# Asymmetric Cyclopropanation of Vinyl Fluorides: Access to Enantiopure Monofluorinated Cyclopropane Carboxylates

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**Abstract**: The transition metal catalyzed cyclopropanation with alkyl diazoacetates of aliphatic or aromatic vinyl fluorides, prepared from the corresponding alkenes by bromofluorination and subsequent dehydrobromination, provides a smooth access to racemic 1:1 mixtures of *cis/trans* isomeric monofluorinated cyclopropane carboxylates. The application of enantiopure bis(oxazoline) ligands and copper(I) triflate makes the reaction *trans*-diastereoselective and enantioselective. For example, treatment of α-fluorostyrene (**3a**) with *tert*-butyl diazoacetate in the presence of 2 mol% of the catalyst prepared from (*S*)-*tert*-leucine-based **11b** and CuOTf gave a 4:1 mixture of *trans*-2-fluoro-2-phenylcyclopropanecarboxylate (**4e**) with 93% ee and the corresponding *cis*-isomer **5e** with 89% ee. The absolute configuration of the *trans*-isomer **4e** has been determined to be (1*S*,2*S*) by X-ray structure analysis of a derivative.

**Key words**: [2+1]-cycloaddition, asymmetric metal catalysis, diazo compounds, carbenoids, fluoroolefins

The cyclopropyl group is known to be one of the most important structural motifs of biological activity and hence is found in a surprisingly large number of naturally occurring compounds.[1] Hence, this function is continuing to attract a lot of attention in synthetic organic chemistry as well as in medicinal and agricultural chemistry.[2] Particularly in pharmaceuticals and in insecticides, the three membered ring frequently represents an important structural element.[1]

On the other hand, it is known for biologically active molecules that the replacement of a C−H bond with a C−F bond can cause dramatic effects on their physiological properties.[3] Therefore, the development of new synthetic approaches to fluorinated compounds is an important field of research.[4] Almost nothing has been known about enantioselective synthesis of monofluorinated cyclopropane carboxylates until very recently, when Imura et al. described the microbial resolution of *cis*-2-fluorocyclopropanecarboxylic acid, which is an important intermediate for the synthesis of the antibacterial quinolone, 7-[7(*S*)-7-amino-5-azaspiro[2.4]heptan-5-yl]-8-chloro-6-fluoro-1-[(1*R*,2*S*)-2-fluorocyclopropyl]-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid,[5] an analogue of the highly potent drug ciprofloxacin (Ciprobay®).

While continuing our research on the synthesis and reactions of vinyl fluorides,[6] we became interested in their ability to react in transition metal-catalyzed cyclopropanations.[7] A related method has been used for the synthesis of fluorinated chrysanthemic acid derivatives, but the reactions suffered from low selectivity and moderate yields.[8] To the best of our knowledge, there have been no previous reports on asymmetric cyclopropanations of fluoro olefins. Herein we wish to report our results on transition metal catalyzed cyclopropanation of vinyl fluorides, which provide a smooth and efficient route to racemic or enantiopure monofluorinated cyclopropane carboxylates.

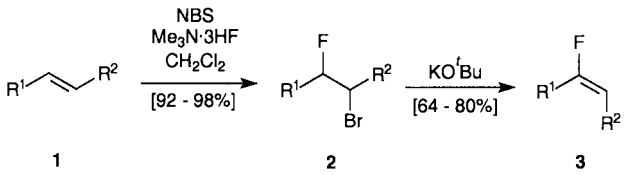
For several years monofluoroolefins proved to be valuable building blocks for the synthesis of new fluorinated compounds by cycloadditions.[6a-d,9] Such monofluoro olefins are easily available by bromofluorination of alkenes and subsequent dehydrobromination of the thus-formed vicinal bromofluorides.[10,11] As fluorination agents, trialkylamine·HF complexes like $Et_3N·3HF$ have been used in combination with *N*-bromosuccinimide (NBS) since these reagents give high yields and are relatively safe to handle.[10] Our studies have shown that $Me_3N·3HF$ is more reactive than $Et_3N·3HF$ and, moreover, led to significantly higher regioselectivity. Bromofluorination of aromatic olefins like **1a−c** exclusively gave the Markovnikov product either with $Et_3N·3HF$ or $Me_3N·3HF$. In contrast, the ratio of regioisomers derived from aliphatic terminal olefins such as hexene was raised from 87:13 ($Et_3N·3HF$) to 95:5 with $Me_3N·3HF$. From these bromofluorides, the corresponding vinyl fluorides have been prepared in good

**Table 1** Bromofluorination of Olefins with NBS/$Me_3N$•3HF and Subsequent Dehydrobromination

| Entry | Olefins **1** | $R^1$ | $R^2$ | Bromo Fluorides **2** | Ratio of Regioisomers | Yield (%) | Vinyl Fluoride **3** | Yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | **1a** | Ph | H | **2a** | >99:1 | 96 | **3a** | 80 |
| 2 | **1b** | *p*-Cl-Ph | H | **2b** | >99:1 | 98 | **3b** | 64 |
| 3 | **1c** | Ph | Me | **2c** | >99:1 | 92 | **3c** | 71 |
| 4 | **1d** | $C_4H_9$ | H | **2d** | 95:5 | 95 | **3d** | 64[a] |

[a] Elimination was carried out without solvent and with KOH as base.

yield by treatment with potassium *tert*-butoxide applying the conditions given in ref.[11] (Scheme 1 and Table 1).



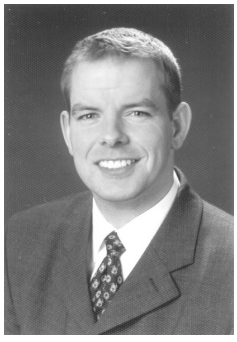

**Scheme 1**

Initial cyclopropanation experiments showed that the conditions and the results concerning the most efficient catalyst reported for non-fluorinated olefins[12] could not simply be applied to vinyl fluorides. By way of example, the reaction of α fluorostyrene (**3a**) with ethyl diazoacetate (EDA) gave much higher yields with copper catalysts, particularly with $Cu(acac)_2$, than with Rh- or Pd-catalysts (Scheme 2 and Table 2), which showed the best results with non-fluorinated alkenes.[12] Moreover, 1:1 mixtures of the *cis*- and *trans*-isomers (The terms *cis* and *trans* with regard to the phenyl and the carboxyl groups are used to make the diastereoselectivity more comparable to the results obtained with non-fluorinated olefins.) were formed independently of the catalyst used, whereas cyclopropanation of styrene with EDA usually gives a 2:1 mixture favoring the *trans*-isomer.[12]

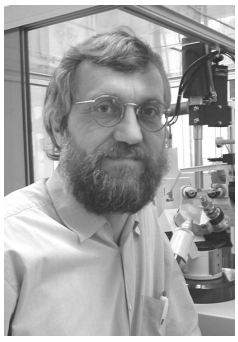
The cyclopropanations of **3a**–**3d** were carried out with $Cu(acac)_2$ (Scheme 3 and Table 3). The reaction mixtures were analyzed by GC and $^{19}F$ NMR. Since an excess of EDA was used in all reactions, small amounts of the ethyl

## Biographical Sketches

**Günter Haufe**, born in 1949 in Saxony, Germany, studied at the University of Leipzig where he received a diploma in chemistry and his doctorate with J. Graefe and M. Mühlstädt in 1975 for work on the mechanism of electrophilic additions. After 18 months of basic military service, he returned to the University of Leipzig and completed his habilitation on transannular cyclizations of unsaturated medium- and large alicyclics in 1985. In the following year, he worked as a research fellow of CNRS with A. Laurent at the University Lyon I, France and as a guest researcher with J. Paasivirta at the University of Jyväskylä, Finland. Since 1988, he was a Lecturer of Bioorganic Chemistry at the University of Leipzig, until he was appointed to his present position as a Professor of Organic Chemistry at the University of Münster in 1991. His work was awarded by the East German Chemical Society with the "Friedrich-Wöhler-Preis" in 1985. In 1994, he was invited as a Visiting Professor to the University of Lyon I, France. His main areas of research relate to the development of selective fluorination methods and synthesis of fluorinated analogues of natural products.



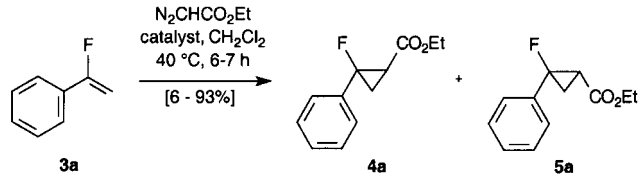
**Oliver Meyer**, born in 1971 in Lemgo, Germany, studied chemistry in Münster and finished his diploma thesis on dihalocarbene addition to vinyl fluorides in 1997. He recently completed his dissertation on the stereoselective cyclopropanation of vinyl fluorides under the supervision of Professor G. Haufe. During his doctorate, he was working as an assistant for the X-ray crystallography department at the Institute of Organic Chemistry.



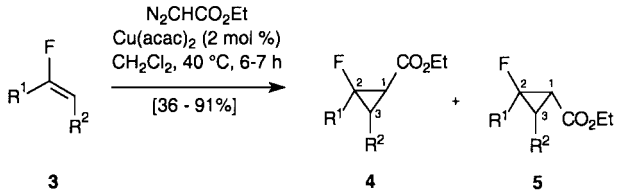
**Roland Fröhlich**, born in 1952 in Soest, Germany, studied chemistry in Münster and Cologne and received his Dr. rer. nat. in 1982. After postdoctoral studies at the Crystallographic Institute of the University of Karlsruhe, he worked as a sales and application manager for Enraf Nonius. Since 1993, he is a senior scientist at the University of Münster and since 1994 a Lecturer of X-ray crystallography at the University of Jyväskylä, Finland.

**Table 2** Cyclopropanation of α-Fluorostyrene (**3a**) with EDA and Different Catalysts

| Catalyst | $PdCl_2$ | $Pd(OAc)_2$ | $RhCl_3$ | $Rh_2(OAc)_4$ | $CuOTf{\cdot}½C_6H_6$ | $Cu(OAc)_2$ | $Cu(acac)_2$ |
|---|---|---|---|---|---|---|---|
| Yield **4a** + **5a** (%, GC) | 16 | 11 | 6 | 25 | 39 | 62 | 93 |




**Scheme 2**




**Scheme 3**

**Table 3** Cyclopropanation of Vinyl Fluorides **3** with EDA Catalyzed by $Cu(acac)_2$

| Entry | Vinyl Fluorides **3** | $R^1$ | $R^2$ | Cyclopropanes **4** and **5** | Ratio **4**:**5** | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | **3a** | Ph | H | **4a** + **5a** | 50:50 | 87 |
| 2 | **3b** | *p*-Cl-Ph | H | **4b** + **5b** | 50:50 | 91 |
| 3 | **3c** | Ph | Me | **4c** + **5c** | 33:67 | 63 |
| 4 | **3d** | $C_4H_9$ | H | **4d** + **5d** | 42:58 | 36 |

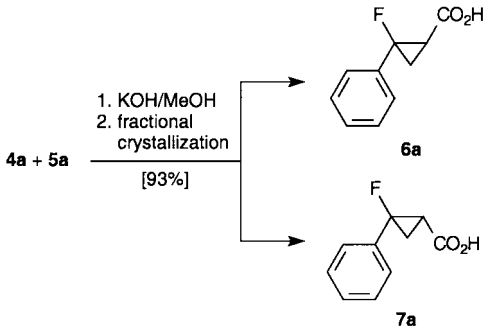
esters of maleic and fumaric acid were formed as byproducts.

It is noteworthy that the cyclopropanation of *cis*-1-fluoro-1-phenylpropene (**3c**) gave an increased portion of **5c** although this isomer can be considered the sterically disfavored one.

Furthermore, the diasteroselectivity of the cyclopropanation of α-fluorostyrene (**3a**) was raised by using *tert*-butyl diazoacetate as a more bulky carbene precursor. The *tert*-butyl 2-fluoro-2-phenylcyclopropanecarboxylates (**4e** and **5e**, not shown) were obtained with a *trans/cis*-ratio of 64:36. The application of $Rh_2(OAc)_4{\cdot}2H_2O$ as the catalyst gave the best yield (70%) in this particular case.

