Organocatalytic Asymmetric Strecker Reaction of Di- and Trifluoromethyl Ketoimines. Remarkable Fluorine Effect

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Supporting Information

Part I

Content **Page**

^1H, ^{13}C, ^{19}F NMR spectra of and HPLC spectra are provided in other files

General: Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refer to pure isolated substances. The $[\alpha]_D$ was recorded using PolAAr 3005 High Accuracy Polarimeter. Infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer.^{1}H and ^{13}C NMR spectra were obtained using a Bruker DPX-400 spectrometer. Chemical shifts are reported in ppm from $CDCl_3$, $(CD_3)_2SO$ or D_2O with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad.

All reactions were carried out in air except noted. Anhydrous toluene was prepared by distillation over sodium-benzophenone ketyl prior to use. All the chiral (thio)urea catalysts were prepared using literature procedures.[1] All the α-trifluoromethylated ketones were commercially available or prepared using literature methods.[2] All the α-difluoromethylated ketones were synthesized according to literature procedures[3]. The difluoromethylketoimine **1** was prepared as a mixture of (Z) and (E) isomers according to the literature report,[4d] which was used directly. The trifluoromethylketoimine **2** was obtained as a pure isomer according to the literature procedures.[4] The ketoimine **7** was obtained as a pure isomer.

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Results of DFT Calculations and Discussion

DFT calculations were carried out using Gaussian 03 program.[5] The Becke's three-parameter nonlocal exchange functional[6] and the Lee, Yang, and Parr nonlocal correlation functional[7] (B3LYP) were utilized, with the standard 6-311G(d,p) basis set. The geometries of hydrogen-bonded complexes and related isolated molecules were fully optimized, followed by vibrational frequency calculations at the same levels of theory to obtain the zero-point energies (ZPE). The interaction energy （ΔE) has been calculated and the basis set superposition error (BSSE) was eliminated by the standard counterpoise (CP) correction method of Boys and Bernardi.[8] The ZPE was also included in the ΔE. Natural Bond Orbital (NBO) analysis[9] was carried out to calculate the NBO charge.

It has been reported that the fluorine in the C-F bond of fluorine-containing organic compounds can act as a weak hydrogen-bond acceptor. In 1994, Shimoni and Glusker carried out an extensive study of intermolecular interactions in fluorine-containing compounds, and concluded that "fluorine is the most electronegative element, but the C-F group is a poor hydrogen-bond former, as was established also from the calculations of the electric charge distribution. On the other hand C-F···H-O and C-F···H-N interactions (like C-H···O and C-H···N) can not be ignored".[10] Their studies revealed that the mean H···F distance tended to be 2.50 Å when the fluorine atom is either a part of a CF_3 group or in a C(sp^3)-F or C(sp^2)-F bond. Based on this result, together with the fact that the sum of the van der Waals radii of hydrogen and fluorine atoms is reported as approximately 2.55 Å,[11] we consider the formation of C-F···H-N hydrogen bonds to be possible if the calculated distance of F···H-N is less than 2.50 Å and the F···H-N angle is greater than 90^o.

The calculation was based on the use of simplified N,N'-dimethylthiourea to interact with difuoromethylketoimine **1a**, trifluoromethylketoimine **2a**, ketoimine **7** and their corresponding

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[5] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.;Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.;Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.;Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision D.01; Gaussian, Inc.: Wallingford, CT, 2004.

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[10] Shimoni, L.; Glusker, J. P. *Struct. Chem.* **1994**, *5*, 383.

[11] Mikami, K.; Itoh, Y.; Yamanaka, M. *Chem. Rev.* **2004**, *104*, 1.

product **5a**, **6a** and **8**. All the complexes are identified as local minima on the potential energy surfaces by vibrational frequency calculations. Their optimized structures are shown in Figure S1.

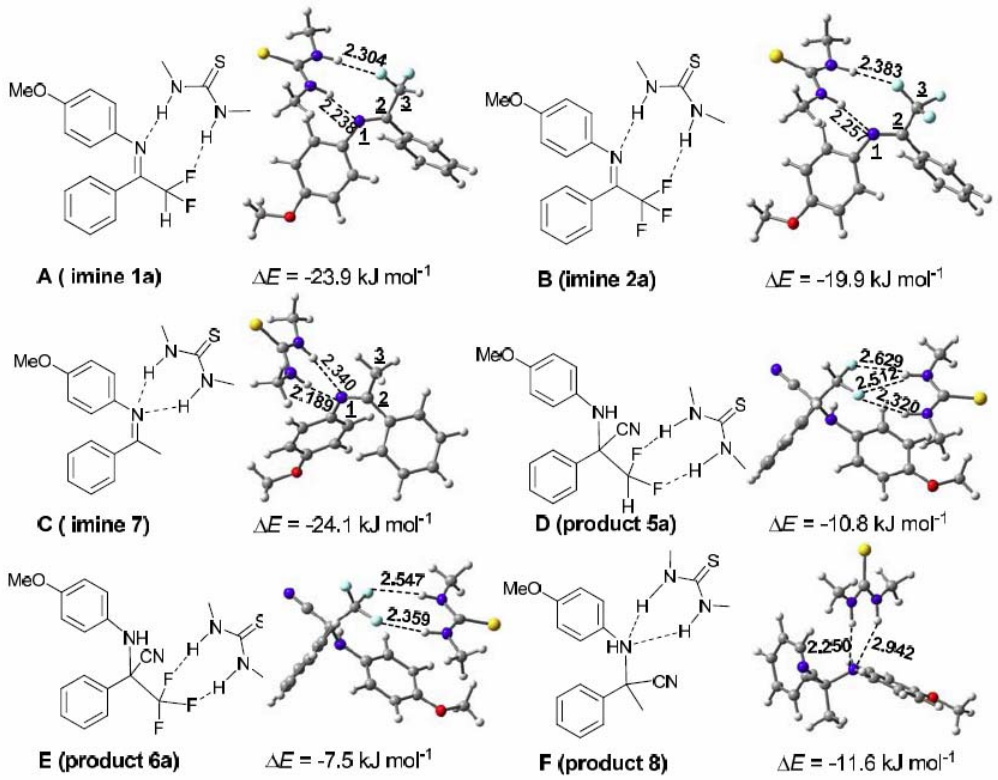


Figure S1. Optimized structures of six hydrogen-bonded complexes. The ΔE with BSSE and ZPE was calculated at the B3LYP/6-311G(d,p) level. Bond distance is in angstrom and the atom number is labeled in the underline font.

First, to understand the possible hydrogen-bonding interactions of imines **1a**, **2a** and **7** with N,N'-dimethylthiourea, we conducted the corresponding calculation. The optimized structures (**A**, **B** and **C**) were shown in Figure S1 as both the 2D chemical structures on the left and the 3D ball and stick models on the right. All the favorable structures of the catalyst-imine complexes have double hydrogen bonds, but the binding model of catalyst-imine **1a** or **2a** (**A** or **B**) is different from that of catalyst-imine **7** (**C**). For the entry **A** and **B**, one fluorine atom of the CHF_2 or CF_3 group may interact with one of the thiourea hydrogen atoms. The F···H-N distance in the nine-membered hydrogen bonds is 2.304 Å for **A** and 2.383 Å for **B**, with the corresponding F···H-N angles are 157.6° for **A** and 156.2° for **B**. All these values are considered to be acceptable for the formation of F···H-N hydrogen bonds, as discussed above. The hydrogen bonding interactions can stabilize complexes **A** and **B** with 23.9 and 19.9 kJ mol^{-1}, respectively. As a result, the thiourea-imine complex **A** and **B** prefer the closed structures with N–H···N and N–H···F hydrogen bonds. The hydrogen bond in the former is stronger

than that of the later. We also tried to optimize the relative bridged structure with double N–H···N hydrogen bonds as Jacobsen proposed,[12] but only obtained the closed structure with N–H···F hydrogen bond. The theoretical results supported our hypothesis that the presence of α fluorine atom of imine **1a** and **2a** indeed interferes with the bifurcated H-bonding pattern proposed by Jacobsen. In addition, we have also designed and optimized other possible hydrogen-bonded models, for instance, the complexes with only one hydrogen bond. However, the final structures we obtained are always the favorable hydrogen-bonded complexes as shown in Figure S1.

Entry **C** is the preferred bridged structure for the non-fluorinated imine **7**-thiourea catalyst complex, featuring imine hydrogen-bonded to both thiourea hydrogen atoms with distances of 2.189 and 2.340 Å which stabilize complexes **C** with 24.1 kJ mol^{-1}. The ΔE with and without BSSE and ZPE corrections are -24.1 and -40.4 kJ mol^{-1}, respectively. Our present ΔE without BSSE and ZPE corrections (-40.4 kJ mol^{-1}) is close to Jacobsen's theoretical result[12] of the ΔE of a thiourea−imine complex without BSSE and ZPE corrections (41.8 kJ mol^{-1}).

Table S1. Natural charges on atoms of isolated imines and relative catalyst-imine complexes. The atom numbers are labeled in Figure S1

entry	*isolated imine*				*catalyst-imine*			
	imine	N1	C2	C3	complex	N1	C2	C3
1	**1a**	-0.42	0.23	0.63	**A**	-0.46	0.24	0.62
2	**2a**	-0.41	0.20	1.09	**B**	-0.45	0.21	1.09
3	**7**	-0.46	0.33	-0.60	**C**	-0.54	0.35	-0.61

We further calculated NBO charges of the isolated imines and imine–thiourea complexes. The results are listed in Table S1. Comparing the natural charge of isolated imine and hydrogen-bonded complex, one can seen that after the formations of hydrogen bonds, the N1 atom has more negative charge and C2 atom has more positive charge, indicating the activation of imines by the hydrogen bonding. However, the charge on C2 atom in complexes **C** (imine 7) is much more positive than those in complexes **A** and **B**. The α fluorine atom in **A** and **B** lead to the result that the C3 atom has much more positive charge and the charge of C2 atom is more negative.

The above results established a plausible explanation for the different reactivity between the fluorinated and non-fluorinated imine: the bifurcated H-bonding pattern in model C can stabilize the

[12] Vachal, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 10012.

negatively charged nitrogen intermediate, as the activation of carbonyl groups by the oxyanion hole of the enzyme in the transition state;[13]

Considering the presence of fluorine atom in the product aminonitriles might lead to a strong hydrogen interaction between product and catalyst, a problem for "catalyst turnover", we conducted calculations for the three catalyst-product complexes (**D**-**F**, Figure S1). For the product **5a**-catalyst complex (**D**), the calculated distance of F···H-N distances and angles showed the presence of only one possible hydrogen-bond (2.320 Å, 159.0°; 2.512 Å, 104.1°; 2.629 Å, 98.8°). Similar result was also obtained for the product **6a**-catalyst complex (**E**). A singly bonded hydrogen-bonded structure was also found for product **8**-catalyst complex (**F**). Complexes **D**, **E** and **F** were stabilized by the single hydrogen-bond interaction with 10.8, 7.5 and 11.6 kJ mol^{-1}, respectively. These results demonstrated that the catalyst turnover is possible if reactions take place because the double hydrogen-bond interactions in catalyst-imine complex **A**-**C** are more than 12.0 kJ mol^{-1} stronger than the corresponding singly hydrogen bond in catalyst-product complex **D**-**F**.

Since we later found that bifunctional hydroquinine derived urea catalyst **9** was slightly better than its thiourea analogue **10**, we further examined the hydrogen-bonding interactions between a simplified N,N'-dimethylurea and imine **1a**, **2a** and **7**, and the corresponding optimized structures of complexes **G**-**I** revealed similar results to those of imine-thiourea complexes discussed above, although the double hydrogen bonding interactions in the imine- urea complexes were slightly weaker than those in the imine-thiourea complexes. For clarity, we omitted discussion here.

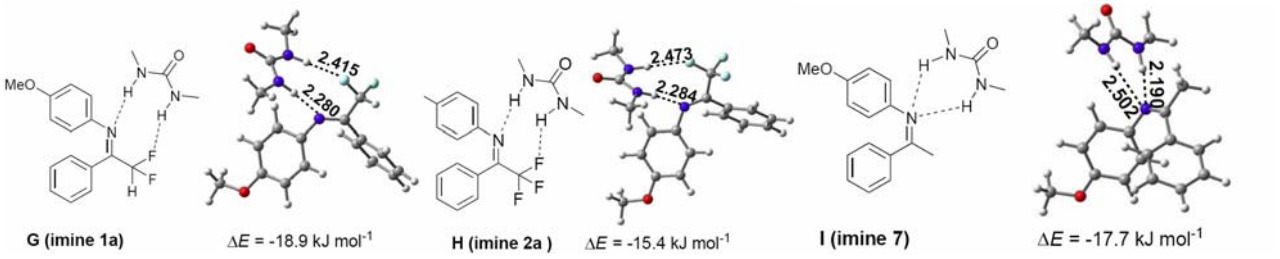


Figure S2. Optimized structures of three hydrogen-bonded urea-imine complexes at the B3LYP/6-311G(d,p) level.

It is also interesting to consider reactivity of the α–CFH_2 ketoimines and compare it with the present α–CF_2H and α–CF_3 ketoimines. We also calculated the postulated hydrogen bond complexes between α–CFH_2 ketoimine **22** and thiourea. As shown in Figure S3, a similar bridged structure **J** with double hydrogen bonds has been identified. The F···H-N distance in the hydrogen bonds is 2.195

[13] a) Branneby, C.; Carlqvist, P.; Magnusson, A.; Hult, K.; Brinck, T.; Berglund, P. *J. Am. Chem. Soc*. **2003**, *125*, 874. b) Svedendahl, M.; Hult, K.; Berglund, P. *J. Am. Chem. Soc*. **2005**, *127*, 17988.

Å and the F···H-N angles is 162.2°. The results show that the F···H-N hydrogen bond is formed in the complex. The interaction energy of the complex is 28.1 kcal mol^{-1}, which is 4.2 and 8.2 kcal mol^{-1} larger than α–CHF_2 and α–CF_3 ketoimines, respectively. The results indicate that the stronger hydrogen bonds in **J** form. Thus, it is expected that the *α*–CH_2F ketoimines may also participate the highly enantioselective titled reaction. The corresponding experiment work is undergoing.

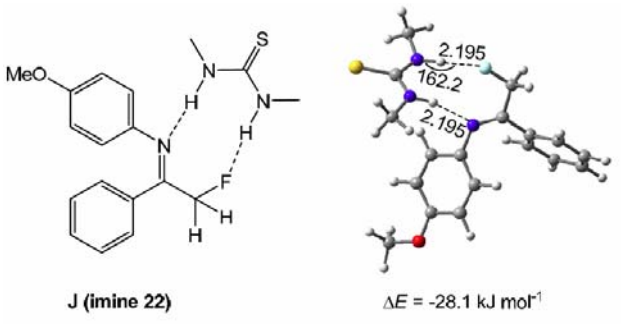


Figure S3. Optimized structure of hydrogen-bonded α-CH_2F ketoimine **22**-thiourea complex **J** at the B3LYP/6-311G(d,p) level.

