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# Enantiopure Fluorous Bis(oxazolines): Synthesis and Applications in Catalytic Asymmetric Reactions

Jerome Bayardon and Denis Sinou*

*Laboratoire de Synthèse Asymétrique, associé au CNRS, ESCPE Lyon, Université Claude Bernard Lyon 1, 43, boulevard du 11 novembre 1918, 69622 Villeurbanne Cedex, France*

*sinou@univ-lyon1.fr*

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Various enantiopure fluorous bis(oxazolines) with fluorine content between 52.7 and 58.7% have been synthesized by a simple reaction sequence that involved the introduction of two fluorinated ponytails by alkylation of the corresponding nonfluorous bis(oxazolines). These new ligands have been used in palladium-catalyzed alkylation of *rac*-(*E*)-1,3-diphenylpropenyl acetate with carbon nucleophiles and in copper-catalyzed oxidation of cycloalkenes; these ligands exhibited enantioselectivities up to 98 and 77%, respectively, quite close to the values obtained using the analogous nonfluorous bis(oxazolines). These ligands could be easily recovered by liquid−liquid extraction or solid−liquid separation and reused with the same enantioselectivities.

## Introduction

The $C_2$-symmetric enantiopure bis(oxazolines) (box) have emerged as one of the most efficient class of ligands in the area of asymmetric organometallic catalysis.[1] The most frequently used bis(oxazolines) are those with one carbon spacer between the two oxazoline rings. These ligands have been successfully used in a variety of catalytic asymmetric transformations over the past decade, including palladium-catalyzed allylic alkylations,[2] Diels−Alder[3] and hetero-Diels−Alder reactions,[4] copper-catalyzed cyclopropanation[5] and aziridination,[5c,6] Mukayama-aldol[7] and nitro-aldol (Henry) reactions,[8] Michael additions,[9] carbonyl−ene reactions,[4a,10] Friedel−Crafts reactions,[11] allylic oxidation,[12] and reduction of ketones,[13] giving generally very high enantioselectivities.

Due to the broad range of applications of this class of ligands and the very high enantioselectivities obtained, much efforts have been devoted to its immobilization on supports in order to recover and recycle the catalyst.

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Effectively, their practical application in asymmetric synthesis is actually limited, due to the low ratio substrate/ligand usually used and the high cost of these ligands. This immobilization could improve the efficiency of asymmetric catalysis by allowing simple catalyst separation and recycling.[14] Different strategies have been employed in the design of immobilized enantiopure bis(oxazoline). In a first type, the heterogenization of the ligand is performed using noncovalent or covalent bonding to solid inorganic[15] as well as organic supports.[16] In a second approach, the bis(oxazoline) is covalently bound to a soluble organic polymer,[17] allowing the reaction to occur under homogeneous conditions, the recovery and recycling of the catalyst being performed by precipitation of the polymer. These different approaches gave enantioselectivities quite close to those obtained when the reaction was performed under homogeneous conditions, the recycling of the supported enantiopure organometallic catalyst being generally possible.

The fluorous biphase catalysis is a quite new concept.[18] This methodology used the markedly temperature-dependent miscibilities of organic and fluorous solvents. The solubilization of the organometallic catalyst in the fluorous phase is obtained by the use of fluorinated ligands. This approach has been extended more or less successfully to some asymmetric organometallic catalysis in a two-phase system organic solvent−fluorous solvent.[19] We recently reported the preparation of fluorous enantiopure bis(oxazolines) and some preliminary results concerning their use as ligands in asymmetric allylic alkylation.[20] At the same time, Benaglia et al.[21] described the preparation of two enantiopure fluorous-substituted bis(oxazolines) and their applications in the ene and cyclopropanation reactions. Here we report a full account concerning the synthesis of a family of fluorinated enantiopure bis(oxazolines) possessing different fluorine content and their use as enantiopure ligands in allylic alkylation and allylic oxidation.

## Results and Discussion

It was crucial to find a very easy and eventually inexpensive access to these enantiopure fluorous bis(oxazolines) from available starting materials; the design of an easily flexible approach in order to modify the oxazoline structure was also needed. Since enantiopure bis(oxazolines) are commercially available or easy to prepare, we expected to introduce two fluorous ponytails on the methylene bridge of these ligands.

In a preliminary experiment, *tert*-butyl-substituted box **1** was treated with BuLi (2.2 molar equiv in THF, −78 °C, 1 h) and then alkylated with nonaflate **2**[22] (2.3 molar equiv in THF, 50 °C, 24 h) (Scheme 1). Only monoalkylated bis(oxazoline) **3** was obtained in 67% isolated yield. All attempts to dialkylated box **1**, for example in the presence of BuLi (1.2 molar equiv in THF, −78 °C), then nonaflate **2** (1.2 molar equiv at 50 °C in THF), followed by addition of BuLi (1.2 molar equiv in THF, −78 °C) in the presence of TMEDA (1.5 molar equiv) and *i*-$Pr_2NH$ (1 molar equiv), followed by addition of nonaflate **2** (1.2 molar equiv in THF) at 50 °C afforded the monoalkylated bis(oxazoline) **3** as the sole product. Sequential treatment of bis(oxazoline) **3** first by BuLi (1.2 molar equiv in THF)

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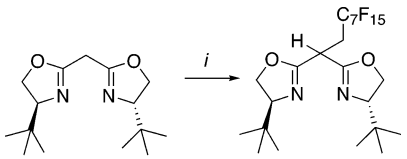
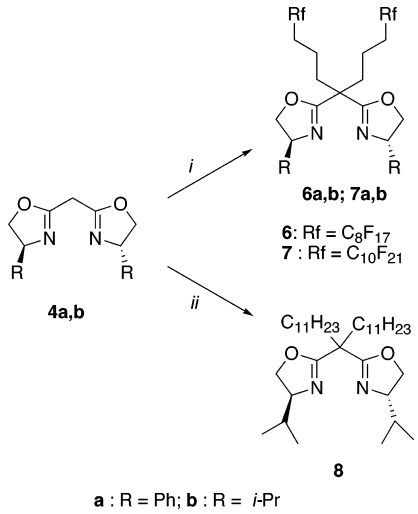
**SCHEME 1. Synthesis of Bis(oxazoline) 3**[a]




[a] Conditions: *n*-BuLi, THF, −78 °C, then $C_7F_{15}CH_2OSO_2C_4F_9$ (**2**), 50 °C.

**SCHEME 2. Synthesis of Bis(oxazolines) 6−8**[a]




[a] Conditions: (i) NaH, DMF, rt, then $C_8F_{17}(CH_2)_3I$ (**5a**) for **6**, $C_{10}F_{21}(CH_2)_3I$ (**5b**) for **7**, 80 °C; (ii) NaH, DMF, rt, then $C_{11}H_{23}Br$, 80 °C.

at −78 °C and then with nonaflate **2** (1.2 molar equiv), or even with MeI (1.2 molar equiv) at 50 °C in THF, afforded only the unreacted substrate **3**.

