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Rearrangement of Differentially Protected *N*-Arylhydroxylamines

Achim Porzelle,[a] Michael D. Woodrow,[b] and Nicholas C. O. Tomkinson*[a]

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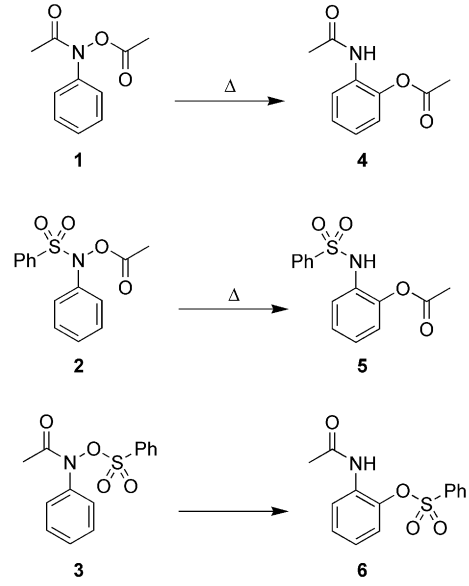
The rearrangement of a series of *N*,*O*-difunctionalised *N*-arylhydroxylamines to generate protected 2-aminophenols has been investigated. *N*-Boc-*N*-Aryl-*O*-acylhydroxylamines are stable, isolable compounds which rearrange smoothly at temperatures between 110 and 140 °C. The corresponding *N*-Boc-*N*-aryl-*O*-sulfonylhydroxylamines were not isolated and rearrange to 1,2-difunctionalised aminophenols at room temperature in excellent yield. Deprotection of either the *N*- or *O*-substituents under standard conditions allows for further synthetic manipulation of either the aniline or phenol functionality.

Introduction

The controlled functionalisation and elaboration of aromatic compounds is of major importance in synthetic research.[1] Of particular interest is the introduction of new carbon–heteroatom bonds. In this context, robust transition-metal-mediated methodology allows access to high-value aromatic and heteroaromatic products of great use in pharmaceutical, agrochemical and natural product research.[2] Much of the fundamental technology developed for the construction of carbon–heteroatom bonds involves the activation of aryl halides or triflates with precious metal catalysts.[3] In recent years, considerable research efforts into C–H activation/functionalisation, has provided important contributions to the arsenal of methods available to the synthetic chemist.[4] Although efficient and practical, the majority of these processes rely on activation of the substrate with transition metals.[5] The development of methodology which allows for the formal metal-free[6] activation of aromatic rings would significantly augment the available methods and provide a valuable synthetic alternative.

In 1957 Horner described the synthesis and thermal rearrangement of *N*-aryl-*N*,*O*-diacylhydroxylamine **1** to provide protected 2-aminophenol **4** (Scheme 1).[7] Subsequent mechanistic studies have shown these reactions proceed via either a [3,3]-sigmatropic rearrangement process or an ion-pair mechanism depending upon the reaction conditions adopted.[8] In contrast, the related rearrangement of *N*-aryl-*N*-sulfonyl-*O*-acylhydroxylamines **2** to give **5**[9] and *N*-aryl-*N*-acyl-*O*-sulfonylhydroxylamines **3** to the 2-functionalised products **6**[10] have been shown to proceed exclusively through a concerted pericyclic process. These overall reactions provide a simple and easily accessible method with which to functionalise anilines at the *ortho* position. The use of these versatile rearrangements is currently limited by the resulting amide or sulfonamide on the aniline nitrogen of the products **4**–**6**, where harsh reaction conditions would be required to unmask the aniline functionality. Having recently developed a simple method for the preparation of differentially protected *N*-arylhydroxylamines through a modified Ullman coupling,[11] we sought to investigate the scope and limitations of subsequent rearrangements that employ synthetically versatile nitrogen protecting groups, providing an important extension to existing technology. Within this paper, we describe a method for the conversion of *N*-arylhydroxylamines to differentially protected 2-ami-



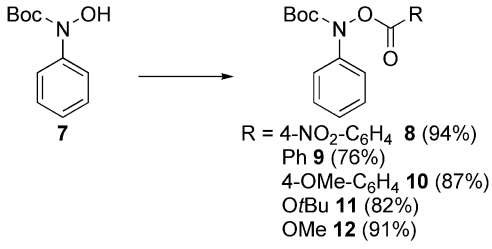
Scheme 1. Rearrangements of *N*-arylhydroxylamines.

[a] School of Chemistry, Main Building, Cardiff University, Park Place, Cardiff, CF10 3AT, UK
E-mail: tomkinsonnc@cardiff.ac.uk
[b] ImmunoInflammation Centre of Excellence for Drug Discovery, GlaxoSmithKline Medicines Research Centre, Stevenage, Hertfordshire, SG1 2NY, UK

nophenols, examine the regiochemical outcome of the rearrangement using non-symmetrical substrates, and report methods for the selective deprotection of both the nitrogen and oxygen substituents.

Results and Discussion

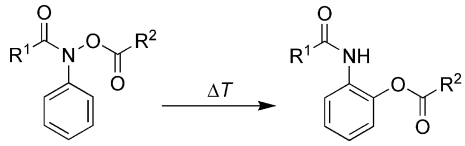
Conversion of *N*-Boc-*N*-phenylhydroxylamine (**7**)[12] to the corresponding *O*-acyl and *O*-carbonate derivatives proceeded smoothly under standard conditions to deliver a series of rearrangement precursors **8**–**12** (76–94%) (Scheme 2). Each of these compounds (**8**–**12**) was bench stable and showed no indication of rearrangement/decomposition at room temperature over the course of this investigation.



Scheme 2. Preparation of rearrangement precursors.

In previous reports, rearrangement of *N*-aryl-*N*-acyl-*O*-acylhydroxylamines (e.g. **1**) was performed at temperatures in the range 150–200 °C.[7] Rationalising that decreasing the electron-withdrawing ability of the nitrogen protecting group would facilitate rearrangement we examined the reaction of **8**–**12** at lower temperatures than those reported, the results of which are collected in Table 1. Rearrangement of **8** proceeded effectively, but slowly at temperatures as low as 110 °C (Table 1, Entry 1) (45%, 48 h) along with recovered starting material (47%). Raising the temperature to 140 °C (refluxing *p*-xylene, 24 h) resulted in complete consumption of starting material giving **13** in a pleasing 75% isolated yield (Entry 2). This trend was reflected with both the *O*-benzoyl **9** (Entries 3 and 4) and *O*-4-methoxybenzoyl **10** (Entries 5 and 6) substrates, suggesting that refluxing xylene provide the most effective conditions for this transformation. Reducing the electron withdrawing ability of the oxygen substituent to a carbonate reduced the propensity of these substrates to undergo rearrangement, however, the expected products could be isolated using refluxing xylene as the reaction medium (Entries 8 and 11). It is worth noting that use of polar solvents such as DMF resulted in complex reaction mixtures, mainly due to loss of carbamate, carbonate, and ester functionalities. Additionally, little benefit was gained by carrying out these reactions under microwave irradiation (300 W, 140 °C, 3 h), with the desired products being isolated in similar yields.

Table 1. Rearrangement of *O*-acylhydroxylamines.



