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Reactions of α-imino ketones derived from arylglyoxals with (trifluoromethyl)trimethylsilane; a new route to β-amino-α-trifluoromethyl alcohols

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ABSTRACT

The reactions of α-imino ketones, derived from arylglyoxals, with (trifluoromethyl)trimethylsilane (CF_3SiMe_3) in DME solution, in the presence of catalytic amount of CsF, at room temperature, yield O-silylated β-imino alcohols in the chemoselective manner. Subsequent reduction of these products with $NaBH_4$ in ethanolic solution leads to the corresponding β-(N-alkyl)amino-α-trifluoromethyl alcohols in good to excellent yields. Trifluoromethylation of enantiomerically pure α-imino ketones (with Ar = Ph or *p*-$MeOC_6H_4$), bearing as a chiral auxiliary the PhCH(Me) group attached to the nitrogen atom, yields mixtures of diastereomeric products in the ratio of ca. 3:2.

1. Introduction

Synthesis of fluoroorganic compounds is a challenging topic of the modern organic chemistry. Especially, the presence of trifluoromethyl moiety in the target molecule often results in significant changes of its physical, chemical and biological properties [1].

The incorporation of the CF_3 group can be conveniently achieved via nucleophilic addition of (trifluoromethyl)trimethylsilane CF_3SiMe_3, the 'Ruppert–Prakash reagent' to electrophilic double bonds [2]. Trifluoromethylation of aldehydes, ketones [3a–d] and esters [3e,f], and other carbonyl derivatives [2a,b], with this extremely useful reagent has been extensively studied. Generally, imines are less reactive towards CF_3SiMe_3 than the corresponding carbonyl analogues. Nevertheless, application of activated imines [4] or special reaction conditions [5] gave the desired α-(trifluoromethyl)amines.

β-Amino alcohols, both achiral and chiral, are versatile reagents for organic synthesis [6,7] and extremely useful building blocks for the preparation of diverse, biologically active compounds [8]. Special attention was focused on the enantiomerically pure β-amino alcohols which are used in asymmetric synthesis as chiral auxiliaries or catalysts [6–8]. Combination of two relevant features, i.e. the synthetic utility of β-amino alcohols and unique properties of the trifluoromethyl group, results in a growing interest in the synthesis of amino alcohols bearing the CF_3 group [9]. β-Amino-α-trifluoromethyl alcohols are reported as effective catalysts in enantioselective reactions and it is well documented that they are more efficient than their non-fluorinated analogues [9c]. β-Amino alcohols, modified with fluorinated alkyl chains, were used as attractive building blocks for the preparation of mimetics of versatile biologically active compounds [9c] as well as diverse heterocycles with variable ring size [10]. In general, three main strategies for the synthesis of β-amino-α-trifluoromethyl alcohols, are presently known. Historically, the oldest one is the Henry reaction (nitro-aldol reaction) with subsequent reduction of the initially formed β-nitro alcohols. Another approach is based on the ring opening of 2-(trifluoromethyl)oxiranes with primary or secondary amines, and finally, nucleophilic trifluoromethylation of appropriate α-amino aldehydes with (trifluoromethyl)-trimethylsilane has been extensively studied in the past two decades [9c].

Recently, we reported on the smooth, diastereoselective additions of CF_3SiMe_3 to easily available α-imino ketones **1**, derived from (1*R*)-camphorquinone, leading to the adducts **2**. These products, upon treatment with sodium borohydride, were smoothly converted into the corresponding β-imino alcohols **3** (Scheme 1) [11]. The subsequent reduction of **3** with DIBAL-H ($NaBH_4$ turned out not to be reactive enough) afforded the β-amino-α-trifluoromethyl alcohols **4** as single *2-exo,3-exo* diastereomers.

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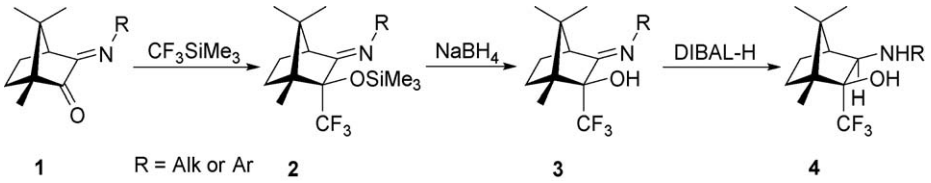


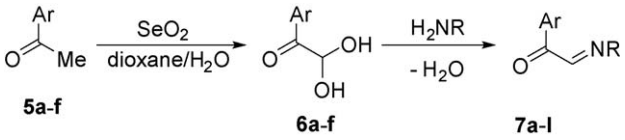
Scheme 1.

The aim of the present study was the elaboration of a simple and reproducible protocol for the conversion of readily available arylglyoxal imines of type **7** into hitherto unknown trifluoromethylated β-amino alcohols **9**, potentially useful for further applications including synthesis of biologically active compounds and organocatalysis. The key step in the presented method is the chemoselective addition of CF_3SiMe_3 to the C=O group and subsequent reduction of the remaining C=N bond.

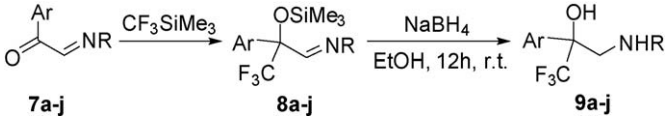
2. Results and discussion

Preparation of 1-aryl-2,2-dihydroxyethanones **6a–f** was based on the known oxidation of aryl-methylketones **5a–f** using SeO_2 in an aqueous dioxane solution (Scheme 2) [12]. A slightly modified literature procedure [13] applied for condensation of primary amines with arylglyoxal hydrates **6a–f** leads to α-imino ketones **7a–j** (Scheme 2, Table 1). Reactions of arylglyoxals **6** with *tert*-butylamine, isopropylamine and (1*S*)-1-phenylethylamine were carried out at room temperature in dichloromethane, in the presence of a dehydrating agent (sodium sulfate). The α-imino ketones **7** obtained in these reactions turned out to be quite unstable compounds, decomposing during the standard purification procedure. For this reason they were used directly (as ^{1}H NMR-pure products) for further conversions. In general, substrates **7** are recommended to be used for the reaction with CF_3SiMe_3 immediately after preparation. However, the non-enolizable representatives **7a–f** were stable enough and could be kept bellow 0 °C for a longer time, without noticeable decomposition.

First experiments were carried out with **7a** in 1,2-dimethoxyethane (DME) using CsF as an initiator. The reaction with CF_3SiMe_3 gave a single product, which showed an absorption signal in the ^{19}F NMR spectrum at −0.68 ppm. The ^{13}C NMR and IR spectra proved the presence of the C=N group. The characteristic ^{1}H NMR signal located at 0.19 ppm revealed the presence of the Me_3SiO-group. All spectroscopic data suggested that the expected 1:1 adduct of type **8** (Scheme 3) was formed as a single product in high yield. Based on our earlier results [11], attempts were made to reduce the C=N group using $NaBH_4$. In contrast to adducts of type **2**, the analogous reaction carried out with **8a** in ethanolic solution at room temperature, afforded after 12 h, in a one-pot procedure, β-amino-α-trifluoromethyl alcohol **9a** (Scheme 3, Table 2) in 90%



Scheme 2.



Scheme 3.

yield. In this case, the ^{13}C NMR and IR spectra confirmed the complete conversion of the C=N group. A strong absorption band located at 3331 cm^{-1} evidenced the presence of the new N–H function. In the ^{1}H NMR spectrum the diastereotopic protons of the CH_2 group appeared as an *AB*-system with two doublets located at 2.87 ppm and 3.39 ppm, correspondingly [14]. Analogous reactions with α-imino ketones **7b–j** were carried out applying the same conditions and they yielded desired β-amino-α-trifluoromethyl alcohols **9b–j** in excellent yields (Table 2).

In order to check the scope and limitations of our protocol, reactions of CF_3SiMe_3 with α-imino ketones **7a–c** were tested in absence of the fluoride anion as an activator; instead other catalysts were applied (Table 2). Thus, the experiments performed in DMF solution, in the presence of K_2CO_3, or in DMSO solution using molecular sieves 4 Å, yielded the corresponding adducts **8** in comparable amounts to the reactions carried under 'classical' conditions. It is worth mentioning that compounds **9e–f** can be considered as a modified ('trifluoromethylated') type of 1-amino 2-(benzofuran-2′-yl)ethan-2-ols, known as anti-hypertensive agents and β-blockers [8a,b].

The diastereoselective version of nucleophilic trifluoromethylation of α-imino ketones **7k–l**, bearing a chiral auxiliary on the nitrogen atom, was also studied (Scheme 4, Table 3).

