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Chemoselective Aldehyde Addition of Zinc Carbenoid Generated from Tribromofluoromethane

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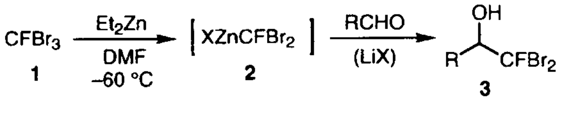
Treatment of tribromofluoromethane with diethylzinc in DMF at −60 °C generated a zinc carbenoid reagent, which reacted with aldehydes RCHO chemoselectively to give $RCH(OH)CFBr_2$ in moderate-to-good yields.

Much attention has been paid recently to organofluorine compounds in the area of pharmaceuticals, agrochemicals, and materials, because introduction of fluorine into organic compounds often leads to remarkable enhancement of their activities and properties.[1] Thus, the development of an efficient and stereoselective synthetic method of organofluorine compounds is a matter of urgency.

Fluorohalomethylmetal reagents[2] are readily prepared from fluorohalomethanes and an organometallic reducing reagent and can be employed for the introduction of a fluorine atom into organic molecules. For example, dibromofluoromethyllithium generated by treatment of tribromofluoromethane (**1**) with butyllithium reacts with aldehydes and ketones to give 1,1-dibromo-1-fluoro-2-alkanols **3**, which are stereoselectively transformed to fluoro olefins and 2-bromo-2-fluoro-1,3-diols.[3] Since the lithium carbenoid is thermally labile owing to the repulsion of p orbitals in fluorine and anionic carbon,[4] all operations need to be performed at −130 °C.

We describe here how the corresponding zinc carbenoid,[5] **2**, can be generated by bromine–zinc exchange of **1** with diethylzinc[6] at −60 °C in DMF. It reacts smoothly with a variety of aldehydes RCHO to give $RCH(OH)CFBr_2$ **3** with high chemoselectivity (Eq. 1). Additional use of a lithium salt is found to improve yields of alcohols **3**.

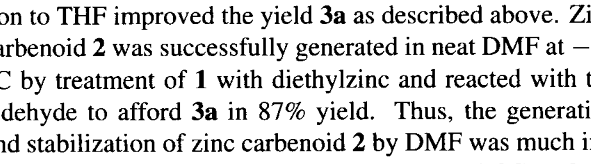


(1)

Results and Discussion

Generation and Carbonyl Addition of Zinc Carbenoid 2.

At first, we examined agents (1.5 mmol) that can metalate **1** (1.5 mmol) at −78 °C and we trapped the metal reagent with 3-phenylpropanal (1 mmol) (Eq. 2). With isopropylmagnesium chloride, the yield of the corresponding alcohol **3a** was only 13% in diethyl ether and 39% in THF. Trimethylaluminium could not give **3a** at all. In contrast, zinc carbenoid **2** generated by treatment of **1** with diethylzinc at −78 °C in THF–DMF was found to be satisfactory and gave **3a** in 60% yield. The solvent effect was remarkable: THF only could not give **3a**; THF–HMPA (10 mmol) was less effective (37% yield) than THF–DMF (10 mmol, 60% yield of **3a**).



(2)

We further studied this solvent effect. Hexane, toluene, or diethyl ether was not effective to produce zinc carbenoid **2**. Use of a polar solvent such as HMPA or DMF in addition to THF improved the yield **3a** as described above. Zinc carbenoid **2** was successfully generated in neat DMF at −60 °C by treatment of **1** with diethylzinc and reacted with the aldehyde to afford **3a** in 87% yield. Thus, the generation and stabilization of zinc carbenoid **2** by DMF was much improved. The same reaction carried out at −40 °C or 0 °C gave **3a** in a lower or null yield. DMF solvent is assumed to solvate diethylzinc to accelerate the reduction to give rise to carbenoid **2**, which is also coordinated by DMF. This aprotic polar solvent apparently stabilizes the otherwise unstable reagent, suppressing the zinc–bromine interaction leading to α-elimination. A similar DMF effect was observed in the reduction of 1,1,1-trichloro-2,2,2-trifluoroethane with zinc metal in DMF; the resulting thermally stable zinc carbenoid reagent CF_3CCl_2ZnCl is shown by X-ray analysis to be coordinated by two DMF molecules.[7]