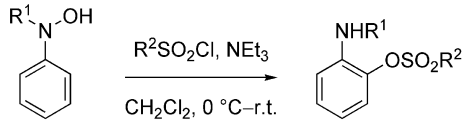
8–12 **13–18**

Entry	R^1	R^2	Product	Solvent[a]	Yield[b]
1	O*t*Bu	4-NO_2-C_6H_4	**13**	toluene	45% (92%)[c]
2	O*t*Bu	4-NO_2-C_6H_4	**13**	*p*-xylene	75%
3	O*t*Bu	Ph	**14**	toluene	30% (82%)[c]
4	O*t*Bu	Ph	**14**	*p*-xylene	55%
5	O*t*Bu	4-OMe-C_6H_4	**15**	toluene	0%
6	O*t*Bu	4-OMe-C_6H_4	**15**	*p*-xylene	33%
7	O*t*Bu	OMe	**16**	toluene	37%[d]
8	O*t*Bu	OMe	**16**	*p*-xylene	62%
9	O*t*Bu	O*t*Bu	**17**	toluene	0%[e]
10	OMe	OMe	**18**	toluene	40% (90)[c]
11	OMe	OMe	**18**	*p*-xylene	65%

[a] Toluene: 110 °C, 48 h; xylene: 140 °C, 24 h. [b] Isolated yield. [c] Yield based on recovered starting material. [d] Conversion by ^{1}H NMR. [e] Loss of *O*-carbonate group.

Our initial results (Table 1) suggested that increasing the electron-withdrawing ability of the oxygen substituent (and/or decreasing that of the nitrogen) lowered the activation barrier of rearrangement. We therefore examined the introduction of a sulfonyl group on the hydroxylamine oxygen with the hope of facilitating the overall rearrangement process further in agreement with previous reports of this class of transformation (Table 2).[10] To our delight, treatment of the *N*-protected hydroxylamines **7** and **20**–**22**[13] with one equivalent of methanesulfonyl chloride and triethylamine at room temperature for 30 min led directly to the rearranged products **23**–**26** in 78–94% isolated yield (Entries 1–4), providing significantly improved reaction conditions for the sequence. Both carbamate (Entries 1 and 2) and sulfonamide (Entries 3 and 4) were well tolerated on the hydroxylamine nitrogen without compromise in reactivity. The protocol was equally effective for the one-pot *O*-tosylation/rearrangement (Entries 5 and 6), with the reactions reaching

Table 2. Rearrangements with sulfonyl chlorides.



7, **20–22** **23–28**

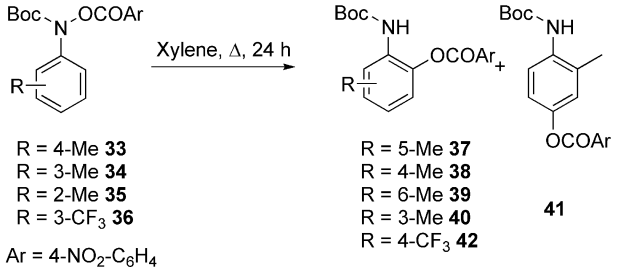
Entry	R^1	R^2	Product	Yield[a]
1	Boc (**7**)	Me	**23**	78%
2	Cbz (**20**)	Me	**24**	94%
3	*p*Ts (**21**)	Me	**25**	85%
4	Ms (**22**)	Me	**26**	93%
5	Boc (**7**)	*p*Tol	**27**	71%
6	Cbz (**20**)	*p*Tol	**28**	89%

[a] Isolated yield.

completion within 1 h at room temperature. In each of these reactions, no indication of the proposed hydroxylamine intermediate was detected, suggesting the rearrangement of *N*-protected *N*-aryl-*O*-sulfonylhydroxylamines is rapid.

Having established effective conditions for the rearrangement of *N*-protected *O*-acyl and *O*-sulfonylhydroxylamines we examined a series of substituted *N*-arylhydroxylamines to gain further insight into the effects of substitution on the aromatic ring on the facility of rearrangement and the regiochemical outcome with non-symmetrical substrates (Table 3 and Table 4). The substituted *N*-Boc-*N*-phenylhydroxylamines **29**–**32** were initially *O*-functionalised with 4-nitrobenzoyl chloride to give stable rearrangement precursors **33**–**36** (86–97%). Heating each of these precursors containing an electron donating methyl group (140 °C, 24 h) gave the protected aminophenol products **37**–**41** in excellent yield (83–90%) (Entries 1–3). Interestingly, rearrangement of the 3-methylhydroxylamine derivative **34** (Entry 2) gave the two possible regioisomers **38** and **39** (83%) in a 55:45 ratio (^{1}H NMR) as an inseparable mixture. Cleavage of the phenolic esters (KOH, DMF/H_2O, 80 °C, 3 h) allowed for simple separation of the isomeric products **49** (42%) and **50** (52%) by column chromatography (Scheme 3). In contrast to all other rearrangements undertaken, both the 1,2- and 1,4-aminophenol derivatives **40** and **41** were obtained from the 2-methyl-substituted aromatic **35** in a 54:46 ratio (^{1}H NMR) (Entry 3). Once again, the isomeric products could readily be separated by solvolysis of the esters (NaOMe, MeOH, Δ, 3 h) to give the phenols **51** (52%) and **52** (42%). Introduction of an electron withdrawing trifluoromethyl group on the aromatic substrate (Entry 4) resulted in decomposition of starting material when heating in refluxing xylene. Lowering the temperature to refluxing chloroform (72 °C) or toluene (110 °C) resulted in isolation of starting material after heating for 24 h. Overall, this suggests that electron deficiency in the aromatic ring disfavours rearrangement and electron-rich aromatic substrates readily undergo rearrangement.

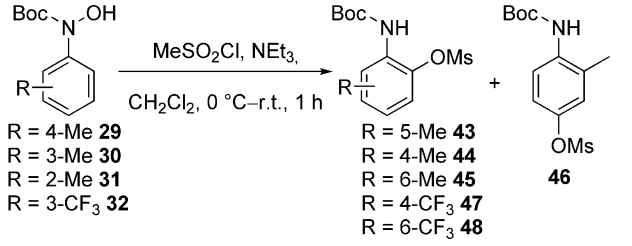
Table 3. Acyl rearrangements with substituted arenes.



Entry	R	Product	Yield[a]
1	4-Me **33**	**37**	90%
2	3-Me **34**	**38** and **39**	83%[b]
3	2-Me **35**	**40** and **41**	85%[b]
4	3-CF_3 **36**	**42**	decomposition
5	3-CF_3 **36**	**42**	0%[c]

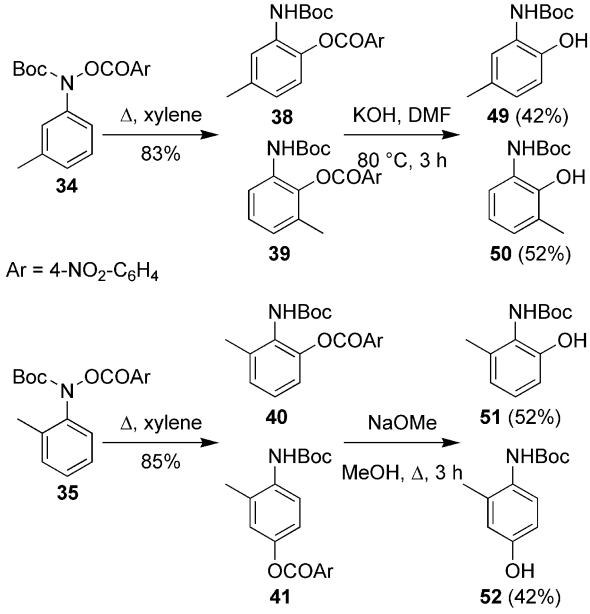
[a] Isolated yield. [b] Product isolated as an inseparable ca. 1:1 mixture of regioisomers. [c] Reaction carried out at 73 °C in $CHCl_3$ or 110 °C in toluene for 24 h.