We assumed that the lack of formation of the bisalkylated oxazoline was probably due to the less nucleophilic character of the carbanion formed by abstraction of the hydrogen of the substituted methylene bond of oxazoline **3**, due to the presence of the fluorous chain bearing one methylenic spacer only. To circumvent this problem, we considered the use of an alkylating agent bearing three methylene units as the spacer. Enantiopure bis(oxazolines) **4a** and **4b** were treated with NaH (3 molar equiv in DMF, 25 °C, 1 h) and then alkylated with 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl iodide (**5a**) (2.3 molar equiv, DMF, 80 °C, 16 h) to afford fluorous bis(oxazolines) **6a** and **6b** in 46% and 62% isolated yield, respectively (Scheme 2). Sequential treatment of **4a** and **4b**, first with NaH (3 molar equiv in DMF, 25 °C, 1 h) and then with 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluorotridecyl iodide (**5b**), afforded the fluorous bis(oxazolines) **7a** and **7b** in 34% and 49% yield, respectively. The nonfluorous bis(oxazoline) **8**, analogue of **6b**, was obtained in 52% yield from **4b** according to the same procedure and using undecyl bromide as the alkylating reagent.

**TABLE 1. Partition Coefficients for the Fluorous Bis(oxazolines)**[a]

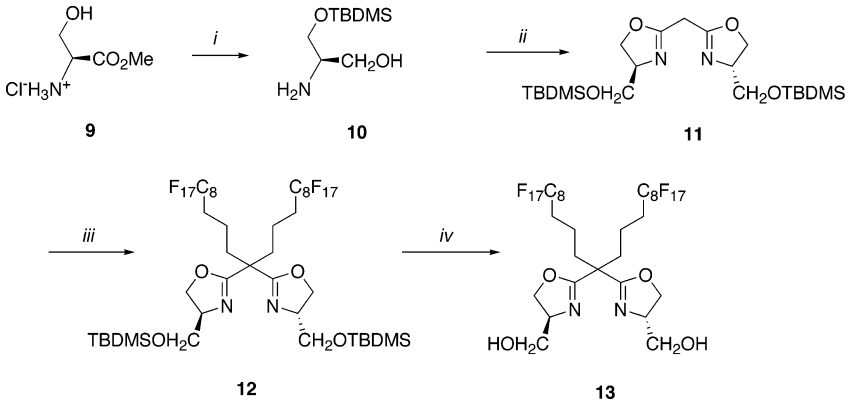
| bis (oxazoline) | F content (wt %) | FC72/$CH_2Cl_2$ % | FC72/$CH_2Cl_2$ $P^b$ | FC72/$CH_3CN$ % | FC72/$CH_3CN$ $P^b$ |
|---|---|---|---|---|---|
| **6a** | 52.66 | 11.8:88.2 | 0.14 | 19.5:80.5 | 0.24 |
| **6b** | 55.75 | 52.3:47.7 | 1.09 | 89.9:11.1 | 8.01 |
| **7a** | 55.93 | 29.7:70.3 | 0.42 | 85.6:14.4 | 5.94 |
| **7b** | 58.73 | 75.7:24.3 | 3.11 | 94.2:5.8 | 16.33 |
| **13** | 56.94 | 24.4:75.6 | 0.32 | 59.4:40.6 | 1.46 |

[a] In a 1:1 mixture of FC72/organic solvent at 25 °C. [b] Partition coefficient $P = c_{FC72}/c_{organic\ solvent}$.

Fluorous functionalized enantiopure bis(oxazoline) **13** was prepared following Scheme 3. Protection and reduction of (*S*)-serine methyl ester **9** according to the literature[23] afforded the protected amino alcohol (*R*)-**10**, which was readily converted to the silyl protected 2,2′methylenebis[(4-hydroxymethyl)-4,5-dihydro-1,3-oxazole] **11** in 78% yield by condensation with malonimidate ethyl ester dihydrochloride in $CH_2Cl_2$.[24] Treatment of bis(oxazoline) **11** with NaH (3 molar equiv in DMF, 25 °C, 1 h) followed by 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl iodide (**5a**) (2.3 molar equiv, DMF, 80 °C, 16 h) afforded the fluorous *O*-silylated bis(oxazoline) **12** in 34% isolated yield. The dihydroxy fluorous bis(oxazoline) **13** was obtained in 70% yield by simple deprotection of compound **12** by $NBu_4F\cdot 3H_2O$ in THF.

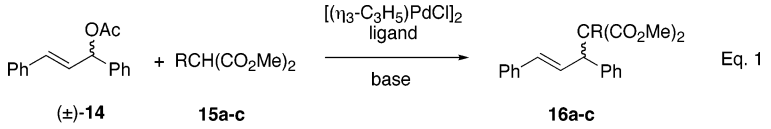
The calculated fluorine contents of some of the fluorous bis(oxazolines) are summarized in Table 1, together with the liquid−liquid partition coefficients *P* between FC72, $CH_2Cl_2$, and $CH_3CN$. Due to the low fluorine content of ligands **3** and **12** (43.9 and 47.4% fluorine, respectively),

**SCHEME 3. Synthesis of Bis(oxazolines) 12 and 13**[a]




[a] Conditions: (i) ref 23; (ii) $EtOC(NH)CH_2C(NH)OEt\cdot 2HCl$, $CH_2Cl_2$; (iii) NaH, DMF, rt, then $C_8F_{17}(CH_2)_3I$ (**5a**), 80 °C; (iv) *n*-$Bu_4NF\cdot 3H_2O$, THF, rt.

