Boron Trifluoride Assisted Perfluoroalkylation of Carbon-Nitrogen Double Bonds

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Received February 12, 1991

In the presence of BF_3·OEt_2, (perfluoroalkyl)lithiums generated in situ from the reaction of primary perfluoroalkyl iodides and MeLi-LiBr reacted with imines, azines, and nitrones to afford perfluoroalkylated nitrogen-containing compounds in moderate to good yields. This method was successfully applied to the preparation of a (perfluoroalkyl)glycine and optically active perfluoroalkylated amines.

Methodology for introducing the perfluoroalkyl group into organic molecules has recently been developed greatly due to increasing needs for fluorine-containing compounds in a variety of industrial fields. These methods can be conveniently divided into three types: cationic perfluoroalkylation represented by the reactions of Umemoto's FITS ((perfluoroalkyl)phenyliodonium trifluoromethanesulfonates) reagents;[2] addition of perfluoroalkyl radicals generated from perfluoroalkyl halides,[3] perfluoroalkanoyl peroxides,[4] or other perfluoroalkyl sources;[5] and nucleophilic or coupling reactions of (perfluoroalkyl)metals represented by (perfluoroalkyl)zinc[6] and (perfluoroalkyl)copper reagents.[7] In the last type of reaction, difficulties are often encountered due to the instability and low reactivity of these metal reagents. Perfluoroalkyl Grignard and lithium reagents react with carbonyl compounds[8] such as aldehydes, ketones, and esters, but they fail to react with less polarized functional groups, leading to self-decomposition into perfluoroalkenes and metal fluorides. In a preliminary form,[9] we have recently reported that in situ generated (perfluoroalkyl)lithiums add smoothly to imines in the presence of BF_3·OEt_2 to produce the corresponding perfluoroalkylated amines. This method has now proven to be applicable to the perfluoroalkylation of other types of carbon-nitrogen double bonds. In this paper, we describe the scope of our method and its successful application to the synthesis of perfluoroalkyl-containing amino acids.

Results and Discussion

Perfluoroalkylation of Imines. Nucleophilic addition of organometallic reagents to imines is a very useful method for the preparation of amines.[10] However, when less reactive nucleophiles such as enol silyl ethers or lithium enolates are employed, the activation of the imine moiety either by transformation into an iminium salt[11] or by coordination with a Lewis acid[12] is often necessary. We found that the latter mode of activation is also applicable to the reaction of imines with (perfluoroalkyl)lithium, which is a poor and labile nucleophile. Thus, MeLi-LiBr (1.1 equiv) was added to a cooled ethereal suspension of *N*-benzylideneethylamine (**1a**), *n*-$C_6F_{13}I$ (1.2 equiv), and BF_3·OEt_2 (1 equiv). Addition of the perfluorohexyl group to the imine function occurred smoothly to afford the perfluorohexylated amine **2ab** in good yield (Table I). Other straight-chain perfluoroalkyl iodides reacted similarly with imines **1** to afford amines **2** in moderate to good yields as shown in Table I. A few observations are worth noting: while *n*-$C_8F_{17}Br$ could also be successfully employed, the reactions using *i*-C_3F_7I and CF_3I gave no perfluoroalkylated products. The presence of a bulky group on the imino nitrogen (**1b** and **1c**) led to diminished yields (35% and 69%, respectively). When 2 equiv each of BF_3·OEt_2, $C_6F_{13}I$, and MeLi-LiBr was used with **1b**, the yield of **2b** improved to 68%. Other Lewis acids such as $TiCl_4$, $SnCl_4$, $ZnCl_2$, $AlCl_3$, $EtAlCl_2$, and Et_3Al were essentially ineffective in promoting the addition of *n*-$C_6F_{13}Li$ to **1a**. The perfluorohexylation was examined in a series of solvents; in toluene and CH_2Cl_2 the reaction proceeded smoothly, giving results similar to those obtained in ether. However, in pentane, DME, or THF, little reaction occurred, as the starting imine **1a** and benzaldehyde were recovered in near-quantitative yield.

In contrast, none of the perfluorohexyl addition products were obtained when an ethereal suspension of imine **1a** and BF_3·OEt_2 (0.9 equiv each) was added to a solution of *n*-$C_6F_{13}Li$ previously prepared from 1 equiv each of *n*-$C_6F_{13}I$ and MeLi-LiBr at −78 °C. The same result was obtained

(1) (a) Ehime University. (b) Kyoto University.

(2) For a review, see: Umemoto, T. *Yuki Gosei Kagaku Kyokaishi*, **1983**, *41*, 251 and references cited therein.

(3) For recent examples: Takeyama, Y.; Ichinose, Y.; Oshima, K.; Uchimoto, K. *Tetrahedron Lett.* **1989**, *30*, 3159. Ishihara, T.; Kuroboshi, M. *Synth. Commun.* **1989**, *19*, 1611. Huang, W.-Y.; Chen, J.-L. *Acta Chim. Sin. (Engl. Ed.)* **1988**, 86. Chen, Q.-Y.; Yang, Z.-Y.; Zhao, C.-X.; Qiu, Z.-M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 563. Wakselman, C.; Tordeux, M. *J. Chem. Soc., Chem. Commun.* **1987**, 1701. Chen, Q.-Y.; Qiu, Z.-M. *J. Fluorine Chem.* **1986**, *31*, 301. Feiring, A. E. *J. Org. Chem.* **1985**, *50*, 3269. Fuchikami, T.; Ojima, I. *J. Fluorine Chem.* **1983**, *22*, 541.

(4) Yoshida, M.; Yoshida, T.; Kobayashi, M.; Kamigata, N. *J. Chem. Soc., Perkin Trans. 1* **1989**, 909. Yoshida, M.; Yoshida, T.; Kamigata, N.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3549. Yoshida, M.; Amemiya, H.; Kobayashi, M.; Sawada, H.; Hagii, H.; Aoshima, K. *J. Chem. Soc., Chem. Commun.* **1985**, 234.

(5) (a) Uneyama, K.; Makio, S.; Nanbu, H. *J. Org. Chem.* **1989**, *54*, 872. (b) Coe, P. L.; Owen, D. M.; Pedler, A. E. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1995. (c) Huang, W.-Y.; Hu, L.-Q.; Xie, Y. *Acta Chim. Sin. (Engl. Ed.)* **1989**, 190. (d) Coe, P. L.; Milner, N. E. *J. Organomet. Chem.* **1972**, *39*, 395; **1974**, *70*, 147; *J. Fluorine Chem.* **1972/1973**, *2*, 167. (e) Schwartz, B.; Cech, D.; Reefschlager, J. *J. Prakt. Chem.* **1984**, *b326*, 985. (f) Umemoto, T.; Ando, A. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 447.

(6) (a) Tordeux, M.; Francese, C.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1951. (b) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186. (c) Benefice, S.; Blancou, H.; Commeyras, A. *Tetrahedron* **1984**, *40*, 1541 and references cited therein.

(7) Clark, J. H.; McClinton, M. A.; Blade, R. J. *J. Chem. Soc., Chem. Commun.* **1988**, 638. Carr, G. E.; Chambers, R. D.; Holmes, T. E.; Perker, D. G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 921. Leroy, J.; Rubinstein, M.; Wakselman, C. *J. Fluorine Chem.* **1985**, *27*, 291. Matsui, K.; Tobita, E.; Ando, M.; Kondo, K. *Chem. Lett.* **1981**, 1719. Kobayashi, Y.; Kumadaki, I. *J. Chem. Soc., Perkin Trans. 1* **1980**, 661. McLouglin, V. C.; Thrower, J. *Tetrahedron* **1969**, *25*, 5921.

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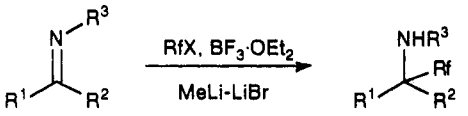
(12) (a) Pirie, D. K.; Welch, W. M.; Weeks, P. D.; Volkmann, R. A. *Tetrahedron Lett.* **1986**, *27*, 1549. (b) Melts, C. N.; Volkmann, R. A. *Tetrahedron Lett.* **1983**, *24*, 4503. (c) Ojima, I.; Inaba, S. *Tetrahedron Lett.* **1980**, *21*, 2081.

0022-3263/92/1957-1504$03.00/0

Table I. Perfluoroalkylation of Imines



1 2

	imine 1					
	R^1	R^2	R^3	R_fX	product	yield,[a] %
a	Ph	H	Et	n-$C_8F_{17}I$	**2aa**	78
a	Ph	H	Et	n-$C_8F^{17}Br$	**2aa**	86
a	Ph	H	Et	n-$C_6F_{13}I$	**2ab**	88
a	Ph	H	Et	n-C_4F_9I	**2ac**	80
a	Ph	H	Et	C_2F_5I	**2ad**	91
b	Ph	H	t-Bu	n-$C_6F_{13}I$	**2b**	35
c	Ph	H	c-Hex	n-$C_6F_{13}I$	**2c**	69
d	Ph	Me	n-Oct	n-$C_6F_{13}I$	**2d**	82
e	i-Pr	H	i-Bu	n-$C_6F_{13}I$	**2e**	84

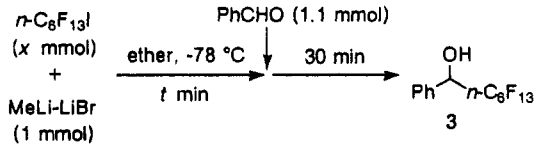
when BF_3·OEt_2 followed by imine **1a** was added to a solution of n-$C_6F_{13}Li$ at −78 °C. Single electron transfer from MeLi to the BF_3–imine complex followed by coupling with perfluoroalkyl iodide is unlikely,[13] because no reductive coupling product was obtained from **1a** even when the perfluoroalkylation did not take place. When n-$C_6F_{13}Li$ was prepared from 2 equiv of n-$C_6F_{13}I$ and 1 equiv of MeLi–LiBr, the reaction with **1a** proceeded to give **2aa** in 76% (addition of BF_3–**1a** complex) and 56% (sequential addition of BF_3·OEt_2 and **1a**) yields. These observations suggest that the reactive species in the perfluoroalkylation may not be the (perfluoroalkyl)lithium.

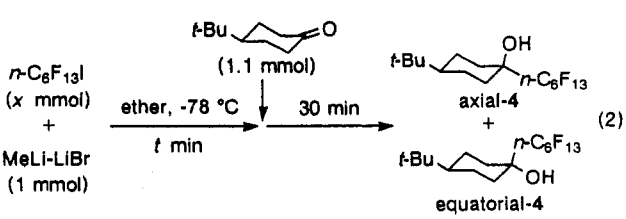
Lithium bis(perfluoroalkyl)halogenanides $[(R_f)_2X^-Li^+]$ become an attractive alternative,[14] although Saveant et al. concluded the insignificance of the $(R_f)_2X^-$ complex on the basis of their electrochemical study of perfluoroalkyl iodides and bromides.[15] If such a halogenanide species plays a role in perfluoroalkyl transfer, the steric bulkiness of the complex will affect the stereochemical outcome of the reaction of the organometallic species with a ketone. To test this hypothesis, the reaction with 4-*tert*-butylcyclohexanone was chosen as a representative case (eq 2). When the ketone was added to n-$C_6F_{13}Li$ prepared from 1 equiv each of n-$C_6F_{13}I$ and MeLi–LiBr at −78 °C, however, 4-*tert*-butyl-1-(perfluorohexyl)-1-cyclohexanol (**4**) was obtained in only 6% yield. On the other hand, the reaction occurred smoothly (82%) when 2 equiv of n-$C_6F_{13}I$ was used. The ratio of axial to equatorial alcohols **4** was 15:85 under both sets of reaction conditions. The stereochemical determination was based on the substituent increment rule of ^{13}C NMR.[16] The stability of n-$C_7F_{15}Li$ derived from the corresponding iodide and n-BuLi in ether was reported to decrease sharply above −90 °C.[17] Therefore, we decided to determine the stability of (perfluoroalkyl)lithium generated under our conditions. In order to estimate the effect of excess perfluoroalkyl iodide on the lifetime of (perfluoroalkyl)lithium, perfluorohexylation of 4-*tert*-butylcyclohexanone and benzaldehyde was carried out as follows (eqs 1 and 2): An ethereal solution of MeLi–LiBr (1 mmol) was added to a stirred solution of n-$C_6F_{13}I$ (x mmol) and tetradecane (1 mmol; internal standard) at −78 °C over 5 min. After the mixture was stirred at −78 °C for t min, 1.1 mmol of 4-*tert*-butylcyclohexanone or benzaldehyde in 10 mL of ether was added to the mixture for 2–3 min. After being stirred for 0.5 h, the reaction mixture was quenched with aqueous $NaHCO_3$. Yields of **3** and **4** determined by capillary GC are listed in Table II.