Table 4. Sulfonyl rearrangements with substituted arenes.



Entry	R	Product	Yield[a]
1	4-Me **29**	**43**	89%
2	3-Me **30**	**44** and **45**	96%
3	2-Me **31**	**46**	92%
4	3-CF_3 **32**	**47**	10%[b]
5	3-CF_3 **32**	**47** and **48**	95%[c]

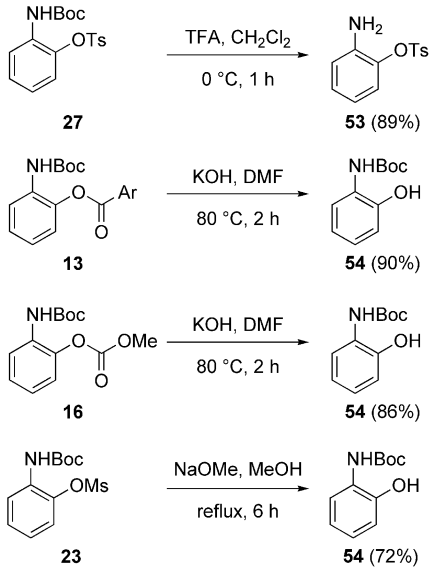
[a] Isolated yield. [b] Isolated yield along with 42% rearrangement precursor. [c] Reaction carried out at 40 °C for 24 h, products isolated in a 60:35 ratio.



Scheme 3. Isomeric products from rearrangement of **34** and **35**.

Rearrangement of the *O*-sulfonylhydroxylamines occurred readily at ambient temperature with methyl-substituted aromatics (Table 4). Treatment of hydroxylamines **29**–**31** with methanesulfonyl chloride under basic reaction conditions gave the rearranged products **43**–**46** in 89–96% isolated yield. Pleasingly, each of these was isolated as single products directly after rearrangement. Difficulties were once again encountered with the electron-deficient substrate **32** (Entry 4), however, this could be circumvented simply by warming the reaction mixture to reflux in dichloromethane to give the rearranged products **47** (60%) and **48** (35%), which could easily be separated by column chromatography (Entry 5).

Selective removal of either the nitrogen or the oxygen protecting groups of the rearranged products proceeded smoothly under standard conditions to unmask these important functionalities for further synthetic manipulation, revealing the potential of this methodology (Scheme 4). Treatment of **27** with trifluoroacetic acid (0 °C, 1 h) provided the aniline **53** (89%). Hydrolysis of the 4-nitrobenzoate **13** and methyl carbonate **16** with potassium hydroxide (DMF, 80 °C, 2 h) gave phenol **54** (90 and 86%, respectively). In addition, it was also possible to remove the sulfonate ester in the presence of the *N*-Boc-aniline under solvolytic conditions (NaOMe, MeOH, Δ, 6 h; 72%), suggesting that each of the rearranged products described in this investigation can easily be selectively deprotected.



Scheme 4. Selective deprotection of rearranged products.

Conclusions

In summary, we have described the preparation and thermal rearrangement of a series of differentially protected *N*-arylhydroxylamines. *N*-Boc-*N*-Aryl-*O*-acylhydroxylamines were found to be stable, isolable compounds, which rearranged smoothly at temperatures between 110 and 140 °C. The corresponding *N*-Boc-*N*-aryl-*O*-sulfonylhydroxylamines were not isolated and rearranged to the 1,2-difunctionalised phenols at room temperature. Deprotection of either the *N*- or *O*-substituents under standard conditions allows for further synthetic manipulation of either the aniline or the phenol functionalities. Substitution of the aromatic ring with electron donating substituents was tolerated, however, electron-withdrawing substituents significantly inhibit rearrangement. Application of this methodology in the preparation of drug-like molecules is currently underway.

Experimental Section

General Information: Commercially available solvents and reagents were used without further purification. Petroleum ether refers to the fraction with a boiling range of 40–60 °C. Flash chromatography was carried out using Merck Kieselgel 60 H silica. Analytical thin-layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF254 that were visualized under UV light (at 254 and/or 360 nm). Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ at 18 °C unless stated otherwise and are reported in ppm; *J* values were recorded in Hz and multiplicities were expressed by the usual conventions. High-resolution mass spectra were obtained courtesy of the EPSRC Mass Spectrometry Service, Swansea using the ionization methods specified. ES refers to electron spray ionization, CI refers to chemical ionization (ammonia) and EI refers to electron ionization. In vacuo refers to evaporation at reduced pressure using a rotary evaporator and diaphragm pump, followed by the removal of trace volatiles using a vacuum (oil) pump.

N-Arylhydroxylamines were obtained by Zn/NH_4Cl reduction of the corresponding nitrobenzenes following literature procedures.[14]

General Procedure for the Rearrangement of *O*-Acylhydroxylamines: *N*-Boc-*N*-Phenyl-*O*-acylhydroxylamines (0.3 mmol) were dissolved in toluene or *p*-xylene (3 mL) and heated to reflux for 48 h (toluene) or 24 h (xylene). After cooling, the crude mixtures were directly subjected to column chromatography (gradient petroleum ether/ethyl acetate, 8:1 to 3:1) to obtain the rearrangement products.

General Procedure for the Rearrangement of *O*-Sulfonylhydroxylamines: *N*-Boc-*N*-Phenylhydroxylamines (0.5 mmol) was dissolved in dichloromethane (2 mL) and NEt_3 (0.14 mL, 1 mmol) was added followed by the addition of methanesulfonyl chloride (0.04 mL, 0.51 mmol) at 0 °C. The ice bath was removed and the reaction mixture stirred at room temperature. After 30 min the crude mixture was directly subjected to column chromatography (gradient petroleum ether/ethyl acetate, 3:1 to 1:1) to obtain the rearrangement products.

***N*-Boc-*N*-Phenyl-*O*-(4-nitrobenzoyl)hydroxylamine (8):** NEt_3 (300 mg, 3 mmol) and a catalytic amount of DMAP (10 mg) was added to a solution of **7** (316 mg, 1.51 mmol) in THF (5 mL) and the reaction mixture was cooled to 0 °C. 4-Nitrobenzoyl chloride (287 mg, 1.55 mmol) was added and the resulting solution was stirred for 1 h at 0 °C and 2 h at room temperature. The reaction mixture was diluted with diethyl ether (20 mL) and washed with saturated $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried with ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the title compound **8** (500 mg, 94%) as pale yellow oil; R_f = 0.63 (petroleum ether/ethyl acetate, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.35–8.28 (m, 4 H), 7.51–7.49 (m, 2 H), 7.41–7.37 (m, 2 H), 7.29–7.26 (m, 1 H), 1.49 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 162.8 (s), 152.1 (s), 152.0 (s), 140.2 (s), 132.9 (s), 131.1 (d), 128.9 (d), 127.4 (d), 124.2 (d), 123.8 (d), 83.7 (s), 28.1 (q) ppm. HRMS (ES) found 376.1501 $[M + NH_4]^{++}$; calculated for $C_{18}H_{22}N_3O_6$ 376.1509.