Conclusion

The above studies revealed that the presence of α-CF_2H or CF_3 group at α-phenylketoimine interfered with the bifurcated H-bonding pattern of non-fluorinated α-methylphenylketoimine-thiourea complex, leading to unprecedented binding models **A**, **B**, **G** and **H** with N–H···N and N–H···F hydrogen bonds. These newly proposed models reasonably explained why α-CF_2H or CF_3 substituted ketoimines **1a** and **2a** failed to react with TMSCN by a simple (thio)urea catalysis. This study encouraged us to try bifuntional catalysis to develop the desired Strecker reactions in the following.

Coordinates for the optimized hydrogen-bonded complexes at the B3LYP/6-311G(d,p) level. The corresponding electronic energies, zero-point energy (ZPE) correction, counterpoise-corrected energy, and basis set superposition error (BSSE) are below, which are in a. u.

A (imine 1a)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	0.283311	-0.537634	-0.439322
2	6	0	0.447265	0.858923	-0.306082
3	6	0	-0.551996	1.550734	0.384700
4	6	0	1.484113	1.592972	-0.907439
5	6	0	-0.499607	2.934133	0.529960

6	1	0	-1.371284	0.991222	0.818980
7	6	0	1.522086	2.971247	-0.796137
8	1	0	2.247314	1.083961	-1.481847
9	6	0	0.539571	3.655293	-0.065669
10	1	0	-1.281752	3.432535	1.085576
11	1	0	2.305790	3.549226	-1.270360
12	8	0	0.678608	5.006266	-0.009681
13	6	0	-0.301620	5.762924	0.691550
14	1	0	0.007557	6.802612	0.601297
15	1	0	-1.295121	5.639902	0.247574
16	1	0	-0.338430	5.486564	1.750824
17	6	0	1.221684	-1.396221	-0.383615
18	6	0	2.664488	-1.198389	-0.055108
19	6	0	3.664476	-1.666190	-0.916371
20	6	0	3.032666	-0.579866	1.146216
21	6	0	5.008671	-1.497857	-0.592895
22	1	0	3.398644	-2.142679	-1.853947
23	6	0	4.374975	-0.426807	1.472902
24	1	0	2.264151	-0.227020	1.823102
25	6	0	5.365904	-0.880110	0.602701
26	1	0	5.774311	-1.852172	-1.273361
27	1	0	4.648904	0.046925	2.408432
28	1	0	6.411820	-0.755533	0.858265
29	6	0	0.823028	-2.855857	-0.578214
30	9	0	-0.499562	-2.983673	-0.890426
31	9	0	1.024988	-3.524503	0.602695
32	6	0	-3.546811	-0.931624	0.009591
33	16	0	-5.134972	-0.412565	0.255248
34	7	0	-2.835328	-0.647740	-1.109136
35	1	0	-1.837864	-0.835774	-1.086430
36	7	0	-2.853424	-1.656438	0.936106
37	1	0	-2.004837	-2.100670	0.614509
38	6	0	-3.336938	0.174295	-2.194768
39	1	0	-3.527639	1.203835	-1.875622
40	1	0	-2.586592	0.177501	-2.987269
41	1	0	-4.270743	-0.232668	-2.585813
42	6	0	-3.458771	-2.207502	2.137084
43	1	0	-2.670028	-2.683931	2.722300
44	1	0	-3.915930	-1.414657	2.729268
45	1	0	-4.235340	-2.944442	1.907157
46	1	0	1.397918	-3.368162	-1.353553

HF = -1536.225024
ZPE = 0.365963
Counterpoise-corrected energy = -1536.219408
BSSE = 0.005616

B (imine 2a)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	5.302149	-0.644651	-0.613028
2	6	0	4.373983	-1.643874	-0.338887
3	6	0	3.004134	-1.347481	-0.319337
4	6	0	2.586114	-0.037870	-0.590663
5	6	0	3.516151	0.953330	-0.881498
6	6	0	4.876965	0.653055	-0.889216
7	1	0	6.359592	-0.881916	-0.611635
8	1	0	4.719970	-2.647442	-0.127452
9	1	0	1.526992	0.187922	-0.584456
10	1	0	3.179164	1.959584	-1.101342
11	1	0	5.603153	1.426571	-1.110833
12	6	0	1.975476	-2.360253	0.050419
13	6	0	2.073655	-3.766331	-0.581331
14	7	0	1.044502	-2.031881	0.852940
15	6	0	-0.056892	-2.908484	1.275794
16	1	0	-0.004843	-3.917410	0.865354
17	1	0	0.028984	-2.982269	2.363573
18	6	0	-1.390154	-2.269941	0.928684
19	6	0	-2.089985	-1.520526	1.877894
20	6	0	-1.932279	-2.422162	-0.351296
21	6	0	-3.313007	-0.936044	1.555273
22	1	0	-1.677778	-1.393231	2.872866
23	6	0	-3.153635	-1.836762	-0.674962
24	1	0	-1.399250	-3.005009	-1.094269
25	6	0	-3.846763	-1.092472	0.278024
26	1	0	-3.848292	-0.362710	2.303538
27	1	0	-3.566487	-1.966400	-1.669143
28	1	0	-4.799582	-0.640062	0.027292
29	6	0	1.066832	0.056862	4.030569
30	16	0	0.702359	0.923422	5.430258
31	7	0	0.727657	0.473569	2.786713
32	1	0	0.855861	-0.178551	2.018112
33	7	0	1.715678	-1.148660	4.052514
34	1	0	2.093603	-1.464363	3.170345
35	6	0	-0.000655	1.700679	2.521182
36	1	0	0.551541	2.568495	2.887882
37	1	0	-0.131799	1.786437	1.441351
38	1	0	-0.982739	1.701638	3.002233
39	6	0	2.313932	-1.709886	5.253619
40	1	0	2.710827	-2.695593	5.003253
41	1	0	3.120311	-1.081980	5.646442

42	1	0	1.561524	-1.815657	6.034786
43	9	0	0.944095	-4.071554	-1.259073
44	9	0	3.087810	-3.887973	-1.450633
45	9	0	2.244427	-4.712776	0.367922

HF = -1560.267103
ZPE = 0.353989
Counterpoise-corrected energy = -1560.263002
BSSE = 0.004102

C (imine 7)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	0.056295	-0.648472	-0.306425
2	6	0	-0.496379	-1.807576	-0.295067
3	6	0	0.394362	-3.009771	-0.496958
4	1	0	1.428418	-2.700933	-0.643328
5	1	0	0.327869	-3.685520	0.361399
6	1	0	0.075698	-3.585668	-1.371285
7	6	0	-1.942405	-2.096861	-0.032150
8	6	0	-2.660086	-2.979892	-0.848923
9	6	0	-2.582618	-1.538364	1.082878
10	6	0	-3.993145	-3.274911	-0.574840
11	1	0	-2.184417	-3.426082	-1.714678
12	6	0	-3.906725	-1.851760	1.367865
13	1	0	-2.038026	-0.861158	1.729250
14	6	0	-4.618620	-2.714944	0.536165
15	1	0	-4.539891	-3.947175	-1.226192
16	1	0	-4.384922	-1.418952	2.239076
17	1	0	-5.653335	-2.952068	0.755545
18	6	0	-0.646175	0.581458	-0.255944
19	6	0	-0.118742	1.607166	0.532097
20	6	0	-1.765062	0.865008	-1.057475
21	6	0	-0.715316	2.865820	0.576878
22	1	0	0.773994	1.417625	1.116836
23	6	0	-2.348259	2.119954	-1.037521
24	1	0	-2.167281	0.101092	-1.710860
25	6	0	-1.838337	3.130257	-0.211219
26	1	0	-0.283305	3.629037	1.209638
27	1	0	-3.203721	2.348282	-1.661581
28	8	0	-2.491566	4.324387	-0.261047
29	6	0	-1.994885	5.401207	0.522439
30	1	0	-0.972351	5.668623	0.234080
31	1	0	-2.656447	6.242584	0.323808

32	1	0	-2.021164	5.165539	1.592221
33	6	0	3.781106	-0.301181	0.059206
34	16	0	5.455069	-0.110773	0.165620
35	7	0	2.999903	-0.577189	1.141433
36	1	0	2.016766	-0.741330	0.967086
37	7	0	3.090815	-0.197116	-1.104347
38	1	0	2.078713	-0.267337	-1.052153
39	6	0	3.519746	-0.844958	2.470060
40	1	0	4.114161	-0.004376	2.832544
41	1	0	2.670494	-0.998264	3.138936
42	1	0	4.156334	-1.734725	2.486501
43	6	0	3.691879	0.187924	-2.367803
44	1	0	2.911672	0.166370	-3.130790
45	1	0	4.121879	1.192837	-2.321630
46	1	0	4.489175	-0.503141	-2.648705

HF = -1337.700419
ZPE = 0.380216
counterpoise-corrected energy = -1337.696421
BSSE = 0.003998

D (product 5a)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.738911	0.301159	-1.642834
2	6	0	-0.581976	-0.508095	-1.392836
3	6	0	0.652836	-0.120528	-1.911600
4	6	0	-0.664252	-1.734019	-0.716584
5	6	0	1.788064	-0.918349	-1.769667
6	1	0	0.740387	0.827070	-2.433070
7	6	0	0.465206	-2.518798	-0.546293
8	1	0	-1.613426	-2.078192	-0.330001
9	6	0	1.703583	-2.122805	-1.070219
10	1	0	2.728394	-0.573340	-2.175923
11	1	0	0.408110	-3.465789	-0.023204
12	8	0	2.747108	-2.964539	-0.837915
13	6	0	4.027456	-2.621495	-1.370166
14	1	0	4.689606	-3.437694	-1.086954
15	1	0	3.991958	-2.547724	-2.462587
16	1	0	4.400252	-1.686106	-0.941504
17	6	0	-2.462293	0.963048	-0.544965
18	6	0	-3.299286	-0.031698	0.286803
19	6	0	-4.123636	-0.917607	-0.416392
20	6	0	-3.310027	-0.053391	1.682097

21	6	0	-4.936620	-1.814573	0.264752
22	1	0	-4.108896	-0.904665	-1.499342
23	6	0	-4.127319	-0.956356	2.363036
24	1	0	-2.676173	0.604870	2.260178
25	6	0	-4.940870	-1.836987	1.659531
26	1	0	-5.568547	-2.495875	-0.293077
27	1	0	-4.120157	-0.967940	3.446697
28	1	0	-5.574645	-2.536977	2.191529
29	6	0	-1.553098	1.875652	0.331515
30	9	0	-0.797933	2.668195	-0.487203
31	9	0	-0.668254	1.133834	1.074263
32	6	0	3.220143	0.970500	0.998259
33	16	0	4.901389	0.792082	0.964344
34	7	0	2.584765	1.983961	0.355770
35	1	0	1.581889	2.050922	0.440271
36	7	0	2.396296	0.120181	1.664256
37	1	0	1.408300	0.178468	1.463899
38	6	0	3.261659	3.043237	-0.372231
39	1	0	3.880041	2.636042	-1.174939
40	1	0	2.497537	3.694149	-0.800320
41	1	0	3.909647	3.629917	0.283949
42	6	0	2.846326	-1.076392	2.357541
43	1	0	2.023831	-1.434535	2.979288
44	1	0	3.139344	-1.869761	1.663433
45	1	0	3.699481	-0.837945	2.991355
46	1	0	-1.538074	0.978171	-2.368129
47	6	0	-3.412738	1.903266	-1.184759
48	7	0	-4.143912	2.650672	-1.668688
49	1	0	-2.108893	2.522203	1.012255

HF = -1629.689101
ZPE = 0.387575
counterpoise-corrected energy = -1629.683478
BSSE = 0.005624

E (product 6a)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	1.624736	-0.051126	-1.666879
2	6	0	0.479707	0.738761	-1.318244
3	6	0	-0.762249	0.413621	-1.862893
4	6	0	0.574423	1.881196	-0.510216
5	6	0	-1.892021	1.195417	-1.622786
6	1	0	-0.859325	-0.468566	-2.487480

7	6	0	-0.549505	2.647090	-0.244956
8	1	0	1.526618	2.174309	-0.090942
9	6	0	-1.794795	2.315942	-0.796904
10	1	0	-2.838031	0.900538	-2.054423
11	1	0	-0.483218	3.528101	0.381881
12	8	0	-2.832122	3.129394	-0.462728
13	6	0	-4.120129	2.847854	-1.013607
14	1	0	-4.777087	3.627569	-0.632711
15	1	0	-4.097951	2.896331	-2.107721
16	1	0	-4.488582	1.870345	-0.687085
17	6	0	2.395881	-0.786188	-0.653781
18	6	0	3.314511	0.148670	0.168970
19	6	0	4.005605	1.137474	-0.539615
20	6	0	3.530373	0.014500	1.541507
21	6	0	4.884330	1.990215	0.117722
22	1	0	3.834872	1.240078	-1.603814
23	6	0	4.408051	0.877258	2.197189
24	1	0	3.028354	-0.748807	2.117815
25	6	0	5.086070	1.865065	1.491456
26	1	0	5.411065	2.752766	-0.444125
27	1	0	4.559814	0.768544	3.264732
28	1	0	5.769211	2.531110	2.005666
29	6	0	1.472647	-1.686104	0.235042
30	9	0	0.603140	-2.370398	-0.541272
31	9	0	0.734726	-0.958053	1.099027
32	6	0	-3.401471	-1.062898	0.814282
33	16	0	-5.069593	-0.795153	0.828215
34	7	0	-2.822447	-2.012795	0.031625
35	1	0	-1.838491	-2.196711	0.158793
36	7	0	-2.529402	-0.349484	1.572497
37	1	0	-1.547985	-0.418718	1.345135
38	6	0	-3.566884	-2.965081	-0.776366
39	1	0	-4.224130	-2.446011	-1.475232
40	1	0	-2.846958	-3.564588	-1.336046
41	1	0	-4.185490	-3.624122	-0.160469
42	6	0	-2.914001	0.757428	2.434442
43	1	0	-2.063506	0.995026	3.075663
44	1	0	-3.190173	1.648700	1.863153
45	1	0	-3.761962	0.467029	3.053589
46	1	0	1.404553	-0.665056	-2.440422
47	6	0	3.265223	-1.722216	-1.401401
48	7	0	3.937646	-2.439319	-2.001377
49	9	0	2.158862	-2.589274	0.952723

HF = - 1728.9651452
ZPE = 0.378864

counterpoise-corrected energy = -1728.960079
BSSE = 0.005066

F (product 8)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	0.037055	0.631901	-1.304115
2	6	0	1.301789	0.188091	-0.789638
3	6	0	2.290634	-0.276845	-1.657389
4	6	0	1.548783	0.126623	0.591869
5	6	0	3.494871	-0.796814	-1.181840
6	1	0	2.122683	-0.242333	-2.729503
7	6	0	2.753741	-0.363539	1.070863
8	1	0	0.795183	0.461108	1.291377
9	6	0	3.738352	-0.834110	0.192397
10	1	0	4.228040	-1.156352	-1.890811
11	1	0	2.950799	-0.406766	2.135080
12	8	0	4.876602	-1.304975	0.770974
13	6	0	5.906600	-1.808867	-0.069543
14	1	0	6.702825	-2.131905	0.598494
15	1	0	5.559958	-2.664537	-0.659453
16	1	0	6.290988	-1.033638	-0.741751
17	6	0	-0.310411	2.092916	-1.168156
18	6	0	-0.669283	2.438545	0.290690
19	6	0	-1.678712	1.712399	0.935036
20	6	0	-0.025577	3.461047	0.988355
21	6	0	-2.026370	1.997041	2.250268
22	1	0	-2.186478	0.910333	0.413392
23	6	0	-0.374537	3.745915	2.309000
24	1	0	0.756102	4.043932	0.519946
25	6	0	-1.373243	3.016184	2.943660
26	1	0	-2.808160	1.421694	2.732243
27	1	0	0.138703	4.541588	2.836775
28	1	0	-1.644866	3.239034	3.969067
29	6	0	0.786444	2.996560	-1.771079
30	6	0	-2.210492	-2.483385	0.033096
31	16	0	-3.383182	-3.643978	0.391439
32	7	0	-0.983367	-2.476571	0.621698
33	1	0	-0.292516	-1.822135	0.284311
34	7	0	-2.416197	-1.473544	-0.852493
35	1	0	-1.657937	-0.820499	-1.021226
36	6	0	-0.527907	-3.491228	1.556254
37	1	0	-0.503773	-4.483396	1.096343
38	1	0	0.477545	-3.218438	1.881165

