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Convenient synthesis of mono- and di-β-hydroxy-β-bis(trifluoromethyl)-(di)imines from β-hydroxy-β-bis(trifluoromethyl)-ketones and (di)amines

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Abstract

A series of novel β-hydroxy-β-bis(trifluoromethyl)-imines (**2a**–**j**) and di(β-hydroxy-β-bis(trifluoromethyl))-diimines (**3a**–**f**) were prepared in moderate to good yields via a simple two-step approach: first, β-hydroxy-β-bis(trifluoromethyl)-ketones (**1a**–**c**) were obtained by a catalyst-free aldol reaction between liquid hexafluoroacetone sesquihydrate and ketones (acetone, acetophenone, and pinacolone, respectively); then, condensation of the latter fluorinated β-ketols **1a**–**c** with primary amines or diamines was achieved in the presence of Lewis (montmorillonite, $InBr_3$, $La(OTf)_3$) or Brönsted (PTSA) acid catalysts. The molecular structures of mono- and di-β-hydroxy-β-bis(trifluoromethyl)-(di)imines **2e**,**h** and **3a**,**f** were determined and found to exhibit strong intramolecular =(R)N···H–O hydrogen bonding.

Keywords: Aldolization; Fluorinated alcohols; Imines; β-Ketols; Lewis acid catalysis

1. Introduction

Fluorinated alkoxy-imino (FAI) ligands of the type $[RN{=}C(R')C{-}C(CF_3)_2O]^-$ were first prepared in the coordination sphere of metal ions, i.e., Cu^{2+}, Ni^{2+}, Co^{2+}, Ce^{3+}, Ce^{4+} by the template condensation of primary (di)amines with the fluorinated β-ketol $MeC(=O)CH_2C(CF_3)_2OH$ (**1a**).[1] A number of complexes based on such FAI ligands and various metal centers (Pd,[2] Ir,[3] Ga,[4] Cu[5]) have recently regained interest due to their attractive application for metal organic chemical vapor deposition (MOCVD)[6] in microelectronics.

Early attempts to prepare directly fluorinated alcohol-imines [protonated equivalent of FAIs] involved the reactions of lithiated imines with anhydrous hexafluoroacetone, but final acidic workup led to the corresponding β-hydroxy-β-bis(trifluoromethyl)-ketones or -aldehydes.[7,8] Similarly, it was found that trifluoroacetaldehyde ethyl hemiacetal reacts with imines and enamines to give the corresponding β-hydroxy-β-trifluoromethyl-ketones in rather good yields after hydrolysis,[9] while the reaction of anhydrous hexafluoroacetone with the enamine derived from acetophenone and morpholine offered the corresponding β-hydroxy-β-bis(trifluoromethyl)-ketone in 31% yield after hydrolysis.[10] An effective entry toward a variety of β-hydroxy-β-(trifluoromethyl)-imines was finally reported by Röschenthaler and co-workers through the room temperature reaction of ketimines or aldimines with activated ketones, like trifluoroacetone, trifluoroacetophenone or 2-hydroxy-trifluoroacetophenone.[11] Recently, this methodology was applied to anhydrous hexafluoroacetone, which led to the efficient preparation of a variety of β-hydroxy-β-bis-(trifluoromethyl)-imines.[12]

Here we describe an alternative, effective, and practical method for preparing known and novel β-hydroxy-β-bis(trifluoromethyl)-imines (**2**) and di(β-hydroxy-β-bis(trifluoromethyl))-diimines (**3**) by the acid-catalyzed condensation of various β-hydroxy-β-bis(trifluoromethyl)-ketones (**1**) with primary mono- and diamines, respectively. This approach involves the preliminary synthesis of fluorinated β-ketols **1**

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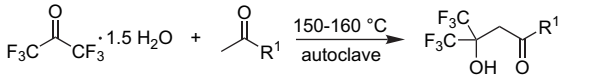
from the aldol reaction of ketones with hexafluoroacetone sesquihydrate. The latter liquid reagent was chosen to avoid the use of gaseous anhydrous hexafluoroacetone,[12] which is a suspected teratogenic reagent, difficult and dangerous to handle. As described in details below, this alternative 'reverse' approach toward fluorinated (di)alcohol-(di)imines relies on the use of effective acid catalysts, based on clays, metal salts or Brönsted acids, to promote the condensation reaction.

2. Results and discussion

2.1. Synthesis of fluorinated β-ketols *1a–c*

The variously substituted β-hydroxy-β-bis(trifluoromethyl)-ketones **1a–c** were obtained by the simple, direct aldol reaction of hexafluoroacetone sesquihydrate with acetone,[5] acetophenone, and pinacolone, respectively, at 150–160 °C (Scheme 1). It is well known that aldol reactions usually proceed under basic or acidic conditions.[13] However, in the present case, the reaction does not require any catalyst due to the strong activation of the carbonyl group of hexafluoroacetone, which shifts the keto-enol equilibrium toward the enol form and allows consuming the latter rapidly under the chosen conditions. β-Ketol **1b** was prepared earlier in 56% yield by the reaction of the corresponding enol-trimethylsilyl ether with anhydrous hexafluoroacetone in the presence of the Lewis acid $SnCl_4$.[14] Here, the fully atom efficient aldol reaction using safer (and cheaper) liquid hexafluoroacetone sesquihydrate offered β-ketol **1b** in a significantly better yield (82%). All the obtained β-ketols are stable compounds under ambient conditions and were recovered as colorless liquids (**1a**,**c**) or white solid material (**1b**).



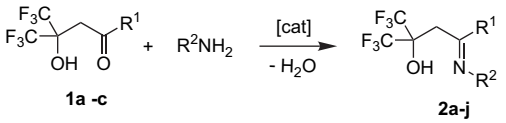
R_1	yield (%)
Me (**1a**)	79
Ph (**1b**)	82
tBu (**1c**)	59

Scheme 1.

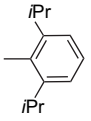
2.2. Synthesis of β-hydroxy-β-bis(trifluoromethyl)-imines

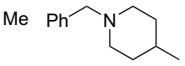
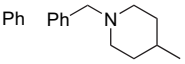
The main strategy to prepare imines involves the acid-catalyzed condensation of primary amines onto carbonyl compounds.[15] Most common, efficient Lewis and Brönsted acids used to perform such reaction include, e.g., $ZnCl_2$,[16] $TiCl_4$,[17] Al_2O_3,[18] montmorillonite clay,[2,19] molecular sieves,[20] and *p*-toluenesulphonic acid (PTSA),[21] or their combination.

Accordingly, we have investigated the synthesis of β-hydroxy-β-bis(trifluoromethyl)-imines (**2a–j**) and di(β-hydroxy-β-bis(trifluoromethyl))-diimines (**3a–f**) via the acid-catalyzed condensation of β-ketols **1a–c** with different primary amines and diamines, respectively (Schemes 2 and 3). Mono β-hydroxy-β-bis(trifluoromethyl) imines (**2a–j**) were prepared by reacting 1.0 equiv of amine with β-ketols, while 2.0 equiv of the latter β-ketols were reacted with diamines to prepare the fluorinated diols-diimines (**3a–f**).

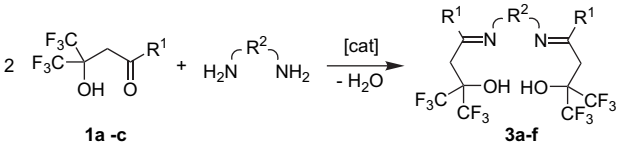


1a -c **2a-j**

R^1	R^2	product
Me	CH_2Ph	**2a**
Ph	CH_2Ph	**2b**
Me	*cyclo*-C_6H_{11}	**2c**
Ph	*cyclo*-C_6H_{11}	**2d**
Me	Ph	**2e**
Ph	Ph	**2f**
Me		**2g**

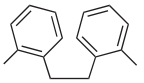
R^1	R^2	product
Me	C_6F_5	**2h**
Me		**2i**
Ph		**2j**
Me	*t*Bu	-
*t*Bu	CH_2Ph	-
*t*Bu	*cyclo*-C_6H_{11}	-

Scheme 2.