Table II. Yield of Perfluorohexylation of Benzaldehyde and 4-*tert*-Butylcyclohexanone

		yield, %			
x, mmol	product	1 min	5 min	10 min	60 min
1.0	**3**	*a*	0	*a*	*a*
	4	6 (15:85)[b,c]	trace	*a*	*a*
1.2	**3**	*a*	9	*a*	*a*
	4	*a*	13 (16:84)[b]	*a*	*a*
1.5	**3**	*a*	34	*a*	*a*
	4	*a*	41 (15:85)[b]	*a*	*a*
2.0	**3**	73	64	56	29
	4	82 (15:85)[b,c]	72 (16:84)[b]	*a*	23 (15:85)[b]
3.0	**3**	*a*	58	*a*	27
	4	*a*	63 (16:84)[b]	*a*	*a*
10.0[d]	**3**	*a*	27	*a*	3

[a] Not examined. [b] The ratio of axial to equatorial alcohols. [c] Isolated yield. [d] A large amount of perfluorohexyl iodide was precipitated.





(13) Trifluoromethylation via single electron transfer from zinc to sulfur dioxide followed by the reaction with trifluoromethyl bromide is known; see ref 5a.

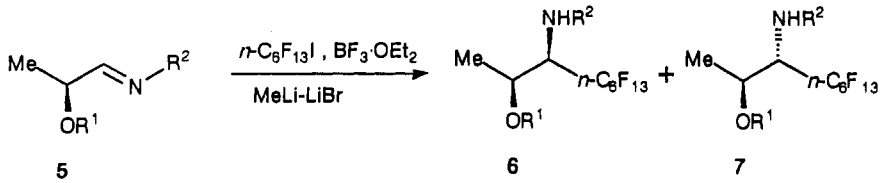
(14) (a) Farnham, W. B.; Calabrese, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 2449. (b) Farnham, W. B.; Dixon, D. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1988**, *110*, 8453. Existence of lithium diphenyliodinate has been proposed in the iodine–lithium exchange reaction of iodobenzene and phenyllithium; see: (c) Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1991**, *113*, 1414; **1989**, *111*, 3444. (d) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101.

(15) Andrieux, C. P.; Gelis, L. Medebielle, M.; Dinson, J.; Saveant, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 3509.

(16) The chemical shift values of the cis isomer (axial alcohol) could be calculated by using the values reported for 1-(pentafluoroethyl)-1-cyclohexanol (ref 8b), whose hydroxyl group is located in the axial position, and *tert*-butylcyclohexane (Kalinowski, H.-O.; Berger, S.; Braun, S. In *Carbon-13 NMR Spectroscopy*; Becconsall, J. K., Transl.; Wiley: New York, 1988). The values thus calculated are 73.58 (C1), 30.24 (C2), 21.12 (C3), and 46.58 (C4), which are closely related to those of the minor alcohol. The larger values of $^4J_{CF}$ coupling constants for the major alcohol (axial R_f) may be ascribed to gauche orientation between the perfluorohexyl group and the C3 carbon.

(17) Johncock, P. *J. Organomet. Chem.* **1969**, *19*, 257. Also see footnote 18 in ref 14b.

Table III. 1,2-Diastereoselectivity in the Perfluorohexylation of Imines 5



5 6 7

	imine 5 R¹	imine 5 R²	solvent[a]	$BF_3·OEt_2$ equiv	yield,[b] %	ratio[c] 6/7
a	$SiMe_2(t\text{-Bu})$	$CH_2CH{=}CH_2$	E	1.2	81	85/15
b	Me	*n*-Pr	E	1.2	46	37/63
b	Me	*n*-Pr	T	1.2	47	19/81
b	Me	*n*-Pr	T	2.0	40	25/75
c	MOM	*n*-Pr	E	1.2	52	19/81
c	MOM	*n*-Pr	T	1.2	42	3/97
d	MOM	$CH_2CH{=}CH_2$	E	1.2	40	19/81

[a] E, ether; T, toluene. [b] Isolated yield. [c] Determined by capillary GC and/or ^{19}F NMR analyses of the reaction mixture.

Table II shows that *n*-$C_6F_{13}Li$ is greatly stabilized in the presence of 1 equiv or more of excess *n*-$C_6F_{13}I$. As the number of equivalents of *n*-$C_6F_{13}I$ was reduced from 2 to 1, the yields of products approached 0%. These results suggest that *n*-$C_6F_{13}Li$ exists as $Li^+,(n\text{-}C_6F_{13})_2I^-$ when *n*-$C_6F_{13}I$ remains in the reaction mixture and that the half-life of $Li^+,(n\text{-}C_6F_{13})_2I^-$ at −78 °C is about 15 min. It should be noted that, in all cases with **4**, the ratio of axial to equatorial alcohols was 15:85–16:84, which may be rather low for the transfer of the perfluorohexyl group from the bulky $Li^+,(n\text{-}C_6F_{13})_2I^-$ species. Although some details of the reaction deserve further study, we suggest that lithium bis(perfluoroalkyl)iodinanide is not the perfluoroalkyl transfer species to electrophiles but instead acts as a more stable carrier of very short-lived (perfluoroalkyl)lithium, which can react with electrophiles.

Diastereoselectivity in Perfluoroalkylation. We next examined the perfluoroalkylation of chiral aldimines. Imines **5a–d** derived from lactic acid were subjected to perfluoroalkylation under reaction conditions described for **1** (Table III). The reaction of α-siloxy imine **5a** produced **6a** and **7a** in an 85:15 ratio, indicating moderate diastereoselectivity (determined by capillary GC). On the other hand, the reverse diastereoselectivity was observed in the reaction of α-alkoxy imines **5b** and **5c** in ether, as indicated by 37:63 and 19:81 ratios, respectively. Changing the solvent from ether to toluene decreased the ratios of **6/7** to 19:81 (**5b**) and 3:97 (**5c**), and the use of a large excess of $BF_3·OEt_2$ (2 equiv) slightly increased it to 25:75 (**5c**).

In order to confirm the stereochemistry, deprotection of silyl and methoxymethyl compounds was carried out. The mixture of amines **6d** and **7d** (19:81) was refluxed with an excess of concd HCl in methanol. After complete disappearance of the original compounds as indicated by GC (2 days), the reaction was quenched with $NaHCO_3$ solution. The reaction mixture contained four components in a 79:11:10:1 ratio. Chromatographic separation of the mixture gave two main fractions (see eq 3); one was composed of two diastereomeric oxazolidines **9** (8%; isomeric ratio, 88:12), and the other contained β-amino alcohols **8** (55%; isomeric ratio, 14:86). The *J*-resolved 2D NMR spectra revealed that the coupling constants between two methine protons of the respective β-amino alcohols **8** are 3.7 Hz for the major isomer and 3.2 Hz for the minor one. The empirical rule regarding the coupling constant of β-amino alcohols ($J_{threo} > J_{erythro}$)[18] thus did not hold properly for **8**. Recrystallization of β-amino alcohols **8** from hexane gave the major isomer in pure form, which on treatment with formalin and concd HCl gave oxazolidine **9**, identical with the minor product from hydrolysis of the amine mixture (**6d** and **7d**). Proton and ^{13}C NMR spectra of this oxazolidine exhibit remarkably large long-range couplings between the methyl and two diastereotopic fluorines ($^4J_{CF}$ = 6 and 3 Hz, $^5J_{HF}$ = 4.1 and 1.4 Hz). Such large couplings were not observed with the minor isomeric oxazolidines.

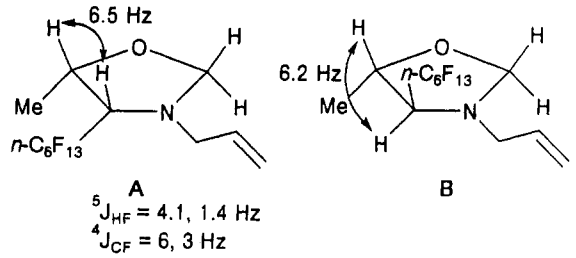
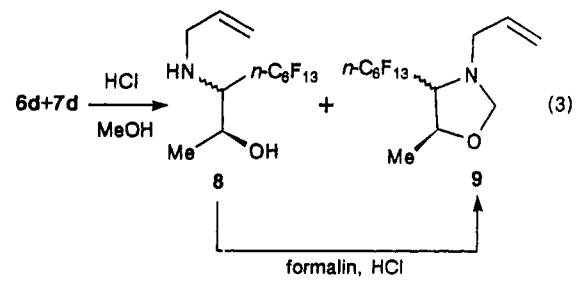


Figure 1. Configurations of **9**.



Similar large long-range couplings were reported in the case of cis methyl and trifluoromethyl groups in cyclopropane derivatives.[19] Large long-range couplings between spatially close fluorine and other atoms are often rationalized by the "through-space" mechanism.[20] In some cases, however, the long-range couplings occurred through intervening bonds which were nicely aligned in the "W" shape.[21] In the case of oxazolidine **9**, $^4J_{CF}/^5J_{HF}$ values are closely related to those reported for 4-fluoro-5-methylphenanthrene derivatives as the "through-space" couplings.[22] Moreover, $^5J_{HF}$ = 4.1 Hz seems too large for

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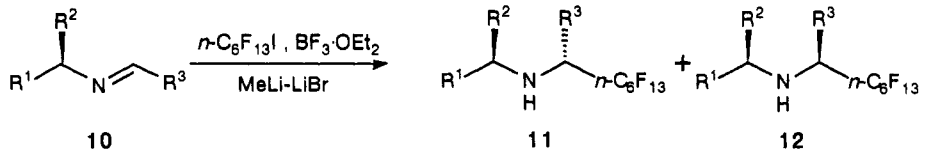
(19) Moss, R. A.; Guo, W.; Denney, D. Z.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1981**, *103*, 6164.

(20) Hilton, J.; Sutcfiffe, L. H. *Prog. Nucl. Magn. Reson. Spectrosc.* **1975**, *10*, 27.

(21) Cushley, R. J.; Wempen, I.; Fox, J. J. *J. Am. Chem. Soc.* **1968**, *90*, 709.

Table IV. Perfluorohexylation of Imines 10 Bearing a Chiral N-Substituent



10 11 12

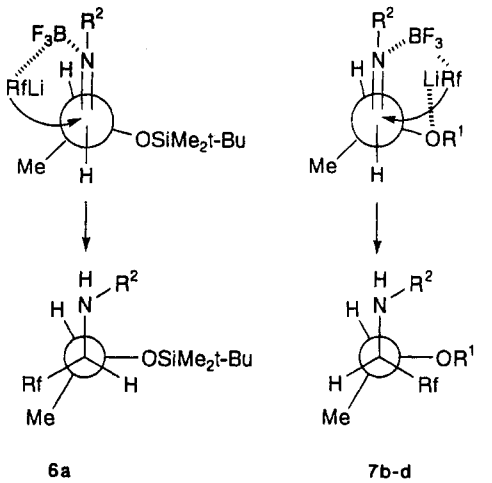
	imine 10					
	R^1	R^2	R^3	solvent[a]	yield,[b] %	ratio[c] 11/12
a	Me	Ph	*i*-Pr	E	90	84/16
a	Me	Ph	*i*-Pr	T	81	84/16
b	Me	Ph	Ph	E	63	77/23
c	Me	Ph	CO_2-*n*-Bu	E	53	77/23
d	*i*-Pr	CO_2Me	Ph	E	54	98/2
d	*i*-Pr	CO_2Me	Ph	T	58	92/8
e	*i*-Bu	CO_2Et	Ph	E	73	94/6
e	*i*-Bu	CO_2Et	Ph	T	87	77/23
f	CH_2Ph	CO_2Et	Ph	E	57	97/3
f	CH_2Ph	CO_2Et	Ph	T	75	96/4
f	CH_2Ph	CO_2Et	Ph	T	25	52/48[d]
g	CH_2Ph	CO_2Et	$CH=CHCH_3$	E	43	96/4
h	CH_2Ph	CO_2Et	*n*-Pr	E	78	88/12

[a] E, ether; T, toluene. [b] Isolated yield. [c] Tentative stereochemical assignment. The ratio was determined by capillary GC analysis of the reaction mixture. [d] The reaction was carried out after the imine and BF_3·OEt_2 were stirred at rt for 1 h.

