Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 4315–4325

TETRAHEDRON

N-(Benzoyloxy)amines: an investigation of their thermal stability, synthesis, and incorporation into novel peptide constructs

Anne Nemchik, Valentina Badescu and Otto Phanstiel, IV*

Department of Chemistry, University of Central Florida, P.O. Box 162366, Orlando, FL 32816-2366, USA

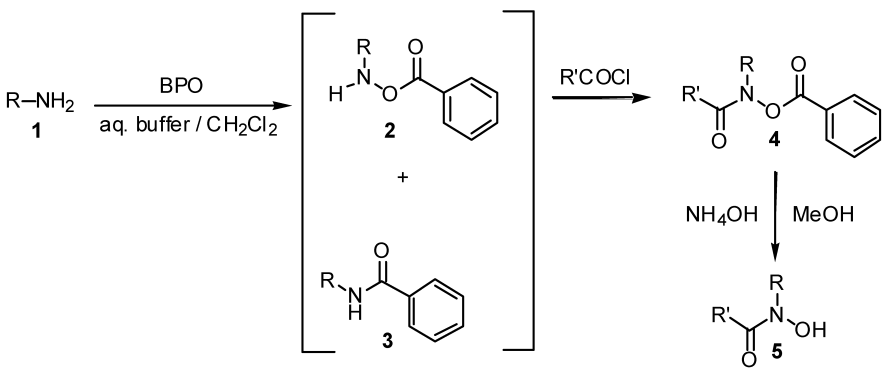
Received 27 September 2002; revised 16 April 2003; accepted 16 April 2003

Abstract—A series of *N*-benzoyloxyamines were pyrolyzed and their decomposition temperatures correlated well with the amine architecture's ability to stabilize a *N*-centered radical. A variety of amine substrates were treated with a biphasic mixture of benzoyl peroxide (BPO), CH_2Cl_2 and an aqueous carbonate buffer (at pH 10.5). Primary and secondary amines were successfully *N*-benzoyloxylated in good yield. Tertiary amines and BPO gave low yields of the corresponding *N*-oxide and complex product mixtures, presumably via radical decomposition. Electron deficient amines (such as fluorinated aliphatic amines, α-aminoacids, α-aminoesters, and α-aminoamides) were not *N*-benzoyloxylated under these conditions. Instead, *N*-benzoylation was observed with the fluorinated amines and the reaction was sensitive to temperature and the pH of the aqueous medium. A one-pot-two-step synthesis of N^{α}-FMOC-L-Leu-N^{β}-(benzoyloxy)-β-alanine ethyl ester, a peptide containing both an α- and a novel β-amino acid framework, was also developed.

1. Introduction

The *N*-oxidation of amines is a chemical reaction that creates at least one N–O bond. This bond offers access to many types of nitrogen chemistries and functional groups. For example, hydroxylamine (NH_2OH) and its derivatives can be converted synthetically into hydroxamates,[1] hydroxamic acids[2] and *N*-(hydroxy)-containing peptides.[3] Early studies by Milewska used benzoyl peroxide (BPO) to directly convert a primary amine **1** into a *N*-(benzoyloxy)amine (RNHOCOPh, **2**, Scheme 1) in moderate yield.[4] This method was heterogeneous and used BPO, anhydrous Na_2CO_3, and CH_2Cl_2 mixtures. Using a biphasic approach, an improved method was developed for the selective monooxidation of primary and secondary amines (Scheme 1).[5] Indeed, an aqueous carbonate buffer (pH 10.5)[5] was shown to enhance the selectivity of the BPO-mediated process and resulted in a significant improvement upon earlier yields.[5]

In recent years we have demonstrated the utility of the *N*-(benzoyloxy)amines in the synthesis of α,β-unsaturated hydroxamic acids (via acylation)[6] and secondary amines (via organoboranes).[7] This work was then extended to include entry to *N*-(hydroxy)-containing peptides[3] and siderophores[8] (e.g. acinetoferrin[6] and nannochelin A[9] shown in Fig. 1). In this report the thermal stability of the *N*-benzoyloxyamines (e.g. **2**) and the synthetic scope of this BPO method were investigated. In addition, the application



Scheme 1.

Keywords: thermal stability; amine oxidation; *N*-benzoyloxyamines; hydroxamic acids; β-peptides.

* Corresponding author. Tel.: +1-407-8235410; fax: +1-407-8232252; e-mail: ophansti@mail.ucf.edu

0040–4020/03/$ - see front matter
doi:10.1016/S0040-4020(03)00635-5

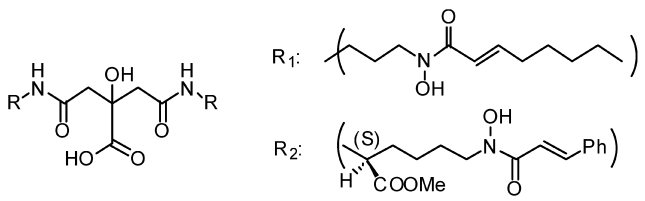


Figure 1. Acinetoferrin (R_1) and Nannochelin A (R_2).

of this method to peptide synthesis was demonstrated. Such studies are important as they identify both the characteristics of the amine architecture required for reaction and the limitations of this technology.

2. Results and discussion

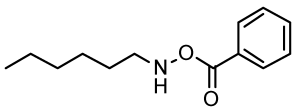
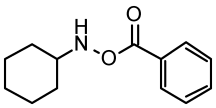
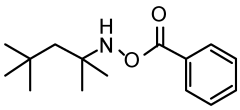
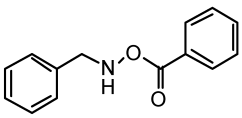
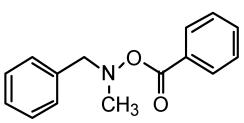
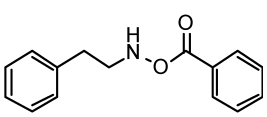
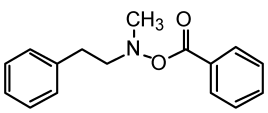
Previous studies probed the effect of substitution on the α-carbon of the primary amine architecture in terms of *N*-benzoyloxyamine yield. In general, 1° amines containing bulky R groups (**1**, Scheme 1) gave higher yields of *N*-(benzoyloxy)amines (Table 1).[7] Secondary amines were also readily converted in high yield.[10] Having developed an improved entry to the *N*-(benzoyloxy)amines (**6-12**) from aliphatic amines, their thermal stability and potential as nitrogen-radical precursors were investigated.

2.1. Thermal studies

A thermal gravimetric analysis–differential thermal analysis (TGA–DTA) study of a homologous series of *N*-benzoyloxyamines is shown in Table 1. All compounds gave positive DTA curves, which is in agreement with the thermal decomposition of **6-12** being an exothermic process. The DTA curve for each compound gave a maxima at a particular temperature. The temperature associated with this maxima was noted as the 'decomposition temperature' for the analyzed compound and is listed in Table 1. To the best of our knowledge, this is the first report on the thermal stabilities of these systems.