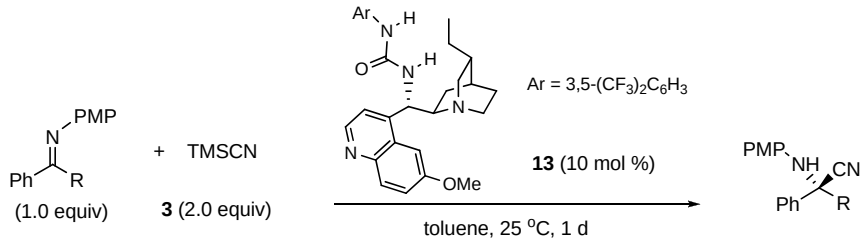
39	1	0	-1.186102	-3.542188	2.425451
40	6	0	-3.630749	-1.317784	-1.636789
41	1	0	-3.545555	-0.393354	-2.209715
42	1	0	-3.775832	-2.158848	-2.320502
43	1	0	-4.507488	-1.260393	-0.988997
44	1	0	-0.000723	0.408796	-2.294806
45	6	0	-1.529007	2.262313	-1.989490
46	7	0	-2.459711	2.379182	-2.659832
47	1	0	0.960943	2.715428	-2.811378
48	1	0	0.490944	4.046265	-1.749493
49	1	0	1.718798	2.872923	-1.219013

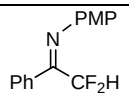
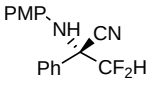
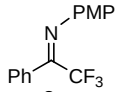
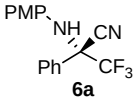
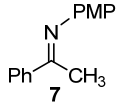
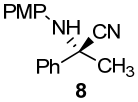
HF =-1431.163397
ZPE =0.402845
counterpoise-corrected energy = -1431.159509
BSSE = 0.003888

Comparing the reactivity of ketomine 1a, 2a and 7

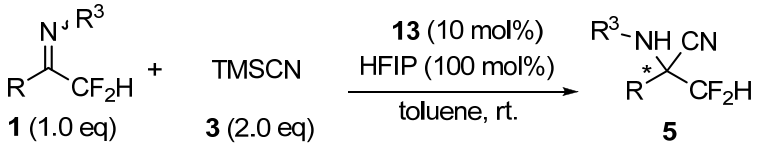
We also compared the reactivity of the fluorinated imine **1a** and **2a** with nonfluorinated ketoimine **7** when using bifunctional catalyst **13**. To get a accurate result, we slowed down the reaction by diluting the concentration of ketoimine to 0.1 mmol/mL, whereas the concentration of ketoimine in our optimum reaction condition was 0.5 mmol/mL. The reactions were run for only one day and then quenched. The products were isolated by column chromatography. By comparing the isolated yields of product **5a**, **6a** and **8** (Table S2), we came to the conclusion that no matter in the presence of HFIP or not, non-fluorinated imine **7** was more reactive than imine **1a** and **2a**, and α-CF_2H ketoimine **1a** was the least reactive under our condition for the Strecker reaction using TMSCN.

Table S2 Comparing the reactivity of ketoimine 1a, 2a and 7

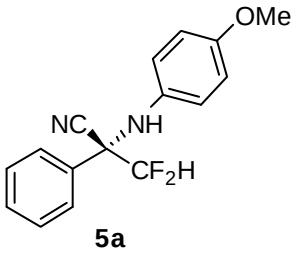


entry	ketoimine	product	isolated yield (%) (In the absence of HFIP)	isolated yield (%) In the presence of HFIP
1	 **1a**	 **5a**	23	31
2	 **2a**	 **6a**	62	84
3	 **7**	 **8**	84	96

General procedure for the Strecker reaction of difluoromethylketoimine 1 and TMSCN 3.

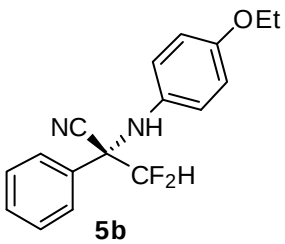


To a 5 mL vial were added catalyst **13** (14.5 mg, 0.025 mmol) and difluoromethylketomine **1** (0.25 mmol), $(CF_3)_2CHOH$ (27 μL, 0.25 mmol), followed by 0.5 mL of anhydrous toluene. The reaction mixture was stirred vigorously at room temperature until the full dissolution of catalyst **13**. The resulting mixture was stirred at indicated temperature for about 15 min before TMSCN **3** (67 μL, 0.50 mmol) was added. After the complete consumption of difluoromethylketomine **1** by TLC analysis, the mixture was directly subjected to column chromatography using petroleum ether/ethyl acetate (from 100:1 to 50:1) as the eluent, affording the desired product **5**.



5a

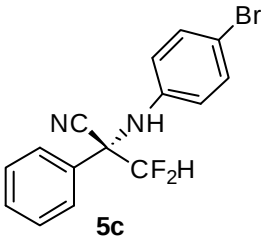
The reaction was carried out at 25 °C for 3 days. Column chromatography afforded the desired product **5a** in 73% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 7.49 min, t_r (minor) = 9.82 min) gave the isomeric composition of the product: 87% ee, $[\alpha]^{20}_D$ = -205.5 (c = 2.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 4H), 5.85 (t, *J* = 55.2 Hz, 1H), 6.59 (ABd, *J* = 8.4 Hz, 2H), 6.69 (ABd, *J* = 8.0 Hz, 2H), 7.47 (s, 3H), 7.69 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.01, 135.05, 131.41, 130.22, 129.38, 129.02, 127.25, 126.22, 119.90, 115.61, 114.49, 114.24 (t, *J* = 255 Hz), 65.77 (t, *J* = 22 Hz), 55.40; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -125.1 (d, *J* = 292 Hz, 1F), -126.6 (d, *J* = 288 Hz, 1F); IR (ATR): 3403, 3373, 3323, 2997, 2956, 2320, 1518, 1480, 1449, 1411, 829; MS (EI): 288 (M^+, 9), 289 [$(M+H)^+$, 2], 122 (100), 77 (26), 41 (22), 51 (21), 237 (20), 95 (17), 43 (15), 166 (6); HRMS (EI): Exact mass calcd for $C_{16}H_{14}N_2OF_2$ $[M]^+$: 288.1074, Found: 288.1078.



5b

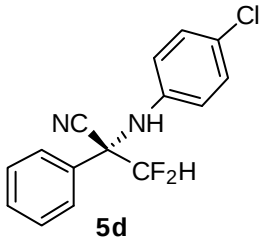
The reaction was carried out at 25 °C for 4 days. Column chromatography afforded the desired product **5b** in 89% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.37 min, t_r (minor) = 7.71 min) gave the isomeric composition of the product: 86% ee; $[\alpha]^{20}_D$ = -141.0 (c = 2.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, *J* = 6.4 Hz, 3H), 3.89 (q, *J* = 6.8 Hz, 2H), 4.27 (s, 1H), 5.84 (t, *J* = 55.2 Hz, 1H), 6.57 (ABd, *J*

= 7.6 Hz, 2H), 6.67 (ABd, *J* = 8.0 Hz, 2H), 7.44-7.45 (m, 3H), 7.68-7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.39, 134.93, 131.45, 130.19, 129.35, 127.26, 119.93, 115.62, 115.12, 114.26 (t, *J* = 255 Hz), 65.79 (t, *J* = 22 Hz), 63.63, 14.78; ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.0 (d, *J* = 292 Hz, 1F), -126.5 (d, *J* = 292Hz, 1F); IR (ATR): 3373, 3051, 2991, 2944, 2889, 2245, 1599, 1513, 1479, 1449, 813; MS (EI): 302 (M^+, 17), 108 (100), 136 (56), 77 (33), 41 (32), 53 (30), 251 (23), 166 (14); HRMS (EI): Exact mass calcd for $C_{17}H_{16}N_2OF_2$ $[M]^+$: 302.1231, Found: 302.1231.



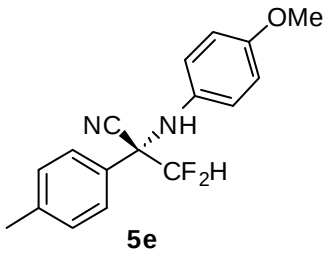
5c

The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **5c** in 89% yield as a white soild. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 8.23 min, t_r (minor) = 9.45 min) gave the isomeric composition of the product: 86% ee, $[\alpha]^{20}_D$ = -74.1 (c = 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (s, 1H), 5.78 (t, *J* = 54.8 Hz, 1H), 6.39-6.46 (m, 2H), 7.01-7.19 (m, 2H), 7.42 (s, 3H), 7.59 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.82, 140.32, 132.01, 130.70, 130.48, 129.64, 129.11, 126.92, 126.54, 118.64, 118.30, 115.09, 114.00 (t, *J* = 255 Hz), 113.85, 64.57 (t, *J* = 22 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.4 (d, *J* = 288 Hz, 1F), -126.6 (d, *J* = 288 Hz, 1F); IR (ATR): 3335, 3094, 2876, 2248, 1628, 1571, 1479, 1398, 1161, 812; MS (EI): 336 (M^+, 12), 337 [$(M+H)^+$, 2], 51 (100), 63 (65), 285 (61), 77 (60), 287 (55), 172 (25), 166 (17); HRMS (EI): Exact mass calcd for $C_{15}H_{11}N_2F_2{}^{79}Br$ $[M]^+$: 336.0074, Found: 336.0066.



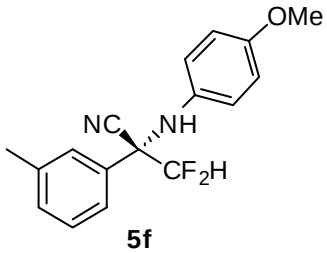
5d

The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **5d** in 85% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 7.81 min, t_r (minor) = 8.93 min) gave the isomeric composition of the product: 89% ee, $[\alpha]^{20}_D$ = -242.8 (c = 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.57 (s, 1H), 5.85 (t, *J* = 54.8 Hz, 1H), 6.46-6.53 (m, 2H), 7.08-7.26 (m, 2H), 7.40-7.52 (m, 3H), 7.58-7.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.81, 140.32, 132.02, 130.77, 130.48, 129.64, 129.12, 126.94, 126.56, 118.64, 118.31, 115.13, 114.01 (t, *J* = 256 Hz), 113.86, 64.59 (t, *J* = 10 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.4 (d, *J* = 288 Hz, 1F), -126.6 (d, *J* = 292 Hz, 1F); IR (ATR): 3340, 2921, 2851, 2244, 1598, 1519, 1492, 1415, 1146, 1098, 817; MS (EI): 292 (M^+, 11), 293 [$(M+H)^+$, 3], 51 (100), 241 (65), 75 (60), 99 (53), 77 (53), 126 (41), 166 (14); HRMS (EI): Exact mass calcd for $C_{15}H_{11}N_2F_2{}^{35}Cl$ $[M]^+$: 292.0579, Found: 292.0588.



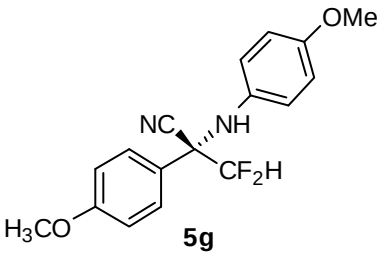
5e

The reaction was carried out at 25 °C for 4 days. Column chromatography afforded the desired product **5e** in 92% yield as yellow oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.70 min, t_r (minor) = 8.50 min) gave the isomeric composition of the product: 85% ee, $[\alpha]^{20}_{D}$ = -139.6 (c = 0.68, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 3.69 (s, 3H), 4.25 (s, 1H), 5.82 (t, *J* = 55.2 Hz, 1H), 6.59 (ABd, *J* = 8.0 Hz, 2H), 6.85 (ABd, *J* = 7.6 Hz, 2H), 7.20-7.30 (m, 2H), 7.50-7.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.99, 140.38, 135.20, 130.08, 129.73, 128.43, 127.13, 126.11, 119.92, 115.73, 114.48, 114.34 (t, *J* = 253 Hz), 65.59 (t, *J* = 21 Hz), 55.41, 21.13; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -125.0 (d, *J* = 292 Hz, 1F), -126.6 (d, *J* = 292 Hz, 1F); IR (ATR): 3359, 2999, 2968, 2841, 2240, 1855, 1618, 1513, 1461, 1367, 813; MS (EI): 302 (M^+, 9), 303 [$(M+H)^+$, 2], 122 (100), 41 (28), 51 (22), 92 (21), 52 (20), 77 (19), 95 (18), 180 (5) ; HRMS (EI): Exact mass calcd for $C_{17}H_{16}N_2OF_2$ $[M]^+$: 302.1231, Found: 302.1230.



5f

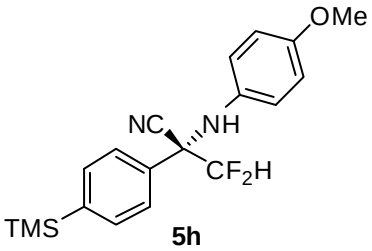
The reaction was carried out at 25 °C for 4 days. Column chromatography afforded the desired product **5f** in 89% yield as yellow oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.19 min, t_r (minor) = 8.05 min) gave the isomeric composition of the product: 86% ee, $[\alpha]^{20}_{D}$ = -143.4 (c = 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H), 3.69 (s, 3H), 4.25 (s, 1H), 5.84 (t, *J* = 54.8 Hz, 1H), 6.59 (ABd, *J* = 7.6 Hz, 2H), 6.69 (ABd, *J* = 8.4 Hz, 2H), 7.25-7.27 (m, 1H), 7.31-7.35 (m, 1H), 7.47-7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.01, 139.39, 135.23, 131.43, 131.01, 129.24, 127.76, 124.25, 119.86, 115.67, 114.50, 114.34 (t, *J* = 253 Hz), 65.83 (t, *J* = 21 Hz), 55.41, 21.47; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -125.0 (d, *J* = 288 Hz, 1 F), -126.5 (d, *J* = 292 Hz, 1 F); IR (ATR): 3372, 2960, 2837, 2481, 1889, 1607, 1512, 1461, 1090, 821; MS (EI): 302 (M^+, 10), 303 [$(M+H)^+$, 2], 122 (100), 51 (31), 91 (30), 41 (28), 92 (27), 65 (24), 95 (23); HRMS (EI): Exact mass calcd for $C_{17}H_{16}N_2OF_2$ $[M]^+$: 302.1231, Found: 302.1232.



