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Cu(I) catalyzed reaction of hydroxylamines

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Erster Gutachter: Prof. Dr. R. Göttlich
Zweiter Gutachter: Prof. Dr. S. Schindler
Tag der mündlichen Prüfung:_____

“Nullus Anxietas”

Terry Pratchet

For my father,
Dr. David M. Bassan, PhD
17 July 1946 to 18 January 2009
Soldier, Father, Scientist

Table of Contents

Abreviations

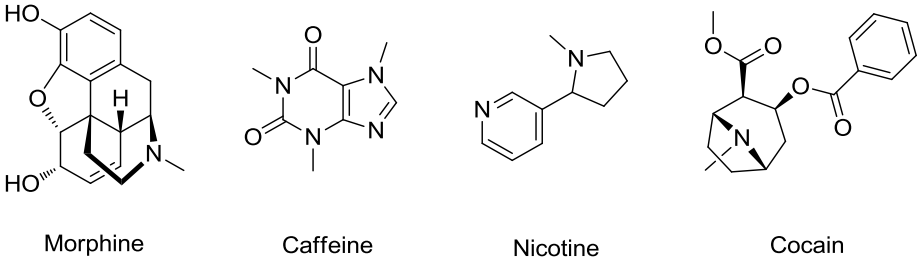
AA	asymmetric aminohydroxylation
CDI	carbonyldiimidazol
Chloramine-T	tosylchloramide
CV	Cyclovoltametry
DCC	*N*,*N'*-Dicyclohexylcarbodiimide
DCM	Dichloromethane
$(DHQ)_2$-PHAL	Hydroquinine 1,4-phthalazinediyl diether
$(DHQD)_2$-PHAL	Hydroquinidine 1,4-phthalazinediyl diether
DMAP	4-Dimethylaminopyridine
DMSO	dimethylsulfoxide
$E_{1/2}$	Halfpotential
ee	enantiomeric excess
EWG	Electron withdrawing group
Eq.	equivalent
FTIR	Fourier transform infrared spectroscopy
H	hour
HPLC	High-performance liquid chromatography
IR	Infrared
LA	Lewis acid
LAH	Lithium Aluminium Hydroxide
Min	minute
mV	mili Volt
Me	methyl
MW	microwave
Ns	Nosyl

p	para
Ph	Phenyl
PhBOX	Phenyl bis(oxazoline)
R	Rest
RT	Room temperature
T	time
TA	Tethered aminohydroxylation
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
THF	tetrahydrofuran
TosCl	4-Toluenesulfonyl chloride
TosOH	*p*-Toluenesulfonic acid
Ts	Tosyl

Introduction

Alkaloids

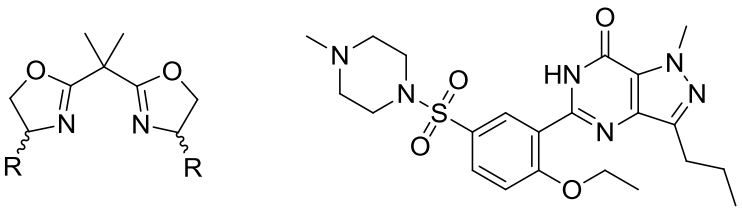
Heterocyclic alkaloids belong to one of the most important classes of molecules. They form a vital part of our everyday and not so everyday lives. Naturally occurring, alkaloids can be extracted, for example, from plants. Examples, depicted in figure 1.1, range from caffeine to nicotine found in coffee, black tee and tobacco and from morphine to cocaine, found in in opium poppy or coca plant leaves.



Morphine Caffeine Nicotine Cocain

Figure 1.1 Alkaloids

Due to the high biological activity of alkaloids, and their capacity to form ligands with transition metals, there is constant interest in their total synthesis. This has also led to many synthetic heterocyclic molecules derived from the naturally occurring alkaloids or mimicking a general structural motif. Just two examples, depicted in figure 1.2, are Bis(oxazoline) derivatives, used as ligands in asymmetric synthesis [1-4] and sildenafil, more commonly known by its trade name Viagra® , used to treat erectile dysfunction [5, 6]. Sildenafil is a perfect example that demonstrates not just the biological activity of an N-heterocyclic structure, but also the economic component. In 2013 it alone accounted for over $1 billion in revenue for Pfizer [7]. Quinine is a quite famous alkaloid. It is one of the earliest drugs for treating malaria, used in the Sharpless asymmetric dihydroxylation, and as a beverage ingredient. It has a bitter taste, and is found in the beverages ‘Bitter Lemon’ and ‘Tonic Water’[8-10]. First isolated in its pure form in 1820, the first total synthesis of Quinine was reported by Woodward and Doering in 1944 [11]. Furthermore, quinine is a vicinal amino alcohol, having the amine and alcohol functional groups in the 1,2 position, as depicted in figure 1.3

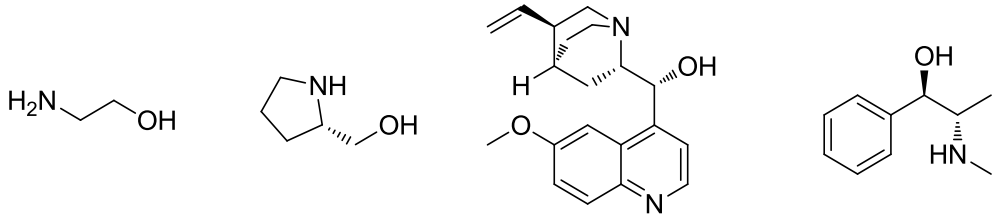


Bis(oxazoline) derivative

sildenafil
(Viagra®)

Figure 1.2 Structures derived from alkaloids

Vicinal amino alcohols are an important subgroup of the alkaloids [12], and several are depicted in figure 1.3. In its most basic form a vicinal amino alcohol is 2-aminoethanol. The molecules prolinol, quinine, and ephedrine, are some examples of well-known vicinal amino alcohols. S-Prolinol is derived from S-proline, a natural amino acid, and its derivatives are commonly found in organocatalysis. Ephedrine is still used as a pharmaceutical today, and its derivatives are used as precursors for the synthesis of oxazolines, molecules used as chiral ligands.



2-aminoethanol

S-prolinol

quinine

ephedrine

Figure 1.3 Vicinal amino alcohols

Now that the importance of this functional class is apparent, one must ask the question, how to prepare them? One of the methods used is the direct oxyamination of an alkene.

Oxyamination Reactions

The first report of the introduction of an amino and an alcohol function across a double bond in one step is B. Sharpless' s 1975 paper [13], followed by Bäckvall's [14], and the first catalytic procedure is reported by Sharpless in a 1976 paper [15]. It wasn't until 1996, a full 20 years later, that the same author published his famous paper on the 'Catalytic Asymmetric Aminohydroxylation (AA) of Olefins'[10].

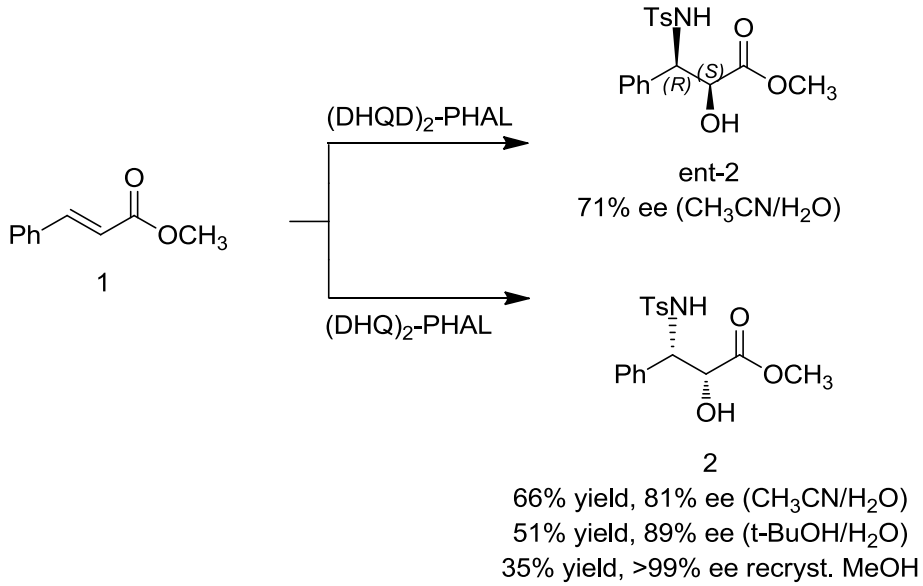


Figure 1.4 Example of the Sharpless Aminohydroxylation

Since the first report in 1975 there has been work published on this subject, but relatively little considering the synthetic importance of vicinal amino alcohols, with fewer than 5000 articles and 3000 patents listed on SciFinder for oxyamination or aminohydroxylation at present. This is due to the difficulty in the regio and stereo selective addition of a nitrogen-oxygen source across an unsymmetrical double bond, with the creation of two new stereogenic centers, as shown in figure 1.5.

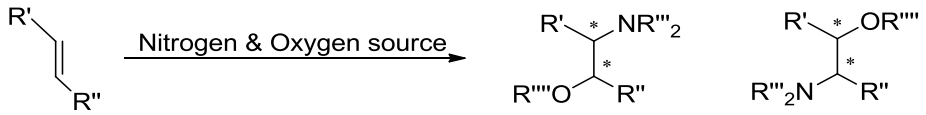


Figure 1.5 Possible outcomes of an aminohydroxylation of an alkene with two distinct rests, leading to a regioselectivity as well as a stereoselectivity conundrum

Osmium-Catalyzed Reactions

The osmium catalyzed oxyamination as typified by the Sharpless AA employs a catalytic amount of $K_2OsO_2(OH)_4$, a ligand derived from a cinchona alkaloid, and a nitrogen source, most commonly chloramine-T, which also serves as the reoxidant. While this is still the most popular method of direct oxyamination as seen in its application in total synthesis protocols [16-20], if suffers two drawbacks. Firstly the choice of substrates is limited to provide for the correct regioselective addition of nitrogen and oxygen, secondly the toxicity of osmium.

To overcome the problem of regioselectivity the workgroup around Donohoe developed the tethered aminohydroxylation (TA). In this novel approach the nitrogen source is tethered to the alkene containing molecule in such a fashion as to limit the addition of said source to only one regional moiety with excellent syn-diastereoselectivity [21, 22].

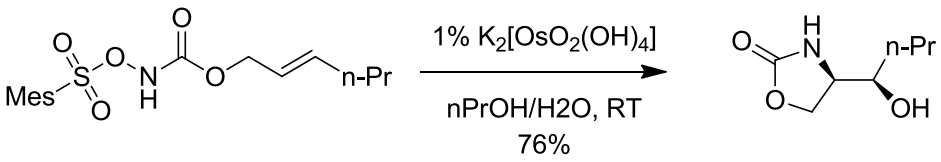


Figure 1.6 Example of a tethered aminohydroxylation (TA)

Palladium-Catalyzed Reactions

In 1975 Bäckvall [14] published the Pd mediated oxyamination. The drawback of this was that it only worked with stoichiometric amounts of Pd. It wasn't until 2005 that Sorensen et. al. [23] reported a catalytic use of palladium by using an iodine (III) oxidant to regenerate the Pd (II) source. This method also uses a tethered N and O source to produce an intramolecular reaction leading to a heterocycle, and in a complementary fashion to the tethered method of Donohoe, produces anti addition across the alkene.

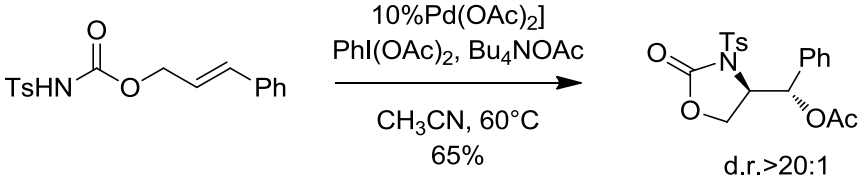


Figure 1.7 Example of a Tethered Pd catalyzed aminohydroxylation

Closely following this work in 2006 Lui et. al. published an intermolecular variety that offered not only excellent regioselectivity, but given an allylic substituent offered diastereoselectivity as well [24].

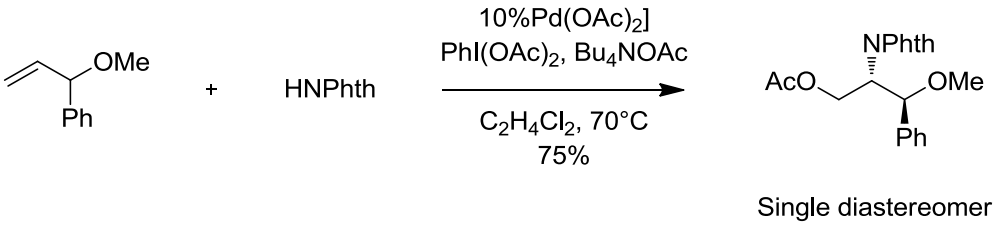


Figure 1.8 Example of a Pd catalyzed intermolecular aminooxygenation

Copper Catalyzed Radical Hydroxylamine Reaction

The first account of a Cu catalyzed oxyamination was in 2002 by the workgroup of Göttlich [25]. Herein was introduced a new method of cyclic vicinal amino alcohol syntheses, the radical aminohydroxylation:

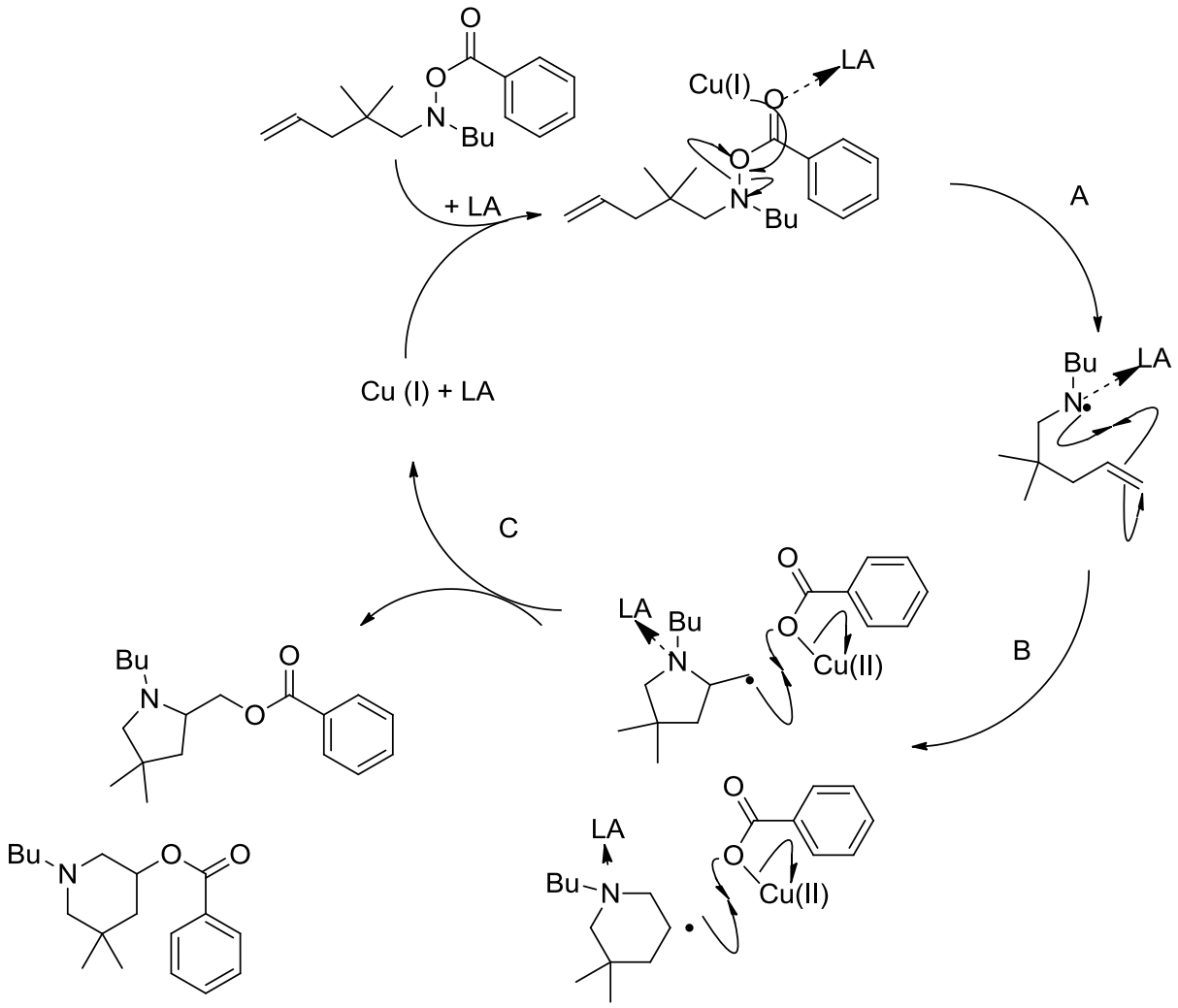


Figure 1.9 Proposed catalytic cycle of Aminohydroxylation

The catalytic cycle as shown in figure 1.9 contains three steps. In step A the LA coordinates to the carbonyl group oxygen, activating it, and the Cu(I) catalyst cleaves, through a single electron transfer, the N-O bond. Now another unit of LA coordinates the aminyl radical. This percipitates, in step B, a 5-exo-trig, or a rare 6-endo-trig cyclisation, by way of a nucleophilic attack of the alkene on the electrophilic LA coordinated aminyl radical. The last step, C, involves forming the products and regenerating the catalyst. Through capture of the radical by the Cu(II) coordinated benzoylic rest the vicinial amino alcohol is formed, at the same time reducing the Cu(II) to Cu(I), regenerating the catalyst for another cycle.

This reaction was a keystone, showing that in principle it should be possible to make much more complex prolinol and piperinol derivatives, for example azasugars. It suffered from two drawback though, 1) a 3:1 selectivity of 5 to 6 ring, and 2) drastic conditions of 100°C for five hours using 1 eq. $BF3 * OEt_2$.

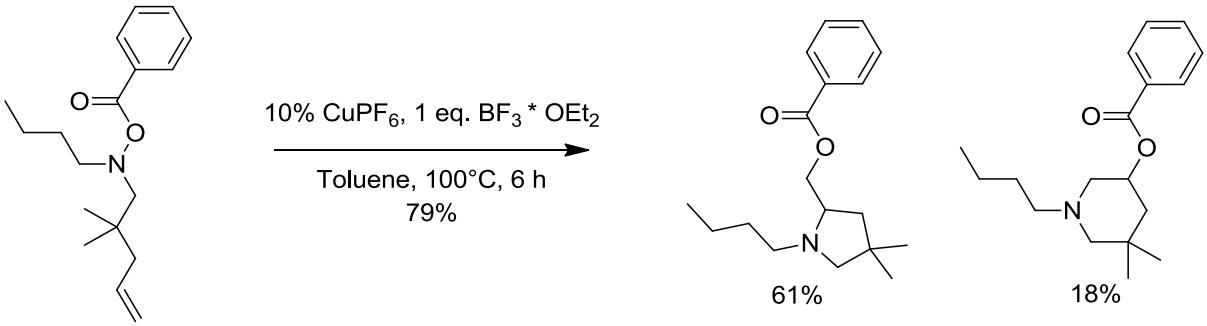


Figure 1.10 Reaction of hydroxylamine to 1,2-aminoalcohol, as optimized by M. Noack

Five years later in 2007 the workgroup of Yoon [26] published an account of the addition of an N-Sulfonyl oxaziridine across a variety of alkene's, using a Cu (II) salt via a Cu (II/III) pathway.

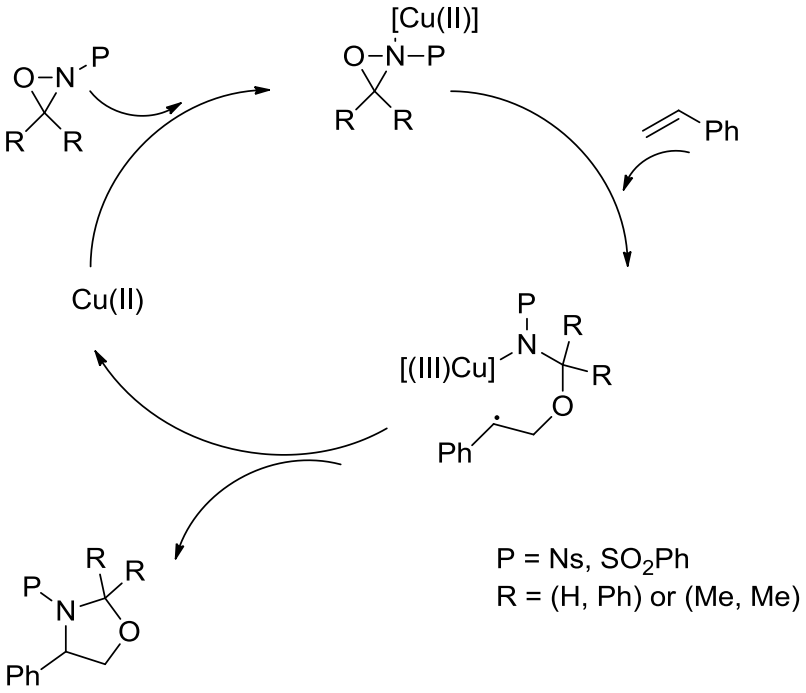


Figure 1.11 Catalytic cycle of Yoon Oxyamination

In 2008 Chemler et. al. published work [27] describing a very similar reaction starting with Cu(II), and achieving a Cu (II) – Cu (I) turnover through the use of 3 equivalents of TEMPO.