The optimized conditions were applied to various aldehydes; the results are summarized in Table 1. Benzaldehyde and napthalene-1-carbaldehyde gave the corresponding alcohols, **3b** and **3c**, in moderate yields (Runs 2 and 3). Whereas 4-nitrobenzaldehyde gave product **3d** in 93% yield (Run 4), 4-methoxybenzaldehyde gave **3f** in only 10% yield (Run 6);

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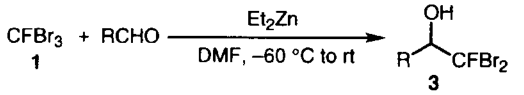
Table 1. Aldehyde Addition of Zinc Carbenoid **2**[a)]

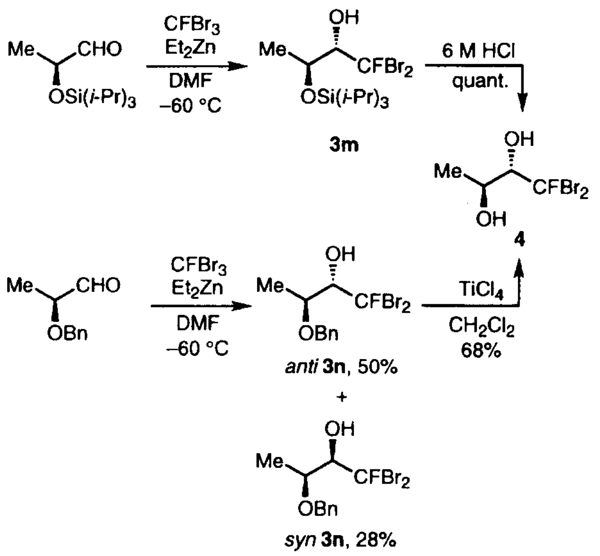


Run	R	Product	Yield (%)[b)]
1	$Ph(CH_2)_2$–	**3a**	87
2	Ph–	**3b**	48
3	1-Napthyl–	**3c**	48
4	4-NO_2–C_6H_4–	**3d**	93
5	4-AcO–C_6H_4–	**3e**	52
6	4-MeO–C_6H_4–	**3f**	10[c)]
7	(*E*)-PhCH=CH–	**3g**	Trace
8	$PhCH_2$–	**3h**	69
9	$CH_3(CH_2)_6$–	**3i**	69
10	*c*-C_6H_{11}–	**3j**	47
11	$(CH_3)_2CH$–	**3k**	53
12	Ph(Me)CH–	**3l**	52[d)]
13	(*S*)-Me[OSi(*i*-Pr)$_3$]CH–	**3m**	61[e)]
14	(*S*)-Me(OCH_2Ph)CH–	**3n**	78[f)]
15	$(Me)_3C$–	**3o**	0

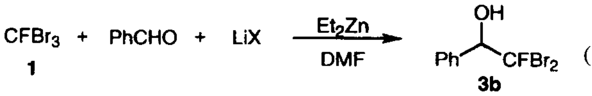
a) Diethylzinc (1.5 mmol) was added to a solution of **1** (1.5 mmol) and aldehyde (1 mmol) in DMF (2 ml) at −60 °C. b) Isolated yields. c) The yield was determined by ^{1}H NMR using 1,1,2-trichloroethene as an internal standard. d) *syn* : *anti* = 95 : 5. e) (2*S*,3*S*) : (2*R*,3*S*) = > 95: < 5. f) (2*S*,3*S*) : (2*R*,3*S*) = 64 : 36.