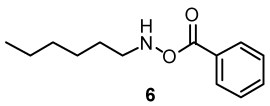
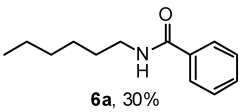
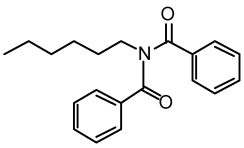
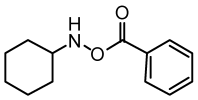
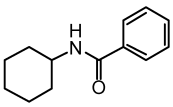
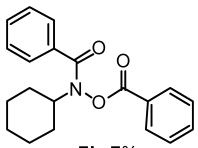
Several trends are evident from Table 1. First, the decomposition temperatures all fall within the 153–218°C temperature range. The effect of α-carbon substitution shows a 10°C lower decomposition temperature for the cyclohexyl derivative **7** (168°C) relative to the *n*-hexylamine **6** (178°C). However, the trend towards lower temperature upon further α-carbon substitution did not hold true for the *tert*-octyl derivative **8**, which had the highest decomposition temperature (218°C) of the series. *N*-Methylation generally resulted in lower decomposition temperatures (see **9-12** in Table 1). Homolytic N–O bond cleavage of **6-12** would generate both a benzoyloxy radical ($PhCOO^{\cdot}$) and an aminyl radical ($RR'N^{\cdot}$). In general, radicals are electron-deficient species. Therefore,

Table 1. Synthesis and TGA–DTA studies of *N*-benzoyloxyamines **6-12**

#	Compound	Yield (%)	Decomposition temperature (°C)	% mass loss[a]
6		74[b]	178	5
7		82[b]	168	11
8		90[b]	218	43
9		63[b]	163	5
10		93	153	14
11		73[b]	167	2
12		86	158	2

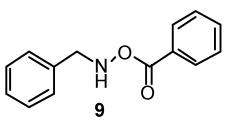
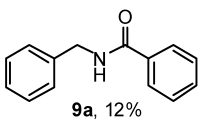
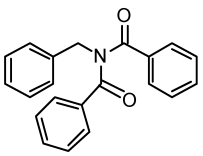
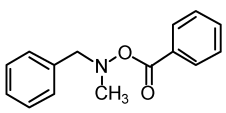
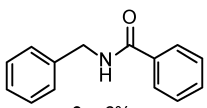
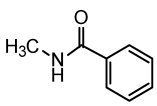
[a] At decomposition temperature.
[b] From Ref. 7.

Table 2. Products isolated from the thermal decomposition of **6** and **7** in the absence and presence of benzaldehyde

Starting material	Pyrolysis products (% yield)	with benzaldehyde (% yield)
 **6**	**6**, 32% recovery  **6a**, 30%	**6a**, 22%  **6b**, 27%
 **7**	 **7a**, 11%	**7a**, 27%  **7b**, 7%

a secondary aminyl radical ($RR'N^{\cdot}$) is usually more stable than its corresponding primary radical ($RHN^{\cdot}$). Since **10** and **12** had lower respective decomposition temperatures than **9** and **11**, the DTA results suggest a direct relationship between thermal decomposition temperature and the stability of the resultant nitrogen radical center.

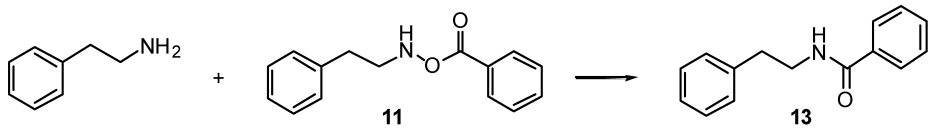
Table 3. Products isolated from thermal decomposition of **9** and **10** in the absence and presence of benzaldehyde

Starting material	Pyrolysis products (% yield)	with PhCHO (% yield)
 **9**	 **9a**, 12%	**9a**, trace
	 **9b**, 8%	**9b**, 13%
 **10**	 **9a**, 6%	
	 **10a**, 11%	

The TGA data tracked %mass loss as a function of increasing temperature. Although large %mass losses occurred at temperatures higher than the listed decomposition temperature, the mass loss measured at the decomposition temperature was typically very low, with the exception of compound **8**. This general observation was rationalized by the relatively low temperatures involved (~153–178°C) and the lag time needed to volatilize the relatively high boiling amine, amide or imide products. The high % mass loss observed with **8** (43%) is likely related to its higher temperature of decomposition. The TGA traces of both **6** and **7** (found in the Supporting Information) also showed significant mass losses at this elevated temperature (218°C) and were ~22 and 32%, respectively.

In order to demonstrate that amine radicals were generated during the thermal decomposition of these *N*-benzoyloxy substrates, several substrates (**6**, **7**, **9** and **10**) were pyrolyzed. In every example (Tables 2 and 3), benzoic acid was formed as a major product (presumably via hydrogen atom abstraction by the benzoyloxy radical). The fate of the amine radical was also monitored. As expected, the thermal decompositions resulted in very complex mixtures as shown by the ^1H NMR spectra and TLC of the crude products. Nevertheless, several products were isolated and characterized. The pyrolysis results with **6** and **7** are shown in Table 2. Analysis of the product architectures suggested that *N*-(benzoyloxy)amines undergo N–O bond cleavage to give aminyl radical formation.

Several experiments support the intermediacy of aminyl radicals. As shown in Table 2, compound **6** was pyrolyzed in refluxing $CHCl_3$ (under N_2) in the presence and absence of excess benzaldehyde (PhCHO), a known radical trap.[11a] The *N*-hexylbenzamide **6a** was formed in 30% isolated yield along with unreacted **6** and benzoic acid. Since benzoic acid was formed during the pyrolysis of every *N*-benzoyloxyamine tested, the discussion will focus on the fate of the amine component. Pyrolysis in refluxing chloroform in the presence of excess benzaldehyde generated the amide **6a**

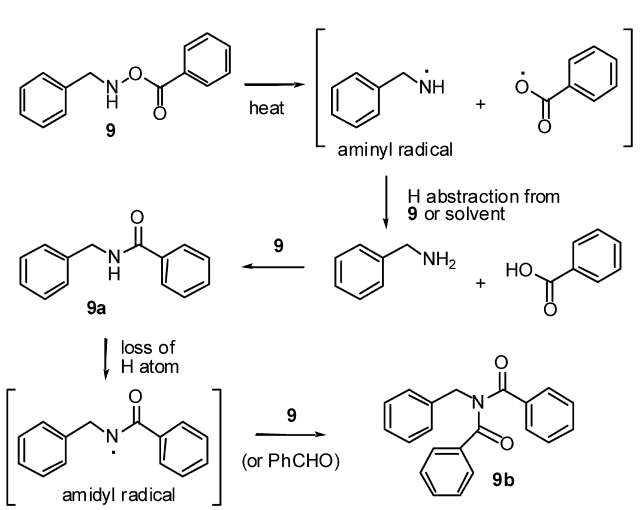


Scheme 2.

(22%) and the symmetrical imide **6b** (27%). Even though the mass recoveries were low, the identification of imide **6b** is compelling evidence for radical intermediates as an ionic pathway to **6b** is unlikely. Likewise, thermolysis of cyclohexyl derivative **7** gave the *N*-cyclohexylbenzamide **7a** (11%). Pyrolysis of **7** in the presence of benzaldehyde gave benzamide **7a** (27%) and a benzoylated adduct **7b** (7%). In short, these product are readily accessed via radical processes involving initial aminyl and later amidyl radicals.

The *N*-(benzoyloxy)-*t*-octylamine **8** had the highest decomposition temperature by DTA and the slowest decomposition rate in solution. After pyrolysis for 42 h in a sealed vessel at 126°C in the presence of CH_3CN, 42% of the unreacted **8** was recovered. Benzoic acid (50% yield) was the only pure product isolated from the crude mixture. Not surprisingly, the decomposition of **8** in the presence of benzaldehyde under refluxing chloroform (e.g. 61°C) also had a very slow rate. Based upon the TLC and ^{1}H NMR of the crude mixture, the bulk of **8** remained after 72 h at reflux. Therefore, the experiment was repeated at higher temperature. Compound **8** and benzaldehyde (2 equiv.) were dissolved in $CDCl_3$ and placed in a sealed reaction vessel and heated to 170°C. CAUTION: a violent explosion took place after 9 h. The products were not determined. Due to safety concerns, the reaction was not repeated and further solution studies with **8** were abandoned.