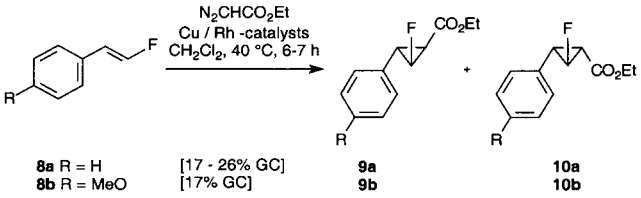
All *cis*- and *trans*-diastereomers were separated by column chromatography. Complete separation of the isomers **4a** and **5a** may also be achieved by fractional crystallization of the corresponding acids **6a** and **7a**, which may be obtained by saponification.

From both isomers (**6a** and **7a**), single crystals were obtained. X-ray structures[13] are shown in Figure 1. The molecules crystallize in the monoclinic space groups $P2_1/c$ (**6a**) or C2/c (**7a**), respectively. In the crystalline state, both diastereomers exist as intermolecularly hydrogen-bonded dimers across the carboxyl groups.




**Scheme 4**

Surprisingly, β-fluorostyrene (**8a**), bearing the fluorine substituent in the terminal position (synthesized as an *E*/*Z*-mixture (86:14) by a Wittig-type reaction),[14] showed a completely different behavior compared to the vinyl fluorides **3a**–**d**. Independent of the catalyst used, only very low conversion of **8** to **9** and **10** was found. Even after the introduction of a *p*-methoxy group, in order to raise the electron density of the double bond, the yield remained as low as 17% (GC) after 6 hours at 40 °C (Scheme 5, shown for the (*E*)-isomers **8**). Elongation of the reaction time (20 hours) did increase the conversion of **8a** slightly to 26%.




**Scheme 5**

These results can be attributed to the mechanism of the cyclopropanation and the different stabilization of cationic positions. It is well known that a fluorine substituent stabilizes cations in α-position by resonance, but destabilizes β-cationic structures.[15] Considering a concerted formation of the cyclopropane carboxylates (Scheme 6, shown for the *trans*-isomers), as proposed by Brookhart et al.[16] and Doyle et al.,[17] the attack of the carbenoid at the terminal position of α-fluorostyrene (**3a**) would create a stabilized positive partial charge in the position α to the fluorine sub-

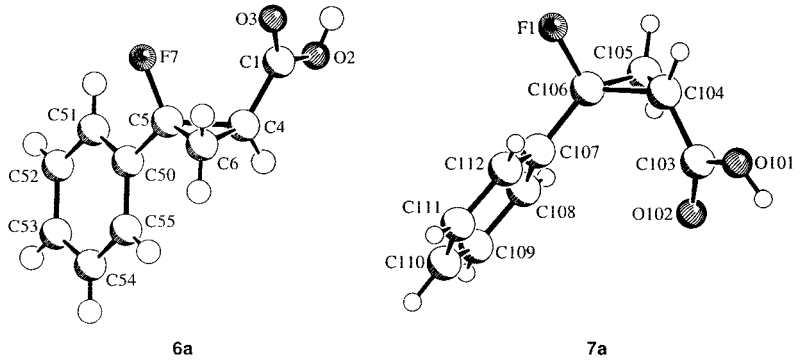
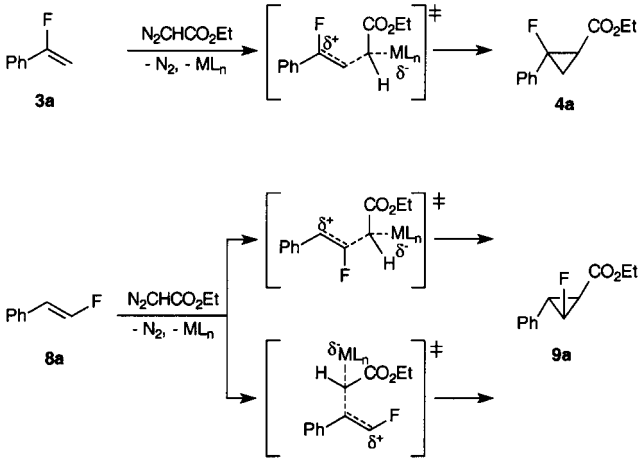



**Figure 1** X-ray Structures of the Fluorinated Cyclopropane Carboxylic Acids **6a** and **7a**.

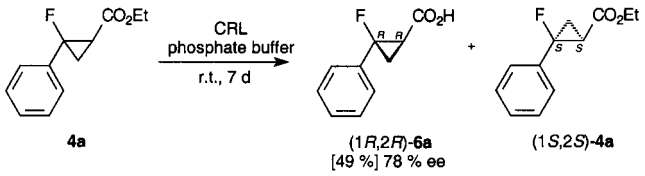
stituent. Subsequent ring closure by nucleophilic attack of the former carbenoid carbon atom and liberation of the metal catalyst leads to the cyclopropane carboxylate **4a**.

In contrast, the analogous attack of the carbenoid to (*E*)-β-fluorostyrene (**8a**) would lead to a cationic benzyl position bearing a β-fluorine substituent. Fluorine in such a position has a strong destabilizing effect and β-fluoroalkyl cations are not known in solution.[15] This could be a reason for the low conversion of 1-fluoroalkenes. On the other hand, the alternative attack of the carbenoid to the benzylic carbon of **8a** leading to a primary homobenzylic cationic structure, which is stabilized by the fluorine, also does not seem to be much favoured. However, the small amount of **9a** is possibly formed in this way (Scheme 6).




**Scheme 6**

In order to obtain optically active monofluorinated cyclopropane carboxylates three different lipases, namely *Candida antarctica* (CAL, Novozym® 435), *Pseudomonas cepacia* (PCL, Amano PS) and *Candida rugosa* (CRL), were screened for their ability to hydrolyze and deracemize the esters **4a** and **5a**, which were separated by column chromatography. Hydrolyses were carried out in phosphate buffer solution ($c$ = 0.1 mol/L) at pH 7.0 and stopped after 7 days. While CAL did not hydrolyse **4a**, PCL converted 15% of this compound to the carboxylic acid **6a**, however with only 6% ee. In contrast, hydrolysis of racemic **4a** with CRL reached 50% conversion after 7 days and yielded 49% of the corresponding cyclopropane carboxylic acid **6a** with 78% ee (Scheme 7). The enantiomeric excesses of the cyclopropane carboxylic acids were determined by $^{19}$F NMR spectroscopy after esterification with enantiopure (−)-menthol using DCC. The absolute configuration of **6a** was assigned to be (1*R*,2*R*) by comparison of the $^{19}$F NMR spectra of the (−)-menthyl ester with that formed from enantiopure (1*S*,2*S*)-**6a** (Table 4, Entry 2, see also Scheme 11). It has to be stressed that under the same conditions no hydrolysis of **5a** took place with any of the tested lipases.



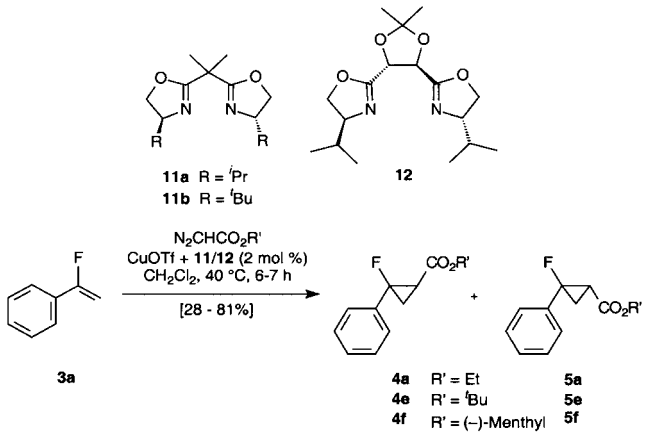

**Scheme 7**

Thus, the asymmetric cyclopropanation of vinyl fluorides using enantiopure catalysts was the way of choice to prepare optically active fluorinated cyclopropane carboxylates. During the last ten years, the asymmetric cyclopropanation of olefins has developed to a very active field of research.[18,19] Nevertheless, there are no reports on the stereoselective cyclopropanation of vinyl fluorides. We expect this method to be a good approach to a wide variety of optically active monofluorinated cyclopropane derivatives.

Among the known ligand systems of enantiopure catalysts for cyclopropanation of alkenes, the $C_2$-symmetric semicorrins, first used by Pfaltz[20] or bis(oxazolines), first used by Masamune[21] and Evans,[22] proved to be highly efficient. Many related catalysts have been shown to be useful as well.[19,23] Moreover, such catalysts have shown their synthetic potential in a wide variety of different asymmet-

ric reactions.[24] While the enantioselectivity of the organometallic ligand is determined by the chiral topology of the catalytic complex, its electronic structure is responsible for the completion of the catalytic cycle.[25]

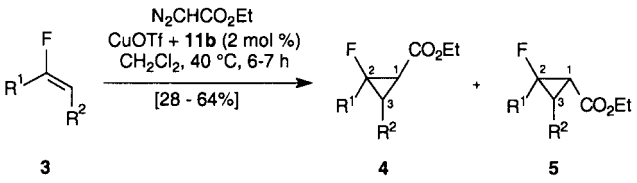
The enantiopure bis(oxazolines) **11** and **12** were synthesized according to published procedures[22,26] from the corresponding amino alcohols, which are readily available from the corresponding amino acids.[27] The enantiopure catalysts were formed in situ by mixing the bis(oxazoline) ligand with a stoichiometric amount of CuOTf·½benzene and used in an amount of 2 mol%. To the solution of the catalyst and the corresponding vinyl fluoride, the diazoacetate was added over a period of about 6 hours at 40 °C and the mixture was stirred for one more hour at this temperature.




**Scheme 8**

The results are summarized in Table 4. Entries 1 and 2 indicate that the bulkiness of the ligand's residue R has no large influence on the diastereoselectivity, but a decisive influence on enantioselectivity. In comparison, the different ligand's "backbones" of **11** and **12** (Table 4, Entries 1 and 3) seem to have almost no effect. Application of a more bulky diazo compound leads to higher diastereo- and enantioselectivity but lower yields (Table 4, Entries 2, 4, and 5).

From other vinyl fluorides such as *p*-chloro-α-fluorostyrene (**3b**), (*E*)-α-fluoro-β-methylstyrene (**3c**), and 2-fluorohex-1-ene (**3d**), the corresponding *cis/trans*-isomeric cyclopropylcarboxylates have been synthesized in an analogous way (Scheme 9 and Table 5).




**Scheme 9**

Scheme 10 illustrates the proposed mechanism for the asymmetric cyclopropanation (shown for the two enantiomers of **4a**).[20b] The bis(oxazoline) ligand and the metal carbene are orthogonal to each other. In case of a *si*-attack by the olefin, a steric interaction with the bulky substituent R would hinder the turn of the ester-group into the plane for cyclopropane formation. Since such an interaction is absent for the *re*-attack, the latter pathway is favored.

In order to prove this mechanistic prediction we determined the absolute configuration of **4a** from Entry 2, Table 4. The pure ester **4a** (89% ee) was hydrolyzed (KOH, MeOH) to **6a** which was recrystallized and subsequently converted to the corresponding amide **13** under Schotten-Baumann conditions using 4-bromoaniline (Scheme 11).

The X-ray structure analysis[13] of the obtained single crystal (triclinic crystal system, space group: P1, enantiopol parameter: −0.017(15) confirmed the configuration of **13** (and therefore of **4a**) to be (1*S*,2*S*) as expected from the proposed mechanism and assumptions regarding the ligand's configuration. Figure 2 just shows one molecule of the unit cell for clarity.