cinnamaldehyde did not give alcohol **3g** (Run 7). Of aliphatic aldehydes, phenylacetaldehyde and octanal gave products **3h** and **3i** in good yields (Runs 8 and 9); the reaction of cyclohexanecarbaldehyde and 2-methylpropanal gave the adducts in low yields (Runs 10 and 11). 2-Phenylpropanal afforded alcohol **3l** in 52% yield with *syn* : *anti* = 95 : 5 selectivity (Run 12). The stereochemistry of **3l** was assigned by comparison of ^{1}H NMR spectra with those of 1,1,1-trichloro-3-phenyl-2-butanol.[8] The stereochemical outcome is in accord with Cram's model.[9] The reaction with (*S*)-2-(triisopropylsiloxy)-propanal[10] gave **3m**, whose stereochemistry was shown to be *anti* (Run 13) by desilylation of **3m** to **4**. Meanwhile, zinc carbenoid **2** reacted with (*S*)-2-benzyloxypropanal to afford a mixture of *anti*- or (2*S*,3*S*)-**3n** and *syn*- or (2*R*,3*S*)-**3n** product (Run 14). The stereochemistry of (2*S*,3*S*)-**3n** was determined by X-ray crystallographic analysis. The *anti* product, (2*S*, 3*S*)-**3n**, was converted with titanium tetrachloride into diol **4**, identical to the diol obtained from **3m** (Scheme 1). The selectivity observed in the formation of **3m** can be understood in terms of the Felkin–Anh model.[11] The reaction of (*S*)-2-(triisopropylsiloxy)-propanol with the corresponding lithium carbenoid gives **3m** (*syn* : *anti* = 74 : 26). The high selectivity attained with zinc carbenoid **2** is thus remarkable. 2,2-Dimethylpropanal that has a quaternary carbon next to a formyl group did not react with zinc carbenoid **2** (Run 15).

Lithium Salt Effect. As discussed above, the carbonyl addition of zinc carbenoid **2** was influenced by the steric and electronic nature of a substrate. Villieras and his co-workers observed that a lithium salt additive contributed remarkably to the stabilization of labile lithium carbenoids. They attributed the improved stability to an *inter*molecular halogen–lithium interaction, weakening an *intra*molecular halogen–lithium interaction.[12] Thus, we studied the effect of a lithium salt in the generation and reaction of zinc carbenoid **2** using benzaldehyde as an electrophile and screened various lithium halides at −60 °C to find that some were effective: none, 48%; LiF, 73%; LiCl, 78%; LiBr, 45%; LiI, 60% (Eq. 3). Thus, lithium chloride was the best. To optimize the reaction temperature, the reaction was carried out at −50, −40, −30, and 0 °C to obtain fluorinated alcohol **3b** in 75, 71, 66, and 12% yields, respectively. Thus, a temperatue range of −60 to −40 °C was pertinent to the reaction. Similar improvement was observed with cyclohexanecarbaldehyde (−60 °C, 66% yield). However, 4-methoxybenzaldehyde was not favored.

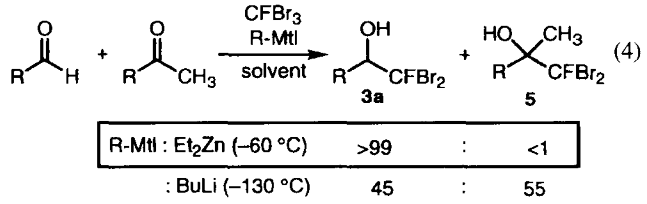


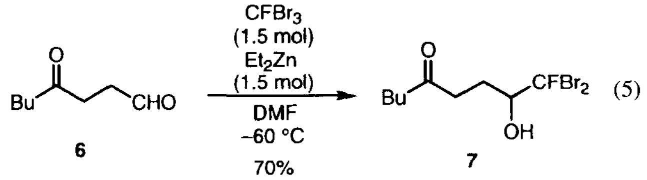
Scheme 1. Determination of the stereochemistry of **3m**.