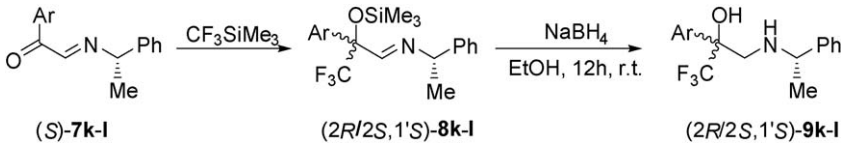
Table 1
Synthesis of α-imino ketones **7** from arylglyoxals hydrates.

Product	R	Ar	**7** Yield [%][a]
7a	*t*-Bu	Ph	93
7b	*t*-Bu	*p*-$MeOC_6H_4$	89
7c	*t*-Bu	*p*-$NO_2C_6H_4$	91
7d	*t*-Bu	*p*-$CF_3C_6H_4$	86
7e	*t*-Bu	Benzofuran-2-yl	83
7f	*t*-Bu	7-Et-benzofuran-2-yl	81
7g	*i*-Pr	Ph	93
7h	*i*-Pr	*p*-$MeOC_6H_4$	92
7i	*i*-Pr	*p*-$NO_2C_6H_4$	95
7j	*i*-Pr	*p*-$CF_3C_6H_4$	92
7k	(*S*)-CH(Me)Ph	Ph	93
7l	(*S*)-CH(Me)Ph	*p*-$MeOC_6H_4$	95

[a] For crude product.

Table 2
Two-step synthesis of β-amino-α-trifluoromethyl alcohols **9**.

Entry	Substrate	Catalyst	Solvent	**9** Yield [%]
1	**7a**	CsF	DME	90
2	**7a**	K_2CO_3	DMF	81
3	**7a**	–	DMSO	75
4	**7b**	CsF	DME	73
5	**7b**	K_2CO_3	DMF	70
6	**7b**	–	DMSO	75
7	**7c**	CsF	DME	82
8	**7c**	K_2CO_3	DMF	76
9	**7c**	–	DMSO	84
10	**7d**	CsF	DME	89
11	**7e**	CsF	DME	70
12	**7f**	CsF	DME	74
13	**7g**	CsF	DME	72
14	**7h**	CsF	DME	69
15	**7i**	CsF	DME	78
16	**7j**	CsF	DME	72



Scheme 4.

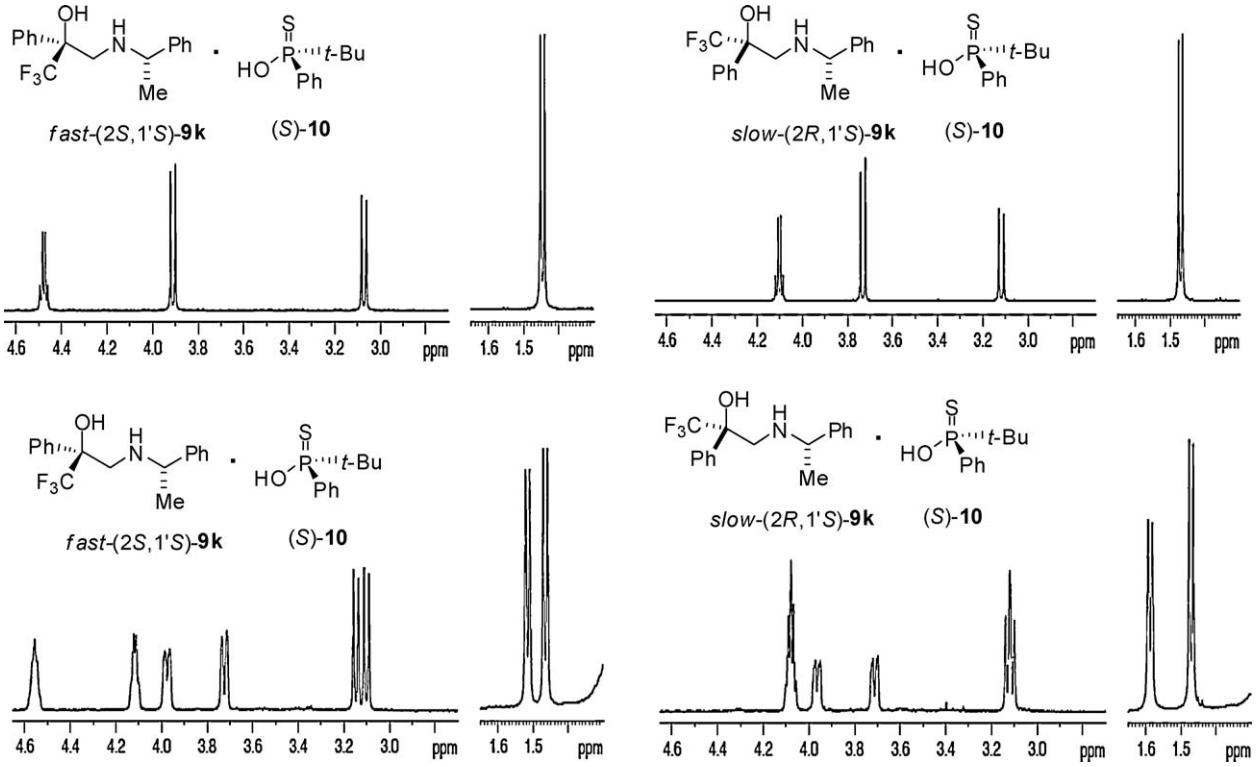


Fig. 1. Comparison of the ^{1}H NMR spectra of racemate and isolated enantiomers of **9k** recorded after addition of 1 equiv. of (−)-(*S*)-(*tert*-butyl)(phenyl)phosponothioic acid (**10**).

Table 3
Diastereoselectivity of CF_3SiMe_3 additions to enantiomerically pure α-imino ketones **7k–l**.

Entry	Substrate	Conditions			d.r.[a]	**9** Yield [%][b]
		kat.	Solvent	Temp.		
1	**7k**	CsF	DME	r.t.	6:4	75
2	**7k**	–	DMSO	r.t.	6:4	70
3	**7k**	CsF	DME	−50 °C	6.5:3.5	68
4	**7l**	CsF	DME	r.t.	6:4	78

[a] On the basis of ^{19}F NMR of crude (2*R*/2*S*, 1′*S*)-**8**.

These reactions were carried out under typical conditions, using cesium fluoride as a catalyst. In both cases, the ^{19}F NMR spectra taken for crude reaction mixtures revealed the presence of diastereomers formed in the ratio of ca. 3:2.

The mixtures of diastereomers (2*R*,1′*S*)-**9k–l** and (2*S*,1′*S*)-**9k–l** were separated by column chromatography and the enantiomeric purity of the isolated *fast*- and *slow*-fractions[2] was proved by the ^{1}H NMR experiments with (*S*)-(*tert*-butyl)phenyltiophosphonic acid (**10**) [15] used as a chiral solvating agent. In each experiment only one set of signals of the corresponding salt was observed (Fig. 1).

In an independent experiment the mixture of diastereomers **9k** was also prepared starting with racemic α-imino ketone **7k** and subsequently, both racemic isomers were separated chromatographically. In each case, the ^{1}H NMR spectrum of *fast*-(*rac*)-**9k** and *slow*-(*rac*)-**9k**, registered in the presence of chiral solvating agent (*S*)-**10**, displayed well separated sets of signals attributed to the in situ formed mixtures of two salts of the corresponding enantiomers (Fig. 1).

The obtained results show that the nucleophilic trifluoromethylation of enolizable α-imino ketones **7k–l**, derived from aryloglyoxal, proceed with no racemization of the 1-phenylethyl substituent. In extension of the results discussed in this paper, the *slow*-isomer of **9l** was used in another work for a cyclization reaction with phosgene yielding selectively the corresponding 1,3-oxazolidin-2-one derivative [10]. The absolute configuration of both stereogenic centers in this compound was determined by X-ray crystallography as (5*R*,1′*S*)-, evidencing thereby the same absolute configuration [(2*R*,1′*S*)-] in the *slow*-**9l** (minor product)

[2] Denotation of *slow*- and *fast*-isomer results from the polarity of separated products; *slow*-**9k,l** relate to the more polar diastereoisomers and *fast*-**9k,l** to the less polar ones.

[10]. By analogy, the same configuration was attributed to the more polar product bearing phenyl substituent, i.e. *slow*-**9k**.

In order to examine the influence of the reaction conditions on the stereochemical outcome, the enantiomerically pure α-imino ketone **7k** was also reacted with CF_3SiMe_3 in DMSO, in the absence of the fluoride anion. In this case the ratio of diastereomeric amino alcohols **9k**, obtained after reduction of the initially formed adduct, was practically unchanged (Table 3). Similarly, another experiment with trifluoromethylation of **7k** at low temperature (−50 °C) in DME solution, under fluoride catalysis, did not result in a noticeable change of the d.r. value.

