Pergamon

Tetrahedron 58 (2002) 3561–3577

TETRAHEDRON

Activated dimethyl sulfoxide dehydration of amide and its application to one-pot preparation of benzyl-type perfluoroimidates☆

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Received 28 December 2001; accepted 13 March 2002

Abstract—Various types of primary amides were treated under an activated dimethyl sulfoxide (DMSO) species, $(COCl)_2$–DMSO and Et_3N, as a dehydrating agent to obtain nitriles in excellent yield. This dehydration system was extended to a one-pot preparation of perfluoroimidates via volatile perfluoronitriles from perfluoroamides. Fifteen benzyl-type perfluoroimidates can be prepared in 70–90% yield as more stable imidates than the trichloro analogue. MPM- and DMPM-perfluoroimidates can be used to protect alcohols in place of the trichloroacetimidate with excellent chemical properties and in comparable yields. © 2002 Elsevier Science Ltd. All rights reserved.

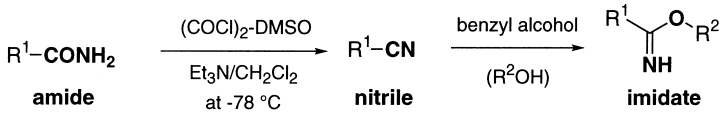
1. Introduction

The dehydration of primary amides offers a convenient approach to nitrile formation. Many nitrile preparation methods by dehydration of amides have been documented in the literature[2] such as phosphorus pentoxide,[3] thionyl chloride,[4] triphenyl phosphine/carbontetrachloride,[5] titanium tetrachloride,[6] phase-transfer conditions,[7] trifluoroacetic anhydride/pyridine,[8] and Vilsmeier reagent.[9] Reagents that are often employed for this transformation are inappropriate in the presence of other functional groups, therefore, requiring protection of the intermediates or an entirely alternative synthesis. Recently, mild and efficient reagents providing higher yields using diphosgene,[10] (methoxycarbonylsulfamoyl)triethylammonium hydroxide (Burgess reagent),[11] ethyl iodide/silver oxide,[12] acetic anhydride/pyridine,[13] refluxing acetonitrile with formic acid,[14] aryl chlorothionoformate[15] have been introduced. We have found that the Swern oxidation conditions[16] was extremely useful for the dehydration of amides.[1a] An important characteristic of this reaction is that the dehydration reaction proceeds at −78°C. We wish to report here in full our observation regarding the details of the dehydration of primary amides. We also describe here one-pot synthesis of benzyl-type perfluoroimidates as the synthetic application (Scheme 1).

2. Background

2.1. Activated dimethyl sulfoxide reagents

Activated dimethyl sulfoxide (DMSO) reagents have been used effectively in organic synthesis. There are many examples of how advantageous the use of DMSO can be, the activators to be discussed are dicyclohexylcarbodiimide (DCC)/polyphosphoric acid, acetic anhydride, thionyl chloride ($SOCl_2$), oxalyl chloride [$(COCl)_2$], sulfur trioxide/pyridine (SO_3·Py), *t*-butyl hypochlorite and halogens. The activated DMSO, ($Me_2S^+ \cdot X^-$) and $Me_2S^+(O)Cl \cdot X^-$, are known for the selective oxidation of various functionalized alcohols to the corresponding carbonyl compounds,[17] and have been reported for the dehydration reaction of oximes and hydroxylamines by Moffatt and co-workers.[18]



Scheme 1.

☆ See Ref. 1.

Keywords: amide; nitrile; dehydration; activated dimethyl sulfoxide; perfluoronitrile; perfluoroamide; perfluoroimidate.

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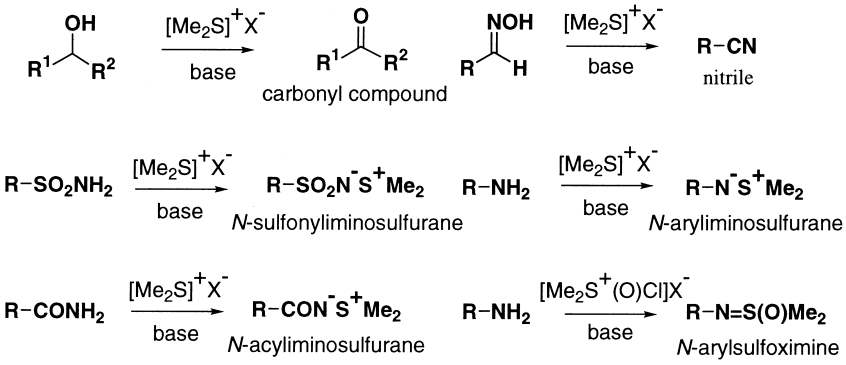
PII: S0040-4020(02)00304-6



Scheme 2.

Swern and co-workers have widely investigated the synthesis of sulfilimines (*N*-sulfony, *N*-acyl and *N*-aryliminosulfuranes) and sulfoximines by using the activated DMSO from sulfonamide, amide, and aromatic amine, although a brief comment with reference to the nitrile formation from amide was given.[16a,19] To date, no detailed study on nitrile formation by amide dehydration using the activated DMSO has been reported (Scheme 2).

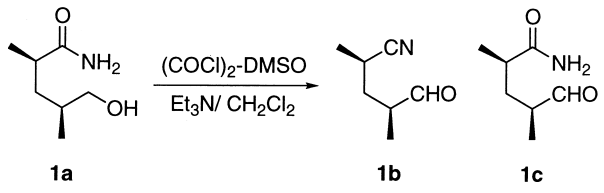
2.2. Imidates

Imidates (imidic acid esters, imido esters, imidoates) are obtained from the condensation of nitriles with alcohols and are important intermediates in organic synthesis of primary and tertiary amines, polymers, orthoesters, amidines, imidazoles, imidazolines, oxazoles, oxazolines, thiazolines and so on.[20] Pinner first prepared imidate hydrochlorides in the presence of anhydrous hydrogen chloride in 1877.[21] The free imidate was obtained by immediate extraction with ether after treatment of the salt with an aqueous potassium carbonate solution. The base-catalyzed conversion of nitriles to imidates has come to be widely used in view of the advantage that the imidate is directly isolated by distillation and the excess nitrile is similarly recovered.[22] In particular, the trichloroacetimidates (R^1=CCl_3)[23] have found widespread use as precursors of (1) protection of a hydroxy group (R^2=benzyl-type),[24] (2) introduction of nitrogen functionality in the molecules via 3,3-sigmatropic rearrangement (R^2=allyl)[25] or Lewis acid-mediated intramolecular cyclization (R^2=epoxy)[26] and (3) synthesis of glycosides and oligosaccharides (R^2=glycosyl).[27]

3. Results and discussion

3.1. Initial studies for dehydration of amide

We first observed an unexpected application of Swern oxidation in a synthetic study of (±)-epiderstatin.[28] When 5-hydroxy-2,4-dimethylpentanamide (**1a**) was oxidized under Swern oxidation conditions with 5.0 equiv. of $(COCl)_2$, 7.5 equiv. of DMSO and 20 equiv. of triethylamine (Et_3N), 4-cyano-2-methylpentanal (**1b**) was isolated in 62% yield instead of the expected 2,4-dimethyl-5-oxopentanamide (**1c**). The dehydration of amide occurred together with the usual alcohol oxidation under Swern oxidation conditions (Scheme 3).



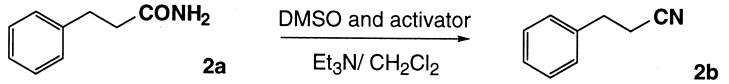
Scheme 3.

We were interested in the dehydration conditions, and the requirement of a reagent was checked using 3-phenylpropanamide (**2a**). The dehydration of **2a** proceeded on treatment with DMSO, $(COCl)_2$ and Et_3N by the Swern oxidation procedure at −78°C for 15 min to give 87% yield of 3-phenylpropionitrile (**2b**) along with a small amount (3%) of the remaining **2a**. Raising the reaction temperature up to room temperature achieved complete reaction to afford **2b** in 92% yield (Table 1, entries 1 and 2). Another DMSO activator, thionyl chloride, trifluoroacetic anhydride (TFAA) and sulfur trioxide/pyridine (SO_3·Py), also afforded **2b** in 86, 85 and 57% yields, respectively (entries 3–5). In the absence of Et_3N or DMSO and the use of phenyl sulfoxide, lacking an α-hydrogen to the sulfur instead of DMSO, no detectable reaction occurred at −78°C (entries 6–8). With the use of 0.5 equiv. of DMSO and $(COCl)_2$, 46% of **2b** with 52% of the starting material were obtained (entry 9). The dehydration also proceeded by dimethyl sulfide (DMS) and *N*-chlorosuccinimide (NCS),[29] although the dehydration yield was only 9% even after 48 h (entry 10). These results show the dehydration reaction needs the combination of DMSO and its activator and results in the formation of an activated DMSO species, followed by Et_3N. The generality and use of an activated DMSO species for the dehydration of amides into nitriles were studied in this paper.

3.2. Dehydration of aromatic amide

The dehydration of aromatic amides (**3a**–**9a**) was next examined. On the treatment of 4-methoxybenzamides (**3a**) and 4-nitrobenzamide (**4a**) with $(COCl)_2$ (1.5 equiv.), DMSO (3.0 equiv.) and Et_3N (6.0 equiv.) for 15 min at −78°C, only 35 and 34% yield of 4-methoxybenzonitrile (**3b**) and 4-nitrobenzonitrile (**4b**) were obtained and iminosulfuranes, *S*,*S*-dimethy-*N*-4-methoxybenzoyliminosulfurane (**3c**) and *S*,*S*-dimethy-*N*-4-nitro-benzoyliminosulfurane (**4c**) were formed in 53 and 41% yield (Table 2, entries 1 and 2). The isolated acyliminosulfuranes (**3c** and **4c**) did not

Table 1. Dehydration of **2a** to **2b** under an activated DMSO conditions



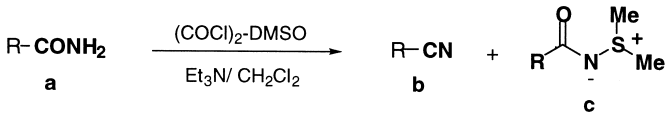
Entry	Activator (equiv.)	DMSO (equiv.)	Et_3N (equiv.)	Temperature	Time (h)	Yield (%)[a]
1	$(COCl)_2$, 1.2	1.6	3.0	−78°C	0.25	87 (3)[b]
2	$(COCl)_2$, 1.2	1.6	3.0	−78°C to rt	0.25 and 1	92
3	$SOCl_2$, 1.2	1.6	3.0	−78°C	0.25	86 (4)[b]
4	TFAA, 1.2	1.6	3.0	−78°C	0.25	85
5	SO_3·Py, 3.0	6.0	15.0	rt	116	57
6	$(COCl)_2$, 3.0	6.0	0	−78°C	0.25	–[c]
7	$(COCl)_2$, 3.0	0	9.0	−78°C	0.25	–[c]
8	$(COCl)_2$, 1.2	1.6[d]	3.0	−78°C	0.25	–[c]
9	$(COCl)_2$, 0.5	0.5	1.5	−78°C	0.25	46 (52)[b]
10	NCS, 1.5	DMS, 2.25	1.75	rt	48	9

[a] Isolation yields after chromatographic purification.
[b] Parentheses show the recovery yield of the starting material.
[c] No reaction occurred.
[d] Phenyl sulfoxide was used for reaction instead of DMSO.

change into the nitriles (**3b** and **4b**) by base treatment. We found the yield of nitrile depended on the amide solubility, increasing solubility tended to increase nitrile yield. The dehydration yields were improved up to 93 and 98% yields using an excess amount of DMSO as solvent (entries 3 and 4). The results of aromatic amide dehydration (**5a**–**9a**) summarized in Table 2. The corresponding nitriles (**5b**–**9b**) were obtained in 64–93% yields without acyliminosulfurane formation.

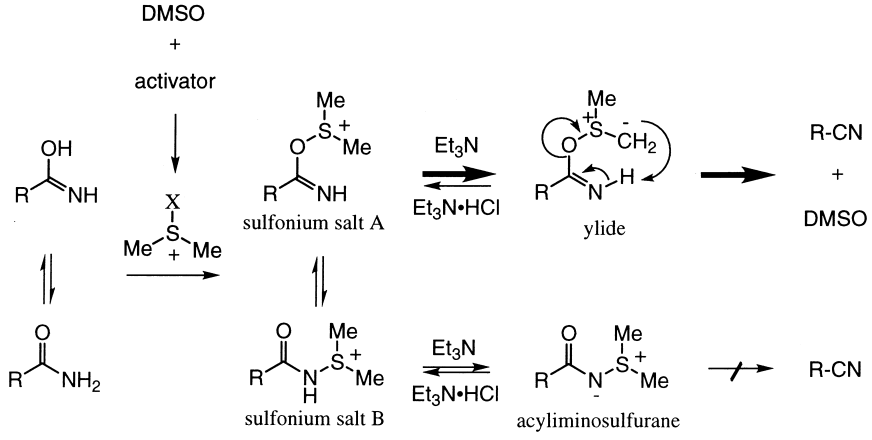
The proposed dehydration mechanism based on our results and a general activated DMSO oxidation mechanism was

Table 2. Dehydration of aromatic amide: iminosulfurane formation under an activated DMSO conditions



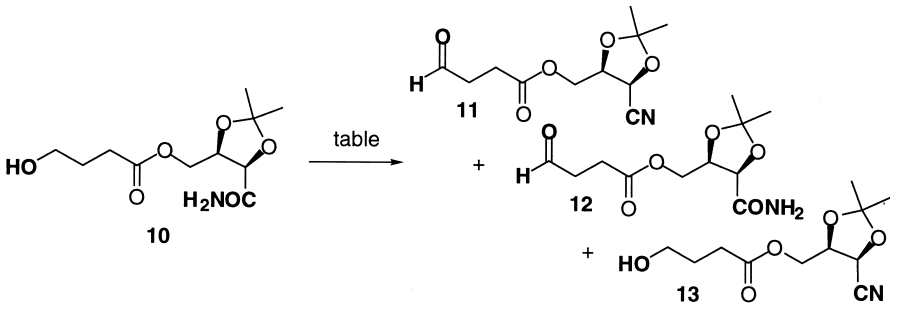
Entry	Amide, R	$(COCl)_2$ (equiv.)	DMSO (equiv.)	Et_3N (equiv.)	Yield (%)[a]	
					b	**c**
1	4-$MeOC_6H_4$ (**3a**)	1.5	3.0	6.0	35	53
2	4-$NO_2C_6H_4$ (**4a**)	1.2	1.6	2.4	34	41
3	**3a**	1.2	7.2	6.0	93	0
4	**4a**	1.2	10.0	2.4	98	0
5	1-Naphtyl (**5a**)	1.2	10.0	2.4	83	0
6	2,6-$Cl_2C_6H_3$ (**6a**)	1.2	10.0	3.0	87	0
7	3,5-$NO_2C_6H_3$ (**7a**)	3.0	10.0	9.0	93	0
8	3-Pyridyl (**8a**)	1.2	3.5	3.0	64	0
9	$C_6H_5CH{=}CH$ (**9a**)	1.2	6.0	2.4	80	0

[a] Isolation yields after chromatographic purification.