***N*-Boc-*N*-Phenyl-*O*-benzoylhydroxylamine (9):** NEt_3 (100 mg, 1 mmol) was added to a solution of **7** (100 mg, 0.48 mmol) in THF (5 mL) and the reaction mixture was cooled to 0 °C. Benzoyl chloride (70 mg, 0.5 mmol) was added and the resulting solution was stirred for 1 h at 0 °C and 2 h at room temperature. The reaction mixture was diluted with diethyl ether (20 mL) and washed with saturated $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried with ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column

chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the title compound **9** (115 mg, 76%) as colourless oil; R_f = 0.52 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, J = 7.5 Hz, 2 H), 7.68–7.65 (m, 1 H), 7.55–7.48 (m, 4 H), 7.43–7.37 (m, 2 H), 7.22–7.17 (m, 1 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 164.5 (s), 152.1 (s), 140.4 (s), 134.3 (s), 130.6 (d), 130.0 (d), 128.9 (d), 128.7 (d), 126.5 (d), 123.3 (d), 83.2 (s), 28.2 (q) ppm. HRMS (ES) found 331.1645 $[M + NH_4]^{\cdot+}$; calculated for $C_{18}H_{23}N_2O_4$ 331.1658.

***N*-Boc-*N*-Phenyl-*O*-(4-methoxybenzoyl)hydroxylamine (10):** NEt_3 (100 mg, 1 mmol) was added to a solution of **7** (100 mg, 0.48 mmol) in THF (2 mL) and the mixture was cooled to 0 °C. 4-Methoxybenzoyl chloride (85 mg, 0.5 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C and 2 h at room temperature. The reaction mixture was diluted with diethyl ether (10 mL) and washed with saturated $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried with ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the title compound **10** (140 mg, 79%) as colourless oil; R_f = 0.47 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.9 Hz, 2 H), 7.52 (d, J = 8.2 Hz, 2 H), 7.35 (dd, J = 8.2 Hz, 2 H), 7.20 (t, J = 8.2 Hz, 1 H), 6.95 (d, J = 8.9 Hz, 2 H) 1.50 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 164.3 (s), 164.1 (s), 152.2 (s), 140.5 (s), 132.2 (d), 128.7 (d), 126.3 (d), 123.0 (d), 119.5 (s), 114.0 (d), 83.0 (s), 55.5 (q), 28.2 (q) ppm. HRMS (ES) found 361.1759 $[M + NH_4]^{\cdot+}$; calculated for $C_{19}H_{25}N_2O_5$ 361.1763.

***N*-Boc-*N*-Phenyl-*O*-Boc-hydroxylamine (11):** A solution of **7** (200 mg, 0.96 mmol) in THF (10 mL) was cooled to 0 °C and Boc_2O (240 mg, 1.1 mmol) was added. The reaction mixture was stirred for 5 h at room temperature, diluted with diethyl ether (30 mL) and washed with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL). The organic phase was dried with ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the product **11** (243 mg, 82%) as colourless oil; R_f = 0.66 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.44 (m, 2 H), 7.37–7.33 (m, 2 H), 7.23–7.19 (m, 1 H), 1.53 (s, 9 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.2 (s), 152.0 (s), 146.8 (s), 128.8 (d), 126.4 (d), 122.9 (d), 85.3 (s), 83.1 (s), 28.1 (q), 27.6 (q) ppm. HRMS (ES) found 327.1917 $[M + NH_4]^{\cdot+}$; calculated for $C_{16}H_{27}N_2O_5$ 327.1920.

***N*-Boc-*N*-Phenyl-*O*-(methoxycarbonyl)hydroxylamine (12):** NEt_3 (72 mg, 0.72 mmol) was added to a solution of **7** (100 mg, 0.48 mmol) in THF (2 mL) and the mixture was cooled to 0 °C. Methyl chloroformate (50 mg, 0.53 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was diluted with diethyl ether (10 mL) and washed with satd. $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried with ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the title compound **12** (117 mg, 91%) as colourless oil; R_f = 0.55 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.42 (m, 2 H), 7.39–7.34 (m, 2 H), 7.25–7.22 (m, 1 H), 3.90 (s, 3 H), 1.51 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.8 (s), 152.1 (s), 140.0 (s), 128.7 (d), 127.0 (d), 123.6 (d), 83.5 (s), 56.1 (q), 28.1 (q) ppm. HRMS (ES) found 285.1456 $[M + NH_4]^{\cdot+}$; calculated for $C_{13}H_{21}N_2O_5$ 285.1450.

***N*-(Methoxycarbonyl)-*N*-phenyl-*O*-(methoxycarbonyl)hydroxylamine:** To a solution of *N*-phenylhydroxylamine (110 mg, 1 mmol) in THF (10 mL) was added NEt_3 (300 mg, 3 mmol) and the mixture was cooled to 0 °C. Methyl chloroformate (200 mg, 2.1 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was diluted with diethyl ether (30 mL) and washed with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL). The organic phase was dried with ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the title compound (182 mg, 81%) as yellow oil; R_f = 0.35 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.47 (m, 2 H), 7.44–7.39 (m, 2 H), 7.34–7.28 (m, 1 H), 3.94 (s, 3 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.7 (s), 154.0 (s), 139.3 (s), 129.0 (d), 127.8 (d), 124.2 (d), 56.4 (q), 54.0 (q) ppm. HRMS (ES) found 226.0706 $[M + H]^{\cdot+}$; calculated for $C_{10}H_{12}NO_5$ 226.0715.

2-(Boc-Amino)phenyl 4-Nitrobenzoate (13): White solid (62 mg, 75%); m.p. 40–42 °C; R_f = 0.46 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42–8.37 (m, 4 H), 8.00 (br. d, J = 8.0 Hz, 1 H), 7.31–7.26 (m, 1 H), 7.22–7.19 (m, 1 H), 7.16–7.12 (m, 1 H), 6.44 (br. s, 1 H), 1.46 (s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8 (s), 152.5 (s), 151.1 (s), 140.3 (s), 134.4 (s), 131.5 (d), 130.3 (s), 127.0 (d), 124.0 (d), 123.9 (d), 122.1 (d), 122.0 (d), 81.1 (s), 28.2 (q) ppm. HRMS (ES) found 376.1501 $[M + NH_4]^{\cdot+}$; calculated for $C_{18}H_{22}N_3O_6$ 376.1509.

2-(Boc-Amino)phenyl Benzoate (14): White solid (63 mg, 55%); m.p. 67–69 °C; R_f = 0.55 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (m, 2 H), 8.10 (br. s, 1 H), 7.71–7.69 (m, 1 H), 7.58–7.54 (m, 2 H), 7.28–7.23 (m, 1 H), 7.20–7.17 (m, 1 H), 7.12–7.08 (m, 1 H), 6.54 (br. s, 1 H), 1.48 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 164.5 (s), 152.4 (s), 140.2 (s), 134.0 (d), 130.7 (s), 130.3 (d), 129.1 (s), 128.8 (d), 126.5 (d), 123.4 (d), 122.2 (d), 121.2 (d), 80.9 (s), 28.3 (q) ppm. HRMS (ES) found 331.1645 $[M + NH_4]^{\cdot+}$; calculated for $C_{18}H_{23}N_2O_4$ 331.1658.