1a -c **3a-f**

R^1	R^2	product
Me	$-(CH_2)_2-$	**3a**
Me	 *trans (R,R/S,S)*	**3b**
Me	 *trans 1R,2R*	**3c**
Me	$-(CH_2)_3-$	**3d**
Ph	$-(CH_2)_3-$	-

R^1	R^2	product
Ph		**3e**
Me		**3f**
Ph		-

Scheme 3.

In both cases, the optimal reaction conditions were found to depend strongly on the amine nucleophilicity and the bulkiness of the β-ketols' R^1 group as well. With the aim to maximize yields of the desired products, a variety of acid catalysts and reaction conditions were evaluated. Condensation reactions catalyzed by the strong Lewis acid $La(OTf)_3$[22] were carried out by adding molecular sieves to trap water eventually produced in the reaction course, and thus helping to shift the reaction equilibrium. Similarly, some condensations were investigated in the presence of the simple, readily available PTSA by carrying out the reactions with Dean–Stark azeotropic removal.[19] Alternatively, we also investigated the use of $InBr_3$, a powerful Lewis acid catalyst,[23] which enables

Table 1
Condensation of (di)amines with β-ketols in the presence of acid catalysts[a]

Entry	Product	Catalyst (mol %)	Reaction conditions[b]	Time (h)	Conv.[c] (%)	Yield[d] (%)
1	**2a**	$InBr_3$ (2.0)	Solvent-free	72[e]	100	71
2	**2b**	PTSA (3.0)	Toluene	72	76	56
3	**2b**	Montmorillonite[a]	$CHCl_3$	48	97	75
4	**2b**	$InBr_3$ (2.0)	Solvent-free	13	90	76
4	**2c**	$InBr_3$ (2.0)	Solvent-free	100	90	72
5	**2d**	Montmorillonite[a]	$CHCl_3$	100	76	50
6	**2e**	PTSA (3.0)	Toluene	12	70	48
7	**2e**	$InBr_3$ (2.0)	Solvent-free	24	68	46
8	**2f**	$La(OTf)_3$ (1.8)	Benzene	144	75	70
9	**2g**	PTSA (3.0)	Toluene	15	45	10
10	**2g**	$La(OTf)_3$ (2.0)	Benzene	72	25	7
11	**2h**	PTSA (3.0)	Toluene	12	60	46
12	**2h**	$La(OTf)_3$ (2.0)	Benzene	12	14	5
13	**2i**	$InBr_3$ (2.0)	Solvent-free	70	80	61
14	**2j**	$La(OTf)_3$ (1.0)	Benzene	72	80	74
15	**4k**	$La(OTf)_3$ (2.0)	Benzene	72	nd	62
16	**3a**	Montmorillonite[a]	$CHCl_3$	72	90	69
17	**3b**	Montmorillonite[a]	$CHCl_3$	72	90	68
18	**3c**	Montmorillonite[a]	$CHCl_3$	72	90	70
19	**3d**	Montmorillonite[a]	$CHCl_3$	72	90	52
20	**3e**	$La(OTf)_3$ (2.0)	Benzene	72	80	79
21	**3f**	PTSA (3.0)	Toluene	100	55	39

[a] See Section 4 for details.
[b] Solvent-free reactions were carried out at 70 °C, and in the other cases under reflux.
[c] Conversion of β-ketol as determined by ^{19}F NMR of reaction mixtures.
[d] Isolated yield of pure product.
[e] Reaction time was not optimized.

performing solvent-free reactions (that is, in the β-ketol/(di)-amine mixture) without specific water trapping. No water trapping was also applied to reactions catalyzed by Montmorillonite K10,[2] to evaluate a potentially very simple system. Representative results are reported in Table 1.

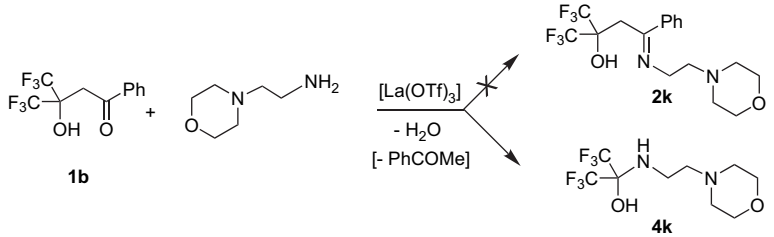
Expectedly, condensation reactions proceed much more easily with aliphatic amines, which are stronger nucleophiles, than with aromatic ones. Thus, many fluorinated alcohol-imines (**2b**,**d**, **3a**–**d**) derived from aliphatic amines, including benzylamine, cyclohexylamine, 1-benzylpiperidin-4-amine, 2-morpholinoethanamine, ethylenediamine, and 1,2-cyclohexyldiamine, were prepared in valuable yields (50–76%) using simply montmorillonite as the catalyst. In those cases, comparative experiments showed that good results (61–76% isolated yields; **2a**–**c**,**i**) can also be achieved using 2.0 mol % of $InBr_3$ under solvent-free conditions. On the other hand, the use of PTSA leads to more modest yields (ca. 50%) (entries 2 and 6).

In the case of aromatic amines such as aniline and the bulky 2,6-diisopropylaniline, we observed that montmorillonite is largely ineffective. The condensation reactions involving such poor nucleophiles were more efficiently performed in the presence of PTSA, affording fluorinated alcohol-imines **2e**,**g**,**h** and **3f** in 10–48% isolated yields. $InBr_3$ did not show improved performances as compared to PTSA for the synthesis of **2e** (entries 6 and 7). The strong Lewis acid $La(OTf)_3$ proved to be quite performant in some cases, e.g., in the preparation of **2f** and **3e** (70 and 79% yields, entries 8 and 20) but was surprisingly found to be completely ineffective in other cases, e.g., for the synthesis of **2g**,**h** (entries 10 and 12). The reasons for these striking differences are still unclear.

On the other hand, we did not succeed to achieve condensation of *tert*-butylamine with the simple β-ketol **1a** neither reactions of different primary aliphatic amines with β-ketol **1c** as well (Scheme 2). Attempts to carry out these reactions under a variety of reaction conditions with the different catalyst systems mentioned above resulted systematically in the recovery of the initial reagents. Obviously, these reactions are hampered by the steric hindrance of the bulky *tert*-butyl substituent present either in the amine or β-ketol. Similar difficulties were also encountered for the condensation of 1,3-diaminopropane and 1,2-diaminobenzene onto the phenyl-substituted β-ketol **1b** (Scheme 3).

More surprisingly, the reaction of 2-morpholinoethanamine and β-ketol **1b** did not offer the expected condensation product (**2k**), but rather the fluorinated hemiaminal **4k** (Scheme 4),[24] which was isolated in 62% yield after sublimation (see Section 4). Apparently, this product results from the condensation of 2-morpholinoethanamine onto hexafluoroacetone. This observation suggests that β-ketol **1b** is not stable under these conditions (i.e., in the presence of 2-morpholinoethanamine, possibly in combination with $La(OTf)_3$) and decomposes via a retro-aldol reaction. The molecular structure of **4k** (Fig. 1) features quite strong intramolecular hydrogen bonding[25] between the morpholine nitrogen atom N(1) and HO(1) group (O–H···N distance=1.722(3) Å).

The prepared β-hydroxy-β-bis(trifluoromethyl)-imines (**2a**–**j**) and di(β-hydroxy-β-bis(trifluoromethyl))-diimines (**3a**–**f**) are all stable compounds at room temperature in air and are readily soluble in a variety of organic solvents (acetone, diethyl ether, hexane, and toluene). They were fully characterized in solution by multinuclear ^1H, ^{13}C, and ^{19}F NMR, as well as by HRMS and elemental analysis (see Section 4). In addition, the solid state structures of **2e**,**h** and **3a**,**f** were determined by single-crystal X-ray diffraction analysis. The



Scheme 4.