**Table 4** Asymmetric Cyclopropanation of α-Fluorostyrene (**3a**) Catalyzed by Different Copper Catalysts

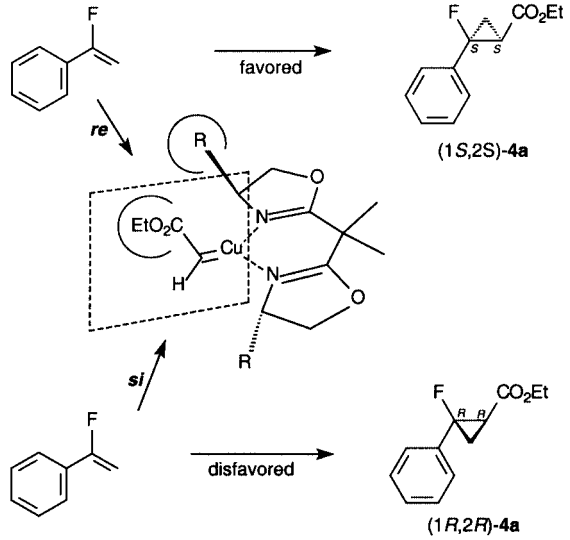
| Entry | Ligands **11** and **12** | R' | Cyclopropane carboxylates **4** and **5** | Ratio **4**:**5** | Yield (%) | ee **4** (%)[a] | ee **5** (%)[a] |
|---|---|---|---|---|---|---|---|
| 1 | **11a** | Et | **4a** + **5a** | 68:32 | 81 | 69 | 54 |
| 2 | **11b** | Et | **4a** + **5a** | 72:28 | 62 | 89 | 80 |
| 3 | **12** | Et | **4a** + **5a** | 66:34 | 75 | 70 | 54 |
| 4 | **11b** | tBu | **4e** + **5e** | 81:19 | 56 | 93[b] | 89[b] |
| 5 | **11b** | (–)-Menthyl | **4f** + **5f** | 81:19 | 28[c] | 92[d] | >98[d] |

[a] The enantiomeric excesses of the cyclopropane carboxylates were determined by $^{19}F$ NMR spectroscopy after hydrolysis and esterification with enantiopure (–)-menthol using DCC.
[b] Determined by chiral GC.
[c] The *cis*-isomer **5f** contains small amounts of the menthyl esters of maleic and fumaric acids as byproducts.
[d] de.

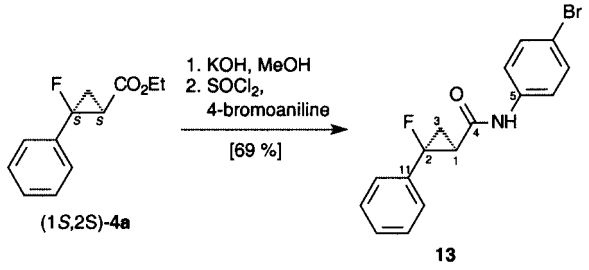
**Table 5** Asymmetric Cyclopropanation of Vinyl Fluorides **3b**, **3c**, and **3d** with EDA and the Copper Catalyst Formed from Ligand **11b**

| Entry | Vinyl Fluoride | $R^1$ | $R^2$ | Cyclopropane carboxylates | Yield (%) | Ratio **4**:**5** | ee **4** (%)[a] | ee **5** (%)[a] |
|---|---|---|---|---|---|---|---|---|
| 6 | **3b** | *p*-Cl-Ph | H | **4b** + **5b** | 64 | 81:19 | 93 | 91 |
| 7 | **3c** | Ph | Me | **4c** + **5c** | 62 | 82:18 | 65 | – |
| 8 | **3d** | $C_4H_9$ | H | **4d** + **5d** | 28 | 64:36 | 16 | – |

[a] The enantiomeric excesses of the cyclopropane carboxylates were determined by $^{19}F$ NMR spectroscopy after hydrolysis and esterification with enantiopure (–)-menthol using DCC.




**Scheme 10**




**Scheme 11**

The thus-formed fluorinated cyclopropane carboxylates **4** are shown to serve as precursors for fluorinated analogues of biogenic amines. By way of example, a fluorinated racemic analogue **15** of the monoamine oxidase inhibitor tranylcypromine has been prepared by Curtius-degradation of racemic **6a** (Scheme 12).

Bromofluoroalkanes **2a**–**d** and vinyl fluorides **3a**–**d** were synthesized according to literature procedures.[10,11] However, in bromofluorinations $Me_3N$•3HF was used instead of $Et_3N$•3HF and elimination of 1-bromo-2-fluorohexane (**2d**) was achieved without solvent using KOH as the base. The spectroscopic data of the bromofluoroalkanes **2a**,[28] **2c**,[28] **2d**[29] and vinyl fluorides **3a**,[30] **3c**,[31] **3d**[32] are in accordance with published data. β-Fluorostyrenes **8a** and

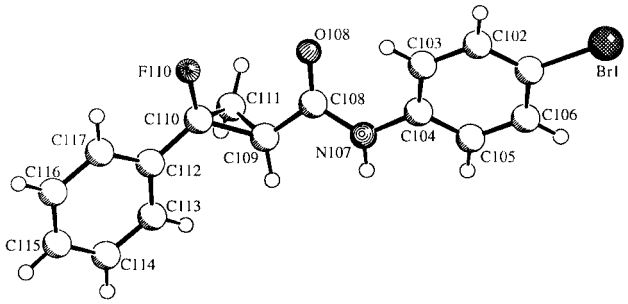
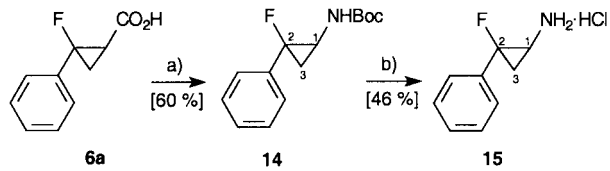



**Figure 2** X-ray Structure of (1*S*,2*S*)-2-Fluoro-2-phenylcyclopropanecarboxylic Acid (4-Bromophenyl)amide (**13**).




a) $NEt_3$, DPPA, $^t$BuOH, Diboc
b) 1N HCl, HOAc

**Scheme 12**

**8b** were prepared by Wittig-type olefination of the corresponding benzaldehydes using *n*-tributylphosphine and trichlorofluoromethane.[14] While (1*R*,3*R*,4*S*)-(−)-menthyl diazoacetate was prepared following the literature procedure,[20b] *tert*-butyl diazoacetate was synthesized by a modified diazo transfer reaction with *p*-acetamidobenzenesulfonyl azide.[33] The bis(oxazoline) ligands **11a**, **11b** and **12** were prepared with little variation according to literature procedures.[22,26] All reagents were obtained from Acros, Merck, or Fluka chemicals. $CH_2Cl_2$ was distilled from $P_4O_{10}$. All cyclopropanation reactions were performed under Ar atm in flame-dried glassware.

If not stated otherwise, $^1H$ (300.13 MHz), $^{13}C$ (75.47 MHz) and $^{19}F$ NMR (282.4 MHz): Bruker WM 300. For some marked cases $^1H$ (600 MHz) and $^{19}F$ NMR (564.3 MHz): Varian 600 MHz apparatus Unity Plus. Carbon multiplicities have been assigned by distortionless enhancement by polarization transfer (DEPT) experiments. Unless otherwise stated, the spectra were obtained in $CDCl_3$ solutions. TMS was used as internal standard for $^1H$-, $CDCl_3$ for $^{13}C$- and $CFCl_3$ for $^{19}F$ NMR spectroscopy. Mass spectra (70 eV): GC/MS coupling: Varian GC 3400/MAT 8230 and data system SS 300 of Finnigan MAT and Varian GC 3400/Varion Saturn IT (Ion Trap) and data system NIST. Elemental analysis: Mikroanalytisches Laboratorium, OC, Universität Münster.

**1-(2-Bromo-1-fluoroethyl)-4-chlorobenzene (2b)**
Prepared from *p*-chlorovinylbenzene (9.7 g, 70 mmol) according to ref.[10] but using $Me_3N{\cdot}3HF$ as fluorinating agent. Yield: 16.4 g (98%).

$^1$H NMR: δ = 3.44−3.59 (m, 2H, $CH_2$), 5.57 (ddd, 1H, $^2J_{H,F}$ = 46.5 Hz, $^3J_{H,H}$ = 4.5 Hz, $^3J_{H,H}$ = 7.2 Hz, CH), 7.20−7.40 (m, 4H, $H_{arom.}$).

$^{13}$C NMR: δ = 33.7 (dt, $^2J_{C,F}$ = 28.0 Hz, C-8), 91.7 (dd, $^1J_{C,F}$ = 179.3 Hz, C-7), 127.0 (dd, $^3J_{C,F}$ = 6.4 Hz, C-2/6), 128.7 (d, C-3/5), 134.9 (s, C-4), 135.4 (ds, $^2J_{C,F}$ = 20.4 Hz, C-1).

$^{19}$F NMR: δ = −174.0 (ddd, $^3J_{H,F}$ = 17.2 Hz, $^3J_{H,F}$ = 22.9 Hz, $^2J_{H,F}$ = 46.5 Hz).

MS (GC/MS): *m/z* (%) = 40/238/236 ($M^+$, 4/13/10), 145/143 ($M^+-CH_2Br$, 38/100), 121 (3), 107 ($M^+$−HCl, 4), 101 (6), 75 ($C_6H_3^+$, 5), 51 ($C_4H_3^+$, 4), 50 (4).

**1-Chloro-4-(1-fluorovinyl)benzene (3b)**
Prepared from **2b** (5.0 g, 21 mmol) according to ref.[11] Yield: 2.1 g (64%).

$^1$H NMR: δ = 4.85 (dd, 1H, $^3J_{H,F(cis)}$ = 17.9 Hz, $^2J_{H,H}$ = 3.6 Hz, $H_A$), 5.00 (dd, 1H, $^3J_{H,F(trans)}$ = 49.4 Hz, $^2J_{H,H}$ = 3.8 Hz, $H_B$), 7.30−7.50 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 90.0 (dt, $^2J_{C,F}$ = 22.9 Hz, C-8), 126.0 (d, C-3/5), 128.7 (d, C-2/6), 130.5 (ds, $^2J_{C,F}$ = 29.2 Hz, C-4), 135.3 (d, C-1),162.0 (ds, $^1J_{C,F}$ = 250.5 Hz, C-7).

$^{19}$F NMR: δ = −108.17 (dd, $^3J_{H,F(trans)}$ = 49.4 Hz, $^3J_{H,F(cis)}$ = 17.9 Hz).

MS (GC/MS): *m/z* (%) = 158/156 ($M^+$, 40/100), 121 ($M^+$−Cl, 55), 101 (121−HF, 40), 75 ($C_6H_3^+$, 12), 51 ($C_4H_3^+$, 16), 50 (8).

**Ethyl 2-Fluoro-2-phenylcyclopropanecarboxylates (4a+5a); Typical Procedure I**
To a solution of **3a** (0.50 g, 4.1 mmol) and $Cu(acac)_2$ (32 mg, 0.12 mmol) in anhyd $CH_2Cl_2$ (5 mL), a solution of ethyl diazoacetate (0.64 mL, 6.15 mmol) in anhyd $CH_2Cl_2$ (3 mL) was added at 40 °C through a syringe pump over a period of 6−7 h. After stirring for one more hour and addition of $CH_2Cl_2$ (100 mL), the mixture was washed successively with sat. $NaHCO_3$ (2 × 50 mL) and $H_2O$ (2 × 50 mL). After drying ($MgSO_4$), the solvent was removed by evaporation (rotary evaporator). Separation of the crude product by column chromatography (silica gel, pentane/$Et_2O$, 40:1) afforded the pure isomers **4a** and **5a** as colorless oils.