**TABLE 2. Enantioselective Palladium-Catalyzed Allylic Alkylation of *rac*-14 with Bis(oxazolines)[a]**




(±)-**14** **15a-c** **16a-c**

**a**: R = H; **b**: R = Me; **c**: R = AcNH

| entry | NuH | L | solvent | Pd (mol %) | base | *t* (h) | convn[b] (%) | ee (%) (config)[c] |
|---|---|---|---|---|---|---|---|---|
| 1 | **15a** | **3** | THF | 5 | NaH | 114 | 75 | 1 (*S*) |
| 2 | **15a** | **3** | $CH_2Cl_2$ | 5 | BSA/KOAc | 114 | nr | |
| 3 | **15a** | **6a** | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 89 | 94 (*S*) |
| 4 | **15a** | **6a** | BTF | 5 | BSA/KOAc | 40 | 93 | 92 (*S*) |
| 5 | **15a** | **6a** | THF | 5 | BSA/KOAc | 46 | 31 | 90 (*S*) |
| 6 | **15a** | **6a** | $CH_2Cl_2$ | 1 | BSA/KOAc | 96 | 53 | 95 (*S*) |
| 7 | **15a** | **6a** | BTF | 1 | BSA/KOAc | 136 | 45 | 91 (*S*) |
| 8 | **15a** | **6a** | BTF[d] | 1 | BSA/KOAc | 72 | 81 | 87 (*S*) |
| 9 | **15a** | **6a** | BTF[d] | 2 | BSA/KOAc | 24 | 100 | 88 (*S*) |
| 10 | **15a** | **6a** | $CH_2Cl_2$ | 5 | NaH | 8 | 98 | 94 (*S*) |
| 11 | **15a** | **6a** | BTF | 5 | NaH | 20 | 100 | 90 (*S*) |
| 12 | **15a** | **6a** | THF | 5 | NaH | 40 | 47 | 78 (*S*) |
| 13 | **15a** | **6b** | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 100 | 93 (*S*) |
| 14 | **15a** | **6b**[e] | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 100 | 94 (*S*) |
| 15 | **15a** | **6b**[f] | $CH_2Cl_2$ | 5 | BSA/KOAc | 40 | 98 | 90 (*S*) |
| 16 | **15a** | **6b**[g] | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 99 | 94 (*S*) |
| 17 | **15a** | **7a** | $CH_2Cl_2$ | 5 | BSA/KOAc | 25 | 97 | 94 (*S*) |
| 18 | **15a** | **7a**[f] | $CH_2Cl_2$ | 5 | BSA/KOAc | 48 | 66 | 98 (*S*) |
| 19 | **15a** | **7b** | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 100 | 94 (*S*) |
| 20 | **15a** | **7b**[f] | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 99 | 93 (*S*) |
| 21 | **15a** | **8** | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 96 | 96 (*S*) |
| 22 | **15a** | **12** | $CH_2Cl_2$ | 5 | BSA/KOAc | 18 | 97 | 96 (*R*) |
| 23 | **15a** | **13** | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 100 | 89 (*R*) |
| 24 | **15b** | **6a** | $CH_2Cl_2$ | 5 | BSA/KOAc | 24 | 93 | 90 (*R*) |
| 25 | **15c** | **6a** | $CH_2Cl_2$ | 5 | BSA/KOAc | 90 | 83 | 93 (*R*) |

[a] Substrate (1 equiv), nucleophile (3 equiv), BSA (3 equiv), KOAc (0.1 equiv), or NaH (3 equiv), $[Pd(C_3H_5)Cl]_2$/ligand L 1:1, 25 °C. [b] The conversion was determined by GC. [c] The ee values were determined by HPLC using a chiral column (Chiralpak AD, *i*-PrOH/*n*-hexane 4:6). The absolute configuration was determined by comparison of the HPLC retention time with literature data. [d] Reaction performed at 50 °C. [e] $[Pd(\eta^3\text{-}C_3H_5)(\mathbf{6b})]PF_6$ was used as the catalyst. [f] Ligands separated by liquid−liquid extraction were used in these entries. [g] Ligand separated by liquid−solid extraction was used in this entry.

their partition coefficients were not determined. This table shows clearly for a compound with a given chain length an increasing partition coefficient by the substitution of the phenyl group by a isopropyl one, whatever the organic solvent used: 0.14 vs 1.09 or 0.24 vs 8.01 for ligands **6a** and **6b**, respectively, using $CH_2Cl_2$ and $CH_3CN$ as the organic solvent, 0.42 vs 3.11 or 5.94 vs 16.33 for ligands **7a** and **7b**. More important, the two fluorous bis(oxazolines) **6b** and **7a** revealed quite different partition coefficients (1.09 and 0.42, in the presence of $CH_2Cl_2$, 8.01 and 5.94 in the presence of $CH_3CN$, respectively), despite their similar fluorine contents; thus, the presence of a phenyl group seemed to be detrimental for the solubilization of the ligand in fluorous solvents, the corresponding bis(oxazolines) showing a higher affinity for organic solvents. Among the two organic solvents tested, acetonitrile seemed the most appropriate for performing organometallic catalysis in a two-phase system.

These ligands were first assessed in palladium-catalyzed allylic substitution of *rac*-(*E*)-1,3-diphenylpropenyl acetate **14** with dimethyl malonate **15a** using $[(\eta^3\text{-}C_3H_5)PdCl]_2$ as the palladium source (eq 1) (Table 2). Bis(oxazoline) **3** gave very low conversion using NaH as the base (Table 2, entry 1) or no transformation at all in the presence of BSA and KOAc (Table 2, entry 2). The use of bis(oxazoline) **6a** as the ligand and BSA/KOAc as the base resulted in high enantioselectivities when the reaction was performed in $CH_2Cl_2$ (94% ee), in BTF (or benzotrifluoride) (92% ee), and in THF (90% ee) as the solvent (Table 2, entries 3−5), although the conversion was sluggish in the later one. Decreasing the amount of palladium precursor from 5 to 1 mol % gave the alkylated product **16a** with the same enantioselectivities (95% and 91% ee, in $CH_2Cl_2$ and BTF, respectively), although the conversions were lower (53 and 45%) (Table 2, entries 6−7). However, performing the reaction at 50 °C in BTF in the presence of 1 mol % palladium increased the conversion to 81%, the obtained enantioselectivity being 87% ee (Table 2, entry 8); it is to be noted that the use of 2 mol % palladium gave a complete conversion after 24 h with an enantioselectivity up to 88% (Table 2, entry 9). The use of NaH as the base gave the alkylated product **16a** with enantioselectivities up to 94, 90, and 78% ee, using $CH_2Cl_2$, BTF, and THF as the solvent, respectively (Table 2, entries 10−12); the observed conversion in THF was again lower. We also observed that the use of fluorous ligands **6b**, **7a**, and **7b** in this alkylation reaction gave quantitatively the expected product **16a** with enantioselectivities up to 93, 94, and 94% ee, respectively (Table 2, entries 13, 17, and 19). A quite similar enan-

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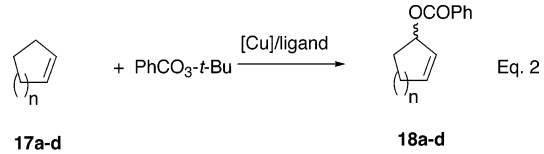
**TABLE 3. Enantioselective Copper-Catalyzed Allylic Oxidation of Cycloalkenes 17 with Bis(oxazolines)[a]**