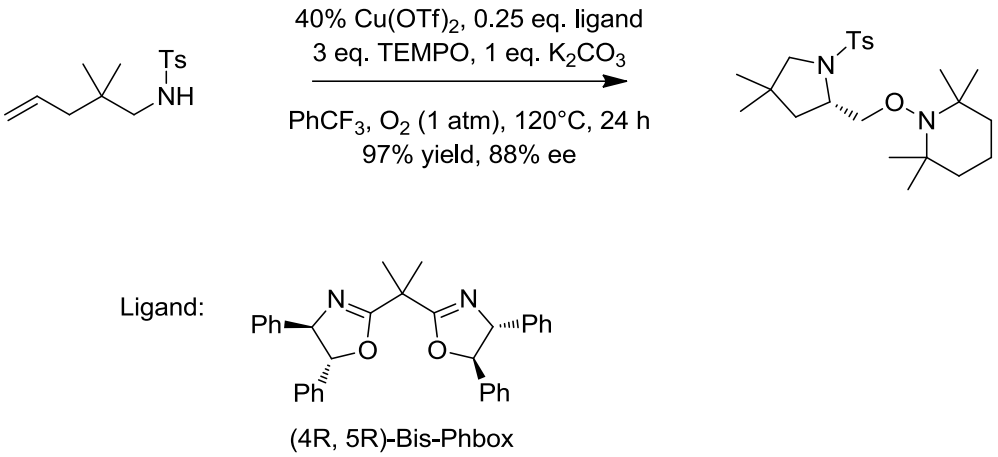


Figure 1.12 Reaction of the Chemler group using TEMPO for Cu(I) generation aminooxygenation

Also in this reaction an ee was achieved using the chiral Bis-PhBox ligand. The reaction as shown also works for aniline analogs with less catalyst and ligand loading, this specific reaction was chosen as an example due to structural and reactive similarity with the aminohydroxylation work published by Göttlich [25].

Goal

The radical Cu(I) catalyzed hydroxyamination pioneered in the Göttlich group has been shown to work, but needs to be optimized. The hypothesis is that by weakening the N-O bond, the molecule will become more reactive. This should lead to milder reaction conditions, and could result in higher yields. It could also be tailored to yield selective 5- or 6-Ring formation. To test this the bond strength of various hydroxylamines should be measured. This could be achieved by cyclovotametric measurement to see the $E_{1/2}$ value of N-O bond breakage and reformation, by ab-inito calculation and FTIR measurement to determine the wavenumber of the bond, or by crystallographic bond length determination.

Further it is hypothesized that by optimizing the bond strength, i.e. the reactivity, an intermolecular reaction could be pursued, leading to the synthesis of open chained vicinal amino alcohols. This could lead to interesting applications with regard to natural product synthesis.

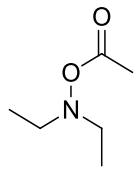
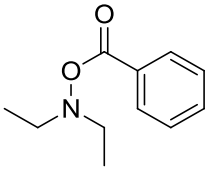
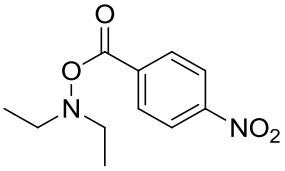
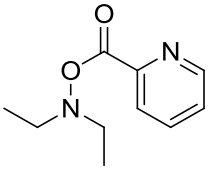
Finally a better understanding of the reaction mechanism is sought. This could be achieved through the use of a radical scavenging molecule such as TEMPO. Further insight into the mechanistic minutia of the reaction would lead to a better understanding of how changing

the molecular structure of substrates would affect the outcome of the reaction. This in turn could lead to stereoselective synthesis.

Main Section

Weakening the N-O Bond

In the first step to determine how to weaken the N-O bond, different groups could be attached to the O, and these molecules then subjected to cyclic voltammetry measurement. In this fashion the aminyl radical would be generated by a single electron transfer, and its redox behavior could be investigated. Several molecules were selected for this investigation as shown in table 2.1. In previous work by Dr. Noack object 2 was already tested in such a way, with an $E_{1/2}$ value of 0.79 mV [28]. These measurements were performed in DCM against a silver/silver chloride electrode in a saturated ethanolic solution of LiCl.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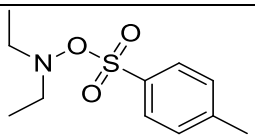
			
(5)			

Table 2.1. Molecules synthesized for cyclic voltammetry measurements to determine the EWG influence on N-O bond cleavage $E_{1/2}$

To this purpose molecules 1 through 4 were synthesized using *N,N*-diethylhydroxylamine and the various acid chlorides, as shown in Figure 2.1. Object 5 was attempted but could not be synthesized, instead leading to a sulfonamide.

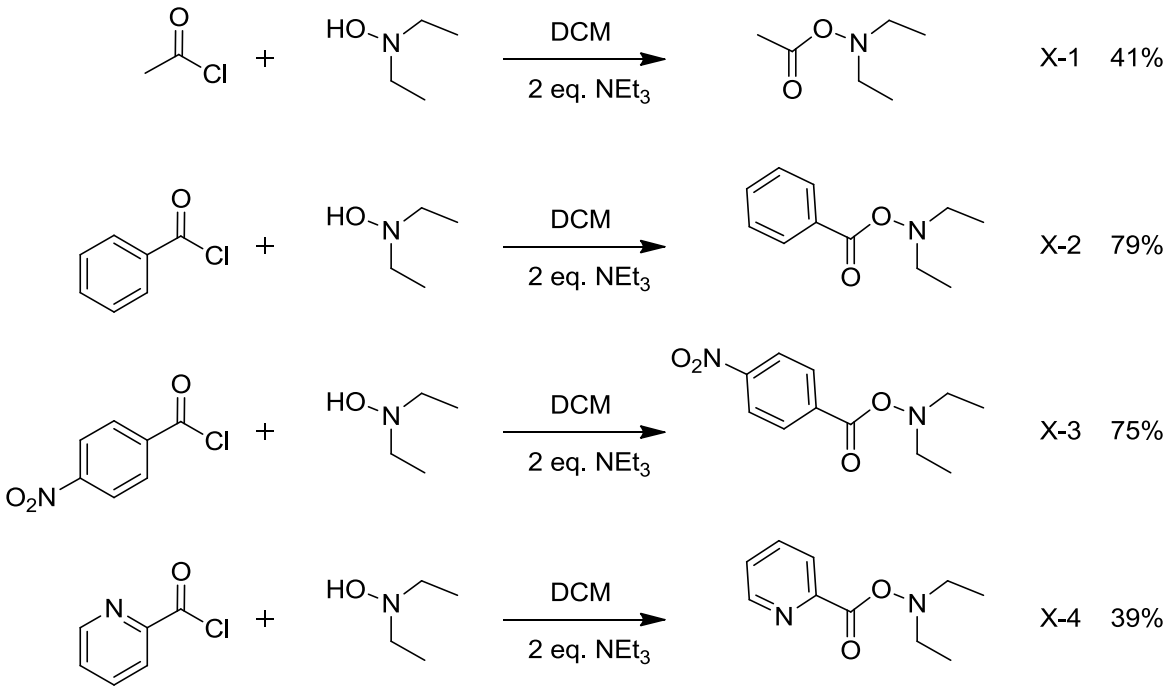


Figure 2.1 Synthesis of various simple hydroxylamines for CV measurement

The calculated $E_{1/2}$ values from the measurements, Appendix 1, are summarized in the following table. However, due to the irreversibility of the redox reactions this was not further investigated.

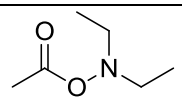
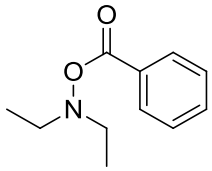
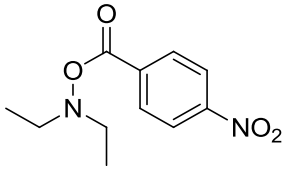
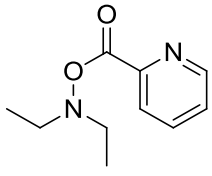
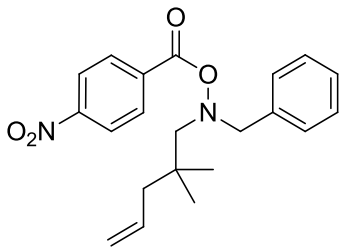
Substance	Molecule	$E_{1/2}$ (n=3) [mV]
	(X-1)	0.69
	(X-2)	0.83
	(X-3)	0.15
	(X-4)	0.55

Table 2.2 $E_{1/2}$ of the various hydroxylamines

The *p*-nitro group containing molecule, X-3, has an $E_{1/2}$ of just 0.15 mV, by far the lowest half potential. This indicates that it has the most easily reducible N-O bond, due to the strong electron withdrawing group. It was deemed the best choice for use in optimizing the cyclization reaction.

It was also thought that computed IR spectra might give insight into the N-O bond strength, therefore geometries were optimized at the B3LYP/6-31G(d) level of theory [29] [30] and harmonic vibrational frequencies were calculated subsequently with Gaussian09 [31], if the stretching vibration could be calculated, and then identified in various synthesized molecules. The B3LYP spectra of X-2 and X-3 were calculated, showing a stretching vibration of 906 cm^{-1} for X-2 and 901 cm^{-1} for X-3. In line with these calculations, X-3 displayed at peak at 876.6 cm^{-1} and X-2 displayed a peak at 872.1 cm^{-1}, with a shoulder peak at 936.2 cm^{-1}. These values proved useful in identifying the peaks in the measured FTIR spectra of said molecules. At the same time, at a difference of 5 cm^{-1}, they (indicated a slightly weaker *N-O* bond, but with this difference it's hardly possible to make a definite statement. For a more precise evaluation computations on a higher level of theory would be required.

Finally the crystal structure of various hydroxylamines was sought. In the course of my work I was only able to grow crystals suitable for measurement of one molecule, X-5 Appendix 2, making a useful comparison impossible.



X-5

N-O Bond length in angstrom

1.479

Figure 2.3a) N-O bond length of Oxymaine

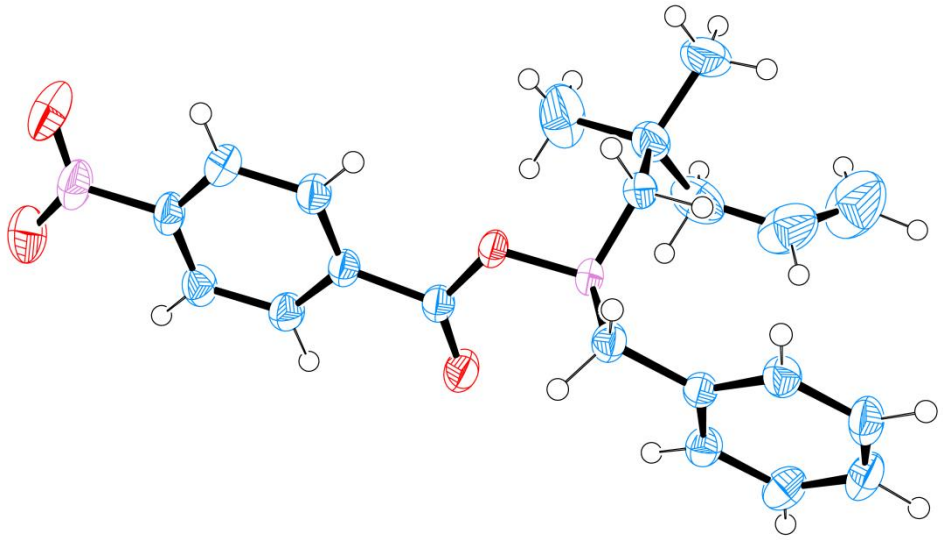
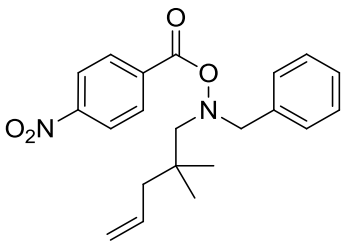


Figure 2.3b) N-O bond length of Oxymaine

Due to the inconclusive result of the IR calculation it was decided to carry on by testing a *p*-nitro derivatized molecule and see if the reactivity had increased, in line with the results of the CV measurements.

Determination of optimal cyclisation precursor

The molecule chosen as an ideal candidate for testing was N-benzyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine, figure 2.4.



X-5

Figure 2.4 The optimal cyclisation precursor

This has two reasons, the Thorpe-Ingold effect [32] and the gem-dialkyl effect [33]. The Thorpe-Ingold effect is the angle compression as a function of substitution, figure 2.5. This slight reduction in angle of 112° 2’ for a secondary to 109° 9’ of a quaternary carbon results in the approach of the double bond to the N-O bond, as applied to X-5.

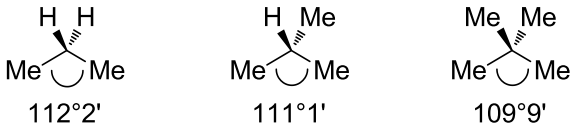


Figure 2.5 Thorpe-Ingold effect

Though undoubtedly the β-carbon angle will be different for the cyclisation precursors, as shown in figure 2.6, compared to the simple molecules depicted in figure 2.5, the trend of smaller angle for higher substituted carbon will be felt.

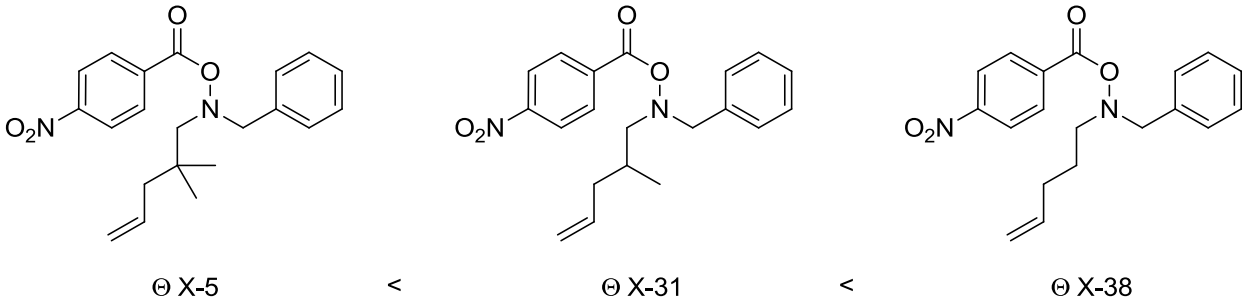


Figure 2.6 Trend of angle compression for cyclisation precursors

More importantly though is the gem-dialkyl effect. As described by Jung [33] this is the 'reactive rotamer effect', the selective destabilization of the groud state conformation and thereby a higher population of the conformation that leads to a cyclization reaction.

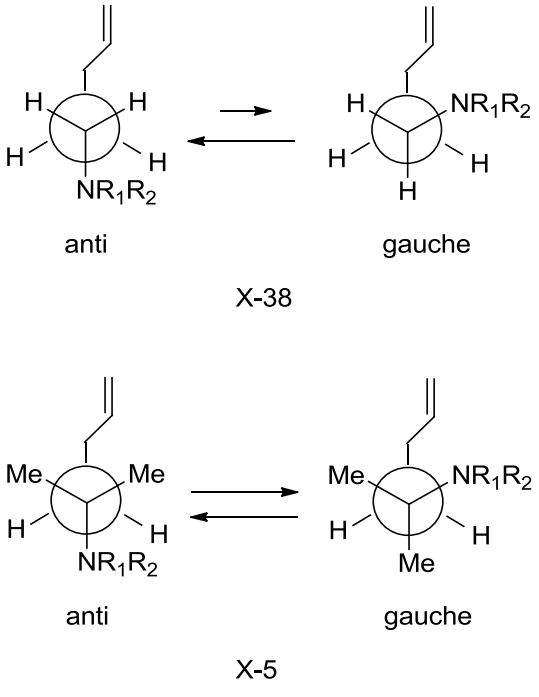


Figure 2.7 Gem-dialkyl effect

In the anti-formation of X-38, the two larger rests of the molecule are farthest from each other, making this conformation more stable. The molecule must first convert to the gauche formation to react, requiring more energy, meaning a lower population of the reactive rotamer. Compare this to X-5 in figure 2.7, in which the anti and gauche formations are relatively similar. This leads to a more equienergetic situation, and leads to the higher population of the gauche formation, the reactive rotamer, than seen in X-38.

Synthesis of optimal cyclisation precursor

Retrosynthetic analysis of X-5 revealed the following steps, as outlined in Figure 2.8. A hydroxyamination of a secondary amine, generated by the reduction of an imin. This would be synthesized by the condensation of a primary amine with an aldehyde, which in turn could be made through a simple Claisen rearrangement.

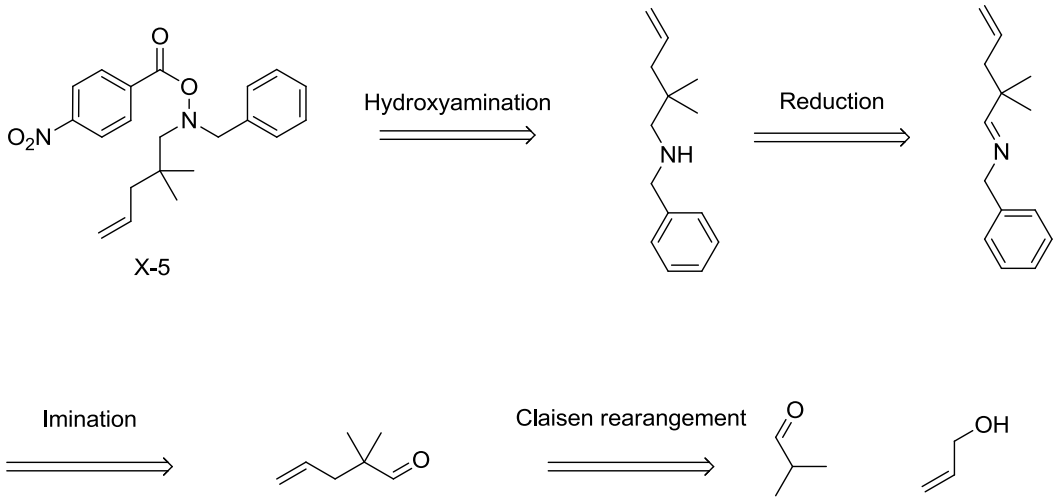


Figure 2.8 Retrosynthetic analysis

The synthesis was performed as follows:

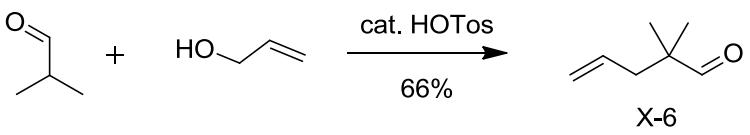


Figure 2.9 Claisen rearrangement of allylic alcohol and aldehyde

2,2-Dimethylpent-4-enal was prepared from allylic alcohol and isobutyr aldehyde with a catalytic amount of p-toluene sulfonic acid, by way of a Claisen rearrangement. This was then

converted to the imine with benzyl amine and reduced to the secondary amine with $NaBH_4$, figure 2.9 and 2.10.

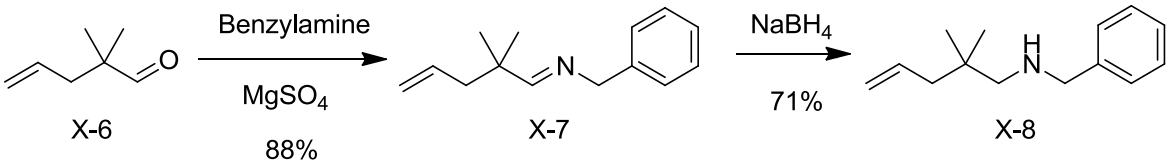


Figure 2.10 Two-step reductive amination leading to the secondary amine

To insert the hydroxylamine function two possible pathways presented themselves. One could use available benzoyl peroxide, and then saponify to give a free –OH function and finally react this with *p*-nitrobenzoyl chloride to give the desired product. This would add three extra steps, resulting in a 6 step synthesis before cyclisation experiments could begin. Alternatively one could make the desired peroxide and react this with X-8, which required only 4 steps or 5 if one includes the step to make the peroxide. This second approach was selected. First *p*-nitro benzoyl peroxide was synthesized to lit. procedure [34], figure 2.11, and then this was reacted with the amine X-8, figure 2.12, in the same manner as benzoyl peroxide with secondary amines by Dr. Noack [28].

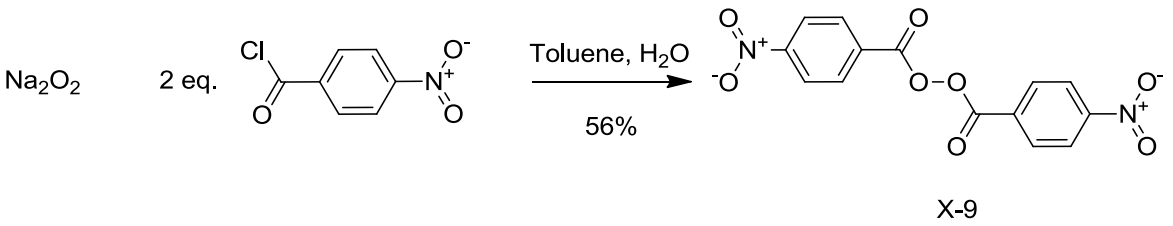


Figure 2.11 Synthesis of p-nitro dibenzoyl peroxide

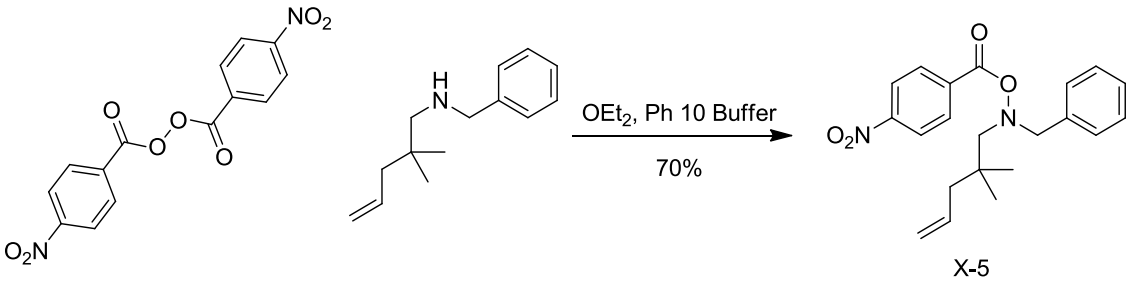


Figure 2.12 Formation of hydroxylamine

Initial cyclisation tests and optimization of reaction conditions

Initially X-5 was tested under the same reaction conditions as those optimized by Dr. Noack. This showed a slightly higher overall reactivity, but less selectivity, with yield of the 6-membered ring going up by 11% and that of the 5-membered ring going down slightly, by 6%, as shown in figure 2.13.

