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A new method for the synthesis of *N*-protected β-amino-α-keto esters from fluoroalkanesulfonylazides and α-keto esters

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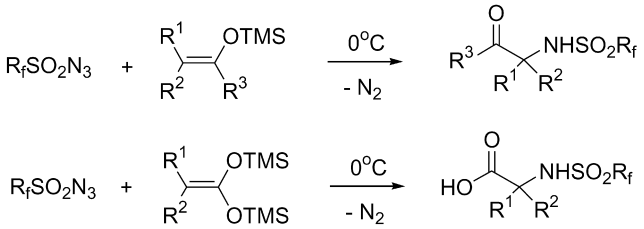
Abstract—In the presence of a secondary amine, treatment of α-keto esters with fluoroalkanesulfonyl azides at room temperature afforded *N*-sulfonyl protected β-amino-α-keto esters in good to excellent yields. This reaction provided a novel, direct and convenient access to *N*-sulfonyl protected β-amino-α-keto esters from α-keto esters and fluoroalkanesulfonyl azides under mild conditions. However, the reaction of fluoroalkanesulfonyl azides with β-ketoester enamines afforded two products: *N*-fluoroalkanesulfonyl amidines and diazoacetate. The reaction mechanism is discussed.

1. Introduction

β-Amino-α-keto acids and ester derivatives have found widespread application as competitive reversible inhibitors of the proteinase family of enzymes.[1] For example, amino acid-derived α-keto acids have been synthesized as inhibitors of the serine proteinase chymotrypsin,[2] whilst their incorporation into appropriate peptide recognition sequences has furnished potent and selective inhibitors of cysteine proteinases such as calpain and cathepsin B,[2] the serine proteinases neutrophil elastase and cathepsin G,[3,4] and the aspartyl proteinase, pepsin.[4] By far the most widely employed route to β-amino-α-keto esters and derivatives has been oxidation of *N*-protected β-amino-α-hydroxy esters prepared by elaboration of *N*-protected α-amino aldehydes.[5] It is obvious that the access to *N*-protected β-amino-α-keto esters is limited by the availability of α-amino aldehydes and the subsequent transformation.

Recently, we reported the direct amination of silyl enol ethers and disilyl ketene acetals by fluoroalkanesulfonyl azides to produce *N*-sulfonyl protected α-amino ketones[6] and α-amino acids,[7] respectively (Scheme 1).

Now, we seek to extend this methodology to the synthesis of *N*-protected β-amino-α-keto esters by the direct amination of α-keto esters. Furthermore, the interest in these fluorine-containing compounds, precursors of biologically and pharmacologically active molecules, encouraged us to develop an introduction of the amino group to the β-position of α-keto esters. Herein, we describe this novel, direct and convenient access to *N*-protected β-amino-α-keto esters, based on the direct amination.



Scheme 1.

2. Results and discussion

It is well known that fluoroalkanesulfonyl azides **1** are more reactive than other organic azides due to the very strong electron-withdrawing properties of the fluoroalkanesulfonyl group, especially in reactions with electron-rich olefins.[8] In previous studies we found that **1** reacted readily with enamines at 0°C giving *N*-fluoroalkanesulfonylamidines.[9,10]

Generally, enamines are prepared by the condensation of ketones with secondary amines,[11] therefore ketones mixed with secondary amines would present an equilibrium between enamine and ketone. As fluoroalkanesulfonyl azides react fast with enamines, the equilibrium between enamine and ketone should be shifted to the enamines. It is clear that the electron density of α-ketoester enamines is less than normal enamines. Therefore, the α-ketoester enamine, which is produced in situ from the α-ketoester and secondary amine, reacted slowly with the azides **1** at room temperature. Under nitrogen atmosphere, the azide **1a** was added into an ether solution of morpholine and ethyl

Keywords: fluorine and compounds; azides; cycloaddition; enamine.

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Table 1. Results of the reaction of azide **1** with **2** in the presence of amine **3**

Entry	Azide **1**	α-Ketoester	Amine **3**	Mole ratio[a]	Time (h)[b]	Product **4**	Yield (%)
1	**1a**	**2a**	**3a**	0.2	120	**4aa**	18
2	**1a**	**2a**	**3a**	0.5	120	**4aa**	40
3	**1a**	**2a**	**3a**	1.0	48	**4aa**	90
4	**1a**	**2a**	**3b**	1.0	12	**4aa**	58
5	**1a**	**2a**	**3b**	1.0	24	**4aa**	78
6	**1a**	**2a**	**3c**[c]	1.0	48	**4aa**	0
7	**1a**	**2a**	**3a**	1.0[d]	48	**4aa**	86
8	**1a**	**2b**	**3a**	1.0	48	**4ab**	87
9	**1a**	**2c**	**3a**	1.0	48	**4ac**	83
8	**1b**	**2a**	**3c**[c]	1.0	72	**4ba**	0
11	**1b**	**2a**	**3b**	1.0[e]	24	**4ba**	74
12	**1b**	**2b**	**3a**	1.0	48	**4bb**	89
13	**1b**	**2c**	**3a**	1.0	48	**4bc**	80
14	**1c**	**2c**	**3a**	1.0	48	**4cc**	78
15	**1d**	**2a**	**3a**	1.0	72	**10a**	80
16	**1d**	**2a**	**3b**	1.0	48	**10b**	86