As shown in Table 3, pyrolysis of *N*-benzyl derivative **9** in refluxing $CHCl_3$ gave both amide **9a** and imide **9b**. The fact that **9b** was isolated in the absence of benzaldehyde suggested that a *N*-benzoyloxyamine could also act as a benzoyl donor. A control experiment using phenethylamine and *N*-benzoyloxyamine **11** revealed efficient *O*- to *N*-benzoyl transfer to phenethylamine to generate *N*-(2-phenylethyl)benzamide **13** in good yield (Scheme 2). This



Scheme 3.

transfer process has also been observed in studies with *N*-benzoyloxy-substituted peptides.[3]

It is plausible that hydrogen atom abstraction by the initially formed aminyl radical (generated from homolysis of **9**) could form benzyl amine in situ. As shown in Scheme 3, this amine in turn could be *N*-benzoylated by **9** to form *N*-benzylbenzamide **9a**. Subsequent H atom abstraction from **9a** would generate a stable amidyl radical, which could *N*-benzoylate via radical addition to **9** followed by formation of imide **9b** and loss of a stable nitroxyl radical. The role of **9** as a benzoyl group donor is likely replaced by benzaldehyde, when benzaldehyde is present and would require a loss of an H atom for **9b** formation.

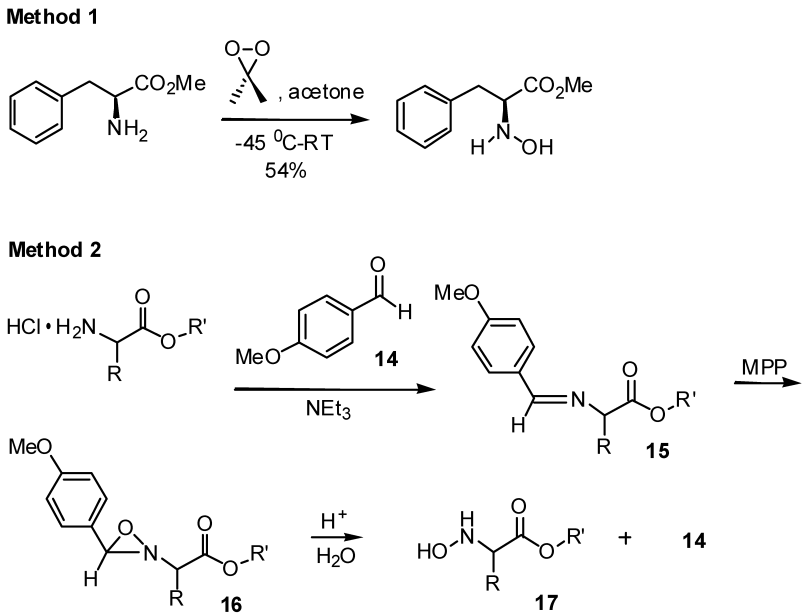
Both imide **6b** and **9b** are formed in higher yields in the presence of benzaldehyde as there are more benzoyl sources present during these reactions. This finding is supported by the fact that the product distribution is also time-dependent. A time-course pyrolysis study with **6** in 2 equiv. of benzaldehyde revealed that the ratio of amide **6a** to imide **6b** went from 1:10 at short reaction times (when copious amounts of benzaldehyde still remained) to approximately 1:1 upon completion of the reaction (with only trace levels of benzaldehyde remaining).

Interestingly, the *N*-methylbenzylamine adduct **10** gave dealkylated products **9a** and **10a** (Table 3). Low levels of benzaldehyde were also generated during the course of this 'benzaldehyde-free' pyrolysis (^{1}H NMR singlet: ~10 ppm). These dealkylated materials (**9a** and **10a**) are likely formed via imine intermediates, which cleave to form the free benzylamine or methylamine. These in turn may be *N*-benzoylated by **10** (or newly generated benzaldehyde) to form the observed adducts. Although speculative, this proposed dealkylation mechanism is supported by the observation of benzaldehyde (an imine cleavage product) during the 'benzaldehyde-free' pyrolysis reaction and the known disproportionation of aminyl radicals to amines and imines.[11b]

Having a better understanding of the thermal properties of **6**-**12**, we explored the scope and limitations of the synthetic method to access the *N*-benzoyloxyamines in general.

2.2. Synthetic scope and limitations

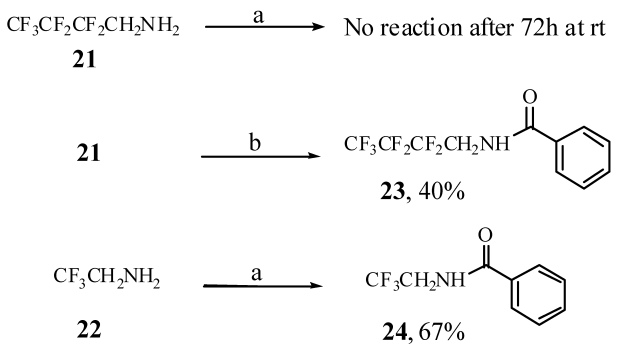
Having already probed the role of steric factors in the BPO-mediated process,[7] we were interested in what electronic perturbations were tolerated by this reaction. How was the yield influenced by substituents adjacent to the amine center? For example, would an electron withdrawing group (EWG) on the α- or β-carbon adjacent to the amine center reduce the yield of **2**? In order to test this premise, several diamines, fluorinated amines, α-aminoacids and α- and



Scheme 4.

β-aminoacid derivatives were chosen as possible substrates for *N*-oxidation (i.e. *N*-benzoyloxylation) with BPO.

Beyond their role as models of electronically-perturbed amines, novel aminoacids have obvious synthetic value. Moreover, there are only limited entries to chiral *N*-(hydroxy)aminoacid derivatives via direct amine oxidation. Prior work by Danishefsky showed that aminoacid derivatives (Method 1, Scheme 4) could be directly oxidized to the corresponding *N*-(hydroxyl)amines with 2,2-dimethyldioxirane.[12] An alternative approach by Chimiak,[13] reacted α-aminoesters (Method 2, Scheme 4) with *p*-anisaldehyde (**14**) to give the corresponding imine **15**. The imine **15** was then oxidized with monoperphthalic acid (MPP) to the corresponding oxaziridine **16**, which gave the *N*-(hydroxy)aminoacid **17** during heating with hydrochloric acid. The yields were typically 40%. The limitations of these earlier methods include low yields and production of the *N*-(hydroxyl)amine component in the uncapped, free *N*-(hydroxyl)amine form. Subsequent acylation of this free hydroxylamine form may be problematic due to selectivity issues (involving N and O). In contrast, the *N*-(benzoyloxy)amines are 'O-capped' systems, which can be selectively *N*-acylated with acid chlorides.[3,5]



Scheme 5. *Reagents*: (a) BPO, CH_2Cl_2, aq. buffer pH 10.5, rt; (b) BPO, aq. buffer pH 10.5, $CHCl_3$, reflux for 48 h.

Previous work with primary and secondary amines resulted in high yields of the respective *N*-(benzoyloxy)amines.[7,10] Initially, the optimized process was expected to allow for selective oxidation of a primary amine in the presence of a tertiary amine, e.g. *N*,*N*-dimethylpropanediamine (Fig. 2). It was presumed that tertiary amines would be inert and would not interfere with distal primary amine oxidation. To test this premise, *N*,*N*-dimethyl-propanediamine was reacted under the standard conditions[7] with BPO. After consumption of the starting amine, multiple products were visible by TLC and column chromatography provided complex mixtures. This suggested that the tertiary amine adducts were unstable. A simpler model was chosen for further investigation.

Tributylamine was selected due to its symmetry and relatively high molecular weight for ease in isolation of reactant products. As shown in Figure 2, tributylamine was reacted with BPO under the standard conditions. Multiple products were observed by TLC and the crude decomposed upon standing overnight. The only product isolated in an appreciable quantity was tributylamine *N*-oxide **18** (9%). This suggested that the *N*-(benzoyloxy)amine **19** was generated in situ and converted to the more stable *N*-oxide or further decomposed. Separate synthesis of *N*-(benzoyloxy)-*N*,*N*-dibutylamine **20** and ^{1}H NMR comparison suggested that none of the major products were generated by *N*-dealkylation of **19** (a pathway demonstrated in our earlier pyrolysis studies with **10**). Indeed, an earlier report by Buckley was consistent with our findings and noted that the tertiary *N*-(benzoyloxy)amines decomposed via radicals.[10,14,15] Therefore, one potential limitation in this BPO-process is the presence of tertiary amine centers, which give rise to radical chemistry at room temperature.

