Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 1259–1266

TETRAHEDRON: *ASYMMETRY*

# Enantioselective reduction of α,β-unsaturated ketones bearing the trifluoromethyl group

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Received 15 March 2001; accepted 4 May 2001

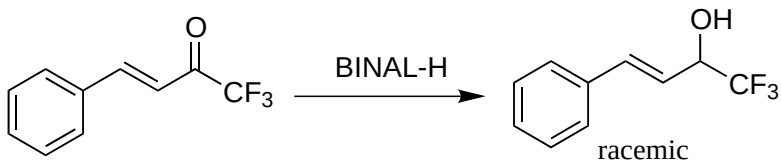
**Abstract**—α,β-Unsaturated ketones bearing the trifluoromethyl group were enantioselectively reduced by a variety of reagents to the corresponding secondary allylic alcohols with e.e. in the range 87–99%. The influence of the trifluoromethyl group on the enantioselectivity is discussed. © 2001 Published by Elsevier Science Ltd.

## 1. Introduction

Organofluorine compounds are promising biologically active materials, and include insecticides and pharmaceuticals. To further understand the mechanism of their action on receptors, individual isomers and enantiomers of such compounds are required for testing.

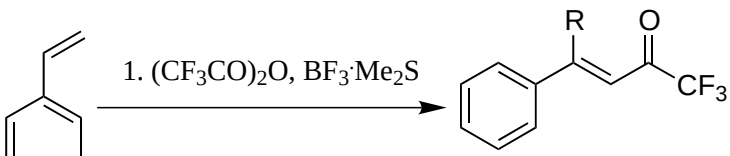
The enantioselective reduction of ketones is one of the most convenient and useful methods for the preparation of homochiral secondary alcohols.[1–3] The reduction of several types of ketones bearing fluoroalkyl groups has been investigated using various reagents[4] and the influence of the fluoroalkyl group on stereoselectivity was found to be unpredictable. Reduction of α,β-unsaturated ketones which possess a $CF_3$ group has not been studied thoroughly. Kitazume et al. have shown that the reduction of 1,1,1-trifluoro-4-phenylbuten-2-one by BINAL-H leads to the formation of racemic allylic alcohol **1a** (Scheme 1).[5]

Some microbiological methods for the reduction of such ketones have also been studied. In the case of baker's yeast, reduction of the double bond takes place and the reaction leads to mixtures of the saturated ketone and saturated alcohol.[5] However, using




**1** **1a**

**Scheme 1.**




**1**, R = H; **2**, **R** = Me

**Scheme 2.**

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PII: S0957-4166(01)00209-9

*Geotrichum candidum*, **1a** was obtained in good yield and excellent enantioselectivity.[6]

The aim of the work reported herein is the investigation of the enantioselective reduction of α,β-unsaturated ketones bearing the trifluoromethyl group by means of various chemical reagents.

## 2. Results and discussion

### 2.1. Synthesis of starting ketones

α,β-Unsaturated ketones bearing the trifluoromethyl group were prepared by three different methods. Ketones **1** and **2** were prepared by direct trifluoroacylation of the corresponding styrenes (Method A) (Scheme 2).[7]

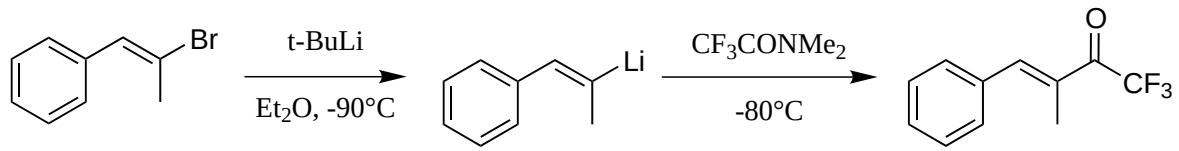
This method is useful for many types of alkenes; however, β-methylstyrenes do not react under these conditions. Therefore, the corresponding ketone **3** was prepared by reaction of *N*,*N*-dimethyltrifluoroacetamide with the appropriate alkenyllithium derivative (Method B) (Scheme 3).

Other ketones were prepared by the reaction of 4-dimethylamino-1,1,1-trifluorobut-3-en-2-one with a variety of aryllithium derivatives (Method C) (Scheme 4).[8]

The yields and methods of preparation of ketones are summarized in Table 1.