3. Conclusions

A new, simple and efficient method for the synthesis of a series of new β-amino-α-trifluoromethyl alcohols of type **9**, based on inexpensive and readily accessible starting materials, was elaborated. In most of the described cases, products **9** were obtained in high yields and could be purified by standard procedures. They can be considered as new, attractive building blocks for the synthesis of other fluorinated organic compounds, e.g. trifluoromethylated heterocyclic compounds [10].

Enantiomerically pure imino ketones **7k**,**l** containing a chiral auxiliary, derived from 1-phenylethylamine, undergo nucleophilic trifluoromethylation, followed by the reduction of the C=N bond, producing in both cases comparable mixtures (ca. 3:2) of the corresponding diastereomeric β-amino-α-trifluoromethyl alcohols **9k** and **9l**, respectively.

4. Experimental

4.1. General experimental procedures

Melting points were determined on a Melt-Temp. II apparatus (Aldrich) in capillaries and are uncorrected. The ^1H, $^{13}C\{^1H\}$ and ^{19}F NMR spectra were recorded in $CDCl_3$ with TMS or CCl_3F as the internal standards using Bruker AC-200 or Bruker ARX-300 spectrometers. Assignments of signals in ^{13}C NMR spectra were made on the basis of DEPT 135 experiments. The IR spectra were measured using a NEXUS FT-IR spectrophotometer. The MS spectra (CI, EI, ESI) were obtained using LKB-2091, Finnigan MAT-95, or Bruker Esquire LC spectrometers. Optical rotations were measured on a PERKIN-ELMER 241 MC spectropolarimeter for λ = 589 nm. Elemental analyses were performed in the Microanalytical Laboratory of the Centre of Molecular and Macromolecular Studies PAS in Lodz.

4.2. Materials

Commercial acetophenone (**5a**), *p*-methoxyacetophenone (**5b**), *p*-nitroacetophenone (**5c**), *p*-(trifluoromethyl)acetophenone (**5d**), sodium borohydride, were purchased from Sigma–Aldrich. Benzofuran-2-ylmethylketone (**5e**) and 7-ethylbenzofuran-2-ylmethylketone (**5f**) were prepared according to the known protocol [8c]. 2,2-Dihydroxyarylethan-2-ones **6a**–**f** were prepared according to the published procedure [12]. Dimethoxyethane (DME) was dried over sodium benzophenone and they were freshly distilled prior to the use. Dimethylsulfoxide (DMSO) was dried over CaH_2, dimethylformamide (DMF) over $CaSO_4$ and both distilled under reduced pressure and stored over activated molecular sieves 4 Å.

4.3. Syntheses of α-imino ketones 7a–l

4.3.1. General procedure

Aryl-2,2-dihydroxyethanones **6a**–**f** (5 mmol) and the corresponding amine (5.05 mmol) were dissolved in methylene chloride (5 ml) and the solution was stirred magnetically, in the presence of anhydrous Na_2SO_4 over 1 h, at room temperature. Then, drying agent was filtered off and next solvent was evaporated to dryness (room temperature bath). Crude products were used for further reactions with no purification.

2-(*tert*-Butylimino)-1-phenylethanone (**7a**). Yield: 1.05 g (93%). Orange colored, viscous oil. ^1H NMR (600 MHz, $CDCl_3$): δ 1.33 (s, 9H, C(CH_3)$_3$), 7.45–7.46 (m, 2 arom. H), 7.56–7.58 (m, 1 arom. H), 8.02 (s, 1H, C*H*=N), 8.19–8.21 (m, 2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 29.1 (C(CH_3)$_3$), 59.2 (*C*(CH$_3$)$_3$), 128.2, 130.7, 133.3 (5 arom. *C*H), 135.3 (1 arom. *C*), 154.3 (*C*H=N), 191.6 (*C*=O). IR (KBr): *ν* 3070*w*, 2971*s*, 2932*m*, 2904*m*, 2871*m*, 1663*vs* (C=O), 1598*s* (C=N), 1578*m*, 1448*s*, 1365*m*, 1286*s*, 1230*m*, 1179*w*, 1068*w*, 1024*w*, *901w*, 762*w* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 190 (38, $[M+1]^+$), 212 (100, $[M+23]^+$).

2-(*tert*-Butylimino)(4′-methoxyphenyl)ethanone (**7b**). Yield: 0.98 g (89%). Yellow colored, viscous oil. ^1H NMR (200 MHz, $CDCl_3$): δ 1.33 (s, 9H, C(CH_3)$_3$), 3.88 (s. 3H, OCH_3), 6.94, 8.25 (2d, $^3J_{H,H}$ = 9.0 Hz, 4 arom. H), 7.99 (s, 1H, *CH*=N). ^{13}C NMR (50 MHz, $CDCl_3$): 28.9 (C(CH_3)$_3$), 59.3 (*C*(CH$_3$)$_3$), 113.4, 113.5, 132.9, 133.1 (4 arom. *C*H), 154.6.1, 154.5 (2 arom. C), 163.8 (*C*H=N), 190.0 (*C*=O). IR (KBr): *ν* 2970*s*, 2933*m*, 2903*m*, 2841*m*, 1656*vs* (C=O), 1601*vs* (C=N), 1574*s*, 1509*s*, 1460*m*, 1419*m*, 1365*m*, 1312*s*, 1258*vs*, 1172*vs*, 1115*w*, 1030*s*, 949*w*, 841*s*, 810*m*, 777*w* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 164 (100), 220 (44, $[M+1]^+$), 242 (44, $[M+23]^+$).

2-(*tert*-Butylimino)(4′-nitrophenyl)ethanone (**7c**). Yield: 1.06 g (91%). Yellow crystals, m.p. 70–74 °C (crude). ^1H NMR (200 MHz, $CDCl_3$): δ 1.33 (s, 9H, C(CH_3)$_3$), 8.00 (s, 1H, C*H*=N), 8.27–8.41 (m, 4 arom. H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 28.8 (C(CH_3)$_3$), 59.5 (*C*(CH$_3$)$_3$), 123.1, 131.8 (4 arom. *C*H), 140.5, 154.2 (2 arom. *C*), 154.2 (*C*H=N), 190.0 (*C*=O). IR (KBr): *ν* 3117*w*, 2975*m*, 2937*w*, 2871*m*, 2899*w*, 1666*vs* (C=O), 1603*s* (C=N), 1524*vs*, 1478*w*, 1364*m*, 1344*vs*, 1287*s*, 1230*m*, 1104*w*, 1010*w*, 951*w*, 905*w*, 863*m*, 754*m* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 179 (100), 193 (38), 235 (47 $[M+1]^+$), 257 (15, $[M+23]^+$).

2-(*tert*-Butylimino)-1-[4′-(trifluoromethyl)phenyl]ethanone (**7d**). Yield: 1.10 g (86%). Yellow colored, viscous oil. ^1H NMR (700 MHz, $CDCl_3$): δ 1.34 (s, 9H, C(CH_3)$_3$), 7.72, 8.34 (2d, $^3J_{H,H}$ = 8.4 Hz, 4 arom. H), 8.01 (s, 1H, C*H*=N). ^{13}C NMR (175 MHz, $CDCl_3$): δ 28.9 (C(CH_3)$_3$), 59.5 (*C*(CH$_3$)$_3$), 123.7 (q, $^1J_{C,F}$ = 271.2 Hz, *C*F$_3$), 125.1 (q, $^3J_{C,F}$ = 3.5 Hz, 2 arom *C*H), 130.9 (2 arom. *C*H), 134.3 (q, $^2J_{C,F}$ = 31.7 Hz, 1 arom. C), 138.1 (1 arom. C), 154.2 (*C*H=N), 190.6 (*C*=O). ^{19}F NMR (235 MHz, $CDCl_3$): δ −63.7 (s, CF_3). IR (film): *ν* 2974*vs*, 2935*m*, 2907*m*, 2873*w*, 1671*vs* (C=O), 1639*m* (C=N), 1578*w*, 1509*w*, 1464*w*, 1411*s*, 1366*m*, 1325*vs*, 1287*vs*, 1230*s*, 1170*vs*, 1131*vs*, 1111*vs*, 1063*s*, 1017*s*, 904*w* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 206 (28), 230 (100, $[M+1]^+$), 252 (89, $[M+23]^+$).