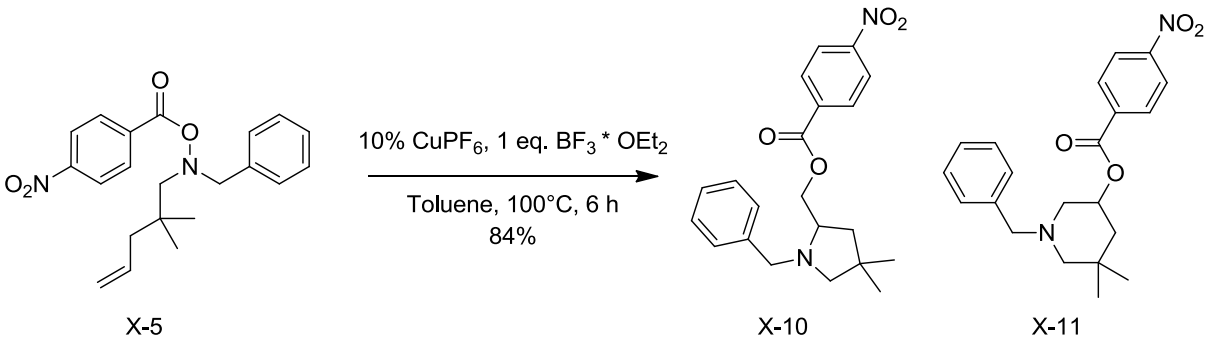


Figure 2.13 Cyclization experiment leading to two products

Entry	cat.Mol% Cu(I)	Eq. BF_3	Solvent	Temp °C	Time h	HPLC conversion %		Isolated yield %	
						5-ring	6-ring	5-ring	6-ring
1	10	1	Toluene	100	5			55	29
2	10	1	Toluene	RT	5	85	15	73	15
3	10	1	Toluene	0	48	0	0		
4	10	0	Toluene	RT	48	0	0		
5	10	0	Toluene	50	48	15	85	2	44
6	10	0	Toluene	100	1	15	85	2	45

Table 2.3 Initial experiments at cyclizing

These yields were isolated, and used to establish an HPLC method for reaction monitoring. These are from now on expressed via HPLC conversion. This in no way means there was a total conversion of educt to product, but that the educt was consumed, and that with this analysis method only product, 5-, and/or 6-membered ring was detected.

In the next steps, entry 2 and 3, the reaction temperature was reduced to RT and 0°C. At RT the reaction required 5 hours to completely consume the educt, and at 0°C no reaction was detected over 48 hours. Entry 2 now shows that at RT the selectivity for 5- versus 6-membered ring is enhanced, yielding a total of 88%, 73% 5-ring and 15% 6-ring. This concluded the initial testing of temperature conditions, and next it was determined what effect the removal of the Lewis acid would have. The initial test at RT showed no reaction over the course of 48 hours, but at 50°C the educt was slowly consumed, over a total of 48 hours. Interestingly, as shown in entry 5, a complete inversion of regioselectivity was achieved. The temperature was raised to 100°C and the reaction was complete in just one hour. The proucts of the reaction without LA at 50°C and 100°C were isolated, and showed similar yields. As determined by HPLC under these reaction conditions there was an inversion of regioselectivity, but the yield was drastically reduced. With just 47% total yield, 45% of which was 6-membered ring at 100°C.

This initial test series showed the hypothesis of inserting an electron withdrawing group into *p*-position of the O-Benzoyl rest made the molecule more reactive, probably by reducing the electron density of the N-O bond. A higher selectivity of 5 or 6-membered ring was achievable as well as a higher isolated yield of 5-, though not of 6-membered ring. It has been discussed by M. Newcomb [35] that Lewis acids, specifically $BF_3{\cdot}OEt_2$, increase the rate constant of 5-exo trig cyclizations, by means of complexing the dialkyl aminyl radical. This correlates with the high yield of 5-membered ring when BF_3 is present, but not the regioselectivity change when BF_3 is not present. As described by Baldwin in his empirically based publication [36], the 5-exo-trig is favored over the 6-endo trig ring closure in a radical reaction, and this is exactly the case with BF_3 present. Why this rare 6-endo trig reaction takes place is still not clear. To determine whether the ionic reaction was taking place, as the 6-endo-trig ring closure for both anionic and cationic reactions are well documented, it was attempted to react X-5 in the presence of 10% Pd(II) or 10 % $N(Bu)_4I$ catalyst, at RT, 50°C and 100°C in toluene over 96 hours. None of these tests resulted in a product as determined by HPLC analysis.

It was hypothesized that side reactions could occur at prolonged exposure to higher temperatures, and maybe a better yield could be achieved by microwave (MW) synthesis. MW assisted synthesis of organic molecules has recently become more common, although the exact nature of the rate enhancement is still unclear [37, 38]. This discussion revolves around whether the enhancement is due to the rapid dielectric heating, specified as specific MW effects, or non-thermal MW effects, not so easily classified. These discussions are not within the scope of this

thesis; suffice to say that there is an observable rate enhancement related to using a synthesis MW, and I was determined to experiment with this and find out if it could be exploited to minimize side reactions in the course of my work.

The initial tests showed a quite surprising result, as shown in table 2.4. The hoped for higher yield of 6 ring did not occur (Entries 1 & 2), indicating that the problem with side products persists even at shorter time intervals. Interestingly though the cyclisation to 5 ring occurs at 75°C in 10 minutes with the same yield as at RT over 5 hours, although 2 eq. of BF_3 are now required. This opens up the possibility of a fast reaction with reactants that are not temperature sensitive at 75°C, or a milder reaction with potentially temperature sensitive reactants at RT. The microwave reaction also has the advantage of needing only 5% catalyst loading. It was also found that the reaction without BF_3 proceeded to completion within 5 minutes. This would indicate that the cyclisation with BF3 proceeds irreversibly through the ammonium radical, producing the kinetic product, while without BF3 it proceeds reversibly through an aminyl radical, producing the thermodynamic product.

Entry	cat.Mol%	Eq. BF_3	Solvent	Temp °C	Time min	HPLC conversion %		Isolated yield %	
						5-ring	6-ring	5-ring	6-ring
1	5	2	Toluene	50	30	46	30		
2	5	2	Toluene	75	10	82	18	76	17
3	10	0	Toluene	100	2	5	25		
4	10	0	Toluene	100	10	16	75	10	49
5	10	0	Toluene	100	5	15	85	11	50

Table 2.4 Initial experiments with MW cyclisation

It was now investigated what effect a change in solvent would have on the reaction products, as shown in table 2.5. DMSO, Dioxane and CCl_4, and THF yielded no results, while Diethylether, CH_3CN, $CHCl_3$ and DCM yielded lower results.

Entry	cat.Mol%	Eq. BF3	Solvent	Temp	Time	HPLC conversion %		Isolated yield %	
						5-ring	6-ring	5-ring	6-ring
1	5	1	OEt_2	RT	24h	<2	<1	0	0
2	5	1	DCM	RT	6h	75	16	70	15
3	10	2	CH_3CN	75°C	30 min	70	30	35	10
4	10	2	$CHCl_3$	75°C	30 min	74	26	30	8

Table 2.5 Various Solvents. Reaction 3 and 4 were performed in the MW

This shows it is possible to perform the reaction in DCM at RT, albeit with a slightly lower yield.

Previous published work has established that Lewis and Brønsted acids activate dialkylaminyl radical reactions. Aminyl radicals are, as compared to aminium cation radicals, less reactive [35, 39, 40]. It was thought that changing the LA or using a BA could be beneficial. This might have an effect on reactivity, selectivity, or be interchangeable with BF_3*OEt_2. Problematic though, is that only LA containing no Cl atoms could be used. As soon as a Cl containing LA is involved, the preferred product is the chlorinated piperidine ring [28], as shown in figure 2.14. This puts a drastic limit to the number of LA's available for us, since these have to also be soluble in the reaction medium.

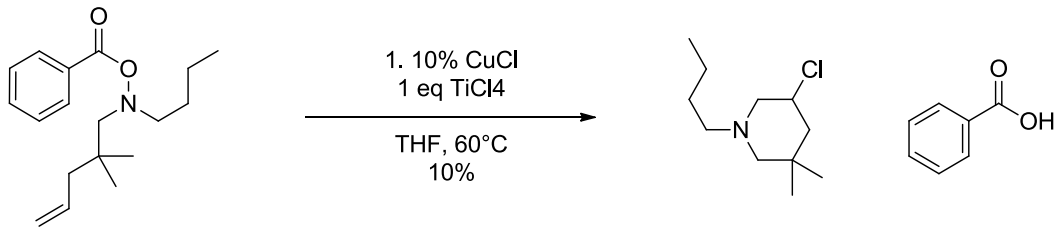


Figure 2.14 Cyclisation producing halogenated piperidine ring

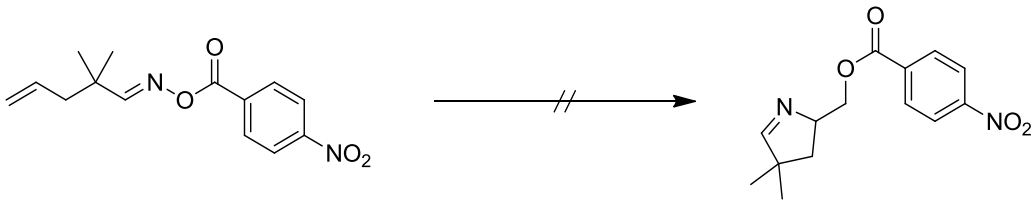
Several LA and BA's were subjected to cyclization conditions, i.e. 75°C, 30 min, in the microwave. Each acid was tested in the solvents OEt_2, DCM, THF, CH_3CN, DMSO, $CHCl_3$, CCl_4, dioxane and toluene. Regretfully these experiments did not even lead to trace amounts of product, though in some cases the reactant was consumed. The probable result of which was the fragmentation of the molecule X-5 into amine and acid. These results indicate that a cationic mechanism is not relevant, and that the reaction proceeds along a radical pathway.

Entry	cat.Mol%	LA/BA	HPLC conversion %	
			5-ring	6-ring
1	10	Scandium(III) triflate	0	0
2	10	Silver(I) triflate	0	0
3	10	$MgBr_2$	0	0
4	10	Copper(II) triflate	0	0
4	10	p-Nitrobenzoic acid	0	0
6	10	Trifluoroacetic acid	0	0
7	10	Benzoic acid	0	0

Table 2.6 Variation of the Lewis acid or Brønsted acid

Attempts at Oxime and Hydroxamic acid cyclisation

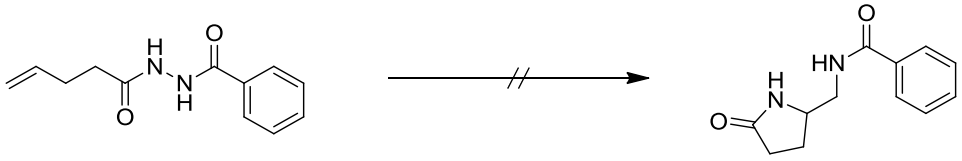
Having determined the optimal reaction conditions for a cyclisation, it was attempted to apply this method to other similar functional groups. It was thought that an imin with an O-*p*-nitrobenzoyl group on it would prove sufficiently reactive to cyclize producing a cyclic imin of the sort shown in figure 2.15. This did not result in a product.



X-75 X-76

Figure 2.15 Attempted cyclization of X-75

Next it was attempted to cyclize a hydrazine amide derivative, as shown in figure 2.16, which also did not result in any product.



X-77 X-78

Figure 2.16 Attempted cyclization of X-77

To determine if the reactions would proceed under harsher conditions, these cyclisation precursors were subjected to the following:

a) 5%. 10% and 100% Cu(I) salt
b) 0, 1, 2, and 5 equivalents of borontrifluoride etherate
c) 0, 25, 50, 75, and 100°C for 48 h.

None of these conditions yielded cyclisation products.

Attempts at intermolecular oxyamination

In the next phase it was determined if the optimal reaction conditions would lend themselves to an intermolecular oxyamination reaction. This was to be tested using two highly reactive oxim's and a hydroxylamine, as the N-O source, with styrene, norbornene and cyclohexene as alkene sources. Styrene and norbornene were picked for their reactivity, and reactions were attempted in DCM and toluene. Though it is not as reactive, cyclohexane was used since it is a liquid, and can act as solvent, thereby increasing the chance of a reactive radical intermediate being in close molecular proximity to the alkene at the time of formation.

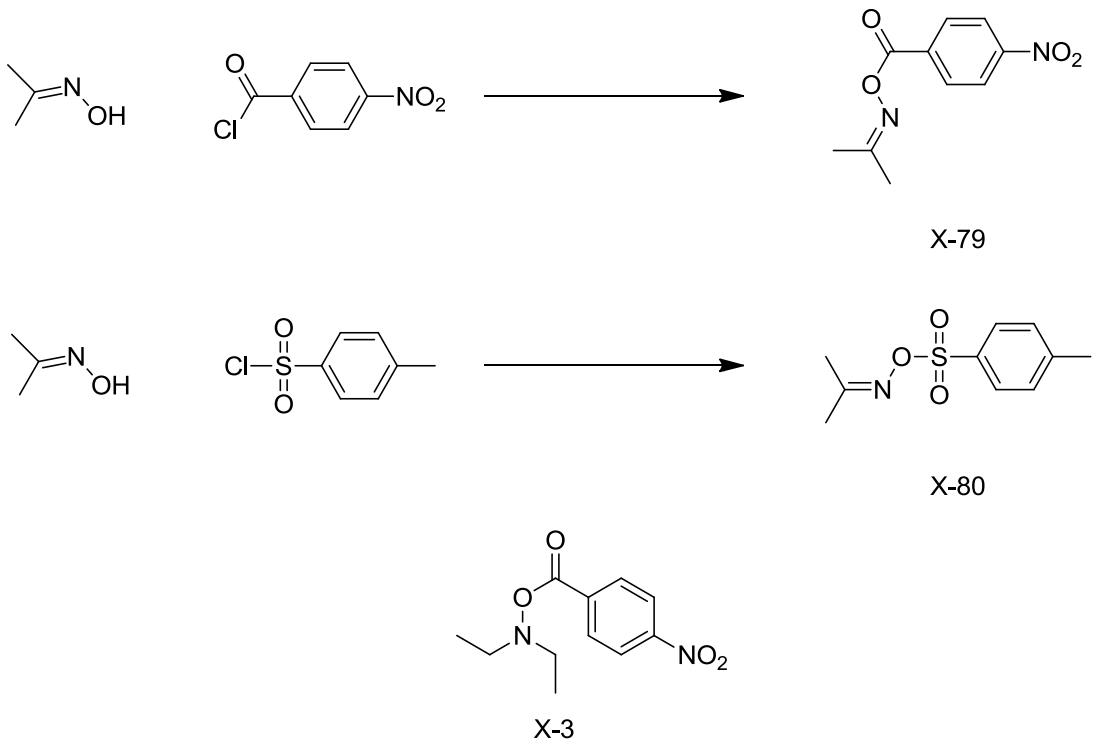


Figure 2.17 Synthesis of molecules for intermoleculare hydroxylamination

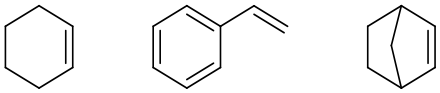


Figure 2.18 Various alkenes used for the intermolecular hydroxylamination

These substrates were subjected to a wide variety of conditions, 5, 10, 25, and 100 % Cu(I) salt, 1, 2, and 5 equivalents of borontrifluoride etherate, 0, 25, 50, 75, 100°C, 1, 2, 5, 10 equivalents of alkene, in DCM and toluene, or in the case of cyclohexene, with said substrate as the solvent. Reaction progress was analyzed by TLC, GC-MS, and ESI TOF to detect possible oxyamination products. None were observed.

Investigating the radical mechanism

It was thought that a better insight into the mechanism of the reaction would lead to ideas for imin, oxim, or intermolecular oxyaminations. Determining whether the reaction was reversible, or if an intermediate could be isolated with a radical scavenger might shed some light on the mechanism. To test whether the reaction to 5- and 6-ring was reversible and an interconversion was possible, the isolated 5-ring and 6-ring were individually subjected to reaction conditions which might lead to an interconversion, as shown in figure 2.19.

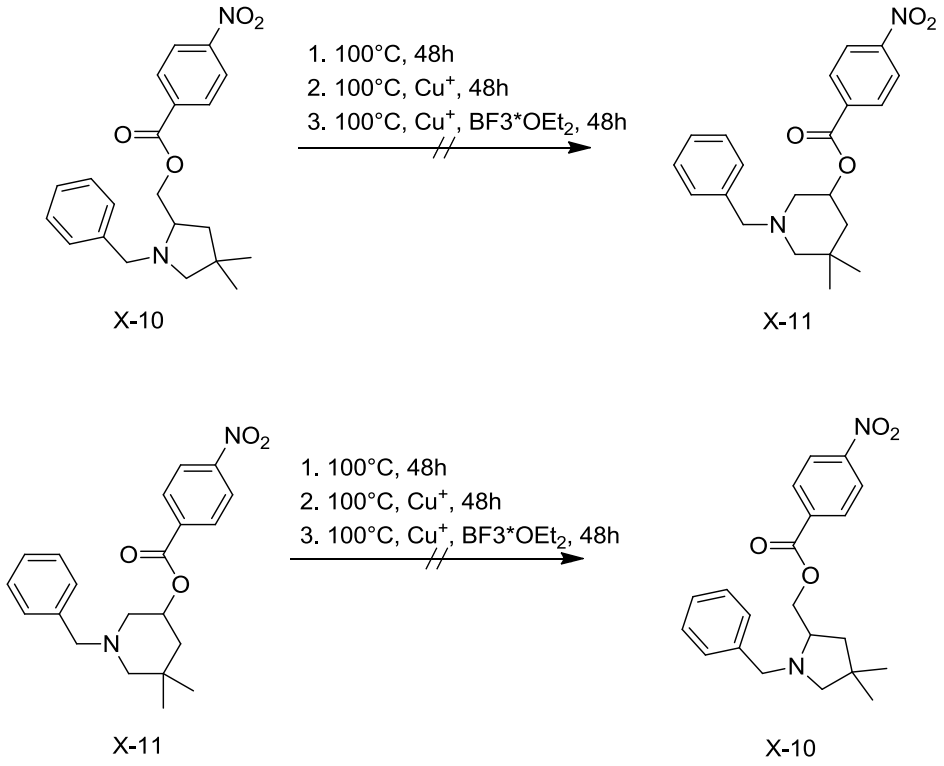


Figure 2.19 Attempts at interconversion of 5- and 6-ring

None of these experiments led to a conversion, lending credence to the hypothesis that this reaction is 1) radical, and 2) non-reversible. In order to cement the hypothesis of a radical cyclisation TEMPO was added in various equivalents, 1 eq., 2 eq., 5 eq., in an attempt to isolate the TEMPO product, as other authors have achieved [27]. This attempt did not result in a product, as shown in figure 2.20. This does not mean however that the reaction is not a radical one; it is simply that TEMPO will not scavenge the radical carbon in this reaction. It may still be possible, with the appropriate radical scavenging molecule, though this was not pursued further.

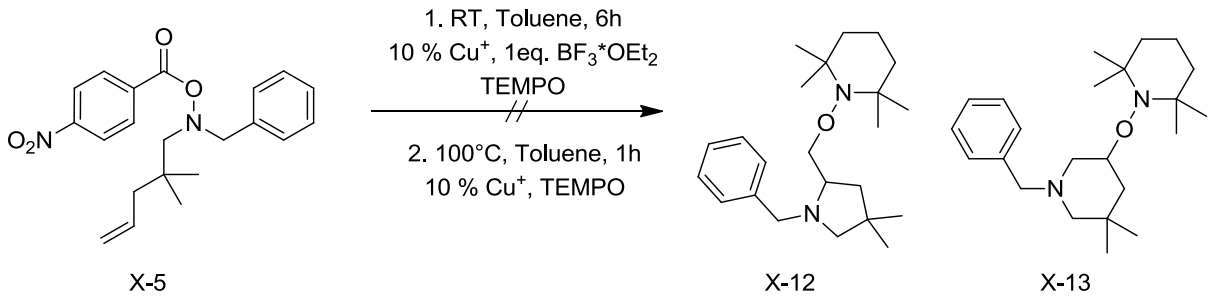


Figure 2.20 Attempt to capture radical intermediate with TEMPO

Scope of milder reaction conditions

Finally, the scope of the milder reactions conditions were tested on a variety of molecules for intramolecular oxyamination. After having optimized the reaction parameters with the ideal reactant X-5, the effects of various substituents on the reaction were investigated. The benzoyl group on the Nitrogen was replaced with a butyl and allyl group, and the germinal dimethyl's were moved along the chain, reduced by one, replaced with phenyl, or removed completely.

In the first instance changing the rest on the nitrogen was investigated. The benzyl group was exchanged for a butyl group to investigate the possible radical stabilization of the benzyl group. Next the benzyl group was exchanged with an allylic group to see if there would be a competing reaction to form a 3- ring via a 3-exo-trig reaction. These molecules were prepared as seen in Figure 2.21 and Figure 2.22 through reductive amination with sodium triacetoxy borohydride and the corresponding amine.