5g

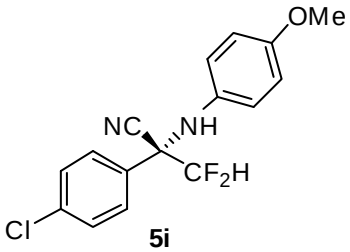
The reaction was carried out at 25 °C for 4 days. Column chromatography afforded the desired product **5g** in 70% yield as pale oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 8.91 min, t_r (minor) = 11.46 min) gave the isomeric

composition of the product: 80% ee, $[\alpha]^{20}_D$ = -111.0 (c = 0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H), 3.83 (s, 3H), 4.27 (s, 1H), 5.82 (t, *J* = 54.8 Hz, 1H), 6.61 (ABd, *J* = 8.0 Hz, 2H), 6.71 (ABd, *J* = 8.4 Hz, 2H), 6.97 (ABd, *J* = 8.0 Hz, 2H), 7.60 (ABd, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.88, 154.96, 135.15, 128.55, 123.02, 119.95, 115.77, 114.70, 114.44, 114.25 (t, *J* = 255 Hz), 65.26 (t, *J* = 20 Hz), 55.37, 55.33; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -125.0 (d, *J* = 292 Hz, 1F), -126.7 (d, *J* = 288 Hz, 1F); IR (ATR): 3377, 3027, 2996, 2968, 2840, 2239, 1697, 1607, 1506, 1462, 820; MS (EI): 318 (M^+, 6), 319 [$(M+H)^+$, 1], 51 (100), 122 (92), 41 (80), 43 (51), 108 (45), 162 (42), 192 (12); HRMS (EI): Exact mass calcd for $C_{17}H_{16}N_2O_2F_2$ $[M]^+$: 318.1180, Found: 318.1178.



5h

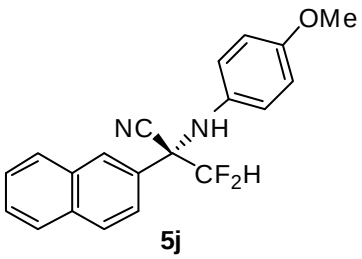
The reaction was carried out at 25 °C for 4 days. Column chromatography afforded the desired product **5h** in 62% yield as a pale solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.29 min, t_r (minor) = 7.51 min) gave the isomeric composition of the product: 86% ee, $[\alpha]^{20}_D$ = -110.2 (c = 0.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.29 (s, 9H), 3.70 (s, 3H), 4.29 (s, 1H), 5.84 (t, *J* = 54.8 Hz, 1H), 6.60 (ABd, *J* = 8.4 Hz, 2H), 6.70 (ABd, *J* = 8.4 Hz, 2H), 7.60 (ABd, *J* = 7.6 Hz, 2H), 7.67 (ABd, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 154.94, 143.38, 135.14, 134.30, 131.74, 126.35, 119.73, 115.58, 114.50, 114.26 (t, *J* = 254 Hz), 65.69 (t, *J* = 20 Hz), 55.40, -1.28; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -125.0 (d, *J* = 292 Hz, 1F), -126.4 (d, *J* = 288 Hz, 1F); IR (ATR): 3389, 3028, 2959, 2850, 2234, 1704, 1595, 1512, 1392, 1107, 822; MS (EI): 360 (M^+, 5), 361 [$(M+H)^+$, 1], 122 (100), 77 (20), 95 (17), 73 (14), 223 (13), 43 (11), 309 (6); HRMS (EI): Exact mass calcd for $C_{19}H_{22}N_2OF_2Si$ $[M]^+$: 360.1469, Found: 360.1469.



5i

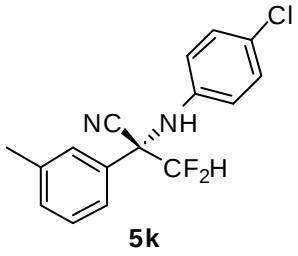
The reaction was carried out at 25 °C for 4 days. Column chromatography afforded the desired product **5i** in 94% yield as yellow oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 7.57 min, t_r (minor) = 9.51 min) gave the isomeric composition of the product: 92% ee, $[\alpha]^{20}_D$ = -121.1 (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.24 (s, 1H), 5.82 (t, *J* = 55.2 Hz, 1H), 6.59 (ABd, *J* = 7.6 Hz, 2H), 6.72 (ABd, *J* = 8.0 Hz, 2H), 7.45 (ABd, *J* = 7.2 Hz, 2H), 7.64 (ABd, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.23, 136.52, 134.65, 129.96, 129.66, 129.27, 128.75, 127.75, 120.04, 115.32, 114.61, 113.94 (t, *J* = 256 Hz), 65.31 (t, *J* = 21 Hz), 55.43; ^{19}F NMR (376 MHz, $CDCl_3$): *δ*

-125.0 (d, J = 292 Hz, 1 F), -126.6 (d, J = 292 Hz, 1 F); IR (ATR): 3386, 3333, 2999, 2883, 2835, 2243, 1594, 1511, 1490, 1403, 820; MS (EI): 322 (M^+, 6), 323 [$(M+H)^+$, 1], 122 (100), 51 (76), 41 (60), 43 (38), 75 (37), 50 (36), 77 (30), 271 (8) ; HRMS (EI): Exact mass calcd for $C_{16}H_{13}N_2OF_2{}^{35}Cl$ $[M]^+$: 322.0684, Found: 322.0684.



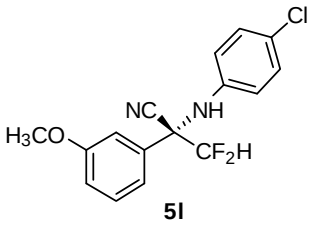
5j

The reaction was carried out at 25 ^oC for 4 days. Column chromatography afforded the desired product **5j** in 81% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 9.01 min, t_r (minor) = 13.01 min) gave the isomeric composition of the product: 87% ee, $[\alpha]^{20}_D$ = -144.5 (c = 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (s, 3H), 4.34 (s, 1H), 5.95 (t, J = 55.2 Hz, 1H), 6.61-6.68 (m, 4H), 7.58-7.59 (m, 2H), 7.74-7.76 (m, 1H), 7.88-7.95 (m, 3H), 8.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.00, 135.10, 133.86, 133.01, 129.47, 128.84, 128.46, 127.77, 127.70, 127.49, 127.01, 123.27, 119.92, 115.72, 114.48, 114.19 (t, J = 254 Hz), 66.05 (t, J = 20 Hz), 55.33; ^{19}F NMR (376 MHz, $CDCl_3$): δ -124.9 (d, J = 292 Hz, 1F), -126.1 (d, J = 292 Hz, 1F); IR (ATR): 3361, 3061, 2924, 2857, 2357, 1701, 1511, 1463, 1244, 1092, 820; MS (EI): 338 (M^+, 9), 339 [$(M+H)^+$, 3], 122 (100), 127 (19), 128 (19), 51 (18), 95 (17), 287 (7), 216 (6); HRMS (EI): Exact mass calcd for $C_{20}H_{16}N_2OF_2$ $[M]^+$: 338.1231, Found: 338.1240.



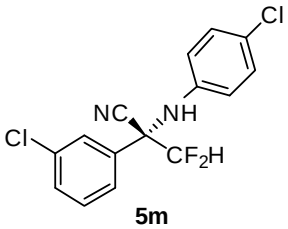
5k

The reaction was carried out at -20 ^oC for 5 days. Column chromatography afforded the desired product **5k** in 75% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.49 min, t_r (minor) = 5.80 min) gave the isomeric composition of the product: 92% ee, $[\alpha]^{20}_D$ = -216.1 (c = 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H), 4.58 (s, 1H), 5.84 (t, J = 54.8 Hz, 1H), 6.53 (ABd, J = 8.4 Hz, 2H), 7.09 (ABd, J = 8.0 Hz, 2H), 7.28-7.29 (m, 1H), 7.33-7.37 (m, 1H), 7.44-7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.44, 139.69, 131.25, 130.72, 129.47, 129.09, 127.39, 126.45, 123.90, 118.24, 115.19, 114.08 (t, J = 254 Hz), 64.69 (t, J = 21 Hz), 21.48; ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.2 (d, J = 288 Hz, 1F), -126.5 (d, J = 292 Hz, 1F); IR (ATR): 3374, 3351, 3044, 2879, 2356, 1609, 1587, 1496, 1083, 817; MS (EI): 306 (M^+, 22), 307 [$(M+H)^+$, 3], 51 (100), 91 (94), 255 (94), 111 (72), 99 (71), 75 (71), 180 (9); HRMS (EI): Exact mass calcd for $C_{16}H_{13}N_2F_2Cl$ $[M]^+$: 306.0735, Found: 306.0733.



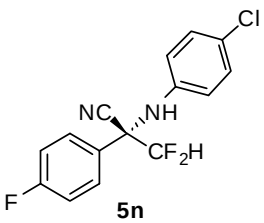
5l

The reaction was carried out at -20 °C for 5 days. Column chromatography afforded the desired product **5l** in 72% yield as colorless oil. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 7.35 min, t_r (minor) = 9.09 min) gave the isomeric composition of the product: 87% ee, $[\alpha]^{20}_{D}$ = -198.5 (c = 0.31, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H), 4.54 (s, 1H), 5.85 (t, *J* = 54.0 Hz, 1H), 6.54 (ABd, *J* = 6.8 Hz, 2H), 6.99-7.01 (m, 1H), 7.00 (ABd, *J* = 6.4 Hz, 2H), 7.18 (s, 1H), 7.26-7.27 (m, 1H), 7.38-7.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.51, 140.37, 132.40, 130.76, 129.15, 126.63, 119.03, 118.28, 115.71, 115.05, 114.03 (t, *J* = 256 Hz), 112.76, 64.67 (t, *J* = 20 Hz), 55.44; ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.2 (d, *J* = 292 Hz, 1F), -126.3 (d, *J* = 292 Hz, 1F); IR (ATR): 3366, 3007, 2945, 2838, 2244, 1599, 1524, 1492, 1460, 1099, 825; MS (EI): 322 (M^+, 24), 323 [$(M+H)^+$, 6], 51 (100), 99 (90), 63 (88), 75 (84), 271 (80), 126 (68), 111 (55); HRMS (EI): Exact mass calcd for $C_{16}H_{13}N_2OF_2Cl$ $[M]^+$: 322.0684, Found: 322.0682.



5m

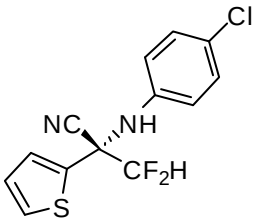
The reaction was carried out at -20 °C for 4 days. Column chromatography afforded the desired product **5m** in 90% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.83 min, t_r (minor) = 6.54 min) gave the isomeric composition of the product: 87% ee, $[\alpha]^{20}_{D}$ = -207.3 (c = 0.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.57 (s, 1H), 5.85 (t, *J* = 54.4 Hz, 1H), 6.52 (ABd, *J* = 7.2 Hz, 2H), 7.13 (ABd, *J* = 7.2 Hz, 2H), 7.41-7.48 (m, 2H), 7.57-7.59 (m, 1H), 7.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.02, 135.98, 133.04, 131.02, 131.00, 129.39, 127.22, 127.07, 125.40, 118.41, 114.72, 113.82 (t, *J* = 256 Hz), 64.39 (t, *J* = 22 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.1 (d, *J* = 292 Hz, 1F), -126.4 (d, *J* = 292 Hz, 1F); IR (ATR): 3390, 2960, 2921, 2860, 2361, 2341, 1617, 1541, 1508, 1437, 818; MS (EI): 326 (M^+, 14), 327 [$(M+H)^+$, 2], 51 (100), 75 (95), 111 (64), 99 (61), 63 (53), 50 (50), 200 (9); HRMS (EI): Exact mass calcd for $C_{15}H_{10}N_2F_2{}^{35}Cl$ $[M]^+$: 326.0189, Found: 326.0190.



5n

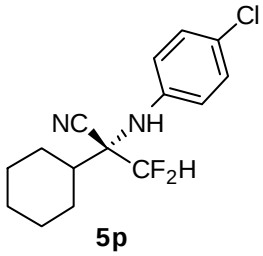
The reaction was carried out at -20 °C for 4 days. Column chromatography afforded the desired product **5n** in 84% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.91 min, t_r (minor) = 6.55 min) gave the isomeric composition of the product: 88% ee, $[\alpha]^{20}_{D}$ = -110.7 (c = 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.55 (s, 1H), 5.82 (t, *J* = 54.4 Hz,

1H), 6.51 (ABd, *J* = 7.2 Hz, 2H), 7.12 (ABd, *J* = 6.8 Hz, 2H), 7.16-7.20 (m, 2H), 7.66 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.08, 162.58, 140.06, 129.25, 129.16, 129.07, 126.93, 126.53, 118.44, 116.96, 116.74, 114.95, 113.85 (t, *J* = 256 Hz), 64.14 (t, *J* = 22 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -109.8 (s, 1F), -125.4 (d, *J* = 292 Hz, 1F), -126.8 (d, *J* = 288 Hz, 1F); IR (ATR): 3373, 2960, 2922, 2852, 2238, 1600, 1507, 1493, 1412, 815; MS (EI): 310 (M^+, 21), 311 [$(M+H)^+$, 3], 51 (100), 75 (88), 99 (72), 126 (59), 259 (59), 63 (52), 111 (47); HRMS (EI): Exact mass calcd for $C_{15}H_{10}N_2F_3{}^{35}Cl$ [M]$^+$: 310.0485, Found: 310.0483.



5o

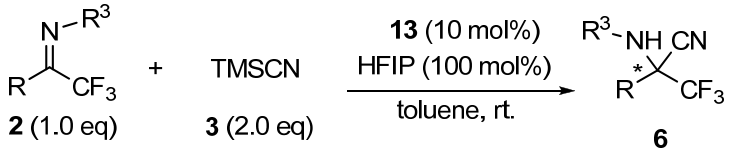
The reaction was carried out at -20 °C for 5 days. Column chromatography afforded the desired product **5o** in 61% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 7.42 min, t_r (minor) = 8.42 min) gave the isomeric composition of the product: 86% ee, $[\alpha]^{20}_D$ = -156.9 (c = 0.51, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.55 (s, 1H), 5.94 (t, *J* = 55.2 Hz, 1H), 6.57 (ABd, *J* = 7.6 Hz, 2H), 7.11-7.16 (m, 3H), 7.40-7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.26, 135.11, 129.24, 128.98, 127.82, 127.44, 118.90, 114.41, 113.54 (t, *J* = 255 Hz), 61.94 (t, *J* = 23 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -127.1 (d, *J* = 288 Hz, 1F), -128.3 (d, *J* = 288 Hz, 1F); IR (ATR): 3360, 3110, 2990, 2883, 2246, 1597, 1555, 1492, 1429, 1127, 820; MS (EI): 298 (M^+, 15), 299 [$(M+H)^+$, 2], 51 (100), 99 (71), 122 (70), 75 (69), 63 (60), 247 (34), 172 (51); HRMS (EI): Exact mass calcd for $C_{13}H_9N_2SF_2{}^{35}Cl$ [M]$^+$: 298.0143, Found: 298.0142.