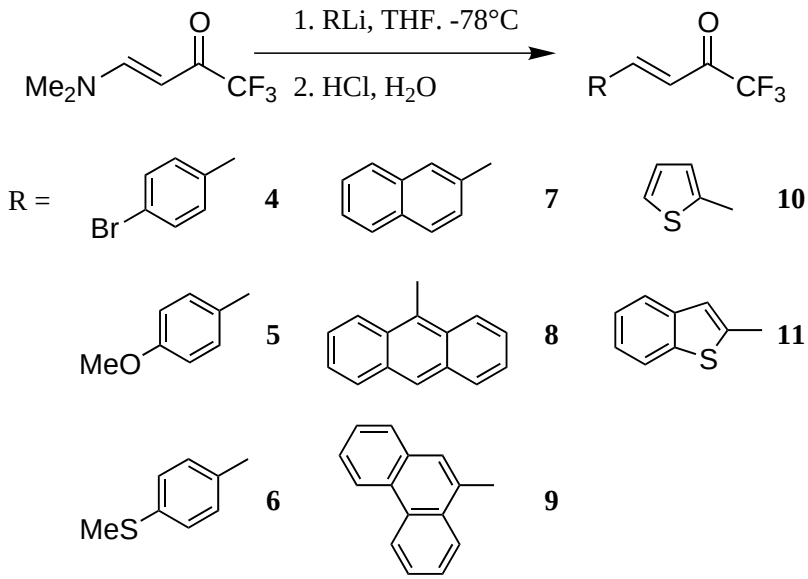
### 2.2. Reduction of ketone 1 by chiral reducing agents

Readily available ketone **1** was chosen as a model substrate in the screening experiments searching for the




**3**

**Scheme 3.**




**Scheme 4.**

**Table 1.** Preparation of the starting ketones

| Ketone | Method | Yield (%) | Ketone | Method | Yield (%) |
|---|---|---|---|---|---|
| **1** | A | 34 | **7** | C | 76 |
| **2** | A | 27 | **8** | C | 68 |
| **3** | B | 85 | **9** | C | 77 |
| **4** | C | 78 | **10** | C | 51 |
| **5** | C | 84 | **11** | C | 95 |
| **6** | C | 76 | | | |

best chiral reducing agent. Alpine-borane **12**,[9] DIP-Chloride **13**,[3] DIP-Bromide **14**,[10] and reduction using CBS catalysts[2] **15–18** by borane–dimethylsulfide complex or catecholborane were tested (Scheme 5).

Reduction of several types of trifluoromethyl-containing ketones by these reagents was reported recently.[4] Ramachandran and Brown made a systematic study on the reduction of aryl,[11] alkyl[11,12] and alkynyl[13] ketones by **13**. CBS reduction of some trifluoromethyl ketones has also been developed.[14,15]

Usually, reduction of most types of ketones by Alpine-borane **12** proceeds very slowly, but α,β-acetylenic ketones are known to react rapidly,[16] furnishing the corresponding propargylic alcohols. Moreover, α,β-acetylenic ketones bearing the trifluoromethyl group react even faster than the non-fluorinated analogues. However, when we tried to use this reagent for the reduction of ketone **1**, we found that the reaction proceeded too slowly and that only traces of the desired product were detected after reacting for one month.

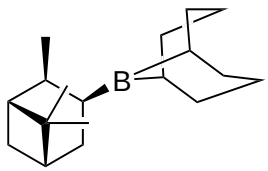
Reduction of ketone **1** by borane–dimethylsulfide complex in the presence of 20 mol% of the catalysts **15–17** led to formation of the racemic alcohol **1a**. It was reported that reduction of aryl trifluoromethyl ketones with such reagents also proceeds with low enantioselectivity.[14] We believe that the absence of stereoselectivity is due to fast reduction of the ketone by borane itself, without participation of a catalyst. To confirm this we investigated the reaction of ketone **1** with borane–dimethylsulfide complex in the absence of the CBS catalyst. It was found that the reaction proceeded exothermically within several minutes, accompanied by the formation of small amounts of the corresponding saturated alcohol. The main product was racemic alcohol **1a**.

We established that application of CBS catalyst **17** with catecholborane reducing agent allowed the preparation of alcohol **1a** in 76% e.e. A better result (87% e.e.) was obtained in the case of oxazaborolidine **18**.[17] We assume that the improvement in the enantioselectivity is due to the bulky $CH_2TMS$ group; some Si–F interactions in the transition state are also possible.

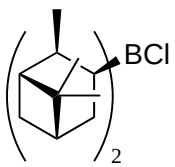
Reaction of ketone **1** with DIP-Chloride proceeded in THF at room temperature over 5 days to give **1a** in 92% isolated yield and 90% e.e. We found that the rate of the reaction was dependent on the polarity of the solvent. For example, the reaction was extremely slow in hexane, but the rate was faster in THF, dichloromethane and ether (reactions in these solvents had approximately the same rate). However, the enantioselectivity of the reaction was not dependent on the nature of solvent.

Reduction with DIP-Bromide proceeded at a higher rate and with excellent enantioselectivity, but the yield of the target product was lower. Being a stronger Lewis acid than **13** it is possible that reagent **14** causes degradation of the product and/or the starting ketone.

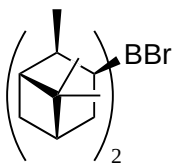
To summarize the first part of our investigation, we found DIP-Chloride to be the best reagent for the reduction of α,β-unsaturated ketones bearing a trifluoromethyl group (Table 2).