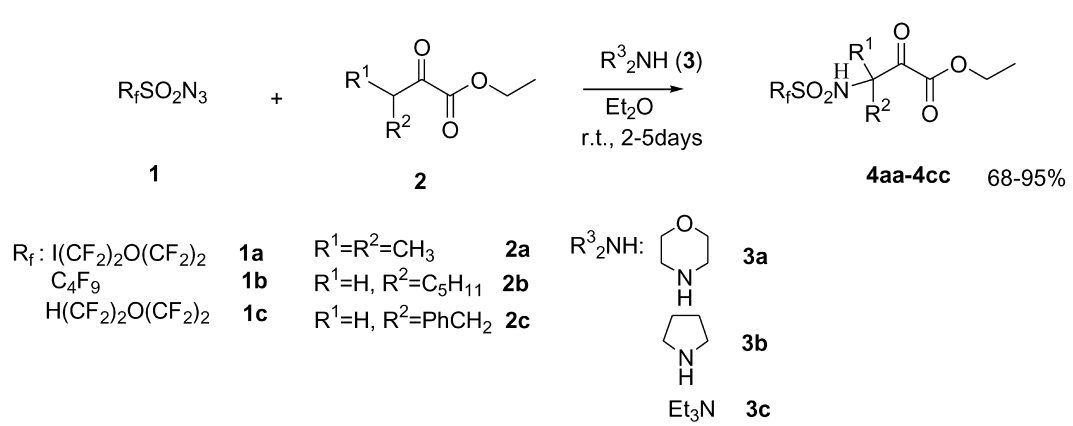
[a] Mole ratio of amine/azide.
[b] Reaction was carried out in Et_2O at room temperature.
[c] In this reaction an equal mole of Et_3N **3c** was added.
[d] In this reaction, an equal mole of toluene was added.
[e] In this reaction, an equal mole of cycohexene was added.

3-methyl-2-oxobutyrate (1:1), the reaction occurred slowly and was finished completely after stirring for 48 h at room temperature (monitored by TLC). After removal the solvent, the residue was chromatographed using EtOAc/petroleum ether as eluant to give the product ethyl 3-methyl-3-(*N*-fluorobutylsulfonyl)amino-2-oxo-butyrate **4aa** in 90% yield.

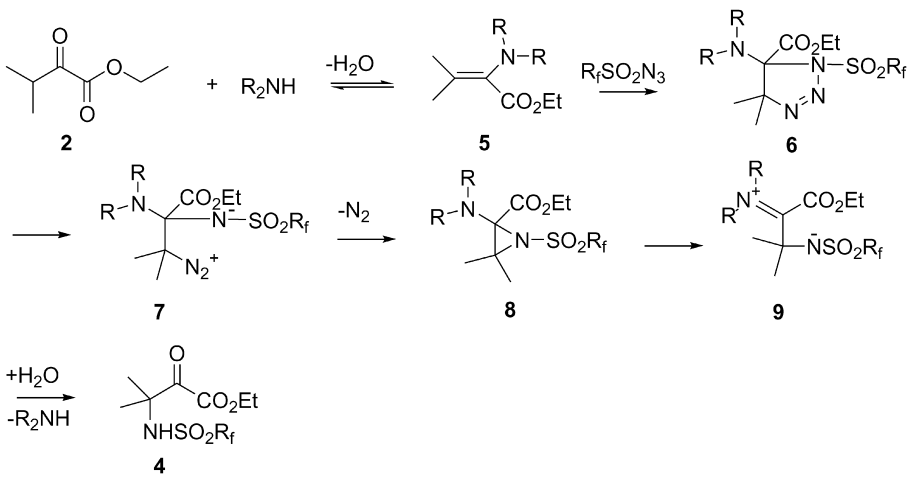
Using other secondary cycloamine such as pyrrolidine **3b** gave the same product and in slightly lower yield, but the reaction rate was increased (see Table 1, entries 4 and 5). It was noticed that the yield of product **4** also depended on the amount of the secondary amine. For example, the yield of **4aa** increased from 18 to 95% when the mole ratio of morpholine and **1a** was increased from 20 to 100%. Due to the acidic character of N–H of *N*-sulfonyl β-amino-α-keto esters, once the final product is produced, it would neutralize and inactivate 1 equiv. of amine. This is the possible reason why this reaction needed 1 equiv. of secondary amine. Under the same reaction conditions other α-ketoester such as n-$C_5H_{11}COCO_2Et$ **2b** and $PhCH_2$-$COCO_2Et$ **2c** reacted with **1** to give good results (see Scheme 2). The results of the reaction of **1** with α-ketoester are summarized in Table 1.