(3)

Chemoselectivity. We next studied the reaction of zinc carbenoid **2** with 4-phenylbutan-2-one as a typical ketone substrate. However, no trace of the desired adduct was produced. Thus, zinc carbenoid **2** appears to be much less reactive than the corresponding lithium carbenoid. This fact suggests possible chemoselective addition to an aldehyde in the presence of a ketone.[13] Indeed, a competitive experiment using 3-phenylpropanal (1 mol) and 4-phenylbutan-2-one (1 mol) demonstrated that zinc carbenoid **2** (1.5 mol) reacted with 3-phenylpropanal selectively to give **3a** in 85% yield; ketone adduct **5** was produced in less than 1% yield. In contrast, the reaction of the corresponding lithium carbenoid gave a 45 : 55 mixture of **3a** and **5** (Eq. 4). Furthermore, an intramolecular chemoselective reaction was realized in the reaction of keto aldehyde **6** with zinc carbenoid **2**; aldehyde adduct **7** was isolated as a sole product in 70% yield (Eq. 5). Thus, high chemoselectivity is the salient features of zinc carbenoid **2**.





In conclusion, we have shown that fluorinated zinc carbenoid **2** can be generated by treatment of tribromofluoromethane (**1**) with diethylzinc and reacts with aldehydes chemoselectively to give fluorinated alcohols **3**. Addition of a lithium salt improved yields of **3** in many cases. Chemoselective aldehyde addition of **2** provides us with a convenient synthetic method for organofluorine compounds which are receiving growing interest in the fields of medicinal, agricultural, and material sciences.

Experimental

General. Melting points were measured with a Yanagimoto micro melting point apparatus. IR spectra were recorded on a Shimadzu FTIR-8100A spectrometer. ^{1}H NMR spectra were measured on a Varian Mercury spectrometer (300 MHz) or a Bruker AC-200 spectrometer (200 MHz) with $CDCl_3$ as a solvent and Me_4Si as an internal standard. ^{13}C NMR spectra were measured on a Varian Mercury spectrometer or a Bruker AC-200 (50 MHz) in a $CDCl_3$ solution. ^{19}F NMR spectra were measured on a Bruker AC-200 (188 MHz) spectrometer in a $CDCl_3$ solution with $CFCl_3$ as an internal standard. Mass spectra were obtained with a Shimadzu QP-5000 GC-MS spectrometer by electron impact ionization at 70 eV; high-resolution MS spectra with a JEOL JMS-700 spectrometer. Elemental analyses were carried out by Elemental Analysis Center, Tokyo Institute of Technology. Preparative HPLC was carried out with a Japan Analytical Industry, LC-908 chromatograph using a JAIGEL-1H or -2H GPC column. Column chromatography was performed using Merck Kieselgel 60 (70—230 mesh and 230—400 mesh) or Wakogel C-200. Diethyl ether, THF, and hexane were distilled from sodium/benzophenone prior to use. Dichloromethane was distilled from CaH_2 prior to use. DMF was purified by distillation from CaH_2 and stored over MS-4A under an argon atmosphere. All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere in a flame dried flask.

Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 143942.

Generation and Aldehyde Addition of Zinc Carbenoid 2: General Procedure. A 1.0 M hexane solution (1 M = 1 mol dm^{-3}) of diethyl zinc (1.50 mmol) was added dropwise over 10 min to a solution of tribromofluoromethane (**1**) (147 μl, 1.50 mmol) and an aldehyde (1.00 mmol) in DMF (3 ml) at −60 °C via a syringe. The resulting mixture was stirred for 3 h at −60 °C before quenching with sat. aq NH_4Cl solution. The organic layer was separated; the aqueous layer was extracted with diethyl ether (20 ml×3). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography to afford fluorinated alcohol **3**.

1,1-Dibromo-1-fluoro-4-phenyl-2-butanol (3a):[3d] This alcohol was produced in 87% yield.

2,2-Dibromo-2-fluoro-1-phenylethanol (3b):[3d] Obtained in 48% yield.

2,2-Dibromo-2-fluoro-1-(1-naphthyl)ethanol (3c):[3d] Isolated in 48% yield.

2,2-Dibromo-2-fluoro-1-(4-nitrophenyl)ethanol (3d):[3d] This compound was obtained in 93% yield.