Scheme 4.

Table 3. Reaction of amide alcohol (**10**) under activated DMSO conditions



Entry	$(COCl)_2$ (equiv.)	DMSO (equiv.)	Et_3N (equiv.)	Yield (%)[a]			
				10	**11**	**12**	**13**
1	3.0	6.0	9.0	0	91	0	0
2	2.0	4.0	6.0	0	76	14	0
3	1.0	2.0	3.0	12	0	75	0

[a] Isolation yields after chromatographic purification.

shown in Scheme 4. The reaction of DMSO and its activator generates an activated DMSO species. The amides react with the activated DMSO to form two sulfonium salts A and B. These two sulfonium salts are in equilibrium. Nitrile formation could occur from the sulfonium salt A via an intramolecular proton abstraction from the ylide, which collapses intramolecularly to the nitrile and DMSO. In the case of aromatic amide dehydration, because the solubility of iminosulfurane is poor, the corresponding benzoyliminosulfuranes should be precipitated out from the supersaturated solution after base treatment.

3.3. Dehydration of amide alcohol

We next investigated the functional group selectivity, amide group vs alcohol, using amide alcohol (**10**). When amide alcohol (**10**) was treated with 3.0 equiv. of $(COCl)_2$, 6.0 equiv. of DMSO and 9.0 equiv. of Et_3N, nitrile aldehyde (**11**) was obtained in 91% yield (Table 3, entry 1). With the use of 2.0 equiv. of $(COCl)_2$, 4.0 equiv. of DMSO and 6.0 equiv. of Et_3N conditions, **11** and amide aldehyde (**12**) were obtained in 76 and 14% yields, respectively (entry 2). The nitrile alcohol (**13**) was not isolated even with the use of 1.0 equiv. of $(COCl)_2$. The activated DMSO species caused alcohol oxidation in preference to amide dehydration to yield **12** in 75% yield along with unconsumed **10** in 12% yield (entry 3).

3.4. General study on dehydration

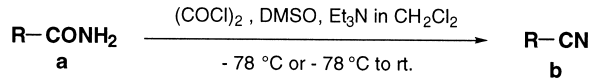
The key to successfully using DMSO as an oxidant for alcohol is to activate the sulfur atom prior to reaction with a nucleophilic alcohol function. Swern oxidation generally requires prior preparation of an activated DMSO species before addition of the substrate, while the dehydration could be achieved without prior preparation of an activated DMSO species. The dehydration proceeded by successively adding $(COCl)_2$ and Et_3N to an amide and DMSO solution in CH_2Cl_2 at $-78°C$. The reaction was successful for various types of primary amides in excellent yield, and the operation is believed to be simple. The results are summarized in Table 4. Protecting groups including acetonide (**14a**, entry 1), *t*-butoxycarbonyl (Boc, **15a** and **16a**, entries 2 and 3), benzyloxycarbonyl (Cbz, **17a**, entry 4), and tosyl (Ts, **18a**, entry 5) were tolerated; however, the presence of a free amino group (**19a**) led to no nitrile formation (entry 6). By employing our methods, optically active *O*-protected cyanohydrins were easily synthesized from the corresponding α-hydroxyamides, which were readily prepared from α-amino acid, sugar and tartaric acid derivatives. The dehydration of sugar derivatives (**20a**, **21a**) α,β-epoxy (**22a**), α-benzoxy (**23a**), α-acetoxy (**24a**, **25a**), α-silyloxy (**23a**, **28a**) and α-glycosyloxyamides (**29a**–**31a**) was carried out to give the corresponding *O*-protected cyanohydrins (**20b**–**31b**) in 80–98% yield (entries 7–18). Neither racemization of the α-carbon nor β-elimination of the nitrile groups was observed.[30] The α-glycosyl cyanohydrins (**29b**–**31b**) were converted into the cyanogen glycosides, (*R*)-prunasin, linamarin (phaseolunatin), (*S*)-heterodendrin (dihydroacacipetalin) in excellent yields.[31]

The dehydration of *syn* and *anti*-aldoxime (**32**),[7,32] urea (**33**), formamide (**34**),[33] and allyl carbamate (**35**)[34] was next studied. These results are summarized in Table 5. When the *syn* and *anti* isomers of oxime (**32**) were separately subjected to the dehydration reaction at $-78°C$, the *syn*-**32** gave no nitrile while the *anti*-**32** gave nitrile (**36**) in 59% yield (entries 1 and 2). The dehydration of urea (**33**) produced cyanamide (**37**)[7] only in 4% (entry 3). No amount of either isonitrile (**38**) or allyl cyanate (**39**) expected to be obtainable from the dehydration of **34** and **35** was isolated (entries 4 and 5).

3.5. One-pot preparation of benzyl-type perfluoroimidates

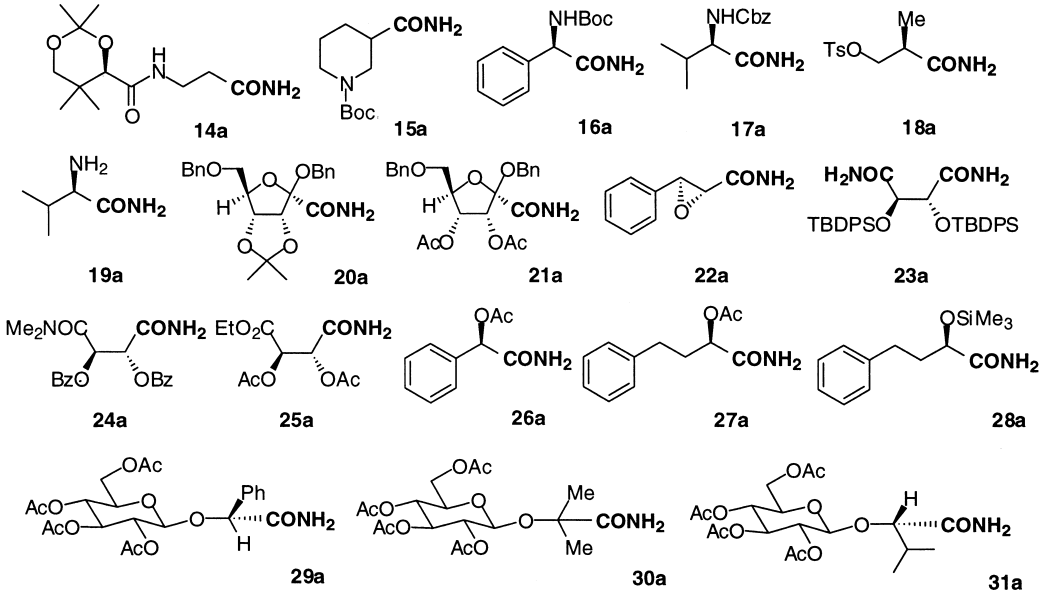
Various types of trichloroacetimidates can be used to install the corresponding protective group in the presence of a variety of other protecting groups under acidic conditions. Both 4-methoxybenzyl (MPM and/or PMB)[35] and 3,4-dimethoxybenzyl (DMPM and/or DMB)[36] trichloroacetimidates are a more reactive protecting reagent than benzyl (Bn) trichloroacetimidate[37] and are not sufficiently stable.

Table 4. General study on dehydration of amides to nitriles



Entry	Amide	$(COCl)_2$ (equiv.)	DMSO (equiv.)	Et_3N (equiv.)	Yield (%)[a]
1	**14a**	1.5	2.0	3.0	93
2	**15a**	1.2	1.6	3.0	89
3	**16a**	1.3	1.7	3.2	81
4	**17a**	1.3	1.6	3.0	67 (16)[b]
5	**18a**	1.4	2.0	3.0	96[c]
6	**19a**	1.2	6.4	7.1	Mess
7	**20a**	1.2	1.5	3.0	95
8	**21a**	1.2	1.6	3.0	94
9	**22a**	1.5	2.0	3.0	87[c]
10	**23a**	2.5	4.0	6.0	80
11	**24a**	1.5	2.0	3.0	94
12	**25a**	1.5	3.0	4.5	91
13	**26a**	1.5	2.0	3.0	90[c]
14	**27a**	1.5	2.0	3.0	91[c]
15	**28a**	1.6	2.4	3.0	83
16	**29a**	4.0	6.0	12.0	97[c]
17	**30a**	4.0	6.0	12.0	93[c]
18	**31a**	4.0	6.0	12.0	98[c]

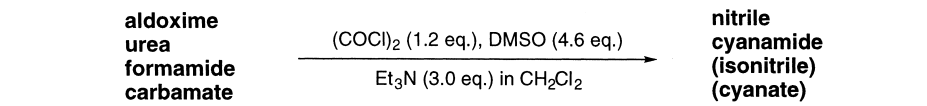
[a] Isolation yields after chromatographic purification.
[b] Parentheses show the recovery yield of the starting material.
[c] Reaction runs at −78°C.



In order to improve the chemical properties of these reagents, we designed and synthesized the perfluoro analogues of MPM- and DMPM-imidates.[1b] Brown and co-workers first reported the preparation of perfluoroimidates from volatile perfluoronitriles and alcohol in a glass ampoule.[38] Thomas and co-workers prepared allylic trifluoroacetimidate by the lithiated alcohol addition to an excess of trifluoroacetonitrile (bp −64°C)[39] which was generated by dehydration of trifluoroacetamide using P_2O_5 and following condensation at −78°C.[40] Trifluoroacetonitrile, pentafluoropropionitrile (bp −35°C) and heptafluorobutyronitrile (bp +2°C) are commercially available packaged in a cylinder. However, the handling of perfluoronitriles is quite troublesome because of their volatile and toxic properties. Therefore, we became interested in a one-pot preparation method of trifluoroacetimidates via generation of perfluoronitriles from perfluoroamide without an isolation step as shown in Scheme 5. The key step in this approach was envisioned to be the in-situ alcohol addition to perfluoronitriles containing electron-withdrawing substituents on the imidate under dehydration conditions.

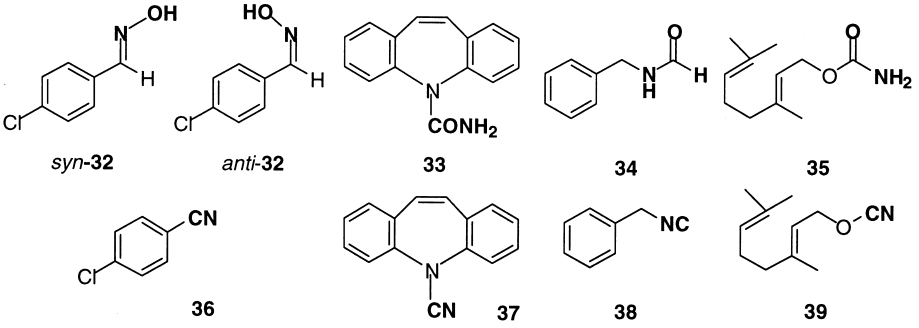
Three equivalents of trifluoroacetonitrile were generated at −78°C from 2,2,2-trifluoroacetamide (3.3 equiv.) by treatment of $(COCl)_2$ (3.0 equiv.), DMSO (15 equiv.), and Et_3N (10 equiv.) in CH_2Cl_2. Benzyl alcohol (1.0 equiv.) was added to the reaction mixture and warmed to room temperature to afford Bn-trifluoroacetimidate (**40A**) in 10% yield (Table 6, entry 1). Other perfluoroalkyl substituents [Rf=$F(CF_2)_2$ (**B**), ClF_2C (**C**), $F(CF_2)_3$ (**D**), $H(CF_2)_2$ (**E**), $H(CF_2)_4$ (**F**) and $H(CF_2)_6$ (**G**)] also produced Bn-perfluoro-

Table 5. Dehydration of aldoxime, urea, formamide, and allyl carbamate



Entry	Substrate	Temperature (°C)	Product	Yield (%)[a]
1	*syn*-**32**	−78	**36**	–[b]
2	*anti*-**32**	−78	**36**	59
3	**33**	−78 to 20	**37**	4
4	**34**	−78 to 20	**38**	–[b]
5	**35**	−78 to 20	**39**	–[b]

[a] Isolation yields after chromatographic purification.
[b] No reaction occurred.



