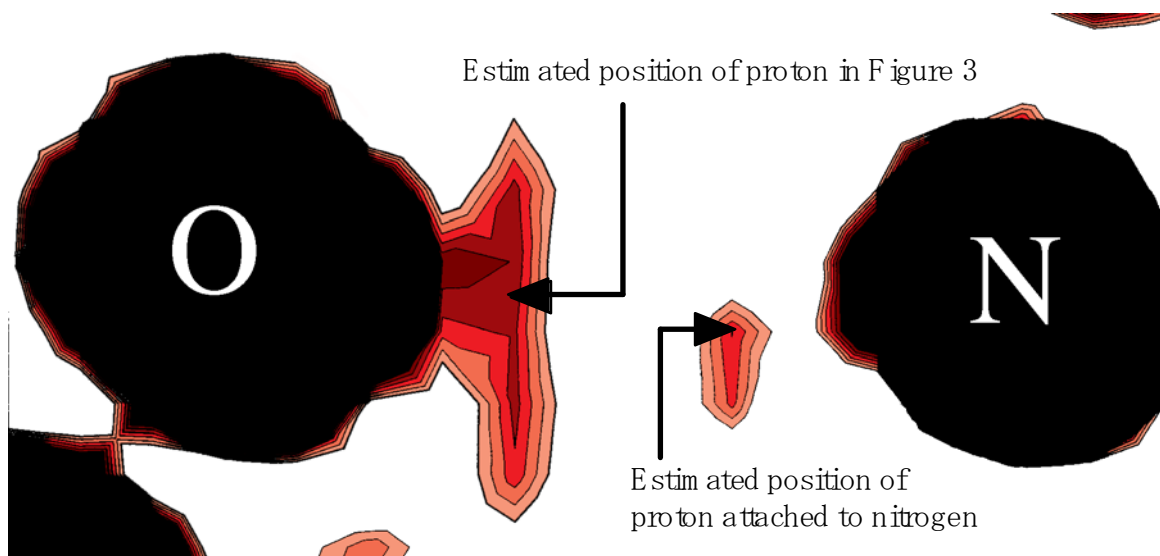


Figure 3. Detailed structure of hydrogen bonds of **2b**.

Another criterion for the classification of the hydrogen bonds is the alignment of the proton donor atom (D), proton (H), and proton acceptor atom (A). A medium hydrogen bond may have a \angle D-H..A degree wider than 130° [18]. Here, elucidation of the location of the proton by X-ray diffraction analysis is not easy due to a little electron density around the proton nucleus. Figure 4(A) illustrates an F_{obs} contour map of the intermolecular hydrogen bonding region. A thin but obvious flare of electron density from the oxygen atom toward the nitrogen atom could be seen, which implies the existence of a proton in this bonding direction [19]. The estimated \angle O-H..N was $164(2)^\circ$. No such flare of electron density could be seen between the intramolecular hydrogen bonding region, as shown in Figure 4(B). The estimated intramolecular \angle N-H..O (a hydrogen bond with nitrogen attached proton) was 97° , which met the criterion for a weak hydrogen bond, but did not meet that for a medium hydrogen bond.

(A)



(B)