2,2-Dibromo-2-fluoro-1-(4-acetoxyphenyl)ethanol (3e): Prepared in 52% yield as a colorless solid, mp 143—144 °C. ^{1}H NMR (200 MHz) δ = 2.30 (s, 3H), 3.17 (brs, 1H), 5.11 (d, J = 9.2 Hz, 1H), 7.09—7.18 (m, 2H), 7.57 (brd, J = 8.2 Hz, 2H). ^{13}C NMR (50 MHz) δ = 21.1, 82.4 (d, J = 22.0 Hz), 102.6 (d, J = 321.8 Hz), 121.3, 129.7, 129.7, 132.3, 169.2. ^{19}F NMR (188 MHz) δ = −62.5 (d, J = 9.2 Hz). IR (KBr) 3410, 1740, 1607, 1509, 1408, 1366, 1258, 1231, 1198, 1165, 1119, 1084, 1019, 997, 955, 939, 922, 864, 855, 795, 768, 708, 666, 640, 592, 573, 523, 503 cm^{-1}. MS m/z (rel intensity) 358 (M^++4; 8), 356 (M^++2; 17), 354 (M^+; 9), 123 (100). HRMS Found: m/z 353.8879. Calcd for $C_{10}H_9Br_2FO_3$: M, 353.8902.

2,2-Dibromo-2-fluoro-1-(4-methoxyphenyl)ethanol (3f):[3d] This alcohol was isolated in 10% yield.

1,1-Dibromo-1-fluoro-3-phenyl-2-propanol (3h): The adduct was obtained in 69% yield as a colorless oil, R_f 0.40 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (200 MHz) δ = 2.60 (brs, 1H), 2.83 (dd, J = 9.8, 14.1 Hz, 1H), 3.28 (d, J = 14.1 Hz, 1H), 4.05—4.20 (m, 1H), 7.10—7.45 (m, 5H). ^{13}C NMR (50 MHz) δ = 38.5 (d, J = 1.5 Hz), 82.1 (d, J = 21.6 Hz), 103.0 (d, J = 320.3 Hz), 127.0, 128.6, 129.4, 136.4. ^{19}F NMR (188 MHz) δ = −60.7; IR (neat) 3520, 3450, 3088, 3065, 3031, 2934, 1719, 1603, 1497, 1455, 1437, 1383, 1273, 1181, 1094, 1032, 934, 912, 874, 843, 826, 789, 754, 720, 700, 629, 569 cm^{-1}. Found: C, 34.50; H, 2.90%. Calcd for $C_9H_9Br_2FO$: C, 34.65; H, 2.91%.

1,1-Dibromo-1-fluoro-2-nonanol (3i): The product was isolated in 69% yield as a colorless oil, R_f 0.73 (hexane–dicholoromethane = 1 : 3). ^{1}H NMR (200 MHz) δ = 0.89 (t, J = 6.6 Hz, 3H), 1.10—2.00 (m, 12H), 2.46 (d, J = 6.1 Hz, 1H), 3.80—3.95 (m, 1H). ^{13}C NMR (50 MHz) δ = 14.1, 22.6, 25.5, 29.1, 29.2, 31.7, 32.1 (d, J = 1.1 Hz), 81.4 (d, J = 21.4 Hz), 104.4 (d, J = 322.2 Hz). ^{19}F NMR (188 MHz) δ = −59.7 (d, J = 6.8 Hz). IR (neat) 3400, 2957, 2928, 2857, 1466, 1379, 1136, 1086, 1046, 1024, 797, 762, 723 cm^{-1}. Found: C, 33.88; H, 5.18%. Calcd for $C_9H_{17}Br_2FO$: C, 33.78; H, 5.35%.

2,2-Dibromo-2-fluoro-1-cyclohexylethanol (3j):[3d] Produced in 47% yield.

1,1-Dibromo-1-fluoro-3-methyl-2-butanol (3k):[3d] This product was obtained in 53% yield.