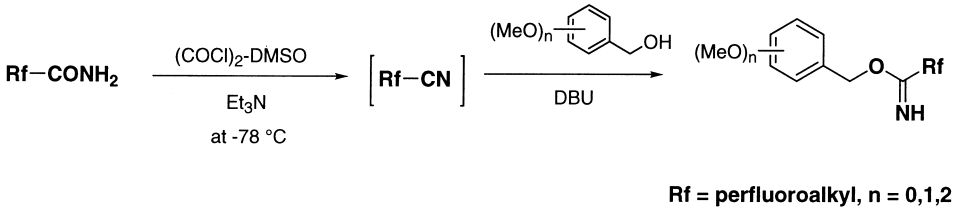
imidates (**40B**–**40G**) in 14–58% yields. As the number of fluorine atoms on perfluoro substituent and the boiling point of nitrile increased, the isolated yield of imidates rose, 10% (**40A**), 14% (**40E**), 29% (**40B**), 58% (**40D**), 35% (**40F**) and 41% (**40G**) (entries 1–7). Unfortunately, the imidate formation was poorly reproducible and was contaminated by benzaldehyde as a major by-product. These results suggested that in situ benzyl alcohol addition to trifluoroacetonitrile was not sufficient; therefore, we sought a way to accelerate nucleophilic alcohol addition to nitrile. After several trials, we were pleased to find that DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) accelerated the alcohol addition and dramatically increased the generation of **40A** up to maximum 87% yield (entry 1). In the presence of DBU, Bn-perfluoroimidates (**40B**–**40G**) were obtained in 74–90% yields without formation of benzaldehyde (entries 2–7). The overall sequence proceeded cleanly on a ten-gram scale and was reproducible. MPM and DMPM alcohol also reacted with perfluoronitriles to afford both MPM and DMPM perfluoroimidates (**41A**–**41D** and **42A**–**42D**) in 80–85% and 70–81% yields as shown in Table 6 (entries 8–11 and 12–15). The described one-pot procedure proved to be operationally simple without requiring special equipment and is useful for the preparation of perfluoroimidates.

3.6. Characterization of benzyl-type perfluoroimidates

Because the basicity of the nitrogen atom is reduced by electron-withdrawing perfluoro substitution on the imidate carbon, 15 perfluoroimidates (**40A**–**42D**) could be purified by usual silica gel short column chromatography. The boiling points of perfluoro analogues were lower than that of the trichloro analogue, nine trifluoroacetimidates (**40A**–**42A**, **40C**–**42C**, and **40D**–**42D**) could be easily distilled without rearrangement as summarized in Fig. 1. In particular, DMPM trifluoroacetimidate (**42A**) was readily distilled at 125°C and 0.3 atm pressure. This boiling point was lower than that of the trichloro analogue by about 90°C at its pressure. MPM and DMPM trichloroacetimidates are reactive and are not sufficiently stable for storage; therefore, they are best prepared fresh before use. The MPM and DMPM perfluoroimidates (**41A**, **B**, **D** and **42A**, **B**, **D**) could be stored for a year in a freezer after distillation.

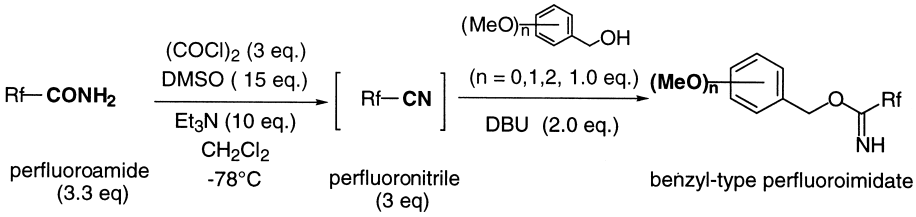
3.7. Benzyl protection of a hydroxy group

We previously reported that MPM- and DMPM-perfluoroimidates could serve as stable protecting reagents for hydroxy functions in place of the trichloroacetimidate with excellent chemical properties and in comparable



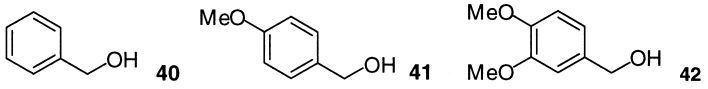
Scheme 5.

Table 6. One-pot preparation of benzyl-type perfluoroimidates



Entry	Rf	Alcohol	Yield (%)[a]			Imidate
			DBU, 0 equiv.	DBU, 1.0 equiv.	DBU, 2.0 equiv.	
1	F_3C	**40**	10	64	87	**40A**
2	$F(CF_2)_2$	**40**	29	54	78	**40B**
3	ClF_2C	**40**	40	61	81	**40C**
4	$F(CF_2)_3$	**40**	58	67	77	**40D**
5	$H(CF_2)_2$	**40**	14	35	74	**40E**
6	$H(CF_2)_4$	**40**	35	82	76	**40F**
7	$H(CF_2)_6$	**40**	41	77	90	**40G**
8	F_3C	**41**	48	54	85	**41A**
9	$F(CF_2)_2$	**41**			80	**41B**
10	ClF_2C	**41**			83	**41C**
11	$F(CF_2)_3$	**41**			80	**41D**
12	F_3C	**42**	56	62	81	**42A**
13	$F(CF_2)_2$	**42**	58	71	82	**42B**
14	ClF_2C	**42**	36	85	81	**42C**
15	$F(CF_2)_3$	**42**		61	70	**42D**

[a] Isolation yields after purification by Kugelrohr distillation and/or SiO_2 column chromatography.



yields.[1b] In the presence of 13 mol% of PPTS (pyridinium *p*-toluenesulfonate) in CH_2Cl_2 as a catalyst, MPM-trifluoroacetimidate (**41A**) reacted with primary alcohol (**43**) to provide the expected MPM ether in 80% yields (entry 1). A small amount of TfOH (trifluoromethanesulfonic acid) in Et_2O was a more effective catalyst, and the MPM protection of **43** with 0.3 mol% of TfOH rapidly proceeded to completion within 5 min (entry 2). The secondary (**44**) and tertiary alcohol (**46**) also provided the expected MPM ether in good yields (entries 3 and 4). The DMPM-trifluoroacetimidate (**42A**) was much more reactive than **41A**. The DMPM protection of **43** with **42A** and PPTS (11 mol%) proceeded within 1 h and 92% yield of DMPM ether was obtained (entries 1 vs 5). The DMPM-pentafluoropropionimidate

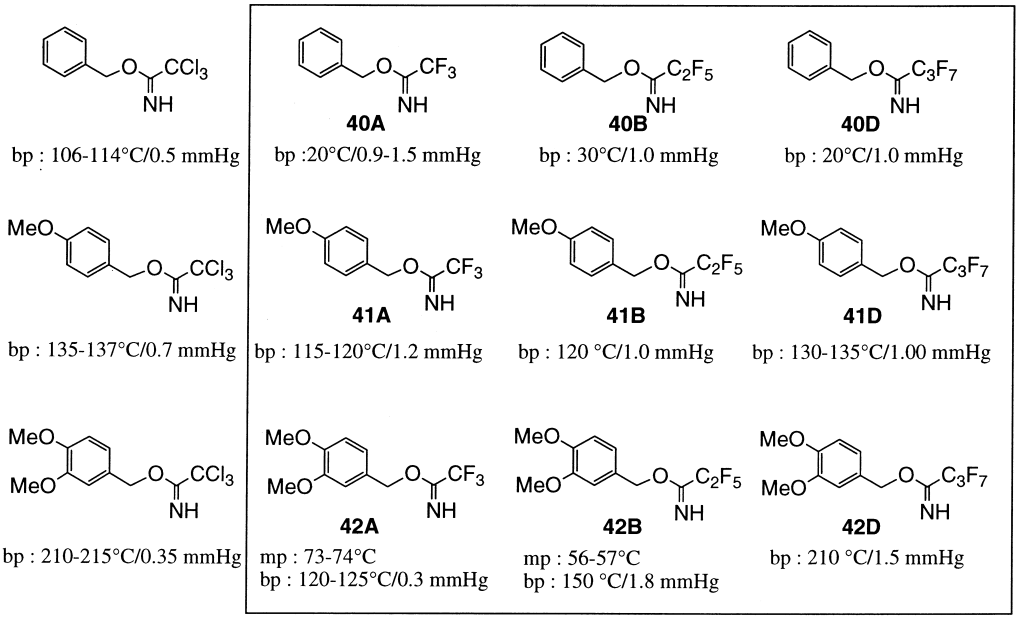
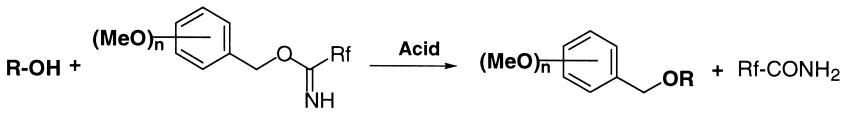


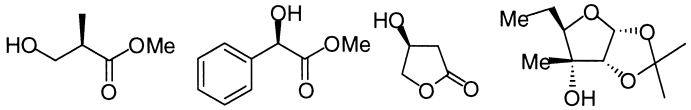
Figure 1.

Table 7. Acid-catalyzed 4-methoxybenzyl (MPM) and 3,4-dimethoxybenzyl (DMPM) protection of alcohol with MPM- and DMPM-perfluoroimidates



Entry	Imidate (equiv.)	Alcohol	Acid (mol%)	Solvent	Time	Yield (%)[a]
1	**41A**, 1.3	**43**	PPTS, 13	CH_2Cl_2	24 h	80
2	**41A**, 1.3	**43**	TfOH, 0.3	Et_2O	5 min	88
3	**41A**, 1.9	**44**	TfOH, 0.3	Et_2O	10 min	74
4	**41A**, 2.5	**46**	TfOH, 0.2	Et_2O	10 min	70
5	**42A**, 1.1	**43**	PPTS, 11	CH_2Cl_2	1 h	92
6	**42B**, 2.0	**43**	PPTS, 50	CH_2Cl_2	1 h	98
7	**42D**, 2.0	**43**	PPTS, 50	CH_2Cl_2	1 h	95
8	**42A**, 2.2	**44**	CSA, 15	CH_2Cl_2	5 h	80
9	**42A**, 1.5	**45**	CSA, 0.5	CH_2Cl_2	6 h	56
10	**42A**, 1.3	**46**	TfOH, 0.3	Et_2O	5 min	-[b]

[a] Isolation yield after chromatographic purification.
[b] Very rapid decomposition of imidate **42A**.



43 **44** **45** **46**

(**42B**) and DMPM-heptafluorobutyrimidate (**42D**) were also useful reagents for DMPM protection, and the DMPM ether of **43** was obtained in 98 and 95% yields, respectively (entries 6, 7). Although secondary alcohol (**44** and **45**) could not be converted to the desired DMPM ether under basic conditions, these transformations were eventually achieved using CSA (10-camphorsulphonic acid) as a catalyst in 80 and 56% yields (entries 8 and 9). Unfortunately, unsuccessful result was obtained for the protection of tertiary alcohol (**46**). No reaction occurred by using CSA and the TfOH catalyst caused rapid decomposition of **42A** (entry 10).

4. Conclusion

We have succeeded in developing a novel preparation method of amide dehydration. The method presented herein is believed to be operationally simple and useful for the conversion of primary amides into nitriles. The extension of amide dehydration to volatile perfluoronitriles and their application to the one-pot preparation of benzyl-type perfluoroimidates were next investigated. The obtained perfluoroimidates were more stable than the trichloro analogue and were purified by silica gel short column chromatography and/or distillation. MPM- and DMPM-perfluoroimidates can serve as stable protecting reagents for hydroxy functions in place of the trichloroacetimidate with excellent chemical properties and in comparable yields.

5. Experimental

5.1. General

^1H, ^{13}C and ^{19}F NMR spectra were recorded on JEOL JNM LA-400 instruments (399.65 MHz ^1H, 100.4 MHz ^{13}C, 376.0 MHz ^{19}F) spectrometer in deuterochloroform ($CDCl_3$), deuteromethanol (CD_3OD) or deuterowater (D_2O) with either tetramethylsilane (TMS) (0.00 ppm ^1H, 0.00 ppm ^{13}C), chloroform (7.26 ppm ^1H, 77.00 ppm ^{13}C) or fluorotribromomethane (7.00 ppm ^{19}F) as an internal reference unless otherwise stated. Data are reported in the following order: chemical shifts are given (δ); multiplicities are indicated [br (broad), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), exch (exchangeable)]; coupling constants, *J*, are reported (Hz); integration is provided; and assignment is indicated. Infrared spectra were measured with a Shimadzu OR-8000 spectrometer. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67–100%), m (medium 40–67%), w (weak 20–40%), and br (broad). Low and high resolution Electron Impact (EI) and Fast Atom Bomberdment (FAB) mass spectra were taken with a JEOL JMS AX-500 spectrometer. Data are reported in the form of *m/z* (intensity relative to base=100). Measurements of optical rotations were carried out with a Horiba SEPA-300 high sensitivity polarimeter and rotation values are reported as follows: $[\alpha]_{wavelength}^{temperature}$, (concentration in g/100 mL, solvent). Analytical thin-layer chromatography was performed using Merck silica gel plates with F-254 indicator. Column chromatography was performed with indicated solvents on Merck silica gel 60 (230–400 mesh ASTM). Visualization was accomplished by UV light, iodine, $KMnO_4$, *para*-anisaldehyde or pancardi solution. Analytical high-pressure liquid chromatography (HPLC) was performed on a GILSON Fast PCLC system and measurement of UV 254 nm absorbance. Melting points (mp) were determined on a Yanaco MP-21 micro melting point apparatus and are uncorrected.