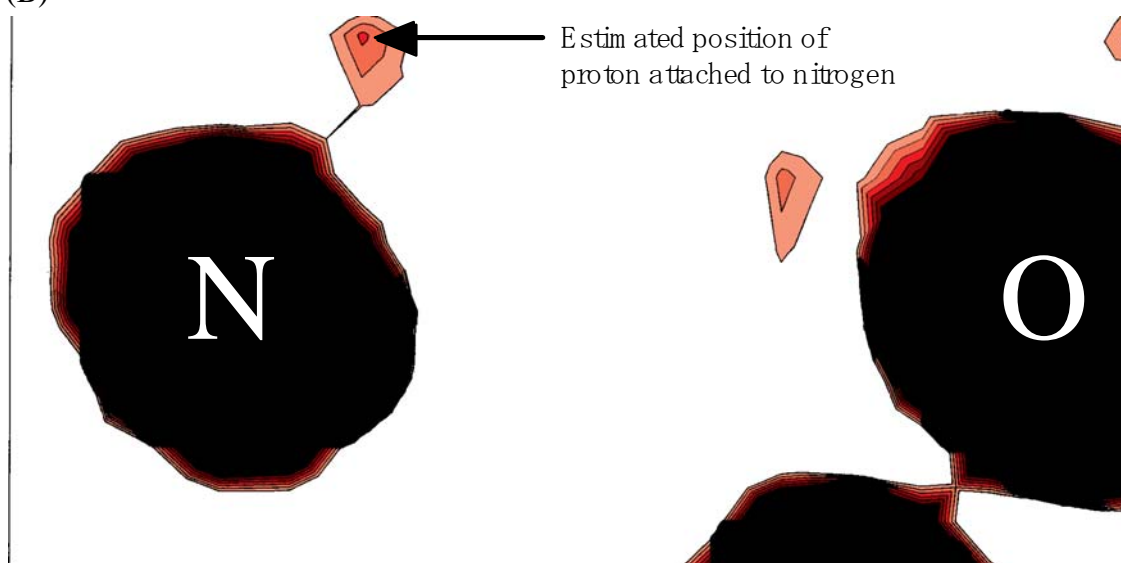
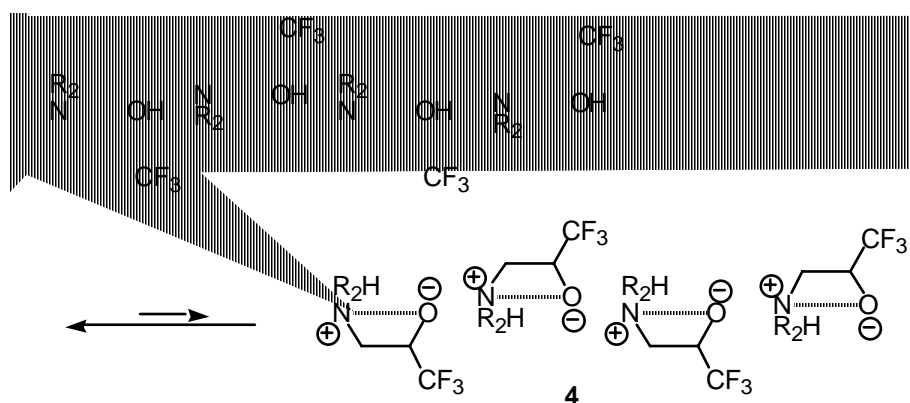


Figure 4. F_{obs} contour map of (A) intermolecular hydrogen bonding region, and (B) intramolecular hydrogen bonding region. Contour interval is $0.10 \text{ e}/\text{\AA}^3$.

Thus, we may conclude that the intermolecular hydrogen bond would be a medium hydrogen bond mediated by proton and the intramolecular hydrogen bond would be a weak hydrogen bond. That is, the hydrogen bonding chain of the **2b** built up with alternating intermolecular medium and intramolecular weak hydrogen bonds.

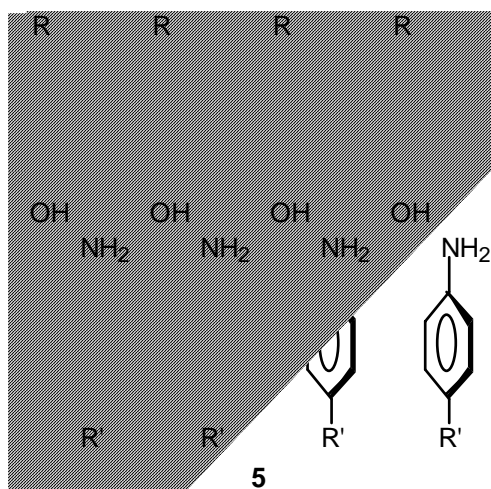
Similarly, the intermolecular distance between the center atom of the donor (oxygen) and that of the acceptor (nitrogen) of amino alcohol **2a** was 2.78 Å and that of the intramolecular was 3.03 Å. Thus, trifluoromethylated amino alcohol **2a** would have a similar alternating medium-weak hydrogen bonding chain structure [20].

The β -fluorinated alcohols have lower pK_a than non-fluorinated analogs. Thus, they have higher hydrogen bond donating ability [α_2^H] and lower hydrogen bond accepting ability [β_2^H] than their parent non-fluorinated alcohols [21,22]. The present aminoalcohols, **2a** and **2b**, have a good hydrogen bond accepting group, amino nitrogen, in their structure. Thus, a certain participation of zwitterionic structure **4** in the crystal would be expected [19]. Furthermore, the medium hydrogen bond which was indicated by detailed structure of the hydrogen bonding system, strongly supported the participation of the structure **4**. Intermolecular protonation of amino nitrogen would induce deprotonation of the hydroxy group and stabilize the zwitterionic structure electrostatically. Then, further protonation of the next amino group would construct infinite hydrogen bonding chains, cooperatively.