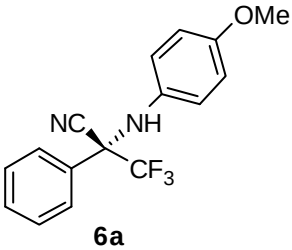
5p

The reaction was carried out at 25 °C for 6 days. Column chromatography afforded the desired product **5p** in 42% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.39 min, t_r (minor) = 7.19 min) gave the isomeric composition of the product: 77% ee, $[\alpha]^{20}_D$ = 13.7 (c = 1.19, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21-1.36 (m, 5H), 1.74-1.76 (m, 1H), 1.77-1.90 (m, 1H), 2.01-2.07 (m, 4H), 3.59 (s, 1H) 5.99 (t, *J* = 54.8 Hz, 1H), 6.95 (ABd, *J* = 7.2 Hz, 2H), 7.23 (ABd, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 141.67, 129.25, 127.28, 120.12, 115.24, 113.43 (t, *J* = 252 Hz), 64.01 (t, *J* = 22 Hz), 42.95, 27.53, 27.39, 26.01, 25.89, 25.69; ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.2 (d, *J* = 300 Hz, 1F), -126.0 (d, *J* = 300 Hz, 1F); IR (ATR): 3336, 2977, 2925, 2858, 2795, 2257, 1599, 1522, 1493, 811; MS (EI): 298 (M^+, 4), 299 [$(M+H)^+$, 2], 41 (100), 55 (94), 51 (44), 43 (39), 53 (25), 75 (25), 247 (11); HRMS (EI): Exact mass calcd for $C_{15}H_{17}N_2F_2{}^{35}Cl$ [M]$^+$: 298.1048, Found: 298.1048.

General procedure for the Strecker reaction of trifluoromethylketoimine 2 and TMSCN 3.

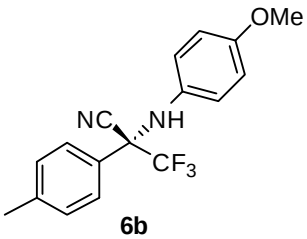


To a 5.0 mL vial were added catalyst **9** (14.5 mg, 0.025 mmol) and trifluoromethylketoimine **2** (0.25 mmol), $(CF_3)_2CHOH$ (27 μL, 0.25 mmol), followed by 0.5 mL of anhydrous toluene. The reaction mixture was stirred vigorously at room temperature until the full dissolution of catalyst **13**. The resulting mixture was stirred for about hour 15min before TMSCN **3** (67 μL, 0.50 mmol) was added. After the complete consumption of trifluoromethylketoimine **2** by TLC analysis (1-2 days except imine **2n**), the mixture was directly subjected to column chromatography using petroleum ether/ethyl acetate (from100:1 to 50:1) as the eluent, affording the desired product **6**.



6a

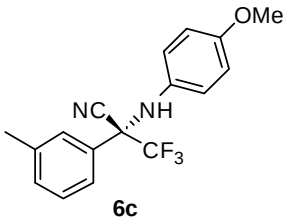
The reaction was carried out at 25 ^oC for 2 days. Column chromatography afforded the desired product **6a** in 97% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.17 min, t_r (minor) = 5.80 min) gave the isomeric composition of the product: 94% ee, $[\alpha]^{20}_D$ = -216.5 (c = 3.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H), 4.31 (s, 1H), 6.59 (ABd, *J* = 7.6 Hz, 2H), 6.70 (ABd, *J* = 7.6 Hz, 2H), 7.45-7.50 (m, 3H), 7.76-7.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.19, 134.55, 130.72, 129.65, 129.13, 127.99, 123.72 (q, *J* = 284 Hz), 119.95, 114.94, 114.48, 66.30 (q, *J* = 30 Hz), 55.38; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.4 (s, 3F); IR (ATR): 3380, 3010, 2969, 2832, 1621, 1512, 1452, 1416, 1241, 1202, 817; MS (EI): 306 (M^+, 9), 307 [$(M+H)^+$, 2], 122 (100), 95 (15), 41 (12), 77 (11), 52 (11), 123 (10), 64 (9); HRMS (EI): Exact mass calcd for $C_{16}H_{13}N_2OF_3$ $[M]^+$: 306.0980, Found: 306.0992.



6b

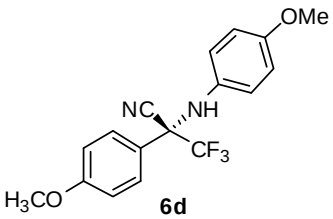
The reaction was carried out at 25 ^oC for 2 days. Column chromatography afforded the desired product **6b** in 93% yield as yellow oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 4.97 min, t_r (minor) = 5.37 min) gave the isomeric composition of the product: 94% ee, $[\alpha]^{20}_D$ = -170.5 (c = 3.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H), 3.61 (s, 3H), 4.24 (s, 1H), 6.52 (ABd, *J* = 8.4 Hz, 2H), 6.62 (ABd, *J* = 8.8 Hz, 2H), 7.17 (ABd, *J* = 7.6 Hz, 2H), 7.55 (ABd, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.16,

140.95, 134.70, 129.82, 127.84, 126.67, 123.8 (q, J = 284 Hz), 119.99, 118.09, 115.06, 114.46, 66.1 (q, J = 31 Hz), 55.37, 21.15; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.6 (s, 3F); IR (ATR): 3365, 2923, 2854, 1612, 1514, 1461, 1417, 1205, 1175, 1028, 718; MS (EI): 320 (M^+, 6), 321 [$(M+H)^+$, 1], 122 (100), 95 (13), 41 (11), 52 (9), 123 (8), 77 (7), 65 (6), 64 (6) ; HRMS (EI): Exact mass calcd for $C_{17}H_{15}N_2OF_3$ $[M]^+$: 320.1136, Found: 320.1135.



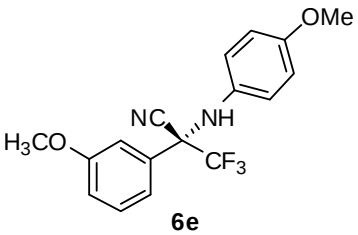
6c

The reaction was carried out at 25 ^{o}C for 2 days. Column chromatography afforded the desired product **6c** in 97% yield as yellow oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 20/80, 1.0 mL/min, 230 nm; t_r (major) = 4.71 min, t_r (minor) = 5.14 min) gave the isomeric composition of the product: 95% ee, $[\alpha]^{20}_D$ = -169.4 (c = 3.80, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 3H), 3.71 (s, 3H), 4.36 (s, 1H), 6.62 (ABd, J = 8.4 Hz, 2H), 6.724 (ABd, J = 8.0 Hz, 2H), 7.30-7.37 (m, 2H), 7.57-7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.20, 139.09, 134.75, 131.48, 129.67, 128.94, 128.43, 125.04, 123.8 (q, J = 284 Hz), 119.98, 115.01, 114.47, 66.4 (q, J = 30 Hz), 55.35, 21.41; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.3 (s, 3F); IR (ATR): 3375, 3019, 2963, 2842, 1728, 1606, 1511, 1460, 1241, 1162, 821; MS (EI): 320 (M^+, 8), 321 [$(M+H)^+$, 2], 122 (100), 95 (13), 41 (10), 52 (10), 123 (9), 77 (8), 65 (7); HRMS (EI): Exact mass calcd for $C_{17}H_{15}N_2OF_3$ $[M]^+$: 320.1136, Found: 320.1136.



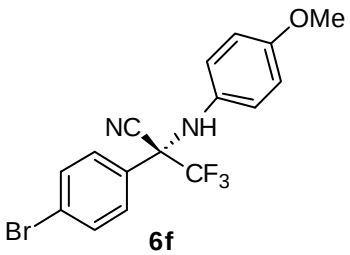
6d

The reaction was carried out at 25 ^{o}C for 2 days. Column chromatography afforded the desired product **6d** in 90% yield as pale oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.21 min, t_r (minor) = 6.71 min) gave the isomeric composition of the product: 94% ee, $[\alpha]^{20}_D$ = -138.7 (c = 3.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.84 (s, 3H), 4.34 (s, 1H), 6.63 (ABd, J = 8.4 Hz, 2H), 6.72 (ABd, J = 8.0 Hz, 2H), 6.97 (ABd, J = 8.0 Hz, 2H), 7.67 (ABd, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.28, 155.19, 134.69, 129.35, 123.8 (q, J = 284 Hz), 121.27, 120.94, 120.09, 115.10, 114.45, 65.9 (q, J = 30 Hz), 55.36, 55.33; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.8 (s, 3F); IR (ATR): 3337, 2940, 2838, 1610, 1511, 1463, 1443, 1239, 1170, 1032, 824; MS (EI): 336 (M^+, 4), 337 [$(M+H)^+$, 1], 122 (100), 95 (13), 41 (13), 5243 (10), 123 (9), 55 (8), 52 (7); HRMS (EI): Exact mass calcd for $C_{17}H_{15}N_2O_2F_3$ $[M]^+$: 336.1086, Found: 336.1091.



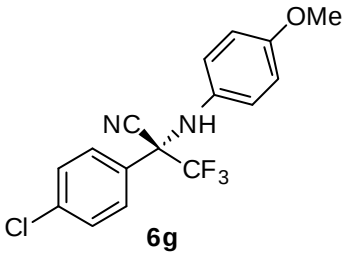
6e

The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6e** in 95% yield as a white soild. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.43 min, t_r (minor) = 6.03 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{20}_{D}$ = -136.6 (c = 3.95, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.81 (s, 3H), 4.36 (s, 1H), 6.63 (ABd, *J* = 8.4 Hz, 2H), 6.72 (ABd, *J* = 8.4 Hz, 2H), 7.02-7.03 (m, 1H), 7.31 (s, 1H), 7.37-7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.03, 155.21, 134.64, 131.17, 130.14, 123.7 (q, *J* = 283 Hz), 120.20, 119.90, 116.12, 114.89, 114.47, 113.70, 66.3 (q, *J* = 30 Hz), 55.36; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.2 (s, 3F); IR (ATR): 3332, 3311, 3078, 2959, 2928, 1608, 1586, 1485, 1458, 806; MS (EI): 336 (M^+, 7), 337[$(M+H)^+$, 2], 122 (100), 41 (13), 95 (13), 123 (10), 43 (8), 52 (8), 77 (7); HRMS (EI): Exact mass calcd for $C_{17}H_{15}N_2O_2F_3$ $[M]^+$: 336.1086, Found: 336.1084.



6f

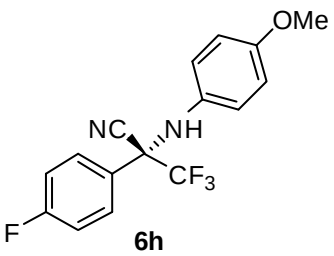
The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6f** in 95% yield as yellow oil. HPLC analysis (Chiralcel OJ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 17.54 min, t_r (minor) = 9.93 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{20}_{D}$ = -81.7 (c = 4.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 3H), 4.35 (s, 1H), 6.60 (ABd, *J* = 8.8 Hz, 2H), 6.73 (ABd, *J* = 8.4 Hz, 2H), 7.60-7.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.43, 134.13, 132.42, 129.67, 128.83, 125.39, 123.5 (q, *J* = 284 Hz), 120.11, 114.59, 65.9 (q, *J* = 30 Hz), 55.40; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.5 (s, 3F); IR (ATR): 3362, 2880, 2386, 1589, 1512, 1460, 1401, 1242, 1177, 818; MS (EI): 384 (M^+, 3), 385 [$(M+H)^+$, 1], 122 (100), 41 (13), 95 (13), 52 (10), 123 (10), 63 (8), 64 (8); HRMS (EI): Exact mass calcd for $C_{16}H_{12}N_2OF_3Br$ $[M]^+$: 384.0085, Found: 384.0084.



6g

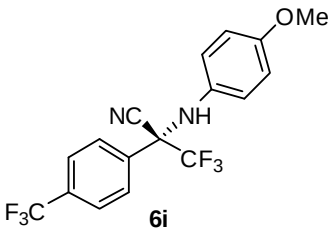
The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6g** in 95% yield as a white soild. HPLC analysis (Chiralcel OJ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 14.53 min, t_r (minor) = 9.29 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{20}_{D}$ = -107.0 (c = 4.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.30 (s, 1H), 6.59 (ABd, *J* = 8.0 Hz, 2H), 6.72

(ABd, J = 7.6 Hz, 2H), 7.44 (ABd, J = 7.6 Hz, 2H), 7.70 (ABd, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.42, 137.11, 134.15, 129.45, 128.69, 128.25, 126.18, 123.5 (q, J = 284 Hz), 120.11, 114.59, 65.9 (q, J = 30 Hz), 55.40; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.49 (s, 3F); IR (ATR): 3362, 2961, 2923, 2844, 1598, 1513, 1491, 1461, 1239, 1201, 819; MS (EI): 340 (M^+, 5), 341 [$(M+H)^+$, 1], 122 (100), 95 (12), 52 (10), 41 (9), 123 (9), 53 (7), 64 (6), 63 (6); HRMS (EI): Exact mass calcd for $C_{16}H_{12}N_2OF_3Cl$ $[M]^+$: 340.0590, Found: 340.0592.



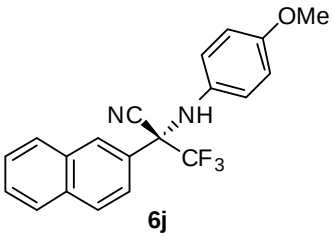
6h

The reaction was carried out at 25 ^{o}C for 2 days. Column chromatography afforded the desired product **6h** in 89% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 12.59 min, t_r (minor) = 8.97 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{20}_D$ = -193.5 (c = 3.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.30 (s, 1H), 6.60 (ABd, J = 8.4 Hz, 2H), 6.72 (ABd, J = 8.4 Hz, 2H), 7.14-7.18 (m, 2H), 7.74-7.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.29, 162.79, 155.47, 134.27, 130.22, 130.13, 125.48, 123.5 (q, J = 284 Hz), 120.23, 116.46, 116.24, 114.79, 114.60, 65.8 (q, J = 30 Hz), 55.43; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.68 (s, 3F), -109.54 (s, 1F); IR (ATR): 3369, 3012, 2895, 2832, 2368, 1604, 1506, 1461, 1443, 819; MS (EI): 324 (M^+, 6), 325 [$(M+H)^+$, 1], 122 (100), 95 (13), 52 (9.5), 152 (9), 123 (8), 64 (6), 63 (6), 53 (6); HRMS (EI): Exact mass calcd for $C_{16}H_{12}N_2OF_4[M]^+$: 324.0886, Found: 324.0888.