5.2. Chemicals

The 2-chloro-2,2-difluoroacetamide, trifluoroacetamide, pentafluoropropionamide, heptafluorobutyramide were

purchased from Fluorochem Limited. The 3*H*-tetrafluoropropionamide, 5*H*-octafluorovaleramide, 7*H*-dodecafluoroheptamide were prepared from ammonia and the corresponding acid chloride which were purchased from Daikin Chemicals Sales.

5.3. The general procedure for amide dehydration

Method A (Tables 1–3). A solution of dimethyl sulfoxide in dry CH_2Cl_2 was added to a stirred solution of oxalyl chloride in dry CH_2Cl_2 at −78°C. After 15 min, a CH_2Cl_2 solution of amide was added to the reaction mixture. Stirring was continued for 20 min at −78°C, and then Et_3N was added. After 30 min at −78°C, the reaction mixture was warmed to room temperature and then reaction was quenched with sat. aqueous NH_4Cl solution. The reaction mixture was diluted with CH_2Cl_2, and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and evaporated in vacuo. Purification of the residue was accomplished by silica gel column chromatography (hexane/EtOAc). Concentration of the appropriate fraction in vacuo gave the indicated yield of products. *Method B* (Tables 4–6). A $(COCl)_2$ and Et_3N were successively added to a solution of and amide in CH_2Cl_2 at −78°C at intervals of 10 min. After 15 min at −78°C, the mixture was quenched by adding sat. aqueous NH_4Cl. The mixture was warmed to room temperature over 10 min, and partitioned between EtOAc and water. The aqueous layer was extracted three times with EtOAc, and the combined organic phases were washed with brine, dried (Na_2SO_4), filtered and concentrated in vacuo. Purification of the residue was accomplished by silica gel column chromatography (hexane/EtOAc). Concentration of the appropriate fraction in vacuo gave the indicated yield of products.

5.3.1. 3-Phenylpropionitrile (2b). Dehydration according to the general procedure using **2a** (85 mg, 0.57 mmol), DMSO (64 μL, 0.91 mmol), $(COCl)_2$ (59 μL, 0.68 mmol) and Et_3N (237 μL, 1.7 mmol) in CH_2Cl_2 (2 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 6/1) to give 68 mg (92%) of **2b** as a colorless oil. The synthetic **2b** was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample.

5.3.2. 4-Methoxybenzonitrile (3b) and *S*,*S*-dimethyl-*N*-4-methoxybenzoylimino-sulfurane (3c). Dehydration according to the general procedure using **3a** (151 mg, 1 mmol), DMSO (213 μL, 3.0 mmol), $(COCl)_2$ (130 μL, 1.5 mmol) and Et_3N (825 μL, 6 mmol) in CH_2Cl_2 (4 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 4/1) to give 46 mg (35%) of **3b**. The *S*,*S*-dimethy-*N*-4-methoxylbenzoyliminosulfurane (**3c**, 112 mg, 53%) was also obtained by continued elution ($CHCl_3$/MeOH, 30/1) and following recrystallization from hexane/EtOAc as colorless plates. The synthetic **3b** (mp 58.5–59.5°C) was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample. Data for **3c**: mp 105.0–106.0°C; ^1H NMR ($CDCl_3$) 8.00 (2H, d, J=8.5 Hz, HC(Ar)), 6.83 (2H, d, J=8.5 Hz, HC(Ar)), 3.79 (3H, s), 2.71 (6H, s); ^{13}C NMR ($CDCl_3$) 176.7, 161.7, 130.2, 128.9, 113.0, 55.2, 32.0; IR (KBr, cm^{-1}) 3010 (w), 1608 (s), 1590 (s), 1417 (s), 1340 (s), 1320 (s), 1306 (s), 1258 (s), 1169 (s), 1028 (s), 982 (s), 849 (s), 808 (m), 774 (s); FAB-MS 240 ($[M+Na]^+$, 10), 213 (14), 212 (MH^+, 100), 176 (25); FAB-HRMS calcd for $C_{10}H_{14}NO_2S$ (MH^+), 212.0745; found, 212.0750. 4-Methoxybenzonitrile (**3b**) was also obtained as colorless needles using **3a** (76.5 mg, 0.5 mmol), DMSO (257 μL, 3.62 mmol), $(COCl)_2$ (53 μL, 0.6 mmol) and Et_3N (420 μL, 3.0 mmol) in 93% yield.

5.3.3. 4-Nitrobenzonitrile (4b) and *S*,*S*-dimethyl-*N*-4-nitrobenzoyliminosulfurane (4c). Dehydration according to the general procedure using **4a** (166 mg, 1.0 mmol), DMSO (114 μL, 1.6 mmol), $(COCl)_2$ (105 μL, 1.2 mmol) and Et_3N (335 μL, 2.4 mmol) in CH_2Cl_2 (4 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 50 mg (34%) of **4b**. The *S*,*S*-dimethyl-*N*-4-nitrobenzoyliminosulfurane (**4c**, 92.8 mg, 41%) was also obtained by continued elution ($CHCl_3$/MeOH, 10/1) and following recrystallization from MeOH as pale yellow plates. The synthetic **4b** (mp 147.5–149°C) was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample. Data for **4c**: mp 219.5–222.0°C; ^1H NMR (CD_3OD) 8.32–8.05 (4H, m, HC(Ar)), 2.85 (6H, s, Me); ^{13}C NMR (CD_3OD) 176.0, 150.8, 143.5, 130.6, 124.1, 31.7; IR (KBr, cm^{-1}) 3018 (w), 3003 (w), 1560 (s), 1518 (s), 1433 (s), 1404 (s), 1358 (s), 1100 (s), 999 (s), 957 (s), 918 (s), 876 (s), 845 (s), 806 (s), 772 (s); FABMS 227 ($[M+H]^+$, 95), 176 (100); FAB-HRMS calcd for $C_9H_{11}O_3N_2S$ (MH^+), 227.0490; found, 227.0508. 4-Nitrobenzonitrile (**4b**) was also obtained as colorless needles using **4a** (166 mg, 1.0 mmol), DMSO (710 μL, 10.0 mmol), $(COCl)_2$ (105 μL, 1.2 mmol) and Et_3N (335 μL, 2.4 mmol) in 98% yield.

5.3.4. 1-Cyanonaphthalene (5b). Dehydration according to the general procedure using **5a** (340 mg, 2.0 mmol), DMSO (1.4 mL, 20 mmol), $(COCl)_2$ (208 μL, 2.4 mmol) and Et_3N (830 μL, 6.0 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 252 mg (83%) of **5b** as colorless prisms. The synthetic **5b** (mp 66.5–67.5°C) was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample.

5.3.5. 2,6-Dichlorobenzonitrile (6b). Dehydration according to the general procedure using **6a** (280 mg, 2.0 mmol), DMSO (1.4 mL, 20 mmol), $(COCl)_2$ (209 μL, 2.4 mmol) and Et_3N (836 μL, 6.0 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 10/1) to give 297 mg (87%) of **6b** as colorless prisms. The synthetic **6b** (mp 145–146°C) was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample.

5.3.6. 3,5-Dinitrobenzonitrile (7b). Dehydration according to the general procedure using **2a** (106 mg, 0.5 mmol), DMSO (355 μL, 5.0 mmol), $(COCl)_2$ (131 μL, 1.5 mmol) and Et_3N (630 μL, 4.5 mmol) in CH_2Cl_2 (2 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 5/1) to give 90 mg (93%) of **7b** as colorless prisms. The synthetic **7b** was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample.

5.3.7. 3-Cyanopyridine (8b). Dehydration according to the general procedure using **8a** (241 mg, 1.97 mmol), DMSO (0.5 mL, 7.0 mmol), $(COCl)_2$ (210 μL, 2.4 mmol) and Et_3N (0.83 mL, 6.0 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 1/1) to give 131 mg (64%) of **8b** as colorless prisms. The synthetic **8b** (mp 49.0–49.5°C) was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample.

5.3.8. Cinnamonitrile (9b). Dehydration according to the general procedure using **9a** (289 mg, 2.0 mmol), DMSO (852 μL, 12.0 mmol), $(COCl)_2$ (209 μL, 2.4 mmol) and Et_3N (670 μL, 4.8 mmol) in CH_2Cl_2 (5 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 6/1) to give 202 mg (80%) of **9b** as a colorless oil. The synthetic **9b** (bp 85–90°C/0.4 mmHg) was spectroscopically (^1H NMR, ^{13}C NMR, IR, MS) identical with authentic sample.

5.3.9. ((5*S*,4*R*)-5-Cyano-2,2-dimethyl-1,3-dioxolan-4-yl)-methyl 4-oxobutanoate (11). Dehydration according to the general procedure using **10** (26 mg, 0.1 mmol), DMSO (43 μL, 0.6 mmol), $(COCl)_2$ (26 μL, 0.3 mmol) and Et_3N (125 μL, 0.9 mmol) in CH_2Cl_2 (2 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 1/1) to give 22 mg (91%) of **11** as a colorless oil: ^1H NMR ($CDCl_3$) 9.80 (1H, s), 4.84–4.82 (1H, m), 4.48–4.40 (1H, m,), 4.37–4.31 (2H, m), 2.78 (2H, t, *J*=6.6 Hz), 2.60 (2H, t, *J*=6.6 Hz), 1.51 (3H, s), 1.33 (3H, s); ^{13}C NMR ($CDCl_3$) 199.7, 171.7, 115.8, 113.0, 74.6, 66.5, 62.5, 38.4, 26.9, 26.2, 25.7; IR (KBr, cm^{-1}) 2994 (m), 2940 (w), 2847 (w), 2737 (w), 1744 (s), 1414 (m), 1387 (s), 1377 (s), 1229 (s), 1163 (s), 1163 (s), 1073 (s), 1038 (m), 862 (m), 776 (w); FAB-MS 264 ($[M+Na]^+$, 60), 243 (16), 242 (MH^+, 100), 184 (77), 85 (97); FAB-HRMS calcd for $C_{11}H_{16}O_5N$ (MH^+), 242.1028; found, 242.1009.

5.3.10. ((4*R*,5*R*)-5-Carbamoyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl 4-oxo-butanoate (12). Dehydration according to the general procedure using **10** (52 mg, 0.2 mmol), DMSO (28.5 μL, 0.4 mmol), $(COCl)_2$ (18 μL, 0.2 mmol) and Et_3N (84 μL, 0.6 mmol) in CH_2Cl_2 (2 mL) afforded a colorless oil. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc, 1/3) to give 39 mg (75%) of **12** as colorless solids from the first fraction. The starting material (**10**, 6.3 mg, 12%) was recovered from the second fraction as colorless solids. Data for **12**: mp 89.0–90.0°C; ^1H NMR ($CDCl_3$) 9.78 (1H, s), 6.51 (1H, br s), 5.69 (1H, br s), 4.59 (1H, ddd, *J*=2.9, 5.6, 7.9 Hz), 4.69 (1H, d, *J*=7.9 Hz), 4.43 (1H, dd, *J*=2.9, 12.4 Hz), 4.10 (1H, dd, *J*=5.6, 12.4 Hz), 2.78 (2H, t, *J*=6.6 Hz), 2.63 (2H, t, *J*=6.6 Hz), 1.55 (3H, s), 1.37 (3H, s); ^{13}C NMR ($CDCl_3$) 199.9, 171.8, 171.1, 110.4, 75.5, 75.0, 63.0, 38.4, 27.0, 26.3, 24.6; IR (KBr, cm^{-1}) 3401 (s), 3310 (s), 2995 (w), 2975 (w), 2930 (w), 1740 (s), 1692 (s), 1663 (s), 1377 (s), 1217 (s), 1171 (s), 1107 (s), 1059 (s), 984 (m), 851 (s); FAB-MS 261 (8), 260 (MH^+, 60), 158 (100), 118 (23), 85 (39); FAB-HRMS calcd for $C_{11}H_{18}O_6N$ (MH^+), 260.1134; found, 260.1142.

5.3.11. 2-Cyanoethylcarboxamido-(3*R*)-3,3-dimethyl-1,3-*O*-isopropylideneoxy-butanoic acid (14b). Dehydration according to the general procedure using **14a** (142.0 mg, 0.55 mmol), DMSO (78 μL, 1.1 mmol), $(COCl)_2$ (67 μL, 0.77 mmol) and Et_3N (0.23 mL, 1.65 mmol) in CH_2Cl_2 (2 mL)) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 2/1) and Kugelrohr distillation to give 123 mg (93%) of **14b** as a colorless oil: bp 185–190°C/0.2 mmHg; $[\alpha]_D^{22}$=44.9 (*c*=1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 7.00 (1H, br d, NH), 4.13 (1H, s, HC(5)), 3.71 (1H, d, *J*=11.7 Hz, HC(7)), 3.65–3.56 (1H, m, HC(3)), 3.56–3.46 (1H, m, HC(3)), 3.32 (1H, d, *J*=11.7 Hz, HC(7)), 2.72–2.60 (2H, m, HC(2)), 1.50 (3H, s, Me), 1.46 (3H, s, Me), 1.06 (3H, s, Me), 1.03 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 170.4, 117.9 (CN), 99.1, 77.0, 71.2, 34.9, 32.9, 29.3, 21.9, 18.8, 18.6, 18.1; IR (neat, cm^{-1}) 3378 (m, NH), 2994 (m), 2957 (m), 2251 (w), 1673 (s), 1526 (s), 1379 (s), 1260 (s), 1223 (m), 1198 (s), 1161 (m), 1100 (s), 1049 (m); EI-MS (70 eV) 241 (0.6), 240 (M^+, 2), 225 (23), 165 (19), 143 (71), 85 (47), 83 (28), 59 (100); Anal. calcd for $C_{12}H_{20}N_2O_3$: C, 59.98; H, 8.39; N, 11.66. Found: C, 60.13; H, 8.45; N, 11.46.