In the reaction of α-ketoester **2** with azides, the fluoroalkanesulfonyl nitrene intermediate should not be involved in the reaction process, because the decomposition of fluoroalkanesulfonyl azides to nitrenes requires thermolysis (100°C) or photolysis.[12] In our previous study on the reaction of azides **1** with cyclohexane or toluene, we noticed that the temperature of formation of the nitrene R_fSO_2N is around 110°C and no corresponding reaction occurred at room temperature.[12] In a comparison test, when toluene or cyclohexene were added into the reaction system of **1** with α-ketoester, no corresponding fluoroalkanesulfonyl nitrene insertion or cycloaddition product was isolated; the yield of normal product **4** was nearly unchanged (see Table 1, entries 7 and 11). Another possible reaction mechanism is through a carbon-anion intermediate. When triethyl amine, even K_2CO_3, which are stronger bases than the secondary amines morpholine and pyrrolidene, were used under the same reaction condition, however no similar reaction occurred (see Table 1 entries 6 and 8). This result ruled out the carbon-anion reaction mechanism. The likely mechanism is as shown in Scheme 3.

When mixing the secondary amines with an α-ketoester, it would present an equilibrium between enamine **5** and



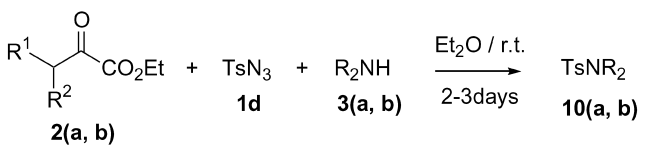
Scheme 2.



Scheme 3.

α-ketoester. As fluoroalkanesulfonyl azides react faster with enamines, the equilibrium between enamine and α-ketoester should be shifted to the enamines and could form the triazoline intermediate **6** by 1,3-dipolar cycloaddition.[13] When the triazoline ring carries an electron-withdrawing group at the 1-position, it is very labile.[13,14] Thus, the first formed triazoline is not readily isolated. It decomposes immediately after formation and produces aziridine **8** through rearrangement and loss of the N_2 at the same time. Since 1 equiv. of water is produced during the condensation of the α-keto ester with amine, the aziridine is hydrolyzed to the corresponding β-amino-α-keto ester and one equivalent of secondary amine is released simultaneously.

Under the same reaction conditions, the tosylazide **1d** reacted with **2** in the presence of morpholine or pyrrolidine and no corresponding *N*-sulfonyl β-amino-α-keto ester was obtained. The product was characterized as tosylamide and the starting ketoester was recovered completely (Scheme 4). From this reaction, it is clear that the fluoroalkanesulfonyl-azide is more reactive than the tosyl azide in a [2+3] polar cycloaddition reaction.

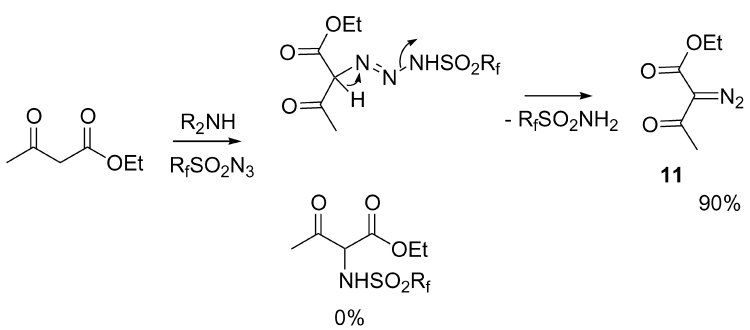


Scheme 4.

We anticipated that this direct amination could be extended to β-ketoesters and hence produce *N*-sulfonyl α-amino-β-keto esters. Unfortunately, ethyl acetoacetate reacted with azides **1** in the presence of morpholine at room temperature to give diazo ethyl acetoacetate as the major product (in 90% yield) and no α-amino-β-keto ester could be detected (Scheme 5). This result indicated that the diazotransfer reaction occurred predominately.

In order to circumvent the diazo-transfer reaction and obtain the α-amino-β-keto esters, we prepared α-ketoester enamines **12** and studied their reaction with azides **1**. α-Ketoester enamines **12** in which the electron-doner group (R_2N) and the electron-withdrawing group (CO_2Et) are bound at each end of the double bond, have a more polar double bond and are more reactive than the α-ketoester enamines in a polar cycloaddition. We found that at room temperature the reaction of **1** with β-ketoester enamine **12** occurred more rapidly than with the α-ketoester enamine. When the azide **1** was added into an ether solution of β-ketoester enamine **12**, the reaction occurred immediately and was finished completely after stirring for 0.5 h at room temperature (monitored by TLC). After evaporating the solvent, the residue was chromatographed using hexane/EtOAc as eluant to give *N*-per(poly)fluoroalkanesulfonyl amidines and diazo-acetate, not the desired α-amino-β-keto esters. The results of the reaction of azides **1** with β-ketoester enamines are summarized in Table 2 and Scheme 6.