Eq. 2

**17a-d** **18a-d**

**a**: n = 1; **b**: n = 2; **c**: n = 3; **d**: n = 4

| entry | alkene | metal salt−ligand | solvent | yield[b] (%) | ee (%) (*S*)[c] |
|---|---|---|---|---|---|
| 1 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **6a** | $CHCl_3/CH_3CN$ | 51 | 73 |
| 2 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **6a** | FC72/$CH_3CN$ | 61 | 69 |
| 3 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **6b** | $CHCl_3/CH_3CN$ | 48 | 62 |
| 4 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **6b**[d] | $CHCl_3/CH_3CN$ | 51 | 57 |
| 4bis[e] | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **6b**[f] | $CHCl_3/CH_3CN$ | 53 | 37 |
| 5 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **6b** | FC72/$CH_3CN$ | 66 | 60 |
| 6 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **8**[g] | $CHCl_3/CH_3CN$ | 64 | 61 |
| 7 | **17b** | $[Cu(CH_3CN)_4]PF_6$ + **6b** | FC72/$CH_3CN$ | 67 | 61 |
| 7bis[h] | **17b** | $[Cu(CH_3CN)_4]PF_6$ + **6b** | FC72/$CH_3CN$ | <10 | nd |
| 8 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **7a** | FC72/$CH_3CN$ | 51 | 71 |
| 9 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **7b** | FC72/$CH_3CN$ | 48 | 60 |
| 10 | **17b** | $[Cu(CH_3CN)_4]PF_6$ + **7b** | FC72/$CH_3CN$ | 39 | 60 |
| 11 | **17b** | $[Cu(CH_3CN)_4]PF_6$ + **7b**[d] | FC72/$CH_3CN$ | 49 | 52 |
| 11bis[h] | **17b** | $[Cu(CH_3CN)_4]PF_6$ + **7b** | FC72/$CH_3CN$ | <10 | nd |
| 12 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **12** | $CHCl_3/CH_3CN$ | 37 | 71 |
| 13 | **17b** | $CuOTf{\cdot}0.5C_6H_6$ + **13** | $CHCl_3/CH_3CN$ | 9 | nd |
| 14 | **17a** | $CuOTf{\cdot}0.5C_6H_6$ + **6a** | FC72/$CH_3CN$ | 86 | 77 |
| 15 | **17c** | $CuOTf{\cdot}0.5C_6H_6$ + **6a** | FC72/$CH_3CN$ | 58 | 49 |
| 16 | **17d** | $CuOTf{\cdot}0.5C_6H_6$ + **6a** | FC72/$CH_3CN$ | 32 | 10 |

[a] Alkene (1 equiv), *tert*-butyl perbenzoate (0.25 equiv), $CuOTf{\cdot}0.5C_6H_6$ or $[Cu(CH_3CN)_4]PF_6$ (0.0125 equiv, 5 mol %), ligand (0.02 equiv, 8 mol %), 7 days, 25 °C. [b] Isolated yield. [c] The ee values were determined by HPLC using a chiral column (Chirapald AD, *i*-PrOH/*n*-hexane 1:150). The absolute configuration was determined by comparison of the HPLC retention time with literature data; nd: not determined. [d] Experiment performed at 50 °C for 2 days. [e] The precipitated catalyst from entry 4 was reused. [f] Experiment performed at 50 °C for 3 days. [g] 9 days. [h] Recycling experiment.

tioselectivity (ee 94%) was obtained when preformed $[Pd(\eta^3\text{-}C_3H_5)$(**6b**)$]PF_6$ was used instead of the catalyst prepared in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand **6b** (Table 2, entry14). The obtained values are quite similar to those published in the literature using nonfluorous bis(oxazolines). Moreover, we performed one experiment using ligand **8**, the nonfluorous analogue of **6b**; an enantioselectivity of 96% was obtained in this alkylation reaction in $CH_2Cl_2$ (Table 2, entry 21), quite close to the value (93% ee) previously obtained using the fluorous ligand **6b**. The functionalized fluorous ligands **12** and **13** gave also quite high enantioselectivities using $CH_2Cl_2$ as the solvent; the alkylation product **16a** was formed with ee up to 96 and 80%, respectively (Table 2, entries 22 and 23).

This alkylation reaction was extended to other carbon nucleophiles using bis(oxazoline) **6a** as the chiral ligand and $CH_2Cl_2$ as the solvent. Dimethyl methylmalonate **15b** and dimethyl acetamidomalonate **15c** gave the expected alkylated products **16b** and **16c** in 90 and 93% ee (Table 2, entries 24 and 25).

We try to recycle the catalyst obtained in situ from $[(\eta^3\text{-}C_3H_5)PdCl]_2$ and ligands **6a**, **7a**, and **7b** or the well-characterized complex $[Pd(\eta^3\text{-}C_3H_5)$(**6b**)$]PF_6$, using the two-phase system FC72/$CH_2Cl_2$. Unfortunatly all attempts to recycle the fluorous-derivatized metal catalyst failed, and this could be due to the low partition coefficient of the formed palladium catalyst or eventually to the desactivation of the catalyst, since formation of black palladium occurred readily. So we studied the recovery of the fluorous ligand and its subsequent reuse in palladium-catalyzed alkylation. In a first procedure, the ligand was recovered at the end of the reaction after evaporation of the organic solvent by liquid−liquid extraction using FC72 as the fluorous solvent. In a second procedure, the ligand was recovered by solid−liquid-phase extraction by using a short column of fluorous reversed-phase silica gel. Ligands **6b**, **7a**, and **7b** were recovered in 76, 68, and 84% yield, respectively, using the first procedure, while ligand **6b** was recovered in 88% yield using the second one; it is to be noted that the conditions for this recovery have not been optimized. The recovered ligands gave NMR spectra identical to those of fresh samples and, more important, gave enantioselectivities very similar to those obtained with a fresh sample of ligand when they were reused in this palladium alkylation reaction. The recovered ligands **6b**, **7a**, and **7b** obtained using the first procedure were reused with a catalyst loading of 5 mol % and gave the alkylated product **16a** with enantioselectivities up to 90, 98, and 93% (Table 2, entries 14, 17, and 19), while the ligand **6b** obtained using the second procedure gave ee up to 94% (Table 2, entry 15).

We then turned our attention to the enantioselective allylic oxidation of cycloalkenes catalyzed by copper complexes associated with the fluorous bis(oxazolines) (eq 2).[12] The reaction was performed at room temperature for 7 days by forming the copper(I) triflate− or copper-(I)hexafluorophosphate−bis(oxazoline) complex (5 mol %) and adding 80 equiv of cycloolefin followed by 20 equiv of *tert*-butyl perbenzoate. The results are summarized in Table 3.