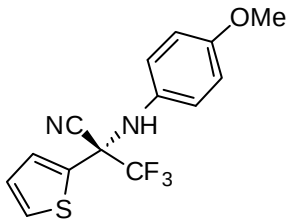
6i

The reaction was carried out at 25 ^{o}C for 2 days. Column chromatography afforded the desired product **6i** in 96% yield as colourless oil. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.05 min, t_r (minor) = 5.38 min) gave the isomeric composition of the product: 96% ee, $[\alpha]^{20}_D$ = -97.6 (c = 4.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.36 (s, 1H), 6.59 (ABd, J = 8.4 Hz, 2H), 6.73 (ABd, J = 8.4 Hz, 2H), 7.74 (ABd, J = 8.0 Hz, 2H), 7.92 (ABd, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.46, 133.94, 133.70, 133.15, 132.82, 128.69, 126.20, 126.17, 124.80, 123.47 (q, J = 278 Hz), 122.09, 120.00, 114.63, 114.43, 65.98 (q, J = 30 Hz), 55.36; ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.0 (s, 3F), -76.2 (s, 3F); IR (ATR): 3401, 2954, 2924, 2855, 2329, 1573, 1457, 1378, 1328, 1126, 829; MS (EI): 374 (M^+, 7), 375 [$(M+H)^+$, 1], 122 (100), 95 (13), 41 (11), 52 (10), 123 (9), 69 (8), 53 (7); HRMS (EI): Exact mass calcd for $C_{17}H_{12}N_2OF_6$ $[M]^+$: 374.0854, Found: 374.0857.



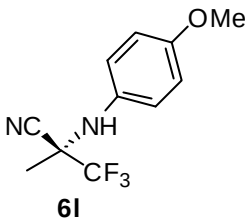
6j

The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6j** in 97% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.19 min, t_r (minor) = 7.75 min) gave the isomeric composition of the product: 96% ee, $[\alpha]^{20}_{D}$ = -178.2 (c = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 4.45 (s, 1H), 6.65-6.70 (m, 4H), 7.57-7.63 (m, 2H), 7.82-7.84 (m, 1H), 7.90-7.95 (m, 3H), 8.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.27, 134.60, 134.10, 132.79, 129.14, 128.73, 128.63, 127.76, 127.70, 127.15, 127.03, 123.91, 120.10, 115.06, 114.52, 66.78, 55.34; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.1 (s, 3F); IR (ATR): 3382, 3343, 3052, 2956, 2858, 1779, 1580, 1523, 1504, 1492, 806; MS (EI): 356 (M^+, 5), 357 [$(M+H)^+$, 2], 122 (100), 41 (23), 95 (17), 43 (16), 57 (17), 55 (13), 123 (9), 69 (9); HRMS (EI): Exact mass calcd for $C_{20}H_{15}N_2OF_3$ $[M]^+$: 356.1136, Found: 356.1136.



6k

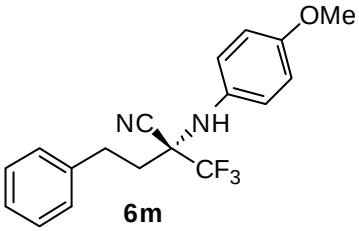
The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6k** in 93% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.90 min, t_r (minor) = 6.47 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{20}_{D}$ = -61.9 (c = 3.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (s, 3H), 4.24 (s, 1H), 6.74-6.79 (m, 4H), 7.07 -7.09 (m, 1H), 7.48-7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.14, 134.21, 133.45, 130.21, 129.44, 127.18, 121.77, 114.47, 114.30, 55.39; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.6 (s, 3F); IR (ATR): 3359, 3080, 2921, 2852, 2057, 1605, 1511, 1462, 1428, 1213, 821; MS (EI): 312 (M^+, 4), 313 [$(M+H)^+$, 1], 122 (100), 41 (18), 95 (18), 52 (14), 43 (11), 53 (9), 55 (9), 69 (9); HRMS (EI): Exact mass calcd for $C_{14}H_{11}N_2OF_3S$ $[M]^+$: 312.0544, Found: 312.0546.



6l

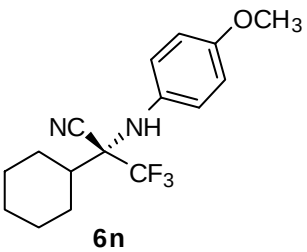
The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6l** in 83% yield as yellow oil . HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.78 min, t_r (minor) = 5.85 min) gave the isomeric composition of the product: 89% ee, $[\alpha]^{20}_{D}$ = -13.4 (c = 2.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65 (s, 3H), 3.59 (s, 1H), 3.80 (s, 3H), 6.87 (ABd, *J* = 7.6 Hz, 2H), 7.11 (ABd, *J* = 7.6 Hz, 2H); ^{13}C NMR

(100 MHz, $CDCl_3$): δ 157.74, 133.18, 126.73, 124.55 (q, *J* = 283 Hz), 116.28, 114.48, 59.27 (q, *J* = 30 Hz), 55.40, 19.92; ^{19}F NMR (376 MHz, $CDCl_3$): δ -78.6 (s, 3F); IR (ATR): 3407, 3327, 3043, 3006, 2882, 1710, 1590, 1511, 1485, 1455, 81; MS (EI): 244 (M^+, 20), 245 [$(M+H)^+$, 2], 122 (100), 52 (24), 149 (21), 41 (21), 175 (19), 69 (18) , 95 (16); HRMS (EI): Exact mass calcd for $C_{11}H_{11}N_2OF_3$ $[M]^+$: 244.0823, Found: 244.0823.



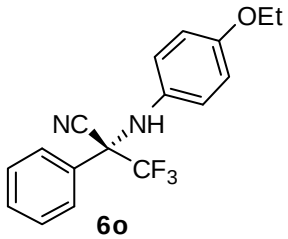
6m

The reaction was carried out at 25 °C for 2 days. Column chromatography afforded the desired product **6m** in 72% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 27.73 min, t_r (minor) = 19.89 min) gave the isomeric composition of the product: 87% ee, $[\alpha]^{20}_D$ = 79.2 (c = 3.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 2.17-2.25 (m, 1H), 2.36-2.43 (m, 1H), 2.91-3.05 (m, 2H), 3.44 (s, 1H), 3.79 (s, 3H), 6.84 (ABd, *J* = 8.4 Hz, 2H), 7.02 (ABd, *J* = 7.6 Hz, 2H), 7.19 (ABd, *J* = 7.2 Hz, 2H), 7.31-7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.81, 139.06, 134.47, 128.84, 128.32, 126.79, 124.73 (q, *J* = 286 Hz), 124.43, 114.84, 114.42, 63.06 (q, *J* = 30 Hz), 55.39, 35.49, 30.24; ^{19}F NMR (376 MHz, $CDCl_3$): δ -75.3 (s, 3F); IR (ATR): 3389, 3360, 3031, 2925, 2870, 2250, 1562, 1500, 1457, 1183, 701; MS (EI): 334 (M^+, 20), 335 [$(M+H)^+$, 3], 91 (100), 122 (64), 41 (38), 77 (37), 123 (30), 79 (30), 65 (29); HRMS (EI): Exact mass calcd for $C_{18}H_{17}N_2OF_3$ $[M]^+$: 334.1293, Found: 334.1292.



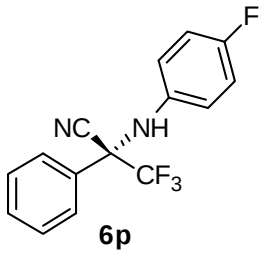
6n

The reaction was carried out at 25 °C for 6 days. Column chromatography afforded the desired product **6n** in 60% yield as a white solid. HPLC analysis (Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 5.36 min, t_r (minor) = 5.77 min) gave the isomeric composition of the product: 86% ee, $[\alpha]^{20}_D$ = 26.4 (c = 2.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.20-1.46 (m, 5H), 1.73-1.76 (m, 1H), 1.90-1.93 (m, 2H), 2.00-2.14 (m, 3H), 3.35 (s, 1H), 3.78 (s, 3H), 6.83 (ABd, *J* = 7.2 Hz, 2H), 7.03 (ABd, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 156.38, 135.45, 125.08 (q, *J* = 288 Hz), 123.76, 114.55, 114.33, 67.13 (q, *J* = 27 Hz), 64.26, 67.04, 55.41, 43.69, 27.75, 27.30, 26.04, 25.99, 25.59; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.9 (s, 3F); IR (ATR): 3381, 3032, 2985, 2948, 2858, 2251, 1509, 1472, 1441, 1167, 820; MS (EI): 312 (M^+, 7), 313 [$(M+H)^+$, 2], 41 (100), 55 (94), 122 (28), 53 (26), 83 (23), 52 (20), 95 (14); HRMS (EI): Exact mass calcd for $C_{16}H_{19}N_2OF_3$ $[M]^+$: 312.1449, Found: 312.1447.



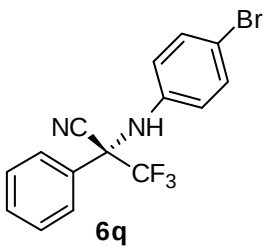
6o

The reaction was carried out at 25 ^{o}C for 2 days. Column chromatography afforded the desired product **6o** in 95% yield as a white solid. HPLC analysis (Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 10.92 min, t_r (minor) = 8.11 min) gave the isomeric composition of the product: 93% ee; $[\alpha]^{20}_{D}$ = -123.3 (c = 3.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, *J* = 6.0 Hz, 3H), 3.91 (q, *J* = 6.8 Hz, 2H), 4.30 (s, 1H), 6.59 (ABd, *J* = 7.6 Hz, 2H), 6.69 (ABd, *J* = 7.6 Hz, 2H), 7.47-7.48 (m, 3H), 7.76-7.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.55, 134.43, 130.67, 129.68, 129.09, 127.97, 123.72 (q, *J* = 288 Hz), 119.97, 115.06, 114.96, 66.31 (q, *J* = 30 Hz), 63.58, 14.75; ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.4 (s, 3F); IR (ATR): 3368, 3058, 2924, 2859, 2399, 1512, 1476, 1453, 1390, 1179, 720; MS (EI): 320 (M^+, 10), 321 [$(M+H)^+$, 2], 108 (100), 43 (64), 57 (54), 136 (53), 41 (48), 55 (43), 81 (30); HRMS (EI): Exact mass calcd for $C_{17}H_{15}N_2OF_3$ $[M]^+$: 320.1136, Found: 320.1139.



6p

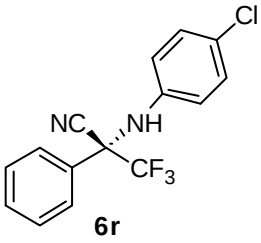
The reaction was carried out at 25 ^{o}C for 1 day. Column chromatography afforded the desired product **6p** in 91% yield as a white soild. HPLC analysis (Chiralcel OJ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 8.71 min, t_r (minor) = 6.31 min) gave the isomeric composition of the product: 91% ee, $[\alpha]^{20}_{D}$ = -162.2 (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.48 (s, 1H), 6.52-6.60 (m, 2H), 6.84-6.88 (m, 2H), 7.48-7.50 (m, 3H), 7.74-7.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.40, 157.00, 137.32, 130.89, 129.28, 129.21, 127.84, 123.62 (q, *J* = 284 Hz), 119.14, 119.07, 115.98, 115.76, 114.65, 65.81(q, *J* = 29 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.66 (s, 3F), -121.66 (s, 1F); IR (ATR): 3380, 3072, 3041, 2926, 2851, 2352, 1510, 1453, 1410, 1180, 720; MS (EI): 294 (M^+, 18), 295 [$(M+H)^+$, 3], 110 (100), 83 (76), 57 (54), 225 (51), 43 (43), 95 (42); HRMS (EI): Exact mass calcd for $C_{15}H_{10}N_2F_4$[$M]^+$: 294.0780, Found: 294.0780.



6q

The reaction was carried out at 25 ^{o}C for 1 day. Column chromatography afforded the desired product **6q** in 98% yield as a white soild. HPLC analysis (Chiralcel OJ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 9.10 min, t_r (minor) = 7.51 min) gave the isomeric composition of the product: 86% ee, $[\alpha]^{20}_{D}$ = -243.7 (c = 4.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.59 (s, 1H), 6.38 (ABd, *J* =7.6 Hz, 2H), 7.15 (ABd, *J* = 8.0 Hz, 2H), 7.37-7.43 (m, 3H), 7.63-7.65 (m, 2H);

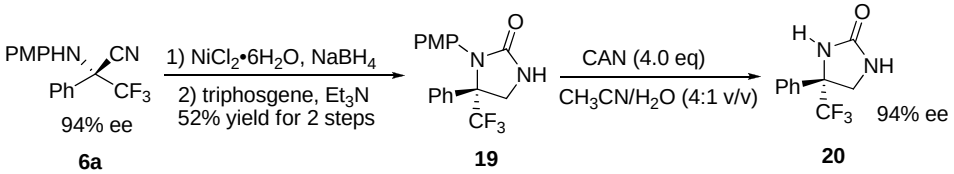
^{13}C NMR (100 MHz, $CDCl_3$): 140.29, 132.06, 130.96, 129.37, 128.91, 127.69, 126.37, 123.53 (q, J = 287 Hz), 118.62, 114.35, 114.21, 65.15 (q, J = 30 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.59 (s, 3F); IR (ATR): 3352, 2885, 2775, 1592, 1514, 1490, 1454, 1244, 1180, 814, 723; IR (ATR): 3352, 2985, 2885, 2775, 1592, 1514, 1490, 1454, 1180, 814; MS (EI): 354 (M^+, 24), 355 [$(M+H)^+$, 5], 91 (100), 43 (94), 41 (88), 170 (73), 55 (72), 172 (71), 57 (65); HRMS (EI): Exact mass calcd for $C_{15}H_{10}N_2F_3Br$ $[M]^+$: 353.9979, Found: 353.9981.



6r

The reaction was carried out at 25 ^{o}C for 1 day. Column chromatography afforded the desired product **6r** in 98% yield as a white solid. HPLC analysis (Chiralcel OJ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 8.45 min, t_r (minor) = 6.80 min) gave the isomeric composition of the product: 88% ee, $[\alpha]^{20}_D$ =-181.8 (c = 3.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.66 (s, 1H), 6.53 (ABd, J =8.4 Hz, 2H), 7.11 (ABd, J = 8.4Hz, 2H), 7.47-7.54 (m, 3H), 7.73-7.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 139.81, 130.96, 129.36, 129.17, 128.98, 127.72, 126.93, 123.55 (q, J = 284 Hz), 118.31, 114.42, 65.25 (q, J = 30 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -76.60 (s, 3F); IR (ATR): 3353, 3048, 2884, 2772, 2382, 1600, 1523, 1493, 1453, 1211, 815; MS (EI): 310 (M^+, 26), 311 [$(M+H)^+$, 5], 126 (100), 241 (59), 99 (55), 75 (38), 111 (35), 128 (33), 63 (29); HRMS (EI): Exact mass calcd for $C_{15}H_{10}N_2F_3Cl$ $[M]^+$: 310.0485, Found: 310.0483.