With primary, secondary, and tertiary amines characterized, the next amine series to be evaluated were the electron-poor fluorinated amines. In general, fluorinated amines typically contain fluorine atoms in the β-position (or even more distal

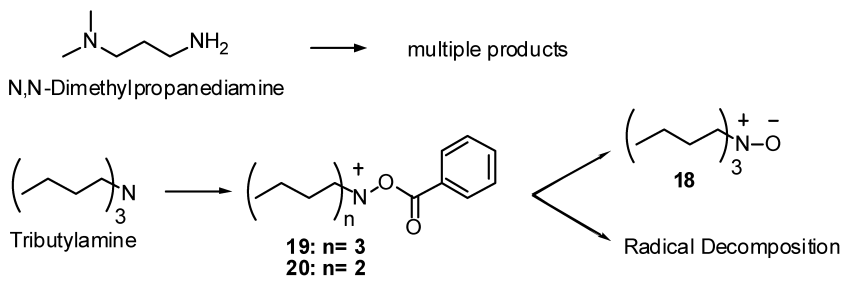


Figure 2. Tertiary amine oxidation products.

to N) due to the instability of α-fluorinated amines. As shown in Scheme 5, the respective amines, 1*H*,1*H*-heptafluorobutylamine **21** and 2,2,2-trifluoroethylamine **22**, were treated with BPO in a biphasic solution (CH_2Cl_2/aqueous buffer pH=10.5) at room temperature.[10] 1*H*,1*H*-heptafluorobutylamine did not react after 72 h under these conditions. The reaction was repeated in refluxing $CHCl_3$ and *N*-(1*H*,1*H*-heptafluorobutyl)benzamide **23** was isolated in 40% yield. In contrast, the reaction of **22** with BPO (biphasic conditions) at 25°C gave *N*-(2,2,2-trifluoroethyl)-benzamide **24** (Scheme 5) in 67% yield. Neither fluorinated alkylamine provided the desired *N*-(benzoyloxy) adduct. Instead, amide products were isolated and assigned by their respective IR and ^{1}H NMR spectra. For example, *N*-(2,2,2-trifluoroethyl)benzamide showed a characteristic band at 1678 cm^{-1} in the IR spectrum; whereas the *N*-benzoyloxy 'ester' carbonyl usually appears at 1720 cm^{-1}. The ^{1}H NMR spectrum of *N*-(2,2,2-trifluoroethyl)benzamide exhibited a multiplet at δ 4.00 ppm and a broad singlet at δ 6.80 ppm, which were indicative of the amide CH_2 and NH, respectively. Based upon these results, the acylation pathway is clearly favored for the fluorinated alkylamines, whereas the *N*-oxidation pathway is preferred with *N*-alkyl-amines under the same conditions. The putative mechanistic pathways are illustrated in Figure 3.

Previous work in our laboratories showed that the *N*-oxidation pathway to form **2** in Figure 3 was pH-dependent and favored at pH 10.5 with aliphatic amines.[5,7] Perhaps not surprisingly, this optimum pH value is in the same range as the pK_a for the ammonium ions of alkylamines.[5] Moreover, the aliphatic 1° amines also generated their corresponding amides (**3**, Fig. 3) at higher pH (11–12), in lieu of the *N*-benzoyloxyamine product **2**.

Fluorinated alkylamines are weaker bases than alkylamines. For example, the ammonium salt of 2,2,2-trifluoroethyl-amine has a pK_a=5.7,[16] whereas the ethylamine counterpart

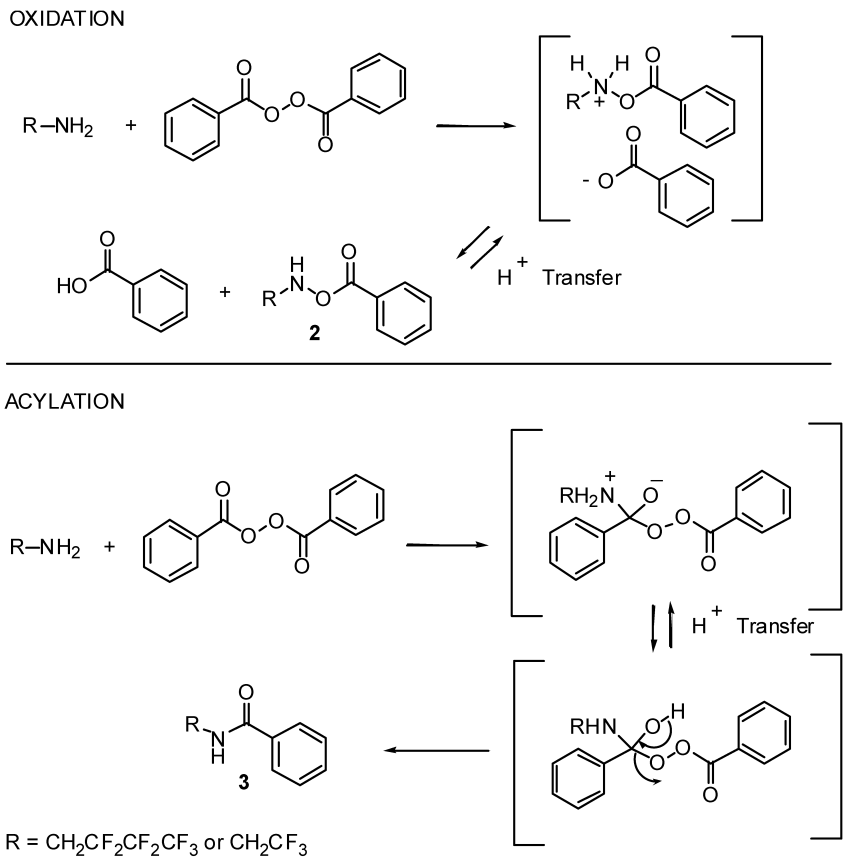
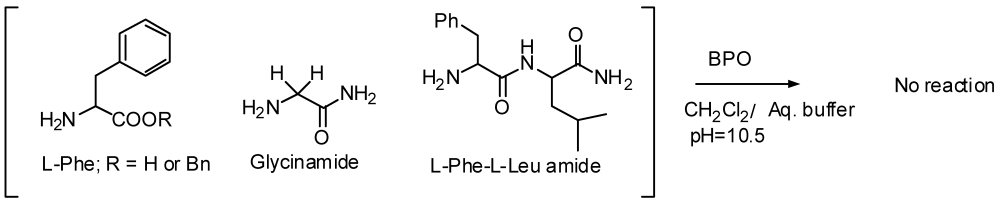
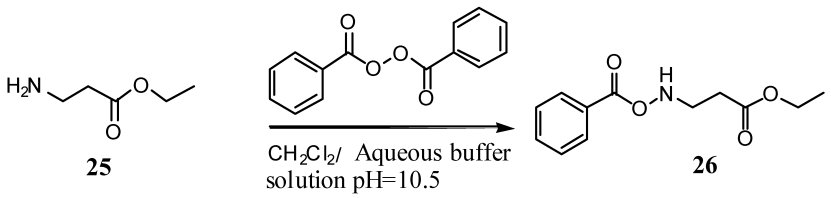


Figure 3. Possible mechanistic pathways for the reaction of fluorinated alkylamines with BPO.



Scheme 6.



Scheme 7.