2-(*tert*-Butylimino)-1-(benzofuran-2′-yl)ethanone (**7e**). Yield: 0.95 g (83%). Yellow crystals, m.p. 109–110 °C (crude). ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 9H, C(CH_3)$_3$), 7.28–7.33, 7.45–7.51, 7.59–7.63, 7.73–7.76 (4m, 4 arom. H), 7.97 (s, 1H, C*H*=N), 8.20 (d, $^4J_{H,H}$ = 0.9 Hz, 1 arom. H) ppm. ^{13}C NMR (175 MHz, $CDCl_3$): δ 29.0 (C(CH_3)$_3$), 59.3 (*C*(CH$_3$)$_3$), 112.5, 119.5, 123.8, 123.9, 128.7 (5 arom. *C*H), 127.2, 150.2, 155.8 (3 arom. *C*), 153.9 (*C*H=N), 180.5 (*C*=O) ppm. IR (KBr): *ν* 2974*m*, 2929*w*, 2900*w*, 2868*w*, 1655*vs* (C=O), 1608*m* (C=N), 1549*s*, 1474*w*, 1362*w*, 1303*w*, 1236*w*, 1210*w*, 1165*s*, 1146*s*, 1069*m*, 1028*w*, 933*w*, 843*w*, 804*w*, 756*s* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 206 (27), 230 (100, $[M+1]^+$), 252 (89, $[M+23]^+$).

2-(*tert*-Butylamino)-1-(7′-ethylbenzofuran-2′-yl)ethanone (**7f**). Yield: 1.04 g (81%). Brownish crystals, m.p. 67–68 °C (crude). ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 9H, C(CH_3)$_3$), 1.36 (t, $^3J_{H,H}$ = 7.8 Hz, 3H, CH_2CH_3), 3.02 (q, $^3J_{H,H}$ = 7.8 Hz, 2H, CH_2CH_3), 7.22–7.33 (m, 2 arom. H), 7.58 (dd, $^1J_{H,H}$ = 1.5 Hz, $^2J_{H,H}$ = 7.5 Hz, 1 arom. H), 7.98 (s, 1H, C*H*=N), 8.15 (s, 1 arom C*H*=N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (CH_2CH_3), 22.7 (CH_2CH_3), 29.0 (C(CH_3)$_3$), 59.3 (*C*(CH$_3$)$_3$), 119.9, 121.1, 124.0, 127.6 (4 arom. *C*H), 126.9,

129.0, 150.0 (3 arom. *C*), 154.0 (1 arom. *C*H), 154.6 (*C*H=N), 180.6 (*C*=O). IR (KBr): *ν* 2968*s*, 2929*w*, 2897*w*, 1657*vs* (C=O), 1635*s* (C=N), 1554*s*, 1488*w*, 1360*w*, 1353*m*, 1314*m*, 1212*w*, 1169*s*, 1071*w*, 966*w*, 904*w*, 849*m*, 745*m* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 202 (89), 258 (100, $[M+1]^+$), 280 (59, $[M+23]^+$).

2-(Isopropylimino)-1-phenylethanone (**7g**). Yield: 0.81 g (93%). Yellow colored viscous oil. ^1H NMR (600 MHz, $CDCl_3$): δ 1.31 (d, $^3J_{H,H}$ = 6.0 Hz, 6H, $CH(CH_3)_2$), 3.62 (dsept., $^3J_{H,H}$ = 6.6 Hz, $^4J_{H,H}$ = 0.6 Hz, 1H, $CH(CH_3)_2$), 7.44–7.47 (m, 2 arom. H), 7.56–7.59 (m, 1 arom. H), 8.07 (d, $^4J_{H,H}$ = 0.6 Hz, 1H, C*H*=N), 8.19–8.21 (m, 2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 23.6 ($CH(CH_3)_2$), 62.2 ($CH(CH_3)_2$), 128.3, 130.6, 133.4 (5 arom. *C*H), 135.2 (1 arom. C), 156.9 (*C*H=N), 191.0 (*C*=O). IR (film): *ν* 3069*w*, 3028*w*, 2971*s*, 2930*m*, 2869*s*, 1663*vs* (C=O), 1598*s* (C=N), 1578*m*, 1448*s*, 1381*w*, 1362*w*, 1317*m*, 1286*vs*, 1180*w*, 1143*m*, 1065*w*, 1026*w*, 944*w*, 853*m* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 167 (33), 176 (100, $[M+1]^+$), 198 (7, $[M+23]^+$).

2-(Isopropylimino)-1-(4′-methoxyphenyl)ethanone (**7h**). Yield: 0.94 g (92%). Yellow colored, viscous oil. ^1H NMR (200 MHz, $CDCl_3$): δ 1.31 (d, $^3J_{H,H}$ = 6.3 Hz, 6H, $CH(CH_3)_2$), 3.60 (sept., $^3J_{H,H}$ = 6.3 Hz, 1H, $CH(CH_3)_2$), 3.87 (s, 3H, OCH_3), 6.94, 8.23 (2d, $^3J_{H,H}$ = 8.8 Hz, 4 arom. H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 23.4 ($CH(CH_3)_2$), 55.2 (OCH_3), 61.9 ($CH(CH_3)_2$), 113.5, 132.8 (4 arom. *C*H), 127.9, 157.9 (2 arom. C), 163.8 (*C*H=N), 189.2 (*C*=O). IR (film): *ν* 2970*vs*, 2933*s*, 2868*m*, 1656*vs* (C=O), 1598*vs* (C=N), 1572*s*, 1509*s*, 1464*s*, 1421*s*, 1362*m*, 1315*s*, 1258*vs*, 1173*s*, 1143*m*, 1116*w*, 1070*w*, 1028*s*, 957*w*, 856*m* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 164 (93), 178 (20), 206 (100, $[M+1]^+$), 228 (25, $[M+23]^+$).

2-(Isopropylimino)-1-(4′-nitrophenyl)ethanone (**7i**). Yield: 1.05 g (95%). Yellow crystals, m.p. 28−34 °C (crude). ^1H NMR (600 MHz, $CDCl_3$): δ 1.31 (d, $^3J_{H,H}$ = 6.6 Hz, 6H, $CH(CH_3)_2$), 3.66 (dsept., $^3J_{H,H}$ = 6.6 Hz, $^4J_{H,H}$ = 0.6 Hz, 1H, $CH(CH_3)_2$), 8.07 (d, $^4J_{H,H}$ = 0.6 Hz, 1H, C*H*=N), 8.27–8.30, 8.37–8.39 (2m, 4 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 23.5 ($CH(CH_3)_2$), 62.2 ($CH(CH_3)_2$), 123.2, 131.7 (4 arom. H), 139.9, 150.3 (2 arom. C), 156.7 (*C*H=N), 196.2 (*C*=O). IR (KBr): *ν* 2973*w*, 2933*w*, 2872*w*, 1661*m* (C=O), 1601*m* (C=N), 1523*vs*, 1467*w*, 1345*s*, 1317*w*, 1288*m*, 1147*w*, 1109*w*, 1014*w*, 952*w*, 866*w* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 179 (40), 203 (16), 218 (70), 221 (100, $[M+1]^+$).

2-(Isopropylimino)-1-[4′-(trifluoromethyl)phenyl]ethanone (**7j**). Yield: 0.94 g (92%). Yellow colored, viscous oil. ^1H NMR (600 MHz, $CDCl_3$): δ 1.31 (d, $^3J_{H,H}$ = 6.6 Hz, 6H, $CH(CH_3)_2$), 3.65 (dsept., $^3J_{H,H}$ = 6.6 Hz, $^4J_{H,H}$ = 0.6 Hz, 1H, $CH(CH_3)_2$), 7.72 (d, $^3J_{H,H}$ = 8.4 Hz, 2 arom. H), 8.32 (dq, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,F}$ = 1.2 Hz, 2 arom. H), 8.52 (d, $^4J_{H,H}$ = 0.6 Hz, 1H, C*H*=N). ^{13}C NMR (150 MHz, $CDCl_3$): δ 23.5 ($CH(CH_3)_2$), 62.2 ($CH(CH_3)_2$), 123.6 (q, $^1J_{C,F}$ = 271.7 Hz, CF_3), 125.2 (q, $^3J_{C,F}$ = 3.0 Hz, 2 arom *C*H), 131.0 (2 arom. *C*H), 134.4 (q, $^2J_{C,F}$ = 33.2 Hz, 1 arom. C), 138.0 (1 arom. C), 156.8 (*C*H=N), 190.1 (C=O). IR (film): *ν* 2974*s*, 2934*w*, 2872*m*, 1671*s* (C=O), 1618*w* (C=N), 1578*w*, 1468*w*, 1411*m*, 1383*w*, 1325*vs*, 1285*s*, 1171*s*, 1131*vs*, 1111*s*, 1077*s*, 1062*s*, 1017*m*, 958*w*, 858*m*, 845*m* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 202 (49), 226 (22), 244 (100, $[M+1]^+$).