5.3.12. (±)-*N*-*t*-Butoxycarbonylpiperidine 3-carbonitrile (15b). Dehydration according to the general procedure using **15a** (456 mg, 2.0 mmol), DMSO (227 μL, 3.2 mmol), $(COCl)_2$ (210 μL, 2.4 mmol) and Et_3N (0.84 mL, 6.0 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 376 mg (89%) of **15b** as a colorless solid: mp 68.0–69.0°C; ^1H NMR ($CDCl_3$) 4.00–3.20 (4H, m, $H_2C(2)$, $H_2C(6)$), 2.70–2.64 (1H, m, HC(3)), 2.05–1.54 (4H, m, $H_2C(4)$, $H_2C(5)$), 1.52 (9H, s, *t*-Bu); ^{13}C NMR ($CDCl_3$) 154.1, 120.0 (CN), 80.4, 46.1, 43.8, 28.2, 27.8, 27.3, 23.0; IR (KBr, cm^{-1}) 2926 (m), 2242 (m), 1688 (s), 1418 (s), 1373 (s), 1134 (s), 1011 (m), 918 (m), 880 (s), 860 (m), 772 (m); EI-MS (70 eV) 210 (M^+, 3.6), 155 (35), 138 (49), 110 (30), 91 (33), 83 (18.5), 57 (100); Anal. calcd for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; N, 13.32. Found: C, 62.44; H, 8.69; N, 13.12.

5.3.13. (*R*)-2-*N*-*t*-Butoxycarbonylamino-2-phenylethanenitrile (16b). Dehydration according to the general procedure using **16a** (331 mg, 1.32 mmol), DMSO (161 μL, 2.27 mmol), $(COCl)_2$ (149 μL, 1.7 mmol) and Et_3N (0.59 mL, 4.3 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 248 mg (81%) of **16b** as a colorless solid: mp 118.5–119.0°C (colorless prisms crystallized from hexane/EtOAc); $[\alpha]_D^{22}$=−1.9 (*c*=1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) 7.48–7.40 (5H, m, HC(Ar)), 5.78 (1H, br s, NH), 5.29 (1H, br s, HC(2)), 1.48 (9H, s, *t*-Bu); ^{13}C NMR ($CDCl_3$) 154.2, 133.5, 129.4, 129.2 126.8, 117.7, 81.5, 46.0, 28.2; IR (KBr, cm^{-1}) 3335 (s), 2980 (s), 2907 (m), 2244 (w), 1693 (s), 1512 (s), 1372 (s), 1165 (s), 1057 (s), 1028 (m), 880 (s), 696 (s); EI-MS (70 eV) 232 (M^+, 0.2), 217 (2), 176 (100), 158 (23), 150 (36), 132 (4), 116 (32), 104 (19), 89 (8), 77 (7), 59 (38), 57 (76); Anal. calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 66.97; H, 6.92; N, 12.03.

5.3.14. (*R*)-2-*N*-Benzyloxycarbonylamino-3-methylbutanenitrile (17b). Dehydration according to the general procedure using **17a** (227 mg, 0.91 mmol), DMSO (114 μL, 3.2 mmol), $(COCl)_2$ (210 μL, 2.4 mmol) and Et_3N

(0.84 mL, 3.0 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 140 mg (67%) of **17b** as a colorless solid. The starting amide (**17a**, 36 mg, 16%) was recovered from the continuing elution (EtOAc) as colorless solids. Data for **17b**: mp 52.0–53.0°C; $[\alpha]_D^{22}$=56.0 (c=1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.40–7.26 (5H, m, HC(Ar)), 5.70–5.40 (1H, br s, NH), 5.07 (2H, s, CH_2Ph), 4.50–4.46 (1H, m, HC(2)), 2.03–1.97 (1H, m, HC(3)), 1.05 (3H, d, J=6.8 Hz, HC(4)), 1.03 (3H, d, J=6.8 Hz, HC(4)); ^{13}C NMR ($CDCl_3$) 155.4, 135.6, 128.5, 128.3, 128.1, 117.7, 67.5, 48.9, 31.6, 18.4, 17.8; IR (KBr, cm^{-1}) 3297 (s), 3065 (s), 3033 (s), 2878 (s), 2243 (w), 1694 (s), 1397 (s), 1258 (s), 988 (s), 963 (s), 779 (m), 752 (s), 725 (s); EI-MS (70 eV) 232 (M^+, 56), 117 (20), 108 (95), 107 (53), 91 (100), 79 (28); Anal. calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.20; H, 6.97; N, 11.81.

5.3.15. (2*S*)-3-(4-Toluenesulfonyloxy)-2-methylpropanenitrile (18b). Dehydration according to the general procedure using **18a** (84.8 mg, 0.33 mmol), DMSO (47 μL, 0.66 mmol), $(COCl)_2$ (40 μL, 0.46 mmol) and Et_3N (0.14 mL, 1.0 mmol) in CH_2Cl_2 (1 mL) at −78°C afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 2/1) to give 76.6 mg (96%) of **18b** as a colorless oil: $[\alpha]_D^{22}$=−16.9 (c=1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.84 (2H, d, J=7.8 Hz, HC(Ar)), 7.42 (2H, d, J=7.8 Hz, HC(Ar)), 4.10 (2H, d, J=6.8 Hz, H_2C(3)), 3.04 (1H, sextet, J=6.8 Hz, HC(2)), 2.50 (3H, s, Me), 1.37 (3H, d, J=6.8 Hz, Me); ^{13}C NMR ($CDCl_3$) 145.5, 131.9, 130.0, 127.9, 119.1, 68.7, 25.8, 21.6, 14.2; IR (neat, cm^{-1}) 2994 (w), 2249 (m), 1364 (s), 1192 (s), 1179 (s), 1098 (s); EI-MS (70 eV) 240 (7), 239 (M^+, 48), 172 (26), 158 (99), 138 (8), 107 (5), 91 (100), 65 (21); EI-HRMS calcd for $C_{11}H_{13}NO_3S$ (M^+), 239.0616; found, 239.0611.

5.3.16. Benzyl 5-*O*-benzyl-1-cyano-1-dehydro-2,3-*O*-isopropylidene-β-D-ribofuranoside (20b). Dehydration according to the general procedure using **20a** (411.0 mg, 0.99 mmol), DMSO (107 μL, 1.5 mmol), $(COCl)_2$ (105 μL, 1.2 mmol) and Et_3N (0.42 mL, 3.0 mmol) in CH_2Cl_2 (6 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 8/1) to give 374 mg (95%) of **20b** as a colorless oil: bp 260–265°C/0.4 mmHg; $[\alpha]_D^{22.6}$=−69.2 (c=1.14, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.40–7.20 (10H, m, HC(Ar)), 4.77 (1H, d, J=11.2 Hz, HC(Bn)), 4.76–4.74 (2H, m, HC(3), HC(4)), 4.71 (1H, d, J=11.2 Hz, HC(Bn)), 4.58 (1H, dd, J=6.8, 6.3 Hz, HC(5)), 4.48 (1H, d, J=12.4 Hz, HC(Bn)), 4.45 (1H, d, J=12.4 Hz, HC(Bn)), 3.50 (1H, dd, J=9.8, 6.3 Hz, HC(6)), 3.42 (1H, dd, J=9.8, 6.3 Hz, HC(6)), 1.59 (3H, s, Me), 1.35 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 137.3, 135.6, 128.44, 128.39, 128.2, 127.8, 127.6, 114.3, 113.4, 105.2, 87.2, 86.4, 81.8, 73.3, 69.8, 67.9, 26.3, 25.1; IR (neat, cm^{-1}) 2292 (w), 2361 (w), 1455 (m), 1385 (m), 1244 (m), 1215 (m), 1159 (m), 1092 (s), 1042 (s), 868 (m), 739 (m), 698 (m); EI-MS (70 eV) 395 (M^+, 0.2), 380 (M^+−15, 17), 304 (33), 289 (56), 272 (11), 231 (41), 220 (2), 198 (26), 180 (5.0), 165 (7), 107 (48), 91 (100); Anal. calcd for $C_{23}H_{25}NO_5$: C, 69.86; H, 6.37; N, 3.54. Found: C, 69.84; H, 6.49; N, 3.50.

5.3.17. Benzyl 5-*O*-benzyl-1-cyano-1-dehydro-2,3-*O*-diacetyl-β-D-ribofuranoside (21b). Dehydration according to the general procedure using **21a** (229 mg, 0.50 mmol), DMSO (57 μL, 0.8 mmol), $(COCl)_2$ (52 μL, 0.6 mmol) and Et_3N (0.21 mL, 1.5 mmol) in CH_2Cl_2 (6 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 206 mg (94%) of **21b** as a colorless oil: $[\alpha]_D^{22.5}$=−10.6 (c=0.99, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.34–7.30 (8H, m, HC(Ar)), 7.30–7.24 (2H, m, HC(Ar)), 5.56 (1H, d, J=4.4 Hz, HC(3)), 5.51 (1H, dd, J=6.2, 4.4 Hz, HC(4)), 4.84 (1H, d, J=10.7 Hz, HC(Bn)), 4.74 (1H, d, J=10.7 Hz, HC(Bn)), 4.57 (1H, d, J=12.0 Hz, HC(Bn)), 4.53 (1H, d, J=12.0 Hz, HC(Bn)), 4.48 (1H, ddd, J=3.2, 4.1, 6.2 Hz, HC(5)), 3.67 (1H, dd, J=3.2, 11.0 Hz, HC(6)), 3.54 (1H, dd, J=4.1, 10.9 Hz, HC(6)), 2.19 (3H, s, Me), 2.06 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 169.5, 168.8, 137.4, 135.5, 128.5, 128.4, 128.3, 128.2, 127.9, 127.7, 113.6 (CN), 101.4, 82.3, 75.8, 73.5, 70.3, 68.8, 68.3, 20.5, 20.4; IR (neat, cm^{-1}) 3034 (s), 2938 (m), 2869 (s), 2244 (w), 1499 (s), 1456 (s), 1374 (s), 1237 (s), 912 (s), 739 (s), 698 (m); EI-MS (70 eV) 440 (0.3), 439 (M^+, 0.1), 413 (0.7), 348 (14), 242 (23), 213 (11), 107 (19), 91 (100); EI-HRMS calcd for $C_{24}H_{25}NO_7$ (M^+), 439.1631; found, 439.1612.

5.3.18. (2*R*,3*S*)-Phenyloxirane-2-carbonitrile (22b). Dehydration according to the general procedure using **22a** (120.0 mg, 0.74 mmol), DMSO (105 μL, 1.5 mmol), $(COCl)_2$ (96.2 μL, 1.1 mmol) and Et_3N (0.31 mL, 2.2 mmol) in CH_2Cl_2 (3 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 6/1) to give 93.2 mg (87%) of **22b** as a pale yellow solid: mp 28.5–29.5°C; $[\alpha]_D^{22}$=−214.5 (c=1.1, benzene); ^{1}H NMR (benzene-d_6) 7.03–6.96 (3H, m, HC(Ar)), 6.68–6.66 (2H, m, HC(Ar)), 3.49 (1H, d, J=1.5 Hz, HC(2)), 2.25 (1H, d, J=1.5 Hz, HC(3)); ^{13}C NMR (benzene-d_6) 133.3, 129.4, 128.6, 125.8, 116.3 (CN), 58.0, 44.2; IR (KBr, cm^{-1}) 3029 (w), 2245 (w), 1495 (m), 1456 (s), 1312 (m), 1287 (m), 1080 (m), 1059 (m), 887 (s), 795 (m), 754 (s), 700 (s), 625 (s); EI-MS (70 eV) 145 (M^+, 42.5), 117 (76), 105 (21), 90 (100), 77 (26), 69 (20), 60 (21), 57 (51); EI-HRMS calcd for C_9H_7NO (M^+), 145.0528; found, 145.0515.

5.3.19. (+)-1,2-Di-*t*-butyldiphenylsilyloxyethane-1,2-dicarbonitrile (23b). Dehydration according to the general procedure using **23a** (206 mg, 0.33 mmol), DMSO (94 μL, 1.32 mmol), $(COCl)_2$ (72 μL, 0.83 mmol) and Et_3N (0.28 mL, 2.0 mmol) in CH_2Cl_2 (2 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 4/1) to give 156.0 mg (80%) of **23b** as a colorless oil: bp 250–255°C/0.1 mmHg; $[\alpha]_D^{20}$=29.0 (c=0.83, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.67–7.65 (4H, m, HC(Ar)), 7.58–7.46 (12H, m, HC(Ar)), 7.38–7.32 (4H, m, HC(Ar)), 4.29 (2H, s), 1.10 (18H, s, Me); ^{13}C NMR ($CDCl_3$) 145.5, 131.9, 130.0, 127.9, 119.1 (CN), 68.7, 25.8, 21.6, 14.2; IR (neat, cm^{-1}) 3034 (m), 2870 (m), 2245 (w), 1499 (m), 1456 (s), 1385 (m), 1275 (m), 1244 (m), 1215 (s), 1179 (m), 1159 (m); EI-MS (70 eV) 588 (M^+, 0.2), 531 (M^+−57, 36), 428 (100), 259 (14), 239 (17), 197 (34), 135 (69); Anal. calcd for $C_{36}H_{40}N_2O_2Si_2$: C, 73.42; H, 6.85; N, 4.76. Found: C, 73.28; H, 6.87; N, 4.73.