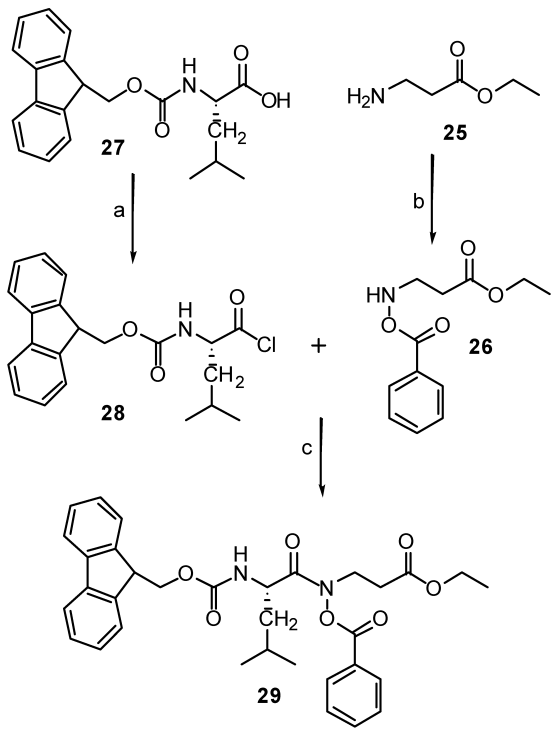
has a pK_a of 10.81.[17] Based upon the earlier pH dependence of the BPO method, it seemed likely that lowering the pH of the water phase closer to the pK_a of the fluorinated amines might influence the mechanism of this process and favor the *N*-oxidation pathway.

The reaction of 2,2,2-trifluoroethylamine with BPO under biphasic conditions at different pH values was performed. This was accomplished by using various aqueous buffer solutions. At pH=7.3 and 8.3, no reaction occurred after stirring overnight. At pH 9.3 traces of *N*-(2,2,2-trifluoroethyl)benzamide **24** were detected. At pH 10.5 the amide **24** was isolated in 67% yield. This study showed that having a lower pH value of the aqueous solution (closer with the pK_a of the ammonium ion of 2,2,2-trifluoroethylamine) did not facilitate the *N*-oxidation pathway. This is in direct contrast to the pH dependency of aliphatic (non-fluorinated) amine systems.

Attempts to apply this biphasic technology to the oxidation of α-aminoacid derivatives were not successful (Scheme 6). The respective systems of L-phenylalanine, L-phenylalanine benzyl ester, glycinamide and L-phenylalanine-L-leucine amide were each treated with BPO, following the general procedure.[7] No reaction occurred after 48 h in each case. These findings were rationalized by relating the amine's propensity for oxidation to the electron richness and nucleophilicity of the amine center.[18] One possible explanation is that the presence of the carbonyl group on the α-carbon inductively withdraws electron density from the nitrogen atom, making it less available for a nucleophilic attack on the peroxy-oxygen of BPO (see oxidation pathway—Fig. 3). This resistance to *N*-oxidation is similar to the fluorinated amines, which are also electron-poor amine systems.

To further illustrate that the oxidation process is strongly dependent upon the electron density of the starting amine, β-alanine ethyl ester **25** was treated with BPO under biphasic conditions at room temperature.[7,10] In this case, *N*-(benzoyloxy)-β-alanine ethyl ester **26** was isolated in 76% (Scheme 7).[3] Therefore, simple insertion of an additional methylene unit was sufficient to regain sufficient amine nucleophilicity. The fact that electron poor amines were not oxidized by BPO illustrated another limitation of this method. However, this finding also suggested that selective *N*-oxidation could be attained with substrates containing both electron rich and electron poor amine centers (e.g. lysine or ornithine).

Although the α-aminoacid substrates were unreactive, their β-derivatives do allow access to *N*-hydroxy-containing peptides. Prior work demonstrated the clean acylation of *N*-(benzoyloxy)amines with acid chlorides.[3] Moreover, Carpino's FMOC-protected aminoacid chloride[19] was shown to acylate *N*-(benzoyloxy)amines without racemization.[3] Recognizing that these two technologies could be combined to form β-aminoacid containing peptides, a



Scheme 8. *Reagents*: (a) $SOCl_2$, reflux, followed by concentration; (b) BPO, CH_2Cl_2, aq. carbonate buffer, pH 10.5; (c) CH_2Cl_2, aq. carbonate buffer, pH 10.5.

convergent approach involving a one-pot, two-step synthesis was developed. As shown in Scheme 8, FMOC-L-leucine **27** was converted to its acid chloride **28** in refluxing thionyl chloride, followed by concentration under high vacuum.[3,19] Conversion was monitored by the IR carbonyl resonance (**27**: 1717 cm^{-1}, **28**: 1789 cm^{-1}). The crude acid chloride acylated **26** to give the final hybrid peptide **29** in 85% isolated yield, for an overall yield of 61% from the starting amine, **25**.

3. Conclusions

By investigating the thermal behavior of a series of *N*-(benzoyloxy)amines, several trends became apparent. First, *N*-(benzoyloxy)amines derived from 2° amines (such as **10**) undergo both N–O and N–C bond cleavage and give rise to very complex product mixtures. Second, *N*-methylation of a *N*-benzoyloxyamine resulted in a lower decomposition temperature by TGA–DTA analysis (e.g. **9** and **10**, **11** and **12**). This is consistent with a more facile homolytic process giving rise to the more stable 2° aminyl radical. Third, both aminyl and amidyl radicals are generated during the thermal decomposition of *N*-(benzoyloxy)amines. In terms of synthetic limitations, BPO-mediated amine oxidation was problematic for both tertiary and electron deficient amines. Tertiary amines were oxidized, but rapidly decomposed. Both the fluoroamine systems and the α-aminoacid derivatives did not undergo *N*-oxidation using the biphasic conditions employed successfully with 1° and 2° *N*-alkylamines.[7] In short, the electron density of the amine nitrogen was shown to strongly influence the BPO-mediated oxidation process.

Lastly, a new method was developed to access the *N*-(hydroxy)-β-aminoacids in an *O*-acylated form conducive for subsequent *N*-acylation. This approach should allow for the synthesis of a new class of *N*-hydroxyamide-containing peptides with unique functionality. In conclusion, the diverse chemistries available to the *N*-benzoyloxyamines make them attractive systems for future study.

4. Experimental

4.1. Materials and methods

All reagents were used without purification unless otherwise noted. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. The fluorinated amine starting materials were generously provided by SynQuest Laboratories, Inc. of Gainesville, FL. The mass spectra data were acquired at the University of Florida by Dr David Powell. The pH 10.5 buffer solution was prepared by adding 1.5N aqueous NaOH to aqueous $NaHCO_3$. The TLC and column chromatography solvents are expressed in vol%. Ammonia-containing solutions were prepared by measuring out concentrated aqueous NH_4OH in the listed vol%. Silica gel (32–63 μm) was used for flash chromatography. Storage recommendations for the oxidized amines are 0°C under argon (months) or as an HCl salt under the same conditions (years). All the thermal decompositions were performed in a sealed glass reactor in dry acetonitrile (unless otherwise indicated), in an inert atmosphere. Benzaldehyde was distilled prior to use. Mass spectra were obtained typically using the fast atom bombardment (FAB) technique in magnetic scan mode. Masses from the matrix (e.g. *meta*-nitrobenzylalcohol) were used as reference points.

4.2. TGA–DTA studies

Respective samples of **6**-**12** were placed into a sample holder and TGA–DTA analysis were performed with a STD 2960 instrument, where the flow rate of the purge N_2 gas is 96 mL/min. A controlled heating rate (at 10°C/min) up to 300°C was used.