**4a:**
Yield: 0.37 g (44%).

$^1$H NMR (600 MHz): δ = 1.26 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, $CH_3$), 1.58 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(cis)}$ = 9.4 Hz, $^3J_{H,F(trans)}$ = 10.7 Hz, $H_A$), 2.15 (ddd, 1H, $^3J_{H,H(cis)}$ = 9.4 Hz, $^3J_{H,H(trans)}$ = 7.8 Hz, $^3J_{H,F(trans)}$ = 2.9 Hz, $H_X$), 2.26 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(trans)}$ = 7.8 Hz, $^3J_{H,F(cis)}$ = 20.4 Hz, $H_B$), 4.2 (m, 2H, $^3J_{H,H}$ = 7.2 Hz, 5-$CH_2$), 7.2−7.4 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 14.1 (q, C-6), 18.9 (dt, $^2J_{C,F}$ = 12.2 Hz, C-3), 29.0 (dd, $^2J_{C,F}$ = 12.7 Hz, C-1), 61.1 (t, C-5), 80.8 (ds, $^1J_{C,F}$ = 226.3 Hz, C-2), 124.6 (dd, $^3J_{C,F}$ = 5.1 Hz, C-8/12), 128.2 (d, C-10), 128.6 (d, C-9/11), 137.5 (ds, $^2J_{C,F}$ = 20.4 Hz, C-7), 167.7 (s, C-4).

$^{19}$F NMR (564.3 MHz): δ = −188.33 (ddd, $^3J_{H,F(trans)}$ = 10.7 Hz, $^3J_{H,F(trans)}$ = 2.9 Hz, $^3J_{H,F(cis)}$ = 20.4 Hz).

MS (GC/MS): *m/z* (%) = 208 ($M^+$, 56), 180 (McLafferty, 18), 163 ($M^+-C_2H_5O$, 20), 160 (180−HF, 14), 153 (40), 135 ($M^+-C_3H_5O_2$, 100), 133 (53), 125 (66), 115 (62) [135−HF], 105 (20), 77 (10), 51 (10).

**5a:**
Yield: 0.36 g (43%).

$^1$H NMR (600 MHz): δ = 0.96 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, $CH_3$), 1.77 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(cis)}$ = 10.4 Hz, $^3J_{H,F(cis)}$ = 19.3 Hz, $H_B$), 1.95 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 12.4 Hz, $H_A$), 2.50 (ddd, 1H, $^3J_{H,H(cis)}$ = 10.4 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 18.1 Hz, $H_X$), 3.9 (q, 2H, $^3J_{H,H}$ = 7.2 Hz, 5-$CH_2$), 7.3−7.5 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 13.9 (q, C-6), 16.4 (dt, $^2J_{C,F}$ = 10.2 Hz, C-3), 27.9 (dd, $^2J_{C,F}$ = 17.3 Hz, C-1), 60.7 (t, C-5), 83.0 (ds, $^1J_{C,F}$ = 221.3 Hz, C-2), 126.3 (ds, $^2J_{C,F}$ = 20.4 Hz, C-7), 128.2 (d, C-8/12), 128.4 (d, C-9/11), 129.2 (d, C-10), 168.8 (s, C-4).

$^{19}$F NMR (564.3 MHz): δ = −154.8 (m).

MS (GC/MS): *m/z* (%) = 208 ($M^+$, 78), 180 (McLafferty, 20), 163 ($M^+-C_2H_5O$, 16), 160 (180−HF, 16), 153 (42), 135 ($M^+-C_3H_5O_2$, 100), 133 (60), 125 (88), 115 (70), 105 (22), 77 (11), 51 (6).

Anal. Calcd for $C_{12}H_{13}FO_2$ (208.23, mixture of **4a** and **5a**): C, 69.22; H, 6.29. Found: C, 69.17; H, 6.55.

**Ethyl 2-(4-Chlorophenyl)-2-fluorocyclopropanecarboxylates (4b, 5b)**
The reaction was carried out following typical procedure I, from **3b** (0.64 g, 4.1 mmol). Separation of the crude product by column chromatography (silica gel, pentane/$CH_2Cl_2$, 1:1) afforded the pure isomers **4b** and **5b** as colorless oils.

**4b:**
Yield: 0.54 g (55%).

$^1$H NMR: δ = 1.29 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, $CH_3$), 1.58 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(cis)}$ = 9.5 Hz, $^3J_{H,F(trans)}$ = 10.7 Hz, $H_A$), 2.15 (ddd, 1H, $^3J_{H,H(cis)}$ = 9.5 Hz, $^3J_{H,H(trans)}$ = 7.9 Hz, $^3J_{H,F(trans)}$ = 3.0 Hz, $H_X$), 2.29 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(trans)}$ = 7.9 Hz, $^3J_{H,F(cis)}$ = 20.0 Hz, $H_B$), 4.15−4.35 (m, 2H, $^3J_{H,H}$ = 7.2 Hz, 5-$CH_2$), 7.15−7.45 (m, 4H, $H_{arom.}$).

$^{13}$C NMR: δ = 14.2 (q, C-6), 18.8 (dt, $^2J_{C,F}$ = 12.7 Hz, C-3), 29.0 (dd, $^2J_{C,F}$ = 11.5 Hz, C-1), 61.2 (t, C-5), 80.3 (ds, $^1J_{C,F}$ = 228.9 Hz, C-2), 126.0 (dd, $^3J_{C,F}$ = 6.35 Hz, C-8/12), 128.8 (d, C-9/11), 134.3 (s, C-10), 136.1 (ds, $^2J_{C,F}$ = 22.9 Hz, C-7), 167.4 (s, C-4).

$^{19}$F NMR: δ = −188.22 (pseudo dd, $^3J_{H,F(trans)}$ = 10.7 Hz, $^3J_{H,F(trans)}$ not resolved, $^3J_{H,F(cis)}$ = 20.0 Hz).

MS (GC/MS): *m/z* (%) = 244/242 ($M^+$, 19/36), 216/214 (McLafferty, 14/32), 187 (40), 185 (34), 171/169 ($M^+-C_3H_5O_2$, 30/96), 159 (92), 151/149 (171/169−HF, 18/31), 139 (28), 134 (66), 133 (169−HCl, 100), 131 (24), 115 (18), 107 (18), 101 (13), 83 (5), 66 (14), 39 (6).

**5b:**
Yield: 0.36 g (36%).

$^1$H NMR: δ = 1.00 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, $CH_3$), 1.81 (ddd, 1H, $^2J_{H,H}$ = 7.2 Hz, $^3J_{H,H(cis)}$ = 10.5 Hz, $^3J_{H,F(cis)}$ = 19.3 Hz, $H_B$), 1.94 (ddd, 1H, $^2J_{H,H}$ = 7.2 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 12.4 Hz, $H_A$), 2.55 (ddd, 1H, $^3J_{H,H(cis)}$ = 10.5 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 17.9 Hz, $H_X$), 3.94 (q, 2H, $^3J_{H,H}$ = 7.2 Hz, 5-$CH_2$), 7.30−7.50 (m, 4H, $H_{arom.}$).

$^{13}$C NMR: δ = 14.0 (q, C-6), 16.6 (dt, $^2J_{C,F}$ = 10.2 Hz, C-3), 28.0 (dd, $^2J_{C,F}$ = 16.5 Hz, C-1), 60.8 (t, C-5), 82.3 (ds, $^1J_{C,F}$ = 221.3 Hz, C-2), 128.5 (d, C-9/11), 129.6 (dd, $^3J_{C,F}$ = 3.8 Hz, C-8/12), 131.7 (ds, $^2J_{C,F}$ = 20.3 Hz, C-7), 135.2 (s, C-10), 168.6 (s, C-4).

$^{19}$F NMR: δ = −155.35 (not resolved ddd, $^3J_{H,F(cis)}$ = 19.3 Hz, $^3J_{H,F(trans)}$ = 12.4 Hz, $^3J_{H,F(cis)}$ = 17.9 Hz).

MS (GC/MS): *m/z* (%) = 244/242 ($M^+$, 18/36), 216/214 (McLafferty, 14/32), 187 (40), 185 (34), 171/169 ($M^+-C_3H_5O_2$, 31/96), 159 (92), 151/149 (171/169−HF, 17/31), 139 (27), 134 (66), 133 (169−HCl, 100), 131 (25), 115 (17), 107 (18), 101 (17), 66 (15), 39 (5).

HRMS: *m/z* calcd for $C_{12}H_{12}O_2ClF$ (**4b**) 242.05098. Found: 242.05057.

**Ethyl 2-Fluoro-3-methyl-2-phenylcyclopropanecarboxylates (4c, 5c)**

The reaction was carried out following typical procedure I, from **3c** (0.55 g, 4.0 mmol). Separation of the crude product by column chromatography (silica gel, pentane/$Et_2O$, 10:1) afforded the pure isomers **4c** and **5c** as colorless oils.

**4c:**

Yield: 0.21 g (24%).

$^1$H NMR: δ = 0.93 (dd, 3H, $^3J_{H,H}$ = 6.7 Hz, $^4J_{H,F}$ = 1.7 Hz, 7-$CH_3$), 1.30 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, 6-$CH_3$), 2.10 (dd, 1H, $^3J_{H,F(trans)}$ = 7.4 Hz, $^3J_{H,H(trans)}$ = 3.1 Hz, $H_B$), 2.38−2.56 (m, 1H, $^3J_{H,F(cis)}$ = 22.2 Hz, $^3J_{H,H}$ = 6.7 Hz, $H_A$), 4.20 (q, 2H, $^3J_{H,H}$ = 7.2 Hz, $CH_2$), 7.30−7.50 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 12.8 (q, C-7), 14.1 (q, C-6), 25.1 (dd, $^2J_{C,F}$ = 15.3 Hz, C-3), 29.0 (dd, $^2J_{C,F}$ = 17.8 Hz, C-1), 61.2 (t, C-5), 85.4 (ds, $^1J_{C,F}$ = 228.9 Hz, C-2), 128.3 (dd, $^3J_{C,F}$ = 5.1 Hz, C-9/13), 128.5 (d, C-10/12), 129.0 (d, C-11), 133.9 (s, C-8), 168.4 (s, C-4).

$^{19}$F NMR (564.3 MHz): δ = −168.87 (dd, $^3J_{H,F(cis)}$ = 22.2 Hz, $^4J_{H,F}$ = 1.7 Hz).

MS(GC/MS): *m/z* (%) = 222 ($M^+$, 14), 204 (4), 177 ($M^+-OC_2H_5$, 15), 153 (36), 149 ($M^+-C_3H_5O_2$, 100), 129 (149−HF, 34), 125 (20), 77 (4), 51 (4).

**5c:**

Yield: 0.35 g (39%).

$^1$H NMR: δ = 1.17 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, 6-$CH_3$), 1.31 (dd, 3H, $^4J_{H,F}$ = 1.7 Hz, $^3J_{H,H}$ = 6.92 Hz, 7-$CH_3$), 2.10−2.30 (m, 1H, $H_A$), 2.49 (dd, 1H, $^3J_{H,F(cis)}$ = 19.1 Hz, $^3J_{H,H}$ = 11.2 Hz, $H_x$), 3.90−4.2 (m, 2H, $CH_2$), 7.30−7.50 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 9.7 (q, C-7), 14.1 (q, C-6), 25.7 (dd, $^2J_{C,F}$ = 12.72 Hz, C-3), 31.2 (dd, $^2J_{C,F}$ = 12.7 Hz, C-1), 60.3 (t, C-5), 85.9 (ds, $^1J_{C,F}$ = 218.7 Hz, C-2), 128.5 (d, C-9/13), 129.6 (d, C-11), 130.8 (d, C-10/12), 131.2 (d, C-8), 168.9 (s, C-4).

$^{19}$F NMR (564.3 MHz): δ = −136.56 (pseudo t, $^3J_{H,F(cis)}$ = 19.1 Hz).

MS (GC/MS): *m/z* (%) = 222 ($M^+$, 18), 177 ($M^+-OC_2H_5$, 12), 153 (42), 149 ($M^+-C_3H_5O_2$, 100), 133 (10), 129 (149−HF, 34), 125 (25), 109 (10), 77 (4), 51 (4).

Anal. Calcd for $C_{13}H_{15}FO_2$ (222.25, mixture of **4c** and **5c**): C, 70.25; H, 6.80. Found: C, 70.29; H, 6.94.