1,1-Dibromo-1-fluoro-3-phenyl-2-butanol (3l): This alcohol was produced in 52% yield as a 95 : 5 mixture of *syn* and *anti* isomers, a pale yellow oil, R_f 0.44 (hexane–ethyl acetate = 5 : 1). The major isomer showed ^{1}H NMR (200 MHz) δ = 1.43 (dd, J = 1.2, 7.0 Hz, 3H), 2.73 (d, J = 5.8 Hz, 1H), 3.47 (dq, J = 4.3, 7.0 Hz, 1H), 4.14 (ddd, J = 4.3, 5.8, 12.2 Hz, 1H), 7.22—7.32 (m, 5H); ^{13}C NMR (50 MHz) A major isomer: δ = 16.2 (d, J = 2.3 Hz), 41.6, 84.6 (d, J = 19.1 Hz), 104.0 (d, J = 329.6 Hz), 127.0, 127.8, 128.8, 144.2 (d, J = 1.2 Hz); ^{19}F NMR (188 MHz) δ = −58.8 (d, J = 12.2 Hz). IR (neat) 3464, 3086, 3063, 3028, 2984, 2937, 1603, 1495, 1454, 1385, 1325, 1271, 1234, 1122, 1084, 1024, 1005, 991, 939, 850, 789, 765, 700 cm^{-1}. Found: C, 36.66; H, 3.37%. Calcd for

$C_{10}H_{11}Br_2FO$: C, 36.84; H, 3.40%.

(2*S*,3*S*)-1,1-Dibromo-1-fluoro-3-triisopropylsiloxy-2-butanol (3m): Obtained in 61% yield as a colorless oil, R_f 0.65 (hexane–ethyl acetate = 4 : 1), $[\alpha]_D$ −4.2° (*c* 1.22, MeOH). ^{1}H NMR (200 MHz) δ = 1.00—1.22 (m, 21H), 1.30 (dd, J = 2.7, 6.3 Hz, 3H), 3.06 (d, J = 3.3 Hz, 1H), 4.15 (ddd, J = 3.3, 3.3, 16.2 Hz, 1H), 4.56 (dddd, J = 3.3, 6.3, 12.5, 12.6 Hz, 1H); ^{13}C NMR (50 MHz) δ = 12.4, 17.6 (d, J = 4.0 Hz), 18.0 (d, J = 2.9 Hz), 68.7, 83.5 (d, J = 18.8 Hz), 97.8 (d, J = 326.2 Hz); ^{19}F NMR (94 MHz) δ = −62.1 (d, J = 16.2 Hz); IR (neat) 3500, 2946, 2869, 1464, 1387, 1248, 1146, 1107, 1071, 1017, 980, 941, 884, 837, 787, 772, 681 cm^{-1}. Found: C, 36.81; H, 6.31%. Calcd for $C_{13}H_{27}Br_2FO_2Si$: C, 36.98; H, 6.45%.

(2*S*,3*S*)-1,1-Dibromo-1-fluoro-3-benzyloxy-2-butanol (3n): Obtained in 50% yield as a colorless solid, mp 69—70 °C, $[\alpha]_D$ −3.50° (*c* 1.07, MeOH). ^{1}H NMR (300 MHz) δ = 1.36 (dd, J = 1.5, 6.3 Hz, 3H), 2.89 (br s, 1H), 4.05 (dq, J = 4.2, 4.5 Hz, 1H), 4.17 (ddd, J = 4.7, 4.8, 11.7 Hz, 1H), 4.56 (d, J = 11.7 Hz, 1H), 4.62 (d, J = 11.7 Hz, 1H), 7.25—7.40 (m, 5H); ^{13}C NMR (75 MHz) δ = 15.0, 71.1, 74.9, 82.0 (d, J = 19.4 Hz), 100.6 (d, J = 324.4 Hz), 127.9 (2 peaks), 128 (2 peaks), 137.5; ^{19}F NMR (188 MHz) δ = −59.9 (d, J = 11.7 Hz); IR (nujor) 3400, 1300, 1210, 1135, 1090, 1075, 1040, 1020, 885, 750 cm^{-1}. Found: C, 36.81; H, 3.93%. Calcd for $C_{11}H_{13}Br_2FO_2$: C, 37.11; H, 3.68%. (2*R*, 3*S*)-Isomer was isolated in 28% yield as a colorless oil, R_f 0.39 (hexane–ethyl acetate = 4 : 1), $[\alpha]_D$ −0.74° (*c* 1.30, MeOH). ^{1}H NMR (300 MHz) δ = 1.35 (d, J = 6.3 Hz, 3H), 3.78 (br s, 1H), 3.80 (q, J = 4.3 Hz, 1H), 4.12 (q, J = 6.3 Hz, 1H), 4.58 (d, J = 11.1 Hz, 1H), 4.66 (d, J = 11.1 Hz, 1H), 7.30—7.43 (m, 5H); ^{13}C NMR (75 MHz) δ = 18.6, 71.8, 83.1 (d, J = 20.6 Hz), 101.2 (d, J = 322.7 Hz), 128.0 (2 peaks), 128.5 (2 peaks), 137.2; ^{19}F NMR (188 MHz) δ = −62.4 (d, J = 9.3 Hz); IR (neat) 3500, 3025, 2970, 2920, 1710, 1690, 1490, 1450, 1400, 1370, 1250, 1140, 1080, 1010, 950, 910, 790, 750, 690 cm^{-1}. Found: C, 37.24; H, 3.70%. Calcd for $C_{11}H_{13}Br_2FO_2$: C, 37.11; H, 3.68%.