2-{1′-[(1′*S*)-1′-Phenylethyl]imino}phenylethanone (**7k**). Yield: 1.11 g (94%). Orange colored semi-solid material. ^1H NMR (300 MHz, $CDCl_3$): δ 1.64 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, CH_3), 4.61 (q, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 7.27–7.49 (m, 7H, 7 arom. H), 7.57–7.62 (m, 1H, 1 arom. H), 8.12 (s. 1H, C*H*=N), 8.21–8.24 (m, 2H, 2 arom. H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.6 (CH_3), 70.6 (CH), 126.6, 127.4, 128.3, 128.7, 130.7, 133.5 (10 arom. *C*H), 135.1, 143.4 (2 arom. C), 158.1 (*C*H=N), 190.9 (C=O). IR (KBr): *ν* 3085*w*, 3061*w*, 3029*w*, 2973*m*, 2927*w*, 2866*w*, 1663*vs* (C=O), 1598*s* (C=N), 1578*w*, 1493*m*, 1488*s*, 1370*w*, 1286*s*, 1179*w*, 1070*w*, 1026*w*, 960*w*, 762*m* cm^{-1}. ESI-MS: *m*/*z* 236 (100, $[M-1]^+$). $[\alpha]_D$ = +10 (*c* = 1.0).

2-{1′-[(1′*S*)-1′-Phenylethyl]imino}-4-methoxyphenylethanone (**7l**). Yield: 1.11 g (94%). Orange colored, semi-solid material. ^1H NMR (600 MHz, $CDCl_3$): δ 1.64 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, CH_3), 3.87 (s, OCH_3), 4.59 (q, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 6.93–6.96 (m, 2 arom. H), 7.27–7.31 (m, 1 arom. H), 7.36–7.39 (m, 2 arom. H), 7.41–7.43 (m, 2 arom. H), 8.10 (s. 1H, C*H*=N), 8.27–8.30 (m, 2H, 2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.5 (CH_3), 55.3 (OCH_3), 70.5 (CH), 113.6, 126.6, 127.3, 128.6, 133.5 (9 arom. CH), 128.1, 143.5, 158.4 (3 arom. C), 164.0 (*C*H=N), 189.1 (C=O). IR (KBr): *ν* 3084*w*, 3060*w*, 3030*w*, 2972*m*, 2931*w*, 2866*w*, 1658*s* (C=O), 1598*vs* (C=N), 1573*w*, 1510*m*, 1453*w*, 1371*w*, 1261*vs*, 1173*s*, 1026*m*, 843*m* cm^{-1}. ESI-MS: *m*/*z* 266 (100, $[M-1]^+$). $[\alpha]_D$ = +40 (*c* = 1.0).

4.4. Synthesis of β-amino-α-trifluoromethyl alcohols 9

4.4.1. Reactions of α-imino ketones 7 with (trifluoromethyl)trimethylsilane

Method A—a general procedure. A solution of the corresponding α-imino ketone **7a**–**l** (1 mmol) in anhydrous DME (1.5 ml), was placed in a dry, two-necked flask, equipped with septum and a tube filled with anhydrous $CaCl_2$. Next, catalytic amount of freshly dried CsF and (trifluoromethyl)trimethylsilane (0.17 ml, 157 mg, 1.1 mmol) were added. The mixture was stirred at room temperature for ca. 1 h and subsequently quenched with water (5 ml). The solution was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated and the crude, oily products **8a**–**l** were used for further reactions without purification.

Method B—a general procedure. A solution of the corresponding α-imino ketone **7a**–**c** (1 mmol) in 1.5 ml of anhydrous DMF was placed in a dry two-necked flask equipped with septum and a tube filled with anhydrous $CaCl_2$. Next, catalytic amount of freshly dried K_2CO_3 and (trifluoromethyl)trimethylsilane (0.17 ml, 157 mg, 1.1 mmol) were added. The reaction solution was stirred magnetically at room temperature and after ca. 3 h was quenched with water (5 ml). The mixture was extracted three times with CH_2Cl_2. The organic layers were separated, combined and dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated and the crude oily products **8a**–**c** were used for further reactions without purification.

Method C—a general procedure. A solution of the corresponding α-imino ketone **7a**–**c** (1 mmol) in anhydrous DMSO (2.0 ml) an freshly activated molecular sieves 4 Å were placed in a dry, two-necked flask equipped with septum and a tube filled with anhydrous $CaCl_2$. Next, (trifluoromethyl)trimethysilane (0.17 ml, 157 mg, 1.1 mmol) was added drop-wise and the reaction solution was stirred magnetically at room temperature for ca. 3 h. After this time, a portion of water (5 ml) was added and the mixture was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated and the crude, oily products **8a**–**c** were used for further reactions without purification.

4.4.2. Reduction of adducts 8a–l with sodium borohydride—a general procedure

To a magnetically stirred solution of the corresponding adduct **8a**–**l** in EtOH (3 ml), sodium borohydride (228 mg, 6 mmol) was added in small portions while cooling the reaction flask in ice-bath. When the evolution of hydrogen was complete, the mixture was stirred at room temperature over next 12 h. After this time the solvent was evaporated and the solid residue was treated with a portion of water (ca. 10 ml), and subsequently extracted with CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated and the crude products were purified by distillation in vacuum or crystallized.

3-(*tert*-Butylamino) 1,1,1-trifluoro-2-phenylpropan-2-ol (**9a**). Crude product was purified by distillation in Kugel–Rohr apparatus

at 100 °C/0.08 Pa. Yield: 196–236 mg (75–90%) (see Table 2). Colorless crystals, m.p. 30–32 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09 (s, 9H, C(CH_3)$_3$), 2.87 (dq, $^2J_{H,H}$ = 12.9 Hz, $^4J_{H,F}$ = 1.2 Hz 1H, CH_2), 3.39 (d, $^2J_{H,H}$ = 12.9 Hz, 1H, CH_2), 5.74 (br. s, 1H, OH) [16], 7.33–7.43 (m, 3 arom. H), 7.57–7.62 (m, 2 arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.9 (C(CH_3)$_3$), 46.4 (CH_2) 50.5 (C(CH$_3$)$_3$), 72.8 (q, $^2J_{C,F}$ = 27.5 Hz, C_q), 127.6 (q, $^1J_{C,F}$ = 286.1 Hz, CF_3), 126.0, 128.1, 128.2 (5 arom. *C*H), 138.0 (1 arom. C). ^{19}F NMR (188 MHz, $CDCl_3$): δ −94.3 (s, CF_3). IR (KBr): ν 3449*m,br* (OH), 3331*s* (NH), 2976*m*, 2938*w*, 1636*w*, 1451*w*, 1397*w*, 1369*w*, 1271*m*, 1231*w*, 1208*w*, 1159*vs*, 1126*w*, 1075*w*, 1059*w*, 1016*w*, 974*w*, 747*m*, 707*s* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 188 (55), 206 (100), 262 (47, [M+1]$^+$), 284 (9, [M+23]$^+$). Anal. Calcd. for $C_{13}H_{18}F_3NO$ (261.23): C, 59.76; H, 6.94; N, 5.36. Found: C, 59.78; H, 6.90; N, 5.46.

3-(*tert*-Butylamino) 1,1,1-trifluoro-2-(4′-methoxyphenyl)propan-2-ol (**9b**). Crude product was distilled in Kugel–Rohr apparatus at 110 °C/0.08 Pa as a thick oil, which at room temperature forms a semi-solid material. Yield: 206–219 mg (70–75%) (see Table 2). Colorless crystals, m.p. 37–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09 (s, 9H, C(CH_3)$_3$), 2.86 (dq, $^2J_{H,H}$ = 12.6 Hz, $^4J_{H,F}$ = 0.9 Hz, 1H, CH_2), 3.34 (d, $^2J_{H,H}$ = 12.9 Hz, 1H, CH_2), 3.82 (s, 3H, OCH_3), 6.89–6.94 (m, 2 arom. H), 7.48–7.53 (m, 2 arom. H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.0 (C(CH_3)$_3$), 46.4 (CH_2), 50.6 (C(CH$_3$)$_3$), 55.2 (OCH_3), 72.7 (q, $^2J_{C,F}$ = 27.5 Hz, C_q), 113.6, 127.4, 127.5 (4 arom. *C*H), 125.8 (q, $^1J_{C,F}$ = 285.7 Hz, CF_3), 130.0, 159.6 (2 arom. C). ^{19}F NMR (188 MHz, $CDCl_3$): δ −2.5 (s, CF_3). IR (KBr): ν 3447*m.br* (OH), 3327*m* (NH), 2963*vs*, 2915*s*, 2891*s*, 2855*s*, 1612*m*, 1515*vs*, 1455*m*, 1366*m*, 1254*vs*, 1172*s*, 1158*s*, 1221*s*, 1083*m*, 1035*m*, 976*w*, 914*w*, 874*m*, 888*s*, 883*m*, 734*s*, cm^{-1}. CI-MS (isobutane): *m*/*z* (rel. int.) 292 (100, [M+1]$^+$). Anal. Calcd. for $C_{14}H_{20}F_3NO$ (291.32): C, 57.72; H, 6.92; N, 4.81. Found: C, 57.98; H, 6.83; N, 4.87.