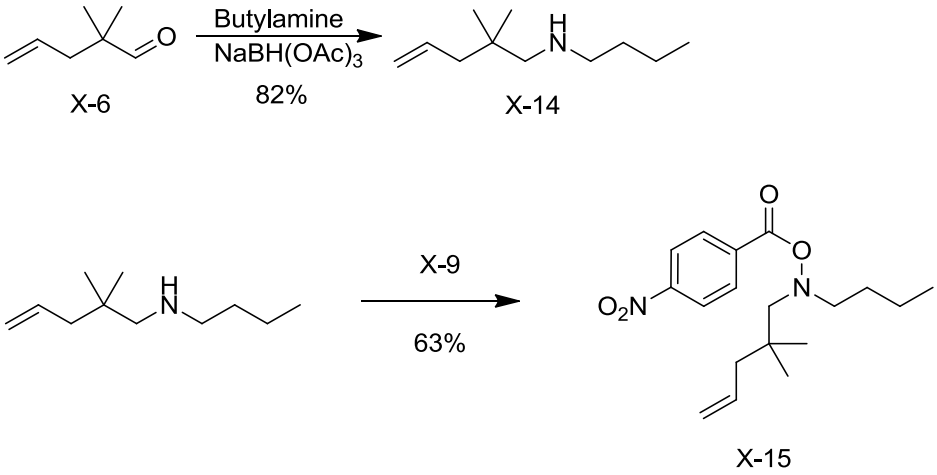


Figure 2.21 Synthesis of N-butyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

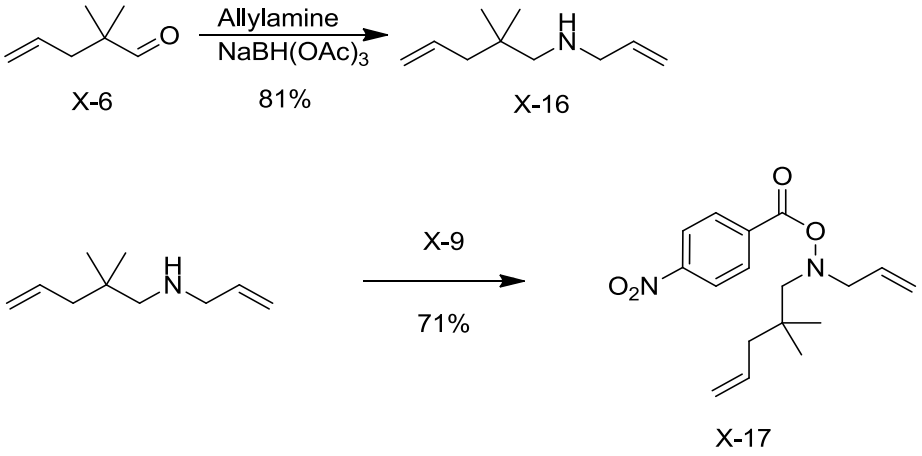


Figure 2.22 Synthesis of N-allyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

Next the placement of methyl or phenyl groups along the carbon skeleton leading to the ring structure was investigated, to determine the scope of the gem dialkyl effect on product yield. First both methyl groups were moved down one carbon to C-3, for which following molecule was synthesized.

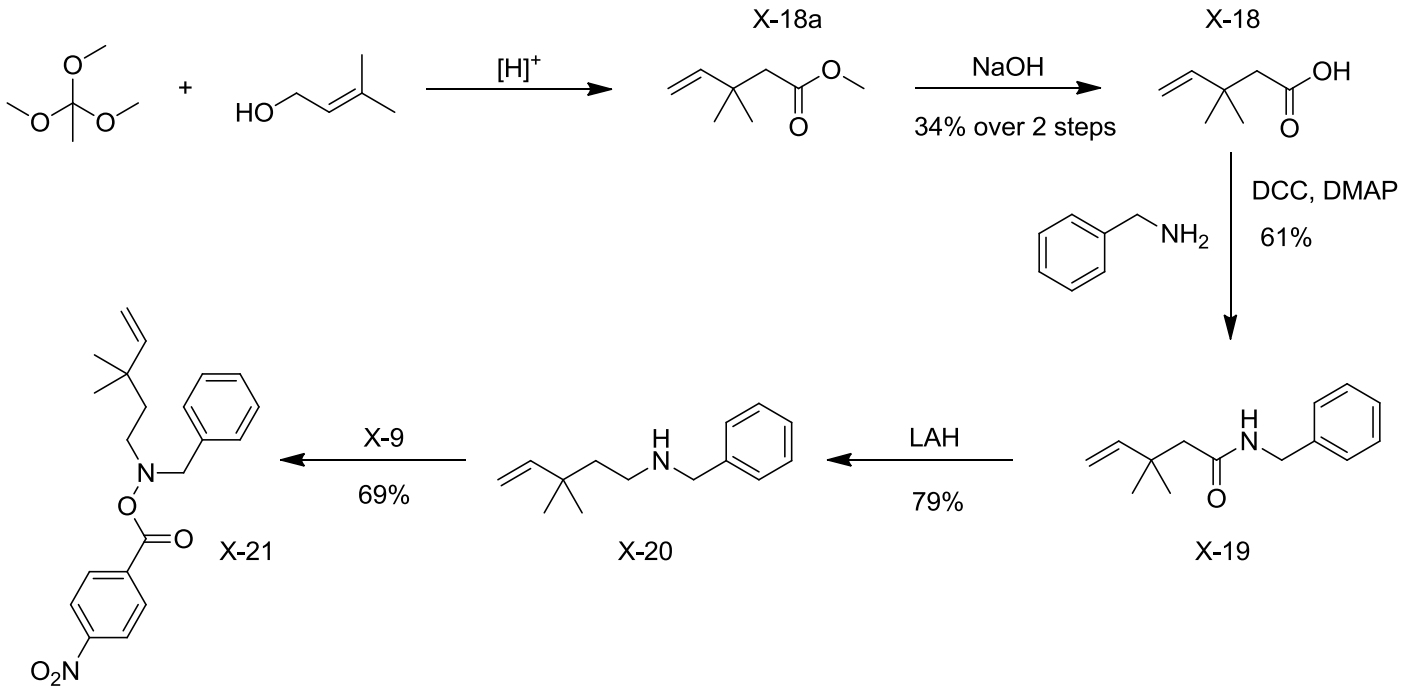


Figure 2.23 Synthesis of N-benzyl-N-(3,3-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

In the first step trimethyl orthoacetate and 2-methylbut-2-en-1-ol were converted to the γ, δ unsaturated ester, X-18a, via Johnsen-Claisen rearrangement. This was then saponified without workup, to yield 3,3-dimethylpent-4-enoic acid in 34% yield over two steps. The acid was then converted to the amide via DCC and DMAP in a Steglich esterification, and reduced to the secondary amine via LAH. The amine was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine, figure 2.23.

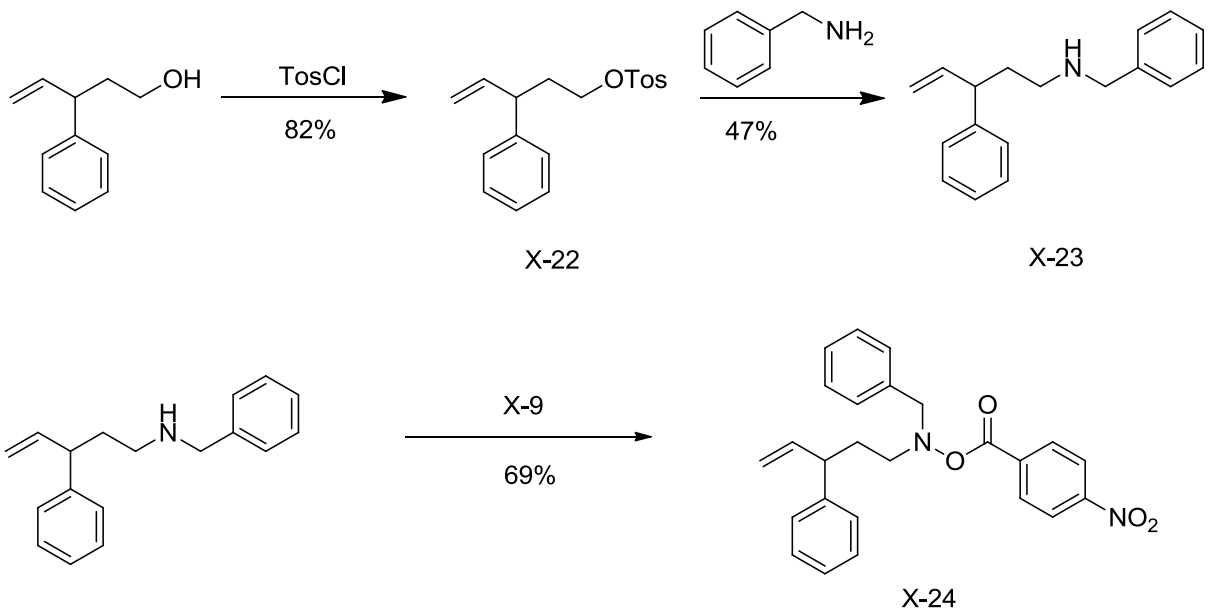


Figure 2.24 Synthesis of N-benzyl-O-(4-nitrobenzoyl)-N-(3-phenylpent-4-en-1-yl)hydroxylamine

Following this it was tested what effect a very large group, phenyl, compared to a small group, methyl, in the C-3 position would have. As depicted in figure 2.24 the alcohol 3-phenylpent-4-en-1-ol was tosylated with p-toluenesulfonyl chloride, and then converted to the secondary amine with benzylamine in a S_N2 reaction. The amine was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine.

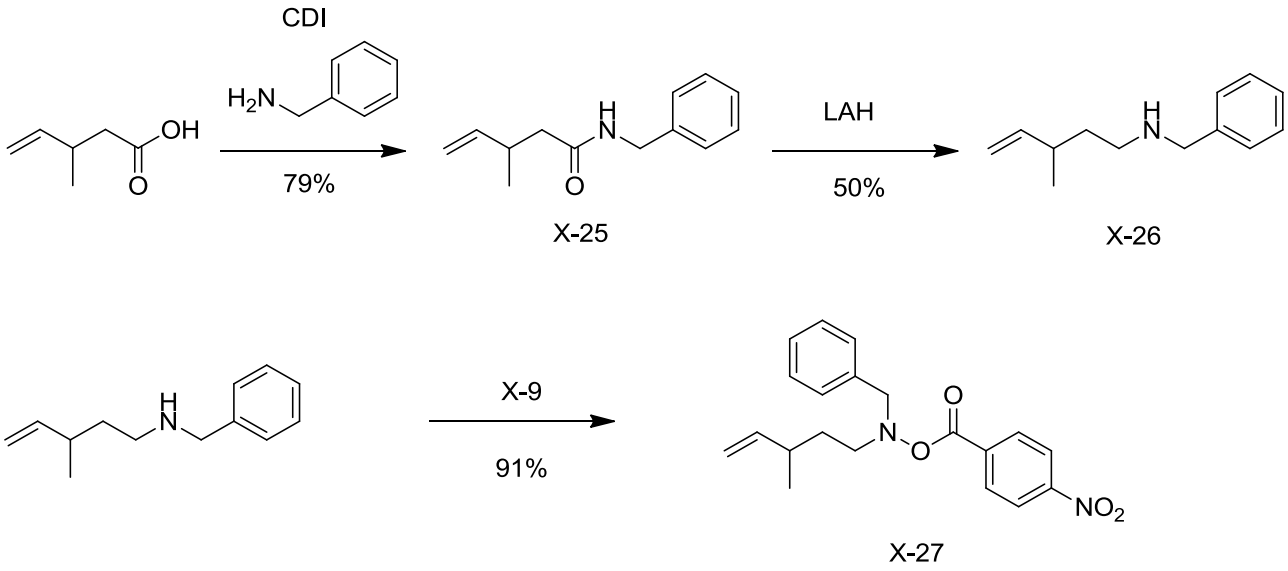


Figure 2.25 Synthesis of N-benzyl-N-(3-methylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

For the methyl substituted molecule, 3-methylpent-4-enoic acid was converted to the benzylamide via CDI activation, which was then reduced to the secondary amine by means of LAH. The amine was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine, as shown in figure 2.25.

Attempts at microwave claisen rearangements

During the course of this work quite a few Claisen and Johnson-Claisen rearrangements were performed. The reactions proceed along the general format as outlined in figure 2.26.

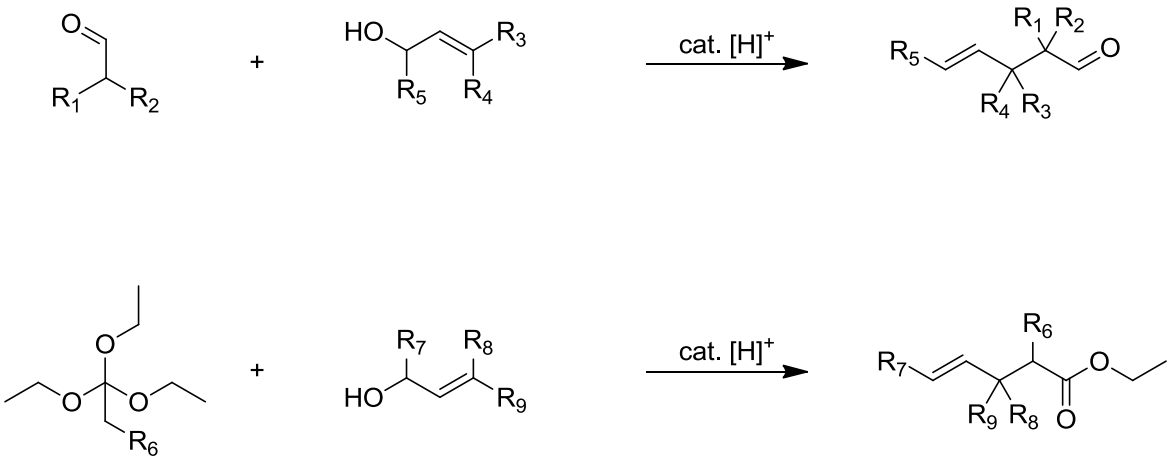


Figure 2.26 General Claisen and Johnson-Claisen rearrangement showing where the rest group will appear

The problem with the Johnson-Claisen rearrangement is that the product does not end up as depicted as an ethyl ester, but will invariable be a mixture, normally to the tune of 3:1, of ethyl and allylic ester, as shown in figure 2.27. This horrendous waste of allylic alcohol is not a problem if one is using allyl alcohol, a cheap and easily available raw material. But if one is to use a more expensive, or self-made, allylic alcohol, to loose upwards of 15% as the ester is galling. In an effort to avoid this loss, I decided to experiment with the microwave assisted Claisen and Johnson-Claisen reactions. To the best of my knowledge this has not been published to date. The idea is simple. In an enclosed reaction vessel, the ethanol generated in the J-C reaction will not be distilled off, and can constantly undergo a transesterification reaction. This would hypothetically increase the yield, if the high temperatures required for the thermally activated reaction can be achieved.

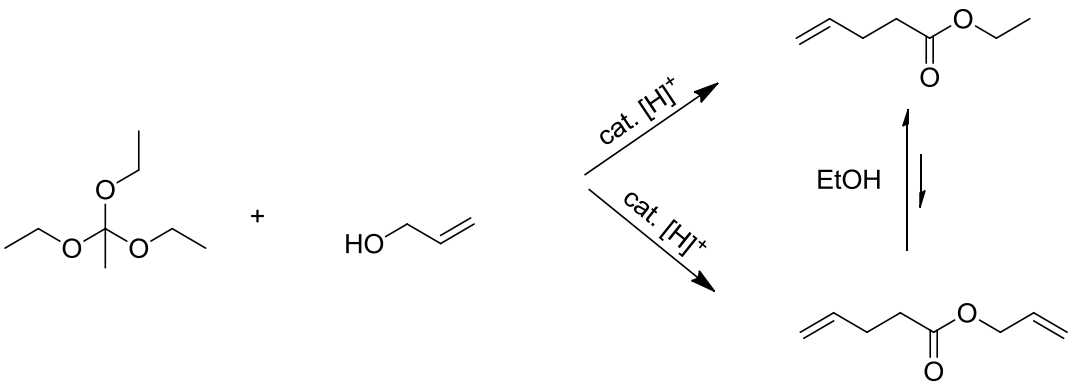


Figure 2.27 Johnson-Claisen rearrangement with equilibrium

The attempted Claisen rearrangement, as depicted in figure 2.28, did not work. The reaction reached the acetal stage, but did not proceeding further. Two different H_2O scavengers were experimented with, neither leading to the hoped for aldehyde, and no further attempts were made in this area.

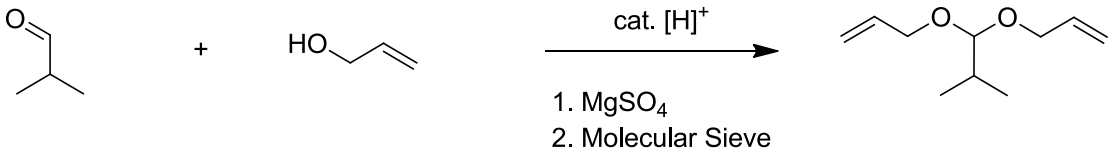


Figure 2.28 Attempted Claisen rearrangement of allylic alcohol and isobutyrl aldehyde

Next the Johnson-Claisen rearrangement was pursued. In a first attempt the microwave was set to 165°C and 17 bar. Due to the low boiling point of the educts, the desired temperature was not reached before the pressure limit of 17 bar was. The reaction was run for 4 hours in this way, after which a GC-MS indicated the product had not formed. In an effort to reach the required temperature for this thermally activated reaction to occur, a silicon carbide passive heating element was used, as shown in figure 2.29.

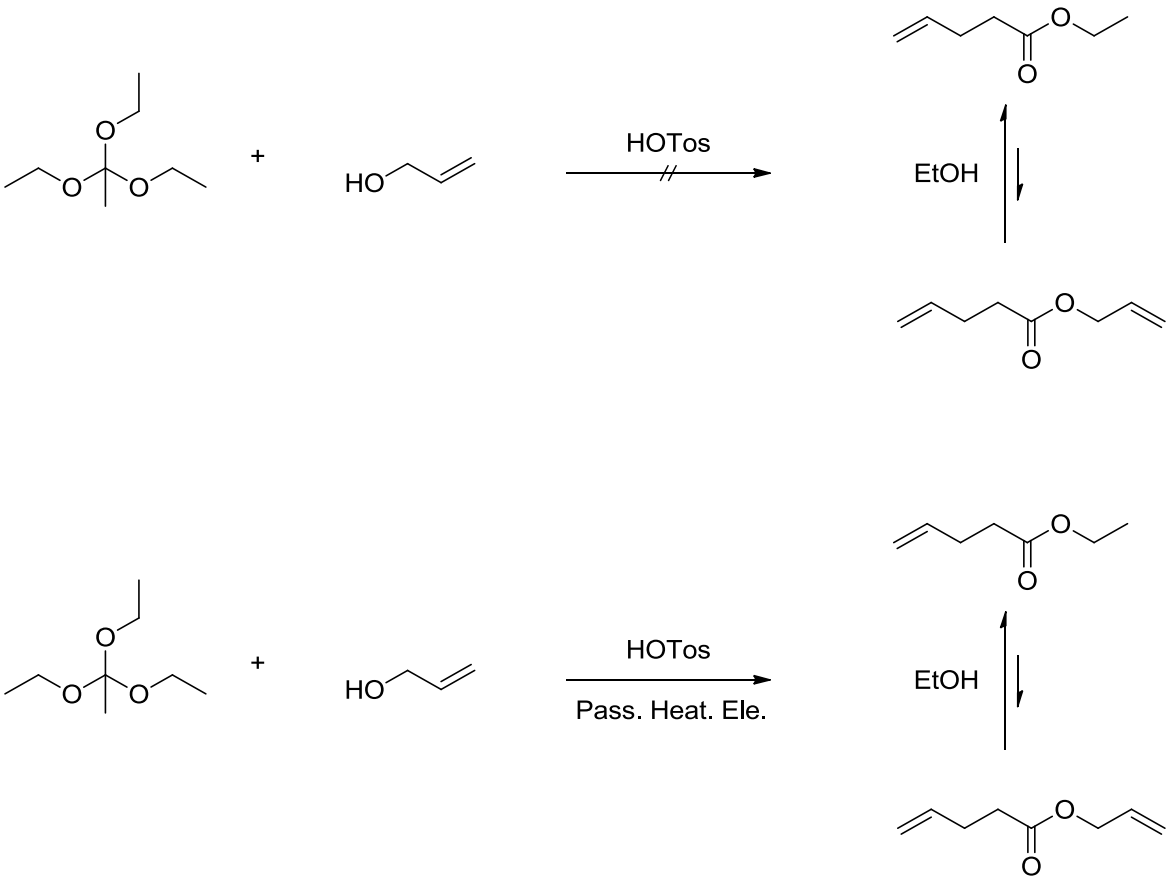


Figure 2.29 Johnson-Claisen rearrangement with passive heating element

With the passive heating element, the Temperature of 160 – 165°C was reached, while the pressure stayed below the 17 bar limit, and the reaction was run for 4 hours. GC-MS indicated the reaction had occurred, and it was run several more times, to determine how long it would take. These results are summarized in table 2.7.

Reaction Time [h]	Educt consumed
4	Yes
3	Yes
2	Yes
1	Partial

Table 2.7 Reaction time variation for the Johnson-Claisen rearangement

At this point the reaction was scaled up from a mere 0,5 gram (8.61 mmol) test run to 3.0 grams (51.7 mmol) to determine the optimal reaction parameters and workup. First the reaction workup was optimized. It was attempted to remove unreacted triethyl orthoacetate by hydrolysis with conc. or dilute HCl, and then extraction with diethylether or t-BME. The extract was washed with sat. $NaHCO_3$ to remove acidic impurities, dried with $MgSO_4$, and the solvents

removed via rotary evaporation. NMR analysis of the product indicated residual EtOH and allyl alcohol impurities, and it was determined the product would require a destillative workup. This yielded the desired product in a 15:1 ratio of ethyl to allyl ester, in 35% yield. Although this yield is basically the same as a classically performed Johnson-Claisen reaction, the usual ratio of 3:1 ethyl to allyl ester had been drastically improved, resulting in an actually higher yield of the desired product due to the higher molecular weight of the allyl alcohol.

Next the amount of triethyl orthoacetate was varied to determine if this could improve the yield. 1.0, 1.5, 2 and 5 equivalents were tried, this factor being limited by the size of the MW glass. For the 5 Eq. experiment the amount of allyl alcohol had to be reduced to 1 gram, to have enough room for the reaction mixture. These experiments did not improve upon the 35% yield achieved with 1.2 equivalents, and went down to 32% at 1.0 equivalents, indicating a slight excess of orthoacetate was required.