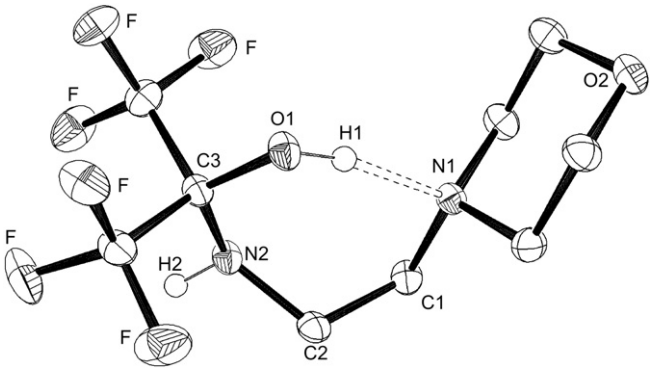


Figure 1. ORTEP view of hemiaminal **4k** depicted with 30% thermal ellipsoids; hydrogen atoms bound to C atoms omitted for clarity. Selected bond lengths (Å) and angles (°): O(1)–C(3) 1.372(2), O(1)–H(1) 0.90(2), N(2)–C(3) 1.441(2), N(2)–C(2) 1.465(2), N(2)–H(2) 0.86(2), N(1)–C(1) 1.475(2), C(1)–C(2) 1.518(2), N(1)–H(1) 1.722(3), N(2)–H(1) 2.346, C(3)–O(1)–H(1) 109.70(1), C(3)–N(2)–C(2) 119.29(1), C(3)–N(2)–H(2) 112.11(2), C(2)–N(2)–H(2) 112.60(1).

molecular structures of these compounds are depicted in Figures 2 (**2e**,**h**) and 3 (**3a**,**f**). Table 2 summarizes the most important bond distances and angles in these molecules. Compounds **2e**,**h** and **3a**,**f** all feature short intramolecular hydrogen bonding[25] between the imino nitrogen atom N(1) and the HO(1) group with O–H···N distances of 1.825 (**2e**), 2.139 (**2h**), 1.834 (**3a**), and 2.039 (**3f**) Å. The angles in the six-membered ring systems N(1)–C(1)–C(2)–C(3)–O(1)–H(1) in **2e**,**h** and **3a**,**f** are in the range 99.86–153.05°. This indicates that these ring systems are much more distorted than that observed in related 4-isopropylimino-3,3,5-trimethyl-1,1,1-trifluoro-2-trifluoromethylhexan-2-ol where the corresponding angles range between 110.9(3) and 114.7(3)8°.[12]

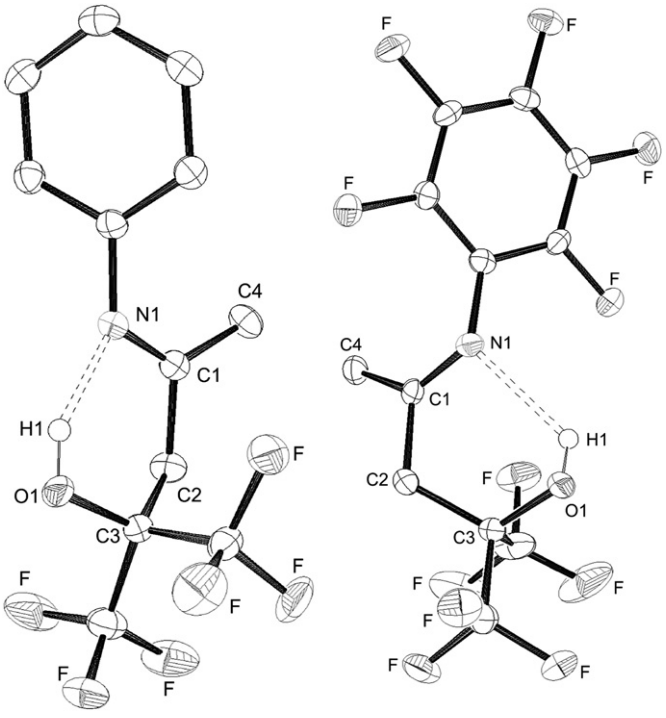


Figure 2. ORTEP view of fluorinated alcohol-imines **2e** (left) and **2h** (right), depicted with 30% thermal ellipsoids; hydrogen atoms bound to C atoms omitted for clarity.

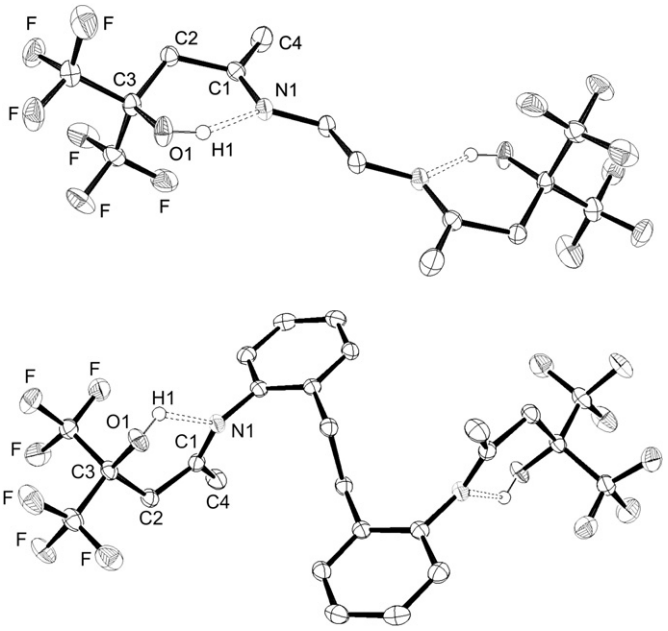


Figure 3. ORTEP views of fluorinated diols-diimines **3a** (top) and **3f** (bottom), depicted with 30% thermal ellipsoids; hydrogen atoms bound to C atoms omitted for clarity.

3. Conclusions

We have shown that β-hydroxy-β-bis(trifluoromethyl)-ketones, readily prepared by the aldol reaction of ketones with relatively cheap and safe hexafluoroacetone sesquihydrate, are convenient precursors toward fluorinated β-alcohol-imines. Condensation of β-hydroxy-β-bis(trifluoromethyl)-ketones with primary aliphatic and aromatic amines and diamines requires the use of appropriate acid catalysts, to be selected upon the specific case. The reaction appears, however, hampered by the presence of very bulky substituent either in the β-ketol or in the amine.

The prepared β-hydroxy-β-bis(trifluoromethyl)-imines (**2a**–**j**) and di(β-hydroxy-β-bis(trifluoromethyl))-diimines

Table 2
Selected bond lengths/contacts (Å) and angles (°) for **2e**, **2h**, **3a**, and **3f**

Compound	**2e**	**2h**	**3a**	**3f**
N(1)–C(1)	1.277(2)	1.278(3)	1.272(2)	1.277(2)
C(1)–C(4)	1.498(2)	1.490(3)	1.497(2)	1.501(2)
C(1)–C(2)	1.521(2)	1.526(3)	1.518(2)	1.513(2)
C(2)–C(3)	1.541(2)	1.544(3)	1.545(2)	1.542(2)
C(3)–O(1)	1.402(1)	1.395(3)	1.397(2)	1.399(2)
N(1)···H(1)	1.825	2.139	1.834	2.039
N(1)–C(1)–C(4)	127.03(1)	127.64(2)	125.69(1)	126.65(1)
C(4)–C(1)–C(2)	114.11(1)	117.34(2)	115.33(1)	114.61(1)
H(1)–N(1)–C(1)	99.86	99.02	101.77	104.37
N(1)–C(1)–C(2)	118.75(1)	115.04(2)	118.96(1)	118.63(1)
C(1)–C(2)–C(3)	115.32(1)	114.03(2)	116.13(1)	116.25(1)
C(2)–C(3)–O(1)	105.86(1)	114.00(2)	114.21(1)	114.18(1)
C(3)–O(1)–H(1)	105.71(2)	109.69(2)	106.10(2)	109.49(1)
O(1)–H(1)–N(1)	153.05	120.48	149.78	127.36

(**3a–f**) are fluorous alkoxy analogs of imino-phenols[26] and Salen derivatives,[27] which are ubiquitous ligands largely used in coordination chemistry. Applications of these new fluorous pro-ligands in the coordination chemistry of oxophilic transition- and main group-metals,[28] and related homogenously catalyzed processes will be reported in due course.