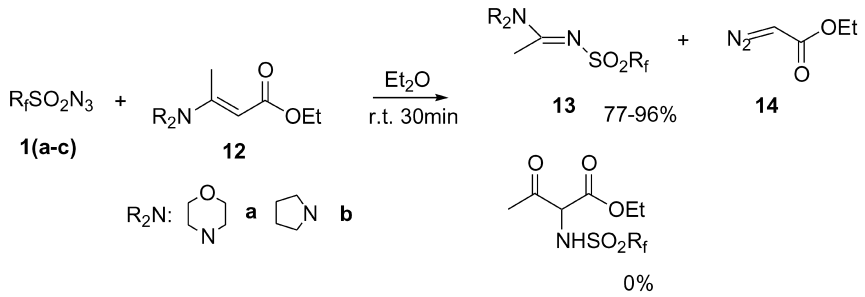
For the formation of the two products **13** and **14**, we



Scheme 5.

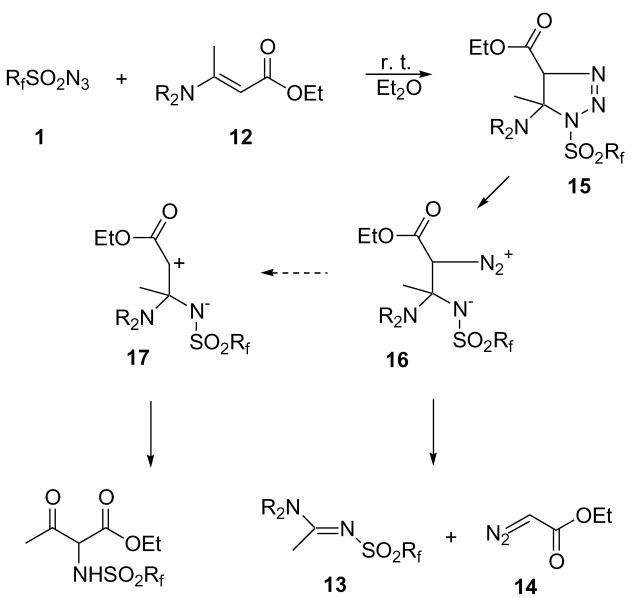
Table 2. The reactions of azides **1** with β-ketoester enamines **12**

Entry	Azides **1**	β-Ketoester enamines	Solvent	Product	Yield (%)
1	**1a**	**12a**	CH_2Cl_2	**13aa**	81
2	**1b**	**12a**	CH_2Cl_2	**13ba**	77
3	**1c**	**12a**	CH_2Cl_2	**13ca**	85
4	**1a**	**12b**	Et_2O	**13ab**	85
5	**1b**	**12b**	Et_2O	**13bb**	96
6	**1c**	**12b**	Et_2O	**13cb**	80



Scheme 6.

supposed that in this reaction the triazoline intermediate should also be formed first. It decomposes immediately after formation in situ and produces amidines and diazo-acetates. To explain the high regiospecificity of this reaction, we assume that the transformations proceed preferentially via intermediate **16** and did not lose N_2 to form a less stable intermediate **17** (Scheme 7).



Scheme 7.

3. Conclusions

In summary, we have investigated the reactions of fluoroalkanesulfonyl azides with ketoester enamines. In the reactions of the azides with α-ketoester enamines, the triazoline intermediates decomposed and released nitrogen to give the *N*-sulfonyl protected β-amino-α-keto esters **4**. This reaction provided a novel, direct and convenient access to *N*-sulfonyl protected β-amino-α-keto esters from α-keto esters and fluoroalkanesulfonyl azides. In the case of the β-ketoester enamine, the formed triazoline intermediate decomposed too. However, it did not eliminate the nitrogen gas and C–C bond cleavage gave amidine and diazoacetate. Further chemical transformations of the fluorine-containing 3-amino ketoester and amidine are under investigation.

4. Experimental

All melting points were determined on a Melt-Temp apparatus and are uncorrected. IR spectra were obtained with a Perkin–Elmer 983G spectrophotometer (KBr disks). ^{1}H NMR and ^{19}F NMR spectra were recorded on Varian-360L and Bruker AM-300 spectrometers operating at 300 and 56.4 MHz with TMS and $CFCl_3$ as an internal and external standard, respectively. NMR spectra were recorded using $CDCl_3$ or $(CD_3)_2CO$ as solvent. Low- and high-resolution mass spectra were obtained on an HP 5989a and a Finnigan MAT spectrometer, respectively. Elemental analyses were performed at this Institute. Column chromatography was performed using silica gel H, particle size 10–40 μm. The per(poly)fluoroalkanesulfonyl azides were prepared by our previously described methods.[12,15]

4.1. General procedure for the reaction of azides 1 with α-ketoester 2

5-Iodo-3-oxa-octafluoropentanesulfonyl azide **1a** (1.35 g, 3 mmol) was added into a solution of the α-ketoester **2a** (0.43 g, 3 mmol) with morpholine **3a** (3 mmol) in anhydrous ether (10 mL) under nitrogen atmosphere. After the solution was stirred at room temperature for 48 h, TLC analysis indicated that the reaction was completely finished. The solution was concentrated and purified by silica gel chromatography (76% EtOAc/hexane) to afford the product **4aa** (1.53 g).