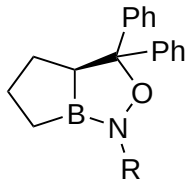

**12**




**13**




**14**




R = H **15**
Me **16**
Bu **17**
$CH_2TMS$ **18**

**Scheme 5.**

**Table 2.** Reduction of ketone **1** by reagents **12–18**

| Reagent | Reaction conditions | Yield (%) | Configuration | E.e. (%) |
|---|---|---|---|---|
| **12** | rt, without solvent | 0 | – | – |
| **13** | rt, THF | 92 | *S* | 90 |
| **14** | rt, $CH_2Cl_2$ | 56 | *S* | >99 |
| $BH_3{\cdot}Me_2S$, 20 mol% of **15** | 30°C, THF | 65 | Racemate | 0 |
| | 0°C, THF | 75 | Racemate | 0 |
| | −30°C, THF | 90 | Racemate | 0 |
| $BH_3{\cdot}Me_2S$, 20 mol% of **16** | −30°C, THF | 65 | Racemate | 0 |
| Catecholborane, 20 mol% of **17** | −87°C, toluene | 85 | *R* | 78 |
| Catecholborane, 20 mol% of **17** | −87°C, $CH_2Cl_2$ | 87 | *R* | 76 |
| Catecholborane, 20 mol% of **18** | −87°C, toluene | 81 | *R* | 87 |

### 2.3. Stereochemistry of reduction

We also investigated the stereochemistry of the reduction reactions. The absolute configuration of alcohol **4a**, prepared by reduction of ketone **4** by (–)-DIP-Chloride, was determined by X-ray analysis.[18] The product was found to have (*S*)-configuration (Fig. 1).

To determine the absolute configuration of alcohol **1a** we analyzed some (*S*)-MPTA[19] derivatives by $^{19}F$ NMR spectroscopy. Comparison of the spectra then allowed assignment of the configuration of **1a** obtained from reaction with the different reducing agents. The signals for the $CF_3$ groups of the (*S*)-MPTA ester of (*S*)-**4a** shifted downfield compared to the signals of the minor diastereomeric ester. The same effect was observed in the spectrum of the (*S*)-MPTA esters of **1a**, which were obtained from the reduction of **1** with **13** and **14**. However, the signals of the main diastereomer in the spectrum of the (*S*)-MPTA ester of **1a** obtained by CBS reduction with catecholborane was shifted upfield. Therefore, we conclude that the configuration of **1a** prepared by means of reagents **13** and **14** by (*S*) and CBS reduction leads to the (*R*)-product (Fig. 2).

The stereochemical outcome of the reductions of trifluoromethyl ketones is in agreement with literature models for the reduction of ketones with both oxazaborolidines[20] and DIP-Chloride.[11] In the postulated transition states for CBS reduction and reduction by DIP-Chloride (Scheme 6) the $CF_3$ group having greater conformational energy occupies the less sterically hindered position rather than the other ketone substituent. Therefore, CBS reduction should lead to the (*R*)-product and reduction by (–)-DIP-Chloride should result in formation of the (*S*)-product.