5.3.20. (2*R*,3*S*) 3-Cyano-2,3-dibenzoyloxy-*N*,*N*-dimethylpropionamide (24b). Dehydration according to the general procedure using **24a** (192 mg, 0.5 mmol), DMSO (71 μL,

1.0 mmol), $(COCl)_2$ (65 μL, 0.75 mmol) and Et_3N (0.31 mL, 1.5 mmol) in CH_2Cl_2 (2 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 4/1) to give 172 mg (94%) of **24b** as a colorless oil: $[\alpha]_D^{20}$=66.4 (c=1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.67–7.65 (2H, m, HC(Ar)), 7.58–7.46 (6H, m, HC(Ar)), 7.38–7.32 (2H, m, HC(Ar)), 6.32 (1H, d, J=7.8 Hz, HC(2)), 6.26 (1H, d, J=7.8 Hz, HC(3)), 3.22 (3H, s, Me), 3.09 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 165.2, 164.6, 164.5, 134.5, 134.4, 130.3, 128.9, 129.0, 127.8, 114.5 (CN), 68.2, 61.3, 37.4, 36.4; IR (neat, cm^{-1}) 2944 (w), 2253 (w), 1732 (s), 1663 (s), 1601 (s), 1586 (m), 1493 (m), 1453 (s), 1420 (m), 1406 (s), 1318 (s), 1267 (s), 1244 (s), 1179 (s), 1161 (m), 1069 (m), 1028 (s), 912 (m), 710 (s); EI-MS (70 eV) 367 (3), 366 (M^+, 7.7), 322 (15), 245 (51), 244 (100), 216 (22), 106 (84), 105 (100), 77 (100), 72 (100); EI-HRMS calcd for $C_{20}H_{18}N_2O_5$ (M^+), 366.1216; found, 366.1190.

5.3.21. Ethyl (±)-(2,3)-*syn*-2,3-diacetoxy-3-cyano-propionate (25b). Dehydration according to the general procedure using **25a** (57 mg, 0.22 mmol), DMSO (46 μL, 0.65 mmol), $(COCl)_2$ (29 μL, 0.33 mmol) and Et_3N (0.14 mL, 1.0 mmol) in CH_2Cl_2 (1 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 2/1) to give 48 mg (91%) of **25b** as a colorless oil: ^{1}H NMR ($CDCl_3$) 5.93 (1H, d, J=3.2 Hz, HC(2)), 5.52 (1H, d, J=3.2 Hz, HC(3)), 4.29 (2H, q, J=6.8 Hz, H_2C), 2.29 (3H, s, Me), 2.20 (3H, s, Me), 1.31 (3H, t, J=6.8 Hz, Me); ^{13}C NMR ($CDCl_3$) 169.5, 168.6, 164.6, 113.6 (CN), 70.2, 63.1, 60.4, 20.5, 20.2, 14.2; IR (neat, cm^{-1}) 2986 (m), 2946 (m), 2361 (m), 1771 (s), 1767 (s), 1761 (s), 1472 (w), 1375 (s), 1281 (m), 1204 (s), 1123 (m), 1060 (s), 1024 (m), 965 (m), 930 (w), 856 (w), 720 (w); FAB-MS 266 ([M+Na]$^+$, 48), 246 (13), 245 (13), 244 (M^+, 100), 184 (31); FAB-HRMS calcd for $C_{10}H_{14}NO_6$ (M^+), 244.0821; found, 244.0813.

5.3.22. (*R*)-2-Acetoxyphenylacetonitrile (26b). Dehydration according to the general procedure using **26a** (96 mg, 0.5 mmol), DMSO (71 μL, 1.0 mmol), $(COCl)_2$ (65 μL, 0.75 mmol) and Et_3N (209 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) at −78°C afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 4/1) to give 79 mg (90%) of **26b** as a colorless solid: bp 95–100°C/1.5 mmHg; $[\alpha]_D^{22}$=8.4 (c=9.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.59–7.32 (5H, m, HC(Ar)), 6.47 (1H, s, HC(2)), 2.22 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 168.9, 131.7, 130.4, 129.2, 127.8, 116.1, 62.8, 20.4; IR (neat, cm^{-1}) 2350 (w), 1755 (s), 1497 (w), 1458 (w), 1374 (m), 1215 (s), 1024 (m); EI-MS (70 eV) 176 (5), 175 (M^+, 26), 133 (100), 116 (71), 115 (95), 105 (37), 89 (25); EI-HRMS calcd for $C_{10}H_9NO_2$ (M^+), 175.0633; found, 175.0620.

5.3.23. (*R*)-2-Acetoxy-4-phenylbutyronitrile (27b). Dehydration according to the general procedure using **27a** (120.0 mg, 0.54 mmol), DMSO (77 μL, 1.1 mmol), $(COCl)_2$ (71 μL, 0.81 mmol) and Et_3N (227 μL, 1.62 mmol) in CH_2Cl_2 (3 mL) at −78°C afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 6/1) to give 93.2 mg (91%) of **27b** as a colorless solid: $[\alpha]_D^{20}$=43.4 (c=4.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.34–7.30 (2H, m, HC(Ar)), 7.24–7.22 (1H, m, HC(Ar)), 7.19–7.17 (2H, m, HC(Ar)), 5.27 (1H, t, J=6.8 Hz, HC(2)), 2.83 (2H, t, J=7.8 Hz, H_2C(4)), 2.24 (2H, dt, J=6.8, 7.8 Hz, H_2C(3)), 2.13 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 169.0, 139.0, 128.7, 128.3, 126.6, 116.7 (CN), 60.4, 33.7, 30.6, 20.3; IR (neat, cm^{-1}) 3030 (w), 2936 (w), 1755 (s), 1605 (w), 1497 (w), 1456 (w), 1374 (m), 1221 (s), 1042 (m), 749 (w), 700 (m); EI-MS (70 eV) 204 (0.6), 203 (M^+, 4), 162 (1), 160 (1), 143 (100), 116 (22), 91 (25); EI-HRMS calcd for $C_{12}H_{13}NO_2$ (M^+), 203.0946; found, 203.0939.

5.3.24. (*R*)-2-Trimethylsilyloxy-4-phenylbutyronitrile (28b). Dehydration according to the general procedure using **28a** (112 mg, 0.44 mmol), DMSO (76 μL, 1.1 mmol), $(COCl)_2$ (62 μL, 0.71 mmol) and Et_3N (186 μL, 1.34 mmol) in CH_2Cl_2 (5 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 5/1) to give 86.4 mg (83%) of **28b** as a colorless oil: $[\alpha]_D^{27}$=26.7 (c=4.0, CCl_4); ^{1}H NMR (benzene-d_6) 7.16–7.06 (3H, m, HC(Ar)), 6.97–6.95 (2H, m, HC(Ar)), 3.95 (1H, dd, J=5.8, 7.1 Hz, HC(2)), 2.64–2.51 (2H, m, H_2C(4)), 1.91–1.74 (2H, m, H_2C(3)), 0.07 (9H, s, Me); ^{13}C NMR ($CDCl_3$) 140.2, 128.7, 126.5, 119.9 (CN), 60.7, 37.7, 30.8, −0.6; IR (neat, cm^{-1}) 2592 (w), 1256 (s), 1150 (s), 968 (w), 847 (s), 749 (m), 700 (m); EI-MS (70 eV) 234 (4), 233 (M^+, 19), 218 (41), 167 (13), 149 (42), 143 (100), 91 (82); EI-HRMS calcd for $C_{13}H_{19}NOSi$ (M^+), 233.1236; found, 233.1236.

5.4. General procedure for perfluoroimidates

In a flame-dried 300 mL 3-necked round-bottom flask equipped with a stirring bar, a thermometer, a septum and a nitrogen inlet were introduced perfluoroamide (3.3 mmol), DMSO (15 mmol) and CH_2Cl_2 (10 mL). This solution was cooled down to −75°C (internal) and $(COCl)_2$ (3.0 mmol) and Et_3N (10 mmol) were slowly added at intervals of 10 min. No rise in temperature was observed during this process. After stirring for 30 min at −78°C, DBU (2.0 mmol) and alcohol (1 mmol) in CH_2Cl_2 (2 mL) were added slowly via syringe. The reaction mixture was stirred for 15 min at −78°C, the mixture was allowed to reach room temperature over 10 h. The reaction mixture was quenched by addition of water; the aqueous layer was extracted with EtOAc. The combined organic phases were washed with brine, dried (Na_2SO_4), and then filtered. Concentration and following purification by silica gel column chromatography and Kugelrohr distillation afforded the indicated yield of products.

5.4.1. Benzyl 2,2,2-trifluoroacetimidate (40A). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 2,2,2-trifluoroacetamide (373 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 177 mg (87%) of the 2,2,2-trifluoroacetimidate as a colorless oil: R_f 0.45 (hexane/EtOAc, 10/1); bp 20°C/0.9 mmHg; ^{1}H NMR ($CDCl_3$) 8.35 (1H, s, NH), 7.42 (5H, m, HC(Ar)), 5.33 (2H, s); ^{13}C NMR ($CDCl_3$) 157.8 (q, J=38.0 Hz, C(1)), 134.9, 128.5, 128.4, 128.0, 115.6 (q, J=280.0 Hz, C(2)),

69.12; ^{19}F NMR ($CDCl_3$) −74.7; IR (neat, cm^{-1}) 3347 (w), 3071 (w), 3038 (w), 2957 (w), 1686 (s), 1501 (w), 1456 (w), 1420 (w), 1356 (m), 1200 (s), 1167 (s), 1078 (m), 1030 (w), 957 (w), 911 (w), 847 (m), 737 (m), 714 (m), 696 (m), 606 (w); EI-MS (70 eV) 204 (9), 203 (M^+, 68), 202 (6), 180 (16), 161 (15), 149 (26), 134 (70), 108 (84), 107 (73), 92 (80), 91 (100); EI-HRMS calcd for $C_9H_8F_3NO$ (M^+), 203.0558; found, 203.0533.

5.4.2. Benzyl 2,2,3,3,3-pentafluoropropionimidate (40B). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 2,2,3,3,3-pentafluoropropionamide (538 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 198 mg (78%) of the 2,2,3,3,3-pentafluoropropionimidate as a colorless oil: R_f 0.45 (hexane/EtOAc, 10/1); bp 30°C/1.0 mmHg; ^{1}H NMR ($CDCl_3$) 8.56 (1H, s, NH), 7.41 (5H, m, HC(Ar)), 5.37 (2H, s); ^{13}C NMR ($CDCl_3$) 158.0 (t, J=28.9 Hz, C(1)), 134.9, 128.5, 128.4, 127.8, 117.9 (tq, J=35.5, 286.6 Hz, C(3)), 106.3 (qt, J=43.1, 257.3 Hz, C(2)), 69.3; ^{19}F NMR ($CDCl_3$) −83.1, −120.5; IR (neat, cm^{-1}) 3355 (w), 3071 (w), 3038 (w), 2959 (w), 1682 (w), 1501 (w), 1456 (m), 1399 (m), 1354 (m), 1325 (s), 1221 (s), 1175 (s), 1086 (s), 1036 (s), 955 (w), 909 (w), 843 (m), 745 (s), 696 (m); EI-MS (70 eV) 253 (M^+, 20), 252 (7), 251 (8), 243 (11), 239 (10), 235 (7), 191 (12), 188 (23), 167 (14), 149 (78), 146 (12), 135 (15), 134 (13), 128 (26), 119 (26), 107 (43), 92 (30), 91 (100); EI-HRMS calcd for $C_{10}H_2F_5NO$ (M^+), 253.0526; found, 253.0508.

5.4.3. Benzyl 2-chloro-2,2-difluoroacetimidate (40C). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 2-chloro-2,2-difluoroacetamide (427 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 178 mg (81%) of the 2-chloro-2,2-difluoroacetimidate as a colorless oil: R_f 0.42 (hexane/EtOAc, 10/1); bp 60°C/1.2 mmHg; ^{1}H NMR ($CDCl_3$) 8.23 (1H, s, NH), 7.47–7.37 (5H, m, HC(Ar)), 5.36 (2H, s); ^{13}C NMR ($CDCl_3$) 159.8 (t, J=32.6 Hz, C(1)), 135.0, 128.5, 128.4, 127.9, 117.8 (t, J=293.2 Hz, C(2)), 69.4; ^{19}F NMR ($CDCl_3$) −61.8; IR (neat, cm^{-1}) 3349 (m), 3094 (w), 3036 (w), 1678 (s), 1499 (m), 1456 (m), 1401 (m), 1343 (s), 1211 (m), 1163 (s), 1080 (s), 980 (s), 909 (m), 839 (s), 779 (m), 737 (m), 696 (s), 617 (m); EI-MS (70 eV) 221 (6), 220 (3), 219 (M^+, 18), 180 (5), 134 (25), 108 (27), 107 (30), 91 (100); EI-HRMS calcd for $C_9H_8ClF_2NO$ (M^+), 219.0262; found, 219.0257.

5.4.4. Benzyl 2,2,3,3,4,4,4-heptafluorobutyrimidate (40D). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 2,2,3,3,4,4,4-heptafluorobutyramide (704 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 234 mg (77%) of the 2,2,3,3,4,4,4-heptafluorobutyrimidate as a colorless oil: R_f 0.45 (hexane/EtOAc, 10/1); bp 20°C/1.0 mmHg; ^{1}H NMR ($CDCl_3$) 8.56 (1H, s, NH), 7.43 (5H, s, HC(Ar)), 5.37 (2H, s); ^{13}C NMR ($CDCl_3$) 158.0 (t, J=28.9 Hz, C(1)), 134.9, 128.6, 128.5, 128.0, 117.6 (tq, J=33.8, 286.6 Hz, C(4)), 108.4 (tqt, J=34.7, 38.9, 228.8 Hz, C(3)), 108.0 (tt, J=32.2, 243.2 Hz, C(2)), 69.7; ^{19}F NMR ($CDCl_3$) −81.2 (t, J=9.2 Hz), −118.2 (sextet, J=9.4 Hz), −127.0 (t, J=9.4 Hz); IR (neat, cm^{-1}) 3355 (w), 3071 (w), 3038 (w), 2959 (w), 1680 (s), 1501 (w), 1456 (w), 1401 (w), 1323 (m), 1221 (s), 1194 (s), 1173 (m), 1125 (s), 1078 (s), 968 (m), 938 (m), 911 (m), 737 (s), 696 (m), 650 (w); EI-MS (70 eV) 303 (M^+, 20), 302 (10), 301 (13), 266 (92), 238 (40), 213 (32), 196 (35), 169 (46), 149 (100), 128 (99.7), 97 (56), 91 (100); EI-HRMS calcd for $C_{11}H_2F_7NO$ (M^+), 303.0494; found, 303.0426.