4. Experimental section

4.1. General

Hexafluoroacetone sesquihydrate (99%) was purchased from ABCR and used as received. All ketones and (di)amines were commercially available and used as received. Montmorillonite K10 (KSF, Acros), $La(OTf)_3$ (99.999%, Aldrich), and $InBr_3$ (99.999%, Strem Chemicals) were used as received.

NMR spectra were recorded at 298 K on Bruker Avance DPX-200, AM-300 or AM-500 spectrometers. ^1H and ^{13}C chemical shifts are reported in parts per million relative to $SiMe_4$ and were determined by reference to the residual solvent resonances. ^{19}F chemical shifts were determined by external reference to an aqueous solution of $NaBF_4$. All coupling constants are given in Hertz. Elemental analyses were performed at the Microanalytical Laboratory at the Institute of Chemistry of Rennes. HRMS spectra were obtained on a high resolution MS/MS spectrometer Micromass ZABSpec-TOF (EI and ESI methods).

4.2. Synthesis

4.2.1. 5,5,5-Trifluoro-4-hydroxy-4-(trifluoromethyl)-pentan-2-one (*1a*)

The synthesis of **1a** was achieved by a slight modification of the literature procedure.[5] A 50 mL stainless steel autoclave was charged with hexafluoroacetone sesquihydrate (12.5 g, 64.7 mmol) and acetone (45 mL, 775 mmol). The autoclave was sealed and heated at 140 °C in an oil bath for 85–100 h. The autoclave was cooled down to room temperature, vented, and diethyl ether (20 mL) and anhydrous $MgSO_4$ were added to the reaction mixture. The solution was filtered and concentrated under vacuum. The oily residue was purified by vacuum distillation (2 mmHg, 32 °C), giving **1a** as a colorless liquid (11.42 g, 79%). ^1H NMR (200 MHz, $CDCl_3$): δ 2.34 (s, 3H, CH_3), 2.96 (s, 2H, CH_2), 6.81 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.7 (s, 6F). HRMS (70 eV, EI): *m/z* calcd for $C_5H_3O_2F_6$ $[M-{}^tCH_3]^{+\bullet}$: 209.00372; found: 209.0036 (0 ppm).

4.2.2. 4,4,4-Trifluoro-3-hydroxy-1-phenyl-3-(trifluoromethyl)butan-1-one (*1b*)

This compound was prepared by following the same procedure as that described above for **1a**, starting from hexafluoroacetone sesquihydrate (13.5 g, 70.0 mmol) and acetophenone (7.8 mL, 66.7 mmol), reacting at 160 °C for 120 h. Compound **1b** was obtained as an off-white crystalline solid (15.5 g, 82%). ^1H NMR (200 MHz, $CDCl_3$): δ 3.49 (s, 2H, CH_2), 7.18 (s, 1H, OH), 7.58 (t, ^3J=7.5, 2H, *m*-H), 7.74 (t, ^3J=7.5, 1H, *p*-H), 7.99 (d, ^3J=7.5, 1H, *o*-H). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.4 (s, 6F). Anal. Calcd for $C_{10}H_6F_6O_2$: C, 44.13; H, 2.22. Found: C, 45.01; H, 2.48. HRMS (70 eV, EI): *m/z* calcd for $C_{11}H_8O_2F_6$ $[M^{+\bullet}]$: 286.04285; found: 286.0430 (0 ppm).

4.2.3. 6,6,6-Trifluoro-5-hydroxy-2,2-dimethyl-5-trifluoromethylhexan-3-one (*1c*)

This compound was prepared by following the same procedure as that described above for **1a**, starting from hexafluoroacetone sesquihydrate (4.30 mL, 37.6 mmol) and pinacolone (4.70 mL, 37.5 mmol), reacting at 160 °C for 100 h. Compound **1c** was obtained as a colorless liquid (5.89 g, 59%). ^1H NMR (200 MHz, $CDCl_3$): δ 1.22 (s, 9H, ^{t}Bu), 3.01 (s, 2H, CH_2), 7.28 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.59 (s, 6F). HRMS (70 eV, EI): *m/z* calcd for $C_5H_3O_2F_6$ $[M-{}^tBu]^+$: 209.00372; found: 209.0036 (0 ppm).

4.2.4. 4-Benzylimino-1,1,1-trifluoro-2-trifluoromethylpentan-2-ol (*2a*)

A Schlenk flask was charged with **1a** (0.50 g, 2.23 mmol) and benzylamine (255 μL, 2.33 mmol) under argon atmosphere. $InBr_3$ (1.57 mg, 2.0 mol %) was added and the flask was heated at 70 °C for 3 days under magnetic stirring. After filtration on Celite, the crude product was distilled in a Kugelrohr apparatus to give **2a** as colorless oil (0.50 g, 71%). ^1H NMR (200 MHz, $CDCl_3$): δ 2.12 (s, 3H, CH_3), 2.81 (s, 2H, CH_2–C=), 4.57 (s, 2H, CH_2–Ph), 7.32 (m, 5H, arom.). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.7 (s, 1C, CH_3), 33.6 (s, 1C, CH_2–C=N), 54.4 (s, 1C, CH_2–Ph), 76.6 (hept, $^2J_{CF}$=29.4, 1C, $C(CF_3)_2$), 123.2 (q, $^1J_{CF}$=288.8, 2C, CF_3), 127.3 (s, 1C, CH_{para}), 127.5 (s, 2C, CH_{ortho}), 128.7 (s, 2C, CH_{meta}), 138.1 (s, 1C, C_{ipso}), 170.5 (s, 1C, C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.72 (s, 6F). HRMS (70 eV, EI): *m/z* calcd for $C_{13}H_{13}NOF_6$ $[M^{+\bullet}]$: 313.09013; found: 313.0893 (2 ppm).

4.2.5. 4-Benzylimino-1,1,1-trifluoro-4-phenyl-2-trifluoromethylbutan-2-ol (*2b*)

This compound was prepared by following the same procedure as that described above for **2a**, starting from **1b** (0.50 g, 1.75 mmol) and benzylamine (200 μL, 1.83 mmol), reacting at 70 °C for 13 h in the presence of $InBr_3$ (1.23 mg, 2.0 mol %). Compound **2b** was obtained as colorless crystals (0.50 g, 76%). Mp=42–43 °C. ^1H NMR (200 MHz, $CDCl_3$): δ 3.12 (s, 2H, CH_2–C=), 4.58 (s, 2H, CH_2–Ph), 7.29 (m, 7H, arom.), 7.51 (m, 3H, arom.), 10.20 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.44 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.7 (s, 1C, CH_2–C=N), 56.3 (s, 1C, CH_2–Ph), 76.9 (hept, $^2J_{CF}$=29.4, 1C, $C(CF_3)_2$), 123.2 (q, $^1J_{CF}$=288.7, 2C, $2CF_3$), 125.9 (s, 2C, *m*-CH), 127.3 (s, 1C, *p*-CH), 127.5 (s, 2C, *o*-CH), 128.7 (s, 2C, *m*-CH), 129.2 (s, 2C, *o*-CH) 130.1 (s, 1C, *p*-CH), 135.8 (s, 1C, C_{ipso}), 138.1 (s, 1C, C_{ipso}), 171.2 (s, 1C, C=N). HRMS (70 eV, EI): *m/z* calcd for $C_{18}H_{15}NOF_6$ $[M^{+\bullet}]$: 375.10578; found: 375.1056 (0 ppm).