2-(Boc-Amino)phenyl 4-Methoxybenzoate (15): Yellow oil (30 mg, 33%); R_f = 0.50 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, J = 10.9 Hz, 2 H), 8.17 (br. s, 1 H), 7.26–7.22 (m, 1 H), 7.17–7.15 (m, 1 H), 7.10–7.01 (m, 1 H), 6.98–6.95 (d, J = 10.9 Hz, 2 H), 6.55 (br. s, 1 H), 3.92 (s, 3 H), 1.48 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 164.3 (s), 164.2 (s), 152.6 (s), 140.5 (s), 132.5 (d), 130.8 (s), 126.3 (d), 123.3 (d), 122.2 (d), 121.3 (s), 121.0 (d), 114.1 (d), 80.8 (s), 55.6 (q), 28.3 (q) ppm. HRMS (ES) found 361.1759 $[M + NH_4]^{\cdot+}$; calculated for $C_{19}H_{25}N_2O_5$ 361.1763.

2-(Boc-Amino)phenyl Methyl Carbonate (16): Colourless oil (48 mg, 62%); R_f = 0.40 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (br. s, 1 H), 7.26–7.19 (m, 2 H), 7.05–7.01 (m, 1 H), 6.69 (br. s, 1 H), 3.94 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.6 (s), 152.3 (s), 140.0 (s), 130.2 (s), 126.6 (d), 122.9 (d), 121.3 (d), 120.4 (d), 81.0 (s), 55.7 (q), 28.3 (q) ppm. HRMS (ES) found 285.1456 $[M + NH_4]^{\cdot+}$; calculated for $C_{13}H_{21}N_2O_5$ 285.1450.

2-[(Methoxycarbonyl)amino]phenyl Methyl Carbonate (18): Colourless oil (98 mg, 65%); R_f = 0.40 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (br. s, 1 H), 7.32–7.26 (m, 2 H), 7.14–7.10 (m, 1 H), 6.95 (br. s, 1 H), 3.98 (s, 3 H), 3.84 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.7 (s), 153.4 (s), 140.1 (s), 129.8 (d), 126.6 (d), 123.5 (d), 121.4 (d), 120.6 (s), 55.7 (q), 52.5 (q) ppm. HRMS (ES) found 226.0706 $[M + H]^{\cdot+}$; calculated for $C_{10}H_{12}NO_5$ 226.0715.

2-(Boc-Amino)phenyl Methanesulfonate (23): White solid (150 mg, 78%); m.p. 63–65 °C; R_f = 0.33 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.1 Hz, 1 H), 7.30–7.26 (m, 2 H), 7.07–7.01 (m, 2 H), 3.20 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.5 (s), 138.3 (s), 131.6 (s), 128.0 (d), 123.5 (d), 122.3 (d), 121.8 (d), 81.3 (s), 37.7 (q), 28.3 (q) ppm. HRMS (ES) found 305.1165 $[M + NH_4]^{\cdot+}$; calculated for $C_{12}H_{21}N_2O_5S$ 305.1171.

2-(Cbz-Amino)phenyl Methanesulfonate (24): White solid (112 mg, 94%); m.p. 65–66 °C; R_f = 0.28 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (br. d, J = 4.0 Hz, 1 H), 7.43–7.28 (m, 8 H), 7.09–7.07 (m, 1 H), 5.21 (s, 2 H), 3.15 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.2 (s), 138.4 (s), 135.9 (s), 131.2 (s), 128.6 (d), 128.4 (d), 128.4 (d), 128.1 (d), 124.1 (d), 122.5 (d), 122.0 (d), 67.4 (t), 37.9 (q) ppm. HRMS (ES) found 322.0741 $[M + H]^{\cdot+}$; calculated for $C_{15}H_{16}NO_5S$ 322.0749.

2-[(4-Tolylsulfonyl)amino]phenyl Methanesulfonate (25): White solid (87 mg, 85%); m.p. 112–115 °C; R_f = 0.19 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.3 Hz, 2 H), 7.64 (d, J = 8.2 Hz, 1 H), 7.39 (br. s, 1 H), 7.32–7.26 (m, 4 H), 7.20–7.15 (m, 1 H), 3.19 (s, 3 H), 2.43 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 144.2 (s), 139.8 (s), 136.5 (s), 130.0 (s), 129.7 (d), 128.2 (d), 127.3 (d), 125.9 (d), 123.7 (d), 123.0 (d), 38.0 (q), 21.5 (q) ppm. HRMS (ES) found 342.0482 $[M + H]^{\cdot+}$; calculated for $C_{14}H_{16}NO_5S_2$ 342.0470.

2-[(Methylsulfonyl)amino]phenyl Methanesulfonate (26): White solid 39 mg, (93%); m.p. 102–103 °C; R_f = 0.12 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.71 (m, 1 H), 7.37–7.34 (m, 2 H), 7.26–7.21 (m, 1 H), 7.08 (br. s, 1 H), 3.33 (s, 3 H), 3.06 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 139.2 (s), 130.4 (s), 128.7 (d), 126.1 (d), 123.6 (d), 123.0 (d), 40.1 (q), 38.3 (q) ppm. HRMS (ES) found 283.0420 $[M + NH_4]^{\cdot+}$; calculated for $C_8H_{15}N_2O_5S_2$ 283.0422.

2-(Boc-Amino)phenyl 4-Toluenesulfonate (27): White solid (130 mg, 71%); m.p. 79–80 °C; R_f = 0.52 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (br. d, J = 8.1 Hz, 1 H), 7.69 (d, J = 8.3 Hz, 2 H), 7.30 (d, J = 8.3 Hz, 2 H), 7.20–7.16 (m, 1 H), 6.99–6.97 (m, 1 H), 6.93–6.89 (m, 1 H), 6.71 (br. s, 1 H), 2.43 (s, 3 H), 1.47 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.1 (s), 146.0 (s), 138.2 (s), 131.9 (s), 131.6 (s), 130.0 (d), 128.5 (d), 127.7 (d), 122.8 (d), 122.6 (d), 120.6 (d), 80.8 (s), 28.2 (q), 21.8 (q) ppm. HRMS (ES) found 363.1126 $[M]^{\cdot+}$; calculated for $C_{18}H_{21}NO_5S$ 363.1140.

2-(Cbz-Amino)phenyl 4-Toluenesulfonate (28): Pale yellow oil (141 mg, 89%); R_f = 0.28 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (br. s, 1 H), 7.69 (d, J = 8.3 Hz, 1 H), 7.44–7.35 (m, 4 H), 7.26–7.20 (m, 4 H), 7.04–6.95 (m, 4 H), 5.14 (s, 2 H), 2.39 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.8 (s), 146.0 (s), 138.7 (s), 135.9 (s), 131.9 (s), 131.1 (s), 129.9 (d), 128.6 (d), 128.5 (d), 128.4 (d), 128.2 (d), 127.8 (d), 123.5 (d), 122.7 (d), 121.0 (d), 67.1 (t), 21.7 (q) ppm. HRMS (ES) found 398.1074 $[M + H]^{\cdot+}$; calculated for $C_{21}H_{20}NO_5S$ 398.1062.