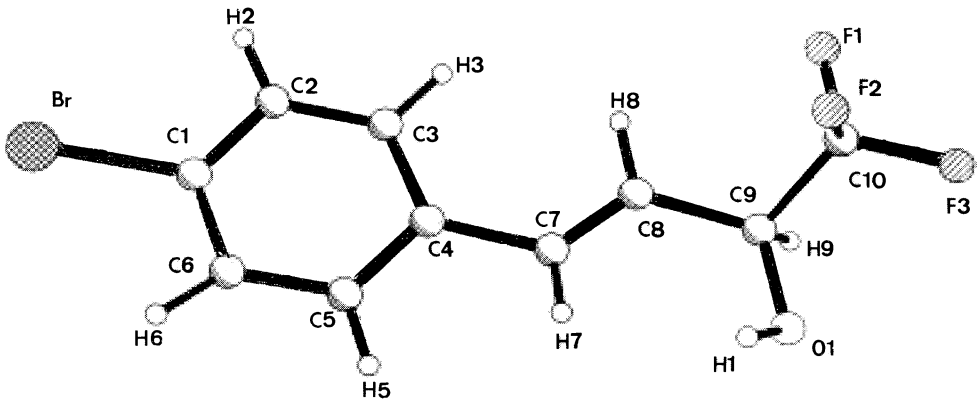



**Figure 1.** X-Ray structure of **4a**.

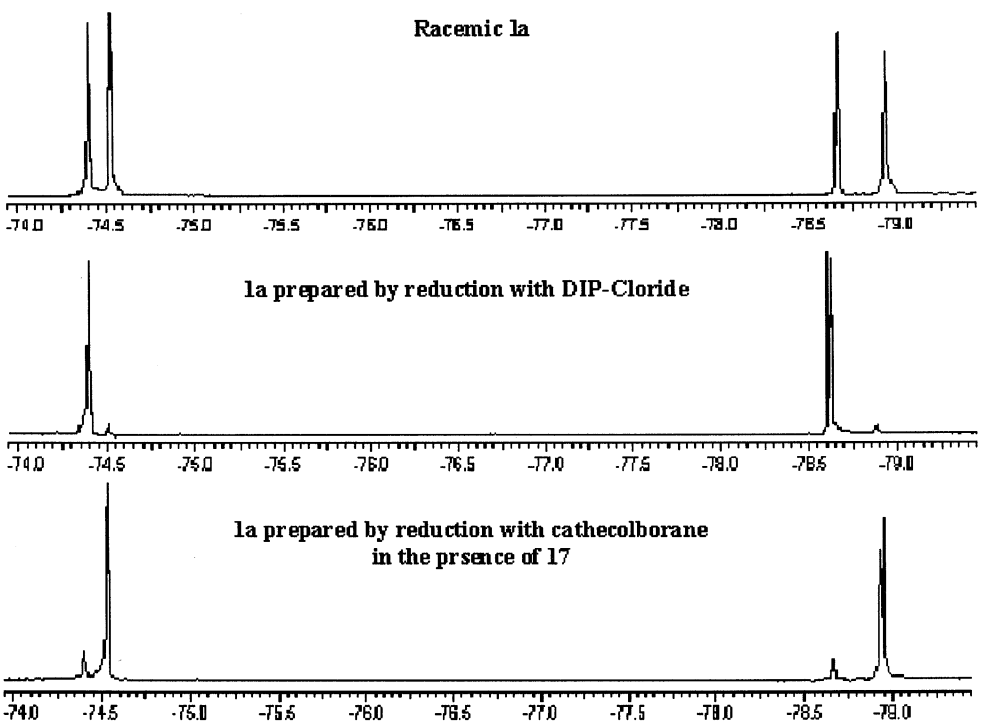
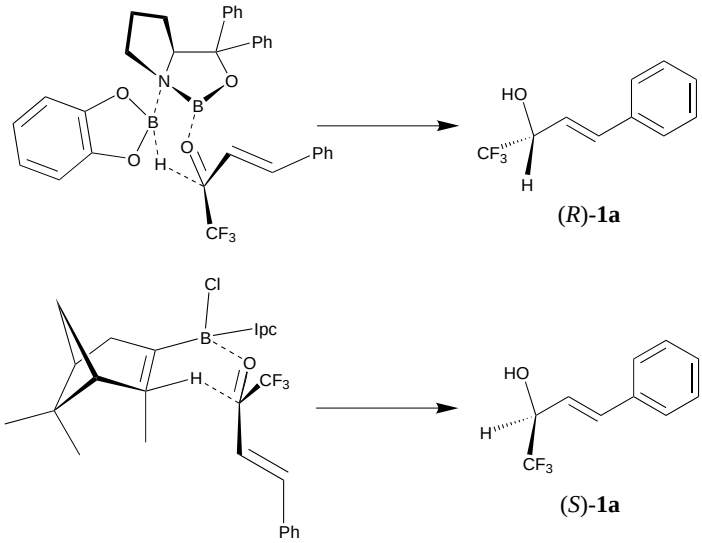



**Figure 2.** $^{19}F$ spectra of (*S*)-MPTA esters of racemic and scalemic **1a**.




**Scheme 6.**

### 2.4. Reduction of other α,β-unsaturated trifluoromethyl ketones

Having found that DIP-Chloride was the optimal reagent for the asymmetric reduction of ketone **1**, we investigated the preparation of other $CF_3$-substituted allylic alcohols (Table 3). The absolute configurations were determined by comparison of chemical shifts of the major diastereomer in $^{19}F$ NMR spectra of (*S*)-MPTA esters of obtained non-racemic alcohols and their racemates, relying on the data for alcohol **4a**. It should be noted that in all cases studied the reduction led to the corresponding (*S*)-alcohols.

## 3. Conclusion

DIP-Chloride was found to be the best reagent for the reduction of α,β-unsaturated trifluoromethyl ketones into the corresponding allylic alcohols. Good enantioselectivities were achieved using a very straightforward experimental procedure.

## 4. Experimental

### 4.1. General

$^1H$ and $^{13}C$ NMR and $^{19}F$ spectra were recorded on Varian VXR-400 spectrometers with TMS or $CFCl_3$ as an internal standard. The IR spectra were obtained on a UR-20 spectrometer in films. HPLC analysis was performed using a Chiracel OD-H column. The e.e.s of the prepared compounds were determined by HPLC or $^{19}F$ NMR spectroscopy using (*S*)-MPTA derivatives.[19] Acylation was performed with the (*S*)-MPTA-chloride in dichloromethane solution in the presence of pyridine and DMAP.[19]

THF, toluene and diethyl ether were dried and distilled according to standard procedures.[21] All operations with air-sensitive compounds were conducted under argon by means of usual Schlenk-type techniques.