4.2.6. 1,1,1-Trifluoro-4-[cyclohexylimino]-2-(trifluoromethyl)pentan-2-ol (**2c**)

This compound was prepared by following the same procedure as that described above for **2a**, starting from **1a** (0.50 g, 2.23 mmol) and cyclohexylamine (270 μL, 2.36 mmol), reacting at 70 °C for 4.5 days in the presence of $InBr_3$ (1.57 mg, 2.0 mol %). Compound **2c** was obtained as a colorless oil (0.49 g, 72%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.00 (s, 3H, CH_3), 2.68 (s, 2H, CH_2), 6.79 (d, ^3J=7.3, 2H, *o*-H), 7.23 (t, ^3J=7.3, 1H, *p*-H), 7.39 (t, ^3J=7.3, 3H, *m*-H), 9.04 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.3 (s, 6F). HRMS (70 eV, EI): *m/z* calcd for $C_{12}H_{17}NOF_6$ [$M^{+\bullet}$]: 305.12143; found: 305.1203 (3 ppm).

4.2.7. 4-[Cyclohexylimino]-1,1,1-trifluoro-4-phenyl-2-(trifluoromethyl)butan-2-ol (**2d**)

A Schlenk flask was charged with **1b** (0.50 g, 1.75 mmol), cyclohexylamine (210 μL, 1.84 mmol), montmorillonite (0.80 g), and chloroform (10 mL) under argon atmosphere. The mixture was heated at 70 °C for 4.5 days. After Kugelrohr distillation of the crude product, **2d** was obtained as an oil, which further crystallized to colorless crystals (0.32 g, 50%). Mp=58–59 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.23 and 1.60 (m, 10H, CH_2 cyclohexyl), 2.99 (s, 2H, CH_2), 3.34 (m, 2H, *o*-H), 7.18 (m, 2H, *m*-H), 7.48 (m, 3H, *o*-H and *p*-H), 10.67 (br s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −8.37 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8 (s, 2C, CH_2 3- and 5-cyclohexyl), 25.4 (s, 1C, CH_2 4-cyclohexyl), 33.3 (s, 2C, CH_2 2- and 6-cyclohexyl), 33.4 (s, 1C, CH_2), 59.7 (s, 1C, CH cyclohexyl), 77.05 (hept, $^2J_{CF}$=28.8, 1C, $C(CF_3)_2$), 123.3 (q, $^1J_{CF}$=189.2, 2C, CF_3), 125.7 (s, 2C, *m*-CH), 129.0 (s, 2C, *o*-CH), 129.5 (s, 1C, *p*-CH), 136.4 (s, 1C, *ipso*-C), 167.9 (s, 1C, *C*=N). HRMS (70 eV, EI): *m/z* calcd for $C_{17}H_{19}NOF_6$ [$M^{+\bullet}$]: 367.13708; found: 367.1386 (4 ppm).

4.2.8. 1,1,1-Trifluoro-4-[phenylimino]-2-(trifluoromethyl)pentan-2-ol (**2e**)

In a 50 mL flask, a mixture of **1a** (2.10 g, 9.4 mmol) and aniline (1.00 mL, 11.0 mmol) in toluene (40 mL), in the presence of a catalytic amount of PTSA (48.4 mg, 3.0 mol %), was refluxed for 12 h using a Dean–Stark apparatus. The reaction mixture was evaporated in vacuum and the residue was distilled in a Kugelrohr apparatus to give **2e** as a colorless oil, which rapidly crystallizes at room temperature (1.35 g, 48%). Mp=40–41 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.00 (s, 3H, CH_3), 2.94 (s, 2H, CH_2), 6.79 (d, ^3J=7.3, 2H, *o*-H), 7.23 (t, ^3J=7.3, 1H, *p*-H), 7.39 (t, ^3J=7.3, 3H, *m*-H), 9.04 (s, 1H, OH). ^{1}H NMR (200 MHz, C_6D_6): δ 1.10 (s, 3H, CH_3), 2.32 (s, 2H, CH_2), 6.42 (d, ^3J=7.3, 2H, *o*-H), 6.87 (t, ^3J=7.3, 1H, *p*-H), 7.01 (t, ^3J=7.4, 3H, *m*-H), 9.13 (br s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.3 (s, 6F). ^{19}F NMR (188 MHz, C_6D_6): δ −77.9 (s, 6F). ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.3 (s, 1C, CH_3), 33.6 (s, 1C, CH_2), 76.3 (hept, $^2J_{CF}$=29.5, 1C, $C(CF_3)_2$), 120.0 (s, 2C, *o*-CH), 123.1 (q, $^1J_{CF}$=287.5, 2C, CF_3), 125.1 (s, 1C, *p*-CH), 129.2 (s, 2C, *m*-CH), 147.1 (s, 1C, C_{ipso}), 171.2 (s, 1C, *C*=N). HRMS (70 eV, EI): *m/z* calcd for $C_{12}H_{11}NOF_6$ [$M^{+\bullet}$]: 299.07448; found: 299.0735 (3 ppm).

4.2.9. 1,1,1-Trifluoro-4-phenyl-4-[phenylimino]-2-(trifluoromethyl)butan-2-ol (**2f**)

A Schlenk flask was charged with **1b** (4.41 g, 15.4 mmol) and benzene (15 mL). Under argon atmosphere, 5 Å molecular sieves (11.0 g), $La(OTf)_3$ (80 mg, 0.14 mmol, 1.0 mol %), and aniline (1.70 mL, 18.64 mmol) were added. The mixture was refluxed for 6 days. The molecular sieves were removed and washed with methylene chloride (15 mL), and the solvents were concentrated under reduced pressure. After trap-to-trap distillation, several drops of pentane were added to the distillate, which crystallized at cold temperature to give **2f** as a pale yellow solid (3.89 g, 70%). Mp=77–78 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.31 (s, 2H, CH_2), 6.73–7.19 (m, 10H, arom.), 9.35 (s, 1H, OH). ^{1}H NMR (200 MHz, C_6D_6): δ 2.95 (s, 2H, CH_2), 6.46–6.79 (m, 10H, arom.), 9.44 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −77.99 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.9 (s, 1C, CH_2), 121.4 (s, 2C, *o*-CH), 125.1 (s, 1C, *p*-CH), 127.7 (s, 1C, *m*-CH), 128.7 (s, 2C, *m*-CH), 128.9 (s, 2C, *o*-CH), 130.2 (s, 1C, *p*-CH), 135.8 (s, 1C, C_{ipso}), 146.8 (s, 1C, C_{ipso}), 169.9 (s, 1C, *C*=N). Resonances for CF_3 groups were not observed due to a too short relaxation period or a non-adapted pulse angle. HRMS (70 eV, EI): *m/z* calcd for $C_{17}H_{13}NOF_6$ [$M^{+\bullet}$]: 361.09013; found: 361.0908 (1 ppm).

4.2.10. 4-[(2,6-Diisopropylphenyl)imino]-1,1,1-trifluoro-2-(trifluoromethyl)pentan-2-ol (**2g**)

This compound was prepared by following the same procedure as that described above for **2e**, starting from **1a** (4.50 g, 20.1 mmol) and 2,6-diisopropylaniline (3.8 mL, 20.1 mmol) in toluene (40 mL), in the presence of PTSA (0.10 g, 3.0 mol %), reacting for 15 h. Compound **2g** was obtained as a pale yellow oil (0.74 g, 10%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.15 (d, 6H, *i*-Pr), 1.19 (d, 6H, *i*-Pr), 1.86 (s, 3H, CH_3), 2.69 (m, 2H, *i*-Pr), 2.97 (s, 2H, CH_2), 7.18 (m, 3H, arom.), 9.68 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −79.1 (s, 6F). Anal. Calcd for $C_{18}H_{23}F_6NO$: C, 56.39; H, 6.05. Found: C, 56.43; H, 5.84.