4.1.1. Ethyl 3-[*N*-(5-iodo-3-oxa-octafluoropentanesulfonyl)]amino-3-methyl-2-oxo-butyrate 4aa. 1.53 g, 90%. White solid; mp 163–164°C; δ_H (300 Hz; $(CD_3)_2CO$): 4.09 (2H, q, J=7.1 Hz, OCH_2), 1.31 (6H, s, $2CH_3$), 1.20 (3H, t, J=7.1 Hz, CH_3CH_2O); δ_F ($(CD_3)_2CO$): −68.8 (2F, s), −81.3 (2F, t, $^4J_{FF}$=17.0 Hz), −86.1 (2F, t, $^4J_{FF}$=17.0 Hz), −117.8 (2F, s). ν_{max} (KBr)/cm^{-1}: 3496, 2990, 1702, 1626, 1460, 1305, 1230–1100; *m/z*: 594 (M^++Et. 85.98), 520 (M^+−OEt, 1.60), 486 (M^+−$NHSO_2$, 6.84), 484 (M^+−H−SO_2−O, 100.00), 227 ($IC_2F_4^+$, 11.83), 177

(ICF_2^+, 14.52), 135 ($M^+-R_fSO_2NH$, 1.18), 127 (I^+, 24.24). (Found: C, 22.98; H, 2.31; N, 2.09%. Calcd for $C_{11}H_{12}F_8O_6SNI$: C, 23.36; H, 2.12; N, 2.48%).

4.1.2. Ethyl 3-[*N*-(5-iodo-3-oxa-octafluoropentanesulfonyl)]amino-2-oxo-octanoate 4ab. 1.58 g, 87%. White solid; mp 168–170°C; δ_H (300 Hz; $(CD_3)_2CO$): 4.14 (2H, q, J=7.2 Hz, OCH_2), 3.19 (1H, m, 3-CH,), 1.82 (2H, m, 4-CH_2), 1.31 (4H, m, 5-CH_2, 6-CH_2), 1.22 (5H, m, 8-CH_3, 7-CH_2), 0.88 (3H, t, J=7.2 Hz, CH_3CH_2O). δ_F ($(CD_3)_2CO$): −68.9 (2F, s), −81.5 (2F, t, $^4J_{FF}$=17.0 Hz), −86.0 (2F, t, $^4J_{FF}$=17.0 Hz), −117.6 (2F, s); ν_{max} (KBr)/cm^{-1}: 3492, 2988, 1695, 1630, 1462, 1220–1100; *m/z*: 562 (M^+−OEt, 3.15), 227 ($ICF_2CF_2^+$, 70.21), 185 ($M^+-NHSO_2R_f$, 47.23), 101 ($COCO_2Et$, 58.28), 64 (SO_2, 100.00). (Found: C, 27.90; H, 2.93; N, 2.09%. Calcd for $C_{14}H_{18}F_8O_6SNI$: C, 27.68; H, 2.97; N, 2.31%).

4.1.3. Ethyl 3-[*N*-(5-iodo-3-oxa-octafluoropentanesulfonyl)]amino-2-oxo-4-phenyl butyrate 4ac. 1.56 g, 83%. Yellow oil; δ_H (300 Hz; $(CD_3)_2CO$): 7.26 (5H, m, Ph), 4.02 (2H, q, J=7.1 Hz, OCH_2), 3.16 (3H, m, 3-CH, 4-CH_2), 1.12 (3H, t, J=7.1 Hz, OCH_2CH_3); δ_F $(CD_3)_2CO$): −69.0 (2F, s), −81.2 (2F, t, $^4J_{FF}$=17.0 Hz), −86.2 (2F, t, $^4J_{FF}$=17.0 Hz), −117.3 (2F, s); ν_{max} (KBr)/cm^{-1}: 3491, 2979, 1694, 1636, 1466, 1216–1108; *m/z*: 626 (M^+, 0.57), 553 (M^+-CO_2Et, 5.99), 119 ($PhCH_2CHNH^+$, 100.00). (Found 626.9440. Calcd for $C_{16}H_{14}F_8O_6SNI$ 626.9459)

4.1.4. Ethyl 3-(*N*-perfluorobutanesulfonyl)amino-3-methyl-2-oxo-butyrate 4ba. 1.18 g, 74%. White solid; mp 187–188°C; δ_H (300 Hz; $(CD_3)_2CO$): 4.08 (2H, q, J=7.1 Hz, OCH_2), 1.31 (6H, s, $2CH_3$), 1.20 (3H, t, J=7.1 Hz, CH_3CH_2O); δ_F $(CD_3)_2CO$): −79.4 (s, 3F), −110.3 (2F, m), −116.7 (2F, m), −122.1 (2F, s); ν_{max} (KBr)/cm^{-1}: 3445, 2993, 1709, 1628, 1468, 1304, 1236–1198; *m/z*: 442 (M^++1, 17.20), 368 (M^+-CO_2Et, 10.53), 219 ($C_4F_9^+$, 4.14), 143 ($M^+-C_4F_9SO_2NH$, 100.00). (Found 441.0293, Calcd for $C_{11}H_{12}O_5F_9SN$: 441.0281).