**Ethyl 2-Butyl-2-fluoro-cyclopropanecarboxylates (4d, 5d)**

The reaction was carried out following typical procedure I, from **3d** (0.50 g, 4.9 mmol). Separation of the crude product by column chromatography (silica gel, pentane/$Et_2O$, 40:1) afforded the pure isomers **4d** and **5d** as colorless oils.

**4d:**

Yield: 0.18 g (20%).

$^1$H NMR: δ = 0.93 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, 10-$CH_3$), 1.05 (ddd, 1H, $^2J_{H,H}$ = 6.4 Hz, $^3J_{H,H(cis)}$ = 9.0 Hz, $^3J_{H,F(trans)}$ = 11.0 Hz, $H_A$), 1.27 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, 6-$CH_3$), 1.3−1.9 (m, 8H, 7−9-$CH_2$/$H_B$/$H_X$), 4.1−4.2 (m, 2H, $^3J_{H,H}$ = 7.2 Hz, 5−$CH_2$).

$^{13}$C NMR: δ = 13.8 (q, C-10), 14.2 (q, C-6), 17.2 (dt, $^2J_{C,F}$ = 12.7 Hz, C-3), 22.2 (t, C-9), 25.3 (dd, $^2J_{C,F}$ = 12.7 Hz, C-1), 27.3 (t, C-8), 35.0 (dt, $^2J_{C,F}$ = 20.3 Hz, C-7), 60.7 (t, C-5), 81.6 (ds, $^1J_{C,F}$ = 231.4 Hz, C-2), 168.6 (s, C-4).

$^{19}$F NMR: δ = −191.0 (m).

MS(GC/MS): *m/z* (%) = 188 ($M^+$, 1), 160 (McLafferty, 5), 159 ($M^+-C_2H_5$, 8), 146 ($M^+-C_3H_6$, 36), 143 ($M^+-C_2H_5O$, 22), 133 (10), 118 (14), 117 (41), 111 (20), 105 (55), 95 (60), 88 (40), 85 (36), 73 ($C_3H_5O_2^+$, 100), 55 (60), 43 (86), 41 (96), 39 (40).

**5d:**

Yield: 0.15 g (16%).

$^1$H NMR: δ = 0.84 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, 10-$CH_3$), 1.2 (t, 3H, $^3J_{H,H}$ = 7.2 Hz, 6-$CH_3$), 1.1−1.6 (m, 6H, 7/8/9-$CH_2$), 1.7−2.15 (m, 3H, $H_A$,$H_B$,$H_X$), 4.08 (q, 2H, $^3J_{H,H}$ = 7.2 Hz, 5-$CH_2$).

$^{13}$C NMR: δ = 14.2 (q, C-10), 14.6 (q, C-6), 18.6 (dt, $^2J_{C,F}$ = 10.2 Hz, C-3), 22.7 (t, C-9), 25.4 (dd, $^2J_{C,F}$ = 15.3 Hz, C-1), 27.9 (t, C-8), 29.8 (dt, $^2J_{C,F}$ = 20.3 Hz, C-7), 61.1 (t, C-5), 83.5 (ds, $^1J_{C,F}$ = 223.8 Hz, C-2), 171.1 (s, C-4).

$^{19}$F NMR: δ = −169.2 (m).

MS (GC/MS): *m/z* (%) = 188 ($M^+$, 3), 168 ($M^+$−HF, 5), 160 (McLafferty, 16), 159 ($M^+-C_2H_5$, 16), 146 ($M^+-C_3H_6$, 100), 143 (30, $M^+-C_2H_5O$), 118 (29), 117 (73), 111 (33), 105 (55), 101 (41), 95 (49), 88 (53), 85 (32), 73 (84, $C_3H_5O_2^+$), 55 (32), 44 (26), 42 ($C_3H_6^+$, 29).

***tert*-Butyl 2-Fluoro-2-phenylcyclopropanecarboxylates (4e, 5e)**

The reaction was carried out following typical procedure I, from **3a** (0.50 g, 4.1 mmol), $Rh_2(OAc)_4{\cdot}2H_2O$ (59 mg, 0.123 mmol) and *tert*-butyl diazoacetate (0.87 mL, 6.15 mmol). Separation of the crude 64:36 mixture of **4e** and **5e** by column chromatography (silica gel, pentane/$Et_2O$, 40:1) afforded the pure isomers as colorless oils.

**4e:**

Yield: 0.40 g (41%).

$^1$H NMR: δ = 1.48 (s, 9H, $C(CH_3)_3$), 1.50−1.57 (m, 1H, $H_A$), 2.11 (ddd, 1H, $^3J_{H,H(cis)}$ = 9.3 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 3.1 Hz, $H_X$), 2.21 (ddd, 1H, $^2J_{H,H}$ = 6.9 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 20.0 Hz, $H_B$), 7.2-7.4 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 18.8 (dt, $^2J_{C,F}$ = 12.7 Hz, C-3), 28.1 (q, C-6/7/8), 30.1 (dd, $^2J_{C,F}$ = 12.7 Hz, C-1), 80.6 (ds, $^1J_{C,F}$ = 227.6 Hz, C-2), 81.2 (s, C-5), 124.3 (dd, $^3J_{C,F}$ = 6.4 Hz, C-10/14), 128.0 (d, C-12), 128.5 (d, C-11/13), 137.9 (ds, $^2J_{C,F}$ = 21.6 Hz, C-9), 166.7 (s, C-4).

$^{19}$F NMR (188.29 MHz): δ = −190.24 (m).

MS (GC/MS): *m/z* (%) = 236 ($M^+$, 0), 221 ($M^+-CH_3$, 2), 207 (1), 180 (McLafferty, 33), 163 ($M^+-C_4H_9O$, 10), 160 (180−HF, 31), 135 ($M^+-C_5H_9O_2$, 43), 125 (19), 115 (135−HF, 31), 105 (22), 77 ($C_6H_5^+$, 4), 57 ($C_4H_9^+$, 100), 41 (34).

**5e:**

Yield: 0.28 g (29%).

$^1$H NMR: δ = 1.15 (s, 9H, $C(CH_3)_3$), 1.71 (ddd, 1H, $^2J_{H,H}$ = 7.2 Hz, $^3J_{H,H(cis)}$ = 10.3 Hz, $^3J_{H,F(cis)}$ = 19.3 Hz, $H_B$), 1.95 (ddd, 1H, $^2J_{H,H}$ = 7.2 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 12.2 Hz, $H_A$), 2.46 (ddd, 1H, $^3J_{H,H(cis)}$ = 10.3 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 18.6 Hz, $H_X$), 7.3−7.5 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 15.9 (dt, $^2J_{C,F}$ = 10.2 Hz, C-3), 27.9 (q, C-6/7/8), 28.8 (dd, $^2J_{C,F}$ = 15.3 Hz, C-1), 81.6 (s, C-5), 82.9 (ds, $^1J_{C,F}$ = 221.3 Hz, C-2), 128.1 (d, C-10/14), 128.7 (d, C-11/13), 129.1 (d, C-12), 133.3 (ds, $^2J_{C,F}$ = 20.4 Hz, C-9), 167.8 (s, C-4).

$^{19}$F NMR (188.29 MHz): δ = −153.80 (m).

MS (GC/MS): *m/z* (%) = 236 ($M^+$, 0), 221 ($M^+-CH_3$, 2), 193 (2), 180 (McLafferty, 48), 163 ($M^+-C_4H_9O$, 11), 160 (180−HF, 39), 135 ($M^+-C_5H_9O_2$, 59), 125 (31), 115 (135−HF, 26), 105 (16), 77 ($C_6H_5^+$, 5), 57 ($C_4H_9^+$, 100), 51 ($C_4H_3^+$, 6), 41 (24).

Anal. Calcd for $C_{14}H_{17}FO_2$ (236.28, mixture of **4e** and **5e**): C, 71.17; H, 7.25. Found: C, 71.20; H, 7.45.

**2-Fluoro-2-phenylcyclopropanecarboxylic Acids (6a, 7a)**

To a solution of KOH (1.51 g, 27 mmol) in dry MeOH (10 mL) a 1:1 mixture of **4a** and **5a** (0.57 g, 2.7 mmol) was added slowly at

0 °C. After strirring at r.t. overnight, the mixture was poured into ice water (50 mL) and extracted successively with $CH_2Cl_2$ (2 × 25 mL). The aqueous phase was adjusted with 2 N hydrochloric acid to pH 1 and extracted with $CH_2Cl_2$ (3 × 25 mL). Drying of the latter extracts ($MgSO_4$) and removing of the solvent by evaporation (rotary evaporator) afforded a mixture of **6a** and **7a** as colorless crystals (total yield: 0.45 g, 93%).

Complete separation of isomers **6a** and **7a** can be achieved by fractional crystallization from $CH_2Cl_2$. One single crystal of each isomer was used for X-ray analysis.

**6a:**
Mp: 102 °C ($CH_2Cl_2$).

$^1$H NMR (250.0 MHz): δ = 1.71 (ddd, 1H, $^2J_{H,H}$ = 6.9 Hz, $^3J_{H,H(cis)}$ = 9.2 Hz, $^3J_{H,F(trans)}$ = 11.3 Hz, $H_A$), 2.20 (ddd, 1H, $^3J_{H,H(cis)}$ = 9.2 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 2.9 Hz, $H_X$), 2.33 (ddd, 1H, $^2J_{H,H}$ = 6.9 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 20.1 Hz, $H_B$), 7.30−7.44 (m, 5H, $H_{arom.}$).

$^{13}$C NMR (62.9 MHz): δ = 19.4 (dt, $^2J_{C,F}$ = 12.4 Hz, C-4), 28.7 (dd, $^2J_{C,F}$ = 11.6 Hz, C-2), 81.5 (ds, $^1J_{C,F}$ = 229.8 Hz, C-3), 124.8 (dd, $^3J_{C,F}$ = 6.2 Hz, C-6/10), 128.6 (d, C-8), 128.7 (d, C-7/9), 132.5 (ds, $^2J_{C,F}$ = 19.9 Hz, C-5), 174.2 (s, C-1).

$^{19}$F NMR: δ = −186.58 (m).

MS (GC/MS) after silylation: *m/z* (%) = 253 ($MH^+$, 6), 252 ($M^+$, 26), 237 ($M^+-CH_3$, 42), 197 (37), 162 ($C_{10}H_7OF^+$, 52), 134 (15), 133 (15), 117 ($C_4H_9O_2Si^+$, 5), 116 (33), 115 (50), 105 (40), 77 ($C_6H_5^+$, 32), 73 ($C_3H_9Si^+$, 100).

**7a:**
Mp: 95 °C ($CH_2Cl_2$).

$^1$H NMR (250.0 MHz): δ = 1.87 (m, 2H, $H_A/H_B$), 2.49 (ddd, 1H, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,H(cis)}$ = 10.2 Hz, $^3J_{H,F(cis)}$ = 17.6 Hz, $H_X$), 7.29−7.45 (m, 5H, $H_{arom.}$).

$^{13}$C NMR (62.9 MHz): δ = 17.3 (dt, $^2J_{C,F}$ = 10.4 Hz, C-4), 27.5 (dd, $^2J_{C,F}$ = 17.3 Hz, C-2), 83.6 (ds, $^1J_{C,F}$ = 221.9 Hz, C-3), 128.3 (d, C-8), 128.3 (d, C-7/9), 128.4 (dd, $^3J_{C,F}$ = 5.6 Hz C-6/10), 132.5 (ds, $^2J_{C,F}$ = 19.9 Hz, C-5), 175.0 (s, C-1).

$^{19}$F NMR: δ = −152.06 (m).

MS (GC/MS) after silylation: *m/z* (%) = 253 ($MH^+$, 9), 252 ($M^+$, 39), 237 ($M^+-CH_3$, 41), 236 (17), 207 (11), 197 (51), 162 ($C_{10}H_7OF^+$, 68), 134 (20), 133 (20), 117 ($C_4H_9O_2Si^+$, 5), 116 (30), 115 (52), 105 (49), 77 ($C_6H_5^+$, 32), 73 ($C_3H_9Si^+$, 100).