4.2.11. 1,1,1-Trifluoro-4-[(pentafluorophenyl)imino]-2-(trifluoromethyl)pentan-2-ol (**2h**)

This compound was prepared by following the same procedure as that described above for **2e**, starting from **1a** (0.81 g, 3.61 mmol) and pentafluoroaniline (0.66 g, 3.60 mmol) in toluene (40 mL), in the presence of PTSA (18.6 mg, 3.0 mol %), reacting for 12 h. Compound **2h** was obtained as colorless crystals (0.65 g, 46%). Mp=63–64 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.13 (s, 3H, CH_3), 3.09 (s, 2H, CH_2), 7.60 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −162.0 (m, 2F, *m*-F), −160.0 (t, ^3J=22.0, 1F, *p*-F), −151.0 (d, ^3J=22.0, 2F, *o*-F), −78.4 (s, 6F, CF_3). Anal. Calcd for $C_{12}H_6F_{11}NO$: C, 37.04; H, 1.55. Found: C, 37.41; H, 2.04.

*4.2.12. 4-(1-Benzylpiperidin-4-ylimino)-1,1,1-trifluoro-2-(trifluoromethyl)pentan-2-ol (**2i**)*

This compound was prepared by following the same procedure as that described above for **2a**, starting from **1a** (4.35 g, 19.4 mmol) and 4-amino-1-benzylpiperidine (3.14 mL, 16.2 mmol), reacting at 70 °C for 70 h in the presence of $InBr_3$ (13.6 mg, 2.0 mol %). Recrystallization of the crude product from pentane gave **2i** as a pale yellow solid (3.92 g, 61%). Mp=126–128 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.64 (m, 4H, $2CH_2$ piperidine), 1.92 (s, 3H, CH_3), 2.12 (m, 2H, CH_2 piperidine), 2.61 (s, 2H, CH_2), 2.73 (m, 2H, CH_2 piperidine), 3.40 (m, 1H, CH of piperidine), 3.46 (s, 2H, C*H*$_2$–Ph), 7.25 (m, 5H, arom.). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.57 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.47 (s, C, CH_3), 32.42 (s, C, *C*H$_2$–Ph), 51.77 (s, C, CH_2), 31.35, 33.76, 56.59, 63.57 (s, 5C piperidine), 126.39 (s, 1C, *p*-CH), 127.43 (s, 1C, *m*-CH), 128.62 (s, 2C, *m*-CH), 129.50 (s, 2C, *o*-CH), 138.81 (s, 1C, *p*-CH), 167.82 (s, C, *C*=N). Resonances for CF_3 groups were not observed due to a too short relaxation period or a non-adapted pulse angle. Anal. Calcd for $C_{19}H_{25}F_6N_2O$: C, 55.47; H, 6.12. Found: C, 55.83; H, 6.58.

*4.2.13. 4-(1-Benzylpiperidin-4-ylimino)-4-phenyl-1,1,1-trifluoro-2-(trifluoromethyl)butan-2-ol (**2j**)*

This compound was prepared by following the same procedure as that described above for **2f**, starting from **1b** (2.40 g, 8.4 mmol) and 1,3-phenylenedimethanamine (0.42 mL, 3.2 mmol) in benzene (15 mL), in the presence of $La(OTf)_3$ (90 mg, 0.15 mmol, 1.8 mol %), reacting for 3 days in a Soxhlet apparatus charged with 5 Å molecular sieves (10.0 g). Compound **2j** was obtained as a pale yellow oil (2.24 g, 74%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.83 (m, 6H, $3CH_2$ of piperidine), 2.80 (m, 2H, CH_2 of piperidine), 3.02 (s, 2H, CH_2), 3.40 (m, 1H, CH of piperidine), 3.51 (s, 2H, C*H*$_2$–Ph), 7.33 (m, 10H, arom.), 10.36 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.24 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.96 (s, C, *C*H$_2$–Ph), 51.49 (s, C, CH_2), 30.14, 33.19, 52.55, 58.09, 63.54 (s, 5C of piperidine), 125.97, 127.11, 127.42, 128.63, 129.51, 129.56, 129.71, 130.08, 136.69, 138.80 (14C of Ph groups), 169.14 (s, C, *C*=N). Resonances for CF_3 groups were not observed due to a too short relaxation period or a non-adapted pulse angle. Anal. Calcd for $C_{24}H_{27}F_6N_2O$: C, 60.88; H, 5.75. Found: C, 70.10; H, 5.42.

*4.2.14. 1,1,1-Trifluoro-4-[(2-{[4,4,4-trifluoro-3-hydroxy-1-methyl-3-(trifluoromethyl)butylidene]amino}ethyl)imino]-2-(trifluoromethyl)pentan-2-ol (**3a**)*

This compound was prepared by following the same procedure as that described above for **2d**, starting from **1a** (2.75 g, 12.3 mmol) and 1,2-ethylenediamine (0.36 g, 6.1 mmol), in the presence of montmorillonite (0.80 g), reacting for 72 h in chloroform (10 mL). Compound **3a** was obtained as an orange solid (3.88 g, 69%) by recrystallization of the crude product from methanol. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.04 (s, 6H, Me), 2.73 (s, 4H, CH_2), 3.66 (s, 4H, CH_2N), 9.88 (s, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.63 (CH_2), 33.41 (Me), 50.42 (CH_2–N), 121.1 (C–OH), 125.5 (C–F), 171.42 (C=N). ^{19}F NMR (182 MHz, $CDCl_3$): δ −78.9 (s, 12F). Anal. Calcd for $C_{14}H_{16}F_{12}N_2O_2$: C, 35.60; H, 3.41. Found: C, 36.44; H, 3.89.

*4.2.15. Racemic trans-4,4′-(cyclohexane-1,2-diylbis(azan-1-yl-1-ylidene))bis(1,1,1-trifluoro-2-(trifluoromethyl)pentan-2-ol) (rac-**3b**)*

Compound *rac*-**3b** was prepared as described for **2d** starting from **1c** (2.50 g, 11.1 mmol), *trans*-1,2-diaminocyclohexane (0.63 g, 5.5 mmol), and montmorillonite (0.80 g) to give *rac*-**3b** as a white solid (3.97 g, 68%). Mp=108.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.38–1.84 (m, 8H, cyclohexyl), 2.01 (s, 6H, Me), 2.65 (m, 2H, CH–N of cyclohexyl), 10.19 (s, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0 (2C, *C*N), 21.10 (2C, *C*H$_2$–C–CF$_3$), 24.20 (2C, *C*H$_3$), 32.02 (2C, CH_2 cyclohexyl), 39.10 (2C, *C*H$_2$–CN cyclohexyl), 64.30 (2C, *C*H–N cyclohexyl), 122.0 (2C, *C*O), 126.0 (q, 2C). ^{19}F NMR (182 MHz, $CDCl_3$): δ −78.72 (q, J=10.35, 6F), −79.20 (q, J=10.34, 6F). HRMS (70 eV, EI): *m/z* calcd for $C_{18}H_{22}F_{12}N_2O_2$: 526.1490; found: 526.1521 (6 ppm). $[M-CF_3]^+$ ($C_{17}H_{22}N_2O_2F_9$) calcd: 457.1538; found: 457.1568.

*4.2.16. 4,4′-((1R,2R)-Cyclohexane-1,2-diylbis(azan-1-yl-1-ylidene))bis(1,1,1-trifluoro-2-(trifluoromethyl)pentan-2-ol) ((R,R)-**3c**)*

Compound (*R*,*R*)-**3c** was prepared in a similar manner as that described above for *rac*-**3b**, starting from **1a** (4.24 g, 19.0 mmol), (1*R*,2*R*)-diaminocyclohexane (0.63 g, 5.5 mmol), and montmorillonite (1.20 g), to give (*R*,*R*)-**3c** (6.97 g, 70%) as a white solid. $[\alpha]_D^{20}$ −32 (*c* 0.01, CH_2Cl_2). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.42–1.85 (m, 8H, cyclohexyl), 2.02 (s, 6H, 2Me), 2.66 (s, 4H, cyclohexyl), 3.57 (m, 2H, CH–N), 10.19 (s, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0 (2C, *C*N), 21.1 (2C, *C*H$_2$–C–CF$_3$), 24.2 (2C, *C*H$_3$), 32.0 (2C, CH_2 cyclohexyl), 39.1 (2C, *C*H$_2$–CN cyclohexyl), 64.3 (2C, *C*H–N cyclohexyl), 122.0 (2C, *C*O), 126.0 (q, 2C). ^{19}F NMR (182 MHz, $CDCl_3$): δ −78.74 (q, J=10.35, 6F), −79.22 (q, J=10.35, 6F).