Diphenylprolinol,[22] catecholborane,[23] butylboronic acid,[24] trimethylsilylmethaneboronic acid,[17] boroxines,[22,25] 9-BBN[26] and Alpine-borane[27] were prepared by literature procedures. Oxazaborolidines were prepared by reaction of corresponding boroxines with diphenylprolinol,[22] except **17**, which was prepared from trimethylsilylmethaneboronic acid,[17] and **15**, which was obtained by reaction of $BH_3{\cdot}Me_2S$ and diphenylprolinol.[28] DIP-Bromide was prepared by hydroboration of (+)-α-pinene by $BH_2Br$–dimethylsulfide complex in dichloromethane at room temperature, followed by recrystallization in hexane.[29]

### 4.2. Preparation of ketones

**4.2.1. Preparation of (*E*)-1,1,1-trifluoro-3-methyl-4-phenyl-3-buten-2-one 3**. [(*E*)-2-Bromo-1-propenyl]benzene was prepared from (*E*)-2-methyl-3-phenyl-2-propenoic acid by a literature procedure.[30]

**Table 3.** Reduction of α,β-unsaturated $CF_3$ ketones

| Ketones | Alcohol obtained | | | |
|---|---|---|---|---|
| | Alcohols | Configuration | Yield (%) | E.e. (%) |
| **2** | **2a** | *S* | 85 | 90 |
| **3** | **3a** | *S* | 92 | 92 |
| **4** | **4a** | *S* | 85 | >99 |
| **5** | **5a** | *S* | 90 | 88 |
| **6** | **6a** | *S* | 88 | >99 |
| **7** | **7a** | *S* | 81 | >99 |
| **8** | **8a** | *S* | 91 | 92 |
| **9** | **9a** | *S* | 89 | >99 |
| **10** | **10a** | *S* | 78 | 91 |
| **11** | **11a** | *S* | 75 | 87 |

To a solution of [(*E*)-2-bromo-1-propenyl]benzene (10 mmol) in ether at −95°C was slowly added a solution of *tert*-BuLi in pentane (22 mmol). After stirring at this temperature for 15 min, the temperature was allowed to rise to −78°C and the reaction mixture was stirred for an additional 15 min. During this time a suspension of organolithium derivatives was seen to form. A solution of 2,2,2-trifluoro-*N*,*N*-dimethylacetamide (22 mmol) was added over 20 min at −78°C. The cooling bath was removed and the temperature of the mixture was allowed to rise to 0°C with stirring. The mixture was cooled to −30°C and quenched by the addition of a saturated $NH_4Cl$ solution (10 mL). The organic layer was removed, the aqueous was extracted three times with ether and the combined organic layers were dried over $Na_2SO_4$ and evaporated. The residue was dissolved in a mixture of hexanes and benzene (1:1) and was passed through a short column of $SiO_2$. The solvent was removed in vacuo and the crude product was purified by distillation (bp 89–92°C/2 mmHg). 85% yield. IR ($\nu$, $cm^{-1}$): 1605, 1720. $\delta_H$ ($CDCl_3$) 2.12 (3H, s), 6.62 (1H, s), 7.15–7.54 (5H, m); $\delta_C$ ($CDCl_3$) 17.05, 116.43 (q, $J=293.12$ Hz), 126.47, 128.56, 129.77, 130.46, 142.52, 164.12, 179.34 (q, $J=34.32$ Hz). Anal. calcd for $C_{11}H_9F_3O$: C, 61.68; H, 4.24. Found: C, 61.72; H, 4.27%.

**4.2.2. Ketones 4–11**. Ketones **4–11** were prepared by procedures reported in the literature.[8]

**4.2.2.1. (*E*)-4-(4-Bromophenyl)-1,1,1-trifluoro-3-buten-2-one 4**. Light yellow solid, mp 55–57°C; IR ($\nu$, $cm^{-1}$): 1620, 1720; $\delta_H$ ($CDCl_3$) 6.91 (1H, dd, $J=15.86$, 0.82 Hz), 7.40 (2H, d, $J=8.43$ Hz), 7.49 (2H, d, $J=8.43$ Hz), 7.80 (2H, d, $J=15.86$ Hz); $\delta_C$ ($CDCl_3$) 114.09 (q, $J=291.46$ Hz), 117.05, 126.92, 130.41, 132.14, 132.51, 148.55, 179.80 (q, $J=36.8$ Hz). Anal. calcd for $C_{10}H_6BrF_3O$: C, 43.04; H, 2.17. Found: C, 43.24; H, 2.20%.

**4.2.2.2. (*E*)-1,1,1-Trifluoro-4-(4-methoxyphenyl)-3-buten-2-one 5**. Light yellow solid, mp 50–52°C; IR ($\nu$, $cm^{-1}$): 1560, 1790; $\delta_H$ ($CDCl_3$) 3.84 (3H, s), 6.86 (1H, d, $J=15.86$ Hz), 6.93 (2H, d, $J=8.68$ Hz), 7.57 (2H, d, $J=8.68$), 7.90 (1H, d, $J=15.86$ Hz); $\delta_C$ ($CDCl_3$) 55.39, 113.88, 114.67, 119.41 (q, $J=291.32$ Hz), 126.07, 131.32, 149.89, 163.16, 179.59 (q, $J=35.10$ Hz). Anal. calcd for $C_{11}H_9F_3O_2$: C, 57.40; H, 3.94. Found: C, 57.55; H, 3.96%.