3-(*tert*-Butylamino) 1,1,1-trifluoro-2-(4′-nitrophenyl)propan-2-ol (**9c**). Crude product was preliminarily purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 1:1) and subsequently crystallized. Yields: 234–257 mg (76–84%) (see Table 2). Colorless crystals, m.p. 101–104 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09 (s, 9H, C(CH_3)$_3$), 1.25 (br. s, 1H, NH), 2.78, 3.47 (2d, $^2J_{H,H}$ = 13.2 Hz, 1H, CH_2), 6.00 (br. s, 1H, OH), 7.77–7.80 (m, 2 arom. H), 8.21–8.26 (m, 2 arom. H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.0 (C(CH_3)$_3$), 46.5 (CH_2) 50.9 (C(CH$_3$)$_3$), 72.9 (q, $^2J_{C,F}$ = 27.8 Hz, C_q), 125.3 (q, $^1J_{C,F}$ = 286.3 Hz, CF_3), 123.4, 127.32, 127.34 (4 arom. *C*H), 145.3, 148.0 (2 arom. C). ^{19}F NMR (188 MHz, $CDCl_3$): δ −1.9 (s, CF_3). IR (KBr): ν 3447*m.br* (OH), 3320*m* (NH), 3124*w*, 2982*m*, 2964*m*, 1607*w*, 1523*vs*, 1397*w*, 1491*w*, 1352*vs*, 1280*m*, 1273*m*, 1227*m*, 1173*vs*, 1152*vs*, 1102*s*, 977*w*, 897*w*, 850*s*, 743*w*, 703*m*, cm^{-1}. CI-MS (isobutane): *m*/*z* (rel. int.) 293 (14), 307 (100, [M+1]$^+$). Anal. Calcd. for $C_{13}H_{17}F_3N_2O_3$ (306.29): C, 50.98; H, 5.59; N, 8.61. Found: C, 51.55; H, 5.67; N, 8.91.

3-(*tert*-Butylamino) 1,1,1-trifluoro-2-[4′-(trifluoromethyl)phenyl]propan-2-ol (**9d**). Crude product was distilled in Kugel–Rohr apparatus at 100 °C/0.08 Pa; thick oil, forms a semi-solid material at room temperature. Yield: 291 mg (89%). Colorless crystals, m.p. 23–25 °C. ^{1}H NMR (700 MHz, $CDCl_3$): δ 1.09 (s, 9H, C(CH_3)$_3$), 2.81, 3.44 (2d, $^2J_{H,H}$ = 12.6 Hz, 2H, CH_2), 3.82 (s, 3H, OCH_3), 7.66, 7.73 (2d, $^3J_{H,H}$ = 8.4 Hz, 4 arom. H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.4 (C(CH_3)$_3$), 46.9 (CH_2) 51.2 (C(CH$_3$)$_3$), 72.2 (q, $^2J_{C,F}$ = 28.2 Hz, C_q), 124.3 (q, $^1J_{C,F}$ = 272.9 Hz, CF_3), 125.6 (q, $^3J_{C,F}$ = 3.5 Hz, 2 arom. H), 125.9 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 127.0 (2 arom. *C*H), 131.1 (q, $^2J_{C,F}$ = 33.5 Hz, 1 arom. C), 142.6 (1 arom. C). ^{19}F NMR (235 MHz, $CDCl_3$): δ −63.2 (s, CF_3), −78.7 (s, CF_3). IR (KBr): ν 3432*m.br*, 2971*m*, 2939*w*, 2875*w*, 1622*w*, 1473*w*, 1416*w*, 1369*w*, 1329*vs*, 1271*w*, 1211*w*, 1170*vs*, 1130*s*, 1107*s*, 1071*s*, 1019*w*, 977*w*, 839*w*, 735*w*, 656*w* cm^{-1}. CI-MS (isobutane): *m*/*z* 330 (100, [M+1]$^+$). Anal. Calcd for $C_{14}H_{17}F_6NO$ (329.29): C, 51.07; H, 5.20. Found: C, 51.23; H, 5.46.

2-(Benzofuran-2′-yl)-3-(*tert*-butylamino) 1,1,1-trifluoropropan-2-ol (**9e**). Crude product was preliminarily purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 1:1) and subsequently recrystallized from hexane. Yield: 210 mg (70%). Colorless crystals, m.p. 45–48 °C (hexane). ^{1}H NMR (700 MHz, $CDCl_3$): δ 1.13 (s, 9H, C(CH_3)$_3$), 3.22, 3.29 (2d, $^2J_{H,H}$ = 12.6 Hz, 2H, CH_2), 6.97 (s, 1H, 1 arom. H), 7.25–7.27, 7.31–7.34, 7.51–7.53, 7.60–7.61 (4m, 4 arom. H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 29.4 (C(CH_3)$_3$), 44.3 (CH_2) 51.2 (C(CH$_3$)$_3$), 72.1 (q, $^2J_{C,F}$ = 29.9 Hz, C_q), 106.8, 111.8, 121.7, 123.4, 125.0 (5 arom. CH), 125.2 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 128.0, 154.1, 155.5 (3 arom. *C*). ^{19}F NMR (235 MHz, $CDCl_3$): δ −79.3 (s, CF_3). IR (KBr): ν 3358*m.br* (OH), 3129*m* (NH), 2962*s*, 2934*m*, 2899*m*, 2870*m*, 1618*w*, 1484*m*, 1455*s*, 1407*m*, 1369*s*, 1354*m*, 1302*m*, 1268*s*, 1252*s*,1210*s*, 1175*vs*, 1164*vs*, 1093*m*, 1064*s*, 1017*m*, 944*s*, 939*w*, 860*m*, 756*s*, 726*m*, 699*m*, 654*w* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 228 (27), 302 (100, [M+1]$^+$), 324 (27, [M+23]$^+$). Anal. Calcd. for $C_{15}H_{18}F_3NO_2$ (301.31): C, 59.79; H, 6.02. Found: C, 60.08; H, 6.20.

3-(*tert*-Butylamino) 2-(7′-ethylbenzofuran-2′-yl)-1,1,1-trifluoropropan-2-ol (**9f**). Crude product was purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 1:1) and subsequently crystallized. Yield: 244 mg (74%). Colorless crystals, m.p. 23–25 °C (hexane). ^{1}H NMR (700 MHz, $CDCl_3$): δ 13 (s, 9H, C(CH_3)$_3$), 1.35 (t, $^3J_{H,H}$ = 7.7 Hz, 3H, CH_2CH_3) 2.91–2.97 (m, 2H, CH_2CH$_3$), 3.21, 3.29 (2d, $^2J_{H,H}$ = 12.6 Hz, 2H, CH_2), 6.95 (s, 1 arom. H), 7.17–7.19 (m, 1 arom. H), 7.14, 7.42 (2d, $^3J_{H,H}$ = 7.7 Hz, 2 arom. H) ppm. ^{13}C NMR (176 MHz, $CDCl_3$): δ 14.3 (CH_2CH_3), 23.3 (CH_2CH$_3$), 29.4 (C(CH_3)$_3$), 44.3 (CH_2) 51.4 (C(CH$_3$)$_3$), 72.2 (q, $^2J_{C,F}$ = 29.9 Hz, C_q), 107.1, 119.3, 123.6, 124.5 (4 arom. CH), 125.1 (q, $^1J_{C,F}$ = 287.0 Hz, CF_3), 127.7, 128.2, 153.5, 154.2 (4 arom. C). ^{19}F NMR (235 MHz, $CDCl_3$): δ −79.4 (s, CF_3) ppm. IR (film): ν 3338*m.br*, 3126*m*, 3063*m*, 3032*m*, 2969*vs*, 2936*m*, 2876*m*, 1716*w*, 1601*w*, 1484*m*, 1464*m*, 1427*m*, 1368*m*, 1277*m*, 1257*m*, 1180*vs*, 1146*vs*, 1096*m*, 1052*m*, 986*m*, 937*w*, 870*m*, 823*m*, 784*m*, 707*w* cm^{-1}. ESI-MS: *m*/*z* (rel. int.) 256 (58), 274 (14), 330 (100, [M+1]$^+$), 352 (48, [M+23]$^+$). Anal. Calcd. for $C_{17}H_{22}F_3NO_2$ (329.37): C, 61.99; H, 6.73. Found: C, 61.92; H, 6.55.