*4.2.17. 1,1,1-Trifluoro-4-[(2-{[4,4,4-trifluoro-3-hydroxy-1-methyl-3-(trifluoromethyl)butylidene]amino}propyl)imino]-2-(trifluoromethyl)pentan-2-ol (**3d**)*

This compound was prepared by following the same procedure as that described above for **2d**, starting from **1a** (1.77 g, 7.9 mmol), 1,3-propanediamine (335 μL, 4.0 mmol), and montmorillonite (0.50 g), reacting in chloroform (5 mL) for 3 days at 70 °C. Compound **3d** was obtained as a colorless oil that crystallizes (1.00 g, 52%). Mp=30 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.01 (s, 6H, CH_3), 2.01 (qt, $^3J_{HH}$=6.6, 2H, CH_2–C*H*$_2$–CH_2), 2.73 (s, 4H, C*H*$_2$–C=N), 3.42 (t, $^3J_{HH}$= 6.6, 4H, C*H*$_2$–N), 10.0 (br s, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.1 (s, 2C, CH_3), 30.2 (s, 1C, CH_2–*C*H$_2$–CH_2), 33.0 (s, 2C, *C*H$_2$–C=N), 47.4 (s, 2C, *C*H$_2$–N), 76.6 (hept, $^2J_{CF}$=29.3, *C*(CF$_3$)$_2$), 123.2 (q, $^1J_{CF}$=288.7, 4C, CF_3), 170.8 (s, 2C, C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.9 (s, 12F). HRMS (70 eV, EI): *m/z* calcd for $C_{15}H_{18}N_2O_2F_{12}$ [$M^{+\bullet}$]: 486.11767; found: 486.1202 (5 ppm).

4.2.18. 4,4′-(Phenylenedimethane-1,3-diylbis(azan-1-ylidene))bis(1,1,1-trifluoro-2-(trifluoromethyl)-pentan-2-ol) (**3e**)

This compound was prepared by following the same procedure as that described above for **2f**, starting from **1b** (1.87 g, 6.55 mmol), 1,3-phenylenedimethanamine (0.42 mL, 3.17 mmol), and La(OTf)$_3$ (90 mg, 0.15 mmol, 2.0 mol %), reacting in benzene (15 mL) for 3 days in a Soxhlet apparatus charged with 5 Å molecular sieves (10.0 g). Compound **3e** was obtained as a pale yellow solid (1.69 g, 79%) by recrystallization of the crude product from hexane. Mp=106–107 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.14 (s, 4H, CH_2), 4.58 (s, 4H, CH_2–Ph), 7.3 (m, 14H, arom.), 10.21 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −78.44 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.09 (s, 2C, CH_2–Ph), 56.46 (s, 2C, CH_2), 122.48, 126.28, 129.62, 130.48, 136.13, 139.07 (14C of Ph groups), 171.85 (s, 2C, C=N). Resonances for CF_3 groups were not observed because of a too short relaxation period or a non-adapted pulse angle. HRMS (70 eV, ES): *m/z* calcd for $C_{30}H_{25}F_{12}N_2O_2$ [$M^{+\bullet}$]: 673.1724; found: 673.1711 (2 ppm). Anal. Calcd for $C_{30}H_{25}F_{12}N_2O_2$: C, 54.86; H, 4.03. Found: C, 55.12; H, 4.48.

4.2.19. 4,4′-(2,2′-(Ethane-1,2-diyl)bis(2,1-phenylene))-bis(azan-1-yl-1-ylidene)bis(1,1,1-trifluoro-2-(trifluoromethyl)pentan-2-ol) (**3f**)

This compound was prepared by following the same procedure as that described above for **2e**, starting from **1a** (3.00 g, 13.39 mmol) and 2-[2-(2-aminophenyl)ethyl]phenylamine (0.95 g, 4.48 mmol) in toluene (40 mL), in the presence of PTSA (23.1 mg, 3.0 mol %), reacting for 100 h in a Dean–Stark apparatus. Compound **3f** was obtained as colorless crystals (1.10 g, 39%) by recrystallization of the crude product from a 1:2 CH_2Cl_2/toluene mixture. ^{1}H NMR (200 MHz, CD_2Cl_2): δ 1.95 (s, 6H, CH_3), 2.70 (s, 4H, CH_2), 2.97 (s, 4H, CH_2), 6.62 (m, 2H, arom.), 7.19 (m, 6H, arom.), 9.35 (s, 2H, OH). ^{19}F NMR (188 MHz, CD_2Cl_2): δ −78.9 (s, 12F). Anal. Calcd for $C_{26}H_{24}F_{12}N_2O_2$: C, 50.01; H, 3.87. Found: C, 51.00; H, 4.28.

4.2.20. 1,1,1,3,3,3-Hexafluoro-2-(2-morpholinoethyl-amino)propan-2-ol (**4k**)

This compound was prepared by following the same procedure as that described above for **2f**, starting from **1b** (2.00 g, 7.0 mmol) and 2-morpholinoethanamine (0.97 mL, 7.4 mmol) in benzene (15 mL), in the presence of La(OTf)$_3$ (74 mg, 0.15 mmol, 1.8 mol %), reacting for 3 days in a Soxhlet apparatus. Sublimation of the crude product at 65 °C (0.1 mmHg) for 12 h gave **4k** as colorless crystals (2.07 g, 62%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.43 (m, 3H, CH_2 and NH), 2.69 (m, 4H, 2CH_2 of morpholine), 3.15 (m, 2H, CH_2), 3.81 (m, 4H, 2CH_2 of morpholine), 11.07 (s, 1H, OH). ^{19}F NMR (188 MHz, $CDCl_3$): δ −81.10 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.28 and 53.88 (2C, 2CH_2), 59.03, 61.63, 66.41 and 67.08 (4C of morpholine). Resonances for CF_3 groups were not observed due to a too short relaxation period or a non-adapted pulse angle. Anal. Calcd for $C_9H_{14}F_6N_2O_2$: C, 36.49; H, 4.76. Found: C, 36.80; H, 4.98.

4.3. Crystal structure determination of **2e**,**h**, **3a**,**f**, and **4k**

Suitable crystals for X-ray diffraction analysis of **2e**,**h**, **3a**,**f**, and **4k** were obtained by recrystallization of purified products (see Section 4). Diffraction data were collected at 100 K using a Bruker APEX CCD diffractometer with graphite-monochromatized Mo Kα radiation (λ=0.71073 Å). A combination of ω and ϕ scans was carried out to obtain at least a unique data set. The crystal structures were solved by means of the Patterson method and remaining atoms were located from difference Fourier synthesis followed by full matrix least-squares refinement based on F^2 (programs SHELXS-97 and SHELXL-97).[29] Many hydrogen atoms could be found from the Fourier difference analysis. Carbon- and oxygen-bound hydrogen atoms were placed at calculated positions and forced to ride on the attached atom. The hydrogen atom contributions were calculated but not refined. All non-hydrogen atoms were refined with anisotropic displacement parameters. The locations of the largest peaks in the final difference Fourier map calculation as well as the magnitude of the residual electron densities were of no chemical significance. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. 661370–661374 for **2e**,**h**, **3a**,**f**, and **4k**. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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References and notes