**4.2.2.3. (*E*)-1,1,1-Trifluoro-4-[4-(methylsulfanyl)phenyl]-3-buten-2-one 6**. Yellow solid, mp 68–69°C; IR ($\nu$, $cm^{-1}$): 1590, 1690; $\delta_H$ ($CDCl_3$) 2.52 (1H, s), 6.97 (1H, d, $J=15.88$ Hz), 7.26 (2H, d, $J=8.43$ Hz), 7.50 (2H, d, $J=8.43$ Hz), 7.91 (1H, d, $J=15.88$ Hz); $\delta_C$ ($CDCl_3$) 14.68, 114.5 (q, $J=290.83$ Hz), 115.15, 118.36, 125.63, 129.52, 145.35, 149.52, 179.82 (q, $J=35.19$ Hz). Anal. calcd for $C_{11}H_9F_3OS$: C, 53.65; H, 3.68. Found: C, 53.61, H, 3.69%.

**4.2.2.4. (*E*)-1,1,1-Trifluoro-4-(2-naphthyl)-3-buten-2-one 7**. Light yellow solid, mp 62–64°C; IR ($\nu$, $cm^{-1}$): 1620, 1730; $\delta_H$ ($CDCl_3$) 7.13 (1H, d, $J=15$, 73 Hz), 7.49–7.63 (4H, m), 7.88–7.91 (2H, m), 7.98 (1H, d, $J=8.21$ Hz), 8.17 (1H, d, $J=15$, 73 Hz); $\delta_C$ ($CDCl_3$) 116.45 (q, $J=292.42$ Hz), 118.41, 122.73, 125.32, 126.05, 126.59, 127.59, 128.96, 130.23, 131.72, 132.76, 133.71, 146.583, 180.85 (q, $J=35.18$ Hz). Anal. calcd for $C_{14}H_9F_3O$: C, 67.20; H, 3.63. Found: C, 67.23; H, 3.75%.

**4.2.2.5. (*E*)-1,1,1-Trifluoro-4-(9-phenanthryl)-3-buten-2-one 9**. Yellow solid, mp 130–132°C; IR ($\nu$, $cm^{-1}$): 1610, 1720; $\delta_H$ ($CDCl_3$) 7.21 (1H, d, $J=15.65$ Hz), 7.63–7.76 (4H, m), 7.95 (1H, d, $J=7.99$ Hz), 8.12 (1H, s), 8.18–8.21 (1H, m), 8.67 (1H, d, $J=8.21$ Hz), 8.72–8.74 (1H, m), 8.83 (1H, d, $J=15.65$ Hz); $\delta_C$ ($CDCl_3$) 116.45 (q, $J=288.22$ Hz), 118.88, 122.62, 123.25, 123.67, 127.22, 127.31, 128.00, 128.65, 129.32, 129.58, 129.65, 130.38, 130.54, 131.81, 180.32 (q, $J=35.09$ Hz). Anal. calcd for $C_{18}H_{11}F_3O$: C, 72.00; H, 3.69. Found: C, 72.05; H, 3.71%.

### 4.3. Reduction of ketones

#### 4.3.1. Reduction with boranes in the presence of oxazaborolidines

**4.3.1.1. General procedure for reductions with $BH_3$·$Me_2S$**. To a stirred solution of oxazaborolidine (1 mmol) and $BH_3$·$Me_2S$ (0.5 mmol) in THF at −30°C, ketone **1** (0.5 mmol) was added. The reaction was monitored by TLC. After a few minutes the reaction mixture was quenched with methanol and evaporated. The residue was suspended in diethyl ether, washed twice with 10% NaOH and dried over $Na_2SO_4$. The solvent was removed in vacuo and the crude product was purified by column chromatography (hexane/ethyl acetate, 9:1). The yields of product are given in Table 2.

**4.3.1.2. General procedure for reductions with catecholborane**. To a stirred solution of oxazaborolidine (1 mmol) in toluene was added ketone **1** (5 mmol). The reaction mixture was immersed in an ethyl acetate–liquid nitrogen bath and stirred for 30 min. A solution of catecholborane (10 mmol) in toluene was added dropwise within 30 min. The reaction was monitored by TLC and was complete within 2 h. The reaction mixture was quenched with methanol and evaporated. The residue was suspended in diethyl ether, washed with 10% NaOH until aqueous layer did not change color, and dried with $Na_2SO_4$. The solvent was removed in vacuo and the crude product was purified by column chromatography (hexane/ethyl acetate, 9:1). The yields and enantiomeric purities of product are given in Table 2.

**4.3.1.3. General procedure for reductions with DIP-Chloride**. The ketone (1 mmol) was placed in a flame dried Schlenk bottom flask fitted with a rubber septum. A solution of DIP-Cl in THF (1.1 mmol) was added and the reaction mixture was allowed to stand at room temperature with TLC analysis. After 5 days the reaction was quenched by the addition of acetaldehyde (1.2 mmol) and the mixture was allowed to stand for an additional 12 h. The reaction mixture was evaporated in vacuo and the residue was dissolved in ether and

washed three times with 1 M NaOH. The organic layer was dried over $Na_2SO_4$ and the solvent was removed. The product was purified by column chromatography (100 g of silica gel, hexanes/ethyl acetate, 10:1, as eluent). The crude compounds were recrystallized from hexanes or a mixture of hexanes and benzene. Compounds **7**, **8**, **9** and **11** were purified by recrystallization instead of chromatographic purification.