(2*S*,3*S*)-1,1-Dibromo-1-fluoro-2,3-butanediol (4): To a solution of (2*S*,3*S*)-**3n** in dichloromethane (1 ml) was added $TiCl_4$ (31 μl) dropwise at room temperature under an argon atmosphere. The resulting mixture was stirred for 1 h at room temperature before quenching with a sat. $NaHCO_3$ aq solution and neutralization with 1 M HCl solution. The aq. layer was extracted with diethyl ether (20 ml×2). The combined extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was purified by silica-gel column chromatography to afford diol **4** in 68% yield as a white solid, mp 55—56 °C, $[\alpha]_D$ −3.5° (*c* 0.34, MeOH). ^{1}H NMR (200 MHz) δ = 1.37 (d, J = 6.3 Hz, 3H), 1.98 (brs, 1H), 2.90 (brs, 1H), 4.03 (ddd, J = 5.1, 5.1, 11.4 Hz, 1H), 4.29 (m, 1H); ^{13}C NMR (50 MHz) δ = 18.1, 98.2, 83.2 (d, J = 19.5 Hz), 100.3 (d, J = 330.2 Hz); ^{19}F NMR (188 MHz) δ = −60.3 (J = 11.4 Hz); IR (nujor) 3450, 3250, 1290, 1120, 1090, 1000, 950, 910, 840, 780 cm^{-1}; MS *m*/*z* (rel intensity) 253 (M^+−Me+4; 0.5), 251 (M^+−Me+2; 0.7), 249 (M^+−Me; 0.4), 142 (97), 140 (100). HRMS Found: *m*/*z* 248.8586. Calcd for $C_3H_4Br_2FO_2$: M^+−Me, 248.8562.

1,1-Dibromo-1-fluoro-5-oxo-2-nonanol (7): The reaction was run with **1** (193 μl, 1.97 mmol), 4-oxo-octanal (**6**) (94 mg, 0.66 mmol), and diethyl zinc (1.00 M in hexane, 1.97 ml, 1.97 mmol) in DMF (2 ml) according the representative procedure and quenched with a sat. aq NH_4Cl solution at −60 °C. Workup and chromatography (hexane–ethyl acetate) afforded **7** (155 mg, 70% yield) as a colorless oil, R_f 0.61 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (200 MHz) δ = 0.91 (t, J = 7.0 Hz, 3H), 1.20—1.45 (m, 2H), 1.45—1.70 (m, 2H), 1.75—2.05 (m, 2H), 2.10—2.35 (m, 1H), 2.46 (t, J = 7.2 Hz, 1H), 2.65—2.80 (m, 2H), 3.32 (brs, 1H), 3.85—4.00 (m, 1H); ^{13}C NMR (50 MHz) δ = 13.8, 22.3, 25.9 (d, J = 1.5 Hz), 25.9, 38.2, 42.6, 80.67 (d, J = 21.2 Hz), 103.5 (d, J = 320.3 Hz), 211.5; ^{19}F NMR (188 MHz) δ = −60.2 (d, J = 6.8 Hz); IR (neat) 3428, 2959, 2934, 2874, 1707, 1466, 1410, 1379, 1312, 1262, 1117, 1084, 1040, 905, 789, 767, 766 cm^{-1}. Found: C, 32.54; H, 4.66%. Calcd for $C_9H_{15}Br_2FO_2$: C, 32.36; H, 4.53%.