Anal. Calcd for $C_{10}H_9FO_2$ (180.17, mixture of **6a** and **7a**): C, 66.66; H, 5.03. Found: C, 66.69; H, 5.35.

### Ethyl 2-Fluoro-3-phenylcyclopropanecarboxylates (9a+10a)

The reaction was carried out following general procedure I, from **8a** (0.50 g, 4.1 mmol) which was synthesized as an *E*/*Z*-mixture (86:14) by a Wittig-type reaction.[14] Three of the four possible diastereomers were found in the crude product by $^{19}$F NMR spectroscopy and GC/MS. Since the mass spectra of the three isomers are almost identical, just one is given below. Because of low conversion, the esters **9a** and **10a** were not isolated, but the configuration can be assigned from the $^{19}$F NMR spectrum of the mixture.

$^{19}$F NMR: δ = −218.11 (ddd, $^2J_{H,F}$ = 64.9 Hz, $^3J_{H,F(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 19.1 Hz), ethyl *t*-2-fluoro-*t*-3-phenylcyclopropane-*r*-1-carboxylate (not shown in Scheme 5); −214.11 (ddd, $^2J_{H,F}$ = 64.9 Hz, $^3J_{H,F(trans)}$ = 3.8 Hz, $^3J_{H,F(cis)}$ = 21.0 Hz), ethyl *c*-2-fluoro-*t*-3-phenylcyclopropane-*r*-1-carboxylate (**9a**); −206.72 (ddd, $^2J_{H,F}$ = 61.0 Hz, $^3J_{H,F(cis)}$ = 17.2 Hz, $^3J_{H,F(cis)}$ = 21.0 Hz), ethyl *t*-2-fluoro-*c*-3-phenylcyclopropane-*r*-1-carboxylate (**10a**); (ratio 27:28:45).

MS (GC/MS): *m/z* (%) = 208 ($M^+$, 20), 188 ($M^+$−HF, 7), 179 ($M^+$−CHO/$M^+-C_2H_5$, 2), 163 ($M^+-C_2H_5O$, 20), 160 (6), 136 (20), 135 ($M^+-C_3H_5O_2$, 100), 133 (20), 116 (9), 115 (52), 109 (8), 89 (6), 77 (5) [$C_6H_5^+$], 73 (6), 63 (4), 51 ($C_4H_3^+$, 6).

### Ethyl 2-Fluoro-3-(4-methoxyphenyl)cyclopropanecarboxylates (9b+10b)

The reaction was carried out following typical procedure I, from **8b** (0.60 g, 4.1 mmol) which was synthesized as an *E*/*Z*-mixture (86:14) by a Wittig-type reaction.[14] Three of the four possible diastereomers were found in the crude product by $^{19}$F NMR spectroscopy and GC/MS. Since the mass spectra of the three isomers are almost identical, just one is given below. Because of low conversion, the esters **9b** and **10b** were not isolated, but the configuration can be assigned from the $^{19}$F NMR spectrum of the mixture.

$^{19}$F NMR: δ = −218.13 (ddd, $^2J_{H,F}$ = 64.9 Hz, $^3J_{H,F(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 19.1 Hz), ethyl *t*-2-fluoro-*t*-3-(4-methoxyphenyl)cyclopropane-*r*-1-carboxylate (not shown in Scheme 5); −214.44 (ddd, $^2J_{H,F}$ = 62.9 Hz, $^3J_{H,F(trans)}$ = 3.8 Hz, $^3J_{H,F(cis)}$ = 22.9 Hz), ethyl *c*-2-fluoro-*t*-3-(4-methoxyphenyl)cyclopropane-*r*-1-carboxylate (**9b**); −206.06 (ddd, $^2J_{H,F}$ = 62.9 Hz, $^3J_{H,F(cis)}$ = 17.2 Hz, $^3J_{H,F(cis)}$ = 22.9 Hz), ethyl *t*-2-fluoro-*c*-3-(4-methoxyphenyl)cyclopropane-*r*-1-carboxylate (**10b**); (ratio 23:29:48).

MS (GC/MS): *m/z* (%) = 238 ($M^+$, 22), 218 ($M^+$−HF, 6), 209 ($M^+$−CHO/$M^+-C_2H_5$, 4), 193 ($M^+-C_2H_5O$, 10), 189 (209−HF, 3), 165 ($M^+-C_3H_5O_2$, 100), 145 (15), 133 (7), 121 (5), 101 (4), 91 (5), 77 (3), 59 (4), 51 (3).

### Lipase-Catalyzed Hydrolysis of Racemic 4a in a Phosphate Buffer

Compound **4a** (104 mg, 0.50 mmol) was suspended in a phosphate buffer solution (20 mL, 0.1 M, pH 7.0) and the respective enzyme (20 mg) was added. The reaction mixture was stirred at r.t. for 7 d. After addition of 2 N HCl (5 mL), the mixture was extracted with $CH_2Cl_2$ (3 x 20 mL) and the conversion was determined by $^{19}$F NMR spectroscopy. Afterwards, the combined organic layers were extracted with sat. $NaHCO_3$•2 N HCl was added to the combined $NaHCO_3$ layers until pH 1−2 was reached and this mixture was extracted twice with $CH_2Cl_2$. After drying ($MgSO_4$) and removal of the solvent, the enantiomerically enriched (1*R*,2*R*)-**6a** (hydrolysis of racemic **4a** with CRL: 88 mg, 49%) was isolated. The enantiomeric excess of the remaining ester (1*S*,2*S*)-**4a** was not determined.

### Determination of the Enantiomeric Excesses of Carboxylic Acids 6

According to ref.,[34] the fluorocarboxylic acids **6** (0.5 mmol) prepared from the esters **4** by saponification (KOH, MeOH) and enantiopure (−)-menthol (224 mg, 1.5 mmol) were dissolved in anhyd $CH_2Cl_2$ (2 mL). *N*,*N*-dicyclohexyl carbodiimide (113 mg, 0.55 mmol) and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (approx. 5 mg) was added and the mixture was stirred at r.t. for 12 h. The precipitated dicyclohexyl urea was filtered off and washed with $CH_2Cl_2$ (1 mL). The combined organic layer was evaporated and the diastereomeric excess of the crude esters was determined by $^{19}$F NMR spectroscopy.

### Asymmetric Cyclopropanation of α-Fluorostyrene (3a); Typical Procedure II

The bis(oxazoline) ligand **11a**, **11b** or **12** (0.15 mmol) and CuOTf·½benzene (30 mg, 0.12 mmol) were dissolved in anhyd $CH_2Cl_2$ (5 mL) and stirred at r.t. for 1 h. Then **3a** (0.50 g, 4.1 mmol) was added. Afterwards, a solution of diazoacetate (6.15 mmol) in anhyd $CH_2Cl_2$ (3 mL) was added at 40 °C through a syringe controlled by a syringe pump over a period of 6−7 h. After stirring for one more hour and addition of $CH_2Cl_2$ (100 mL), the mixture was washed successively with sat. $Na_2CO_3$ (2 × 50 mL) and $H_2O$ (2 × 50 mL). After drying ($MgSO_4$) and evaporation of the solvent, the crude product was purified by column chromatography (silica gel,

**Table 6** Optical Rotations of Enantiomerically Enriched Monofluorinated Cyclopropane Carboxylates

| Compounds | ee **4** [%] | ee **5** [%] | $[\alpha]_D^{20}$ **4** (*c* 1, $CH_2Cl_2$) | $[\alpha]_D^{20}$ **5** (*c* 1, $CH_2Cl_2$) |
|---|---|---|---|---|
| **a** | 89 | 80 | −161.0 | −29.8 |
| **c** | 65 | n.d[a] | −30.2 | −1.2 |
| **d** | 16 | n.d. | −34.8 | −42.4 |
| **e** | 93 | 89 | 152.3 | n.d. |

[a] n.d = not determined.

same eluents as for the racemic products). The spectroscopic data of all optically active products agree with those obtained for the corresponding racemic compounds. If not stated otherwise (cf. Table 4), the enantiomeric excess was determined by $^{19}F$ NMR spectroscopy after saponification of the cyclopropane carboxylates (KOH in MeOH) and esterification with enantiopure (−)-menthol using the above described method. The enantiomeric excesses and optical rotations are given in Table 6.

### (−)-Menthyl 2-Fluoro-2-phenylcyclopropanecarboxylate (4f, 5f)

**4f:**

Yield: 0.29 g (22%).

$^1H$ NMR: δ = 0.80 (d, 3H, $^3J_{H,H}$ = 6.9 Hz, $CH_3$), 0.90 (d, 3H, $^3J_{H,H}$ = 6.9 Hz, $CH(CH_3)_2$), 0.91 (d, 3H, $^3J_{H,H}$ = 6.4 Hz, $CH(CH_3)_2$), 0.83−1.15 (m, 3H), 1.34−1.54 (m, 2H), 1.59 (ddd, 1H, $^2J_{H,H}$ = 6.7 Hz, $^3J_{H,H(cis)}$ = 9.3 Hz, $^3J_{H,F(trans)}$ = 10.7 Hz, $H_A$), 1.64−1.76 (m, 2H), 1.82−1.98 (m, 1H), 2.0−2.1 (m, 1H), 2.16 (ddd, 1H, $^3J_{H,H(cis)}$ = 9.3 Hz, $^3J_{H,H(trans)}$ = 7.8 Hz, $^3J_{H,F(trans)}$ = 3.2 Hz, $H_X$), 2.28 (ddd, 1H, $^2J_{H,H}$ = 6.7 Hz, $^3J_{H,H(trans)}$ = 7.8 Hz, $^3J_{H,F(cis)}$ = 20.0 Hz, $H_B$), 4.75−4.88 (m, 1H, 11-CH), 7.2−7.5 (m, 5H, $H_{arom.}$).

$^{13}C$ NMR: δ = 16.5 (q, $CH(CH_3)_2$), 18.5 (dt, $^2J_{C,F}$ = 12.7 Hz, C-3), 20.6 (q, $CH(CH_3)_2$), 22.0 (q, C-17), 23.7 (t, C-14), 26.5 (d, C-18), 29.4 (dd, $^2J_{C,F}$ = 11.5 Hz, C-1), 31.4 (d, C-15), 34.3 (t, C-13), 41.0 (t, C-16), 47.1 (d, C-12), 75.2 (d, C-11), 80.7 (ds, $^1J_{C,F}$ = 227.6 Hz, C-2), 124.7 (dd, $^3J_{C,F}$ = 6.4 Hz, C-6/10), 128.3 (d, C-8), 128.6 (d, C-7/9), 137.7 (ds, $^2J_{C,F}$ = 21.6 Hz, C-5), 167.2 (s, C-4).

$^{19}F$ NMR: δ = −187.35 (m) [(1*S*,2*S*)-**4f**]; −188.59 (m) [(1*R*,2*R*)-**4f**]; (ratio 96:4).

MS (GC/MS): *m/z* (%) = 318 ($M^+$, 0), 180 (McLafferty, 25), 160 (180−HF, 12), 139 ($C_{10}H_{19}^+$, 24), 135 ($M^+-C_{11}H_{19}O_2$, 14), 115 (135−HF, 14), 105 (6), 97 (16), 83 (100), 71 (6), 69 (32), 57 (28), 55 (31), 43 (12), 41 (12).

**5f:**

Yield: 0.15 g (6%).

$^1H$ NMR: δ = 0.47 (d, 3H, $^3J_{H,H}$ = 6.9 Hz, $CH_3$), 0.79 (d, 3H, $^3J_{H,H}$ = 7.2 Hz, $CH(CH_3)_2$), 0.80 (d, 3H, $^3J_{H,H}$ = 6.4 Hz, $CH(CH_3)_2$), 0.8−1.0 (m, 3H), 1.14−1.37 (m, 3H), 1.45−1.70 (m, 3H), 1.78 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(cis)}$ = 10.5 Hz, $^3J_{H,F(cis)}$ = 19.8 Hz, $H_B$), 2.01 (ddd, 1H, $^2J_{H,H}$ = 7.1 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 12.6 Hz, $H_A$), 2.54 (ddd, 1H, $^3J_{H,H(cis)}$ = 10.5 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 18.1 Hz, $H_X$), 4.3−4.5 (m, 1H, 11-CH), 7.3−7.5 (m, 5H, $H_{arom.}$).