General Procedure for the preparation of 20 from 6a.[14]



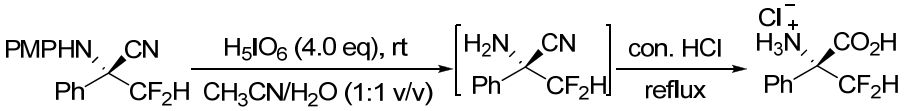
To a stirred solution of **6a (**75.0 mg, 0.24 mmol, 94% ee) and $NiCl_2$•$6H_2O$ (65.5 mg, 0.24 mmol) in 5.0 mL MeOH was added $NaBH_4$ (65.3 mg, 1.72 mmol) at 0 ^oC in three portions over 5 minutes. The resulting mixture was stirred until the generation of gas stopped, and then heated to 60 ^oC until the complete consumption of **6a** as indicated by TLC. The reaction was quenched by the addition of 0.2 mL of saturated NH_4Cl aqueous solution, and the resulting mixture was stirred at room temperature until the generation of gas ceased. Anhydrous Na_2SO_4 was added (about 1.0 g) to the reaction mixture, followed by a filtration. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1-1/1) to give the 1,2-diamine (55.9 mg) as colorless viscous oil, which was directly used for the next step. To a solution of 1,2-diamine (55.9 mg, 0.18 mmol) and triethylamine (72.0 μL, 0.54 mmol) in dry CH_2Cl_2 (10.0 mL) under nitrogen at 0 °C was added a solution of triphosgene (53.4 mg, 0.18 mmol) in dry CH_2Cl_2 dropwise. The reaction mixture was warmed to room temperature and stirred for 3 h until the complete consumption of diamine as indicated by TLC. Then the reaction was quenched using a reported work-up procedure.[14b] The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate =10/1-2/1) to give **19** (43.5 mg) in 52% yield for two steps as a white soild. The NMR data of **19:** ^1H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 3H), 3.81 (ABd, *J* = 10.0 Hz, 1H), 4.09 (ABd, *J* = 10.4 Hz, 1H), 6.72 (ABd, *J* = 8.0 Hz, 2H), 6.84 (ABd, *J* = 8.0 Hz, 2H), 6.91 (s, br, 1H), 7.41-7.43 (m, 3H), 7.59-7.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.93, 158.80, 137.25, 130.07, 129.06, 128.84, 128.33, 127.06, 126.89 (q, *J* = 285 Hz), 114.02, 70.20 (q, *J* = 28 Hz), 55.24, 49.89; ^{19}F NMR (376 MHz, $CDCl_3$): δ -70.89 (s, 3 F); MS (EI): 336 (M^+, 1), 41 (100), 43 (91), 55 (68), 57 (58), 69 (29), 56 (36), 149 (25); HRMS (EI): Exact mass calcd for $C_{17}H_{15}N_2O_2F_3$ $[M]^+$: 336.1086, Found: 336.1089.

To a solution of **19** (43.5 mg, 0.13 mmol) in dry acetonitrile (4.0 mL) was added dropwise a solution of CAN (283.0 mg, 0.52 mmol) in H_2O (1.0 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 6 h until the complete consumption of **19** as indicated by TLC. After a reported work-up procedure,[14c] the residue was purified by chromatography (petroleum ether/ethyl acetate =10/1-1/1) to give **20** (20.1 mg) in 67% yield as a yellow soild. HPLC analysis

[14] a) Caddick, S.; Judd, D. B.; de K. Lewis, A. K.; Reich, M. T.; Williams, M. R. V. *Tetrahedron*, **2003**, *59*, 5417.
b) Bégis, G.; Cladingboel, D. E.; Jerome, L.; Motherwell, W. B.; Sheppard, T. D. *Eur. J. Org. Chem.* **2009**, 1532.
c) Amii, H.; Kishikawa,Y.; Kageyama, K.; Uneyama, K. *J. Org. Chem.* **2000,** *65,* 3404.

(Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 19.92 min, t_r (minor) = 23.85 min) confirmed the isomeric composition of the product **20** to be 94%. $[\alpha]^{20}_{D}$ = -95.8 (c = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 3.66 (ABd, *J* = 10.0 Hz, 1H), 4.01 (ABd, *J* = 10.4 Hz, 1H), 6.81 (s, br, 1H), 7.42-7.49 (m, 5H), 8.32 (s, 1H) ; ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ 161.65, 137.58, 129.69, 129.19, 128.87, 127.69 (q, *J* = 284 Hz), 127.20, 64.82 (q, *J* = 28 Hz), 48.08; ^{19}F NMR (376 MHz, $CDCl_3$): δ -78.66 (s, 3F); IR (ATR): 3437, 3225, 3084, 2920, 2852, 1709, 1537, 1496, 1466, 1173, 706; HRMS (ESI): Calculated for $C_{10}H_9F_3N_2O$ ($M+H^+$): 231.0740, found: 231.0749.

General Procedure for the preparation of CF_2H- containing amino acids 21 from 5a.[15, 14c]



5a 87% ee **21**

The α-amino nitrile **5a** (52.0 mg, 0.18 mmol) was dissolved in CH_3CN/H_2O (1:1, 4.0 mL), followed by the addition of periodic acid (164 mg, 0.72 mmol) and sulfuric acid (0.36 mmol, 360 μL). The mixture was stirred until complete consumption of **5a** by TLC analysis. Then 2 mL of water and 5.0 mL of ether were added to the reaction mixture. The phases were separated and the aqueous phase was extracted with diethyl ether (8.0 mL × 4). The combined organic phases were dried over sodium sulfate and concentrated under vacuum. The crude product was dissolved in concentrated hydrochloric acid (5.0 mL) and refluxed until completion of the reaction as indicated by TLC (ca. 24 h). The resulting solution was washed with diethyl ether and ethyl acetate and concentrated under vacuum to afford the 2-amino-3,3-difluoro- 2-phenylpropanoic acid hydrochloride **21** as crude product. The crude product was purified by silica gel column chromatography (MeOH) to give **21** as a white soild (28.6 mg, 66%). $[\alpha]^{20}_{D}$ = -5.2 (c = 1.43, $CHCl_3$); ^{1}H NMR (400 MHz, D_2O): δ 6.76 (t, *J* = 52.4 Hz, 1H), 7.45 (s, 5H); ^{13}C NMR (100 MHz, D_2O): δ 168.63, 134.54, 130.67, 130.61, 130.24, 130.13, 129.63, 128.45, 125.99, 124.66, 114.76 (t, *J* = 256 Hz), 67.42 (t, *J* = 16 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -126.5 (d, *J* = 296 Hz, 1F), -129.9 (d, *J* = 300 Hz, 1F); IR (ATR): 3453, 3127, 3034, 2808, 2328, 1641, 1544, 1353, 1066, 695; MS (EI): 202 ($M-Cl^-$), HRMS (EI): Exact mass calcd for $C_9H_{10}NO_2F_2{}^{35}Cl$ $[M]^+$: 237.0368, Found: 237.0363.

[15] a) Enders, D.; Gottfried, K.; Raabe, G. *Adv. Synth. Catal.* **2010**, *352*, 3147.. b) Verkade, J. M. M.; van Hermert, L. J. C.; Quaedflieg, P. J. L. M.; Alsters, P. L.; van Delft, F. L.; Rutjes, F. P. J. T. *Tetrahedron Lett.* **2006**, *47*, 8109.

Single-Crystal X-ray Crystollgraphy[16]

Data intensity of **6p** was collected using a Bruker SMART APEX II (Mo radiation). The X-ray condition of was 50 kV × 30 mA. Data collection and reduction were done by using the Bruker ApexII software package. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for **6p**: $C_{15}H_{10}N_2F_3Br$, M = 355.15, T = 296(2) K, λ = 0.71073 Å, Orthorhombic, space group P2(1)2(1)2(1), a = 5.9903(2) Å, b = 16.9203(3) Å, c = 28.8205(10) Å, V = 2922.73(17) Å^3, z = 8, d_{calc} = 1.614 mg/m^3, 34105 reflections measured, 5144 unique [R_{int} = 0.0757], R_1 = 0.0384, wR_2 = 0.0660 ($I > 2\sigma(I)$), final R_1 = 0.0853, wR_2 = 0.0797 (all data), GOF = 1.021, and 379 parameters.

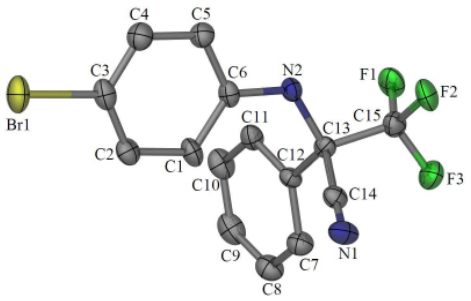


Table 1. Crystal data and structure refinement for z.

Identification code	z
Empirical formula	C15 H10 Br F3 N2
Formula weight	355.16
Temperature	296 (2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 5.9903(2) A alpha = 90 deg.
	b = 16.9293(6) A beta = 90 deg.
	c = 28.8205(10) A gamma = 90 deg.
Volume	2922.73(17) A^3

[16] Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. (CCDC 804952)

Z, Calculated density	8, 1.614 Mg/m^3
Absorption coefficient	2.839 mm^-1
F(000)	1408
Crystal size	0.14 x 0.06 x 0.05 mm
Theta range for data collection	1.39 to 25.01 deg.
Limiting indices	-6<=h<=7, -20<=k<=18, -34<=l<=34
Reflections collected / unique	34105 / 5144 [R(int) = 0.0757]
Completeness to theta = 25.01	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8711 and 0.6920
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5144 / 0 / 379
Goodness-of-fit on F^2	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0384, wR2 = 0.0660
R indices (all data)	R1 = 0.0853, wR2 = 0.0797
Absolute structure parameter	0.002(9)
Largest diff. peak and hole	0.362 and -0.393 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for z.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br(1)	2913(1)	4923(1)	1807(1)	76(1)
F(1)	318(5)	6258(2)	-1086(1)	69(1)
F(2)	1517(5)	7352(2)	-806(1)	70(1)
F(3)	3580(5)	6674(2)	-1264(1)	76(1)
N(2)	1480(6)	6199(2)	-137(1)	45(1)
N(1)	6700(8)	6951(2)	-254(1)	62(1)
C(1)	3832(9)	5499(3)	426(1)	50(1)
C(2)	4109(8)	5210(3)	870(2)	52(1)
C(3)	2483(9)	5328(3)	1198(2)	52(1)

C(4)	552(9)	5731(3)	1089(2)	59(2)
C(5)	269(8)	6011(3)	648(2)	50(1)
C(6)	1887(9)	5903(2)	310(1)	42(1)
C(7)	5646(8)	5143(3)	-868(2)	53(1)
C(8)	6058(10)	4382(3)	-1020(2)	63(2)
C(9)	4478(11)	3805(3)	-964(2)	66(2)
C(10)	2520(10)	3980(3)	-746(2)	63(2)
C(11)	2077(8)	4736(3)	-597(1)	50(1)
C(12)	3652(8)	5324(3)	-657(1)	40(1)
C(13)	3090(8)	6168(2)	-504(1)	39(1)
C(14)	5157(9)	6612(3)	-369(2)	47(1)
C(15)	2111(9)	6622(3)	-920(2)	52(1)
Br(2)	-1591(1)	6498(1)	-4860(1)	97(1)
F(4)	-97(4)	7985(2)	-1734(1)	65(1)
F(5)	-3389(5)	8112(2)	-2018(1)	60(1)
F(6)	-2094(5)	6965(2)	-1870(1)	68(1)
N(3)	3042(8)	6752(2)	-2458(1)	60(1)
N(4)	-2205(6)	7242(2)	-2808(1)	49(1)
C(16)	-3546(10)	6496(3)	-3966(2)	64(1)
C(17)	-3670(8)	6673(3)	-3496(2)	52(1)
C(18)	-1927(8)	7070(2)	-3278(1)	43(1)
C(19)	-83(8)	7277(3)	-3536(2)	50(1)
C(20)	39(9)	7100(3)	-4007(2)	56(1)
C(21)	-1713(11)	6724(3)	-4215(2)	61(1)
C(22)	-1578(9)	8906(3)	-2926(1)	50(1)
C(23)	-1126(10)	9677(3)	-3051(2)	62(2)
C(24)	875(10)	10021(3)	-2934(2)	66(2)
C(25)	2410(10)	9589(3)	-2695(2)	69(2)
C(26)	2002(9)	8818(3)	-2573(2)	56(1)
C(27)	-9(8)	8474(3)	-2685(1)	45(1)
C(29)	1509(9)	7140(3)	-2487(2)	48(1)
C(28)	-567(7)	7638(3)	-2526(2)	41(1)
C(30)	-1549(9)	7677(3)	-2031(1)	47(1)

Table 3. Bond lengths [A] and angles [deg] for z.

Br(1)-C(3)	1.902(4)
F(1)-C(15)	1.327(5)
F(2)-C(15)	1.327(5)
F(3)-C(15)	1.329(5)
N(2)-C(6)	1.401(5)
N(2)-C(13)	1.432(5)
N(2)-H(2B)	0.8600
N(1)-C(14)	1.136(5)
C(1)-C(2)	1.382(6)
C(1)-C(6)	1.392(6)
C(1)-H(1A)	0.9300
C(2)-C(3)	1.371(6)
C(2)-H(2A)	0.9300
C(3)-C(4)	1.379(6)
C(4)-C(5)	1.368(6)
C(4)-H(4A)	0.9300
C(5)-C(6)	1.386(6)
C(5)-H(5A)	0.9300
C(7)-C(12)	1.376(6)
C(7)-C(8)	1.383(7)
C(7)-H(7A)	0.9300
C(8)-C(9)	1.369(7)
C(8)-H(8A)	0.9300
C(9)-C(10)	1.363(7)
C(9)-H(9A)	0.9300
C(10)-C(11)	1.377(6)
C(10)-H(10A)	0.9300
C(11)-C(12)	1.383(6)
C(11)-H(11A)	0.9300
C(12)-C(13)	1.532(6)
C(13)-C(14)	1.500(7)
C(13)-C(15)	1.541(6)
Br(2)-C(21)	1.901(4)

F(4)-C(30)	1.327(5)
F(5)-C(30)	1.326(5)
F(6)-C(30)	1.332(5)
N(3)-C(29)	1.132(6)
N(4)-C(18)	1.395(5)
N(4)-C(28)	1.440(5)
N(4)-H(4B)	0.8600
C(16)-C(21)	1.367(7)
C(16)-C(17)	1.389(6)
C(16)-H(16A)	0.9300
C(17)-C(18)	1.392(6)
C(17)-H(17A)	0.9300
C(18)-C(19)	1.376(6)
C(19)-C(20)	1.394(6)
C(19)-H(19A)	0.9300
C(20)-C(21)	1.365(7)
C(20)-H(20A)	0.9300
C(22)-C(27)	1.378(6)
C(22)-C(23)	1.381(6)
C(22)-H(22A)	0.9300
C(23)-C(24)	1.375(7)
C(23)-H(23A)	0.9300
C(24)-C(25)	1.362(7)
C(24)-H(24A)	0.9300
C(25)-C(26)	1.375(6)
C(25)-H(25A)	0.9300
C(26)-C(27)	1.376(6)
C(26)-H(26A)	0.9300
C(27)-C(28)	1.526(6)
C(29)-C(28)	1.506(7)
C(28)-C(30)	1.544(6)
C(6)-N(2)-C(13)	123.2(4)
C(6)-N(2)-H(2B)	118.4
C(13)-N(2)-H(2B)	118.4
C(2)-C(1)-C(6)	119.9(4)