5.4.5. Benzyl 3*H*-2,2,3,3-tetrafluoropropionimidate (40E). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 3*H*-2,2,3,3-tetrafluoropropionamide (493 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 175 mg (74%) of the 3*H*-2,2,3,3-tetrafluoropropionimidate as a colorless oil: R_f 0.36 (hexane/EtOAc, 10/1); bp 60°C/0.7 mmHg; ^{1}H NMR ($CDCl_3$) 8.49 (1H, s, NH), 7.41 (5H, br m, HC(Ar)), 6.00 (1H, tt, J=5.2, 53.0 Hz, H(3)), 5.34 (2H, s); ^{13}C NMR ($CDCl_3$) 159.5 (t, J=29.7 Hz, C(1)), 135.0, 128.6, 128.5, 128.0, 108.7 (tt, J=36.6, 251.9 Hz, C(3)), 108.2 (tt, J=28.9, 251.1 Hz, C(2)), 69.2; ^{19}F NMR ($CDCl_3$) −122.7 (q, J=6.8 Hz), −137.9 (td, J=6.8, 52.6 Hz); IR (neat, cm^{-1}) 3347 (w), 3038 (w), 1386 (s), 1501 (w), 1456 (w), 1391 (w), 1339 (m), 1246 (s), 1163 (s), 1136 (s), 1111 (s), 1063 (s), 955 (w), 911 (w), 851 (m), 824 (m), 764 (m), 752 (m), 696 (m); EI-MS (70 eV) 236 (11), 235 (M^+, 63), 234 (6), 233 (15), 192 (13), 191 (81), 167 (18), 149 (56), 134 (37), 107 (49), 101 (20), 92 (58), 91 (100), 90 (35), 59 (37), 58 (35); EI-HRMS calcd for $C_{10}H_9F_4NO$ (M^+), 235.0520; found, 235.0548.

5.4.6. Benzyl 5*H*-2,2,3,3,4,4,5,5-octafluorovalerimidate (40F). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 5*H*-2,2,3,3,4,4,5,5-octafluorovaleramide (749 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 253 mg (76%) of the 5*H*-2,2,3,3,4,4,5,5-octafluorovalerimidate as a colorless oil: R_f 0.36 (hexane/EtOAc, 10/1); bp 100°C/2.0 mmHg; ^{1}H NMR ($CDCl_3$) 8.56 (1H, s, NH), 7.44 (5H, br m, HC(Ar)), 6.02 (1H, tt, J=5.36, 52.0 Hz, H(5)), 5.37 (2H, s); ^{13}C NMR ($CDCl_3$) 158.1 (t, J=29.3 Hz, C(1)), 134.9, 128.6, 128.4, 128.0, 113.8–107.0 (m, C(3), C(4)), 108.5 (tt, J=32.2, 260.0 Hz, C(2)), 107.7 (tt, J=31.4, 255.0 Hz, C(5)), 69.6; ^{19}F NMR ($CDCl_3$) −117.6 (br t, J=10.3 Hz), −124.4 (br t, J=9.2 Hz), −130.0 (br m), −137.5 (d, J=54.5 Hz); IR (neat, cm^{-1}) 3069 (w), 3036 (w), 2953 (w), 2859 (w),

1784 (w), 1686 (m),1499 (w), 1456 (w), 1356 (m), 1202 (s), 1167 (s), 1082 (m), 957 (w), 911 (w), 847 (w), 737 (m), 696 (m), 606 (w); EI-MS (70 eV) 336 (4), 335 (M^+, 24), 279 (26), 256 (15), 239 (12), 213 (7), 185 (9), 167 (40), 149 (100), 134 (30), 107 (19), 91 (97), 71 (42), 57 (65); HRMS calcd for $C_{12}H_9F_8NO$ (M^+), 335.0556; found, 335.0581.

5.4.7. Benzyl 7*H*-2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptimidate (40G). Imidate formation according to the general procedure using benzyl alcohol (108 mg, 1 mmol), 7*H*-2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptamide (1.14 g, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 10/1) and following Kugelrohr distillation to give 390 mg (90%) of the 7*H*-2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptimidate as a colorless oil: R_f 0.33 (hexane/EtOAc, 10/1); bp 120°C/0.9 mmHg; ^1H NMR ($CDCl_3$) 8.57 (1H, s, NH), 7.41 (5H, m, HC(Ar)), 5.99 (1H, tt, J=5.1, 52.0 Hz, HC(7)), 5.39 (2H, s); ^{13}C NMR ($CDCl_3$) 158.2 (t, J=28.9 Hz, C(1)), 135.1, 128.6, 128.4, 128.0, 114.2–106.8 (m, C(3), C(4), C(5), C(6)), 108.8 (tt, J=33.1, 262.2 Hz, C(2)), 107.9 (tt, J=31.4, 254.8 Hz), 69.7; ^{19}F NMR ($CDCl_3$) −117.2 (t, J=9.4 Hz), −122.2 (s), −122.5 (br s), −123.7 (s), −129.8 (s), −137.5 (dt, J=55.3, 9.4 Hz); IR (neat, cm^{-1}) 3357 (m), 3071 (w), 3038 (w), 2961 (w), 1680 (s), 1601 (w), 1557 (w), 1501 (m), 1456 (m), 1401 (m), 1348 (s), 1316 (m), 1140 (s), 1088 (s), 967 (m), 911 (m), 843 (s), 797 (m), 739 (s), 696 (s), 669 (m), 542 (m); EI-MS (70 eV) 436 (8), 435 (M^+, 46), 423 (8), 403 (7), 370 (23), 328 (8), 308 (6), 278 (5), 255 (13), 236 (31), 208 (9), 194 (11), 166 (11), 152 (20), 134 (85), 111 (39), 91 (100), 79 (76), 58 (63), 56 (100); EI-HRMS calcd for $C_{14}H_9F_{12}NO$ (M^+), 435.0492; found, 435.0490.

5.4.8. 4-Methoxybenzyl 2,2,2-trifluoroacetimidate (41A). Imidate formation according to the general procedure using 4-methoxybenzyl alcohol (138 mg, 1 mmol), 2,2,2-trifluoroacetamide (373 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 6/1) and following Kugelrohr distillation to give 200 mg (85%) of the 2,2,2-trifluoroacetimidate as a colorless oil: R_f 0.61 (hexane/EtOAc, 3/1); bp 115–120°C/1.2 mmHg; ^1H NMR ($CDCl_3$) 8.32 (1H, s, NH), 7.34 (2H, d, J=8.55 Hz, HC(Ar)), 6.90 (2H, d, J=8.79 Hz, HC(Ar)), 5.24 (2H, s), 3.78 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 159.8, 157.7 (q, J=37.95 Hz, C(1)), 130.0, 126.9, 115.6 (q, J=280.0 Hz, C(2)), 113.9, 69.1, 55.0; ^{19}F NMR ($CDCl_3$) −74.6; IR (neat, cm^{-1}) 3332 (w), 3007 (w), 2961 (m), 2842 (w), 1686 (s), 1617 (s), 1588 (m), 1518 (s), 1466 (m), 1352 (m), 1304 (m), 1252 (s), 1163 (s), 1080 (s), 1036 (s), 953 (m), 924 (s), 828 (s), 758 (w), 735 (w), 718 (w), 702 (w), 596 (w), 558 (w), 517 (m); EI-MS (70 eV) 234 (9), 233 (M^+, 56), 232 (18), 221 (12), 200 (11), 185 (13), 167 (34), 149 (82), 137 (97), 122 (100), 121 (100), 120 (77), 91 (53), 67 (65), 58 (43); EI-HRMS calcd for $C_{10}H_{10}F_3NO_2$ (M^+), 233.0663; found, 233.0658.

5.4.9. 4-Methoxybenzyl 2,2,3,3,3-pentafluoropropionimidate (41B). Imidate formation according to the general procedure using 4-methoxybenzyl alcohol (138 mg, 1 mmol), 2,2,3,3,3-pentafluoropropionamide (538 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 6/1) and following Kugelrohr distillation to give 228 mg (80%) of the 2,2,3,3,3-pentafluoropropionimidate as a colorless oil: R_f 0.61 (hexane/EtOAc, 3/1); bp 120°C/1.0 mmHg; ^1H NMR ($CDCl_3$) 8.43 (1H, s, NH), 7.31 (2H, d, J=8.55 Hz, HC(Ar)), 6.90 (2H, d, J=8.51 Hz, HC(Ar)), 5.26 (2H, s), 3.81 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 159.8, 158.0 (t, J=28.9 Hz, C(1)), 130.1, 127.2, 117.9 (qt, J=287.0, 35.6 Hz, C(3)), 113.9, 106.3 (tq, J=39.7, 258.1 Hz, C(2)), 69.4, 55.0; ^{19}F NMR ($CDCl_3$) −83.1, −120.6; IR (neat, cm^{-1}) 3334 (w), 2840 (w), 2362 (w), 2342 (w), 1684 (m), 1617 (m), 1518 (m), 1325 (m), 1252 (m), 1221 (s), 1175 (s), 1082 (m), 1032 (s), 741 (w), 419 (m); EI-MS (70 eV) 284 (9), 283 (M^+, 70), 282 (100), 281 (8), 240 (87), 228 (30), 197 (30), 176 (13), 162 (30), 137 (89), 134 (70), 122 (100), 121 (100), 120 (54), 119 (69), 109 (49), 91 (100), 88 (48), 69 (100), 67 (100), 51 (68); EI-HRMS calcd for $C_{11}H_{10}F_5NO_2$ (M^+), 283.0631; found, 283.0590.

5.4.10. 4-Methoxybenzyl 2-chloro-2,2-difluoroacetimidate (41C). Imidate formation according to the general procedure using 4-methoxybenzyl alcohol (138 mg, 1 mmol), 2-chloro-2,2-difluoroacetamide (427 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) in CH_2Cl_2 (10 mL) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 6/1) and following Kugelrohr distillation to give 207 mg (83%) of the 2-chloro-2,2-difluoroacetimidate as a colorless oil: R_f 0.55 (hexane/EtOAc, 3/1); bp 140°C/1.8 mmHg; ^1H NMR ($CDCl_3$) 8.09 (1H, s, NH), 7.35 (2H, d, J=8.51 Hz, HC(Ar)), 6.90 (2H, d, J=8.75 Hz, HC(Ar)), 5.24 (2H, s, H_2C), 3.81 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 160.0 (t, J=32.6 Hz, C(1)), 159.8, 129.9, 127.1, 117.8 (t, J=294.2 Hz, C(2)), 114.0, 69.4, 55.3; ^{19}F NMR ($CDCl_3$) −62.1; IR (neat, cm^{-1}) 1680 (s), 1614 (s), 1518 (s), 1339 (m), 1304 (m), 1250 (s), 1078 (s), 1036 (s), 972 (s), 824 (s), 689 (m); EI-MS (70 eV) 251 (31), 250 (26), 249 (M^+, 90), 248 (50), 247 (27), 240 (27), 227 (24), 214 (19), 207 (15), 196 (35), 184 (18), 164 (41), 162 (50), 148 (50), 137 (100), 136 (83), 135 (97), 134 (53), 122 (100), 120 (100), 91 (100), 90 (51), 69 (100), 67 (100), 55 (44), 51 (55); EI-HRMS calcd for $C_{10}H_{10}ClF_2NO_2$ (M^+), 249.0368; found, 249.0350.

5.4.11. 4-Methoxybenzyl 2,2,3,3,4,4,4-heptafluorobutyrimidate (41D). Imidate formation according to the general procedure using 4-methoxybenzyl alcohol (138 mg, 1 mmol), 2,2,3,3,4,4,4-heptafluorobutyramide (704 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 6/1) and following Kugelrohr distillation to give 265 mg (80%) of the 2,2,3,3,4,4,4-heptafluoropropionimidate as a colorless oil: R_f 0.55 (hexane/EtOAc, 3/1); bp 130–135°C/1.0 mmHg; ^1H NMR ($CDCl_3$) 8.51 (1H, s, NH), 7.34 (2H, d, J=7.99 Hz, HC(Ar)), 6.91 (2H, d, J=7.99 Hz, HC(Ar)),

5.23 (2H, s, H_2C), 3.79 (3H, s, H_3C); ^{13}C NMR ($CDCl_3$) 159.9, 158.0 (t, J=28.4 Hz, C(1)), 130.0, 126.9, 117.5 (tq, J=33.8, 287.8 Hz, C(4)), 113.9, 108.2 (tq, J=38.9, 267.1 Hz, C(3)), 108.0 (tt, J=32.2, 259.7 Hz, C(2)), 69.6, 55.0; ^{19}F NMR ($CDCl_3$) −81.2, −118.2, −126.9; IR (neat, cm^{-1}) 2842 (w), 1682 (m), 1617 (m), 1559 (w), 1541 (w), 1518 (m), 1354 (m), 1323 (m), 1306 (m), 1221 (s), 1177 (s), 1125 (s), 1075 (m), 1036 (m), 967 (m), 934, (m), 826 (m), 749 (m); EI-MS (70 eV) 333 (M^+, 32), 332 (42), 331 (31), 316 (46), 271 (25), 257 (72), 256 (100), 255 (72), 242 (76), 241 (100), 227 (44), 211 (21), 169 (92), 136 (67), 135 (85), 122 (100), 121 (100), 91 (74), 68 (58), 67 (85), 56 (33); EI-HRMS calcd for $C_{12}H_{10}F_7NO_2$ (M^+), 333.0599; found, 333.0574.