$^{13}C$ NMR: δ = 15.9 (q, $CH(CH_3)_2$), 16.1 (dt, $^2J_{C,F}$ = 9.7 Hz, C-3), 20.7 (q, $CH(CH_3)_2$), 21.9 (q, C-17), 23.2 (t, C-14), 26.0 (d, C-18), 28.5 (dd, $^2J_{C,F}$ = 16.64 Hz, C-1), 31.2 (d, C-15), 34.1 (t, C-13), 40.4 (t, C-16), 46.8 (d, C-12), 74.6 (d, C-11), 83.1 (ds, $^1J_{C,F}$ = 220.6 Hz, C-2), 128.2 (d, C-6/7/9/10), 129.1 (d, C-8), 133.2 (ds, $^2J_{C,F}$ = 19.4 Hz, C-5), 168.2 (s, C-4).

$^{19}F$ NMR: δ = −153.56 (m) [(1*R*,2*R*)-**5f**]; −154.85 (m) [(1*S*,2*S*)-**5f**]; (ratio 1:99).

MS (GC/MS): *m/z* (%) = 318 ($M^+$, 0), 180 (McLafferty, 26), 160 (180−HF, 12), 139 ($C_{10}H_{19}^+$, 32), 135 ($M^+-C_{11}H_{19}O_2$, 15), 115 (135−HF, 12), 105 (8), 97 (19), 83 (100), 71 (6), 69 (32), 57 (28), 55 (38), 41 (20).

### Determination of the Absolute Configuration of (1*S*,2*S*)-2-Fluoro-2-phenylcyclopropanecarboxylic (4-Bromophenyl)amide (13)

Enantiopure compound **6a** (315 mg, 1.75 mmol), prepared by saponification of **4a** (89% ee) and recrystallization, and $SOCl_2$ (0.30 mL, 4.14 mmol) were dissolved in dry benzene (10 mL) and heated under reflux for 5 h. After removing the solvent and excess $SOCl_2$ by evaporation, the residue was dissolved in $CH_2Cl_2$ (3 mL). This solution was added slowly to a cold (0 °C) solution of 4-bromoaniline (310 mg, 1.8 mmol) and $Et_3N$ (0.5 mL) in $CH_2Cl_2$ (5 mL) and stirred overnight. The mixture was poured into sat. $NH_4Cl$ (20 mL) and extracted with $CH_2Cl_2$ (3 × 10 mL). The organic phase was washed successively with sat. $NaHCO_3$, $H_2O$, and brine (50 mL each). After drying ($MgSO_4$), the solvent was removed by evaporation (rotary evaporator). Purification of the crude product by recrystallization from EtOAc afforded **13** (400 mg, 69%) as white crystals; mp 160 °C (sublimation). One of the single crystals of **13** was used for X-ray analysis.

$^1H$ NMR (acetone-$d_6$): δ = 1.69 (ddd, 1H, $^2J_{H,H}$ = 6.7 Hz, $^3J_{H,H(cis)}$ = 9.1 Hz, $^3J_{H,F(trans)}$ = 10.3 Hz, $H_A$), 2.32 (ddd, 1H, $^2J_{H,H}$ = 6.7 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(cis)}$ = 20.3 Hz, $H_B$), 2.42 (ddd, 1H, $^3J_{H,H(cis)}$ = 9.1 Hz, $^3J_{H,H(trans)}$ = 7.6 Hz, $^3J_{H,F(trans)}$ = 4.0 Hz, $H_X$), 7.31−7.48 (m, 7H, $H_{arom.}$), 7.62−7.70 (m, 2H, $H_{arom.}$).

$^{13}C$ NMR: δ = 18.3 (dt, $^2J_{C,F}$ = 12.7 Hz, C-3), 32.9 (dd, $^2J_{C,F}$ = 12.7 Hz, C-1), 82.0 (ds, $^1J_{C,F}$ = 225.1 Hz, C-2), 116.3 (s, C-8), 122.0 (dd, $^3J_{C,F}$ = 6.4 Hz, C-12/16), 125.0 (dd, $^4J_{C,F}$ = 6.4 Hz, C-13/15), 129.0 (d, C-14), 129.7 (d, C-6/10), 132.7 (d, C-7/9), 139.8 (ds, $^2J_{C,F}$ = 21.6 Hz, C-11), 140.0 (s, C-5), 165.0 (s, C-4).

$^{19}F$ NMR: δ = −189.97 (m).

MS (GC/MS): *m/z* (%) = 336/334 ($M^+$+H, 12/14), 335/333 ($M^+$, 70/68), 315/313 ($M^+$−HF, 7/6), 280/278 (10/12), 260/258 (280/278−HF, 4/5), 213/211 ($C_8H_6NOBr^+$, 18/20), 173/171 ($C_6H_6NBr^+$, 30/32), 162 ($M^+-C_6H_6NBr$, 78), 135 ($C_9H_8F^+$, 82), 115 (135−HF, 100), 109 (18), 91 (15), 76 (8), 63 (14), 39 (12).

Anal. Calcd for $C_{16}H_{13}NBrFO$ (334.18): C, 57.51; H, 3.92; N, 4.19. Found: C, 57.15; H, 3.99; N, 3.94.

### *trans*-*N*-(2-Fluoro-2-phenylcyclopropyl)carbamic Acid *tert*-Butyl Ester (14)

A two-neck 250 mL flask, which had been thoroughly dried, pumped and purged with Ar, was charged with racemic **6a** (834 mg, 4.55 mmol), anhyd cyclohexane (85 mL), $Et_3N$ (0.73 mL, 5.31 mmol, freshly distilled from $CaH_2$), *t*-BuOH (4.38 mL, 46.1 mmol, freshly distilled from $CaH_2$), and diphenylphosphoryl azide (1.0 mL, 4.8 mmol). The mixture was heated at 70 °C for 18 h under Ar and then di-*tert*-butyl dicarbonate (1.55 mL, 6.8 mmol) was added, and the mixture was heated for a further 2 h. The reaction was then cooled to r.t., and the solvent was removed by evaporation (rotary evaporator) leaving a thick oil. EtOAc (120 mL) was added, and the organic layer was washed successively with 5% aqueous citric acid, $H_2O$, sat. $NaHCO_3$, and brine (75 mL each). The excess dicarbonate was removed by Kugelrohr distillation (60 °C at $1.2 \bullet 10^{-1}$ mbar), and the residue was purified by column chromatography (silica gel, EtOAc/cyclohexane, 6:1) to give **14** (0.68 g, 60%) as a white solid; mp 103 °C (EtOAc).

$^1$H NMR: δ = 1.35−1.68 (m, 3H, $H_A/H_B/H_X$), 1.47 (s, 9H, $C(CH_3)_3$), 7.25−7.41 (m, 5H, $H_{arom.}$).

$^{13}$C NMR: δ = 20.2 (dt, $^2J_{C,F}$ = 11.4 Hz, C-3), 28.3 (q, C-6/7/8), 34.0 (br s, C-1), 79.1 (ds, $^1J_{C,F}$ = 219.2 Hz, C-2), 80.0 (s, C-5), 125.0 (d, C-10/14), 128.1 (d, C-12), 128.5 (d, C-11/13), 137.5 (ds, $^2J_{C,F}$ = 20.3 Hz, C-9), 156.3 (s, C-4).

$^{19}$F NMR: δ = −191.04 (m).

MS (GC/MS): *m/z* (%) = 251 ($M^+$, 1), 250 ($M^+$−H, 1), 236 ($M^+$−$CH_3$, 1), 195 (McLafferty, 6), 175 (195 - HF, 4), 151 ($C_9H_{10}NF^+$, 18), 130 (70), 103 (16), 77 ($C_6H_5^+$, 14), 59 ($CHNO_2^+$, 40), 57 ($C_4H_9^+$, 100), 51 ($C_4H_3^+$, 20), 41 (56).

Anal. Calcd for $C_{14}H_{18}FNO_2$ (251.30): C, 66.91; H, 7.22; N, 5.57. Found: C, 66.70; H, 7.00; N, 5.55.

### *trans*-(2-Fluoro-2-phenylcyclopropyl)amine Hydrochloride (15)

A suspension of **14** (145 mg, 0.58 mmol) in 1.2 N HCl/HOAc (5 mL) was stirred at r.t. for 1 h. After evaporation, HOAc (10 mL) was added twice and evaporated to remove traces of HCl. Washing of the residue with $Et_2O$ (5 mL) and drying of the solid at r.t./15 mbar for 1 h yielded 50 mg (46%) of **15** as a white solid (46%); mp 160 °C (decomposition).

$^1$H NMR (methanol-$d_4$): δ = 1.79−1.96 (m, 2H, $CH_2$), 3.05−3.15 (m, 1H, CH), 7.40−7.50 (m, 5H, $H_{arom.}$).

$^{13}$C NMR (methanol-$d_4$): δ = 18.1 (dt, $^2J_{C,F}$ = 12.7 Hz, C-3), 32.7 (dd, $^2J_{C,F}$ = 10.2 Hz, C-1), 79.5 (ds, $^1J_{C,F}$ = 218.7 Hz, C-2), 127.0 (dd, $^3J_{C,F}$ = 6.4 Hz, C-5/9), 130.2 (d, C-6/8), 130.5 (d, C-7), 136.8 (ds, $^2J_{C,F}$ = 20.3 Hz, C-4).

$^{19}$F NMR (methanol-$d_4$): δ = −187.94 (m).

MS (direct inlet): *m/z* (%) = 188/186 ($M^+$, 0/0), 151 ($M^+$−HCl, 12), 150 ($C_9H_9FN^+$, 22), 131 (12), 130 (150−HF, 100), 103 (32), 99 (11), 77 ($C_6H_5^+$, 16), 74 (18), 57 (11), 51 ($C_4H_3^+$, 13).

Anal. Calcd for $C_9H_{11}ClFN$ (187.64): C, 57.61; H, 5.91; N, 7.46. Found: C, 57.34; H, 5.95; N, 7.29.

### X-Ray Crystal Data

**6a:**

Formula $C_{10}H_9O_2F$, $M$ = 180.17, colorless crystal 0.40 × 0.20 × 0.20 mm, $a$ = 5.492(1), $b$ = 7.569(2), $c$ = 20.451(2) Å, β = 93.78(1)°, $V$ = 848.3(2) Å$^3$, $\rho_{calc}$ = 1.411 g cm$^{-3}$ μ = 1.12 cm$^{-1}$, no absorption correction (0.957 ≤ $T$ ≤ 0.978), $Z$ = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 0.71073 Å, $T$ = 293 K, ω/2θ scans, 1654 reflections collected (+$h$, +$k$, ±$l$), [(sinθ)/λ] = 0.59 Å$^{-1}$, 1489 independent ($R_{int}$ = 0.009) and 1118 observed reflections [$I \geq 2\ \sigma(I)$], 120 refined parameters, $R$ = 0.029, $wR^2$ = 0.079, max. residual electron density 0.18 (−0.16) e Å$^{-3}$, hydrogens calculated and refined as riding atoms.

**7a:**

Formula $C_{10}H_9O_2F$, $M$ = 180.17, colorless crystal 0.5 × 0.05 × 0.05 mm, $a$ = 24.124(3), $b$ = 5.543(1), $c$ = 40.282(6) Å, β = 98.20(1)°, $V$ = 5331.4(14) Å$^3$, $\rho_{calc}$ = 1.347 g cm$^{-3}$, μ = 9.05 cm$^{-1}$, no absorption correction, $Z$ = 24, monoclinic, space group $C2/c$ (No. 15), λ = 1.54178 Å, $T$ = 223 K, ω/2θ scans, 4032 reflections collected (±$h$, -$k$, -$l$), [(sinθ)/λ] = 0.56 Å$^{-1}$, 3961 independent ($R_{int}$ = 0.141) and 2023 observed reflections [$I \geq 2\ \sigma(I)$], 355 refined parameters, $R$ = 0.068, $wR^2$ = 0.170, max. residual electron density 0.39 (−0.34) e Å$^{-3}$, hydrogens calculated and refined as riding atoms.