***N*-Boc-*N*-(4-Methylphenyl)hydroxylamine (29):** A solution of 4-methyl-*N*-phenylhydroxylamine (123 mg, 1 mmol) in THF (10 mL) was cooled to –78 °C and a precooled solution of Boc_2O (240 mg, 1.1 mmol) in THF (10 mL) was added. The reaction mixture was warmed slowly to room temperature overnight, diluted with diethyl ether (40 mL) and washed with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give the product **29** (189 mg, 85%) as a white solid; m.p. 82–84 °C; R_f = 0.41 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.5 Hz, 2 H), 7.14 (d, J = 8.5 Hz, 2 H), 2.34 (s, 3 H), 1.49 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.5 (s), 138.4 (s), 135.1 (s), 129.0 (d), 121.9 (d), 83.1 (s), 28.3 (q), 20.9 (q) ppm. HRMS (ES) found 224.1284 $[M + H]^{\cdot+}$; calculated for $C_{12}H_{18}NO_3$ 224.1281.

***N*-Boc-*N*-(4-Methylphenyl)-*O*-(4-nitrobenzoyl)hydroxylamine (33):** Waxy pale yellow solid (165 mg, 89%); R_f = 0.56 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33–8.26 (m, 4 H), 7.39 (d, J = 8.4 Hz, 2 H), 7.19 (d, J = 8.4 Hz, 2 H), 2.35 (s, 3 H), 1.51 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 162.9 (s), 152.4 (s), 151.1 (s), 137.8 (s), 137.7 (s), 133.1 (s), 131.1 (d), 129.5 (d), 124.9 (d), 123.7 (d), 83.5 (s), 28.1 (q), 21.0 (q) ppm. HRMS (ES) found 390.1679 $[M + NH_4]^{\cdot+}$; calculated for $C_{19}H_{24}N_3O_6$ 390.1665.

2-(Boc-Amino)-5-methylphenyl 4-Nitrobenzoate (37): Pale yellow oil (68 mg, 90%); R_f = 0.58 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40–8.35 (m, 4 H), 7.81 (br. d, J = 4.0 Hz), 7.09–7.07 (m, 1 H), 7.01 (br. s, 1 H), 6.32 (br. s, 1 H), 2.34 (s, 3 H), 1.44 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 162.9 (s),152.7 (s), 151.1 (s), 140.8 (s), 134.5 (s), 131.4 (d), 127.6 (d), 127.5 (s), 123.8 (d), 122.7 (d), 122.5 (d), 80.9 (s), 28.3 (q), 20.8 (q) ppm. HRMS (ES) found 390.1679 $[M + NH_4]^{\cdot+}$; calculated for $C_{19}H_{24}N_3O_6$ 390.1665.

***N*-Boc-*N*-(3-Methylphenyl)hydroxylamine (30):** A solution of *N*-(3-methylphenyl)hydroxylamine (123 mg, 1 mmol) in THF (10 mL) was cooled to –78 °C and a precooled solution of Boc_2O (240 mg, 1.1 mmol) in THF (10 mL) was added. The reaction mixture was warmed slowly to room temperature overnight, diluted with diethyl ether (40 mL) and washed with satd. $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give **30** (194 mg, 87%) as a pale yellow solid; m.p. 63–65 °C; R_f = 0.45 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (br. s, 1 H), 7.26–7.21 (m, 2 H), 6.99 (br. d, J = 8 Hz, 1 H); 2.38 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.5 (s), 140.9 (s), 138.2 (s), 128.1 (d), 126.0 (d), 122.3 (d), 118.9 (d), 83.2 (s), 28.3 (q), 21.5 (q) ppm. HRMS (EI) found 223.1209 $[M]^{\cdot+}$; calculated for $C_{12}H_{17}NO_3$ 223.1208.

***N*-Boc-*N*-(3-Methylphenyl)-*O*-(4-nitrobenzoyl)hydroxylamine (34):** Pale yellow oil (172 mg, 96%); R_f = 0.53 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.25 (m, 4 H), 7.31 (br. s, 1 H), 7.26–7.22 (m, 2 H), 7.07 (br. d, J = 4.0 Hz, 1 H), 2.34 (s, 3 H), 1.47 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 162.9 (s), 152.2 (s), 151.1 (s), 139.9 (s), 138.9 (s), 132.9 (s), 131.2 (d), 128.8 (d), 128.3 (d), 124.9 (d), 123.8 (d), 121.3 (d), 83.6 (s), 28.1 (q), 21.4 (q) ppm. HRMS (ES) found 390.1664 $[M + NH_4]^{\cdot+}$; calculated for $C_{19}H_{24}N_3O_6$ 390.1665.

2-(Boc-Amino)-4-methylphenyl 4-Nitrobenzoate (38) and 2-(Boc-Amino)-6-methylphenyl 4-Nitrobenzoate (39): Mixture of regioisomers, isomer **38** (1,2,4-trisubstituted), isomer **39** (1,2,6-trisubstituted). White solid (85 mg, 83%); R_f = 0.50 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44–8.35 (m, 8 H), 7.85–7.80 (br. m, 2 H, *o*-CH), 7.19 (t, J = 7.9 Hz, 1 H), 7.07 (d, J = 8.2 Hz, 1 H), 7.00 (d, J = 7.2 Hz, 1 H), 6.93 (d, J = 7.2 Hz, 1 H), 6.43 (br. s, 1 H, NH), 6.37 (br. s, 1 H, NH), 2.37 (s, 3 H), 2.17 (s, 3 H), 1.46 (s, 9 H), 1.44 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.0 (s), 162.4 (s), 152.6 (s), 152.5 (s), 151.2 (s), 151.1

(s), 139.5 (s), 138.0 (s), 137.1 (s), 134.5 (s), 134.0 (s), 131.6 (d), 131.5 (d), 130.6 (s), 129.8 (s), 126.8 (d), 126.0 (d), 124.5 (d), 124.0 (d), 123.9 (d), 122.3 (d), 121.7 (d), 119.9 (d), 81.1 (s), 28 (m, 2 C), 21.3 (q), 16.6 (q) ppm. HRMS (ES) found 390.1664 $[M + NH_4]^{+}$; calculated for $C_{19}H_{24}N_3O_6$ 390.1665.

***N*-Boc-*N*-(2-Methylphenyl)hydroxylamine (31):** A solution of *N*-(2-methylphenyl)hydroxylamine (123 mg, 1 mmol) in THF (10 mL) was cooled to –78 °C and a precooled solution of Boc_2O (240 mg, 1.1 mmol) in THF (10 mL) was added. The reaction mixture was warmed slowly to room temperature overnight, diluted with diethyl ether (40 mL) and washed with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give **31** (176 mg, 79%) as a pale yellow solid; m.p. 60–62 °C; R_f = 0.38 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.29 (m, 1 H), 7.23–7.19 (m, 3 H), 2.33 (s, 3 H), 1.45 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 156.0 (s), 139.8 (s), 135.9 (s), 130.6 (d), 128.3 (d), 127.1 (d), 126.3 (d), 82.3 (s), 28.3 (q), 17.8 (q) ppm. HRMS (APCI) found 223.1205 $[M]^{+}$; calculated for $C_{12}H_{17}NO_3$ 223.1208.