"through-bond" coupling, because the H–F coupling was the averaged value of three protons on the methyl group. Thus, the large long-range couplings in the oxazolidine can be attributed to "through-space" coupling, suggesting a cis orientation of the methyl and perfluorohexyl groups (**A** in Figure 1). This structure determination was further supported by the apparent behavior of **6d** and **7d** under the hydrolytic conditions mentioned above; **6** was mainly transformed to trans oxazolidine **9B**, while **7d** was hydrolyzed to β-amino alcohol **8**, presumably because of the severe steric interaction between methyl and perfluorohexyl groups. Thus, the major compound obtained from the perfluorohexylation of **5d** is assigned the threo structure (**7d**). Desilylation of the mixture (**6a** and **7a**) obtained in the perfluorohexylation of **5a** gave a diastereomeric mixture of **8**, the major isomer of which was the same as the minor one derived from the mixture of **6d** and **7d**. By comparison of NMR spectra, the major products from the perfluorohexylation of **5b** and **5c** were identified as **7b** and **7c**, respectively.

The diastereofacial selectivity observed in the reaction of **5** does not agree with the prediction according to Cram's chelation model.[23] This disagreement is not surprising, considering similar observations in reactions carried out in the presence of a Lewis acid.[24] Although the mechanism of perfluoroalkylation is not clearly understood, possible transition states accounting for the diastereoselectivity are illustrated in Figure 2. This proposal is based on the assumption that the interaction of BF_3 with the (perfluoroalkyl)lithium should be similar to that which occurs with MeLi.[25]

Diastereoselective addition of organometallics to imines derived from aldehydes and chiral amines is a useful method for the preparation of optically active secondary



6a 7b-d

Figure 2. Proposed transition states for the diastereoselectivity.

amines and amino acid derivatives.[26] 1-Phenylethylamine and α-amino acid derivatives have been widely used for such purposes. The general BF_3-assisted perfluoroalkylation procedure also proved to be successful, and the results obtained with chiral imines **10** are shown in Table IV. The reaction of imines **10a–c**, derived from 1-phenylethylamine, showed moderate diastereoselectivity without showing any dependence on the solvent used. In the reaction of imines **10d–h**, however, better selectivity was realized by using ether rather than toluene as a solvent. This tendency was most enhanced in the case of imine **10e**, where the steric effect would be smallest toward the nucleophilic attack on the imine moiety. In the reaction of **10d**, almost the same degree of diastereoselectivity was observed in both solvents with 2 equiv each of *n*-$C_6F_{17}I$, BF_3·OEt_2, and MeLi–LiBr. These findings suggest that the apparent bulkiness of perfluoroalkylating species increases through solvation by ether.

The relative stereochemistry of (perfluoroalkyl)amines were determined as follows. Pirkle and Hauske have synthesized chiral perfluoroalkylated amines via the reduction of chiral imines derived from perfluoroalkyl ke-

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(25) A MeLi–BF_3 complex is known; see: Lipshutz, B. H.; Ellsworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 1351. Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 5869.

(26) Fiaud, J.-C.; Kagan, H. B. *Tetrahedron Lett.* **1970**, 1813; **1971**, 1019.

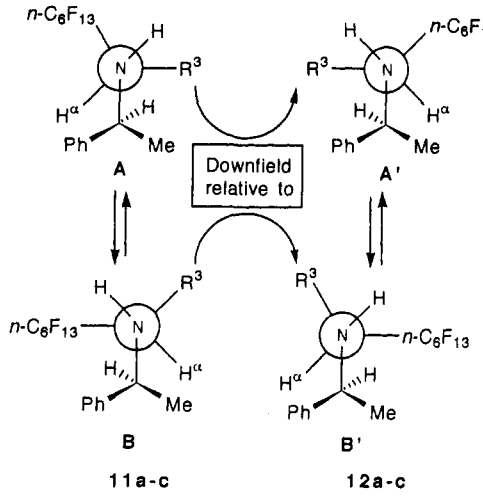


Figure 3. Proposed conformations and stereochemical assignments for **11a–c** and **12a–c** based on ^{1}H NMR chemical shifts.

tones and 1-phenylethylamine,[27] and they reported detailed ^{1}H NMR data for the *S,S* isomer of 2,2,3,3,4,4,4-heptafluoro-1-phenyl-*N*-(1′-phenylethyl)butylamine. By comparison of our ^{1}H NMR data with the above, the relative stereochemistry of the minor isomer (**12b** in Table IV) was confirmed to be *S*,S**. In the ^{1}H NMR spectra, signals for the methine proton (H^α in Figure 3) of the major products from **10b** and **10c** appear at higher field than those of the minor ones, while the opposite is observed in the reaction of **10a** (see Experimental Section). On the other hand, isopropyl (**11a** and **12a**) and *n*-butyl ester (**11c** and **12c**) groups of the minor isomers show an upfield shift relative to the major ones. These NMR data can be rationalized by considering the steric bulk of n-C_6F_{13}, *i*-Pr, Ph, and CO_2-*n*-Bu (n-$C_6F_{13} \cong$ *i*-Pr > Ph $\cong$ CO_2-*n*-Bu).[28] Stable conformers of both isomers **11a–c** and **12a–c** are illustrated in Figure 3. In the isomers from **10a**, both conformers (**A** and **B** for **11a**; **A′** and **B′** for **12a**) may be comparable because the steric effects of n-C_6F_{13} and *i*-Pr groups are similar, while the conformers **A** and **A′** may be predominant in the isomers from **10b** and **10c**. In the conformer **B′**, both H^α and R^3 are expected to show upfield shifts due to the phenyl anisotropy,[29] whereas in the conformer **A′**, H^α and R^3 are expected to show downfield and upfield shifts, respectively. Thus, the major products derived from **10a** and **10c** are proposed to be *S*,R** isomers **11a** and **11c** as shown in Table IV.

The relative stereochemistry of the other (perfluoroalkyl)amines **11d–f** and **12d–f** can be determined from their ^{1}H NMR chemical shift nonequivalence.[29] Chemical shifts of the ester groups of the minor isomers show a marked upfield shift, while signals due to the α'-methine proton ($H^{\alpha'}$) and R^1 groups of the major isomers appear at higher field than those of the minor ones (see Experimental Section). Considering the fact that the ester groups are smaller in steric bulk than any of R^1 groups (*i*-Pr, *i*-Bu, and Bz),[28] the most favorable conformations of **11d–f** (*S,R*) and **12d–f** (*S,S*) may be illustrated as shown in Figure 4. In **12d–f**, the ester alkyl groups are expected to show upfield shifts due to the phenyl anisotropy.[29] The α'-methine proton ($H^{\alpha'}$) and R^1 group of **11d–f** are expected to behave similarly. Thus, the major isomers are proposed to possess

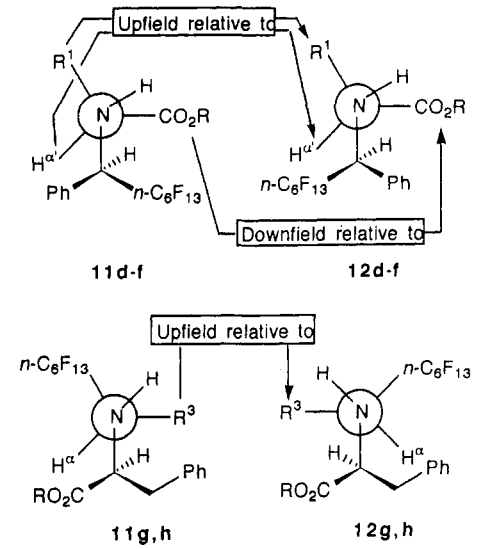
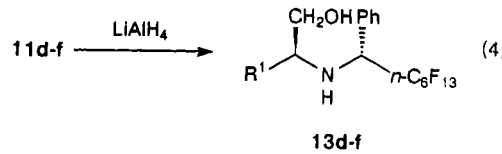


Figure 4. Proposed conformations and stereochemical assignments for **11d–h** and **12d–h** based on ^{1}H NMR chemical shifts.

structures **11d–f**, which is consistent with the diastereofacial selectivity observed in the addition of hydrogen cyanide,[30] ketene silyl acetal,[12c] and Grignard reagents[31] to chiral imines from amino acid esters. Similarly, the major products from **10g** and **10h** are assigned structures **11g** and **11h** (Figure 4), respectively, assuming that the n-C_6F_{13} group is far larger than the R^3 groups (allyl and propyl).[28]

Neither column chromatography nor GPC could effect separation of these isomers (**11d–h** and **12d–h**), however. HPLC analysis of the isomers using a chiral column (Chiralcel-OJ) did not allow exact estimation of the optical purity owing to insufficient separation and/or interference from impurities. Therefore, these isomers were reduced with $LiAlH_4$ to β-amino alcohols, and the major isomers **13d–h** were then isolated by column chromatography (eq 4). Enantiomers of **13f** were well separated by HPLC using the above chiral column (3% 2-propanol/hexane as eluent), and the enantiomeric purity was 86% ee. As the optical purity of (*S*)-phenylalanine ethyl ester hydrochloride used was >96%, this lower than expected optical purity may be attributed to racemization during the preparation of imine **10f**.



(4)

Preparation of Perfluoroalkylated Primary Amines. Perfluoroalkylated primary amines could be easily obtained by removal of the N-protecting alkyl group from the amines obtained above. Thus, treatment of *N-tert*-butylamine **2b** with concd HCl in acetic acid at 110 °C gave **14** in quantitative yield (eq 5). The *N*-1-phenylethyl group of **11c** and **12c** could be removed by hydrogenolysis over $Pd(OH)_2/C$ under 10–15 kg/cm^2 hydrogen pressure, giving butyl (perfluorohexyl)glycinate (**15c**) in 66% yield (eq 6). Palladized charcoal was ineffective for the present purpose. As the basicity and nucleophilicity of the amino group in **15c** are greatly reduced by the presence of the perfluorohexyl group, this amino

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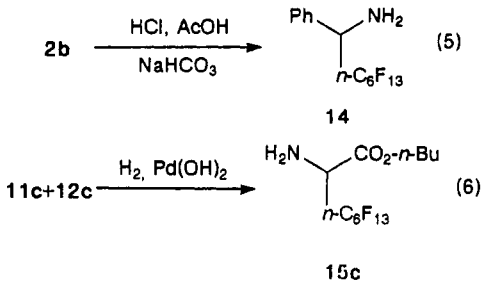
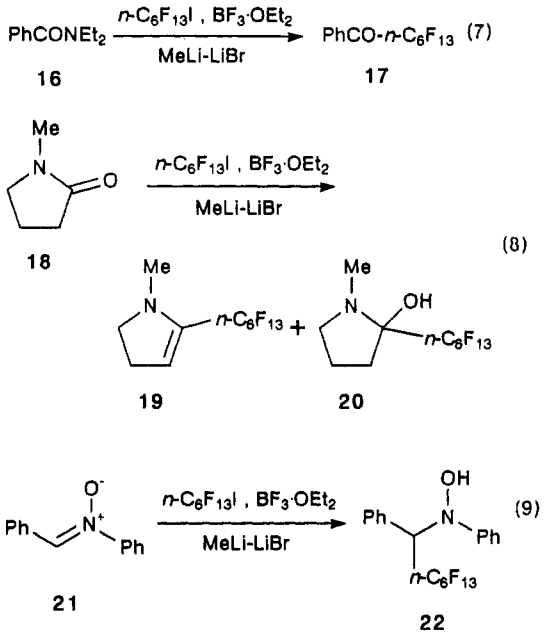
(30) Yamada, S.; Hashimoto, S.-i. *Chem. Lett.* **1976**, 921.
(31) Hashimoto, S.-i.; Yamada, S.; Koga, K. *J. Am. Chem. Soc.* **1976**, *98*, 7450; *Chem. Pharm. Bull.* **1979**, *27*, 771.

acid ester can be distilled without decomposition and stored as the free base.