Elmer and Eling reported X-ray crystallographic study on hydrogen bonding chains found in the six complexes by phenols and anilines **5** [23,24]. The neighboring hydrogen bonds in the chains of **5** were non-equivalent; that is, the distances of the hydrogen bonds are quite different depending on the proton-donating group. The distances of the hydrogen bond with the proton-donating oxygen atom were 2.77-2.81 Å, and that with nitrogen atom were 3.13 - 3.15 Å. Similar to the our case, these non-

equivalent hydrogen bonding chains of phenols and anilines would also be made by alternating medium-weak hydrogen bonds.



4. Conclusion

Here we showed that the β,β,β -trifluoroalcohol with an intramolecular proton-accepting group constructs an infinite hydrogen bonding chain. The chain would be made by alternating medium and weak hydrogen bonds. The strong protonating ability of β,β,β -trifluoroalcohol results in the contribution of a zwitterionic structure, which would make the weak hydrogen bonds rather strong. This hydrogen bonding chain could be a method to align molecules infinitely in its crystal. Thus, it could be applicable for construction of crystalline supramolecular architecture [25].

5. Experimental

General Experimental Procedures

Trifluoromethylated amino alcohols were prepared from a common starting material, 75% ee (*S*)-2,3-epoxy-1,1,1-trifluoropropane **3**, which is commercially available [26]. Preparations and reactions of the epoxide were summarized in our previous reviews [9,10]. Nucleophilic ring-opening reactions of the epoxide with amines gave a series of trifluoromethylated amino alcohols [9,10]; 1,1,1-trifluoro-3-(*N*-piperidyl)-2-propanol **2a** was prepared with piperidine [13-15,27] and 1,1,1-trifluoro-3-(*N,N*-dimethylamino)-2-propanol **2b** was prepared with dimethylamine [13].

Intensity measurements for X-ray crystallographic analyses were made on a Rigaku RAXIS-IV imaging plate area detector with graphite monochromated Mo-K α radiation at 150 K. The results were solved by SIR92 in TEXSAN package program. The CIF data of the compounds **2a**, **2b** were deposited at the Cambridge Crystallographic Data Centre and allocated deposition number of the compound **2a** is 244474, and the compound **2b** is 244475.

Crystallographic data for 2a: (CCDC 244474)

Mw = 197.20 colorless needles, orthorhombic, space group $P2_12_12_1$ (#19), $a = 16.619(4)$, $b = 9.224(4)$, $c = 6.013(2)$, $V = 921.7(5)$ Å³, $Z = 4$, $D_c = 1.421$ g/cm³, $\mu(\text{MoK}\alpha) = 1.33$ cm⁻¹, $2\theta_{\text{max}} = 51.2^\circ$, No. of measured = 978, No. observations ($I > 0.00\sigma(I)$) = 965, No. of parameter = 135, $R = 0.078$, $R_w = 0.113$, GOF = 1.13, residual electron density = 0.24/-0.32 e/Å⁻³.

Crystallographic data for 2b: (CCDC 244475)

Mw = 157.14 colorless platelet, orthorhombic, space group $P2_12_12_1$ (#19), $a = 16.736(1)$, $b = 7.5394(4)$, $c = 5.7115(2)$, $V = 720.67(6)$ Å³, $Z = 4$, $D_c = 1.448$ g/cm³, $\mu(\text{MoK}\alpha) = 1.50$ cm⁻¹, $2\theta_{\text{max}} = 54.9^\circ$, No. of measured = 1529, No. observations ($I > 2.00\sigma(I)$) = 888, No. of parameter = 131, $R = 0.027$, $R_w = 0.041$, GOF = 1.10, residual electron density = 0.17/-0.15 e/Å⁻³.