4.1.5. Ethyl 3-(*N*-perfluorobutanesulfonyl)amino-2-oxo-octanoate 4bb. 1.29 g, 89%. White solid; mp 192–194°C; δ_H (300 Hz; $(CD_3)_2CO$): 4.12 (2H, q, J=7.1 Hz, OCH_2), 3.22 (1H, m, 3-CH), 1.81 (2H, m, 4-CH_2), 1.29 (4H, m, 5-CH_2, 6-CH_2), 1.21 (5H, m, 8-CH_3, 7-CH_2), 0.88 (3H, t, J=7.1 Hz, CH_3CH_2O); δ_F ($(CD_3)_2CO$): −79.4 (3F, s), −110.3 (2F, m), −116.7 (2F, m), −122.1 (2F, s); ν_{max} (KBr)/cm^{-1}: 3445, 2993, 1709, 1628, 1468, 1304, 1236–1198; *m/z*: 528 (M^++OEt, 49.45), 512 (M^++Et, 33.32), 300 ($M^+H-C_{10}H_{17}O_3$, 2.47), 219 ($C_4F_9^+$, 4.52), 185 ($M^+-NHSO_2C_4F_9$, 14.40), 101 (M^+-COCO_2Et, 21.43), 69 (CF_3^+, 100.00). (Found: C, 34.92; H, 3.81; N, 2.65%. Calcd for $C_{14}H_{18}F_9O_5SN$: C, 34.78; H, 3.73; N, 2.90%).

4.1.6. Ethyl 3-(*N*-perfluorobutanesulfonyl)amino-2-oxo-4-phenyl butyrate 4bc. 1.21 g, 80%. Yellow oil; δ_H (300 Hz; $CDCl_3$): 7.28 (5H, m, Ph), 4.03 (2H, q, J=7.1 Hz, OCH_2), 3.95 (3H, m), 3.33 (1H, m, NH), 1.12 (3H, t, J=7.1 Hz, CH_3CH_2O); δ_F ($CDCl_3$): −80.0 (3F, s), −113.8 (2F, m), −120.2 (2F, m), −125.3 (2F, m); ν_{max} (KBr)/cm^{-1}: 3424, 1708, 1487, 1620, 1231, 1310; *m/z*: 503 (M^+, 3.18), 177 ($M^+-C_4F_9SO_2NH$-Et, 29.96), 146 (M^++1−$C_4F_9SO_2-C_6H_5CH_2$, 100.00), 77 ($C_6H_5^+$, 10.23). (Found 503.0435. Calcd for $C_{16}H_{14}F_9O_5NS$: 503.0449).

4.1.7. Ethyl 3-[*N*-(5-H-3-oxa-octafluoropentanesulfonyl)]amino-2-oxo-4-phenyl butyrate 4cc. 1.17 g, 78%. Yellow oil; δ_H (300 Hz; $CDCl_3$): 7.19 (5H, m, Ph), 5.74 (1H, t-t, $^2J_{H-F}$=53.5 Hz, $^3J_{F-F}$=3.3 Hz, HCF_2), 4.02 (2H, q, J=7.1 Hz, OCH_2), 3.68 (1H, m, 3-CH), 3.14 (2H, m, $PhCH_2$), 0.96 (3H, t, J=7.1 Hz, CH_3CH_2O); δ_F ($CDCl_3$): δ_F ($CDCl_3$): −82.0 (2F, t, $^4J_{FF}$=17.0 Hz), −89.3 (2F, t, $^4J_{FF}$=17.0 Hz), −120.2 (2F, s), −140.3 (2F, d, J=53 Hz); ν_{max} (KBr)/cm^{-1}: 3428, 1710, 1624, 1468, 1190–1100; *m/z*: 501 (M^+, 1.41), 205 ($M^+-HCF_2CF_2OCF_2CF_2SO_2NH$, 4.45), 176 ($M^+-HCF_2CF_2OCF_2CF_2SO_2NH$ -Et, 27.73), 91 ($PhCH_2$, 49.85), 77 ($C_6H_5^+$, 20.45), 43 ($C_3H_3O_2^+$, 100.00). (Found 501.3421. Calcd for $C_{16}H_{15}F_8O_6NS$: 501.3504).

4.1.8. *N*-Tosyl-pyrrolidine[16] 10a. 0.723 g, 80%. White solid, mp 123–124°C; δ_H (300 Hz; $CDCl_3$): 7.72 (2H, d, J=8.1 Hz,), 7.32 (2H, d, J=8.1 Hz,), 3.23 (4H, m,), 2.43 (3H, s), 1.75 (4H, m); ν_{max} (KBr)/cm^{-1}: 3089, 2974, 1595, 1334, 1166, 819, 753; *m/z*: 225 (M^+, 44.27), 224 (M^+−1, 39.41), 155 ($C_7H_7SO_2^+$, 23.42), 91 ($C_7H_7^+$, 82.00), 70 ($C_4H_8N^+$, 100.00).