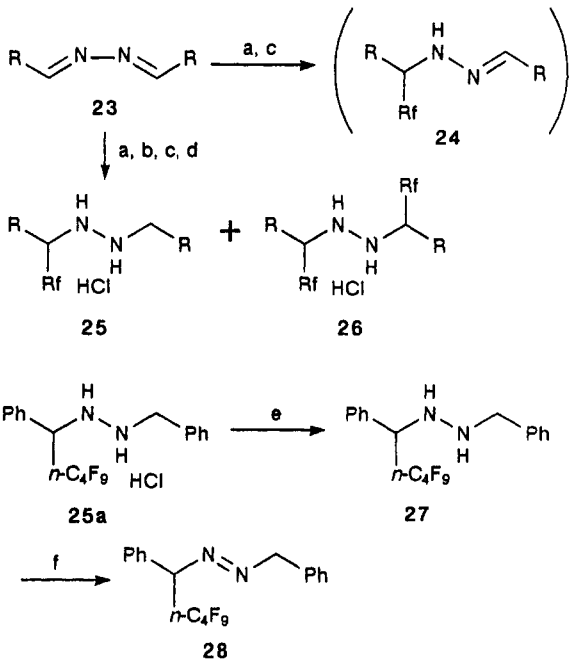


Perfluoroalkylation of Other Compounds. To further define the scope and limitations of our perfluoroalkylation method, reactions with other carbon–nitrogen functionalities were carried out. In the presence of BF_3·OEt_2, the amide carbonyl group participated in perfluoroalkylation. Thus, *N,N*-diethylbenzamide (**16**) gave, under the general perfluorohexylation conditions, (perfluoroheptanoyl)benzene (**17**)[8a] in 66% yield (eq 7). The reaction of *N*-methyl-2-pyrrolidone (**18**) with *n*-$C_6F_{13}I$ gave a mixture of cyclic enamine **19** and cyclic hemiacetal **20** in a ratio of 2:1 (eq 8). Distillation of the reaction mixture caused spontaneous loss of water from the hemiacetal (**20**) to provide pure **19** in 55% yield. Similarly, nitrone **21** was transformed to perfluorohexylated hydroxylamine **22** in 66% yield (eq 9).



The reaction of aldazine **23a** with 2 equiv each of *n*-C_4F_9I, BF_3·OEt_2, and MeLi–LiBr gave a mixture of hydrazone **24a**, *N*-(1-phenylethyl)-*N'*-benzylidenehydrazine, and unchanged **23a** (Scheme I). Disappointingly, all attempts, such as fractional crystallization, column chromatography, and preparative GPC, failed to separate **24a** from the product mixture. Therefore, the mixture was treated with $LiAlH_4$ before the aqueous workup to obtain hydrazine derivatives, from which hydrazine hydrochloride **25a** could be easily isolated by crystallization from HCl-containing ethanol. Free hydrazine base **27** was quantitatively obtained by treatment of **25a** with aqueous NaOH. Compound **27** was rather unstable and easily oxidized even in $CDCl_3$ to form azo compound **28**, which could be isolated by column chromatography on silica gel. The preparative oxidation of hydrazine **27** was incomplete in commercially available chloroform which contains methanol as a stabilizer, but it proceeded under daylight irradiation. Chlorine derived from the decomposition of chloroform may be responsible for the reaction.[32] The perfluoroalkylations of other azines were carried out under similar conditions, and the results are summarized in Table V. *N,N'*-Bis(1-phenylethylidene)hydrazine could not be perfluoroalkylated. Sterically less crowded azine **23b** underwent double perfluoroalkylation, perfluorooctyl groups being introduced on both azine carbons to give **26b**. Monoperfluorooctyl derivative **25b** present as a minor component in the reaction mixture could not be isolated.

Scheme I[a]



[a] Reagents and conditions: (a) R_fI, BF_3·OEt_2, MeLi–LiBr. (b) $LiAlH_4$, BF_3·OEt_2. (c) Aqueous NaOH. (d) HCl. (e) Aqueous NaOH. (f) *hν*, $CHCl_3$.

Table V. Perfluoroalkylation of Azines

azine			yield,[a] %	
23	R	R_fI	25	26
a	Ph	*n*-C_4F_9I	31	–
b	Me	*n*-$C_8F_{17}I$	–	31
c	*i*-Pr	*n*-$C_8F_{17}I$	59	–

Formation of **26b** prompted us to examine the perfluoroalkylation of hydrazone. However, under similar reaction conditions *N,N*-dimethyl-*N'*-benzylidenehydrazine failed to react and the starting material was recovered. Attempted perfluoroalkylation of benzonitrile, *N*-ethylphenylnitrilium tetrafluoroborate,[33] 1-cyclohexyl-2-phenylaziridine,[34] and cyclohexyl isocyanide[35] gave negative results. The former three did not react, and the latter afforded only an intractable polymeric substance.

In summary, an efficient method for the perfluoroalkylation of carbon–nitrogen double bonds including imines, nitrones, azines, 2-isoxazolidines,[36] and azaarenes[37]

(32) An ionic oxidation mechanism was proposed for the reaction of 1,2-dibenzylhydrazine with carbon tetrachloride; see: Kano, K.; Anselme, J.-P. *Bull. Soc. Chim. Belg.* **1988**, *97*, 461.
(33) Fly, J. L.; Ott, R. A. *J. Org. Chem.* **1981**, *46*, 602.
(34) Okada, I.; Ichimura, K.; Sudo, R. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1185.
(35) In refluxing benzene, perfluoroalkyl iodides reacted with isonitriles in the presence of copper to give perfluoroalkyl imidoyl iodides; see: Tordeux, M.; Wakselman, C. *Tetrahedron* **1981**, *37*, 315.

has been developed. The role of perfluoroalkyl organometallic species involved in this reaction is unclear, but (perfluoroalkyl)lithium, which transfers the perfluoroalkyl group to imines, may be stabilized by forming lithium bis(perfluoroalkyl)iodinanide with unreacted perfluoroalkyl iodide. Optically active perfluoroalkylated amines have been prepared via imines using 1-phenethylamine and amino acid esters.

Experimental Section

Melting points are uncorrected. Unless otherwise noted, all NMR spectra were obtained on a JEOL GSX-270 spectrometer at rt using $CDCl_3$ as solvent, tetramethylsilane as an internal standard for ^1H and ^{13}C, and $CFCl_3$ as an internal standard for ^{19}F. Mass spectra were measured under the following ionizing conditions: EI (20 eV) and CI (70 eV, methane as CI gas). Column chromatography was carried out using Wakogel C-200. Gas–liquid chromatography was performed with a 3% OV-1 packed column (1 m) and/or a CBP10-M25 capillary column (25 m). Preparative gel permeation chromatography was performed using JAI LC-08 with JAI-1H (20 mm ID × 60 cm) and JAI-2H (20 mm ID × 60 cm) columns. Ether, THF, and DME were distilled from sodium benzophenone ketyl. Pentane, CH_2Cl_2, benzene, and toluene were distilled from CaH_2 and stored over 4-Å molecular sieves. Perfluoroalkyl iodides were purified by washing with aqueous $NaHSO_3$, drying over Na_2SO_4, and fractional distillation. MeLi–LiBr was prepared from Li and MeBr in ether and titrated prior to use. Other commercially available materials were used without further purification. Imines **1a**,[38] **1b**,[39] **5e**,[40] **10a**,[40] and **10c**[40] were prepared according to the reported methods. Imines **1d** and **1e** were prepared according to the similar methods reported for *N*-[1-(2-thienyl)propylidene]aniline[41] and *N*-isobutylidenepropylamine,[42] respectively. Imines **1c**, **5a**, **5c**, **5d**, **10b**,[43] **10d**,[44] **10e**, **10f**, **10g**, and **10h** were prepared according to a modified method for *N*-2-butenylidenevaline *tert*-butyl ester:[45] A solution of aldehyde (11 mmol) in 10 mL of dry benzene was added to a cooled solution of amine (10 mmol) in 10 mL of dry benzene. Molecular sieves (4 Å) (2 g) were added to the mixture, and the mixture was allowed to warm to rt. After being left overnight, the mixture was filtered, and the filtrate was concentrated in vacuo. In the cases of **10g** and **10h**, the imines were used without further purification, because these imines considerably decomposed on distillation. In other cases, imines were purified by Kugelrohr distillation. 2-[(*tert*-Butyldimethylsilyl)oxy]propanal[46] and 2-(methoxymethoxy)propanal[47] were prepared from the corresponding lactates, and 2-methoxypropanal was prepared by ozonolysis of (*E*)-3-methoxy-2-butene.[48] Azines[49] and nitrone[50] were prepared according to the reported procedures. All perfluoroalkylated products were purified by column chromatography on silica gel followed either by Kugelrohr distillation (liquid) or by recrystallization (solid). Compounds **27** and **28** were purified only by column chromatography, while compounds **25** and **26** were purified only by recrystallization.

***N*-(1-Phenylethylidene)octylamine (1d)**: colorless oil, oven temperature 83 °C/0.07 mmHg (solidified in a freezer); ^1H NMR δ 0.89 (3 H, t, J = 7.0 Hz), 1.1–1.5 (10 H, m), 1.74 (2 H, m), 2.23 (3 H, s), 3.47 (2 H, t, J = 7.3 Hz), 7.35 (3 H, m), 7.76 (2 H, m); ^{13}C NMR δ 14.11, 15.43, 22.67, 27.71, 29.33, 29.55, 30.94, 31.82, 31.87, 52.29, 126.53, 128.16, 129.22, 141.52, 164.75; IR (neat) 2924, 2856, 1634, 1448, 1282 cm^{-1}; MS (EI) m/e 231 (M^+), 230 (M^+ – 1), 216, 202, 188, 174, 160, 146, 132 (base peak). Anal. Calcd for $C_{16}H_{25}N$: C, 83.06; H, 10.89; N, 6.05. Found: C, 83.13; H, 10.80; N, 6.05.

***N*-[2-[(*tert*-Butyldimethylsilyl)oxy]propylidene]allylamine (5a)**: colorless oil, oven temperature 55 °C/0.5 mmHg; ^1NMR δ 0.06 (3 H, s), 0.08 (3 H, s), 0.89 (9 H, s), 1.28 (3 H, d, J = 6.4 Hz), 4.01 (2 H, dd, J = 5.8, 1.3 Hz), 4.33 (1 H, m), 5.05–5.20 (2 H, m), 5.95 (1 H, ddt, J = 17.4, 10.4, 5.8 Hz), 7.55 (1 H, dt, J = 5.2, 1.3 Hz); ^{13}C NMR δ –4.68, –4.59, 18.18, 21.69, 25.82, 62.79, 70.65, 115.96, 135.55, 168.79; IR (neat) 2956, 2860, 1680, 1256, 1094 cm^{-1}; MS (EI) m/e 227 (M^+), 212, 199, 170 (base peak). Anal. Calcd for $C_{12}H_{25}NO_2$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.82; H, 12.07; N, 10.54.

***N*-Benzylidene-1-phenylethylamine (10b)**: colorless oil, oven temperature 105 °C/0.07 mmHg; ^1H NMR δ 1.59 (3 H, d, J = 6.7 Hz), 4.54 (1 H, q, J = 6.7 Hz), 7.2–7.5 (8 H, m), 7.78 (2 H, m), 8.37 (1 H, s); ^{13}C NMR 24.84, 69.72, 126.61, 126.80, 128.24, 128.40, 128.51, 130.54, 136.39, 145.17, 159.43; IR (neat) 3060, 2972, 2844, 1646, 1452 cm^{-1}; MS (EI) m/e 209 (M^+), 194, 105 (base peaks). Anal. Calcd for $C_{15}H_{15}N$: 86.06; H, 7.22; N, 6.68. Found: C, 86.02; H, 7.43; N, 6.38.