Further it was investigated if one could simply add NaOH after the 2 hour reaction time to induce a saponification, without prior workup. This led to the formation of a solid cake like reaction mixture, causing the reaction vessel to crack. This was probably the result of the amount of NaOH required, and the possibility of a MW saponification was pursued no further.

Finally the general applicability of the reaction was investigated with a few simple and available allylic alcohols, as shown in table 2.8.

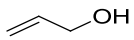
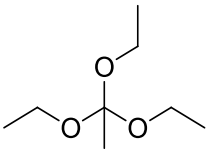
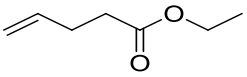
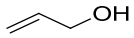
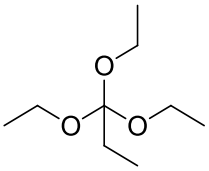
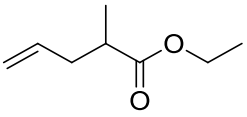
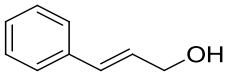
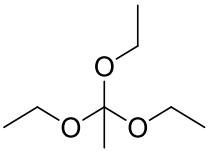
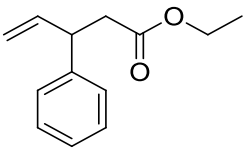
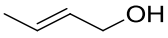
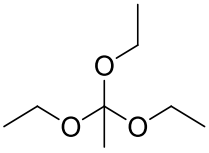
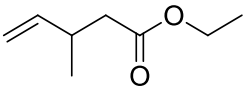
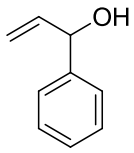
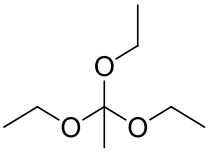
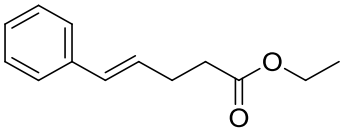
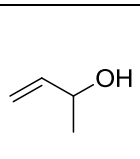
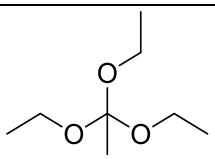
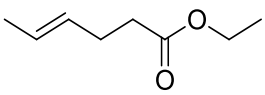
Allyl alcohol	Orthoester	Product	Yield
			35
			45
			0
			0
			0
			0

Table 2.8 Various allylic alcohols attempted

These attempted reactions only yielded the desired result when the simple allyl alcohol was used. The reaction was then attempted for longer periods of time, up to 4 hours, and for the methyl substituted alcohols some product was determined via GC-MS. For the benzylic substituted alcohols no product was observed. The reason for this is unclear, as the reactions do take place using the traditional method of slowly heating up to 160°C and holding the temperature for 3 to 6 hours while distilling off EtOH. Since the MW method would not yield any benefits over the traditional method, this research was pursued no further.

Returning to the Scope of milder reaction conditions

Next it was tested what effect a single group in the C-2 position would have. For this purpose, as shown in figure 2.29, allyl alcohol and triethyl orthopropionate were converted to the γ,δ-unsaturated ester in the MW at 165°C and 15 bar for 2 hours, and then without further purification saponified to yield 2-methylpent-4-enoic acid. This was then converted to the amide via CDI activation, and then reduced to the secondary amine via LAH. The amine was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine.

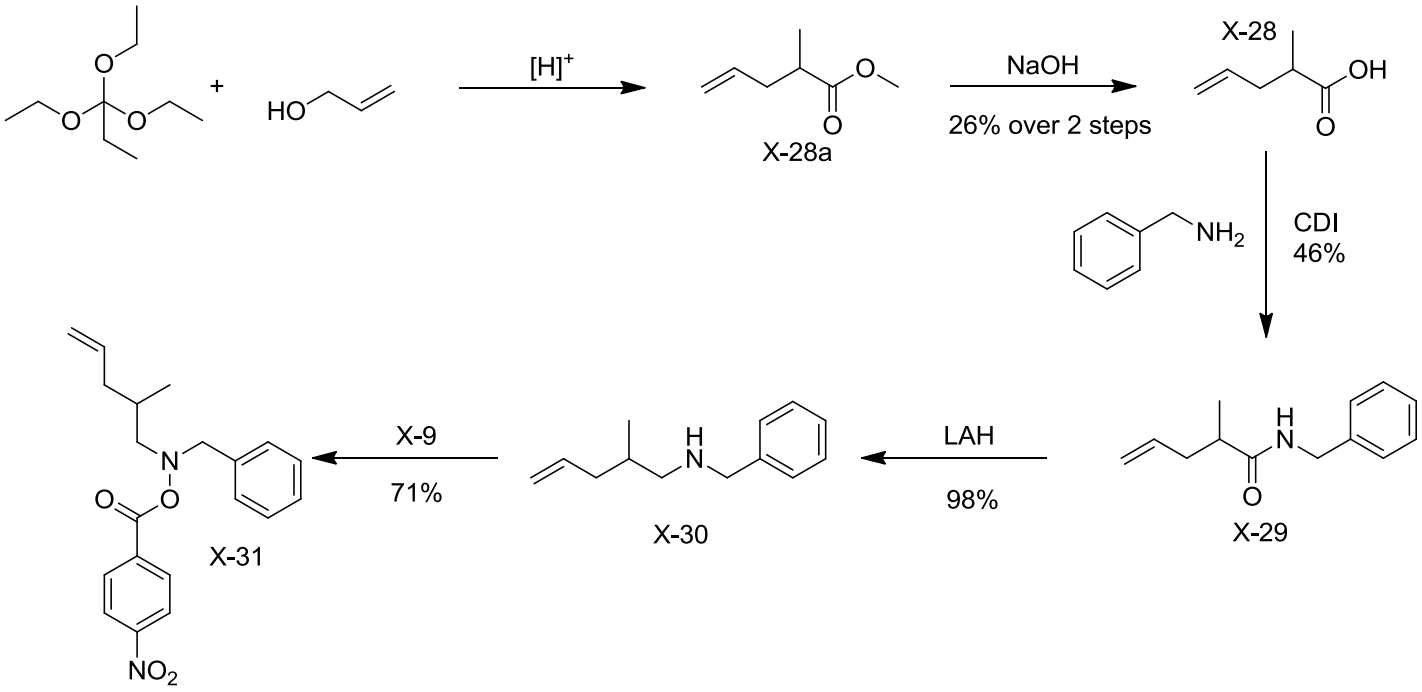


Figure 2.29 Synthesis of N-benzyl-N-(2-methylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

For the phenyl substituted molecule, 2-phenylpent-4-enoic acid was converted to the benzyl amide via CDI activation. This was converted to the secondary amine via a LAH reduction, which was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine, as shown in figure 2.30.

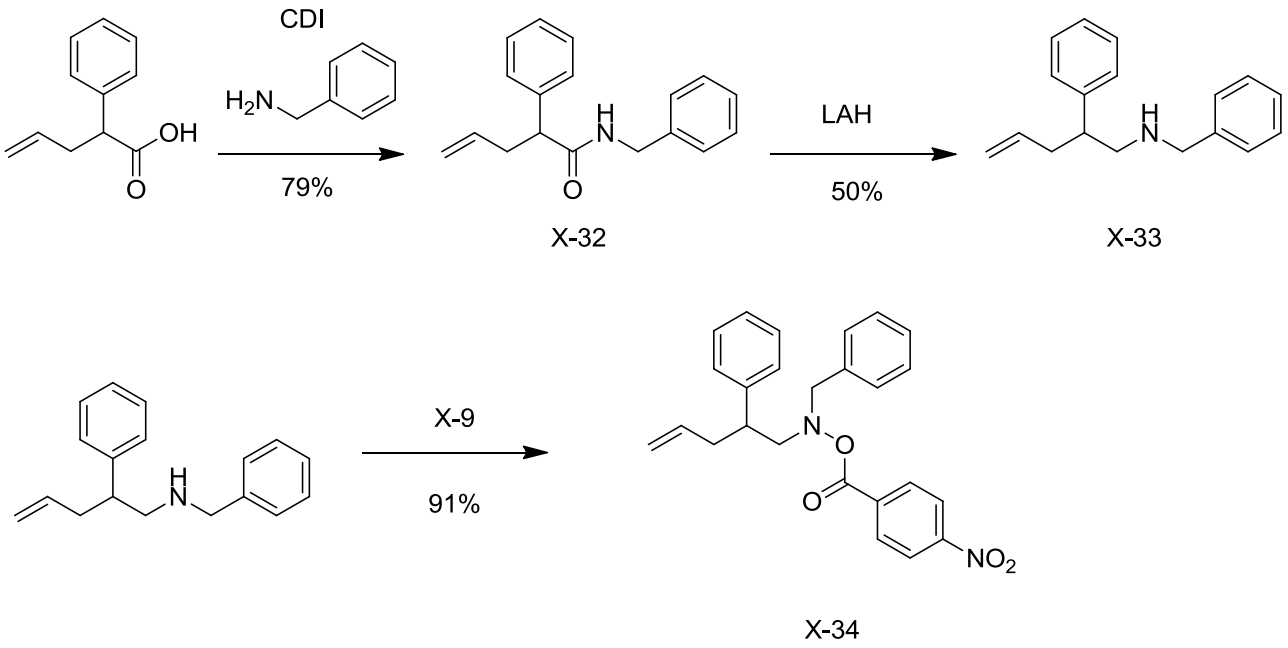


Figure 2.30 Synthesis of N-benzyl-O-(4-nitrobenzoyl)-N-(2-phenylpent-4-en-1-yl)hydroxylamine

Finally the molecule with no substitution on the carbon skeleton was tested, to determine the reactivity without any gem alkyl effect in the molecule. This was synthesized by Claisen rearrangement of trimethyl orthoacetate and allyl alcohol, followed by saponification with NaOH. This was then converted to the amide via CDI activation and reduced to the secondary amine via LAH, and converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine, as shown in figure 2.31.

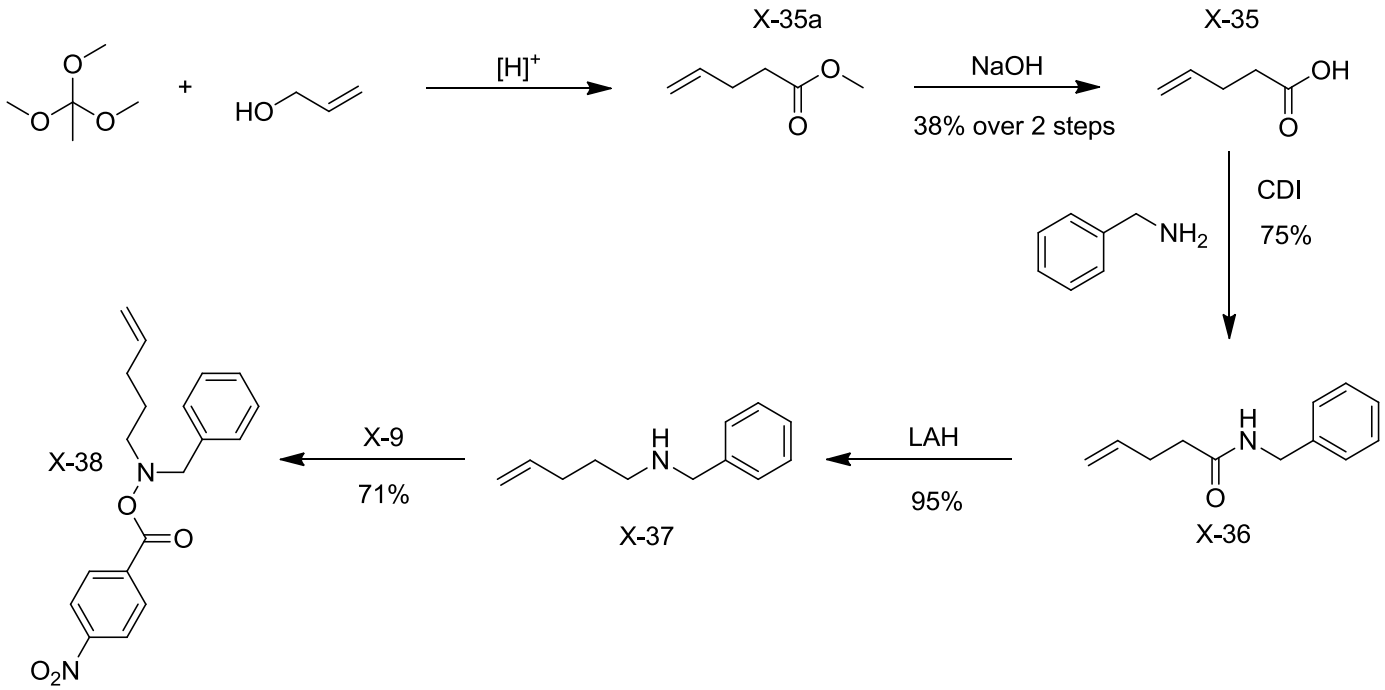


Figure 2.31 Synthesis of N-benzyl-O-(4-nitrobenzoyl)-N-(pent-4-en-1-yl)hydroxylamine

Next the reactivity of sterically hindered alkenes was tested. Three molecules were selected for the purpose. The first would have a terminal methyl group, with the two geminal methyl groups giving the full gem alkyl effect, the next would have the terminal methyl group, but no gem methyl groups, and the third would have the alkene inside a 5-ring, and no gem methyl groups, leading to a very sterically hindered alkene, with no further group activation. To that purpose the following molecules were synthesized. The first with two methyl groups in the 2 position, giving the full germinal dialkyl affect, was made as shown in figure 2.32. In a Claisen rearrangement of but-3-en-2-ol with isobutyraldehyde, (E)-2,2-dimethylhex-4-enal was synthesized, which was then converted to the benzylic imin, reduced to the secondary amine with $NaBH_4$ and converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine.

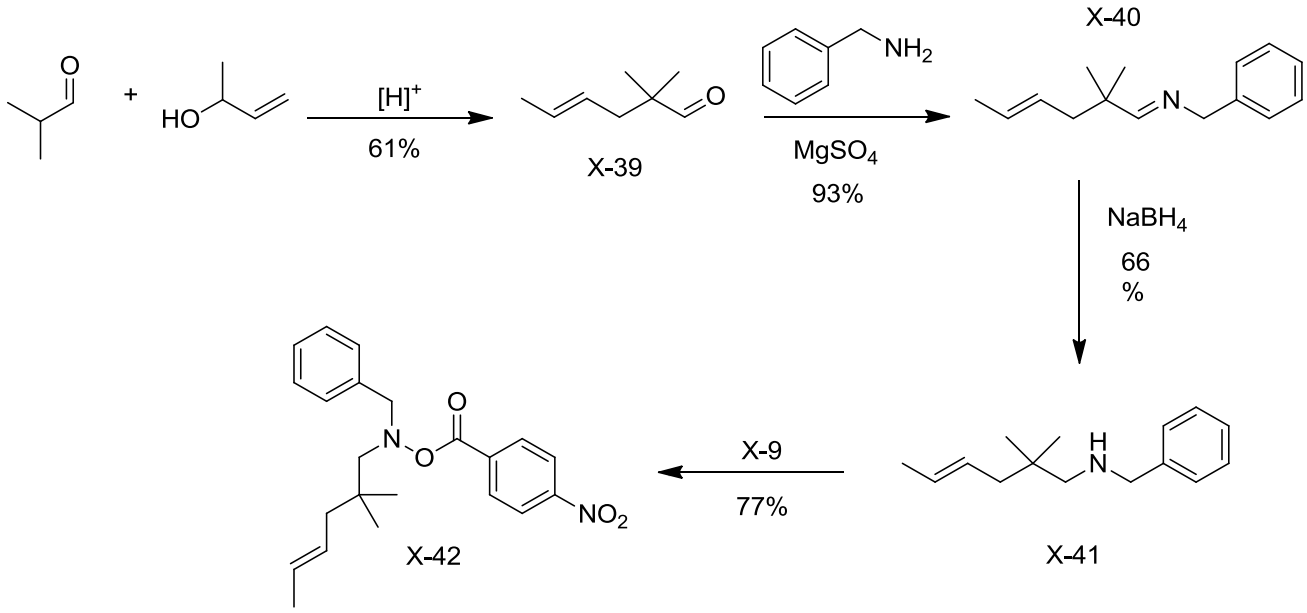


Figure 2.32 (E)-N-benzyl-N-(2,2-dimethylhex-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

To synthesize the variant without the dimethyl group in the 2 position following plan was followed. Starting from (E)-hex-4-enoic acid, the benzylic amide was formed via CDI activation, then the secondary amine via LAH reduction. This was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine, as shown in figure 2.33.

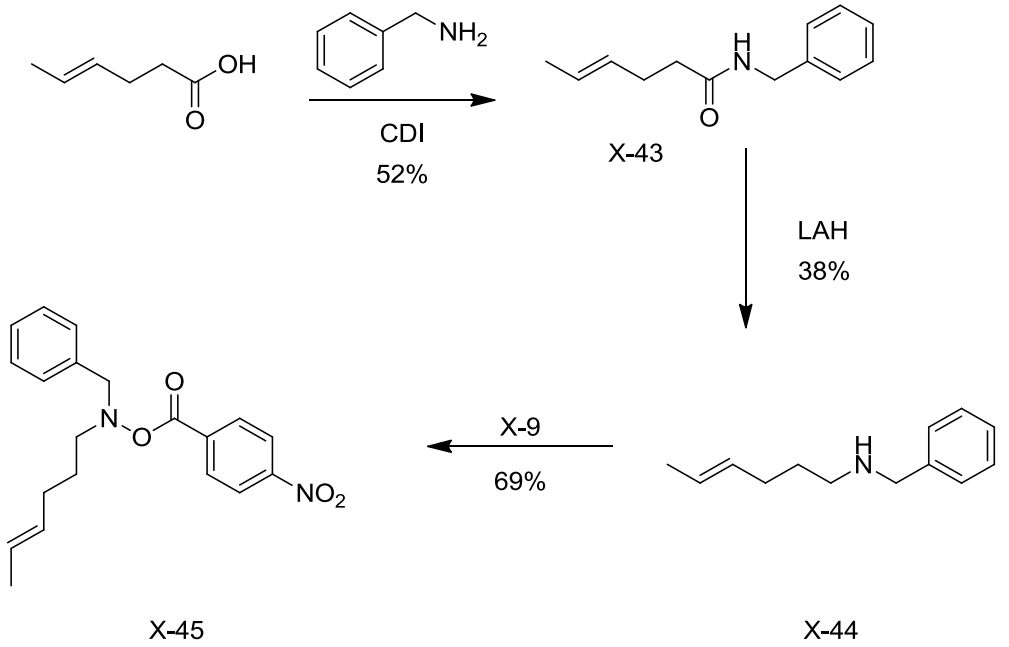


Figure 2.33 Synthesis of (E)-N-benzyl-N-(hex-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

Finally it was determined how a very sterically hindered alkene would react by synthesis of an alkene within a ring. This could potentially lead to a double five ring. To this end 2-

(cyclopent-2-en-1-yl)acetic acid was converted to the benzyl amide with CDI and benzylamine, followed by LAH reduction to the secondary amine. This was then converted in the final step to the O-*p*-nitro Benzoyl hydroxylamine, as shown in figure 2.34.

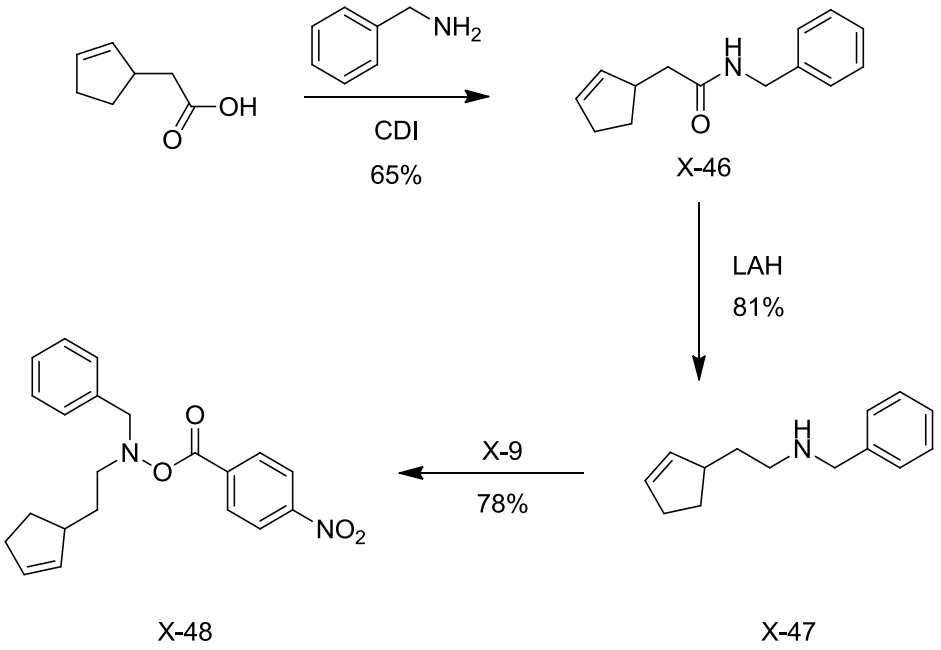


Figure 2.34 Synthesis of N-benzyl-N-(2-(cyclopent-2-en-1-yl)ethyl)-O-(4-nitrobenzoyl)hydroxylamine

Next was tested the applicability of the reaction to form rings of other sizes, utilizing a cyclisation precursor with 3, 4, and 6 carbon atoms in the carbon skeleton, as shown in figure 2.35. This was done in the assumption that an ally group might undergo a 3-exo-trig reaction, the butene might also undergo a 4-exo-trig or 5-endo-trig reaction, and the hexene moiety might undergo a 6-exo-trig or a 7-endo trig reaction. Although the 3-exo-trig reaction is desricbed by Baldwin as being a radical reaction supported by empirical data, the 4 and 6 exo as well as 5 and 7 endo reactions are only described for anionic reactions. Performing these cyclizations might be able to help shed some light on the mechanistic aspect of the Cu(I) mediated hydroxyamination.