Oxidation reaction of cyclohexene **17b** catalyzed by the complex CuOTf-ligand **6a** afforded (*S*)-cyclohex-2-enyl benzoate **18b** in 73 and 69% ee when the reaction was performed using a monophasic system $CHCl_3/CH_3CN$ or

a biphasic system FC72/$CH_3CN$, respectively (Table 3, entries 1 and 2). It is to be noted that 59% ee was obtained in the literature when the reaction was performed in $CH_3CN$ in the presence of 2,2-bis[(4*S*)-4-phenyl-1,3-oxazolin-2-yl]propane as the ligand.[12b] Oxidation of **17b** at room temperature catalyzed by copper complex Cu(OTf)−**6b** gave **18b** with ee up 62 and 60% in $CHCl_3$/$CH_3CN$ and FC72/$CH_3CN$, respectively (Table 3, entries 3 and 5), while ee up to 57% was obtained when the reaction was performed in $CHCl_3$/$CH_3CN$ at 50 °C for 2 days (Table 3, entry 4). The use of the nonfluorous ligand **8**, analogue of **6b**, gave ee up to 61% using $CHCl_3$/$CH_3CN$ as the solvent, quite close to the value previously obtained with the fluorous ligand **6b** under the same conditions (Table 3, entry 6). Changing the catalyst precursor from CuOTf·0.5$C_6H_6$ to $Cu(CH_3CN)_4PF_6$ and using the bis(oxazoline) **6b** as the ligand gave almost the same enantioselectivity (61% in the two-phase system FC72/$CH_3CN$) (Table 3, entry 7).

Ligands **7a** and **7b**, associated with CuOTf or $Cu(CH_3CN)_4PF_6$, in the two-phase system FC72/$CH_3CN$ gave enantioselectivities up to 71 and 60% ee, respectively (Table 3, entries 8−10). Higher conversion was obtained when the reaction was performed at 40 °C (49% after 2 days), but a low decrease of the enantioselectivity was observed (Table 3, entry 11). Finally, the functionalized ligands **12** and **13** were also used. When the fluorous silylated bis(oxazoline) **12** gave benzoate **18b** in 37% yield and 71% ee after 7 days, dihydroxy ligand **13** gave a very low yield (9%) (Table 3, entries 12 and 13).

The reaction was extended to other cycloalkenes using the enantiopur catalyst CuOTf·0.5$C_6H_6$−**6a**. The efficiency of the oxidation of other cycloalkenes as well as the enantioselectivity were in quite good agreement with the results obtained previously under the same conditions using various 2,2-bis[4-substituted-1,3-oxazolin-2-yl]propanes.[12] The highest enantioselectivity and yield were obtained for cyclopentene **17a** (77% ee and 86% yield), when cycloheptene **17c** and cyclooctene **17d** gave lower yields and enantioselectivities (49% ee and 58% yield for **17c**, only 10% ee and 32% yield for **17d**) (Table 3, entries 14−16).

The recycling of the catalytic systems $Cu(CH_3CN)_4PF_6$−**6b** and $Cu(CH_3CN)_4PF_6$−**7b**, having the highest fluorine content, was studied using FC72/$CH_3CN$ as the two-phase system. Although the fluorine contents of the postulated catalytic species $CuPF_6$−**6b** and $CuPF_6$−**7b** were 55.6 and 58.2%, respectively, the recycling of the catalyst was very disappointing in these cases, less than 10% yield being observed after 7 days reaction (Table 3, entries 7bis and 11bis). According to the blue color of the organic solution, it seemed that most of the catalyst was in the organic phase and not in the fluorous phase. So, to try to recycle more efficiently the catalyst, cyclohexene (**17b**) was oxidized at 50 °C for 2 days in a mixture $CHCl_3$/$CH_3CN$ using CuOTf·0.5$C_6H_6$−**6b** as the catalyst; at the end of the reaction, evaporation of the solvents followed by addition of hexane allowed the precipitation of the complex and the very easy separation of the allylic benzoate in 51% yield and 57% ee (Table 3, entry 4). The precipitaded complex was reused in another reaction giving the allylic benzoate in 53% yield and 37% ee, after 3 days (Table 3, entry 4bis).

## Conclusion

An easy access to enantiopure fluorous bis(oxazolines) with different fluorine content has been described. These ligands have been used in two catalytic reactions: the palladium−allylic substitution of unsaturated acetates and the copper-catalyzed allylic oxidation of cyclic alkenes. The obtained enantioselectivities are as high as those described in the literature or obtained using non fluorous analogues: ee up to 98 and 77% for the allylic substitution and oxidation, respectively. Although the recycling of the catalyst was unsuccessful, recovery of the fluorous bis(oxazolines) was possible by liquid−liquid extraction using a fluorous solvent or by solid−liquid extraction via a fluorous silica gel. The recovered ligands could be recycled affording the product in quite similar yield and enantioselectivity to those obtained in the first cycle. The development of an efficient recyclable catalyst for both allylic alkylation and oxidation required ligands with higher fluorine content, and bis-hydroxy fluorous bis(oxazoline) **13** seemed a good precursor for this purpose.

## Experimental Section

**1,1-Bis[(4*S*)-4-*tert*-butyl-1,3-oxazolin-2-yl]-(1*H*,2*H*,2*H*)-perfluorononane (3).** To a stirred solution of bis(oxazoline) **1** (300 mg, 1.13 mmol) in dry THF (5 mL) cooled to −78 °C under nitrogen was added dropwise a 2.5 M solution of *n*-BuLi in hexane (0.5 mL, 1.24 mmol). After being stirred for 1 h at −78 °C, a solution of $C_7F_{15}CH_2OSO_2C_4F_9$ (**2**) (0.92 g, 1.35 mmol) in dry THF (5 mL) was added dropwise, and the reaction mixture was stirred overnight at 50 °C. The reaction was quenched by the addition of a saturated aqueous solution of $NH_4Cl$ (10 mL), and the resulting mixture was extracted with ether (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried over $Na_2SO_4$, and concentrated under vacuum. The residue was purified by chromatography on silica gel, using petroleum ether/ethyl acetate (1:1, v/v) as the eluent to afford the fluorinated bis(oxazoline) **3** as a pale yellow solid (0.49 g, 67% yield): mp = 66−68 °C; $R_f$ 0.58 (petroleum ether/ethyl acetate 1:1); $[\alpha]^{25}_D$ +36.8 (*c* 0.2, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.88 (s, 18H), 2.96−3.09 (m, 2H), 3.78 (dd, $J$ = 6.4, 8.6 Hz, 1H), 3.86−3.92 (m, 2H), 4.09−4.14 (m, 2H), 4.20−4.26 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 25.8, 26.0, 27.2 (t, $J$ = 23.0 Hz), 34.6, 69.1, 70.5, 110.0−120.0, 166.1; $^{19}$F NMR ($CDCl_3$) $\delta$ −126.6 (m, 2F), −124.0 (m, 2F), −123.2 (m, 2F), −122.6 (m, 2F), −122.1 (m, 2F), −114.8 (m, 2F), −81.3 (t, $J$ = 10.3 Hz, 3F); HRMS calcd for $C_{23}H_{28}F_{15}N_2O_2$ $[MH]^+$ 649.1911, found 649.1911.