4.3. General procedure for amine oxidation

A solution of benzoyl peroxide (BPO, 1 equiv.) in CH_2Cl_2 (5 mL/mmol BPO) was added quickly to a mixture of the amine (1 equiv.) and a pH 10.5 aqueous buffer solution (5 mL/mmol amine) at room temperature. [Note: using 1–1.1 equiv. of BPO facilitated the isolation of the intermediate *N*-(benzoyloxy)amines, which often had R_f values close to that of BPO.][7] TLC was used to monitor the consumption of the starting amine, using both UV and iodine vapor staining for visualization as needed. After the reaction was complete, the aqueous layer was extracted three times with fresh CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude residue was subjected to flash column chromatography for purification of the products. In this manner, compounds **6**-**9** and **11** were prepared by published methods.[7]

4.4. General pyrolysis procedure

Compounds **6** and **9** were initially pyrolyzed in $CHCl_3$ with and without benzaldehyde. For pyrolyses with benzaldehyde, benzaldehyde (0.181 g, 1.8 mmol) and the *N*-(benzoyloxy)amine (0.9 mmol) were dissolved in $CHCl_3$ (7 mL). In experiments without added benzaldehyde, the *N*-(benzoyloxy)amine (0.9 mmol) was dissolved in $CHCl_3$ (7 mL). The respective solution was refluxed under a N_2 atmosphere. Compounds **7**, **8**, and **10** were pyrolyzed in CH_3CN at 126°C due to the slow rates observed in $CHCl_3$. The pyrolyses in CH_3CN were also conducted in the presence and absence of benzaldehyde using the molar ratios listed above in $CHCl_3$. The conversion of the *N*-(benzoyloxy)amine was monitored by TLC and ^1H NMR. Multiple new spots were visible by TLC. The mixture was concentrated under high vacuum and the residue was dissolved in $CDCl_3$. An ^1H NMR spectrum of the crude mixture was used to quantify the reaction mixture via an internal standard, $C_2H_2Cl_4$ (47.0 mg, 0.28 mmol). The standard was added to the crude and gave a quantifiable ^1H NMR singlet at 5.90 ppm. The crude was then subjected to flash column chromatography (often eluting with 100% $CHCl_3$). Several products were isolated (typically the amide and imide) along with benzoic acid. Using the above ^1H NMR integration information, the respective yields were determined. The quantified NMR signals were well-resolved from other pyrolysis products and easily identified by their chemical shifts.

4.4.1. *N*-Hexylbenzamide 6a.[20] R_f=0.3 in 100% $CHCl_3$; ^1H NMR ($CDCl_3$): δ 7.77 (m, 2H, aromatic), 7.41 (m, 3H, aromatic), 6.30 (br s, 1H), 3.4 (q, 2H), 1.60 (m, 2H), 1.30 (m, 6H), 0.90 (t, 3H); ^{13}C NMR ($CDCl_3$): δ 167.5, 134.8, 131.1, 128.4, 126.8, 40.1, 31.5, 29.5, 27.6, 22.5, 14.0.

4.4.2. *N*-Hexyldibenzamide 6b. R_f=0.40 in 100% $CHCl_3$; ^1H NMR ($CDCl_3$): δ 7.41 (m, 4H, aromatic), 7.20 (m, 6H, aromatic), 4.00 (t, 2H), 1.80 (m, 2H), 1.40 (m, 2H), 1.36 (m, 4H), 0.90 (t, 3H); ^{13}C NMR: δ 175.4, 137.9, 132.7, 129.7, 129.2, 48.5, 32.5, 30.0, 27.8, 23.5, 15.0.

4.4.3. *N*-Cyclohexylbenzamide 7a.[20] R_f=0.35 in 100% $CHCl_3$; ^1H NMR ($CDCl_3$): δ 7.75 (m, 2H, aromatic), 7.45 (m, 3H, aromatic), 6.0 (br, s, 1H), 4.0 (m, 1H), 1.62 (m, 10H).

4.4.4. *N*-(Benzoyloxy)-*N*-cyclohexylbenzamide 7b. R_f=0.42 in 100% $CHCl_3$; ^1H NMR ($CDCl_3$): δ 8.0 (m, 2H, aromatic), 7.59 (m, 2H, aromatic), 7.35 (m, 6H, aromatic) 4.35 (m, 1H), 1.65 (m, 10H). High resolution mass spectrum: theory for $C_{20}H_{21}NO_3$ (M+1)=324.1599, found M+1=324.1556.

4.4.5. *N*-Benzylbenzamide 9a.[20] R_f=0.23 in 20% EtOAc/hexane; ^1H NMR ($CDCl_3$) δ 7.80 (m, 2H, aromatic), 7.40 (m, 8H, aromatic), 6.42 (br, s, 1H), 4.62 (d, 2H). High resolution mass spectrum: theory for $C_{14}H_{13}NO$ (M+1)=212.1075, found M+1=212.1021.

4.4.6. *N*-Benzyldibenzamide 9b. ^1H NMR ($CDCl_3$): δ 7.80 (m, 4H, aromatic), 7.41 (m, 6H, aromatic), 7.20 (m, 5H, aromatic), 5.22 (s, 2H).

4.4.7. *N*-Methylbenzamide 10a.[20] R_f=0.3 in 20% EtOAc/hexane; ^1H NMR ($CDCl_3$) δ 7.70 (m, 2H, aromatic), 7.40 (m, 3H, aromatic), 6.1 (br, s, 1H), 2.95 (d, 3H).

4.4.8. *N*-(Benzoyloxy)benzylmethylamine 10. A solution of BPO (0.96 g, 4 mmol) in CH_2Cl_2 (30 mL) was added quickly to a mixture of benzylmethylamine (0.484 g, 4 mmol) in 30 mL of an aqueous buffer solution (pH=10.5) at room temperature. The disappearance of the starting material was monitored by TLC (2% NH_4OH/MeOH, R_f=0.30). After the reaction was complete, the organic layer was separated and the water layer was extracted twice with 25 mL of CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. The product mixture was subjected to flash column chromatography, eluting with 20% EtOAc/hexane, to isolate the *N*-(benzoyloxy)benzylmethylamine **10** (0.90 g, 93%).

Compound **10**. R_f=0.37 in 20% EtOAc/hexane. IR ($CDCl_3$) 3155, 2900, 1735, 1602, 1452, 1263, 1093, 1059, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.90 (m, 2H, aromatic), 7.35 (m, 8H, aromatic), 4.15 (s, 2H), 2.9 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.9, 135.6, 132.9, 129.4, 129.3, 128.3, 128.2, 127.7, 65.0, 46.0. Note: there was significant overlap in the 129–128 ppm range.

4.4.9. *N*-(Benzoyloxy)methylphenethylamine 12. A solution of BPO (0.96 g, 4 mmol) in CH_2Cl_2 (30 mL) was added quickly to a mixture of methylphenethylamine (0.543 g, 4 mmol) in 30 mL of an aqueous buffer solution (pH=10.5) at room temperature. The disappearance of the starting material was monitored by TLC (2% NH_4OH/MeOH, R_f=0.35). After the reaction was complete, the organic layer was separated and the water layer was extracted twice with 25 mL of CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. The product mixture was subjected to flash column chromatography, eluting with 20% EtOAc/hexane, to isolate the *N*-(benzoyloxy)-methylphenethylamine **12** (0.88 g, 86%).

Compound **12**. R_f=0.47 in 20% EtOAc/hexane. IR ($CDCl_3$): 3154, 2968, 1732, 1602, 1452, 1261, 1081, 1061, 1025 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.01 (m, 2H, aromatic), 7.35 (m, 8H, aromatic), 3.22 (t, 2H), 2.90 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 165.1, 139.2, 133.0, 129.4, 129.1, 128.6, 128.4, 128.3, 126.2, 62.6, 47.0, 33.7. Anal/calcd for $C_{16}H_{17}NO_2$: C,75.27; H, 6.71; N, 5.48. Found: C, 75.23; H, 6.68; N, 5.44.

4.4.10. Reaction of phenethylamine with 11 to give 13. Phenethylamine (0.050 g, 0.413 mmol) and *N*-(benzoyloxy)phenethylamine[7] (0.099 g, 0.413 mmol) were dissolved in CH_3CN (10 mL). The solution was stirred under nitrogen. No reaction occurred after 24 h at room temperature by TLC. The solution was heated to reflux (81°C). The starting material *N*-(benzoyloxy)phenethylamine was consumed after 6 h as shown by TLC (R_f=0.45 in 100% $CHCl_3$). The crude product was subjected to prep TLC (100% $CHCl_3$) to give *N*-(phenethyl)benzamide (66 mg, 0.293 mmol) in 71% yield. *N*-(Phenethyl)-benzamide, **13**: ^1H NMR ($CDCl_3$): δ 7.60–7.10 (m, 10H), 6.08 (br s, 1H), 3.61 (q, 2H), 2.85 (t, 2H).