4.1.9. *N*-Tosyl-morpholine[16] 10b. 0.58 g, 86%. Mp 148–149°C; δ_H (300 Hz; $CDCl_3$): 7.64 (4H, ab, J=6.6 Hz, Ph), 3.74 (4H, m, 2O−CH_2), 2.98 (4H, m, 2N−CH_2), 2.45 (3H, s, Ph−CH_3); ν_{max} (KBr)/cm^{-1}: 2852, 1735, 1453, 1597, 1231, 1310; *m/z*: 241 (M^+, 24.99), 155 (M^+−morpholine, 42.50), 91 ($PhCH_3$, 78.10), 86 (morpholine, 100.00). (Found 241.0772. Calcd for $C_{11}H_{15}O_3NS$: 241.0738).

4.2. General procedure for the reaction of azides 1 with β-ketonester enamines 12

To a solution of the β-ketoester enamines **12a** (0.270 g, 1.357 mmol) in anhydrous dichloromethane (10 mL) at room temperature under nitrogen atmosphere was added dropwise, an equimolar amount of azides **1b** (0.441 g, 1.357 mmol). TLC analysis indicated that the reaction was completely finished in 30 min. The solution was concentrated to give an oily residue. Purification by silicon gel chromatography (20% EtOAc/hexane) afforded diazoacetate **14** (0.880 g, 57%; R_f: 0.66, 20% EtOAc/hexane), then changed eluant (50% EtOAc/hexane) afforded amidine **13ba** (0.448 g, 81%; R_f: 0.46, 50% EtOAc/hexane).

4.2.1. *N*-(5-Iodo-3-oxa-octafluoropentanesulfonyl) morpholino ethylideneimine 13aa. 0.587 g, 81%. White solid; mp 69–70°C; δ_H (300 Hz; $(CD_3)_2CO$): 3.90 (2H, t, J=5.5 Hz, O-CH_2), 3.80 (4H, m, 2×N−CH_2), 3.70 (2H, t, J=5.5 Hz, O−CH_2), 2.55 (3H, s, CH_3); δ_F ($(CD_3)_2CO$): −64.2 (2F, s), −80.6 (2F, t, $^4J_{FF}$=17.0 Hz), −84.8 (2F, t, $^4J_{FF}$=17.0 Hz), −111.0 (CF_2, s); ν_{max} (KBr)/cm^{-1}: 2995, 2961, 1576, 1485, 1440, 1210, 1220–1100; *m/z*: 535 (M^++1, 53.96), 406 (M^++1−I, 9.74), 356 (M^++1−CF_2I, 1.40), 227 (C_2F_4I, 5.18), 191 (M^+-R_f, 87.52), 175 (M^+-OR_f, 31.29), 127 ($M^+-SO_2R_f$, 37.05), 86 ($C_4H_8NO^+$, 100.00), (Found: C, 22.17; H, 1.83; N, 5.19%. Calcd for $C_{10}H_{11}F_8O_4SN_2I$: C, 22.47; H, 2.06; N, 5.24%).

4.2.2. *N*-(5-Iodo-3-oxa-octafluoropentanesulfonyl)pyrrolidinyl ethylideneimine 13ab. 0.597 g, 85%. Colorless oil; δ_H ($CDCl_3$): 3.60 (4H, m, 2×N–CH_2), 2.55 (3H, s, CH_3), 2.00 (4H, m, 2×CH_2); δ_F ($CDCl_3$): −64.2 (2F, s), −80.1 (2F, t, $^4J_{FF}$=17.0 Hz), −84.4 (2F, t, $^4J_{FF}$=17.0 Hz), −115.9 (2F, s); ν_{max} (KBr)/cm^{-1}: 2982, 2887, 1572, 1466, 1419, 1331, 1293, 1230–1195, 1092, 1037, 986, 971, 859, 829; *m/z*: 519 (M^++1, 24.19), 392 (MH^+−I, 4.93), 227 ($C_2F_4I^+$, 3.49), 175 (M^+-R_f, 89.05), 159 (M^+-OR_f, 14.47), 111 ($M^+-SO_2R_f$, 4.38), 100 ($C_2F_4^+$, 7.68), 70 ($C_4H_8N^+$, 100.00). (Found 517.9372. Calcd for $C_{10}H_{11}F_8N_2O_3SI$: 517.9375).

4.2.3. *N*-Perfluorobutanesulfonyl morpholino ethylideneimine 13ba. 0.43 g, 77%. White solid; mp 67–68°C; δ_H (300 Hz; $(CD_3)_2CO$): 3.90 (2H, t, *J*=5.5 Hz, O–CH_2), 3.80 (4H, m, 2×N–CH_2), 3.70 (2H, t, *J*=5.5 Hz, O–CH_2), 2.55 (3H, s, CH_3); δ_F ($(CD_3)_2CO$): −79.8 (2F, s), −113.0 (2F, t, $^4J_{FF}$=17.0 Hz), −120.0 (2F, s), −125.2 (2F, t, $^4J_{FF}$=17.0 Hz); ν_{max} (KBr)/cm^{-1}: 2987, 2934, 1568, 1495, 1452, 1432, 1397, 1354, 1220–1140; *m/z*: 411 (M^++1, 26.60), 410 (M^+, 25.77), 191 (M^+-R_f, 64.57), 175 (M^+-OR_f, 12.81), 150 ($C_3F_6^+$, 6.59), 127 ($M^+-SO_2R_f$, 20.54), 86 ($C_4H_8NO^+$, 100.00). (Found: C, 29.06; H, 2.36; N, 6.75%. Calcd for $C_{10}H_{11}F_9O_3SN_2$: C, 29.27; H, 2.68; N, 6.38%).