**General Procedure for the Synthesis of Bis(oxazolines) 6−8.** To a solution of 2,2′-methylenebis[(4*S*)-4-phenyl-2-oxazoline] (**4a**) or methylenebis[(4*S*)-4-isopropyl-2-oxazoline] (**4b**) (2 mmol) in anhydrous DMF (20 mL) was added NaH (144 mg, 6 mmol). After the mixture was stirred for 1 h at rt, a solution of $R_f(CH_2)_3I$ (**5a**,**b**) or $CH_3(CH_2)_{10}Br$ (4.6 mmol) in anhydrous DMF (7 mL) was slowly added. After being stirred at 80 °C for 16 h, half of the DMF was removed under reduced pressure, water (20 mL) was added, and the resulting mixture was extracted with ether (4 × 20 mL). The organic layers were washed with brine and dried over $Na_2SO_4$. Concentration of the organic solution under reduced pressure followed by purification of the residue by chromatography on silica gel afforded the corresponding bis(oxazolines) **6**−**8**.

**12,12-Bis[(4*S*)-4-phenyl-1,3-oxazolin-2-yl](9*H*,9*H*,10*H*,-10*H*,11*H*,11*H*,13*H*,13*H*,14*H*,14*H*,15*H*,15*H*)perfluorotricosane (6a):** yield 46%; pale yellow solid; mp 68−70 °C; $R_f$ 0.38 (petroleum ether/ethyl acetate 7:1); $[\alpha]^{25}_D$ −34.7 (*c* 0.3, $C_6H_5CF_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.61−1.64 (m, 4H), 2.03−2.13 (m, 8H), 4.17 (dd, $J$ = 8.3, 8.3 Hz, 2H), 4.68 (dd, $J$ = 8.3, 9.6

Hz, 2H), 5.27 (dd, $J$ = 8.3, 9.6 Hz, 2H), 7.16−7.21 (m, 10H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.9, 31.5 (t, $J$ = 22.3 Hz), 33.3, 46.5, 70.0, 75.6, 127.0, 128.1, 129.1, 142.4, 168.2; $^{19}$F NMR ($CDCl_3$) $\delta$ −126.9 (4F), −124.0 (4F), −123.4 (4F), −122.4 (12F), −114.7 (4F), −81. 7 (t, $J$ = 9.2 Hz, 6F). Anal. Calcd for $C_{41}H_{28}F_{34}N_2O_2$: C, 40.13; H, 2.28. Found: C, 40.19; H, 2.38.

**12,12-Bis[(4*S*)-4-isopropyl-1,3-oxazolin-2-yl](9*H*,9*H*,10*H*,10*H*,11*H*,11*H*,13*H*,13*H*,14*H*,14*H*,15*H*,15*H*)perfluorotricosane (6b):** yield 62%; white solid; mp = 34−36 °C; $R_f$ 0.58 (petroleum ether/ethyl acetate 5:1); $[\alpha]^{25}_D$ −25.7 (*c* 0.18, $C_6H_5CF_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.87 (d, $J$ = 6.6 Hz, 6H), 0.93 (d, $J$ = 6.6 Hz, 6H), 1.56−1.60 (m, 4H), 1.75−1.79 (m, 2H), 2.01−2.07 (m, 8H), 3.97−4.00 (m, 4H), 4.18−4.26 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.7, 18.1, 18.9, 31.5 (t, $J$ = 21.7 Hz), 32.8, 33.0, 46.1, 70.3, 72.2, 109.0−121.0, 166.6; $^{19}$F NMR ($CDCl_3$) $\delta$ −126.7 (m, 4F), −124.0 (m, 4F), −123.3 (m, 4F), −122.5 (m, 12F), −144.7 (m, 4F), −81.4 (t, $J$ = 9.3 Hz, 6F). Anal. Calcd for $C_{35}H_{32}F_{34}N_2O_2$: C, 36.27; H, 2.76. Found: C, 36.19; H, 2.86.

**14,14-Bis[(4*S*)-4-phenyl-4,5;1,3-oxazolin-2-yl](11*H*,11*H*,12*H*,12*H*,13*H*,13*H*,15*H*,15*H*,16*H*,16*H*,17*H*,17*H*)perfluoroheptacosane (7a):** yield 34%; white solid; mp 78−80 °C; $R_f$ 0.48 (petroleum ether/ethyl acetate 4:1); $[\alpha]^{25}_D$ −25.1 (*c* 0.2, $C_6H_5CF_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.61−1.64 (m, 4H), 2.08−2.14 (m, 8H), 4. 08 (dd, $J$ = 8.4, 8.4 Hz, 2H), 4.60 (dd, $J$ = 8. 4, 9.6 Hz, 2H), 5.18 (dd, $J$ = 8.4, 9.6 Hz, 2H), 7.16−7.27 (m, 10H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.8, 31.5 (t, $J$ = 22.3 Hz), 33.1, 46.4, 70.0, 75.6, 127.0, 128.1, 129.2, 142.3, 168.2; $^{19}$F NMR ($CDCl_3$) $\delta$ −126.7 (m, 4F), −123.9 (m, 4F), −123.2 (m, 4F), −122.2 (m, 20F), −114.5 (m, 4F), −81.4 (t, $J$ = 10.3 Hz, 6F). Anal. Calcd for $C_{45}H_{28}F_{42}N_2O_2$: C, 37.87; H, 1.96. Found: C, 38.15; H, 1.92.

**14,14-Bis[(4*S*)-4-isopropyl-1,3-oxazolin-2-yl](*11H*,*11H*,*12H*,12*H*,13*H*,13*H*,15*H*,15*H*,16*H*,16*H*,17*H*,17*H*)perfluoroheptacosane (7b):** yield 49%; white solid; mp 74−76 °C; $R_f$ 0.50 (petroleum ether/ethyl acetate 4:1); $[\alpha]^{25}_D$ −23.4 (*c* 0.24, $C_6H_5CF_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.86 (d, $J$ = 6.6 Hz, 6H), 0.93 (d, $J$ = 6.6 Hz, 6H), 1.55−1.59 (m, 4H), 1.76−1.80 (m, 2H), 2.04−2.07 (m, 8H), 3.97−3.99 (m, 4H), 4.18−4.22 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.7, 18.1, 18.9, 31.5 (t, $J$ = 21.7 Hz), 32.8, 46.1, 70.3, 72.2, 110.1−119.0, 166.5; $^{19}$F NMR ($CDCl_3$) $\delta$ −126.8 (m, 4F), −124.1 (m, 4F), −123.4 (m, 4F), −122.4 (m, 20F), −114.8 (m, 4F), −81.5 (t, $J$ = 10.3 Hz, 6F). Anal. Calcd for $C_{39}H_{32}F_{42}N_2O_2$: C, 34.46; H, 2.37. Found: C, 34.68; H, 2.34.