***N*-Boc-*N*-(2-Methylphenyl)-*O*-(4-nitrobenzoyl)hydroxylamine (35):** Pale yellow oil (185 mg, 97%); R_f = 0.48 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.23 (m, 4 H), 7.31 (br. d, *J* = 8.0 Hz, 1 H), 7.30–7.24 (m, 3 H), 2.48 (s, 3 H), 1.47 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 162.6 (s), 153.1 (s), 151.0 (s), 138.7 (s), 137.3 (s), 133.2 (s), 131.1 (d), 131.0 (d), 129.5 (d), 128.4 (d), 126.7 (d), 123.8 (d), 83.3 (s), 28.1 (q), 17.8 (q) ppm. HRMS (ES) found 373.1397 $[M + H]^{+}$; calculated for $C_{19}H_{21}N_2O_6$ 373.1394.

2-(Boc-Amino)-3-methylphenyl 4-Nitrobenzoate (40) and 4-(Boc-Amino)-3-methylphenyl 4-Nitrobenzoate (41): Mixture of isomers; white solid (85 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30–8.25 (m, 8 H) 7.85 (br. d, *J* = 9.4 Hz, 1 H), 7.23 (t, *J* = 7.8 Hz, 1 H), 7.18–7.16 (m, 1 H), 7.12–7.10 (m, 1 H), 7.07–7.04 (m, 2 H), 6.28 (br. s, 1 H), 5.84 (br. s, 1 H), 2.33 (s, 3 H), 2.27 (s, 3 H), 1.53 (s, 9 H), 1.34 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.5 (s), 162.9 (s), 153.1 (s), 150.9 (s), 150.9 (s), 146.8 (s), 146.1 (s), 135.1 (s), 134.8 (s), 134.6 (s), 131.4 (d), 131.2 (d), 129.1 (d), 127.9 (d), 123.7 (d), 123.7 (d), 123.0 (d), 120.1 (d), 119.4 (d), 80.8 (s), 80.4 (s), 28.3 (q), 28.1 (q), 18.1 (q), 17.9 (q) ppm. HRMS (ES) found 390.1663 $[M + NH_4]^{+}$; calculated for $C_{19}H_{24}N_3O_6$ 390.1665.

***N*-Boc-*N*-(3-Trifluoromethylphenyl)hydroxylamine (32):** A solution of *N*-(3-trifluoromethylphenyl)hydroxylamine (177 mg, 1 mmol) in THF (10 mL) was cooled to –78 °C and a precooled solution of Boc_2O (240 mg, 1.1 mmol) in THF (10 mL) was added. The reaction mixture was warmed slowly to room temperature overnight, diluted with diethyl ether (40 mL) and washed with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$) and the volatiles removed under reduced pressure. The crude product was purified by column chromatography on silica eluting with petroleum ether/ethyl acetate (3:1) to give **32** (188 mg, 68%) as a white solid; m.p. 67–68 °C; R_f = 0.46 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (s, 1 H), 7.67 (br. d, *J* = 8.0 Hz, 1 H), 7.45 (dd, *J* = 8.0 Hz, 1 H), 7.39–7.37 (m, 1 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.9 (s), 141.2 (s), 131.0 (CF_3), 128.9 (d), 123.4 (d), 121.3 (d), 121.2 (d), 117.6 (s), 84.5 (s), 28.2 (q) ppm. HRMS (ES) found 295.1267 $[M + NH_4]^{+}$; calculated for $C_{12}H_{18}F_3N_2O_3$ 295.1264.

***N*-Boc-*N*-(3-Trifluoromethylphenyl)-*O*-(4-nitrobenzoyl)hydroxylamine (36):** Colourless oil (183 mg, 86%); R_f = 0.51 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38–8.30 (m, 4 H), 7.78 (s, 1 H), 7.69–7.66 (m, 1 H), 7.51–7.50 (m, 2 H), 1.50 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1 (s), 151.7 (s), 151.6 (s), 140.9 (s), 132.8 (s), 132.0 (s), 131.7 (d), 129.9 (d), 126.1 (d), 123.8 (d), 123.0 (q, CF_3) 122.6 (s), 120.2 9 (d), 80.5 (s), 28.5 (q) ppm. HRMS (ES) found 444.1374 $[M + NH_4]^{+}$; calculated for $C_{19}H_{21}O_6N_3F_3$ 444.1377.

2-(Boc-Amino)-5-methylphenyl Methanesulfonate (43): White solid (134 mg, 89%); m.p. 104–106 °C; R_f = 0.44 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 4.0 Hz, 1 H), 7.09–7.07 (m, 2 H), 6.88 (br. s, 1 H), 3.18 (s, 3 H), 2.31 (s, 3 H), 1.50 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.7 (s), 138.5 (s), 134.0 (s), 128.8 (s), 128.6 (d), 122.7 (d), 122.1 (d), 81.0 (s), 37.7 (q), 28.3 (q), 20.6 (q) ppm. HRMS (ES) found 319.1321 $[M + NH_4]^{+}$; calculated for $C_{13}H_{23}N_2O_5$ 319.1328.

2-(Boc-Amino)-4-methylphenyl Methanesulfonate (44): Pale yellow waxy solid (73 mg, 48%); R_f = 0.39 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (s, 1 H), 7.18–7.14 (m, 1 H), 6.95–6.92 (m, 1 H), 6.85 (br. d, *J* = 8.0 Hz, 1 H), 3.18 (s, 3 H), 2.34 (s, 3 H), 1.51 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.6 (s), 138.2 (s), 132.1 (s), 131.1 (s), 127.5 (d), 124.1 (d), 122.0 (d), 81.2 (s), 37.5 (q), 28.3 (q), 21.4 (q) ppm. HRMS (ES) found 319.1335 $[M + NH_4]^{+}$; calculated for $C_{13}H_{23}N_2O_5S$ 319.1328.

2-(Boc-Amino)-6-methylphenyl Methanesulfonate (45): Colourless oil (72 mg, 48%); R_f = 0.39 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (br. d, *J* = 8.0 Hz, 1 H), 7.30 (br. s, 1 H), 6.95–6.92 (m, 1 H), 6.88–6.85 (m, 1 H), 3.32 (s, 3 H), 2.34 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.8 (s), 138.2 (s), 136.1 (s), 131.9 (s), 125.9 (d), 122.1 (d), 120.0 (d), 80.9 (s), 38.7 (q), 28.3 (q), 17.2 (q) ppm. HRMS (ES) found 319.1335 $[M + NH_4]^{+}$; calculated for $C_{13}H_{23}N_2O_5S$ 319.1328.

4-(Boc-Amino)-3-methylphenyl Methanesulfonate (46): Colourless liquid (139 mg, 92%); R_f = 0.29 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (br. d, *J* = 8 Hz, 1 H), 7.09–7.07 (m, 2 H), 6.30 (br. s, 1 H), 3.10 (s, 3 H), 2.25 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.9 (s), 144.7 (s), 135.7 (s), 129.0 (s), 123.8 (d), 121.9 (d), 120.0 (d), 81.0 (s), 37.1 (q), 28.3 (q), 17.8 (q) ppm. HRMS (ES) found 324.0875 $[M + Na]^{+}$; calculated for $C_{13}H_{19}NO_5NaS$ 324.0882.