1. (a) Martin, J. W. L.; Willis, C. J. *Can. J. Chem.* **1977**, *55*, 2459–2464; (b) Konefal, E.; Loeb, S. J.; Stephan, D. W.; Willis, C. J. *Inorg. Chem.* **1984**, *23*, 538–545 and references cited therein.
2. Liu, Y.-H.; Cheng, Y.-C.; Tung, Y.-L.; Chi, Y.; Chen, Y.-L.; Lui, C.-S.; Peng, S.-M.; Lee, G.-H. *J. Mater. Chem.* **2003**, *13*, 135–142.
3. Chen, Y.-L.; Hsu, C.-C.; Song, Y.-H.; Chi, Y.; Carty, A. J.; Peng, S.-M.; Lee, G.-H. *Chem. Vap. Deposit.* **2006**, *12*, 442–447.
4. Chi, Y.; Chou, T.-Y.; Wang, Y.-J.; Huang, S.-F.; Carty, A. J.; Scoles, L.; Udachin, K. A.; Peng, S.-M.; Lee, G.-H. *Organometallics* **2004**, *23*, 95–103.
5. Lay, E.; Song, Y.-H.; Chiu, Y.-C.; Lin, Y.-M.; Chi, Y.; Carty, A. J.; Peng, S.-M.; Lee, G.-H. *Inorg. Chem.* **2005**, *44*, 7226–7233.
6. For Ru complexes incorporating related fluorinated alkoxy-imino ligands, see Ref. 2.
7. (a) Abele, H.; Haas, A.; Lieb, M. *Chem. Ber.* **1986**, *119*, 3502–3506; (b) Schlosser, M.; Keller, H. *Liebigs Ann.* **1995**, 1587–1589.

8. For the synthesis of 5,5,5-trifluoro-4-(trifluoromethyl)-4-hydroxy-2-pentanone (38% yield) by the reaction of anhydrous hexafluoroacetone and acetone, see: Simonyan, L. A.; Gambaryan, N. P.; Knunyants, I. L. *Zh. Vses. Khim. Obshchestva D.I. Mendeleeva* **1966**, *11*, 467–468; *Chem. Abstr.* **1966**, *65*, 18489.
9. (a) Funabiki, K.; Nojiri, M.; Matsui, M.; Shibata, K. *Chem. Commun.* **1998**, 2051–2052; (b) Funabiki, K.; Matsanaga, K.; Matsui, M.; Shibata, K. *Synlett* **1999**, 1477–1479.
10. Funabiki, K.; Isomura, A.; Yamaguchi, Y.; Hashimoto, W.; Matsunaga, K.; Shibata, K.; Matsui, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2578–2582.
11. Barten, J. A.; Funabiki, K.; Röschenthaler, G.-V. *J. Fluorine Chem.* **2002**, *113*, 105–109.
12. Barten, J. A.; Lork, E.; Röschenthaler, G.-V. *J. Fluorine Chem.* **2004**, *125*, 1039–1049.
13. (a) Mahrwald, R. *Modern Aldol Reactions*; Wiley-VCH: Weinheim, Germany, 2004; Vols. 1 and 2, pp 1218–1223; (b) Wade, L. G. *Organic Chemistry*, 6th ed.; Prentice Hall: Upper Saddle River, New Jersey, NJ, 2005; pp 1056–1066; (c) Smith, M. B.; March, J. *Advanced Organic Chemistry*, 5th ed.; Wiley-Interscience: New York, NY, 2001; pp 1218–1223.
14. Ishihara, T.; Shinjo, H.; Inoue, Y.; Ando, T. *J. Fluorine Chem.* **1983**, *22*, 1–19.
15. (a) *The Chemistry of Carbon Nitrogen Double Bond*; Patai, S., Ed.; Wiley-Interscience: New York, NY, 1970; (b) Layer, W. *Chem. Rev.* **1963**, *63*, 489–510; (c) Marc, J. *Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, 3rd ed.; John Wiley & Sons: New York, NY, 1985; (d) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part B*, 4th ed.; Springer: New York, NY, 2000.
16. Billman, J. H.; Tai, K. M. *J. Org. Chem.* **1958**, *23*, 535–539.
17. White, W. A.; Weingarten, H. *J. Org. Chem.* **1967**, *32*, 213–214.
18. Texier-Boullet, F. *Synthesis* **1985**, 679–681.
19. Varma, M.; Dahiya, R.; Kumar, S. *Tetrahedron Lett.* **1997**, *38*, 2039–2042 and references cited therein.
20. Taguchi, K.; Westheimer, F. H. *J. Org. Chem.* **1971**, *36*, 1570–1572.
21. (a) Kuehne, M. E. *J. Am. Chem. Soc.* **1959**, *81*, 5400–5404; (b) Stork, G.; Terrell, R.; Szmuszkovicz, J. *J. Am. Chem. Soc.* **1954**, *76*, 2029–2030; (c) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207–222.
22. For the use of $La(OTf)_3$ as Lewis catalyst: (a) Kobayashi, S.; Manabe, K. *Pure Appl. Chem.* **2000**, *72*, 1373–1380; (b) Engberts, J.; Feringa, B.; Keller, E.; Otto, S. *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 457–464; (c) Barrett, A.; Braddock, D. *Chem. Commun.* **1997**, 351–352; (d) Xie, W.; Jin, Y.; Wang, P. *Chem. Technol.* **1999**, *29*, 23–29.
23. For the use of $InBr_3$ as Lewis catalyst: (a) Huang, J.-M.; Wong, C.-M.; Xu, F.-X.; Loh, T.-P. *Tetrahedron Lett.* **2007**, *48*, 3375–3377; (b) Yadav, J. S.; Reddy, B. V. S.; Rao, K. V.; Raj, K. S.; Prasad, A. R.; Kumar, S. K.; Kunwar, A. C.; Jayaprakash, P.; Jagannath, B. *Angew. Chem., Int. Ed.* **2003**, *42*, 5198–5201; (c) Yadav, J. S.; Reddy, B. V. S.; Bhaishya, G. *Green Chem.* **2003**, *5*, 264–271.
24. For related fluorinated hemiaminals of type $R^1R^2NC(CF_3)_2OH$, see: (a) Burger, K.; Penninger, S.; Greisel, M.; Daltrozzo, E. *J. Fluorine Chem.* **1980**, *15*, 1–27; (b) Korenchenko, O. V.; Sokolov, V. B.; Aksinenko, A. Y.; Martynov, I. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1990**, *2*, 373–378.
25. Steiner, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 48–76.
26. (a) Fujita, T.; Tohi, Y.; Mitani, M.; Matsui, S.; Saito, J.; Nitabaru, M.; Sugi, K.; Makio, H.; Tsutsui, T. Eur. Pat. Appl. 0,874,005, 1998 (b) Makio, H.; Kashiwa, N.; Fujita, T. *Adv. Synth. Catal.* **2002**, *344*, 477–493; (c) Makio, H.; Fujita, T. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 52–66; (d) Nakayama, Y.; Saito, J.; Bando, H.; Fujita, T. *Chem.—Eur. J.* **2006**, *12*, 7546–7556.
27. (a) Atwood, D. A.; Harvey, J. M. *Chem. Rev.* **2001**, *101*, 37–52; (b) Baleizao, C.; Garcia, H. *Chem. Rev.* **2006**, *106*, 3987–4043.
28. (a) Lavanant, L.; Chou, T.-Y.; Chi, Y.; Lehmann, C. W.; Toupet, L.; Carpentier, J.-F. *Organometallics* **2004**, *23*, 5450–5458; (b) Amgoune, A.; Lavanant, L.; Thomas, C. M.; Chi, Y.; Welter, R.; Dagorne, S.; Carpentier, J.-F. *Organometallics* **2005**, *24*, 6279–6282; (c) Kirillov, E.; Lavanant, L.; Thomas, C. M.; Roisnel, T.; Chi, Y.; Carpentier, J.-F. *Chem.—Eur. J.* **2007**, *13*, 923–935.
29. (a) Sheldrick, G. M. *SHELXS-97: Program for the Determination of Crystal Structures*; University of Gottingen: Germany, 1997; (b) Sheldrick, G. M. *SHELXL-97: Program for the Refinement of Crystal Structures*; University of Gottingen: Germany, 1997.