**4.3.1.4. (*S*)-(*E*)-1,1,1-Trifluoro-4-phenyl-3-penten-2-ol 2a**. Colorless oil, $[\alpha]_D=-12$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 1.88 (3H, s), 2.44 (1H, bs), 4.45 (1H, q, $J=6.92$ Hz), 6.60 (1H, s), 7.15–7.29 (5H, m); $\delta_C$ ($CDCl_3$) 13.63, 75.8 (q, $J=32.05$ Hz), 124.5 (q, $J=283.82$ Hz), 127.3, 128.22, 129.07, 131.01, 131.83, 136.17. Anal. calcd for $C_{11}H_{11}F_3O$: C, 61.11; H, 5.13. Found: C, 61.42; H, 5.01%.

**4.3.1.5. (*S*)-(*E*)-1,1,1-Trifluoro-3-methyl-4-phenyl-3-buten-2-ol 3a**. Colorless oil, $[\alpha]_D=-8$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 2.17 (3H, s), 2.95 (1H, bs), 4.81 (1H, dq, $J=2.2$ Hz, 8.65 Hz), 5.76 (1H, d, $J=8.65$ Hz), 7.35–7.42 (5H, m); $\delta_C$ ($CDCl_3$) 16.70, 67.90 (q, $J=31.4$ Hz), 119.18, 123.33, 124.72 (q, $J=282.22$ Hz), 126.13, 128.21, 141.75, 144.46. Anal. calcd for $C_{11}H_{11}F_3O$: C, 61.11; H, 5.13. Found: C, 61.77; H, 5.81%.

**4.3.1.6. (*S*)-(*E*)-4-(4-Bromophenyl)-1,1,1-trifluoro-3-buten-2-ol 4a**. Colorless solid, mp 87–89°C; $[\alpha]_D=-9.1$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 2.87 (1H, s), 4.63 (1H, m), 6.57 (1H, dd, $J=6.82$ Hz, 15.11 Hz), 6.78. (1H, d, $J=15.11$ Hz), 7.09 (2H, d, $J=8.18$ Hz), 7.19 (2H, d, $J$ 8.57 Hz); $\delta_C$ ($CDCl_3$) 72.57 (q, $J=32.00$ Hz), 119.05, 123.42, 124.55 (q, $J=282.78$ Hz), 130.00, 132.73, 134.44, 142.47. Anal. calcd for $C_{10}H_8BrF_3O$: C, 42.73; H, 2.87. Found: C, 42.75; H, 2.88%.

**4.3.1.7. (*S*)-(3*E*)-1,1,1-Trifluoro-4-(4-methoxyphenyl)-3-buten-2-ol 5a**. Colorless solid, $[\alpha]_D=-12$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 2.85 (1H, s), 4.58 (1H, m), 6.05 (1H, dd, $J=6.98$ Hz, 15.87 Hz), 6.76 (1H, d, $J=15.87$ Hz), 6.87 (2H, d, $J=8.57$ Hz), 7.33 (2H, d, $J=8.57$ Hz); $\delta_C$ ($CDCl_3$) 55.17, 71.75 (q, $J=32.05$ Hz), 114.10, 118.28, 124.35 (q, $J=280.78$ Hz), 128.10, 128.18, 135.94. Anal. calcd for $C_{11}H_{11}F_3O_2$: C, 56.90; H, 4.77. Found: C, 56.93; H, 4.79%.

**4.3.1.8. (*S*)-(*E*)-1,1,1-Trifluoro-4-[4-(methylsulfanyl)-phenyl]-3-buten-2-ol 6a**. Colorless solid, mp 72–74°C; $[\alpha]_D=-7.5$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 2.40 (3H, s), 4.52 (1H, m), 6.06 (1H, dd, $J=16.1$ Hz, 6.69 Hz), 6.70 (1H, d, $J=16.1$ Hz), 7.2 (2H, d, $J=7.93$ Hz), 7.23 (2H, d, $J=7.93$ Hz); $\delta_C$ ($CDCl_3$) 15.45, 71.55 (q, $J=32.05$ Hz), 119.85, 124.25 (q, $J=279.25$ Hz), 126.32, 127.2, 132.08, 135.61, 139.36. Anal. calcd for $C_{11}H_{11}F_3OS$: C, 53.22; H, 4.47. Found: C, 53.31; H, 4.51%.

**4.3.1.9. (*S*)-(*E*)-1,1,1-Trifluoro-4-(2-naphthyl)-3-buten-2-ol 7a**. Colorless solid, mp 67–69°C; $[\alpha]_D=-9$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 2.77 (1H, s), 4.77 (1H, m), 6.26 (1H, dd, $J=15.75$ Hz, 6.47 Hz), 7.44–7.65 (5H, m), 7.83–7.89 (2H, m), 8.07–8.10 (1H, m); $\delta_C$ ($CDCl_3$) 71.64 (q, $J=32.04$ Hz), 123.48, 123.78, 124.37 (q, $J=282.3$ Hz), 124.39, 125.549, 126.03, 126.4, 128.64, 129.02, 131.06, 133.12, 133.59, 133.73. Anal. calcd for $C_{14}H_{11}F_3O$: C, 66.67; H, 4.40. Found: C, 66.73; H, 4.43%.