2-(Boc-Amino)-4-trifluoromethylphenyl Methanesulfonate (47): White solid (130 mg, 65%); m.p. 77–78 °C; R_f = 0.55 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, *J* = 8.0 Hz, 1 H), 7.66 (br. s, 1 H), 7.37–7.32 (m, 2 H), 3.39 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.4 (s), 135.2 (s), 134.4 (s), 127.7 (s), 125.2 (d), 123.9 (q, *J* = 15.7 Hz, CF_3), 123.8 (d), 120.9 (q, *J* = 5.0 Hz), 81.5 (s), 39.2 (q), 28.2 (q) ppm. HRMS (ES) found 373.1031 $[M + NH_4]^{+}$; calculated for $C_{13}H_{20}N_2O_5F_3S$ 373.1045.

2-(Boc-Amino)-6-trifluoromethylphenyl Methanesulfonate (48): Colourless oil (53 mg, 30%); R_f = 0.29 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (br. s, 1 H), 7.42 (d, *J* = 8.5 Hz, 1 H), 7.32–7.30 (m, 1 H), 7.08 (br. s, 1 H), 3.27 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.1 (s), 144.4 (s), 139.6 (s), 130.3 (q, *J* = 33.0 Hz, CF_3), 124.5 (s), 122.7 (d), 120.0 (m), 118.3 (d), 82.1 (s), 38.3 (q), 28.2 (q) ppm. HRMS (ES) found 373.1037 $[M + NH_4]^{+}$; calculated for $C_{13}H_{20}N_2O_5F_3S$ 373.1045.

2-(Boc-Amino)-4-methylphenol (49): Colourless oil (25 mg, 42%); R_f = 0.49 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (br. s, 1 H), 6.91 (s, 1 H), 6.87–6.82 (m, 2 H), 6.60 (br. s, 1 H), 2.24 (s, 3 H), 1.52 (s, 9 H) ppm. HRMS (EI) found 223.1208 $[M]^{\cdot+}$; calculated for $C_{12}H_{17}NO_3$ 223.1208.

2-(Boc-Amino)-6-methylphenol (50): Colourless oil (31 mg, 52%); R_f = 0.53 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (br. s, 1 H), 6.94 (d, J = 7.5 Hz, 1 H), 6.85 (d, J = 7.5 Hz, 1 H), 6.75 (dd, J = 7.5, 7.5 Hz, 1 H), 6.57 (br. s, 1 H), 2.28 (s, 3 H), 1.53 (s, 9 H) ppm. HRMS (EI) found 223.1201 $[M]^{\cdot+}$; calculated for $C_{12}H_{17}NO_3$ 223.1208.

2-(Boc-Amino)-3-methylphenol (51): Colourless oil (31 mg, 52%); R_f = 0.36 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (br. s, 1 H), 7.02 (dd, J = 7.8, 7.8 Hz, 1 H), 6.89 (d, J = 7.8 Hz, 1 H), 6.76 (d, J = 7.8 Hz, 1 H), 6.24 (br. s, 1 H), 2.26 (s, 3 H), 1.52 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.7 (s), 153.6 (s), 132.2 (s), 128.2 (s), 125.9 (d), 117.3 (d), 113.5 (d), 80.5 (s), 28.4 (q), 17.8 (q) ppm. HRMS (EI) found 223.1201 $[M]^{\cdot+}$; calculated for $C_{12}H_{17}NO_3$ 223.1208.

4-(Boc-Amino)-3-methylphenol (52): White solid (25 mg, 42%); m.p. 42–43 °C; R_f = 0.20 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (br. d, J = 5.5 Hz, 1 H), 6.53–6.49 (m, 2 H), 6.08 (br. s, 2 H), 2.13 (s, 3 H), 1.51 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.4 (s), 149.8 (s), 129.7 (s), 125.5 (d), 122.8 (s), 122.5 (d), 121.4 (d), 81.3 (s), 27.3 (q), 17.2 (q) ppm. HRMS (EI) found 223.1208 $[M]^{\cdot+}$; calculated for $C_{12}H_{17}NO_3$ 223.1208.

2-Aminophenyl 4-Toluenesulfonate (53):[15] Compound **27** (45 mg, 0.12 mmol) was dissolved in dichloromethane (2 mL) and cooled to 0 °C. TFA (0.2 mL) was added via syringe and the resulting solution was warmed to room temperature over 2 h. The reaction mixture was diluted with dichloromethane (10 mL) and washed with $NaHCO_3$, water (10 mL) and brine (10 mL). The organic layer was evaporated and the crude product purified by column chromatography on silica to give the title compound (29 mg, 89%) as a brown waxy solid; R_f = 0.22 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, J = 8.9 Hz, 2 H), 7.33 (d, J = 8.9 Hz, 2 H), 7.02 (ddd, J = 8.0, 8.0, 1.3 Hz, 1 H), 6.78 (dd, J = 6.8, 1.4 Hz, 1 H), 6.72 (dd, J = 6.8, 1.4 Hz, 1 H), 6.60 (ddd, J = 8.0, 8.0, 1.3 Hz, 1 H), 3.6 (br. s, 2 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 145.5 (s), 139.7 (s), 137.0 (s), 132.8 (s), 129.8 (d), 128.5 (d), 127.8 (d), 122.9 (d), 118.3 (d), 117.2 (d), 21.7 (q) ppm.

***N*-Boc-2-Aminophenol (54):**[16] Compound **13** (80 mg, 0.22 mmol) was dissolved in DMF (6 mL) and KOH (1 M, 2 mL) was added. The mixture was heated to 80 °C for 2 h, diluted with ethyl acetate (20 mL) and water (10 mL). The organic layer was washed with HCl (1 M, 5 mL), water (10 mL) and brine (10 mL). The organic layer was concentrated and the crude product was purified by column chromatography (petroleum ether/ethyl acetate, 3:1) to give the title compound **54** as a colourless oil (42 mg, 90%); R_f = 0.46 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (br. s, 1 H), 7.09 (br. d, J = 8.8 Hz, 1 H), 7.06–7.01 (m, 1 H), 6.97–6.95 (m, 1 H), 6.88–6.83 (m, 1 H), 6.69 (br. s, 1 H), 1.51 (s, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.0 (s), 147.5 (s), 125.6 (s), 125.6 (d), 121.4 (d), 120.8 (d), 118.8 (d), 82.1 (s), 28.3 (q) ppm.

***N*-Boc-2-Aminophenol (54):** Compound **16** (215 mg, 0.81 mmol) was dissolved in DMF (6 mL) and KOH (1 M, 2 mL) was added. The mixture was heated to 80 °C for 2 h, diluted with ethyl acetate (20 mL) and water (10 mL). The organic layer was washed with HCl (1 M, 5 mL) water (10 mL) and brine (10 mL). The organic layer was concentrated and the crude product purified by column chromatography (petroleum ether/ethyl acetate, 3:1) to give the title compound **54** (145 mg, 86%).

***N*-Boc-2-Aminophenol (54):** Compound **23** (50 mg, 0.17 mmol) was dissolved in MeOH (4 mL) and NaOMe (5 mg) was added. The mixture was heated to reflux for 6 h after which time it was cooled, evaporated and diluted with diethyl ether (10 mL). The organic layer was washed with HCl (1 M, 5 mL), water (10 mL) and brine (10 mL). The organic layer was concentrated and the product was isolated by column chromatography (petroleum ether/ethyl acetate, 3:1) to give the title compound **54** (26 mg, 72%).

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