Ethyl 2-(benzylideneamino)-3-phenylpropanoate (10f): colorless oil, oven temperature 130 °C/0.06 mmHg; ^1H NMR δ 1.25 (3 H, t, J = 7.0 Hz), 3.15 (1 H, dd, J = 13.6, 8.7 Hz), 3.36 (1 H, dd, J = 13.6, 5.3 Hz), 4.16 (1 H, dd, J = 8.7, 5.3 Hz), 4.20 (2 H, q, J = 7.0 Hz), 7.1–7.3 (5 H, m), 7.40 (3 H, m), 7.69 (2 H, m), 7.93 (1 H, s); ^{13}C NMR 14.15, 39.76, 61.14, 75.02, 126.51, 128.27, 128.45, 128.49, 129.74, 131.01, 135.62, 137.46, 163.63, 171.63; IR (neat) 3028, 2980, 1738, 1644, 1172 cm^{-1}; MS (CI) m/e 310 (M^+ + Et), 282 (M^+ + 1, base peak), 208, 190. Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.73; H, 6.70; N, 4.98.

Perfluoroalkylation of Imines. General Procedure. A solution of the imine (1 mmol) and perfluoroalkyl iodide (1.2 mmol) in 10 mL of dry ether (or dry toluene) was stirred and cooled at –78 °C. As 0.13 mL (1 mmol) of BF_3·OEt_2 was added, in most cases, precipitation of the BF_3–imine complex soon occurred. An ethereal solution of MeLi–LiBr (1.1 mmol) was added to the mixture at –78 °C over 10 min. The mixture became clear near the end of the addition. After the mixture was stirred for 1 h at –78 °C, aqueous $NaHCO_3$ was added to it. The organic phase was separated, and the aqueous phase was extracted with ether. The combined extracts were washed with brine and dried over Na_2SO_4. Isolated yields and structures of starting materials and products are shown in Tables I, III, and IV.

***N*-Ethyl-2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluoro-1-phenylnonylamine (2aa)**: oven temperature 82–84 °C/0.08 mmHg; ^1H NMR δ 1.05 (3 H, t, J = 7.0 Hz), 1.50 (1 H, br s), 2.52 (2 H, m), 4.28 (1 H, dd, J = 18.3, 9.5 Hz), 7.35 (5 H, m); ^{13}C NMR δ 14.80, 41.75, 63.22 (dd, J = 23, 20 Hz), 100–125 (8 C), 128.64, 128.83, 128.96, 134.58; IR (neat) 3036, 2976, 1370, 1326, 1300–1100 cm^{-1}; MS (CI) m/e 554 (M^+ + 1, base peak), 552, 537, 534, 509, 476, 134. Anal. Calcd for $C_{17}H_{12}F_{17}N$: C, 36.91; H, 2.19; N, 2.53. Found: C, 36.65; H, 2.07; N, 2.70.

(*R*,S)-*N*-Allyl-2-[(*tert*-butyldimethylsilyl)oxy]-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-3-nonylamine (6a)**: oven temperature 73 °C/0.6 mmHg; ^1H NMR δ 0.66 (3 H, s), 0.09 (3 H, s), 0.89 (9 H, s), 1.29 (3 H, d, J = 6.4 Hz), 2.72 (1 H, br s), 3.05 (1 H, dd, J = 19.5, 8.2 Hz), 3.47 (2 H, m), 4.34 (1 H, m), 5.11 (1 H, m), 5.21 (1 H, m), 5.87 (1 H, m); ^{13}C NMR δ –5.32, –4.16, 14.09, 23.22, 25.68, 52.58, 62.08 (dd, J = 24, 18 Hz), 65.16 (m), 100–125 (6 C), 116.05, 136.78; IR (neat) 3368, 2956, 1364, 1300–1100 cm^{-1}; MS (EI) m/e 547, 496, 159 (base peak), 115. Anal. Calcd for

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$C_{18}H_{26}F_{13}NOSi$: C, 39.13; H, 4.80; N, 2.90. Found: C, 39.49; H, 4.79; N, 2.56.

(*R,*R**)-*N*-Allyl-2-[(*tert*-butyldimethylsilyl)oxy]-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-3-nonylamine (7a)**: ^{1}H NMR (typical signal) δ 1.25 (d, *J* = 6.4 Hz).

(*S,*R**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-methoxy-*N*-propyl-3-nonylamine (6b)**: ^{1}H NMR δ 0.91 (3 H, t, *J* = 7.3 Hz), 1.29 (3 H, d, *J* = 6.4 Hz), 1.28 (1 H, br s), 1.47 (2 H, m), 2.74 (2 H, m), 3.30 (1 H, dd, *J* = 18.6, 9.8 Hz), 3.34 (3 H, m), 3.72 (1 H, m).

(*S,*S**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-methoxy-*N*-propyl-3-nonylamine (7b)**: oven temperature 62–65 °C/0.3 mmHg; ^{1}H NMR δ 0.92 (3 H, t, *J* = 7.3 Hz), 1.22 (3 H, dt, *J* = 6.4, 1.0 Hz), 1.28 (1 H, br s), 1.47 (2 H, m), 2.64 (1 H, dt, *J* = 11.3, 7.3 Hz), 2.84 (1 H, dt, *J* = 11.3, 7.0 Hz), 3.35 (3 H, s), 3.45 (1 H, m), 3.72 (1 H, m); ^{13}C NMR δ 11.46, 14.61 (t, *J* = 3 Hz), 23.63, 51.75, 56.72, 60.59 (dd, *J* = 22, 19 Hz), 75.46, 100–125 (6 C); IR (neat) 3380, 2968, 1364, 1318, 1300–1100 cm^{-1}; MS (CI) *m/e* 450 (M^+ + 1, base peak), 448, 430, 420, 418, 390, 371, 112. Anal. Calcd for $C_{13}H_{16}F_{13}NO$: C, 34.76; H, 3.59; N, 3.12. Found: C, 34.56; H, 3.52; N, 3.10.

(*S,*R**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-(methoxymethoxy)-*N*-propyl-3-nonylamine (6c)**: ^{1}H NMR (typical signals) δ 1.35 (3 H, d, *J* = 6.4 Hz), 3.07 (1 H, ddm, *J* = ca. 22, 6 Hz), 3.38 (3 H, s), 4.64 (1 H, d, *J* = 7 Hz), 4.67 (1 H, d, *J* = 7.0 Hz); ^{13}C NMR δ 11.45, 19.19, 23.96, 52.35, 55.67, 62.77 (dd, *J* = 24, 20 Hz), 70.34 (br), 95.44, 100–125 (6 C).

(*S,*S**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-(methoxymethoxy)-*N*-propyl-3-nonylamine (7c)**: oven temperature 64 °C/0.25 mmHg; ^{1}H NMR δ 0.92 (3 H, t, *J* = 7.3 Hz), 1.22 (3 H, d, *J* = 6.4 Hz), 1.49 (2 H, sextet, *J* = 7.3 Hz), 1.5 (1 H, br s), 2.64 (1 H, dt, *J* = 11.0, 7.3 Hz), 2.85 (1 H, dt, *J* = 11.0, 7.0 Hz), 3.39 (3 H, s), 3.43 (1 H, ddm, *J* = 20.4, 6.4 Hz), 4.15 (1 H, m), 4.65 (1 H, d, *J* = 7.0 Hz), 4.67 (1 H, d, *J* = 7.0 Hz); ^{13}C NMR δ 11.44, 15.59 (t, *J* = 3 Hz), 23.63, 51.60, 55.51, 61.87 (dd, *J* = 22, 19 Hz), 71.56, 95.30, 100–125 (6 C); IR (neat) 3384, 2964, 1364, 1300–1100 cm^{-1}; MS (CI) *m/e* 480 (M^+ + 1), 448 (base peak), 418. Anal. Calcd for $C_{14}H_{18}F_{13}NO_2$: C, 35.08; H, 3.79; N, 2.92. Found: C, 34.94; H, 3.80; N, 2.82.

(*S,*R**)-*N*-Allyl-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-(methoxymethoxy)-3-nonylamine (6d)**: ^{1}H NMR (typical signals) δ 1.35 (3 H, d, *J* = 6.4 Hz), 3.11 (1 H, ddm, *J* = 19.5, 8.9 Hz), 3.37 (3 H, s), 4.63 (1 H, d, *J* = 7.0 Hz), 4.67 (1 H, d, *J* = 7.0 Hz); ^{13}C NMR δ 19.30, 52.38, 55.75, 61.48 (dd, *J* = 24, 20 Hz), 70.23, 95.43, 100–125 (6 C), 116.45, 136.54.

(*S,*S**)-*N*-Allyl-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-(methoxymethoxy)-3-nonylamine (7d)**: oven temperature 64 °C/0.25 mmHg; ^{1}H NMR δ 1.27 (3 H, d, *J* = 6.4 Hz), 1.54 (1 H, br s), 3.38 (3 H, s), 3.4–3.6 (3 H, m), 4.14 (1 H, m), 4.63 (1 H, d, *J* = 7.0 Hz), 4.66 (1 H, d, *J* = 7.0 Hz), 5.10 (1 H, dm, *J* = 10.7 Hz), 5.21 (1 H, dm, *J* = 18.9 Hz), 5.87 (1 H, m); ^{13}C NMR δ 15.53 (t, *J* = 3 Hz), 51.84, 55.60, 60.51 (dd, *J* = 22, 19 Hz), 71.26, 95.16, 100–125 (6 C), 116.54, 136.39; IR (neat) 2932, 1364, 1300–1100 cm^{-1}; MS (CI) *m/e* 478 (M^+ + 1), 446 (base peak), 89. Anal. Calcd for $C_{14}H_{16}F_{13}NO_2$: C, 35.23; H, 3.38; N, 2.93. Found: C, 35.57; H, 3.30; N, 2.89.

(*S,*R**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-methyl-*N*-(1-phenylethyl)-3-nonylamine (11a)**: oven temperature 100–105 °C/0.15 mmHg; ^{1}H NMR δ 0.94 (3 H, dd, *J* = 6.9, 1.4 Hz), 1.12 (3 H, d, *J* = 7.0 Hz), 1.31 (3 H, d, *J* = 6.4 Hz), 1.50 (1 H, br s), 2.19 (1 H, m), 3.19 (1 H, dm, *J* = 14.6 Hz, H), 4.08 (1 H, m), 7.2–7.4 (5 H, m); ^{13}C NMR δ 16.44 (d, *J* = 3 Hz), 21.21, 23.30, 27.69, 56.04, 59.13 (t, *J* = 20 Hz), 100–125 (6 C), 127.10, 127.43, 128.47, 145.26; IR (neat) 3372, 3032, 2972, 1366, 1318, 1300–1100 cm^{-1}; MS (CI) *m/e* 496 (M^+ + 1), 494, 480, 452, 418, 176, 133, 105 (base peak). Anal. Calcd for $C_{18}H_{18}F_{13}N$: C, 43.65; H, 3.66; N, 2.83. Found: C, 43.47; H, 3.68; N, 2.99.

(*S,*S**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-methyl-*N*-(1-phenylethyl)-3-nonylamine (12a)**: ^{1}H NMR δ 0.74 (3 H, d, *J* = 7.0 Hz), 0.89 (3 H, d, *J* = 6.7 Hz), 1.35 (3 H, d, *J* = 6.4 Hz), 1.50 (1 H, br s), 1.97 (1 H, m), 2.99 (1 H, ddm, *J* = 17.4, 12.5 Hz, H), 4.07 (1 H, m), 7.2–7.4 (5 H, m); ^{13}C NMR δ (typical signals) 16.01 (d, *J* = 4 Hz), 21.09, 24.20, 56.76 (t, *J* = 20 Hz), 127.43, 128.36, 144.70.