4.2.4. *N*-Perfluorobutanesulfonyl pyrrolidinyl ethylideneimine 13bb. 0.51 g, 96%. White solid; mp 73–74°C; δ_H ($CDCl_3$): 3.60 (4H, m, 2×N–CH_2), 2.55 (3H, s, CH_3), 2.00 (4H, m, 2×CH_2). δ_F ($CDCl_3$): −79.3 (2F, s), −112.5 (2F, t, $^4J_{FF}$=17.0 Hz), −119.4 (2F, s), −124.5 (2F, t, $^4J_{FF}$=17.0 Hz); ν_{max} (KBr)/cm^{-1}: 2984, 2887, 1575, 1475, 1458, 1420, 1340, 1318, 1270–1115, 1042, 1010, 858, 820; *m/z*: 395 (M^++1, 5.96), 394 (M^+, 42.15), 374 (M^++1−F, 1.38), 175 (M^+-R_f, 64.26), 159 (M^+-OR_f, 13.82), 111 ($M^+-SO_2R_f$, 4.38), 100 ($C_2F_4^+$, 2.54), 70 ($C_4H_8N^+$, 100.00). (Found: C, 30.54; H, 2.67; N, 7.03%. Calcd for $C_{10}H_{11}F_9N_2O_3S$: C, 30.46; H, 2.79; N, 7.11%).

4.2.5. *N*-(5-*H*-3-Oxa-octafluoropentanesulfonyl) morpholino ethylideneimine 13ca. 0.47 g, 85%. Colorless oil; δ_H ($CDCl_3$): 5.88 (1H, t-t, $^2J_{H-F}$=53.5 Hz, $^3J_{F-F}$=3.3 Hz, CF_2H), 3.90 (2H, t, *J*=5.5 Hz, O–CH_2), 3.80 (4H, m, 2×N–CH_2), 3.70 (2H, t, *J*=5.5 Hz, O–CH_2), 2.55 (3H, s, CH_3). δ_F ($CDCl_3$): −80 (2F, t, $^4J_{FF}$=17.0 Hz), −87.2 (2F, t, $^4J_{FF}$=17.0 Hz), −116.7 (2F, s), −136.8 (2F, d, *J*=53 Hz); ν_{max} (KBr)/cm^{-1}: 2938, 2866, 1559, 1495, 1450, 1421, 1324, 1278, 1210, 1190–1100, 1001, 980, 865; *m/z*: 408 (M^+, 13.31), 388 (M^++1−C_2F_4H, 1.02), 191 (M^+-R_f, 87.52), 175 (M^+-OR_f, 31.29), 127 ($M^+-SO_2R_f$, 37.05), 119 ($C_2F_5^+$, 16.58), 101 ($C_2F_4H^+$, 15.75), 86 ($C_4H_8NO^+$, 100.00). (Found: C, 29.44; H, 2.89; N, 6.66%. Calcd for $C_{10}H_{12}F_8N_2O_4S$: C, 29.41; H, 2.94; N, 6.86%).

4.2.6. *N*-(5-*H*-3-Oxa-octafluoropentanesulfonyl) pyrrolidinyl ethylideneimine 13cb. 0.426 g, 80%. Colorless oil; δ_H ($CDCl_3$): 5.91 (1H, t-t, *J*=53, 5 Hz, CF_2H), 3.60 (4H, m, 2×N–CH_2), 2.55 (3H, s, CH_3), 2.00 (4H, m, 2×CH_2); δ_F ($CDCl_3$): −87.2 (2F, t, $^4J_{FF}$=17.0 Hz), −95.0 (2F, t, $^4J_{FF}$=17.0 Hz), −123.7 (2F, s), −143.7 (2F, d, *J*=53 Hz); ν_{max} (KBr)/cm^{-1}: 2984, 2887, 1575, 1466, 1421, 1326, 1285, 1205–1100, 1037, 985, 960, 829; *m/z*: 392 (M^+, 13.68), 372 (M^++1−F, 1.00), 175 (M^+-R_f, 62.09), 159 (M^+-OR_f, 9.23), 119 ($C_2F_5^+$, 9.18), 111 ($M^+-SO_2R_f$, 6.12), 101 ($C_2F_4H^+$, 9.62), 70 ($C_4H_8N^+$, 100.00). (Found: C, 30.70; H, 3.09; N, 7.13%. Calcd for $C_{10}H_{12}F_8N_2O_3S$ C, 30.61; H, 3.06; N, 7.14%.)

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