1,1,1-Trifluoro-3-(isopropylamino) 2-phenylpropan-2-ol (**9g**). Crude product was purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 9:1). Yield: 178 mg (72%). Colorless, thick oil. ^{1}H NMR (700 MHz, $CDCl_3$): δ 1.07, 1.11 (2d, $^3J_{H,H}$ = 6.3 Hz, 6H, CH(CH_3)$_2$), 2.79–2.83 (m, 1H, CH(CH$_3$)$_2$), 2.94 (dq, $^2J_{H,H}$ = 13.3 Hz, $^4J_{H,F}$ = 0.7 Hz, 1H, CH_2), 3.52 (d, $^2J_{H,H}$ = 13.3 Hz, 1H, CH_2), 7.38–7.44 (m, 3 arom. H), 7.64 (d, $^3J_{H,H}$ = 7.7 Hz, 2 arom H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 23.0, 23.2 (CH(CH_3)$_2$), 49.5 (CH_2), 50.8 (CH(CH$_3$)$_2$), 73.2 (q, $^2J_{C,F}$ = 26.4 Hz, C_q), 125.8 (q, $^1J_{C,F}$ = 286.0 Hz, CF_3), 126.2, 128.3, 128.5 (5 arom. H), 138.1 (1 arom. C). ^{19}F NMR (235 MHz, $CDCl_3$): δ −78,9 (s, CF_3). IR (film): ν 3340*m.br*, 3094*m*, 3064*m*, 3038*m*, 2968*s*, 2934*m*, 2873*m*, 1605*w*, 1497*m*, 1470*m*, 1452*s*, 1387*m*, 1372*m*, 1247*s*, 1215*s*, 1154*vs*, 1123*s*, 1074*s*, 1045*s*, 1028*m*, 983*m*, 923*w*, 880*w*, 766*s*, 702*s* cm^{-1}. CI-MS (isobutane): *m*/*z* (rel. int.) 248 (100, [M+1]$^+$). ESI-HRMS: (*m*/*z*) for $C_{12}H_{17}F_3NO$ ([M+1]$^+$) calcd.: 248.12568. Found: 248.12543.

1,1,1-Trifluoro-3-(isopropylamino) 2-(4′-methoxyphenyl)propan-2-ol (**9h**). Crude product was purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 9:1). Yield: 175 mg (69%). Colorless semi-solid material, m.p. 24–27 °C. ^{1}H NMR (700 MHz, $CDCl_3$): δ 1.06, 1.10 (2d, $^3J_{H,H}$ = 6.3 Hz, 6H, CH(CH_3)$_2$), 2.78–2.83 (m, 1H, CH(CH$_3$)$_2$), 2.93, 3.46 (2d, $^2J_{H,H}$ = 12.6 Hz, 2H, CH_2), 3.84 (s, 3H, OCH_3), 6.95, 7.53 (2d, $^3J_{H,H}$ = 9.1 Hz, 4 arom. H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 23.1, 23.2 (CH(CH_3)$_2$), 49.4 (CH_2), 50.7 (CH(CH$_3$)$_2$), 55.2 (OCH_3), 73.0 (q, $^2J_{C,F}$ = 27.8 Hz, C_q), 125.8 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 113.6, 127.5 (4 arom. *C*H), 130.4, 159.7 (2 arom. *C*). ^{19}F NMR (235 MHz, $CDCl_3$): δ −79.2 (s, CF_3). IR (KBr): ν 3425*m.br*, 2967*m*, 2937*m*, 2873*w*, 2841*w*, 1612*m*, 1516*s*, 1467*m*, 1443*w*, 1387*w*, 1308*m*, 1254*s*, 1158*vs*, 1106*m*, 1034*m*, 983*w*, 831*m* cm^{-1}. CI-MS (isobutane): *m*/*z* (rel. int.) 278 (100, [M+1]$^+$). Anal. Calcd. for $C_{13}H_{18}F_3NO_2$ (277.29): C, 56.31; H, 6.54. Found: C, 56.37; H, 6.95.

1,1,1-Trifluoro-3-(isopropylamino) 2-(4′-nitrophenyl)propan-2-ol (**9i**). Crude product was purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 8:2) and subsequently crystallized. Yield: 228 mg (78%). Yellowish crystals, m.p. 41–44 °C (hexane). ^{1}H NMR (700 MHz, $CDCl_3$): δ 1.06, 1.11 (2d, $^3J_{H,H}$ = 7.0 Hz, 6H, CH(CH_3)$_2$), 2.77–2.81 (m, 1H, C*H*(CH$_3$)$_2$), 2.82, 3.58 (2d, $^2J_{H,H}$ = 13.3 Hz, 2H, CH_2), 7.80, 8.24 (2d, $^3J_{H,H}$ = 8.6 Hz, 4 arom. H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 23.0, 23.1 (CH(CH_3)$_2$), 49.6 (CH_2), 50.6 (*C*H(CH$_3$)$_2$), 73.1 (q, $^2J_{C,F}$ = 26.4 Hz, C_q), 125.3 (q, $^1J_{C,F}$ = 287.0 Hz, CF_3), 123.4, 127.6 (4 arom. *C*H), 145.3, 148.0 (2 arom. C). ^{19}F NMR (235 MHz, $CDCl_3$): δ −78.7 (s, CF_3). IR (KBr): ν 3358*m.br*, 3115*w*, 2974*m*, 2873*w*, 1601*m*, 1523*vs*, 1468*m*, 1454*m*, 1416*m*, 1355*s*, 1306*m*, 1261*m*, 1218*m*, 1161*vs*, 1122*m*, 1100*m*, 1041*m*, 1030*m*, 974*w*, 873*w*, 848*m*, 811*w*, 699*m* cm^{-1}. CI-MS (isobutane): *m*/*z* 293 (100, [M+1]$^+$). Anal. Calcd. for $C_{12}H_{15}F_3N_2O_3$ (292.26): C, 49.32; H, 5.17. Found: C, 49.50; H, 5.15.

1,1,1-Trifluoro-3-(isopropylamino) 2-[4-(trifluoromethyl)phenyl]propan-2-ol (**9j**). Crude product was purified by filtration trough neutral Al_2O_3 plug (hexane/CH_2Cl_2 9:1). Yield: 227 mg (72%). Colorless, thick oil. ^{1}H NMR (700 MHz, $CDCl_3$): δ 1.05, 1.10 (2d, $^3J_{H,H}$ = 6.3 Hz, 6H, CH(CH_3)$_2$), 2.76–2.85 (m, 1H, C*H*(CH$_3$)$_2$), 2.84, 3.53 (2d, $^2J_{H,H}$ = 13.3 Hz, 2H, CH_2), 7.65, 7.72 (2d, $^3J_{H,H}$ = 8.4 Hz, 4 arom. H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.4, 23.5 (CH(CH_3)$_2$), 49.9 (CH_2), 51.0 (*C*H(CH$_3$)$_2$), 73.4 (q, $^2J_{C,F}$ = 26.4 Hz, C_q), 124.3 (q, $^1J_{C,F}$ = 271.2 Hz, CF_3), 125.6 (q, $^3J_{C,F}$ = 3.5 Hz, 2 arom. *C*H), 125.8 (q, $^1J_{C,F}$ = 287.0 Hz, CF_3), 127.0 (2 arom. *C*H), 131.1 (q, $^2J_{C,F}$ = 31.7 Hz, 1 arom. *C*), 142.5 (1 arom. C). ^{19}F NMR (235 MHz, $CDCl_3$): δ −63.2 (s, CF_3), – 78.8 (s, CF_3). IR (film): ν 3343*m.br*, 2970*s*, 2936*m*, 2875*m*, 1932*w*, 1622*m*, 1471*m*, 1417*m*, 1388*m*, 1329*vs*, 1248*s*, 1166*vs*, 1128*vs* 1106*vs*, 1070*vs*, 1044*m*, 1018*s*, 984*m*, 923*w*, 838*s*, 790*w* cm^{-1}. CI-MS (isobutane): *m*/*z* (rel. int.) 316 (100, [M+1]$^+$). Anal. Calcd for $C_{13}H_{15}F_6NO$ (315.26): C, 49.53; H, 4.88. Found: C, 49.74; H, 4.85.

(2*R*/2*S*)-1,1,1-Trifluoro-3-{1′-[(1′*S*)-1′-phenylethylamino]}-2-phenylpropan-2-ol ((2*R*/2*S*,1′*S*)-**9k**). Total yield of preliminarily purified mixture of diastereomers: 210–232 mg (68–75%) (see Table 3). Separation of diastereomers was performed by column chromatography on silica gel using mixture of hexane and Et_2O (85:15).