**4.3.1.10. (*S*)-(*E*)-4-(9-Anthryl)-1,1,1-trifluoro-3-buten-2-ol 8a**. Light yellow solid, mp 114–117°C; $[\alpha]_D=-8.7$ ($c=1.6$, acetone); $\delta_H$ ($(CD)_3CO$) 4.96–5.03 (m, 1H), 6.45 (1H, dd $J=6.52$ Hz, 15.58 Hz), 7.59–7.74 (4H, m), 7.98–8.02 (2H, m), 7.78 (1H, d, $J=15.58$ Hz); $\delta_C$ ($(CD)_3CO$) 71.51 (q, $J=32.1$ Hz), 122.17, 123.40, 124.05, 125.22, 125.81, 126.06 (q, $J=282.3$ Hz), 126.83, 127.63, 127.71, 127.78, 127.81, 129.65, 131.14, 131.18, 132.50, 133.43, 133.56. Anal. calcd for $C_{18}H_{13}F_3O$: C, 71.52; H, 4.33. Found: C, 71.49; H, 4.37%.

**4.3.1.11. (*S*)-(*E*)-1,1,1-Trifluoro-4-(9-phenanthryl)-3-buten-2-ol 9a**. Light yellow solid, mp 165–167°C; $[\alpha]_D=-9.5$ ($c=1.6$, acetone); $\delta_H$ ($(CD)_3CO$) 4.99 (1H, m), 6.46 (1H, dd, $J=15.48$ Hz, 6.30 Hz), 7.37–7.83 (5H, m), 8.00–8.08 (2H, m), 8.23 (1H, dd, $J=8.31$ Hz, $J=2.22$ Hz), 8.81 (1H, d, $J=7.62$ Hz), 8.89 (1H, dd, $J=7.65$ Hz, $J=1.86$ Hz); $\delta_C$ ($(CD)_3CO$) 71.92 (q, $J=32.1$ Hz), 123.7 (q, $J=280.36$ Hz), 123.81, 124.54, 125.69, 126.26, 127.31, 128.12, 128.20, 128.26, 128.29, 130.13, 131.61, 131.67, 132.99, 133.91, 134.01. Anal. calcd for $C_{18}H_{13}F_3O$: C, 71.52; H, 4.33. Found: C, 71.18; H, 4.52%.

**4.3.1.12. (*S*)-(*E*)-1,1,1-Trifluoro-4-(2-thienyl)-3-buten-2-ol 10a**. Colorless solid, mp 55–57°C; $[\alpha]_D=-11$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($CDCl_3$) 2.65 (1H, s), 4.5 (1H, m), 5.93 (1H, dd, $J=15.87$ Hz, 6.61 Hz), 6.88 (1H, d, $J^3_{H\text{-}H}=15.87$ Hz), 6.91 (1H, dd, $J=3.66$ Hz, 4.88 Hz), 6.97 (1H, d, $J=3.66$ Hz), 7.16 (1H, d, $J=4.88$ Hz); $\delta_C$ ($CDCl_3$) 71.22 (q, $J=32.04$ Hz), 119.71, 122.65 (q, $J^1_{C\text{-}F}=282.31$ Hz), 125.78, 127.52 (2C), 129.16, 140.22. Anal. calcd for $C_8H_7F_3OS$: C, 46.15; H, 3.39. Found: C, 47.02; H, 3.27%.

**4.3.1.13. (*S*)-(*E*)-4-(1-Benzothien-2-yl)-1,1,1-trifluoro-3-buten-2-ol 11a**. Colorless solid, mp 122–123°C; $[\alpha]_D=-21$ ($c=1.6$, $CHCl_3$); $\delta_H$ ($(CD_3)_2CO$) 4.83 (1H, m), 6.17 (1H, dd, $J=15.57$ Hz, 5.94 Hz), 7.23 (1H, d, $J=15.57$ Hz), 7.32–7.37 (2H, m), 7.42 (1H, s), 7.75–7.79 (1H, m), 7.83–7.88 (1H, m); $\delta_C$ ($(CD_3)_2CO$) 71.52 (q, $J=32.2$ Hz), 122.92, 123.04, 124.8 (q, $J=280.56$ Hz), 125.57, 125.35, 125.73, 130.44, 140.01, 140.56, 141.03. Anal. calcd for $C_{12}H_9F_3OS$: C, 55.81; H, 3.51. Found: C, 55.87; H, 3.52%.

## Acknowledgements

The research described in this publication was supported by the Russian Fundamental Investigation Foundation (Grant N 00-03-32760a). Dr. David Lindsay (LMU, München) is gratefully acknowledged for his help with correction of the text.

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