(*S,*R**)-2,2,3,3,4,4,5,5,6,6,7,7,7-Tridecafluoro-1-phenyl-*N*-(1-phenylethyl)-1-heptylamine (11b)**: oven temperature 112 °C/0.2 mmHg; ^{1}H NMR δ 1.28 (3 H, d, *J* = 6.4 Hz), 2.00 (1 H, br s), 3.48 (1 H, q, *J* = 6.4 Hz), 4.00 (1 H, dd, *J* = 19.5, 8.2 Hz, H), 7.2–7.4 (10 H, m); ^{13}C NMR δ 24.99, 54.71, 60.59 (dd, *J* = 25, 20 Hz), 100–125 (6 C), 127.24, 127.58, 128.57, 128.71, 128.92, 128.98, 134.10, 143.45; IR (neat) 3068, 3036, 2968, 1364, 1300–1100 cm^{-1}; MS (CI) *m/e* 530 (M^+ + 1), 514, 452, 426, 105 (base peak). Anal. Calcd for $C_{21}H_{16}F_{13}N$: C, 47.65; H, 3.05; N, 2.65. Found: C, 47.34; H, 2.29; N, 2.86.

(*S,*S**)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-1-phenyl-*N*-(1-phenylethyl)-1-heptylamine (12b)**: ^{1}H NMR δ 1.30 (3 H, d, *J* = 6.4 Hz), 1.99 (1 H, br s), 3.73 (1 H, q, *J* = 6.4 Hz), 4.37 (1 H, ddm, *J* = 18.1, 8.4 Hz, H), 7.2–7.4 (10 H, m).

(*S,*R**)-Butyl 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-2-[(1-phenylethyl)amino]octanoate (11c)**: oven temperature 83–85 °C/0.15 mmHg; ^{1}H NMR δ 0.94 (3 H, t, *J* = 7.3 Hz), 1.37 (3 H, d, *J* = 6.4 Hz), 1.38 (2 H, m), 1.64 (2 H, m), 2.28 (1 H, br s), 3.66 (1 H, m), 3.75 (1 H, m, H), 4.23 (2 H, m, CO_2CH_2), 7.30 (5 H, m); ^{13}C NMR δ 13.33, 18.94, 24.78 (d, *J* = 2 Hz), 30.50, 56.74, 60.01, 60.16 (dd, *J* = 25, 21 Hz), 100–125 (6C), 127.21, 127.77, 128.55, 142.79, 168.09; IR (neat) 3336, 3032, 2968, 1744, 1300–1100 cm^{-1}; MS (CI) *m/e* 554 (M^+ + 1), 552, 538, 120, 105 (base peak). Anal. Calcd for $C_{20}H_{20}F_{13}NO_2$: C, 43.41; H, 3.64; N, 2.53. Found: C, 43.12; H, 3.62; N, 2.73.

(*S,*S**)-Butyl 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-2-[(1-phenylethyl)amino]octanoate (12c)**: ^{1}H NMR δ 0.88 (3 H, t, *J* = 7.3 Hz), 1.32 (2 H, m), 1.37 (3 H, d, *J* = 6.4 Hz), 1.49 (2 H, m), 2.28 (1 H, br s), 3.77 (1 H, m), 3.9 (1 H, m, H), 3.99 (2 H, m, CO_2CH_2), 7.30 (5 H, m); ^{13}C NMR δ (typical signals) 18.86, 22.69 (d, *J* = 2 Hz), 30.30, 56.78, 57.58, 60.32 (dd, *J* = 26, 22 Hz), 126.71, 127.59, 128.61, 144.11, 167.77.

(*S,*R**)-Methyl 3-methyl-2-[(1-phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)amino]butanoate (11d)**: oven temperature 106 °C/0.2 mmHg; ^{1}H NMR δ 0.88 (3 H, d, *J* = 6.7 Hz), 0.90 (3 H, d, *J* = 6.7 Hz), 1.92 (1 H, m), 2.42 (1 H, br s), 2.78 (1 H, d, *J* = 5.8 Hz, H), 3.71 (3 H, s, CO_2CH_3), 4.32 (1 H, t, *J* = 12.7 Hz), 7.37 (5 H, m); ^{13}C NMR δ 18.01, 19.34, 31.52, 51.58, 61.80 (dd, *J* = 22, 21 Hz), 63.21, 100–125 (6 C), 128.47, 129.27, 129.79, 132.79, 174.47; IR (neat) 3040, 2968, 1738, 1366, 1300–1100 cm^{-1}; MS (CI) *m/e* 540 (M^+ + 1, base peak), 520, 480, 437, 409, 220, 140. Anal. Calcd for $C_{19}H_{18}F_{13}NO_2$: C, 42.31; H, 3.36; N, 2.60. Found: C, 42.26; H, 3.38; N, 2.65.

(*S,*S**)-Methyl 3-methyl-2-[(1-phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)amino]butanoate (12d)**: ^{1}H NMR δ (typical signals) 2.93 (1 H, d, *J* = 6.7 Hz, H), 3.28 (3 H, s, CO_2CH_3), 4.19 (1 H, dd, *J* = ca. 20, 7 Hz).

(*S,*R**)-Ethyl 4-methyl-2-[(1-phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)amino]pentanoate (11e)**: oven temperature 101 °C/0.2 mmHg; ^{1}H NMR δ 0.70 (3 H, d, *J* = 6.7 Hz), 0.86 (3 H, d, *J* = 6.7 Hz), 1.24 (3 H, t, *J* = 7.0 Hz), 1.43 (2 H, m), 1.79 (1 H, m), 2.20 (1 H, br s), 2.98 (1 H, dd, *J* = 8.2, 6.1 Hz, H), 4.15 (2 H, m, CO_2CH_2), 4.41 (1 H, t, *J* = 12.7 Hz), 7.37 (5 H, m); ^{13}C NMR δ 14.10, 21.58, 22.94, 24.52, 42.76, 56.13, 60.72, 61.51 (dd, *J* = 23, 20 Hz), 100–125 (6 C), 128.51, 129.30, 129.71, 132.94, 174.68; IR (neat) 2964, 1734, 1370, 1300–1100 cm^{-1}; MS (CI) *m/e* 568 (M^+ + 1, base peak), 548, 510, 494, 409. Anal. Calcd for $C_{21}H_{22}F_{13}NO_2$: C, 44.45; H, 3.91; N, 2.47. Found: C, 44.31; H, 3.93; N, 2.48.

(*S,*S**)-Ethyl 4-methyl-2-[(1-phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)amino]pentanoate (12e)**: ^{1}H NMR δ (typical signals) 0.90 (6 H, d, *J* = 6.4 Hz), 1.02 (3 H, t, *J* = 7.0 Hz), 1.44 (2 H, m), 3.28 (1 H, dd, *J* = 8.2, 6.1 Hz, H), 3.72 (2 H, m, CO_2CH_2), 4.20 (1 H, m).

(*S*,*R*)-Ethyl 3-phenyl-2-[(1-phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)amino]propanoate (11f): oven temperature 121 °C/0.2 mmHg; ^{1}H NMR δ 1.19 (3 H, t, *J* = 7.0 Hz), 2.36 (1 H, br s), 2.84 (1 H, dd, *J* = 13.4, 8.6 Hz), 2.99 (1 H, dd, *J* = 13.4, 5.5 Hz), 3.22 (1 H, dd, *J* = 8.6, 5.4 Hz, H), 4.13 (2 H, m, CO_2CH_2), 4.43 (1 H, dd, *J* = 13.7, 11.6 Hz), 7.19–7.77 (10 H, m); ^{13}C NMR δ 13.95, 39.44, 58.94, 60.91, 61.49 (dd, *J* = 24, 20 Hz), 100–125 (6 C), 126.86, 128.44 (2 C), 129.05, 129.34 (2 C), 132.55 (br), 136.76, 173.15; IR (neat) 3352, 3032, 2984, 1734, 1368, 1352, 1300–1100 cm^{-1}; MS (CI) *m/e* 602 (M^+ + 1, base peak), 528, 510. Anal. Calcd for $C_{24}H_{20}F_{13}NO_2$: C, 47.93; H, 3.35; N, 2.33. Found: C, 47.78; H, 3.46; N, 2.40.

(*S*,*S*)-Ethyl 3-phenyl-2-[(1-phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)amino]propanoate (12f): ^{1}H NMR δ 0.97

(3 H, t, J = 7.0 Hz), 2.32 (1 H, br s), 2.93 (2 H, m), 3.46 (1 H, t, J = 7.2 Hz, H), 3.75 (2 H, q, J = 7.3 Hz, CO_2CH_2), 4.12 (1 H, dd, J = 18.3, 9.2 Hz), 7.1–7.4 (10 H, m).

(S*,R*)-Ethyl 3-phenyl-2-[(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluoro-2-decen-4-yl)amino]propanoate (11g): oven temperature 114 °C/0.2 mmHg; ^{1}H NMR δ 1.18 (3 H, t, J = 7.0 Hz), 1.68 (3 H, dd, J = 6.4, 1.5 Hz), 1.77 (1 H, br s), 2.92 (1 H, dd, J = 13.4, 7.6 Hz), 2.99 (1 H, dd, J = 13.4, 6.4 Hz), 3.56 (1 H, dd, J = 7.6, 6.4 Hz), 3.75 (1 H, m), 4.11 (2 H, q, J = 7.0 Hz), 5.07 (1 H, ddm, J = 14.4, 9.0 Hz), 5.63 (1 H, dq, J = 14.4, 7.0 Hz), 7.1–7.4 (5 H, m); ^{13}C NMR δ 14.02, 17.80, 39.51, 58.88, 60.36 (t, J = 22 Hz), 60.80, 100–125 (6 C), 122.33 (t, J = 3 Hz), 126.88, 128.43, 129.27, 134.39, 136.80, 173.37; IR (neat) 3336, 3032, 2984, 1736, 1368, 1352, 1300–1100 cm^{-1}; MS (CI) m/e 566 (M^+ + 1, base peak), 492, 474. Anal. Calcd for $C_{21}H_{20}F_{13}NO_2$: C, 44.61; H, 3.57; N, 2.48. Found: C, 44.36; H, 3.80; N, 2.52.

(S*,S*)-Ethyl 3-phenyl-2-[(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluoro-2-decen-4-yl)amino]propanoate (12g): ^{1}H NMR δ (typical signals) 1.17 (3 H, t, J = 7.0 Hz), 1.59 (3 H, dd, J = 7.0, 1.8 Hz), 5.29 (1 H, m), 5.87 (1 H, dq, J = 14, 7.0 Hz).

(S*,R*)-Ethyl 3-phenyl-2-[(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluorodec-4-yl)amino]propanoate (11h): oven temperature 110 °C/0.2 mmHg; ^{1}H NMR δ 0.75 (3 H, t, J = 7.0 Hz), 1.08 (1 H, m), 1.18 (3 H, t, J = 7.2 Hz), 1.32 (2 H, m), 1.49 (1 H, m), 1.99 (1 H, br s), 2.84 (1 H, dd, J = 13.6, 7.9 Hz), 2.97 (1 H, dd, J = 13.6, 6.1 Hz), 3.10 (1 H, m), 3.61 (1 H, dd, J = 7.9, 6.1 Hz), 4.11 (2 H, m), 7.1–7.4 (5 H, m); ^{13}C NMR δ 13.64, 13.91, 18.59, 30.95 (t, J = 3 Hz), 40.89, 58.81 (t, J = 21 Hz), 60.87, 62.36, 100–125 (6 C), 126.75, 128.41, 129.35, 137.25, 173.82; IR (neat) 3364, 3032, 2968, 1736, 1366, 1352, 1300–1100 cm^{-1}; MS (CI) m/e 568 (M^+ + 1, base peak), 494, 476, 91. Anal. Calcd for $C_{21}H_{22}F_{13}NO_2$: C, 44.45; H, 3.91; N, 2.47. Found: C, 44.45; H, 3.75; N, 2.42.

(S*,S*)-Ethyl 3-phenyl-2-[(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluorodec-4-yl)amino]propanoate (12h): ^{1}H NMR δ (typical signals) 0.89 (3 H, t, J = 7.0 Hz), 1.14 (3 H, t, J = 7.3 Hz), 2.91 (2 H, m), 3.16 (1 H, m), 3.67 (1 H, dd, J = 7.6, 6.1 Hz), 4.07 (2 H, m); ^{13}C NMR δ 13.84, 14.02, 18.84, 31.26 (m), 40.40, 58.94 (t, J = 22 Hz), 60.79, 62.38, 126.72, 128.28, 129.28, 136.72, 174.44.