**12,12-Bis[(4*S*)-4-isopropyl-1,3-oxazolin-2-yl]tricosane (8):** yield 52%; colorless oil; $R_f$ 0.58 (petroleum ether/ethyl acetate 1:1); $[\alpha]^{25}_D$ −53.8 (*c* 0.7, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.86 (d, $J$ = 6.6 Hz, 6H), 0.90 (m, 6H), 0.93 (d, $J$ = 6.6 Hz, 6H), 1.24−1.29 (m, 36H), 1.77−1.99 (m, 6H), 3.90−3;99 (m 4H), 4.12−4.20 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.4, 18.0, 19.0, 23.0, 24.1, 29.6, 29.7, 29.8, 29.9, 30.0, 30.1, 32.2, 32.6, 32.7, 46.2, 69.7, 72.0, 167.8. Anal. Calcd for $C_{35}H_{66}N_2O_2$: C, 76.85; H, 12.17. Found: C, 76.96; H, 12.45.

**Preparation of Complex [Pd($\eta^3$-$C_3H_5$)(6b)]$PF_6$.** A solution of [Pd($\eta^3$-$C_3H_5$)Cl]$_2$ (60 mg, 165 $\mu$mol) and ligand **6b** (401 mg, 347 $\mu$mol) in $CH_2Cl_2$ (9 mL) was stirred at rt under nitrogen for 1 h and then treated with $AgPF_6$ (90 mg, 360 $\mu$mol) in THF (7 mL). After 15 min, the mixture was filtered through a pad of Celite, and the filtrate was washed with a saturated aqueous solution of NaCl and dried over $Na_2SO_4$. The solid obtained after evaporation of the solvent under reduced pressure was triturated with hexane to afford the complex [Pd($\eta^3$-$C_3H_5$(**6b**)]$PF_6$ as a pale yellow solid (431 mg, 90% yield): mp 76−78 °C; $[\alpha]^{25}_D$ +13.8 (*c* 0.24, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.79 (d, $J$ = 6.8 Hz, 6H), 0.97 (d, $J$ = 7.0 Hz, 6H), 1.53−1.56 (m, 4H), 2.07−2.17 (m, 10H), 3.13 (d, $J$ = 12.1 Hz, 1H), 3.34 (d, $J$ = 12.8 Hz, 1H), 4.01 (d, $J$ = 6.0, 1H), 4.07 (d, $J$ = 6.8 Hz, 1H), 4.35−4.55 (m, 6H), 5.76 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.2, 16.6, 18.9, 29.9, 30.2 (t, $J$ = 23 Hz), 36.9, 49.7, 60.6, 63.1, 69.2, 74.2, 117.4, 170.0; $^{19}$F NMR ($CDCl_3$) $\delta$ −72.3 (s, 3F), −74.8 (s, 3F), −81.2 (t, $J$ = 9.3 Hz, 6F), −114.4 (m, 4F), −122.3 (m, 12F), −123.2 (m, 8F), −126.6 (m, 4F). Anal. Calcd for $C_{38}H_3F_{40}N_2O_2$-PPd: C, 31.45; H, 2.57. Found: C, 31.50; H, 2.77.

**2,2-Methylenebis[(4*R*)-4-[[[*tert*-butyl(dimethyl)silyl]-oxy]methyl]-1,3-oxazoline] (11).** To the amino alcohol (*R*)-**10**[23] (0.87 g, 4.23 mmol) dissolved in $CH_2Cl_2$ (20 mL) was added portionwise over 10 min diethyl malonimidate dihydrochloride (0.49 g, 2.15 mmol). Afetr being stirred at rt for 48 h, the solution was poured into water (20 mL), and the mixture was extracted with $CH_2Cl_2$ (3 × 20 mL). The organic layers were washed with brine (20 mL), dried over $Na_2SO_4$, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel, using $CH_2Cl_2$/$CH_3OH$ (9:1, v/v) as the eluent to afford the bis(oxazoline) **11** as a pale yellow oil (0.74 g, 78% yield): $R_f$ 0.78 ($CH_2Cl_2$/$CH_3OH$ 9:1); $[\alpha]^{25}_D$ −41.5 (*c* 0.34, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.00 (s, 12H), 0.83 (s, 18H), 3.27 (s, 2H), 3.49−3.54 (m, 2H), 3.74 (m, 2H), 4.19−4.30 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ −5.0, 18.5, 26.2, 28.7, 64.9, 68.9, 70.9, 163.2. Anal. Calcd for $C_{21}H_{42}N_2O_4Si_2$: C, 56.98; H, 9.57. Found: C, 56.42; H, 9.52.

**12,12-Bis[[(4*R*)-4-[*tert*-butyl(dimethyl)silyl]oxy]methyl-1,3-oxazolin-2-yl](9*H*,9*H*,10*H*,10*H*,11*H*,11*H*,13*H*,13*H*,14*H*,14*H*,15*H*,15*H*)perfluorotricosane (12).** This bis(oxazoline) was obtained from **11** by the general procedure previously described in 34% yield: white solid; mp 33−35 °C; $R_f$ 0.50 (petroleum ether/ethyl acetate 4:1); $[\alpha]^{25}_D$ −14.0 (*c* 0.2, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.00 (s, 12H), 0.83 (s, 18H), 1.49−1.53 (m, 4H), 1.98−2.03 (m, 8H), 3.48−3.50 (m, 2H), 3.75−3.78 (m, 2H), 4.17−4.23 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ −5.3, 15.5, 18.5, 26.0, 31.3 (t, $J$ = 21.7 Hz), 33.2, 46.1, 64.5, 68.0, 70.7, 168.1; $^{19}$F NMR ($CDCl_3$) $\delta$ −81.7 (t, $J$ = 10.3 Hz, 6F), −114.8 (m, 4F), −122.6 (m, 12F), −123.5 (m, 4F), −124.2 (m, 4F), −126.9 (m, 4F). Anal. Calcd for $C_{43}H_{52}F_{34}N_2O_4Si_2$: C, 37.89; H, 3.82. Found: C, 37.98; H, 3.89.