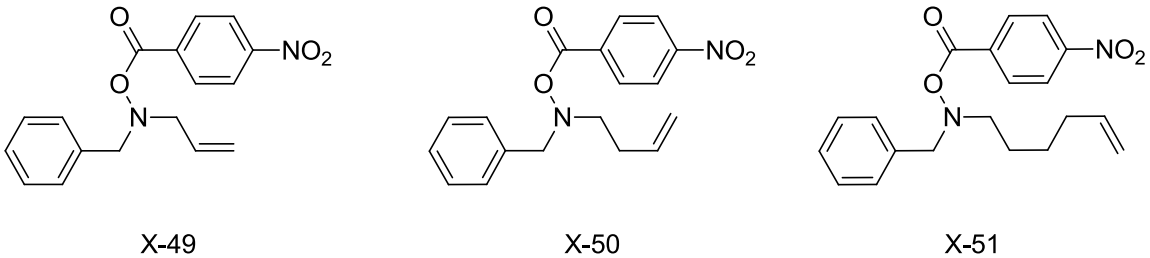


Figure 2.35 The 3, 4 and 6 carbon skeleton cyclisation precursors

The three and four carbon skeleton moieties' were synthesized in the same way, as shown in figure 2.36 by the S_N2 reaction of alkene bromide with benzylamine, then converted to the O-*p*-nitro Benzoyl hydroxylamine.

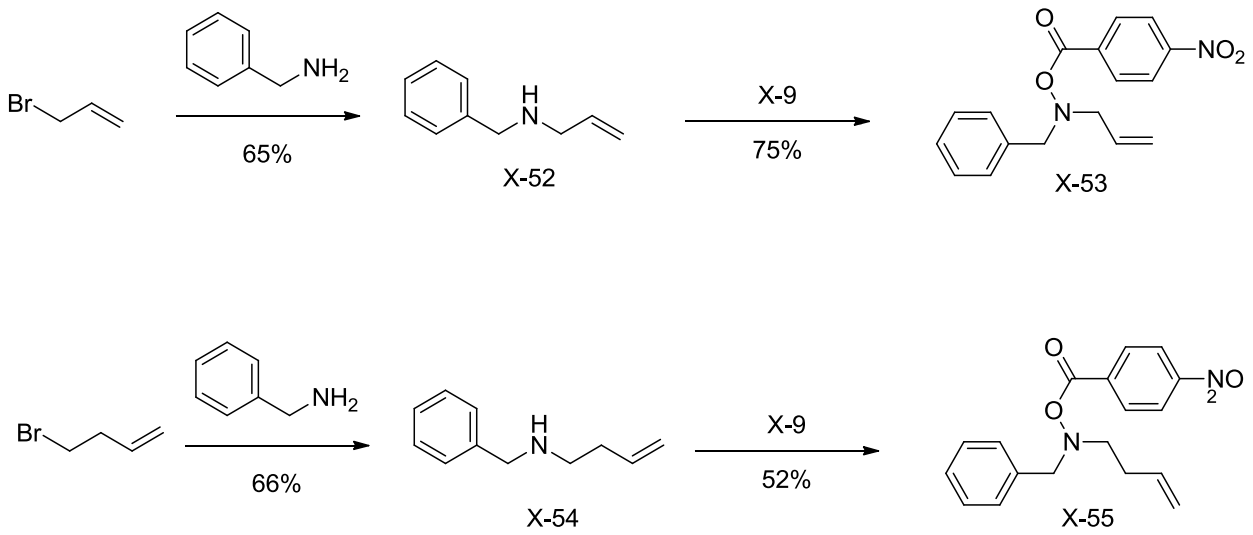


Figure 2.36 Synthesis of the allyl and butenyl variants, X-53 and X-55

The 6 carbon skeleton was synthesized by way of the alcohol, which was tosylated, and then aminated via S_N2 reaction with benzylamine, and converted to the O-*p*-nitro Benzoyl hydroxylamine, as shown in figure 2.37.

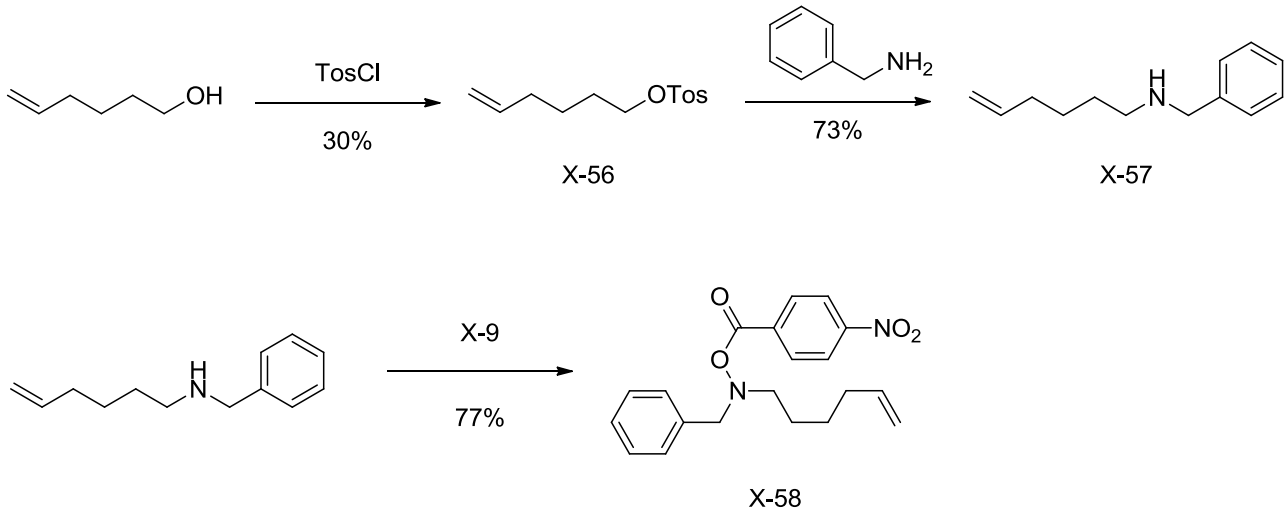


Figure 2.37 Synthesis of N-benzyl-N-(hex-5-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

Results of cyclisation

Cyclisations were carried in out 1 mL Toluene under four reaction conditions:

a) RT for 6 hours, 1 eq. BF3*OET2, 10 % Cu(I)
b) 75°C for 10 min in the MW, 2 eq. BF3*OET2, 5% Cu(I)
c) 100°C, 1 hour, 10% Cu(I)
d) 100°C, 5 min in the MW, 5 % Cu(I)

The substrates were subjected to reaction conditions a) and c) three times and an average was formed for a) and c). The substrates were also subjected to conditions b) and d), but these results were the same (+- 2%) as a) and c) and are not reported separately.

1. Changing the rest on the nitrogen

The change of the group on the nitrogen from a benzyl to a butyl or an allyl group had a marked change on the stability and reactivity of the molecule. While the benzyl moiety is bench stable for at least six months, the butyl and allyl varieties decomposed completely over the course of two days, and had to be stored at -20°C.

Under condition a) the cyclisation of X-14 led to 71% overall yield, 62% 5-ring and 9% 6-ring, figure 2.38. Compared to the 79% of Dr. Noack, 61% 5-ring and 18% 6-ring yield. This indicates a stabilizing effect of the benzyl group on the aminyl radical in X-5.

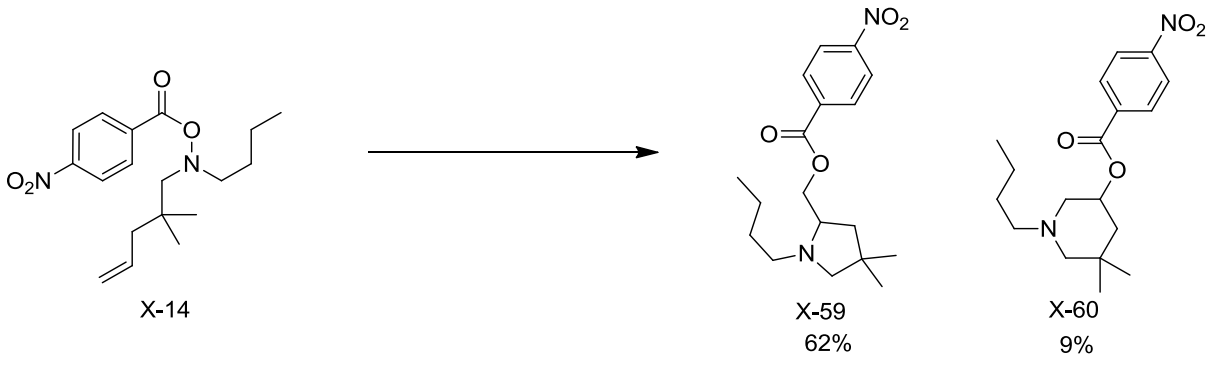


Figure 2.38 Cyclization of X-14

Conditions	5-Ring	6Ring
a)	62	9
c)	0	30

The cyclisation of X-17, figure 2.39, led to 54% yield of just the 5-ring, slightly better than Dr. Noacks 45% yield, and just as previously, there was no isolable 6-ring. This indicates that the allyl group does not stabilize the radical intermediate, and that it contributes to side products leading to a lower yield. This opens up the possibility, however, of cyclizing an allyl-N-Hydroxylamine, with a benzyl group on the nitrogen, which will be investigated later, although a double cyclisation leading to a pyrrolizin type molecule was not isolated.

Figure 2.39 Cyclization of X-17

Conditions	5-Ring	6Ring
a)	54	0
c)	0	0

2. Changing the rest's on the carbon skeleton forming the ring.

Changing the placement of both methyl groups to the C-3 position on the chain resulted in a lower yield of 5-ring and no 6-ring with BF_3*OEt_2 at RT and 75°C MW. At 100°C without BF_3*OEt_2 15% 6-ring was isolated as the sole product, as depicted in figure 2.40.

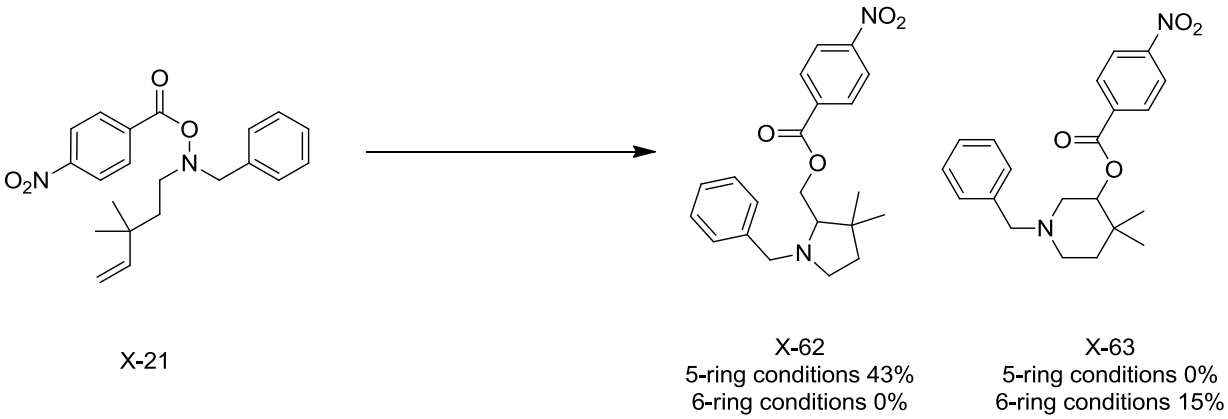


Figure 2.40 Cyclization of X-21

Conditions	5-Ring	6Ring
a)	43	0
c)	0	15

This could be because although the gem dialkyl affect is still present, the two methyl groups are now close enough to the double bond that they prove to be a steric hindrance. This thought is proven to an extent by the higher yield in 5-ring resulting from just one methyl group in this position X-64, 50%, figure 2.41, and no methyl groups, 51%, X-66, figure 2.43a). Although at the same time, the 6-ring cannot be produced under 6-ring conditions with these molecules. This indicates that in some was the double methyl group encourages 6-ring formation. Before reaction workup TLC indicated a diastereomeric mixture, but after chromatographic workup only one spot remained on the TLC and NMR shows only signals for one molecule.

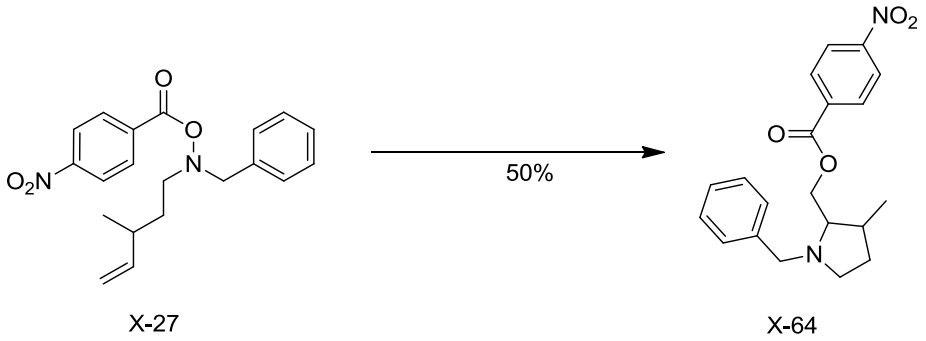


Figure 2.41 Cyclization of X-27

Conditions	5-Ring	6Ring
a)	50	0
c)	0	0

When the methyl group is exchanged for a phenyl group, the steric hindrance becomes so great so as to affect a drop in yield of 5-ring to 28%, and again no 6-ring.

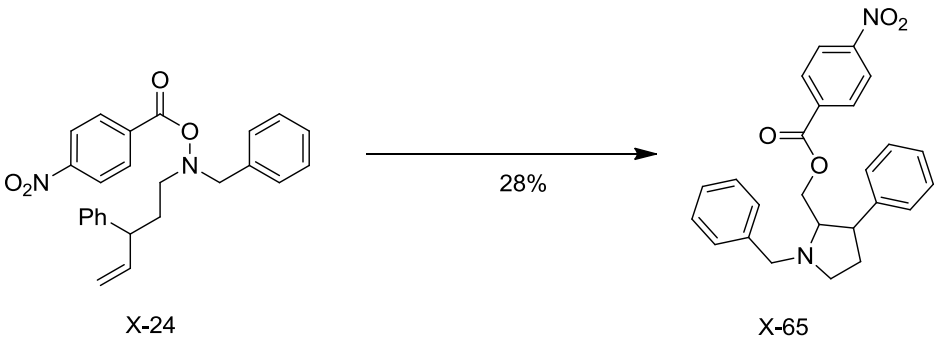


Figure 2.42 Cyclization of X-24

Conditions	5-Ring	6Ring
a)	28	0
c)	0	0

As compared to the moiety with no groups on the chain, yielding 51% 5-ring, only the single methyl moiety has a comparable yield. This indicates that a non-active group placed in the 3 position is only a hindrance to product formation.

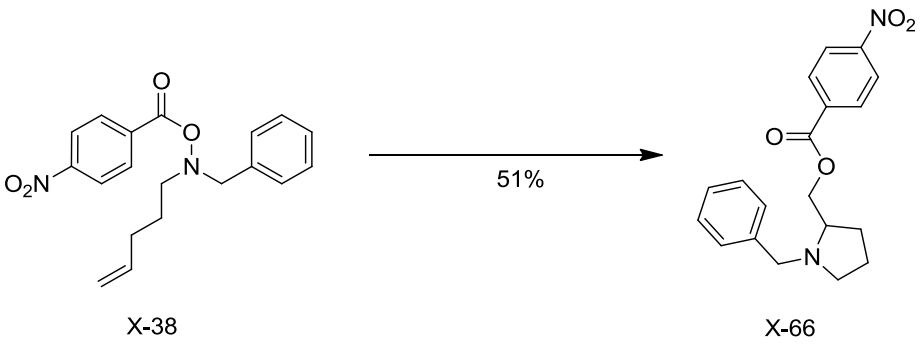


Figure 2.43a) Cyclization of X-38

Conditions	5-Ring	6Ring
a)	51	0
c)	0	0

Though attempted with all cyclization products, it was only possible to generate a crystal for XRD structure determination of the HCl salt of X-66, figure 2.43b), leading to the definite determination of a 5-ring. It is very difficult if not impossible, based solely on NMR and MS data, to determine for certain which molecule is a 5 or 6 ring. Fortuitously the crystal which succeeded in being measured and identified was of the molecule with no extra carbon atoms on the ring, one could describe this as the base molecule. While all the other molecules vary slightly in their NMR shifts of the carbon atoms within the ring, there is a definite difference between 5 and 6 ring, with a definite trend for either ring. This made the determination of the rings by proxy slightly more reliable.

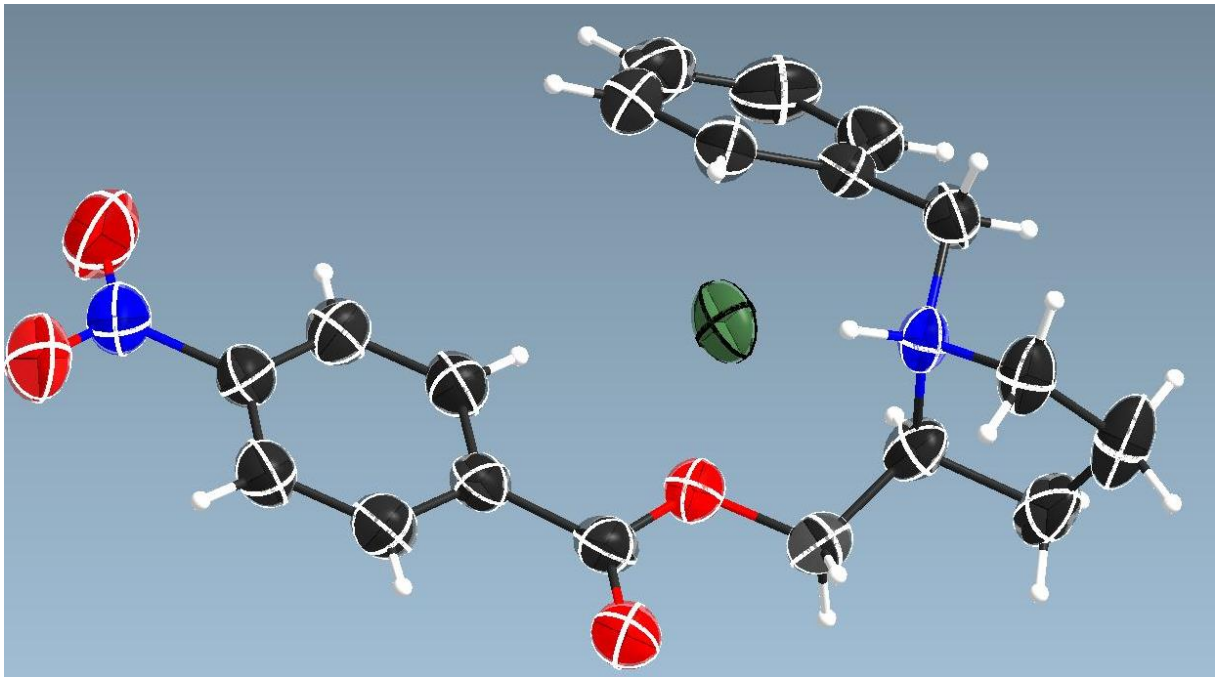
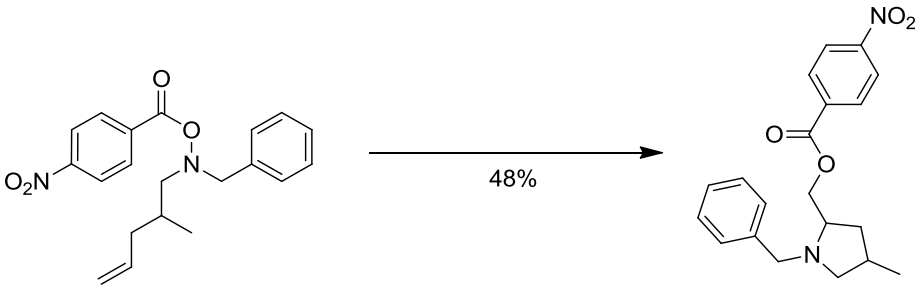


Figure 2.43b) Crystal structure of X-38

When the methyl and phenyl groups are placed in the optimal C-2 position, the yield is generally higher. For the single methyl group, it reaches 48%, comparable to X-66 (no groups). The cyclization of X-31 led to a diastereomeric mixture, which could not be separated. The minor diastereomer was obtained in such small quantities that its signals could not be used to determine de.

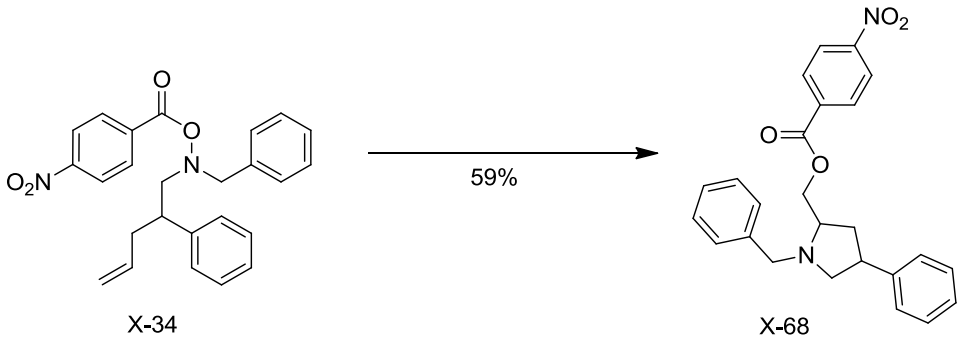


X-31 X-67

Figure 2.44 Cyclization of X-31

Conditions	5-Ring	6Ring
a)	48	0
c)	0	0

And when the C-2 position is fitted with a phenyl group, the yield becomes better than that with no groups, 59%, figure 2.45. This shows that although there is only one group present, the size of the phenyl group partially makes up for the lack of a second methyl group. Before reaction workup TLC indicated a diastereomeric mixture, but after chromatographic workup only one spot remained on the TLC and NMR shows only signals for one molecule.



X-34 X-68

Figure 2.45 Cyclization of X-34

Conditions	5-Ring	6Ring
a)	59	0
c)	0	0

Finally it was investigated how a terminal substitution on the alkene would affect the reaction performance. To this end three molecules were cyclized. In the first instance to the optimal cyclisation precursor was added a terminal methyl group, figure 2.46. The minor diastereomer was obtained in such small quantities that its signals could not be used to determine de.