(X-Ray Analysis). A colorless prismatic crystal of $C_{11}H_{13}Br_2FO_2$ having approximate dimensions of 0.40×0.20×0.15 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC5S diffractometer with graphite-monochromated Mo $K\alpha$ radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 252 carefully centered reflections in the range $20.25 < 2\theta < 24.66°$, corresponded to a primitive orthorhombic cell with dimensions: a = 10.205(2), b = 13.237(3), c = 9.538(2) Å, V = 1288.4(3) Å^3. For Z = 4 and F.W. = 356.03, the calculated density is 1.84 g cm^{-3}. Based on packing considerations, a statistical analysis of the intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be $P2_12_12_1$ (#19). The data were collected at a temperature of 23±1 °C using the ω–2θ scan technique to a maximum 2θ value of 55.0°. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.12° with a take-off angle of 6.0°. Scans of $(1.10+0.50 \tan\theta)°$ were made at a speed of 8.0 ° min^{-1} (in omega). The weak reflections ($I < 10.0\sigma(I)$) were rescanned (maximum of 5 scans) and the counts were accumulated to ensure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2 : 1. The diameter of the incident beam collimator was 1.0 mm, the crystal to detector length was 258 mm, and the detector aperture was 9.0×13.0 mm (horizontal×vertical). A total of 1724 reflections was collected. The intensities of three representative reflection were measured after every 150 reflections. An empirical correction for the absorption was based on azimuthal (x) scans of three reflections. The struc-

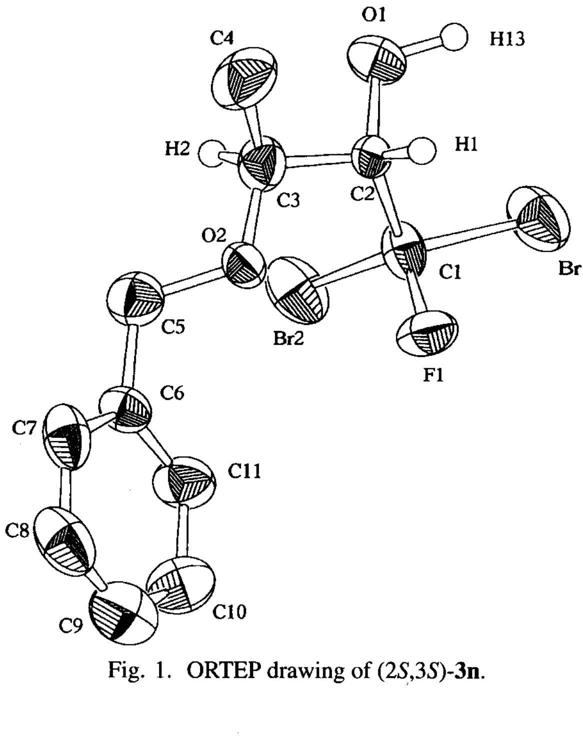


Fig. 1. ORTEP drawing of (2*S*,3*S*)-**3n**.

ture was solved by the direct method using the DIRDIF92 RATTY program. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were refined isotropically. Calculations were carried out on a VAX station 3200 computer with teXsan programs which used the atomic scattering factors taken from "International Tables for X-Ray Crystallography". The final cycle of full-matrix least-squares refinement yields $R = 0.038$, $R_w = 0.025$, and goodness-of-fit = 1.85 for 850 observed reflections $[I > 3.00s(I)]$ and 145 variable parameters. The final atomic parameters are deposited as Document No. 73040 at the Office of the Editor of Bull. Chem. Soc. Jpn. The ORTEP drawing of (2*S*,3*S*)-**3n** was shown in Fig. 1.

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