Fast-(2*S*,1′*S*)-**9k** (major). Yield: 123 mg (40%). Yellowish oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.27 (d, $^3J_{H,H}$ = 6.6 Hz,3H, CH_3), 2.74 (dq, $^2J_{H,H}$ = 13.2 Hz, $^4J_{H,F}$ = 1.2 Hz 1H, CH_2), 3.23 (d, $^2J_{H,H}$ = 13.2 Hz, 1H, CH_2), 3.57 (q, $^3J_{H,H}$ = 6.6 Hz,1H, CH), 7.07–7.12 (m, 2 arom. H), 7.17–7.21 (m, 1 arom. H), 7.26–7.34 (m, 5 arom. H), 7.46–7.47 (m, 2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 23.92 (CH_3), 51.2 (CH_2), 58.6 (CH), 73.5 (q, $^2J_{C,F}$ = 27.2 Hz, C_q), 125.6 (q, $^1J_{C,F}$ = 286.8 Hz, CF_3), 126.3, 127.5, 128.3, 128.5, 128.8 (10 arom. *C*H), 137.8, 144.2 (2 arom. C). ^{19}F NMR (565 MHz, $CDCl_3$): δ −78.4. IR (film): ν 3344*m* (NH), 3063*m*, 3030*m*, 2929*m*, 2872*m*, 1956*w*, 1495*s*, 1451*vs*, 1404*m*, 1376*m*, 1305*m*, 1280*m*, 1242*s*, 1177*vs*, 1155*vs*, 1074*m*, 1029*m*, 998*m*, 899*w* cm^{-1}. ESI-HRMS: (*m*/*z*) for $C_{17}H_{19}F_3NO$ ([M+1]$^+$) calcd.: 310.14133 Found: 310.14137. $[\alpha]_D$ = −54 (*c* = 1.0).

Slow-(2*R*,1′*S*)-**9k** (minor). Yield: 83 mg (27%). Yellowish oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.39 (d, $^3J_{H,H}$ = 6.6 Hz,3H, CH_3), 2.88 (dq, $^2J_{H,H}$ = 12.6 Hz, $^4J_{H,F}$ = 1.2 Hz 1H, CH_2), 3.31 (d, $^2J_{H,H}$ = 12.6 Hz, 1H, CH_2), 3.82 (q, $^3J_{H,H}$ = 6.6 Hz,1H, CH), 7.20–7.22 (m, 2 arom. H), 7.24–7.27 (m, 1 arom. H), 7.32–7.38 (m, 5 arom. H), 7.50–7.52 (2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (CH_3), 50.9 (**C**H$_2$), 58.2 (CH), 73.8 (q, $^2J_{C,F}$ = 28.7 Hz, C_q), 125.5 (q, $^1J_{C,F}$ = 283.8 Hz, CF_3), 126.2, 126.3, 127.4, 128.3, 128.5, 128.8 (10 arom. H), 137.4, 144.0 (2 arom. C). ^{19}F NMR (565 MHz, $CDCl_3$): δ −78.2. IR (film): ν 3344*m* (NH), 3063*m*, 3030*m*, 2969*m*, 2929*m*, 2872*m*, 1956*w*, 1495*m*, 1451*s*, 1403*m*, 1376*m*, 1302*s*, 1278*s*, 1243*s*, 1174*vs*, 1155*vs*, 1074*s*, 1026*m*, 998*m*, 919*w* cm^{-1}. ESI-HRMS: (*m*/*z*) for $C_{17}H_{19}F_3NO$ ([M+1]$^+$) calcd.: 310.14133 Found: 310.14130. $[\alpha]_D$ = −32 (*c* = 1.0).

(2*R*/2*S*)-1,1,1-Trifluoro-3-{1′-[(1′*S*)-1′-phenylethylamino]}-2-(4′′-methoxyphenyl)propan-2-ol ((2*R*/2*S*,1′*S*)-**9l**). Total yield of preliminarily purified mixture of diastereomers: 264 mg (78%). Separation of diastereomers was performed by column chromatography on silica gel using the mixture of hexane and Et_2O (85:15).

Fast-(2*S*, *1′S*)-**9l** (major). Yield: 142 mg (42%). Yellowish semi-solid material. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.36 (d, $^3J_{H,H}$ = 6.6 Hz,3H, CH_3), 2.82, 3.28 (2d, $^2J_{H,H}$ = 12.6 Hz, 2H, CH_2), 3.68 (q, $^3J_{H,H}$ = 6.6 Hz,1H, CH), 3.82 (s, 3H, OCH_3), 6.90–6.92 (m, 2 arom. H), 7.20–7.23 (m, 2 arom. H), 7.29–7.30 (m, 1 arom. H), 7.35–7.37 (m, 2 arom. H), 7.47–7.49 (2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.2 (CH_3), 51.4 (CH_2), 55.6 (OCH_3), 58.8 (CH), 73.5 (q, $^2J_{C,F}$ = 28.7 Hz, C_q), 125.9 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 113.9, 126.4, 127.7, 129.0 (9 arom. *C*H), 130.0, 144.5, 160.0 (3 arom. C). ^{19}F NMR (565 MHz, $CDCl_3$): δ −78.8 (CF_3). IR (film): ν 3063*w*, 3034*w*, 2968*w*, 2935*w*, 2878*w*, 1612*w*, 1514*w*, 1455*w*, 1372*w*, 1261*m*, 1238*m*, 1183*s*, 1160*vs*, 1173*vs*, 1150*s*, 1174*vs*, 1117*m*, 1032*m*, 977*w* cm^{-1}. ESI-HRMS: (*m*/*z*) for $C_{18}H_{21}F_3NO_2$ ([M+1]$^+$) calcd.: 340.15189. Found: 340.15172. $[\alpha]_D$ = −45 (*c* = 1.0).

Slow-(*2R,1′S*)-**9l** (minor). Yield: 101 mg (30%). Yellowish oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.40 (d, $^3J_{H,H}$ = 6.6 Hz,3H, CH_3), 2.90 (d, $^2J_{H,H}$ = 12.6 Hz, 1H, CH_2), 3.29 (dq, $^2J_{H,H}$ = 12.6 Hz, $^4J_{H,F}$ = 1.2 Hz 1H, CH_2), 3.81 (s, 3H, CH_3), 3.83 (q, $^3J_{H,H}$ = 6.6 Hz,1H, CH), 6.90–6.91 (m, 2 arom. H), 7.23–7.24 (m, 2 arom. H), 7.26–7.29 (m, 1 arom. H), 7.34–7.36(m, 2 arom. H), 7.45–7.46 (m, 2 arom. H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 23.1 (CH_3), 50.1 (CH_2), 54.37 (OCH_3), 57.4 (CH), 73.0 (q, $^2J_{C,F}$ = 27.2 Hz, C_q), 124.8 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 112.9, 125.5, 126.6, 126.8, 127.9 (9 arom. *C*H), 128.6, 143.3, 158.9 (3 arom. C). ^{19}F NMR (565 MHz, $CDCl_3$): δ −78.6 (CF_3). IR (film): ν 3343*m* (NH), 3063*w*, 3028*w*, 2966*m*, 2934*m*, 2840*m*, 1896*w*, 1611*s*, 1583*m*, 1515*s*, 1465*m*, 1403*m*, 1375*m*, 1305*s*, 1281*s*, 1254*vs*, 1174*vs*, 1158*vs*, 1031*s*, 969*m* cm^{-1}. ESI-HRMS: (*m*/*z*) for $C_{18}H_{21}F_3NO_2$ ([M+1]$^+$) calcd.: 340.15189. Found: 340.15163. $[\alpha]_D$ = −13 (*c* = 1.0).

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[14] It is worth mentioning that the first of these two signals appears as a *dq*, but the second one as a *doublet*. Additional splitting of the more shielded signal, located at 2.87 ppm might results from trough-space interaction of one of the CH_2 protons with CF_3 moiety. The same phenomenon has not been observed in all other amino alcohols of type **9**. In some instances, e.g. **9e**–**f**, only broadening of the more deshielded signals, were observed. Additionally, for compounds **9e**–**f** the observed difference of chemical shifts is smaller. As the result, the low resolved spectra of both compounds showed only one, broad pseudo-singlet.

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[16] (a) Signals related to dynamic NH and/or OH protons have not been always registered in the ^{1}H NMR spectra of amino alcohols **9**;
(b) In the IR spectra, absorption bands related to the N-H and/or O-H stretching bonds could not be always found. Very likely, this effect results from strong inter- and intramolecular H-bonding in compounds **8**.