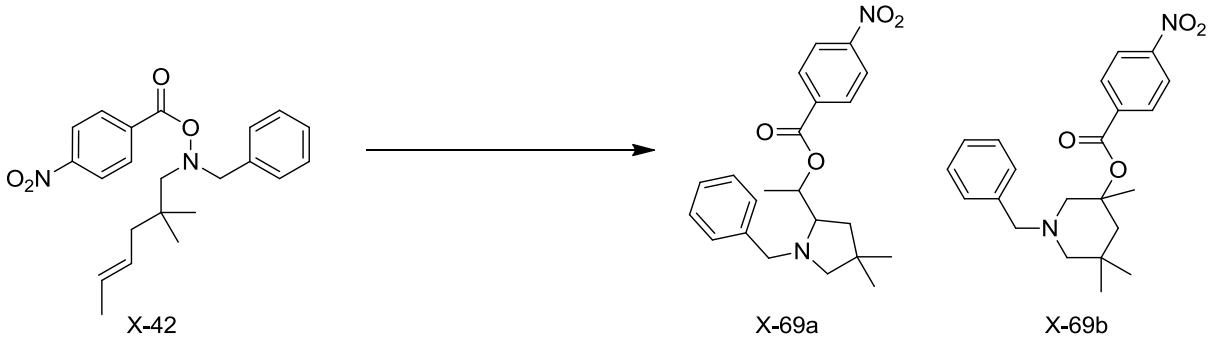


Figure 2.46 Cyclization of X-42

Conditions	5-Ring	6Ring
a)	53	33
c)	<0	58

This molecule did cyclize quite well under 5-ring conditions, with a yield of 86%, especially when compared to the previous attempt by Dr. Noack, without the p-nitro group, which only led to 63%. Problematic though, was that the product was a quite inseparable mixture of erythro/threo products of both 5 (3.2 to 1) and 6 ring (1.1 to 1). This mixture of products was just separable enough on an analytical HPLC column to be able to make this fairly rough determination. It was not feasible to determine the makeup of erythro or threo beyond a ratio by NMR. Also notworthy is that the selectivity for 5-ring over 6-ring goes down with the terminal methyl group. This could be due to a stabilization of the radical intermediate, resulting in enough time to form the thermodynamically favored 6-ring.

Under 6-ring conditions, the yield goes up, as compared to the cyclization of X-5 to X-11. This is again indicative of a stabilizing effect by the terminal methyl group leading to more suitable conditions for the thermodynamically favored product.

Next, the geminal alkyl groups were removed. This led to a lower overall yield of 44 %, und 5-ring conditions, and 22 % under 6-ring conditions. These were relatively cleanly one diastereomer, figure 2.47.

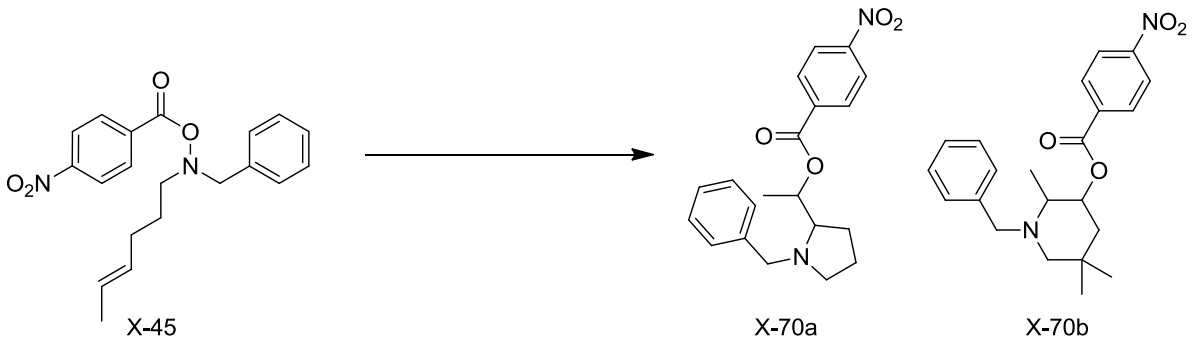


Figure 2.47 Cyclization of X-45

Conditions	5-Ring	6Ring
a)	32	12
c)	7	15

Finally an alkene within a 5 ring was tested, in the hope of forming a pyrrolizine structure, figure 2.48. The initial test for reactivity showed no conversion. In the hopes of isolating just a few milligrams, the reaction was carried out with 500 mg educt, allowing for 5 mg product if just 1% converted. Regretfully no such product was found, or any for that matter. It seems this kind of alkene is far too sterically hindered for an intermolecular reaction to take place.

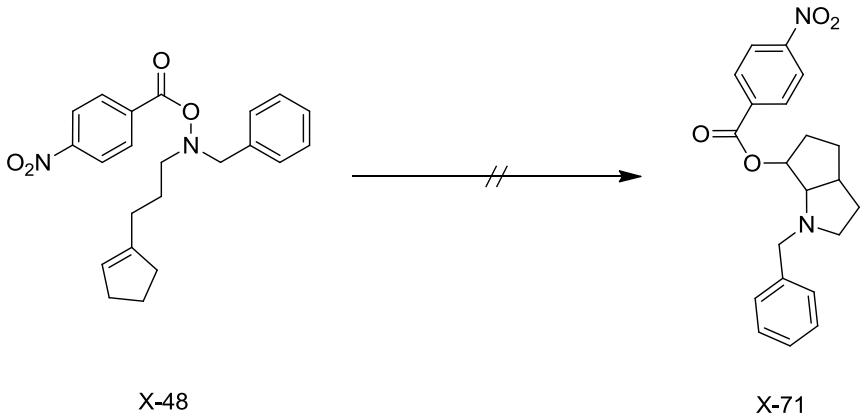


Figure 2.48 Attempted cyclization of X-48

In the last set of cyclisation experiments it was investigated whether other sizes of rings were possible, figure 2.49. To this end the cyclisation of three molecules of varying sizes was attempted. Interestingly, although a 3-exo trig reaction should be favored, this reaction did not occur.

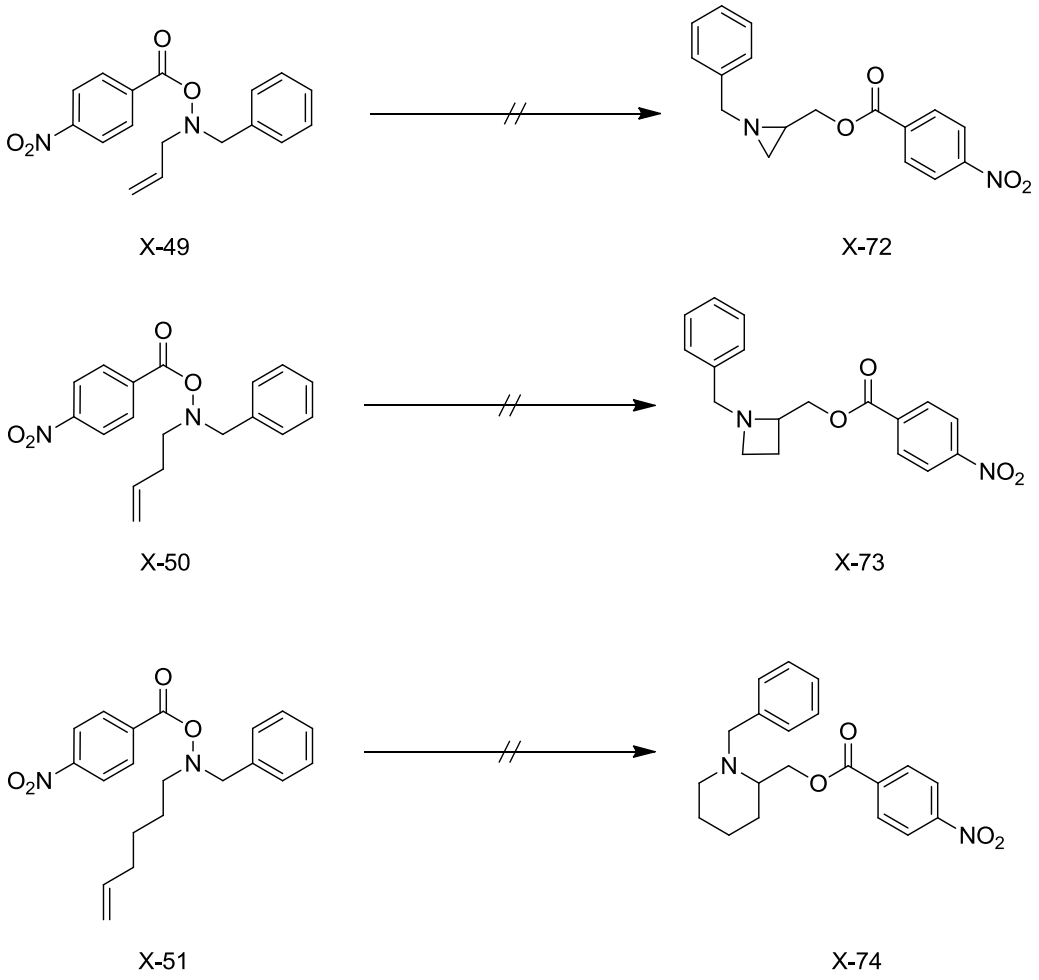


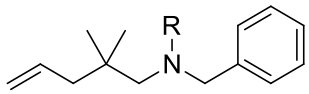
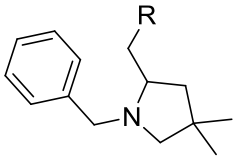
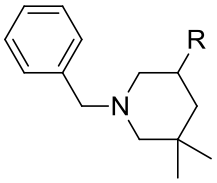
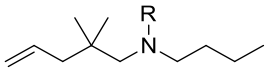
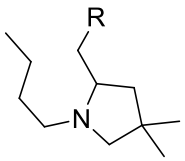
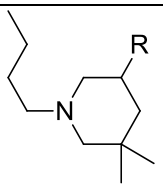
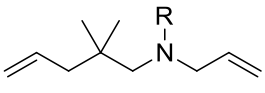
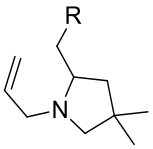
Figure 2.49 Attempted cyclization of molecules X-49, 50 and 51

The butene did not undergo a 4-exo-trig or 5-endo-trig reaction, and the hexene moiety did not undergo a 6-exo-trig or a 7-endo trig reaction. This indicates that the reaction is indeed radical, since these reactions are known to occure in nucleophilic closures, with the exception of the 5-endo-trig variety[36].

Summary and Outlook

In the course of my PhD I was able to further optimize the intramolecular Cu(I) catalyzed amino oxygenation of hydroxylamines. I found that by inserting a *p*-NO_2 group on the benzoyl rest of the O increased the reactivity of the hydroxylamine. Both the selectivity and general yield were improved, under different reaction conditions. At RT with the activation through 1eq. BF_3OEt after 6 hours, or in the MW at 75°C with 2 eq. BF_3OEt after 10 minutes, the five ring is formed relatively selectivly. At 100°C after 1 hour in an oil bath, or 5 minutes in the MW without BF_3OEt the selectivity reverses, although in much lower yield. The general applicability of this reaction was tested for benzylic, allylic and alkan substituted Hydroxylamines, as well as for the placement of carbon substituents along the carbon skeleton resulting in the ring. It was found that the formation of the 6-ring is highly dependent on the geminal dialkyl groups. It was also determined that varying the length of the carbon chain to form 3, 4 or 7 membered rings did not occur, even with the higher reactivity.

Further studies could delve into the effects of substitution on the N, swapping the benzyl group for a more electron withdrawing configuration. This could hypothetically lead to better selectivity for the 6 ring, and reduced reaction conditions, lower temperature and other Lewis Acid catalysts.

N-*p*-nitro benzoyloxyamine	Product	Yield % (5/6)-Ring
 X-5	 X-10  X-11	76/17
 X-14	 X-59  X-60	62/9
 X-17	 X-61	54/0

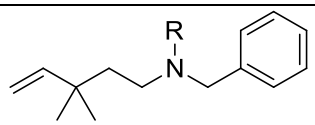
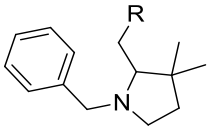
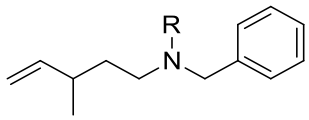
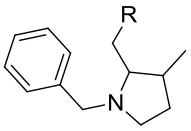
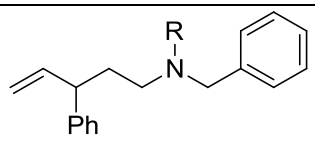
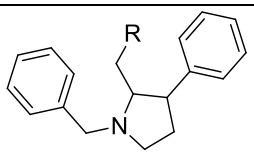
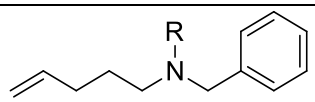
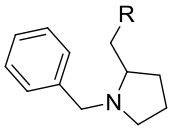
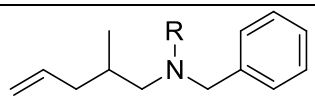
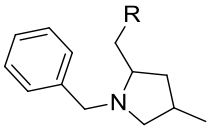
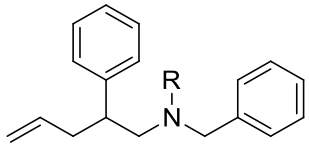
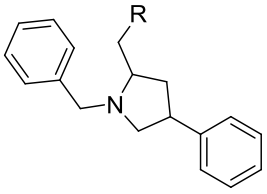
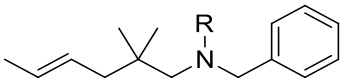
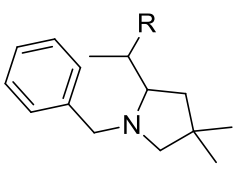
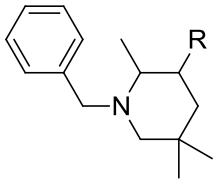
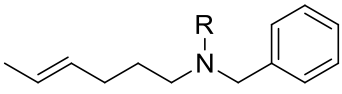
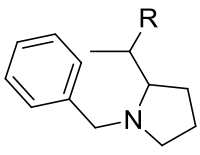
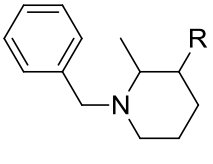
 X-21	 X-62	43/0
 X-27	 X-64	50/0
 X-24	 X-65	28/0
 X-38	 X-66	51/0
 X-31	 X-67	48/0
 X-34	 X-68	59/0
 X-42	 X-69a  X-69b	53/33
 X-45	 X-70a  X-70b	32/12

Table 3.1 Summary of cyclisation reactions under 5-ring conditions

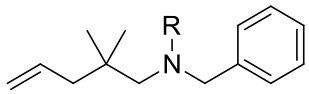
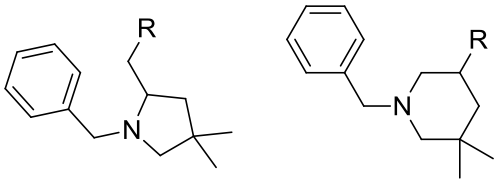
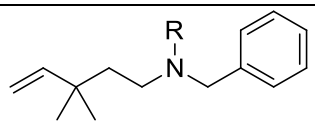
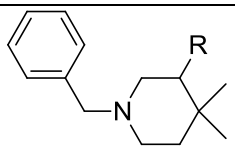
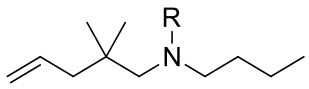
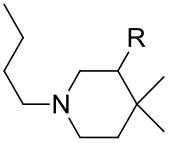
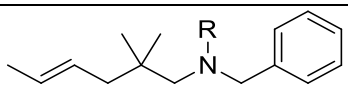
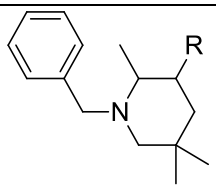
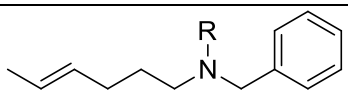
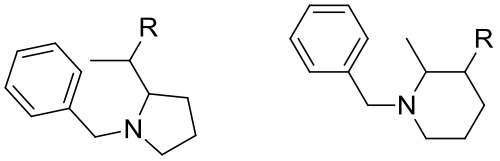
N-*p*-nitro benzoyloxyamine	Product	Yield % (5/6)-Ring
 X-5	 X-10 X-11	2/48
 X-21	 X-63	0/15
 X-14	 X-60	0/15
 X-42	 X-69b	0/58
 X-45	 X-70a X-70b	7/15

Table 3.2 Summary of cyclisation reactions under 6-ring conditions

Generation of two crystals suitable for XRD analysis led to the determination of the N-O bond length, as well as the definitive identification of a 5-Ring, X-66. Further XRD analysis could show how the bond length changes with various EWG's attached the O.

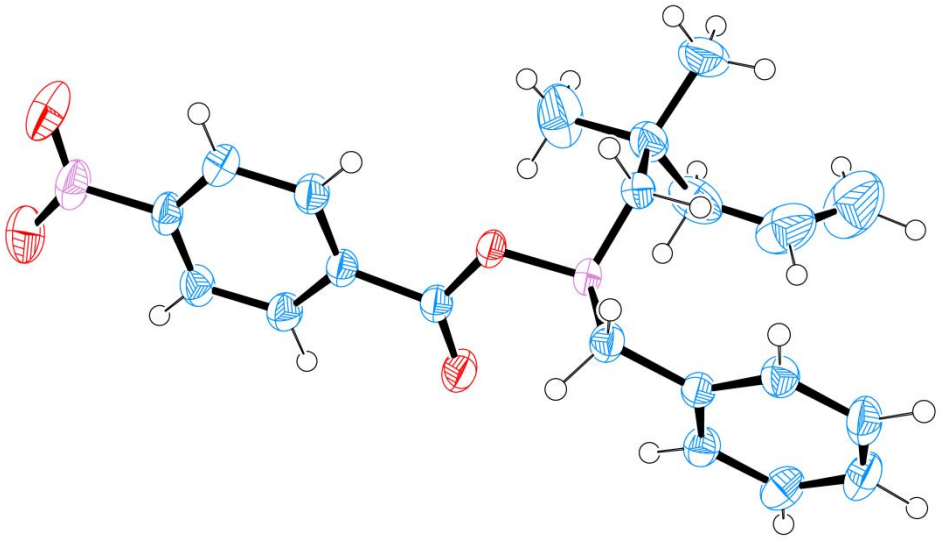


Figure 3.1 Crystal structure of X-5, determination of N-O bond length

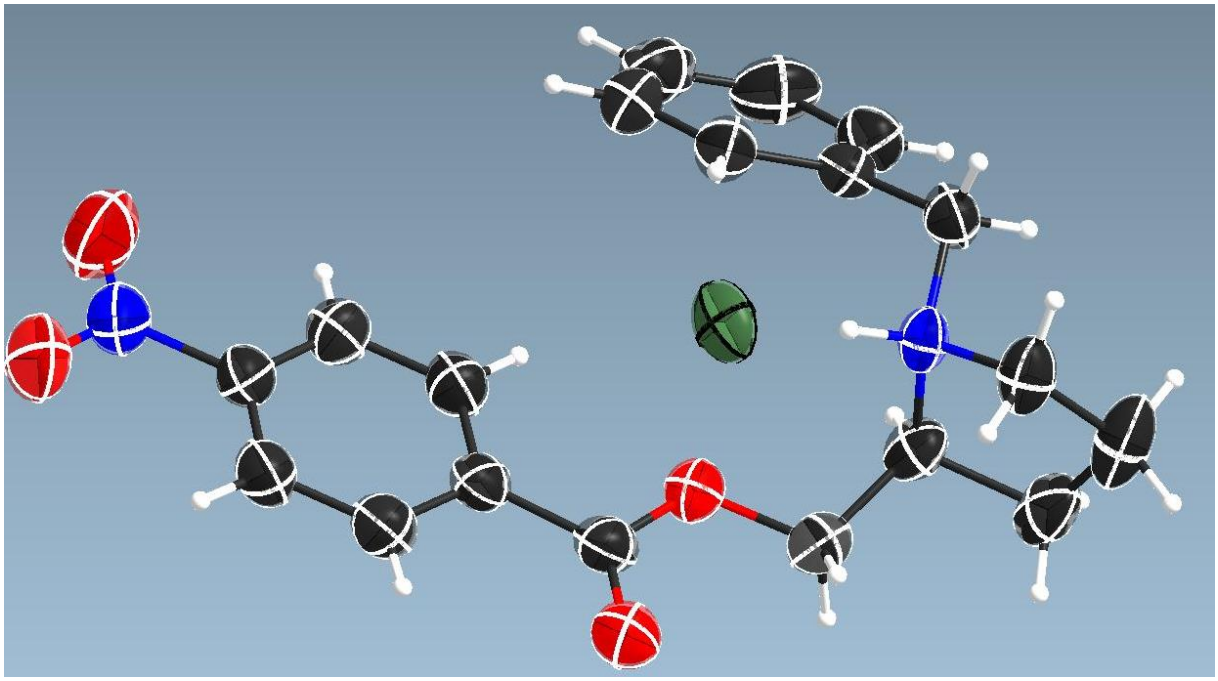
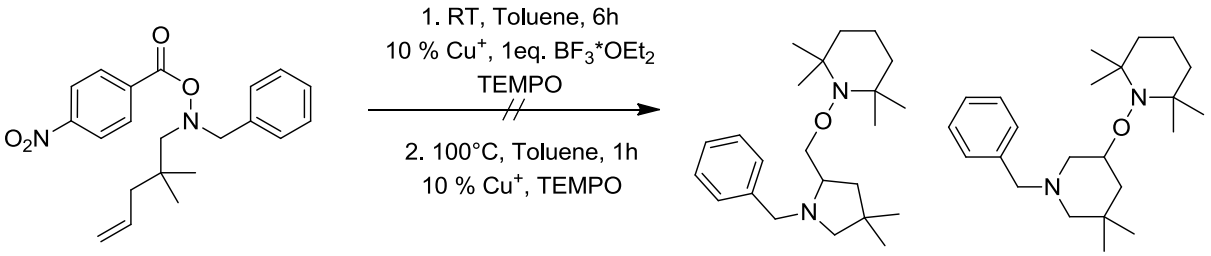


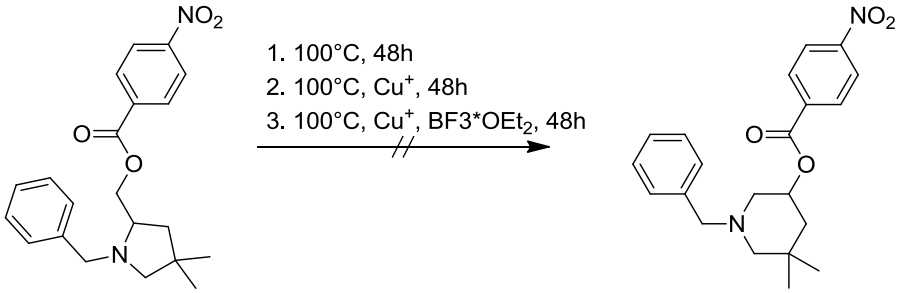
Figure 3.2 Crystal structure of X-66, definitive identification of 5-ring

The attempted capture of the radical intermediate via TEMPO was not possible. This would have helped prove the radical reaction mechanism.