Postaddition Procedure of BF_3–1a. To a solution of n-$C_6F_{13}I$ (0.892 g, 2 mmol) in ether (10 mL) was added an ethereal solution of MeLi–LiBr (1.2 M, 0.83 mL, 1 mmol) with stirring at −78 °C over 10 min. Immediately after the addition, an ethereal suspension (10 mL) of imine **1a** (0.133 g, 1 mmol) and BF_3·OEt_2 (0.13 mL, 1 mmol) was added to the colorless solution through a dropping funnel for 5 min. The mixture was stirred for 1 h and then quenched with aqueous $NaHCO_3$. Usual workup of the mixture gave 0.344 g (76%) of **2ab**.

4-*tert*-Butyl-1-(perfluorohexyl)-1-cyclohexanol (4): cis:trans = 1:4; colorless needles (hexane), mp 76–82 °C (subl); ^{1}H NMR δ 0.87 (9 H of major isomer, s), 0.88 (9 H of minor isomer, s), 1.0–2.5 (10 H, m); ^{13}C NMR cis isomer (axial alcohol) 21.24 (br s, C3), 27.35, 30.44 (t, J = 2 Hz, C2), 32.33, 47.01 (C4), 73.75 (t, J = 23 Hz, C1), 100–125 (6 C); trans isomer (equatorial alcohol) 22.86 (t, J = 2 Hz, C3), 27.47, 32.39, 34.24 (t, J = 1 Hz, C2), 45.95 (C4), 73.78 (t, J = 23 Hz, C1), 100–125 (6 C); IR (KBr) 3420, 2960, 1300, 1100 cm^{-1}; MS (CI) m/e 475 (M^+ + 1), 473 (M^+ − 1), 459, 455, 451, 416, 401 (base peak), 381, 155. Anal. Calcd for $C_{16}H_{19}F_{13}O$: C, 40.52; H, 4.04. Found: C, 40.59; H, 4.27.

(S,R)-3-Phenyl-2-[(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-1-phenylheptyl)amino]propanol (13f). To a suspension of $LiAlH_4$ (70 mg, 2 mmol) in 20 mL of ether was slowly added a solution of **11f** (520 mg, 0.87 mmol) in 10 mL of ether with stirring at 0 °C. After the addition, the reaction mixture was allowed to warm up to rt. After being stirred for 2 h, the reaction mixture was quenched by addition of aqueous $NaHCO_3$. The mixture was filtered through a Celite pad, which was washed with ether. The ethereal phase was separated, and the aqueous phase was extracted with ether: yield, 446 mg (87%); colorless crystals (ether/hexane), mp 63–65 °C, 87% ee, $[\alpha]^{20}_D$ = −25.7 (c = 0.59, MeOH); ^{1}H NMR δ 0.92 (1 H, br s), 2.38 (1 H, br s), 2.70 (3 H, m), 3.41 (1 H, d, J = 11.3 Hz), 3.70 (1 H, dd, J = 11.3, 2.1 Hz), 4.31 (1 H, dd, J = 19.2, 8.5 Hz), 6.85 (2 H, m), 6.98 (2 H, m), 7.15–7.35 (6 H, m); ^{13}C NMR δ 38.51, 57.18, 60.70 (dd, J = 25, 20 Hz), 62.27, 100–125 (6 C), 126.76, 128.47, 128.57, 128.75, 128.84, 129.17, 133.23, 137.67; IR (neat) 3352, 2928, 1300–1100 cm^{-1}; MS (CI) m/e 560 (M^+ + 1, base peak) 542, 528, 468, 409, 240, 140, 117. Anal. Calcd for $C_{22}H_{18}F_{13}NO$: C, 47.24; H, 3.24; N, 2.50. Found: C, 46.92; H, 3.27; N, 2.24.

Deprotection of 6d and 7d. To a solution of 3.13 g (6.56 mmol) of the amines **6d** and **7d** (**6d**:**7d** = 81:19) in 30 mL of methanol was added 1.4 mL of 6 N HCl. Then the mixture was refluxed overnight. After the starting material was consumed (monitored by GC, OV-1, 1 m), the reaction was quenched by slow addition of aqueous $NaHCO_3$ and the mixture was extracted three times with ether. The ether extracts were washed with brine, dried over Na_2SO_4, and concentrated to give 2.249 g of a mixture (**8** and **9**, 79:11:10:1) as a pale yellow oil. The mixture was chromatographed on silica gel (hexane/$CHCl_3$) to give 0.239 g (8.2%) of **9** (less polar fractions, diastereomeric ratio = 12:88) as a colorless oil and 1.562 g (55%) of **8** (more polar fractions, diastereomeric ratio = 86:14) as colorless crystals. Recrystallization of the diastereomeric **8** from hexane gave the major isomer of **8** in a pure form.

3-(Allylamino)-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-nonanol (8). *S*,S** isomer (major isomer): colorless crystals (hexane), mp 55–58 °C; ^{1}H NMR δ 1.16 (3 H, d, J = 6.3 Hz), 1.60 (1 H, br s), 2.75 (1 H, br s), 3.34 (1 H, ddt, J = 13.8, 6.1, 1.2 Hz), 3.45 (1 H, tdm, J = 15.0, 3.7 Hz), 3.61 (1 H, ddt, J = 13.8, 6.1, 1.2 Hz), 4.14 (1 H, m), 5.15 (1 H, ddt, J = 10.1, 1.8, 1.2 Hz), 5.23 (1 H, ddt, J = 17.1, 1.8, 1.2 Hz), 5.86 (1 H, ddt, J = 17.1, 10.1, 6.1 Hz); ^{13}C NMR δ 17.86, 52.19, 61.77 (dd, J = 22, 19 Hz), 64.93 (d, J = 2 Hz), 100–125 (6 C), 116.95, 135.98; IR (KBr) 3308, 3250, 2984, 1368, 1314, 1300–1100 cm^{-1}; MS (CI) m/e 434 (M^+ + 1, base peak), 416, 388. Anal. Calcd for $C_{12}H_{12}F_{13}NO$: C, 33.27; H, 2.79; N, 3.23. Found: C, 33.08; H, 2.84; N, 3.24. *S*,R** isomer (minor isomer): colorless oil; ^{1}H NMR δ 1.30 (3 H, d, J = 6.5 Hz), 1.70 (2 H, br s), 3.05 (1 H, dddm, J = 14.3, 10.6, 3.2 Hz), 3.38 (1 H, ddt, J = 13.8, 6.4, 1.2 Hz), 3.51 (1 H, ddt, J = 13.8, 6.1, 1.2 Hz), 4.14 (1 H, qd, J = 6.5, 3.2 Hz), 5.16 (1 H, ddt, J = 10.1, 1.8, 1.2 Hz), 5.22 (1 H, ddt, J = 17.1, 1.8, 1.2 Hz), 5.86 (1 H, ddt, J = 17.1, 10.1, 6.1 Hz).

3-Allyl-5-methyl-4-(tridecafluorohexyl)oxazolidine (9): colorless oil, oven temperature 70 °C/0.15 mmHg. *S*,R** isomer (major isomer): ^{1}H NMR δ 1.46 (3 H, d, J = 6.2 Hz), 3.16 (1 H, ddd, J = 19.8, 6.6, 6.2 Hz), 3.34 (1 H, dd, J = 13.6, 5.5 Hz), 3.41 (1 H, dd, J = 13.6, 7.6 Hz), 4.19 (1 H, quint-d, J = 6.2, 0.9 Hz), 4.27 (1 H, ddd, J = 6.9, 0.9, 0.6 Hz), 4.49 (1 H, dt, J = 6.9, 0.6 Hz), 5.15–5.25 (2 H, m), 5.85 (1 H, m); ^{13}C NMR δ 20.41, 59.96, 69.39 (dd, J = 26, 19 Hz), 73.18, 86.25, 100–125 (6 C), 118.34, 135.08; IR (KBr) 2988, 1352, 1300–1100 cm^{-1}; MS (CI) m/e 446 (M^+ + 1, base peak), 426, 126. Anal. Calcd for $C_{13}H_{12}F_{13}NO$: C, 35.07; H, 2.72; N, 3.15. Found: C, 35.02; H, 2.61; N, 3.11. *S*,S** isomer (minor isomer): colorless oil; ^{1}H NMR δ 1.48 (3 H, ddd, J = 6.9, 4.1, 1.4 Hz), 3.34 (1 H, ddm, J = 13.8, 7.4 Hz), 3.41 (1 H, ddm, J = 13.8, 5.3 Hz), 3.54 (1 H, ddm, J = 26.8, 6.5 Hz), 4.28 (1 H, quint, J = 6.7 Hz), 4.28 (1 H, d, J = 4.8 Hz), 4.62 (1 H, dd, J = 4.8, 0.9 Hz), 5.1–5.3 (2 H, m), 5.84 (1 H, dddd, J = 17.1, 10.2, 7.4, 5.3 Hz); ^{13}C NMR δ 15.13 (dd, J = 6, 3 Hz), 58.29, 64.19 (dd, J = 30, 20 Hz), 73.78, 85.70 (d, J = 2 Hz), 100–125 (6 C), 118.34, 134.21.

Conversion of 8 to 9. To a suspension of the major isomer of **8** (433 mg, 1 mmol) in 10 mL of 37% formalin was added 0.2 mL of concd HCl with stirring at rt. The reaction mixture gradually became clear during 15 min. After 45 min, an aqueous solution of $NaHCO_3$ and ether was added to the mixture. The organic phase was separated, and the aqueous phase was extracted twice with ether: yield, 421 mg (95%). The oxazolidine corresponded to the minor isomer of **9** obtained in the above experiment.

1-Phenyl-2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptylamine (14). A solution of *N*-*tert*-butylamine **2b** (241 mg, 0.5 mmol) in a mixture of acetic acid (1 mL) and concd HCl (1 mL) was heated at 110 °C for 1 day. During this period, white solids appeared. The reaction mixture was quenched by addition of aqueous $NaHCO_3$ and ether. The ethereal layer was separated, and the aqueous layer was extracted twice with ether: yield, 197 mg (93%); colorless oil, oven temperature 68–70 °C/0.3 mmHg; ^{1}H NMR δ 1.81 (2 H, br s), 4.48 (1 H, dd, J = 15.0, 11.9 Hz), 7.36 (5 H, m); ^{13}C NMR δ 57.03 (t, J = 23 Hz), 100–125 (6 C), 128.20, 128.64, 128.95, 135.68 (d, J = 3 Hz); IR (neat) 3336, 3040, 1364, 1316, 1300–1100 cm^{-1}; MS (CI) m/e 426 (M^+ + 1), 409, 406, 386, 348,

106 (base peak). Anal. Calcd for $C_{13}H_8F_{13}N$: C, 36.72, H, 1.90; N, 3.29. Found: C, 36.38; H, 1.89; N, 3.37.

Butyl 2-Amino-3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctanoate (15c). The mixture of **11c** and **12c** (**11c:12c** = 77:23, 1.103 g, 2 mmol), $Pd(OH)_2/C$ (0.5 g), and THF (50 mL) were placed in a stainless steel autoclave. The pressure vessel was sealed and pressured to 10–13 kg/cm^2 with H_2. The mixture was stirred under the H_2 pressure at rt for 5 h. Then the pressure on the vessel was released, the vessel was opened, and the mixture was filtered: yield, 0.476 g (66%); pale yellow oil, oven temperature 65–68 °C/0.4 mmHg; ^{1}H NMR δ 0.94 (3 H, t, J = 7.3 Hz), 1.42 (2 H, m), 1.61–1.72 (2 H, m), 1.85 (2 H, br s), 4.13 (1 H, dd, J = 14.2, 10.2 Hz), 4.23 (2 H, t, J = 6.6 Hz); ^{13}C NMR δ 13.39, 18.86, 30.28, 56.25 (t, J = 24 Hz), 66.29, 167.45; IR (neat) 2968, 1750, 1300–1100 cm^{-1}. Anal. Calcd for $C_{12}H_{12}F_{13}NO_2$: C, 32.09, H, 2.69; N, 3.12. Found: C, 31.81; H, 2.70; N, 3.12.