4.4.11. Tributylamine *N*-oxide 18.[20] Tributylamine (0.45 g, 2.4 mmol) was reacted with BPO (0.65 g, 2.7 mmol) using the general procedure. After stirring overnight, the reaction was worked up. The crude was subjected to flash chromatography using the following gradient: 5% EtOH/$CHCl_3$ to 60% EtOH/$CHCl_3$ and then 3% NH_4OH/MeOH. A complex mixture of products was recovered. The *N*-oxide was isolated in 9% yield (0.05 g). TLC with 3% NH_4OH/MeOH (R_f=0.45) detected the *N*-oxide by iodine vapor.

Compound **18**. ^1H NMR ($CDCl_3$): δ 3.34 (m, 6H), 1.72 (m, 6H), 1.36 (m, 6H), 0.93 (t, 9H); high resolution mass spectrum (FAB) theory for ($C_{12}H_{28}NO$) M+1=202.2171, found M+1=202.2149. Note: tributylamine gave the following: ^1H NMR ($CDCl_3$): δ 2.38 (t, 6H), 1.40 (m, 6H), 1.28 (m, 6H), 0.90 (t, 9H).

4.4.12. *N*-(Benzoyloxy)-dibutylamine 20. Dibutylamine (0.21 g, 1.6 mmol) was reacted with BPO (0.40 g, 1.6 mmol) using the general procedure. Disappearance of the starting amine was monitored by TLC ($CHCl_3$). Since the amine was not fully consumed after a day, an additional amount of BPO (0.17 g, 0.71 mmol) was added. Upon completion, the reaction was worked up and the crude product was subjected to flash chromatography (30% hexane/$CHCl_3$ to 10% hexane/$CHCl_3$). The oxidized amine (R_f=0.24 in 10% hexane/$CHCl_3$) was isolated in

94% yield (0.38 g). ^{1}H NMR ($CDCl_3$) δ 8.03 (d, 2H), 7.58 (t, 1H), 7.44 (t, 2H), 2.98 (t, 4H), 1.59 (m, 4H), 1.37 (m, 4H), 0.92 (t, 6H). Anal. calcd for $C_{15}H_{23}O_2N$: C, 72.25; H, 9.30; N, 5.62. Found: C, 71.95; H, 9.22; N, 5.56.

4.4.13. Reaction of 22 and BPO using different aqueous buffer solutions. A solution of BPO (0.960 g, 4 mmol, dissolved in 20 mL CH_2Cl_2) was added quickly at room temperature to a vigorously stirred mixture of 2,2,2-trifluoroethylamine hydrochloric acid salt (0.484 g, 4 mmol) and 20 mL of either a pH 7.3 buffer solution (50 mL of 0.1 M KH_2PO_4 and 41.1 mL of 0.1 M NaOH mixed together and diluted with deionized water to a final volume of 100 mL) or a pH 8.3 buffer solution (50 mL of 0.025 M borax and 17.7 mL of 0.1 M HCl mixed together and diluted with deionized water to a final volume of 100 mL) or a pH 9.3 buffer solution (50 mL of 0.025 M borax and 3.6 mL of 0.1 M NaOH mixed together and diluted with deionized water to a final volume of 100 mL). The organic layer was checked by TLC. After 40 h there was no evidence of product formation at pH 7.3 or 8.3 (the only spot visible by UV and iodine detection was BPO, R_f=0.6 in 100% $CHCl_3$). After 24 h a trace of 2,2,2-trifluoroethylbenzamide **24** was detected in the pH 9.3 reaction. Overall, there was no evidence of *N*-(benzoyloxy)-2,2,2-trifluoroethylamine formation.

4.4.14. *N*-(1*H*,1*H*-Heptafluorobutyl)benzamide 23. A solution of BPO (0.484 g, 2 mmol, dissolved in 10 mL CH_2Cl_2) was added quickly at room temperature to a vigorously stirred mixture of 1*H*,1*H*-heptafluorobutylamine (0.398 g, 2 mmol) and 10 mL of a pH 10.5 carbonate buffer solution. Since it was difficult to monitor the consumption of the 1*H*,1*H*-heptafluorobutylamine by TLC (it is not visible by iodine or UV detection), the organic layer was checked by TLC for the formation of the expected UV active products. After 58 h at room temperature, BPO was the only visible spot on the TLC plate (R_f=0.6 in 100% chloroform).

The reaction was run again in deuterated chloroform. BPO (0.242 g, 1 mmol) was dissolved in $CDCl_3$ (7 mL) and 1*H*,1*H*-heptafluorobutylamine (0.199 g, 1 mmol) was added to the mixture. A ^{1}H NMR spectrum was taken at time zero. 1*H*,1*H*-Heptafluorobutylamine gave a characteristic triplet at δ 3.50 ppm (CF_2CH_2N). After 24 h at room temperature, the TLC showed only BPO (R_f=0.6 in 100% chloroform). There was no evidence of product formation by TLC or ^{1}H NMR. Therefore, the reaction mixture was heated to reflux ($CDCl_3$ bp=60.9°C, 1*H*,1*H*-heptafluorobutylamine bp=72°C). After another 24 h under reflux, TLC showed only one new UV and iodine active spot (R_f=0.32 in 20% EtOAc/hexane). The ^{1}H NMR spectrum of the crude indicated that the starting material 1*H*,1*H*-heptafluorobutylamine was not totally consumed and two multiplets were observed at δ 3.85 and 4.20 ppm. The crude product was subjected to flash chromatography. Only *N*-(1*H*,1*H*-heptafluorobutyl)-benzamide **23** (R_f=0.32 in 20% EtOAc/hexane) was isolated in a 40% yield (based on approximate 70% conversion of the starting material). The compound, which gave rise to the other multiplet at δ 3.85 ppm, was not isolated. **23**: IR ($CDCl_3$): 3461, 1682, 1520, 1489, 1262, 1230, 918 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.79 (m, 2H, aromatic), 7.45 (m, 3H, aromatic), 6.40 (broad s, 1H, NH), 4.22 (m, 2H, CF_2CH_2N).

4.4.15. *N*-(2,2,2-Trifluoroethyl)benzamide 24.[20] A solution of BPO (0.960 g, 4 mmol, dissolved in 20 mL CH_2Cl_2) was added quickly at room temperature to a vigorously stirred mixture of 2,2,2-trifluoroethylamine hydrochloric acid salt (0.484 g, 4 mmol) and a pH 10.5 carbonate buffer solution (20 mL). The 2,2,2-trifluoroethylamine was consumed after 15 h as shown by TLC (R_f=0.21 in 2% NH_4OH/MeOH). The organic layer was separated. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. The residue was subjected to flash column chromatography, eluting with 100% methylene chloride to give 2,2,2-trifluoroethylbenzamide **24** as a white crystalline solid (0.55 g, 67%).

Compound **24**. R_f=0.23 in 100% methylene chloride. IR ($CDCl_3$) 3460, 1679, 1523, 1490, 1391, 1260, 914, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.69 (m, 2H, aromatic), 7.35 (m, 3H, aromatic), 6.89 (s, 1H, NH), 4.00 (m, 2H, CF_3CH_2N).

4.4.16. *N*-(Benzoyloxy)-β-alanine ethyl ester 26. A solution of BPO (1.21 g, 5 mmol) dissolved in 30 mL CH_2Cl_2 was added quickly at room temperature to a vigorously stirred mixture of β-alanine ethyl ester HCl salt (0.768 g, 5 mmol) and 30 mL of a pH 10.5 carbonate buffer solution. The starting material was consumed after 10 h as shown by TLC (R_f=0.23 in 2% NH_4OH/MeOH). The organic layer was separated. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. The residue was subjected to flash column chromatography, eluting with 100% methylene chloride to give *N*-(benzoyloxy)-β-alanine ethyl ester **26** as a colorless oil (0.85 g, 76%). R_f=0.35 in 100% methylene chloride. IR ($CDCl_3$) 3240, 2985, 1725, 1602, 1452, 1270, 1194, 1026, 926, 720 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.03 (m, 2H, aromatic), 7.45 (m, 3H, aromatic), 4.18 (q, 2H, OCH_2), 3.45 (t, 2H, $NHCH_2$), 2.65 (t, 2H, CH_2CO), 1.27 (t, 3H, CH_3). Anal. calcd for $C_{12}H_{15}O_4N$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.85; H, 6.34; N, 5.90. ^{13}C NMR ($CDCl_3$): δ 171.74, 166.56, 133.36, 129.31, 128.45, 128.17, 60.76, 47.78, 32.15, 14.09. High resolution mass spectrum (FAB) theory for ($C_{12}H_{15}O_4N$) M+1=238.1000; found: M+1=238.1080.