**13:**

Formula $C_{16}H_{13}NOFBr$, $M$ = 334.18, colorless crystal 0.20 × 0.10 × 0.05 mm, $a$ = 5.706(1), $b$ = 7.890(1), $c$ = 15.613(4) Å, α = 90.55(1), β = 94.90(1), γ = 91.84(2)°, $V$ = 699.9(2) Å$^3$, $\rho_{calc}$ = 1.586 g cm$^{-3}$, μ = 29.42 cm$^{-1}$, empirical absorption correction via SORTAV (0.591 ≤ $T$ ≤ 0.867), $Z$ = 2, triclinic, space group $P1$ (No. 1), λ = 0.71073 Å, $T$ = 198 K, ω and φ scans, 4298 reflections collected (±$h$, ±$k$, ±$l$), [(sinθ)/λ] = 0.65 Å$^{-1}$, 3298 independent ($R_{int}$ = 0.041) and 2933 observed reflections [$I \geq 2\ \sigma(I)$], 367 refined parameters, $R$ = 0.050, $wR^2$ = 0.129, max. residual electron density 0.45 (−0.43) e Å$^{-3}$, Flack parameter −0.02(2), hydrogens calculated and refined as riding atoms.

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## References

+ X-ray structures

(1) Liu, H. -W.; Walsh, C. T. Biochemistry of the Cyclopropyl Group. In *The Chemistry of the Cyclopropyl Group;* Rappoport, Z., Ed.; Wiley: New York, 1987; pp 959−1025. Salaün, J. *Top. Curr. Chem.* **2000**, *207*, 1.

(2) For recent reviews, see: *Houben-Weyl*, 4th ed., Vol. E17a/b; de Meijere, A., Ed.; Thieme: Stuttgart, 1997.

(3) *Biomedical Frontiers of Fluorine Chemistry;* Ojima, I.; McCarthy, J. R.; Welch, J. T., Eds.; ACS Symposium Series 639, Washington DC, 1996.
*Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications;* Filler, R.; Kobayashi, Y.; Yagupolski, L. M., Eds.; Elsevier: Amsterdam, 1993.
Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley: New York, 1991.

(4) *Asymmetric Fluoroorganic Chemistry. Synthesis, Applications, and Future Directions;* Ramachandran, P. V., Ed.; ASC Symposium Series 746: American Chemical Society: Washington, DC, 2000.
*Enantiocontrolled Synthesis of Fluoro-Organic Compounds;* Soloshonok, V. A., Ed.; Wiley: New York, 1999.
*Chemistry of Organic Fluorine Compounds II;* Hudlický, M.; Pavlath, A. E., Eds.; ACS Monograph 187: Washington, DC, 1995.
*Organofluorine Chemistry;* Banks, R. E.; Smart, B. E.; Tatlow, J. C., Eds.; Plenum Press: New York, 1994.
*Synthetic Fluorine Chemistry;* Olah, G. A.; Chambers, R. D.; Prakash, G. K. S., Eds.; Wiley: New York, 1992.

(5) Imura, A.; Itoh, M.; Miyadera, A. *Tetrahedron: Asymmetry* **1998**, *9*, 3047.

(6) a) Ernet, T.; Haufe, G. *Tetrahedron Lett.* **1996**, *37*, 7251.
b) Ernet, T.; Haufe, G. *Synthesis* **1997**, 953.
c) Laue, K. W.; Haufe, G. *Synthesis* **1998**, 1453.
d) Laue, K. W.; Mück-Lichtenfeld, C.; Haufe, G. *Tetrahedron* **1999**, *55*, 10413.
e) Bogachev, A. A.; Kobrina, L. S.; Meyer, O. G. J.; Haufe, G. *J. Fluorine Chem.* **1999**, *97*, 135.
f) Kovtonyuk V. N.; Kobrina, L. S.; Gatilov, Y. V.; Bagryanskaya, I. Y.; Fröhlich, R.; Haufe, G. *J. Chem. Soc., Perkin Trans. I* **2000**, in press.

(7) Meyer, O. G. J.; Haufe, G. presented in part at the 12th European Symposium on Fluorine Chemistry, Berlin, 1998, Abstracts of Papers, A5.

(8) Cottens, S.; Schlosser, M. *Tetrahedron* **1988**, *44*, 7127.

(9) Buddrus, J.; Nerdek, F.; Hentschel, P.; Klamann, D. *Tetrahedron Lett.* **1966**, 5379.

Jeong, I. -H.; Kim, Y. -S. *Bull. Korean Chem. Soc*. **1990**, *11*, 178.
Iwaoka, T.; Katagiri, N.; Sato, M.; Kaneko, C. *Chem. Pharm. Bull.* **1992**, *40*, 2319.
Crowley, P. J.; Percy, J. M.; Stansfield, K. *Tetrahedron Lett*. **1996**, *37*, 8233.
Crowley, P. J.; Percy, J. M.; Stansfield, K. *Tetrahedron Lett*. **1996**, *37*, 8237.
Ito, H.; Saito, A.; Taguchi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1979.
Ito, H.; Saito, A.; Taguchi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1989.

(10) Alvernhe, G.; Laurent, A.; Haufe, G. *Synthesis* **1987**, 562.
Haufe, G.; Alvernhe, G.; Laurent, A.; Ernet, T.; Goj, O.; Kröger, S.; Sattler, A. *Org. Synth.* **1999**, *76*, 159.

(11) Eckes, L.; Hanack, M. *Synthesis* **1978**, 217
Suga, H.; Hamatani, T.; Guggisberg, Y.; Schlosser, M. *Tetrahedron* **1990**, *46*, 4255.

(12) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.
Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75.
Doyle, M. P. In *Comprehensive Organometallic Chemistry;* Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Elsevier: Oxford, 1995; pp 387−420.

(13) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (no. CCDC-145029, **6a**; CCDC-145030, **7a**; CCDC-145031, **13**). Copies of the data can be obtained free of charge on application to The Director CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax int. code+44(1223)1336033, e-mail: deposit@ccdc.cam.ac.uk].

(14) Cox, D. G.; Gurusamy, M.; Burton, D. J. *J. Am. Chem. Soc.* **1985**, *107*, 2811.

(15) Smart, B. E., In *Organofluorine Chemistry;* Banks, R. E.; Smart, B. E.; Tatlow, J. C., Eds.; Plenum Press: New York, 1994; pp 58−88.
Smart, B. E., In *Chemistry of Organic Fluorine Compounds II;* Hudlický, M.; Pavlath, A. E., Eds.; American Chemical Society; Monograph 187: Washington DC, 1995; pp 979−1010.

(16) Brookhart, M.; Tucker, J. R.; Husk, G. R. *J. Am. Chem. Soc*. **1983**, *105*, 258.

(17) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometallics* **1984**, *3*, 44.
Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53.

(18) Bolm, C. *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 542.
Brunner, H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1183.

(19) For recent reviews, see: Pfaltz, A. Cyclopropanation and C-H Insertion with Cu. In *Comprehensive Asymmetric Catalysis;* Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. II, pp 513−538.
Lydon, K. M.; McKervey M. A. Cyclopropanation and C-H Insertion with Rh. In *Comprehensive Asymmetric Catalysis;* Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. II, pp 540−580.
Charette, A. B.; Lebel, H. Cyclopropanation and C-H Insertion with Metals other than Cu and Rh. In *Comprehensive Asymmetric Catalysis;* Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. II, pp 581−603.
Davies, H. M. L. *Eur. J. Org. Chem.* **1999**, 2459.
Doyle, M. P.; Forbes, D.C. *Chem. Rev.* **1998**, *98*, 911.
Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919.
Singh, V. K.; Gupta, A. D.; Sekar, G. *Synthesis* **1997**, 137.
Noels, A. F.; Demonceau, A. Catalytic Cyclopropanation. In *Applied Homogeneous Catalysis with Organometallic Compounds;* Cornils, B.; Herrmann, W. A., Eds.; VCH: Weinheim, 1996; pp 733−747.
Eilbracht, P. In *Houben-Weyl*, 4th ed., Vol. E21c; Kelmchen, G.; Hoffmann, R. W.; Mulzer, J.; Schaumann, E., Eds.; Thieme: Stuttgart, 1995; pp 2650−2658.
Reißig, H. -U. In *Houben-Weyl*, 4th ed., Vol. E21c; Helmchen, G.; Hoffmann, R. W.; Mulzer, J.; Schaumann, E., Eds.; Thieme: Stuttgart, 1995; pp 3220−3270.

(20) a) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1005.
b) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* **1988**, *71*, 1553.
c) Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232.
d) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339.

(21) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005.

(22) Evans, D. A.; Woerpel, K. A.; Hinman, K. A.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726.

(23) Selected recent papers not cited in the reviews [19]:
Nishiyama, H.; Soeda, N.; Naito, T.; Motoyama, Y. *Tetrahedron: Asymmetry* **1998**, *9*, 2865.
Fraile, J. M.; Garcia, J. I.; Mayoral, J. A.; Tarnai, T. *Tetrahedron: Asymmetry* **1998**, *9*, 3997.
Wu, X. -Y.; Li, X. -H.; Zhou, Q. -L. *Tetrahedron: Asymmetry* **1998**, *9*, 4143.
Cai, L.; Mahmoud, T.; Han, Y. *Tetrahedron: Asymmetry* **1999**, *10*, 411.
Ikeno, T.; Sato, M.; Yamada, T. *Chem. Lett.* **1999**, 1345.
Uchida, T.; Irie, R.; Katsuki, T. *Synlett* **1999**, 1793.
Löffler, F.; Hagen, M.; Lüning, U. *Synlett* **1999**, 1826.
Cho, D. -J.; Jeon, S. -J.; Kim, H. -S.; Cho, C. -S.; Shim, S. -C. Kim, T. -J. *Tetrahedron: Asymmetry* **1999**, *10*, 3833.
Boulch, R.; Scheurer, A.; Mosset, P.; Saalfrank, R. W. *Tetrahedron Lett.* **2000**, *41*, 1023.
Li, Z.; Zheng, Z.; Chen, H. *Tetrahedron: Asymmetry* **2000**, *11*, 1157.

(24) Ghosh, A. K.; Mathivanan, P.; Capiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1.

(25) Kovac, B.; Klasinc, L.; Raza, Z.; Šunjic, V. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2455.

(26) Denmark, S. E.; Nakajima, N.; Nicaise, O. J. -C.; Faucher, A. -M.; Edwards, J. P. *J. Org. Chem.* **1995**, *60*, 4884.
Bedekar, A. V.; Koroleva, E. B.; Andersson, P. G. *J. Org. Chem.* **1997**, *62*, 2518.

(27) McKennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarm, M. *J. Org. Chem.* **1993**, *58*, 3568.

(28) Tamura, M.; Shibakami, M.; Sekiya, A. *Synthesis* **1995**, 515.

(29) Kröger, S.; Haufe, G. *Liebigs Ann./Recueil* **1997**, 1201.

(30) Lermontov, S. A.; Zavorin, S. I.; Bakhtin, I. V.; Pushin, A. N.; Zefirov, N. S.; Stang, P. J. *J. Fluorine Chem.* **1998**, *87*, 75.

(31) Kuroboshi, M.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1799.

(32) Dolbier, W. R.; Rong, X. X.; Bartberger, M. D.; Koroniak, H.; Smart, B. E.; Yang, Z. -Y. *J. Chem. Soc., Perkin Trans. 2* **1998**, 219.

(33) O'Bannon, P. E.; Dailey, W. P. *Tetrahedron* **1990**, *46*, 7341.

(34) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, 4475.

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