**12,12-Bis[(4*S*)-4-(hydroxymethyl)-1,3-oxazolin-2-yl]-(9*H*,9*H*,10*H*,10*H*,11*H*,11*H*,13*H*,13*H*,14*H*,14*H*,15*H*,15*H*)-perfluorotricosane (13).** A solution of $NBu_4F{\cdot}3H_2O$ (0.14 g, 0.52 mmol) in THF (3 mL) was added dropwise to a solution of bis(oxazoline) **12** (0.18 g, 0.13 mmol) in THF (2 mL). The mixture was stirred at rt for 2 h. After evaporation of the solvent, the mixture was diluted with diethyl ether (10 mL), and the solution was washed with water (3 × 10 mL) and dried over $Na_2SO_4$. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on silica gel ($CH_2Cl_2$/$CH_3OH$ 12:1) to yield the fluorous bis(oxazoline) **13** as a solid (100 mg, 70% yield): white solid; mp 43−45 °C; $R_f$ 0.46 ($CH_2Cl_2$/$CH_3OH$ 12:1); $[\alpha]^{25}_D$ −30.2 (*c* 0.2, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.64−1.69 (m, 4H), 2.00−2.16 (m, 8H), 3.52−3.55 (m, 2H), 3.78−3.82 (m, 4H), 4.28−4.40 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 16.0, 31.3 (t, $J$ = 21.7 Hz), 33.7, 47.0, 61.1, 67.4, 70.2, 169.8; $^{19}$F NMR ($CDCl_3$) $\delta$ −81.4 (t, $J$ = 10.3 Hz, 6F), −114.6 (m, 4F), −122.4 (m, 12F), −123.2 (m, 4F), −124.0 (m, 4F), −126.7 (m, 4F). Anal. Calcd for $C_{31}H_{24}F_{34}N_2O_4$: C, 32.80; H, 2.12. Found: C, 33.16; H, 2.19.

**Determination of Partition Coefficients.** The partition coefficients were determined by dissolving 20 mg of the bis(oxazoline) in a biphasic system consisting of FC72 (1 mL) and the organic solvent (1 mL). The resulting mixture was stirred at rt for 20 min. The two phases were separated, the solvents evaporated to dryness, and the residues weighed.

**General Procedure for the Catalytic Allylic Alkylation.** Ligand (31.2 $\mu$mol, 6.5 mol %) and [($\eta^3$-$C_3H_5$)PdCl]$_2$ (4.6 mg, 12.5 $\mu$mol, 2.5 mol %) were dissolved in the solvent (1.5 mL) under nitrogen in a Schlenk tube. The reaction mixture was stirred for 1 h at 50 °C, and 1,3-(*E*)-diphenyl-2-propenyl acetate **14** (126 mg, 0.5 mmol) in the solvent (1.5 mL) was transferred to this Schlenk tube. After 20 min, this solution was transferred into another reaction vessel containing *N*,*O*-bis(trimethylsilyl)acetamide (305 mg, 1.5 mmol), KOAc (4.9 mg, 0.05 mmol, 10 mol %), and the nucleophile (1.5 mmol) in the corresponding solvent (2 mL). When NaH was used as the base, the solution containing the acetate **14** and the catalyst was transferred into another reaction vessel containing NaH (36 mg, 1.5 mmol) and the nucleophile (1.5 mmol) in the solvent (2 mL). The reaction mixture was stirred at the desired

temperature for the appropriate time. The mixture was then diluted with diethyl ether, and the organic layer was washed with a saturated aqueous $NH_4Cl$ solution and then dried over $Na_2SO_4$. Evaporation of the solvent under reduced pressure gave a residue that was purified by chromatography on silica gel to afford the alkylated product **15**. The conversion was determined by GC using a Quadrex OV1 column (30 m × 0.25 mm) and the enantioselectivity by HPLC with a Chiralpak AD (25 cm × 0.46 cm) and eluting with hexane/*i*-PrOH (6:4).

**Recycling. Method A:** At the end of the reaction, the solvent was removed under reduced pressure, and the residue was extracted with FC72 (3 × 2 mL). The fluorous phase was washed with $CH_3CN$ (2 × 2 mL), and the fluorous solvent was removed under reduced pressure to afford the corresponding fluorous bis(oxazoline). The alkylated product was purified by chromatography on silica gel.

**Method B:** At the end of the reaction, the solvent was removed under reduced pressure, and diethyl ether (2 mL) was added followed by (1*H*,1*H*,2*H*,2*H*)perfluorooctyldimethyl bound silica gel (1 g). Evaporation of the solvent gave a powder that was charged on a column of chromatography containing fluorous silica. Elution was performed successively with $CH_3CN$ and then FC72. Evaporation of the fluorous phase afforded the fluorous bis(oxazoline), when evaporation of the organic phase followed by column chromatography gave the alkylation product.

**General Procedure for the Catalytic Allylic Oxidation.** To a stirred solution of $CuOTf{\cdot}0.5C_6H_6$ (4 mg, 16 $\mu$mol, 5 mol %) or $Cu(CH_3CN)_4PF_6$ (5.9 mg, 16 $\mu$mol, 5 mol %) in the $CHCl_3$ or FC72 (2 mL) was added the bis(oxazoline) (25 $\mu$mol, 8 mol %). This solution was warmed at 50 °C for 1 h. The alkene **17** (1.28 mmol, 80 equiv) in 2 mL of $CH_3CN$ was added to the solution cooled at rt, followed by dropwise addition of *tert*-butyl perbenzoate (61.3 mg, 0.32 mmol, 20 equiv). The resulting solution was then stirred at rt for the time indicated in Table 3. The mixture was then diluted with ether (10 mL), and the organic solution was washed with water (5 mL), HCl 2 N (5 mL), and water (5 mL). The solvent was removed in vacuo to afford a residue that was purified by column chromatography on silica gel to give the corresponding allylic benzoate **18**. The ee was determined by HPLC using a Chiralpak AD (25 cm × 0.46 cm) and eluting with hexane/*i*-PrOH (150:1)

**Recycling Using a Two-Phase System.** After reaction, the organic phase was separated from the fluorous phase at 0 °C, and a new solution of alkene and *tert*-butyl perbenzoate was added.

**Recycling by Precipitation.** After reaction, the solvent was evaporated. Hexane (3 × 2 mL) was added and the catalyst precipitated as a blue-green solid that was recovered by simple decantation of the supernatant liquid. The catalyst was reused in another catalytic oxidation without further addition of copper or ligand. Evaporation of hexane afforded a residue that was purified by chromatography on silica to give the allylic benzoate.

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**Supporting Information Available:** Preparation of fluorous iodide **5b** and $^1H$, $^{13}C$, and $^{19}F$ NMR spectra of compounds **3**, **6a**,**b**, **7a**,**b**, **8**, **12**, **13**, and $[Pd(\eta^3\text{-}C_3H_5)(\mathbf{6b})]PF_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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