4.4.17. *S*-3-{Benzoyloxy-[2-(9*H*-fluoren-9-ylmethoxycarbonylamino)-4-methyl-pentanoyl]-amino}-propionic acid ethyl ester, 29. A solution of BPO (0.79 g, 3.3 mmol) in CH_2Cl_2 (17 mL) was quickly added to a stirring solution of β-alanine ethyl ester hydrochloride salt (0.50 g, 3.2 mmol) in pH 10.5 buffer (17 mL). The consumption of the β-aminoester was monitored by TLC (2% NH_4OH/MeOH, R_f=0.23). The *N*-oxidized β-aminoester **26** was generated in 72% yield as evidenced by ^{1}H NMR integration of the crude.

N-FMOC-L-Leucine **27** (1.27 g, 3.6 mmol) was refluxed for 4 h in an excess of freshly distilled thionyl chloride (4.5 mL,

59 mmol) dissolved in CH_2Cl_2 (25 mL). The reaction was monitored by the conversion of the carbonyl IR stretch from 1717 to 1789 cm^{-1}. The acid chloride **28** was concentrated down to provide a residue. Benzene was added and the solution was re-concentrated under vacuum in order to remove the remaining $SOCl_2$. The crude was then transferred to the oxidized alanine mixture **26** with a minimum of CH_2Cl_2. The reaction was stirred at room temperature for 2 days. The aqueous phase was extracted three times with fresh CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. The residue was subjected to flash chromatography (1% EtOH/1% EtOAc/$CHCl_3$, R_f=0.34). The peptide **29** was isolated in 85% yield. The overall yield was 61% for the 2 steps. **29**: ^{1}H NMR ($CDCl_3$): δ 8.08 (d, 2H), 7.73 (d, 2H), 7.63 (t, 1H), 7.57 (t, 2H), 7.47 (t, 2H), 7.36 (t, 2H), 7.28 (t, 2H), 5.41 (d, 1H), 4.63 (m, 1H), 4.38 (d, 2H), 4.18 (m, 3H), 4.04 (q, 2H), 2.71 (t, 2H), 1.61 (m, 1H), 1.50 (m, 2H), 1.20 (t, 3H), 0.85 (d, 3H), 0.70 (br s, 3H); ^{13}C NMR with DEPT analysis ($CDCl_3$): δ 173.65 (C═O), 171.00 (C═O), 164.12 (C═O), 156.15 (C═O), 144.14 (quaternary C), 143.92 (quaternary C), 141.44 (quaternary C), 134.89 (CH), 130.30 (CH), 129.57 (CH), 129.13 (CH), 128.74 (CH), 127.88 (CH), 127.26 (CH), 126.48 (CH), 125.34 (CH), 120.16 (CH), 67.32 (CH_2), 61.20 (CH_2), 50.07 (CH), 47.52 (CH), 44.83 (CH_2), 42.57 (CH_2), 32.66 (CH_2), 24.86 (CH), 23.73 (CH_3), 21.86 (CH_3), 14.49 (CH_3). High resolution mass spectrum (FAB) theory for ($C_{33}H_{37}O_7N_2$) M+1=573.2601; found: M+1=573.2593. Anal/calcd for $C_{33}H_{36}O_7N_2 \cdot 1H_2O$: C, 67.10; H, 6.48; N, 4.74; found: C, 67.45; H, 6.20; N, 4.75. Optical rotation $[\alpha]_D$=+25° (c=3.8, $CDCl_3$, 23°C).

Acknowledgements

The authors thank Dr Adam Alty and SynQuest Laboratories for their generous gift of the fluorinated amine starting materials. In related experiments Omar Shami generated the *N*-benzoyloxyamine HCl salts and conducted their long-term stability studies. The stable HCl salts allow for the long-term storage of these materials. Dr Richard Gardner assisted with the characterization of peptide **29**.

References

1. Bauer, L.; Exner, O. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 376–384.
2. Yale, H. L. *Chem. Rev.* **1943**, *33*, 209–256.
3. Wang, L.; Phanstiel, O., IV. *J. Org. Chem.* **2000**, *65*, 1442–1447.
4. Milewska, M. J.; Chimiak, A. *Synthesis* **1990**, 233–234.
5. Wang, Q. X.; King, J.; Phanstiel, O., IV. *J. Org. Chem.* **1997**, *62*, 8104–8108.
6. Wang, Q. X.; Phanstiel, O., IV. *J. Org. Chem.* **1998**, *63*, 1491–1495.
7. Phanstiel, O., IV; Wang, Q. X.; Powell, D. H.; Ospina, M. P.; Leeson, B. A. *J. Org. Chem.* **1999**, *64*, 803–806.
8. Guo, H.; Naser, S. A.; Ghobrial, G.; Phanstiel, O., IV. *J. Med. Chem.* **2002**, *45*, 2056–2063.
9. Bergeron, R. J.; Phanstiel, O., IV. *J. Org. Chem.* **1992**, *57*, 7140–7143.
10. Badescu, V. Synthesis and Thermal Study of a Series of *N*-Benzoyloxyamines and the Scope and Limitations of an Amine Oxidation Process. Masters Thesis, Department of Chemistry, University of Central Florida, 2000.
11. (a) Gitchell, A.; Simonaitis, R.; Heiklen, J. The Inhibition of Photochemical Smog. *J. Air Pollut. Control Assoc.* **1974**, *24*, 357–361. (b) Mackay, D.; Waters, W. A. *J. Chem. Soc. C* **1966**, 813.
12. Wittman, M. D.; Halcomb, R. L.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 1981–1983.
13. Pokonski, T.; Chimiak, A. *Tetrahedron Lett.* **1974**, *28*, 2453–2456.
14. Buckley, D.; Dunstan, S.; Henbest, H. B. *J. Chem. Soc.* **1957**, 4901–4904.
15. Geiger, W. B. *J. Org. Chem.* **1958**, *23*, 298–299.
16. Koppel, I.; Prodel, A.; Koppel, *J. Org. React. (Tartu)* **1990**, *27*(1–2), 74–86.
17. McMurry, J. *Organic Chemistry*; 4th ed. Brooks and Cole: New York, 1996; pp 942–943.
18. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part A: Structure and Mechanisms*; 4th ed. Kluwer Academic: New York, 2000; p 293 and references therein.
19. Carpino, L. A.; Cohen, B. J.; Stephens, K. E., Jr.; Sadat-Aalaee, S. Y.; Tien, J.; Langridge, D. C. *J. Org. Chem.* **1986**, *51*, 3732–3734.
20. These are known compounds with matching literature NMR data. *N*-Hexylbenzamide **6a**: Katritzky, A. R.; Drewniak, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2339–2344. *N*-Cyclohexyl-benzamide **7a**: Kunishima, M.; Kawachi, C.; Hioki, K.; Terao, K.; Tani, S. *Tetrahedron* **2001**, *57*, 1551–1558. *N*-Benzylbenzamide **9a**: Wan, Y.; Alterman, M.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2002**, *67*, 6232–6235. *N*-Methylbenzamide **10a**: Hajipour, A. R.; Ghasemi, M. *Indian J. Chem.* **2001**, 504–507. Tributylamineoxide **18**: Ferrer, M.; Sanchez-Baeza, F.; Messeguer, A. *Tetrahedron* **1997**, *53*, 15877–15888. *N*-(2,2,2-Trifluoroethyl)-benzamide **24**: Hegarty, A. F.; Eustace, S. J.; Tynan, N. M.; Pham-Tran, N.-N.; Nguyen, M. T. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1239–1246.