C(2)-C(1)-H(1A)	120.1
C(6)-C(1)-H(1A)	120.1
C(3)-C(2)-C(1)	120.1(5)
C(3)-C(2)-H(2A)	120.0
C(1)-C(2)-H(2A)	120.0
C(2)-C(3)-C(4)	120.8(4)
C(2)-C(3)-Br(1)	119.1(4)
C(4)-C(3)-Br(1)	120.1(4)
C(5)-C(4)-C(3)	119.1(5)
C(5)-C(4)-H(4A)	120.4
C(3)-C(4)-H(4A)	120.4
C(4)-C(5)-C(6)	121.4(5)
C(4)-C(5)-H(5A)	119.3
C(6)-C(5)-H(5A)	119.3
C(5)-C(6)-C(1)	118.7(4)
C(5)-C(6)-N(2)	118.5(4)
C(1)-C(6)-N(2)	122.8(4)
C(12)-C(7)-C(8)	120.1(5)
C(12)-C(7)-H(7A)	119.9
C(8)-C(7)-H(7A)	119.9
C(9)-C(8)-C(7)	120.3(5)
C(9)-C(8)-H(8A)	119.9
C(7)-C(8)-H(8A)	119.9
C(10)-C(9)-C(8)	119.7(5)
C(10)-C(9)-H(9A)	120.2
C(8)-C(9)-H(9A)	120.2
C(9)-C(10)-C(11)	120.8(5)
C(9)-C(10)-H(10A)	119.6
C(11)-C(10)-H(10A)	119.6
C(10)-C(11)-C(12)	120.0(5)
C(10)-C(11)-H(11A)	120.0
C(12)-C(11)-H(11A)	120.0
C(7)-C(12)-C(11)	119.2(4)
C(7)-C(12)-C(13)	121.7(4)
C(11)-C(12)-C(13)	119.0(4)

N(2)-C(13)-C(14)	110.3(3)
N(2)-C(13)-C(12)	113.2(3)
C(14)-C(13)-C(12)	111.1(4)
N(2)-C(13)-C(15)	107.5(4)
C(14)-C(13)-C(15)	105.4(4)
C(12)-C(13)-C(15)	108.9(3)
N(1)-C(14)-C(13)	178.1(5)
F(1)-C(15)-F(2)	107.7(4)
F(1)-C(15)-F(3)	107.3(4)
F(2)-C(15)-F(3)	107.5(4)
F(1)-C(15)-C(13)	110.9(4)
F(2)-C(15)-C(13)	112.0(4)
F(3)-C(15)-C(13)	111.2(4)
C(18)-N(4)-C(28)	124.4(4)
C(18)-N(4)-H(4B)	117.8
C(28)-N(4)-H(4B)	117.8
C(21)-C(16)-C(17)	119.5(5)
C(21)-C(16)-H(16A)	120.2
C(17)-C(16)-H(16A)	120.2
C(16)-C(17)-C(18)	120.3(5)
C(16)-C(17)-H(17A)	119.9
C(18)-C(17)-H(17A)	119.9
C(19)-C(18)-C(17)	118.8(4)
C(19)-C(18)-N(4)	124.5(4)
C(17)-C(18)-N(4)	116.7(4)
C(18)-C(19)-C(20)	120.9(5)
C(18)-C(19)-H(19A)	119.6
C(20)-C(19)-H(19A)	119.6
C(21)-C(20)-C(19)	119.2(5)
C(21)-C(20)-H(20A)	120.4
C(19)-C(20)-H(20A)	120.4
C(20)-C(21)-C(16)	121.3(4)
C(20)-C(21)-Br(2)	119.6(4)
C(16)-C(21)-Br(2)	119.1(4)
C(27)-C(22)-C(23)	119.9(5)

C(27)-C(22)-H(22A)	120.0
C(23)-C(22)-H(22A)	120.0
C(24)-C(23)-C(22)	120.5(5)
C(24)-C(23)-H(23A)	119.7
C(22)-C(23)-H(23A)	119.7
C(25)-C(24)-C(23)	119.0(5)
C(25)-C(24)-H(24A)	120.5
C(23)-C(24)-H(24A)	120.5
C(24)-C(25)-C(26)	121.4(5)
C(24)-C(25)-H(25A)	119.3
C(26)-C(25)-H(25A)	119.3
C(25)-C(26)-C(27)	119.8(5)
C(25)-C(26)-H(26A)	120.1
C(27)-C(26)-H(26A)	120.1
C(26)-C(27)-C(22)	119.4(5)
C(26)-C(27)-C(28)	120.9(4)
C(22)-C(27)-C(28)	119.6(4)
N(3)-C(29)-C(28)	178.6(5)
N(4)-C(28)-C(29)	110.1(4)
N(4)-C(28)-C(27)	114.2(4)
C(29)-C(28)-C(27)	111.1(4)
N(4)-C(28)-C(30)	106.4(4)
C(29)-C(28)-C(30)	105.7(4)
C(27)-C(28)-C(30)	108.7(4)
F(5)-C(30)-F(4)	108.0(4)
F(5)-C(30)-F(6)	106.8(4)
F(4)-C(30)-F(6)	107.0(4)
F(5)-C(30)-C(28)	111.5(3)
F(4)-C(30)-C(28)	111.3(4)
F(6)-C(30)-C(28)	112.0(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for z.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Br(1)	118(1)	63(1)	47(1)	8(1)	-14(1)	-10(1)
F(1)	66(2)	79(2)	63(2)	11(2)	-29(2)	-13(2)
F(2)	89(2)	49(2)	70(2)	13(1)	-17(2)	12(2)
F(3)	76(2)	95(2)	55(2)	21(2)	8(2)	1(2)
N(2)	41(2)	51(2)	42(2)	2(2)	-8(2)	10(2)
N(1)	48(3)	57(3)	81(3)	-6(2)	-7(2)	1(3)
C(1)	57(4)	54(3)	40(3)	1(2)	-7(2)	10(3)
C(2)	57(3)	41(3)	56(3)	-4(2)	-14(3)	8(3)
C(3)	73(4)	40(3)	44(2)	-4(2)	-14(3)	-3(3)
C(4)	66(4)	67(4)	44(3)	-6(3)	8(3)	-2(3)
C(5)	47(3)	53(3)	48(3)	-4(2)	-3(3)	11(3)
C(6)	54(3)	34(3)	39(2)	-3(2)	-13(2)	-2(3)
C(7)	51(3)	51(4)	58(3)	-11(3)	-2(3)	-5(3)
C(8)	58(4)	72(4)	59(3)	-17(3)	-2(3)	15(3)
C(9)	90(5)	51(4)	57(3)	-18(3)	-19(3)	11(4)
C(10)	78(5)	42(3)	68(3)	-8(2)	-13(3)	-5(3)
C(11)	44(3)	50(3)	54(3)	-1(2)	-7(2)	-9(3)
C(12)	38(3)	44(3)	39(2)	-5(2)	-2(2)	0(3)
C(13)	33(3)	45(3)	39(2)	-3(2)	-10(2)	-6(2)
C(14)	46(3)	44(3)	52(3)	0(2)	-3(2)	3(3)
C(15)	53(3)	50(3)	53(3)	7(2)	-2(3)	-3(3)
Br(2)	144(1)	96(1)	51(1)	-16(1)	-3(1)	31(1)
F(4)	62(2)	86(2)	47(2)	-7(2)	-11(2)	4(2)
F(5)	56(2)	67(2)	57(2)	-2(1)	5(1)	21(2)
F(6)	88(2)	55(2)	62(2)	16(1)	18(2)	8(2)
N(3)	49(3)	59(3)	72(3)	0(2)	3(2)	9(3)
N(4)	39(2)	60(2)	50(2)	-4(2)	5(2)	-9(2)
C(16)	80(4)	53(3)	60(3)	-13(3)	-7(3)	-1(4)
C(17)	51(3)	47(3)	58(3)	-14(2)	2(3)	1(3)
C(18)	47(3)	38(3)	44(2)	0(2)	1(3)	7(3)
C(19)	52(3)	50(3)	48(3)	-3(2)	6(3)	5(3)

C(20)	62(4)	51(3)	56(3)	4(3)	19(3)	13(3)
C(21)	83(4)	48(3)	52(3)	-10(2)	-5(3)	22(3)
C(22)	50(3)	54(3)	46(2)	2(2)	-1(2)	4(3)
C(23)	74(4)	50(4)	61(3)	12(2)	-1(3)	15(3)
C(24)	86(4)	40(3)	72(3)	7(3)	17(3)	-3(4)
C(25)	67(4)	52(4)	90(4)	-3(3)	7(3)	-8(3)
C(26)	44(3)	51(3)	73(3)	1(3)	1(3)	0(3)
C(27)	44(3)	46(3)	43(2)	0(2)	3(2)	3(3)
C(29)	52(4)	43(3)	50(3)	3(2)	8(3)	6(3)
C(28)	38(3)	45(3)	40(2)	-2(2)	0(2)	7(2)
C(30)	56(3)	43(3)	42(2)	5(2)	-3(3)	3(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for z.

	x	y	z	U(eq)
H(2B)	200	6408	-193	54
H(1A)	4943	5425	205	60
H(2A)	5400	4934	947	62
H(4A)	-542	5811	1313	71
H(5A)	-1038	6278	573	59
H(7A)	6720	5534	-910	64
H(8A)	7413	4261	-1160	76
H(9A)	4740	3297	-1074	79
H(10A)	1472	3583	-697	75
H(11A)	718	4852	-456	59
H(4B)	-3437	7103	-2679	59
H(16A)	-4702	6224	-4111	77
H(17A)	-4923	6525	-3327	62
H(19A)	1098	7538	-3393	60
H(20A)	1297	7237	-4178	68
H(22A)	-2940	8678	-3004	60
H(23A)	-2185	9966	-3215	74

H(24A)	1176	10541	-3017	79
H(25A)	3762	9821	-2614	83
H(26A)	3081	8529	-2414	67

Table 6. Torsion angles [deg] for z.

C(6)-C(1)-C(2)-C(3)	-0.8(7)
C(1)-C(2)-C(3)-C(4)	0.4(7)
C(1)-C(2)-C(3)-Br(1)	-179.9(3)
C(2)-C(3)-C(4)-C(5)	0.3(7)
Br(1)-C(3)-C(4)-C(5)	-179.4(4)
C(3)-C(4)-C(5)-C(6)	-0.6(7)
C(4)-C(5)-C(6)-C(1)	0.2(7)
C(4)-C(5)-C(6)-N(2)	179.4(4)
C(2)-C(1)-C(6)-C(5)	0.5(6)
C(2)-C(1)-C(6)-N(2)	-178.7(4)
C(13)-N(2)-C(6)-C(5)	175.7(4)
C(13)-N(2)-C(6)-C(1)	-5.1(6)
C(12)-C(7)-C(8)-C(9)	0.6(7)
C(7)-C(8)-C(9)-C(10)	-1.9(8)
C(8)-C(9)-C(10)-C(11)	2.5(8)
C(9)-C(10)-C(11)-C(12)	-1.7(7)
C(8)-C(7)-C(12)-C(11)	0.2(6)
C(8)-C(7)-C(12)-C(13)	-177.2(4)
C(10)-C(11)-C(12)-C(7)	0.4(6)
C(10)-C(11)-C(12)-C(13)	177.9(4)
C(6)-N(2)-C(13)-C(14)	-60.0(5)
C(6)-N(2)-C(13)-C(12)	65.2(5)
C(6)-N(2)-C(13)-C(15)	-174.4(4)
C(7)-C(12)-C(13)-N(2)	-155.8(4)
C(11)-C(12)-C(13)-N(2)	26.8(5)
C(7)-C(12)-C(13)-C(14)	-31.0(5)
C(11)-C(12)-C(13)-C(14)	151.6(4)
C(7)-C(12)-C(13)-C(15)	84.7(5)

C(11)-C(12)-C(13)-C(15)	-92.7(5)
N(2)-C(13)-C(14)-N(1)	9(16)
C(12)-C(13)-C(14)-N(1)	-118(16)
C(15)-C(13)-C(14)-N(1)	124(16)
N(2)-C(13)-C(15)-F(1)	-65.5(5)
C(14)-C(13)-C(15)-F(1)	176.9(4)
C(12)-C(13)-C(15)-F(1)	57.5(5)
N(2)-C(13)-C(15)-F(2)	54.8(5)
C(14)-C(13)-C(15)-F(2)	-62.8(5)
C(12)-C(13)-C(15)-F(2)	177.9(4)
N(2)-C(13)-C(15)-F(3)	175.1(4)
C(14)-C(13)-C(15)-F(3)	57.5(5)
C(12)-C(13)-C(15)-F(3)	-61.8(5)
C(21)-C(16)-C(17)-C(18)	-0.9(7)
C(16)-C(17)-C(18)-C(19)	-0.5(7)
C(16)-C(17)-C(18)-N(4)	178.5(4)
C(28)-N(4)-C(18)-C(19)	-2.1(7)
C(28)-N(4)-C(18)-C(17)	179.0(4)
C(17)-C(18)-C(19)-C(20)	0.6(7)
N(4)-C(18)-C(19)-C(20)	-178.3(4)
C(18)-C(19)-C(20)-C(21)	0.7(7)
C(19)-C(20)-C(21)-C(16)	-2.2(7)
C(19)-C(20)-C(21)-Br(2)	178.8(3)
C(17)-C(16)-C(21)-C(20)	2.3(8)
C(17)-C(16)-C(21)-Br(2)	-178.7(4)
C(27)-C(22)-C(23)-C(24)	-0.3(7)
C(22)-C(23)-C(24)-C(25)	0.2(8)
C(23)-C(24)-C(25)-C(26)	0.5(8)
C(24)-C(25)-C(26)-C(27)	-1.1(8)
C(25)-C(26)-C(27)-C(22)	1.0(7)
C(25)-C(26)-C(27)-C(28)	-176.0(4)
C(23)-C(22)-C(27)-C(26)	-0.3(6)
C(23)-C(22)-C(27)-C(28)	176.7(4)
C(18)-N(4)-C(28)-C(29)	-64.1(5)
C(18)-N(4)-C(28)-C(27)	61.8(5)
C(18)-N(4)-C(28)-C(30)	-178.3(4)

N(3)-C(29)-C(28)-N(4)	-39(19)
N(3)-C(29)-C(28)-C(27)	-166(100)
N(3)-C(29)-C(28)-C(30)	76(19)
C(26)-C(27)-C(28)-N(4)	-156.0(4)
C(22)-C(27)-C(28)-N(4)	27.0(5)
C(26)-C(27)-C(28)-C(29)	-30.6(5)
C(22)-C(27)-C(28)-C(29)	152.4(4)
C(26)-C(27)-C(28)-C(30)	85.3(5)
C(22)-C(27)-C(28)-C(30)	-91.7(5)
N(4)-C(28)-C(30)-F(5)	-63.7(5)
C(29)-C(28)-C(30)-F(5)	179.2(4)
C(27)-C(28)-C(30)-F(5)	59.8(5)
N(4)-C(28)-C(30)-F(4)	175.7(4)
C(29)-C(28)-C(30)-F(4)	58.6(5)
C(27)-C(28)-C(30)-F(4)	-60.8(5)
N(4)-C(28)-C(30)-F(6)	56.0(5)
C(29)-C(28)-C(30)-F(6)	-61.1(5)
C(27)-C(28)-C(30)-F(6)	179.5(4)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for z [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)