5.4.12. 3,4-Dimethoxybenzyl 2,2,2-trifluoroacetimidate (42A). Imidate formation according to the general procedure using 3,4-dimethoxybenzyl alcohol (841 mg, 5 mmol), 2,2,2-trifluoroacetamide (1.8 g, 16 mmol), DMSO (3.41 mL, 48 mmol), $(COCl)_2$ (1.31 mL, 15 mmol), Et_3N (5.35 mL, 38 mmol) and DBU (1.5 mL, 10 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) and following Kugelrohr distillation to give 1.07 g (81%) of the 2,2,2-trifluoroacetimidate as a colorless solid: R_f 0.39 (hexane/EtOAc, 3/1); mp 73–74°C; bp 120–125°C/0.3 mmHg; ^1H NMR ($CDCl_3$) 8.25 (1H, s, NH), 6.84 (3H, m, HC(Ar)), 5.19 (2H, s, H_2C), 3.83 (3H, s, Me), 3.82 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 157.5 (q, J=38.0 Hz, C(1)), 149.1, 148.8, 127.1, 121.0, 115.4 (q, J=280.0 Hz, C(2)), 111.4, 110.8, 69.1, 55.5; ^{19}F NMR ($CDCl_3$) −74.7; IR (neat, cm^{-1}) 3305 (w), 2961 (w), 2840 (w), 1744 (w), 1686 (s), 1595 (m), 1520 (s), 1466 (m), 1422 (m), 1354 (m), 1269 (s), 1242 (s), 1202 (s), 1161 (s), 1080 (s), 1028 (s), 849 (m), 808 (m), 768 (w), 642 (w), 556 (w); EI-MS (70 eV) 264 (10), 263 (M^+, 65), 262 (36), 261 (10), 248 (22), 232 (10), 193 (13), 192 (51), 165 (46), 152 (100), 151 (100), 135 (62), 107 (100), 106 (63), 73 (60), 69 (54), 67 (69), 51 (25); EI-HRMS calcd for $C_{11}H_{12}F_3NO_3$ (M^+), 263.0769; found, 263.0768.

5.4.13. 3,4-Dimethoxybenzyl 2,2,3,3,3-pentafluoropropionimidate (42B). Imidate formation according to the general procedure using 3,4-dimethoxybenzyl alcohol (168 mg, 1 mmol), 2,2,3,3,3-pentafluoropropionamide (538 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) and following Kugelrohr distillation to give 255 mg (82%) of the 2,2,3,3,3-pentafluoropropionimidate as a colorless solid: R_f 0.39 (hexane/EtOAc, 3/1); mp 56–57°C; bp 150°C/1.8 mmHg; ^1H NMR ($CDCl_3$) 8.46 (1H, s, NH), 6.83 (3H, m, HC(Ar)), 5.21 (2H, s, H_2C), 3.80 (6H, s, Me); ^{13}C NMR ($CDCl_3$) 157.7 (t, J=28.6 Hz, C(1)), 149.1, 148.9, 127.2, 120.7, 117.7 (tq, J=35.5, 286.6 Hz, C(3)), 111.1, 110.8, 106.1 (qt, J=39.7, 257.7 Hz, C(2)), 69.4, 55.53, 55.46; ^{19}F NMR ($CDCl_3$) −83.0, −120.4; IR (KBr) 3305 (s), 2963 (m), 2840 (m), 1692 (s), 1609 (m), 1595 (m), 1520 (s), 1472 (m), 1426 (m), 1387 (m), 1321 (s), 1275 (s), 1252 (s), 1240 (s), 1181 (s), 1161 (s), 1142 (s), 1082 (s), 1028 (s), 999 (m), 909 (m), 880 (m), 855 (m), 812 (m), 749 (m), 642 (m), 577 (w), 423 (w); EI-MS (70 eV) 314 (8), 313 (M^+, 54), 312 (7), 311 (8), 298 (18), 27 (4), 263 (4), 248 (3), 194 (11), 166 (15), 152 (32), 151 (100), 150 (29), 149 (19), 135 (37), 108 (20), 107 (58), 106 (20), 67 (25), 56 (21); EI-HRMS calcd for $C_{11}H_{12}F_5NO_3$ (M^+), 313.0737; found, 313.0742.

5.4.14. 3,4-Dimethoxybenzyl 2-chloro-2,2-difluoroacetimidate (42C). Imidate formation according to the general procedure using 3,4-dimethoxybenzyl alcohol (168 mg, 1 mmol), 2-chloro-2,2-difluoroacetamide (427 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (150 μL, 1.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) and following Kugelrohr distillation to give 238 mg (85%) of the 2-chloro-2,2-difluoroacetimidate as a colorless oil: R_f 0.45 (hexane/EtOAc, 3/1); bp 140°C/1.8 mmHg; ^1H NMR ($CDCl_3$) 8.12 (1H, s, NH), 6.81 (3H, m, HC(Ar)), 5.15 (2H, s, H_2C), 3.77 (3H, s, Me) 3.76 (3H, s, Me); ^{13}C NMR ($CDCl_3$) 159.5 (t, J=32.9 Hz, C(1)), 149.0, 148.7, 127.3, 120.8, 117.6 (t, J=293.2 Hz, C(2)), 111.3, 110.8, 69.3, 55.5; ^{19}F NMR ($CDCl_3$) −61.7; IR (neat, cm^{-1}) 3305 (w), 3006 (w), 2959 (w), 2840 (w), 1742 (m), 1680 (s), 1595 (m), 1520 (s), 1466 (m), 1422 (m), 1331 (m), 1269 (s), 1242 (m), 1161 (s), 1142 (s), 1080 (s), 1028 (s), 976 (s), 853 (m), 806 (m), 766 (w), 689 (w), 613 (w), 556 (w); EI-MS (70 eV) 281 (31), 280 (18), 279 (M^+, 92), 278 (15), 269 (63), 264 (27), 244 (14), 194 (30), 166 (41), 152 (100), 151 (100), 150 (65), 135 (100), 121 (36), 108 (80), 107 (100), 106 (98), 105 (70), 90 (65), 71 (87), 69 (87), 67 (100), 51 (36); EI-HRMS calcd for $C_{11}H_{12}ClF_2NO_3$ (M^+), 279.0474; found, 279.0480.

5.4.15. 3,4-Dimethoxybenzyl 2,2,3,3,4,4,4-heptafluorobutyrimidate (42D). Imidate formation according to the general procedure using 3,4-dimethoxybenzyl alcohol (168 mg, 1 mmol), 2,2,3,3,4,4,4-heptafluorobutyramide (704 mg, 3.3 mmol), DMSO (1.07 mL, 15 mmol), $(COCl)_2$ (260 μL, 3.0 mmol), Et_3N (1.38 mL, 10 mmol) and DBU (300 μL, 2.0 mmol) afforded a colorless oil, which was purified by silica gel column chromatography (hexane/EtOAc, 3/1) and following Kugelrohr distillation to give 255 mg (70%) of the 2,2,3,3,4,4,4-heptafluorobutyrimidate as a colorless oil: R_f 0.39 (hexane/EtOAc, 3/1); bp 210°C/1.5 mmHg; ^1H NMR ($CDCl_3$) 8.43 (1H, s, NH), 6.86 (3H, m, HC(Ar)), 5.23 (2H, s, H_2C), 3.84 (6H, s, Me); ^{13}C NMR ($CDCl_3$); 157.7 (t, J=28.8 Hz, C(1)), 149.2, 148.9, 127.2, 120.9, 117.3 (tq, J=33.8, 286.7 Hz, C(4)), 111.3, 110.9, 108.0 (tqt, J=33.9, 38.9, 266.8 Hz, C(3)), 107.8 (tt, J=32.2, 259.3 Hz, C(2)), 69.5, 55.5, 55.4; ^{19}F NMR ($CDCl_3$) −81.1 (t, J=9.1 Hz), −118.3 (sextet, J=9.0 Hz), −127.0 (t, J=9.1 Hz); IR (neat, cm^{-1}) 3355 (w), 3306 (w), 2961 (w), 2840 (w), 1742 (w), 1680 (s), 1595 (m), 1520 (s), 1466 (m), 1424 (m), 1399 (w), 1321 (m), 1269 (s), 1229 (s), 1163 (s), 1125 (s), 1076 (m), 1030 (m), 968 (m), 926 (m), 851 (m), 806 (m), 749 (m), 648 (w), 556 (w); EI-MS (70 eV) 364 (14), 363 (M^+, 86), 362 (32), 361 (4), 348 (20), 300 (35), 285 (10), 270 (18), 269 (85), 238 (17), 225 (8), 194 (18), 193 (12), 166 (31), 152 (83), 151 (100), 135 (77), 107 (100), 106 (56), 67 (53), 56 (29); EI-HRMS calcd for $C_{13}H_{12}F_7NO_3$ (M^+), 363.0705; found, 363.0711.

5.5. General procedure for benzyl protection

A solution of benzyl imidate, alcohol and acid was stirred at

room temperature. The reaction mixture was diluted with EtOAc (10 mL) and the whole was washed with sat. aqueous NH_4Cl solution. Separated aqueous layer was further extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/EtOAc) to give benzyl ether product as colorless oil.

5.5.1. Methyl (*R*)-3-(4-methoxybenzyloxy)-2-methylpropionate (Table 7 entry 1, MPM-43). 4-Methoxybenzyl protection according to the general procedure using 4-methoxybenzyltrifluoroacetimidate (**41A**) (82 mg, 0.31 mmol), methyl (*R*)-3-hydroxy-2-methylpropionate (**43**, 33 mg, 0.28 mmol) and PPTS (8.7 mg, 13 mol% of imidate) in CH_2Cl_2 (1.0 mL) afforded a colorless oil. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 9/1) to give 53 mg (80%) of the methyl (*R*)-3-(4-methoxybenzyloxy)-2-methylpropionate (MPM-**43**) as a colorless oil: R_f 0.33 (hexane/EtOAc, 5/1); ^{1}H NMR ($CDCl_3$) 7.27–7.22 (2H, m), 6.89–6.86 (2H, m), 4.48–4.41 (2H, m), 3.80 (3H, s, Me), 3.69 (3H, s, Me), 3.62 (1H, dd, J=7.3, 9.0 Hz, HC (3)), 3.45 (1H, dd, J=5.8, 9.0 Hz, HC(3)), 2.76 (1H, ddq, J=5.8, 7.3, 7.1 Hz, HC(2)), 1.16 (3H, d, J=7.1 Hz, Me); ^{13}C NMR ($CDCl_3$); 175.3, 159.2, 130.2, 129.2, 113.7, 72.7, 71.6, 55.2, 51.7, 40.1, 14.0; IR (neat, cm^{-1}) 2951 (m), 2961 (m), 1740 (s), 1613 (m), 1514 (s), 1465 (m), 1364 (m), 1248 (s), 1202 (s), 1175 (s), 1090 (s), 1036 (s), 822 (m); EI-MS (70 eV) 239 (3), 238 (M^+, 22), 137 (M^+-121, 100), 121 (100); EI-HRMS calcd for $C_{13}H_{18}O_4$ (M^+), 238.1205; found, 238.1220.

5.5.2. Methyl (*S*)-α-(3,4-dimethoxybenzyloxy)benzeneacetate (Table 7 entry 8, DMPM-44). 3,4-Dimethoxybenzyl protection according to the general procedure using 3,4-dimethoxybenzyltrifluoroacetimidate (**42A**) (59 mg, 0.22 mmol), methyl (*S*)-(+)-mandelate (**44**, 17 mg, 0.1 mmol) and CSA (3.5 mg, 15 mol% of imidate) in CH_2Cl_2 (1.0 mL) afforded a colorless oil. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 3/1) to give 25 mg (80%) of the methyl (*S*)- α-(3,4-dimethoxybenzyloxy)benzeneacetate as a colorless oil: R_f 0.25 (hexane/EtOAc, 3/1); ^{1}H NMR ($CDCl_3$) 7.49 (5H, m), 6.90–6.82 (3H, m), 4.92 (1H, s, HC (2)), 4.56 (1H, d, J=11.7 Hz), 4.49 (1H, d, J=11.7 Hz), 3.87 (3H, s), 3.85 (3H, s), 3.70 (3H, s); ^{13}C NMR ($CDCl_3$); 171.3, 149.0, 148.9, 136.2, 129.4, 128.7, 127.4, 126.6, 120.9, 111.5, 110.9, 79.1, 71.0, 55.9, 55.8, 52.3; IR (neat, cm^{-1}) 2955 (m), 2840 (m), 1748 (s), 1595 (m), 1518 (s), 1456 (s), 1422 (m), 1267 (s), 1159 (s), 1140 (s), 1098 (m), 1073 (m), 1028 (s), 912 (s), 810 (m), 731 (s); EI-MS (70 eV) 317 (11), 316 (M^+, 58), 167 (M^+-151, 46), 151 (100); EI-HRMS calcd for $C_{18}H_{20}O_5$ (M^+), 316.1311; found, 316.1310.

Acknowledgements

Partial financial support of this research under the Biodesign Research Program of the Institute of Physical and Chemical Research (RIKEN) and a grant-in-aid for Scientific Research for the Japan Ministry of Education, Science and Culture are gratefully acknowledged.

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