1-Methyl-2-(tridecafluorohexyl)pyrroline (19): colorless oil, oven temperature 58 °C/0.26 mmHg; ^{1}H NMR δ 2.51 (2 H, m), 2.58 (3 H, t, J = 1.8 Hz), 3.21 (2 H, t, J = 9.2 Hz), 5.44 (1 H, m); ^{13}C NMR δ 28.65, 39.51, 57.40, 110–125 (6 C), 112.46 (t, J = 6 Hz), 140.97 (t, J = 25 Hz); IR (neat) 2968, 1330, 1312, 1300–1100 cm^{-1}; MS (CI) m/e 402 (M^+ + 1, base peak), 401, 382. Anal. Calcd for $C_{11}H_8F_{13}N$: C, 32.93; H, 2.01; N, 3.49. Found: C, 32.68; H, 2.11; N, 3.60.

2-Hydroxy-1-methyl-2-(tridecafluorohexyl)pyrrolidine (20): ^{1}H NMR δ 1.84 (2 H, m), 2.0 (1 H, br s), 2.46 (3 H, s), 2.8–3.2 (4 H, m); ^{13}C NMR δ (typical signals) 21.41, 33.10 (t, J = 3 Hz), 37.11, 54.66.

***N*-(2,2,3,3,4,4,5,5,6,6,7,7,7-Tridecafluoro-1-phenylheptyl)-*N*-phenylhydroxylamine (22)**: colorless needles (ether/hexane), mp 65–66 °C; ^{1}H NMR δ 5.00 (1 H, dd, J = 20.7, 9.0 Hz), 5.19 (1 H, s), 7.02 (4 H, m), 7.2–7.4 (6 H, m); ^{13}C NMR δ 70.86 (dd, J = 27, 18 Hz), 100–125 (6 C), 117.71, 123.48, 127.96, 128.34, 128.80, 129.21, 131.34, 150.12 (d, J = 2 Hz); IR (KBr) 3552, 1366, 1320, 1300–1100 cm^{-1}; MS (EI) m/e 517, 501, 409, 390, 198, 182 (base peak), 108. Anal. Calcd for $C_{19}H_{12}F_{13}NO$: C, 44.12; H, 2.34; N, 2.71. Found: C, 43.85; H, 2.39; N, 2.71.

Perfluoroalkylation of Azines. Typical Procedure. *N*,*N*′-Dibenzylidenehydrazine (0.416 g, 2 mmol) and *n*-C_4F_9I (2.08 g, 6 mmol) were dissolved in 20 mL of dry ether and cooled down to ca. −30 °C by a dry ice–acetone bath. To the well-stirred solution was added 0.72 mL (5.5 mmol) of BF_3·OEt_2. The resulting yellow suspension was further cooled to −78 °C, and an ethereal solution of MeLi–LiBr (0.93 M, 5.4 mL, 5 mmol) was added at that temperature over 20 min. During the course of the addition, the mixture became clear. After the mixture was stirred for 1 h at −78 °C, 0.72 mL of BF_3·OEt_2 and 0.2 g of $LiAlH_4$ were successively added to the mixture. Then the mixture was allowed to warm up to rt. After being stirred for 1 h, the reaction mixture was quenched with 10% aqueous NaOH. The organic phase was separated, and the aqueous phase was extracted with ether. The combined extracts were washed with brine, dried over Na_2SO_4, and filtered. A sufficient amount of dry HCl was bubbled into the ethereal filtrate, which immediately became cloudy. After removal of the solvent, the residue was recrystallized from ethanol–ether to give 0.287 mg (0.61 mmol, 31%) of ***N*-benzyl-*N*′-(2,2,3,3,4,4,5,5,5-nonafluoro-1-phenylpentyl)hydrazine hydrochloride (25a)** as colorless needles: mp 152 °C dec; ^{1}H NMR (DMSO-d_6, 60 °C) δ 4.12 (1 H, d, J = 13.1 Hz), 4.16 (1 H, d, J = 13.1 Hz), 5.64 (1 H, dd, J = 19.7, 10.1 Hz), 6.8 (1 H, br), 7.3–7.6 (10 H, m), 11.0 (1 H, br s); ^{13}C NMR (DMSO-d_6, 60 °C) δ 53.48, 60.54 (dd, J = 26, 19 Hz), 100–125 (4 C), 127.85, 128.33, 128.42, 129.33, 129.41, 130.41, 130.61, 131.13; IR (KBr) 3192, 3032, 2928, 1414, 1300–1100 cm^{-1}; MS (EI) m/e 430 (M^+ − HCl), 309, 211, 121, 106. Anal. Calcd for $C_{18}H_{16}ClF_9N_2$: C, 46.32; H, 3.45; N, 6.00. Found: C, 46.42; H, 3.55; N, 5.85.

***N*-(2-Methylpropyl)-*N*′-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-methyl-3-undecyl)hydrazine hydrochloride (25c)**: colorless crystals, mp 134–137 °C subl; ^{1}H NMR (CD_3OD) δ 1.01 (3 H, dd, J = 7.0, 2.1 Hz), 1.05 (3 H, d, J = 6.7 Hz), 1.05 (3 H, d, J = 7.0 Hz), 1.19 (3 H, dd, J = 6.7, ca. 1 Hz), 2.24 (2 H, m), 3.02 (2 H, m), 3.88 (1 H, ddm, J = ca. 20, 10 Hz); IR (KBr) 3212, 2968, 1372, 1336, 1300–1100 cm^{-1}; MS (EI) 562 (M^+ − HCl), 519, 463, 143 (base peak). Anal. Calcd for $C_{16}H_{20}ClF_{17}N_2$: C, 32.09; H, 3.37; N, 4.68. Found: C, 32.11; H, 3.33; N, 4.58.

***N*,*N*′-Bis(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-2-decyl)hydrazine hydrochloride (26b)**: colorless crystals, mp 83–86 °C; ^{1}H NMR (CD_3OD) δ 1.31 (6 H, d, J = 6.7 Hz), 3.61 (2 H, m); IR (KBr) 3420, 3168, 1370, 1330, 1300–1100 cm^{-1}; MS (EI) 924 (M^+ − HCl), 905, 505 (base peak), 477, 462. Anal. Calcd for $C_{20}H_{11}ClF_{34}N_2$: C, 25.00; H, 1.15; N, 2.92. Found: C, 24.89; H, 1.07; N, 2.91.

***N*-Benzyl-*N*′-(2,2,3,3,4,4,5,5,5-nonafluoro-1-phenylpentyl)hydrazine (27)**: pale yellow oil; ^{1}H NMR δ 3.33 (1 H, br s), 3.61 (1 H, m), 3.83 (2 H, s), 4.56 (1 H, m), 7.15–7.40 (10 H, m); ^{13}C NMR δ 55.66, 64.83 (dd, J = 24, 19 Hz), 100–125 (4 C), 127.48, 128.53, 128.65, 128.84 (2 C), 129.15, 133.45, 138.00; IR (neat) 3268, 3068, 3036, 2920, 1354, 1300–1100 cm^{-1}; MS (CI) m/e 431 (M^+ + 1), 411, 291, 150, 121 (base peak).

1-(Benzylazo)-2,2,3,3,4,4,5,5,5-nonafluoro-1-phenylpentane (28): pale yellow oil; ^{1}H NMR δ 4.96 (1 H, d, J = 13.1 Hz), 5.02 (1 H, d, J = 13.1 Hz), 5.12 (1 H, m), 7.15–7.55 (10 H, m); ^{13}C NMR δ 74.35 (m), 81.12 (t, J = 20 Hz), 100–125 (4 C), 127.89, 128.73, 128.77, 129.11, 129.34, 129.63, 131.17 (m), 134.33; IR (neat) 3068, 3036, 2932, 1356, 1300–1100 cm^{-1}; MS (CI) m/e 429 (M^+ + 1, base peak), 409, 119, 107, 105; HRMS (CI) M_r calcd for $C_{18}H_{13}F_9N_2$ + H 429.1012, found 429.1016.

Acknowledgment. This work has been partially supported by a Grant-in-Aid for Scientific Research (No. 02750619) from the Ministry of Education, Science and Culture. We thank Dr. Kazuhiro Shimokawa (Daikin Kogyo Co. Ltd.) for a generous gift of perfluoroalkyl iodides.

Registry No. **1a**, 6852-54-6; **1b**, 6852-58-0; **1c**, 2211-66-7; **1d**, 118825-46-0; **1e**, 6898-82-4; **2aa**, 118825-48-2; **2ab**, 118825-49-3; **2ac**, 118825-50-6; **2ad**, 118825-51-7; **2b**, 118825-52-8; **2c**, 118825-53-9; **2d**, 118825-54-0; **2e**, 118825-55-1; **3**, 57242-02-1; **3b**, 137967-29-4; **3c**, 137967-70-5; **3d**, 137967-71-6; *axial*-**4**, 137967-26-1; *equatorial*-**4**, 137967-27-2; **5a**, 137967-28-3; **5b**, 137967-29-4; **5c**, 137967-30-7; **5d**, 137967-31-8; **6a**, 137967-32-9; **6b**, 138008-58-9; **6c**, 137967-33-0; **6d**, 137967-34-1; **7a**, 137967-35-2; **7b**, 137967-36-3; **7c**, 137967-37-4; **7d**, 137967-38-5; (*R**,*S**)-**8**, 137967-39-6; (*R**,*R**)-**8**, 138008-59-0; **8d**, 40216-61-3; **8e**, 2743-41-1; **8g**, 138283-38-2; **8h**, 137967-44-3; *cis*-**9**, 137967-40-9; *trans*-**9**, 137967-41-0; **10a**, 6797-97-3; **10b**, 62696-51-9; **10c**, 67321-50-0; **10d**, 40216-61-3; **10e**, 2743-41-1; **10f**, 137967-42-1; **10g**, 137967-43-2; **10h**, 137967-44-3; **11a**, 137967-45-4; **11b**, 137967-46-5; **11c**, 137967-47-6; **11d**, 137967-48-7; **11e**, 137967-49-8; **11f**, 137967-50-1; **11g**, 138008-60-3; **11h**, 137967-51-2; **12a**, 137967-52-3; **12b**, 137967-53-4; **12c**, 137967-54-5; **12d**, 137967-55-6; **12e**, 137967-56-7; **12f**, 137967-57-8; **12g**, 137967-58-9; **12h**, 137967-59-0; **13d**, 137967-72-7; **13e**, 137967-73-8; **13f**, 137967-60-3; **14**, 118825-60-8; **15c**, 137967-61-4; **16**, 1696-17-9; **17**, 78960-66-4; **18**, 872-50-4; **19**, 137967-62-5; **20**, 137967-63-6; **21**, 1137-96-8; **22**, 137967-64-7; **23a**, 588-68-1; **23b**, 592-56-3; **23c**, 18300-78-2; **25a**, 137967-65-8; **25c**, 137967-66-9; **25aa**, 137967-74-9; **25ab**, 137967-75-0; **25ad**, 138008-61-4; **26b**, 137967-67-0; **27**, 137967-68-1; **28**, 137967-69-2; BF_3·OEt_2, 109-63-7; *n*-C_4F_9I, 423-39-2; *n*-$C_8F_{17}I$, 507-63-1; *n*-$C_8F_{17}Br$, 423-55-2; *n*-$C_6F_{13}I$, 355-43-1; C_2F_5I, 354-64-3; PhCHO, 100-52-7; 4-*tert*-butylcyclohexanone, 98-53-3.

Supplementary Material Available: ^{19}F, ^{1}H, and ^{13}C NMR data and IR data of **1c,e**, **2ab–ad,b–e**, **3b–d**, **6a–c**, **7b–d**, **8**, **8d,e,g,h**, **9**, **11a–h**, **12a**, **13d–f**, **14**, **15c**, **19**, **20**, **22**, **25aa,ab,ad,a,c**, **26b**, and **28** (6 pages). Ordering information is given on any current masthead page.