Acknowledgment

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References and Notes

- [1] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, John Wiley & Sons, New York, 1994.
- [2] J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, John Wiley & Sons, New York, 1995.
- [3] Y. Matsumoto, A. Ohno, S.-J. Lu, T. Hayashi, N. Oguni, M. Hayashi, *Tetrahedron: Asymm.* 4 (1993) 1763-1766.
- [4] M. Hayashi, T. Kaneko, N. Oguni, *J. Chem. Soc. Perkin Trans. 1* (1991) 25-28.
- [5] M. Hayashi, H. Miwata, N. Oguni, *J. Chem. Soc. Perkin Trans. 1* (1991) 1167-1171.
- [6] N. Oguni, Y. Matsuda, T. Kaneko, *J. Am. Chem. Soc.* 110 (1988) 7877-7878.
- [7] J. Jacques, A. Collet, S.H. Wilen, *Enantiomers, Racemates, and Resolutions*, Wiley-Interscience, New York, 1981.
- [8] A. Ishii, M. Kanai, K. Higashiyama, K. Mikami, *Chirality* 14 (2002) 709-712.
- [9] T. Katagiri, Synthesis of stereochemically defined trifluoromethyl-containing compounds through (*S*)-3,3,3-trifluoropropene oxide, in: V.A. Soloshonok (Ed.) *Enantiocontrolled Synthesis of Fluoro-Organic Compounds: Stereochemical Challenges and Biomedical Targets*. Wiley: Chichester, 1999, pp 161-178.
- [10] T. Katagiri, K. Uneyama, *J. Fluorine Chem.* 105 (2000) 285-293.
- [11] T. Katagiri, Y. Fujiwara, S. Takahashi, N. Ozaki, K. Uneyama, *Chem. Commun.* (2002) 986-987.
- [12] Y. Fujiwara, T. Katagiri, K. Uneyama, *Tetrahedron Lett.* 44 (2003) 6161-6162.
- [13] E.T. McBee, C.E. Hathaway, C.W. Roberts, *J. Am. Chem. Soc.* 78 (1956) 3851-3854.
- [14] M.G. Voronkov, U.P. Baryshok, S.N. Tandura, V.Y. Vitkovskii, V.M. Dyakov, V.A. Pestunovich, *Zh. Obshch. Khim.* 48 (1978) 2238-2245.
- [15] P.V. Ramachandran, B. Gong, H.C. Brown, *J. Org. Chem.* 60 (1995) 41-46.
- [16] T. Katagiri, K. Uneyama, *Chem. Lett.* (2001) 1330-1331.

- [17] G.A. Jeffery, *An Introduction to Hydrogen Bonding*, Oxford University Press, Oxford, 1997, p 12.
- [18] G.R. Desiraju, T. Steiner, *The Weak Hydrogen Bonds in Structural Chemistry and Biology*, Oxford, Oxford, 1999, p 13.
- [19] Detailed X-ray diffraction analysis of compound **2a** (without constraint of the occupancies) implied that the disordered occupancy of the proton attached to the oxygen was 0.79 and that on the nitrogen was 0.22 (see Figure 4(A)). That is, the ratio of the zwitterionic structure contribution would be around 20%. Such disorder of the proton, based on X-ray crystallographic analysis, has often been discussed; e.g. H. Takemura, M. Kotoku, M. Yasutake, T. Shinmyozu, *Eur. J. Org. Chem.* (2004) 2019-2024.
- [20] Similar to **2a** and **2b**, 3-amino-1,1,1-trifluoro-2-propanol and 3-(*N*-benzylamino)-1,1,1-trifluoro-2-propanol constructed similar hydrogen bonding chains in their crystals. The intermolecular donor-acceptor distances of the 3-amino-1,1,1-trifluoro-2-propanol and the 3-(*N*-benzylamino)-1,1,1-trifluoro-2-propanol were 2.697(1) and 2.768(7) Å, and those of intramolecular distances were 2.974(1) and 2.807(2), respectively. Thus, hydrogen bonding chains of these two compounds would be made similarly by alternating intermolecular medium and intramolecular weak hydrogen bondings. The CIF data of these compounds were deposited at the Cambridge Crystallographic Data Centre and allocated deposition number of the 3-amino-1,1,1-trifluoro-2-propanol is 244472, the 3-(*N*-benzylamino)-1,1,1-trifluoro-2-propanol is 244473,
- [21] J.P. Begue, D. Bonnet-Delpon, B. Crousse, *Synlett* (2004) 18-29.
- [22] B. Jursic, M. Ladika, D.E. Sunko, *Tetrahedron Lett.* 26 (1985) 5323-5324.
- [23] O. Ermer, A. Eiling, *J. Chem. Soc., Perkin Trans. 2* (1994) 925-944.
- [24] S. Hanessian, M. Simard, S. Roelens, *J. Am. Chem. Soc.* 117 (1995) 7630-7645.
- [25] T. Katagiri, M. Duan, M. Mukae, K. Uneyama, *J. Fluorine Chem.* 120 (2003) 165-172.

- [26] K. Furuhashi, Biological routes to optically active epoxides, in: A.N. Collins, G.N. Sheldrake, J. Crosby (Eds.), *Chirality in Industry*, John Wiley & Sons, 1992.
- [27] T. Katagiri, M. Takahashi, Y. Fujiwara, H. Ihara, K. Uneyama, *J. Org. Chem.* 64 (1999) 7323-7329.