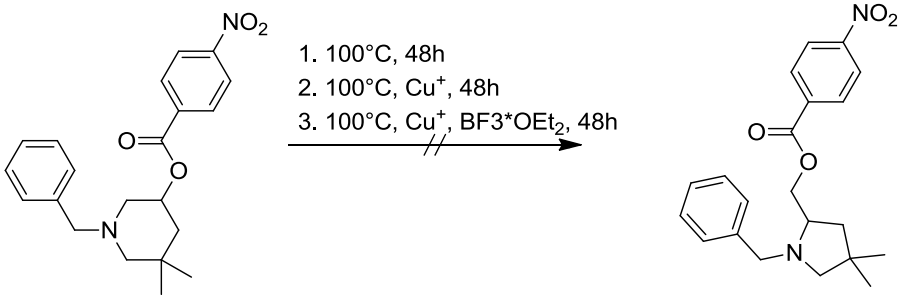


X-5 X-12 X-13

The attempted interconversion of 5 to 6-ring was not possible, which is in line with the results of Dr. Noack.

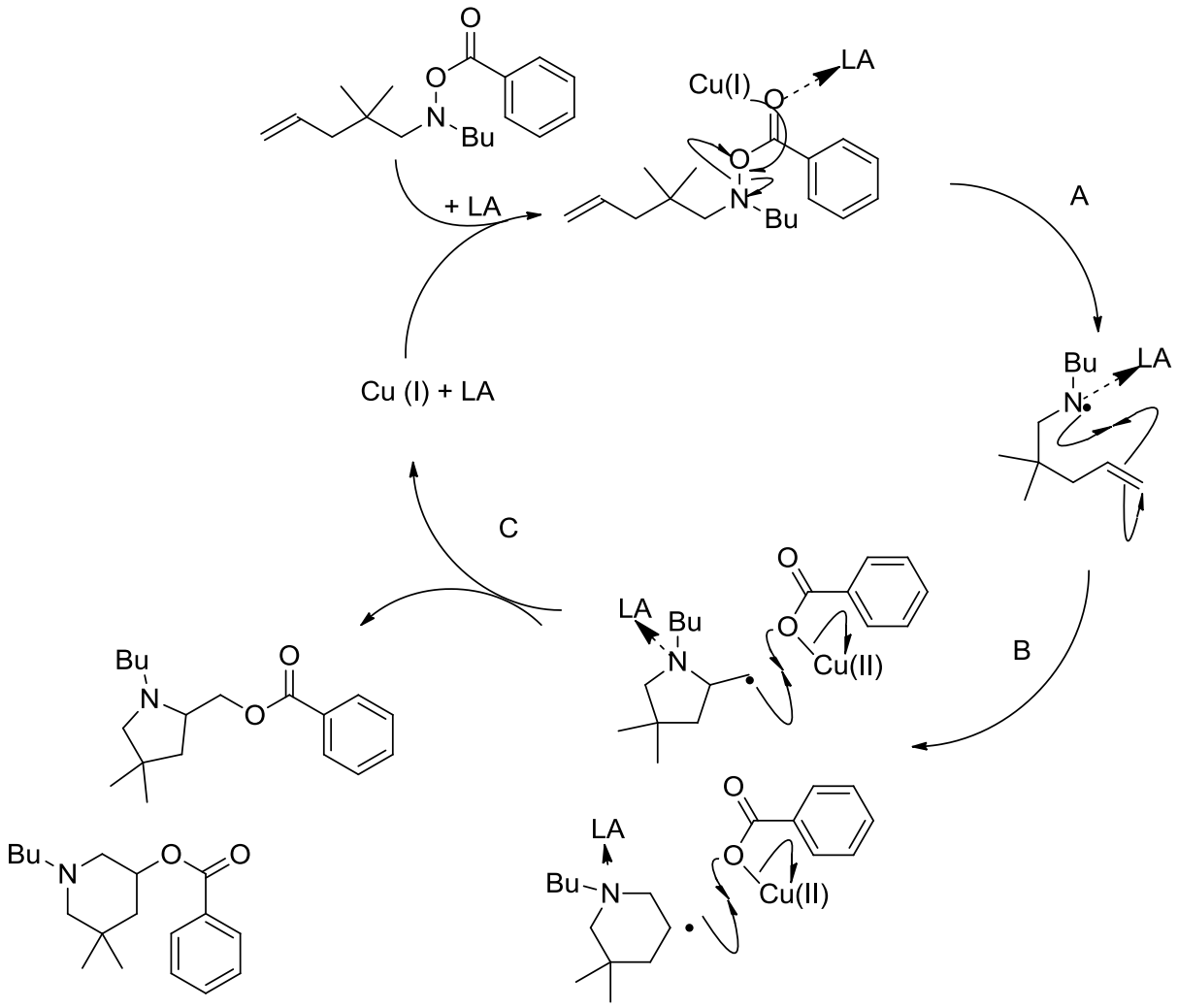


X-10 X-11



X-11 X-10

Further study is needed with other radical scavengers to determine if there is the possibility of capturing the radical intermediate in Step B of the proposed mechanism.



The inability to capture a radical intermediate does not disprove the radical mechanism, but further study is required. The inability to force a 5 to 6-Ring conversion further lends credence to the radical mechanism.

The use of the MW for reaction optimization was shown to be very fruitful. It saved time and resources in a long test series. Further use of this tool is highly recommended. The use of the MW for Johnson Claisen reaction was shown to work for simple molecules, not for all, and for the simple Claisen reaction it did not work. Further studies could delve into the need for water entrapment, to let the reaction move forward. If this method of synthesis could be further optimized for the Johnson Claisen reaction it would lead to ease of use of many rearrangement products in small quantities.

Experimental Section

1. General

1. Working Procedures

Work under inert conditions was performed with glassware flame dried under an oil pump vacuum and then flooded with nitrogen, taken from the in house nitrogen system.

All work done with microwave heating was performed in a Discover Microwave reactor from the company CEM GmbH, Kamp-Lintfort.

2. Solvents

Dry Diethylether, Dichloromethane, Toluene, THF and DMF were provided using a solvent drying machine SPS-800 of the company MBraun, Garching.

All solvents used for chromatography were purified by rotary distillation before use.

Other solvents were used as is, or were purified as the need arose in accordance with published procedures in 'Purification of Organic Laboratory Chemicals, 4th edition'.

3. Chromatography

i. TLC

Analytical TLC was performed using DC-Plates (Silica gel 60 F_{254}) by the company MERCK KGAA (Darmstadt). Detection was performed using a UV lamp (λ = 254 nm or 366 nm) or one of the following stains:

Potasiumpermanganate solution: 3g $KMnO_4$, 250 mg NaOH and 20g K_2CO_3 in 300 mL water

I_2 chamber: I_2 pellets in sand

Ninhydrin: 5 g Ninhydrin in 95 g EtOH

ii. LC

Preparative LC was performed using Silica gel 60, corn size 0.040 - 0.065 mm from the company MERCK KGAA (Darmstadt), or on an automated LC machine of the company Armen

Instrument, Saint Ave, France. Pre packed normal phase silica cartridges from Grace Discovery Sciences (Deerfield, Il., USA) or MERCK KGAA (Darmstadt).

iii. HPLC

Analytical HPCL was conducted on a Kontron (pump 420/422, UV/VIS detector 432) machine set for a detection wavelength of 254 nm, using software from Clarity by DataAPEX (Prague, Czech Republic). A self-pack column, Vertex-Leersäule 250 X 8 mm from Knauer Wissenschaftliche Geräte GmbH, was used with Si-60 gel. Eluents used were n-hexane (A) and t-BME (B), as follows: time 0 min: A:95%, B:5%; time 10 min A:80%, B:20%; time 11 min A:95%, B:5%, time:16.4 min End. Detection time of toluene @ 3.27 min, as seen in the Appendix.

4. NMR Spectroscopy

NMR spectra were measured on Avance II 200 (^{1}H @ 200MHz, ^{13}C @ 50MHz), Avance II 400 (^{1}H @ 400MHz, ^{13}C @ 100MHz), and Avance III 600 (^{1}H @ 600MHz, ^{13}C @ 150MHz), machines from Bruker Biospin GmbH, Reinstetten. Measurements were taken at 298 K, by Mrs. Hausmann, Mrs. Stammler, and Mrs. Pospiech.

The chemical shift is given on a ppm scale. For internal reference tetramethylsilane was used (^{1}H-NMR for $CDCl_3$) or solvent signals as per literature values (^{13}C-NMR).

The analysis of signals was performed using the software MestReC (MestreLabs Research), and the correlation of signals was done using ChemBioDraw 12.0 software (Cambridgesoft) as well as 2D NMR techniques. Numbering of atoms in a molecule for the purpose of assigning signals does not follow the IUPAC rules. The listing of signals in ^{1}H NMR follows the scheme chemical shift (multiplicity, integral, coupling constant(s) in Herz, assignment). The multiplicities are given by the following abbreviations: s (singlet), d (duplet), t (triplet), q (quartet), quin (quintet), sep (septet), oct (octet) and m (multiplet), and combinations thereof.

5. Mass spectrometry

Exact masses were determined using and EI sector field MS (Thermo Finnigan MAT, Bremen) operated by Dr. Röcker, or an ESI MicroToF (Bruker Daltonics, Bremen). Set to the following conditions: Method: tune_low_270308, Source Type: ESI, Focus: Not active, Scan Begin: 50 m/z, Scan End: 1200 m/z, Ion Polarity: Positive, Set Capillary: 4500 V, Set End Plate Offset: -

500 V, Set Nebulizer: 0.4 bar, Set Dry Heater: 180 °C, Set Dry Gas: 4.0 L/min, Set Divert Valve: Waste

GC-MS was measured on an Automass 615 GC machine (ATI UNICAM).

6. *IR-Spectroscopy*

IR-Spectra were measured on an IFS 25-Spectrometer (Bruker Optics, Ettlingen) by Ms. Stammler. The measurement was performed by means of KBr pellets or as a film on NaCl plates. The intensities of the IR peaks are described as follows: vs (very strong), s (strong), m (middle), w (weak) and br (broad).

7. *CHN- Analysis*

Elemental analysis was performed on a Carlo Erba 1106 CHN machine by Mr. Meurer.

8. *Crystallography*

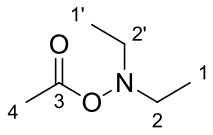
Single crystal X-ray diffraction was performed with a STOE IPDS-diffractometer equipped with a low temperature system, a graphite monochromator and IP detector system. Mo-K_α radiation (λ = 0.71069 Å) was used. The frames were integrated with the STOE software package. No absorption corrections were applied. Analysis was performed by Ms. Löw or Mr. Becker.

9. *Cyclic voltammetry*

CV was measured on an eDAQ potentiostat EA161 and e-corder ED410. Measurements were carried out at room temperature, in DCM with 0.1 mol/L $N(Bu)_4ClO_4$ as electrolyte. Electrodes employed were a gold working electrode, platinum auxiliary electrode and an Ag/AgCl reference electrode. Measurements were performed using a 1 mmol/L solution of oxyamine, as shown in the appendix. 190 mV was measured for Ferrocene, and no reversible electron transfer reactions were observed, as can be seen in the diagrams in the appendix.

2. *Synthesis of the hydroxylamine derivatives for the cyclovoltamometric measurements*

1. *O*-acetyl-*N*,*N*-diethylhydroxylamine



N,N-Diethylhydroxylamine (20.0 mmol, 1.8 g) and triethylamine (20.0 mmol, 2.024 g) were dissolved in DCM (20 mL) at 0°C to give a colorless solution. Acetic anhydride (40.0 mmol, 4.08 g) dissolved in DCM (20 mL) was added drop wise over 5 minutes to give a clear solution. The ice bath was removed and the solution stirred at room temperature for five hours.

Removed solvent via rotary evaporation to give a purple brown residue. Diluted with ice cold diethyl ether (50 mL), washed with ice cold NaOH (20%) (2 x 50 mL), extracted aq. phase with ice cold ether, dried over Na_2SO_4, removed solvent via rotary evaporation. Took up crude product on silica gel and filtered over a silica plug with t-BME.

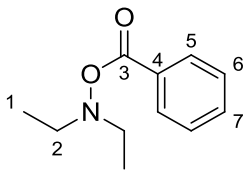
Yield: 1.08 g (8.23 mmol, 41%)

^{1}H-NMR (400 MHz, CDCl3): δ = 1.05 (t, 6H, *J* = 7.1, Hz, H-1, 1’), 2.00 (s, 3H, H-4), 2.83 (q, 4H, *J* = 7.09Hz, H-2, 2’).

^{13}C-NMR (100 MHz, CDCl3): δ = 170.4 (C-4), 53.2 (C-2, 2’), 19.2 (C-4), 11.7 (C-1, 1’).

NMR data agrees with Literature data[41].

2. O-benzoyl-N,N-diethylhydroxylamine



N,N-Diethylhydroxylamine (7.18 mmol, 0.64 g) was added to pyridine (3 mL) under stirring at 0°C. Benzoyl chloride (14.36 mmol, 2.019 g) was added dropwise over 5 minutes. This suspension was stirred for 20 minutes at 0°C, at which point the color becomes a grayish pink. The ice bath is removed, the suspension heated to 50°C for 30 minutes, at which point it becomes a solution. The water bath was removed and the solution stirred at room temperature overnight, after which it turned brown.

The solution was poured onto 50 mL ice water and 5 mL conc. HCl. The organic phase was extracted with diethylether (3 X 50 mL), and the combined organic phases were washed with aq. $NaHCO_3$, dried over Na_2SO_4, and the solvent removed via rotary evaporation. The residue was chromatographed over silica gel, pentane : t-BME (3:1).

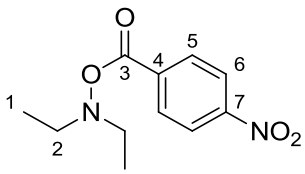
Yield: 1.1 g (5.69 mmol, 79%)

^{1}H-NMR (400 MHz, CDCl3): δ = 1.11 (t, 6H, 3J = 7.1 Hz, H-1), 2.98 (q, 4H, 3J = 7,09 Hz, H-2), 7.35 – 7.97 (m, 5H, H-5, H-6, H-7).

^{13}C-NMR (100 MHz, CDCl3): δ = 165.9 (C-3), 133.0 (C-7), 129.5 (C-5), 129.2 (C-4), 128.4 (C-6), 53.5 (C-2), 11.9 (C-1).

NMR data agrees with Literature data[42].

3. *N*,*N*-diethyl-*O*-(4-nitrobenzoyl)hydroxylamine



N,N-Diethylhydroxylamine (20.0 mmol, 1.78 g) and triethylamine (20 mmol, 2.78 mL) were added to DCM (50 mL) under stirring at 0°C. 4-nitrobenzoyl chloride (20.0 mmol, 3.71 g) dissolved in dichloromethane (20 mL) was added dropwise over 10 minutes. This suspension was stirred for 20 minutes at 0°C, at which point the color turned a bright yellow. The ice bath was removed and the suspension warmed to 40°C for 30 minutes, at which point it turned to a yellow solution, and stirred at room temperature overnight.

The solution was poured onto ice water (25 mL) and the phases separated. The organic phase was washed with aq. $NaHCO_3$, dried over Na_2SO_4, and the solvent removed via rotary evaporation. The residue was filtered over a silica plug with t-BME.

Yield: 3.6 g (15.03 mmol, 75%).

^{1}H NMR (200 MHz, CDCl3) δ = ppm 1.20 (t, *J* = 6.90 Hz, 1H), 3.10 (q, *J* = 6.94, 6.88, 6.88 Hz, 1H), 8.27 (dd, *J* = 17.97, 8.42 Hz, 1H).

^{13}C-NMR (50 MHz, CDCl3): δ = 11.90 (C-1), 53.55 (C-2), 123.59 (C-6), 130.63 (C-5), 134.65 (C-4), 150.57 (C-7), 164.02 (C-3).

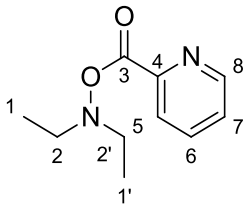
HRMS: m/z = 238.09353 [M+ 238.0954 calc. for $C11H14N2O4^-$]

IR (KBr) *v* = cm^{-1} 3458, 2976, 1756, 1606, 1525, 1446, 1347, 1239, 1071, 876, 851, 717, 480

CHN:

calc.	C:	55.46	H:	5.92	N:	11.76
anal.	C:	55.48	H:	5,89	N:	11.78

4. *N*,*N*-diethyl-*O*-picolinoylhydroxylamine



Picolinic acid (25 mmol, 3.08 g) was added to toluene (22.5 mL) at 0 °C to give a white suspension. Oxalyl chloride (50 mmol, 6.35 g) was added drop wise over 10 minutes, to yield a yellow suspension. After 1 h, the reaction was left to warm to room temperature and stirred overnight.

The solid was filtered and washed with toluene (18 mL), then dried in by vacuum to yield picolinic acid chloride (3.2 g, 22.61 mmol), which was used without further purification or characterization.

In a 250 mL round-bottomed flask triethylamine (13,94 ml, 100 mmol) and N,N-diethyl hydroxylamine (2,049 ml, 20 mmol) were added to DCM (Volume: 30 ml) to give a colorless solution at 0°C.

Picolinoyl chloride (3,2 g, 22,61 mmol) suspended in DCM (20 mL) was added slowly over 10 minutes. The ice bath was removed and the reaction mixture stirred overnight.

The reaction mixture was washed with pH 7 buffer solution (2 X 40 mL), dried with Na_2SO_4, and excess solvent removed by rotary evaporation and then by oil pump vacuum.

Yield: 1.51 g (7.77 mmol, 39%) (NMR shows slight toluene and t-BME impurities)

^{1}H NMR (400 MHz, CDCl3): δ = 1.13 (t, *J* = 7.10, 7.10 Hz, 6H, H-1, 1’), 3.03 (q, *J* = 7.09, 7.09, 7.09 Hz, 4H, H-2, 2’), 7.42 (ddd, *J* = 7.64, 4.76, 1.19 Hz, 1H, H-aromatic), 7.78 (dt, *J* = 7.78, 7.75, 1.77 Hz, 1H, H-aromatic), 8.09-8.03 (m, 1H, H-aromatic), 8.70 (ddd, *J* = 4.75, 1.68, 0.80 Hz, 1H, H-aromatic).

^{13}C-NMR (50 MHz, CDCl3): δ = 164.71 (C-3), 149.88 (C-4), 147.50 (C-8), 136.96 (C-7), 126.95 (C-5), 125.26 (C-6), 53.61 (C-2, 2’), 12.02 (C-1, 1’).

3. *Synthesis of cyclisation precursors*

1. General Procedures

i. Hydroxylamination of secondary amines

In a 100 mL round-bottomed flask p-nitro dibenzoyl peroxide (1.5 eq) and sec-amine (1 eq) were mixed in Diethyl ether: pH 10 buffer (Ratio: 1:1, Volume: 60 to 100 ml), and refluxed till TLC indicated amine was consumed, usually overnight.

The phases were separated, and the aqueous phases made basic with 20% NaOH till pH was ~14, then extracted with diethyl ether (3 X 40 mL). The combined organic phases were washed with water (2 X 30 mL), dried over $MgSO_4$, and the solvent removed by rotary evaporator. The crude product was chromatographed on silica gel with pentane : ether (25:1) to yield product.

ii. Room temperature cyclisation of hydroxylamine's

In a flame dried 10 mL Schlenk glass 5 mol % $[Cu(CH_3CN)_4PF_6$, 1 eq. hydroxylamine, 1 mL toluene and 1 eq. BF3*OEt_2 were added sequentially. The mixture was stirred under N_2 for 6 hours and then quenched by the addition of 2 mL conc. NH_3. The organic phase was extracted with 3 X 10 mL DCM, which was dried over $MgSO_4$, taken up on silica gel, and purified chromatographically pentane : ether (9 : 1) to yield the product(s).

iii. High Temperature cyclisation of hydroxylamines

In a flame dried 10 mL Schlenk glass 5 mol % $[Cu(CH_3CN)_4PF_6$, 1 eq. hydroxylamine and 1 mL toluene were added sequentially. The mixture was stirred and heated to 100°C under N_2 for 1 hour and then quenched by the addition of 2 mL conc. NH_3. The organic phase was extracted with 3 X 10 mL DCM, which was dried over $MgSO_4$, taken up on silica gel, and purified chromatographically pentane : ether (9 : 1) to yield the product(s).

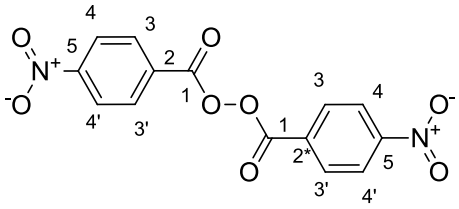
iv. Microwave cyclisation of hydroxylamines at75°C

In a 5 mL MW glass 5 mol % $[Cu(CH_3CN)_4PF_6$, 1 eq. hydroxylamine, 1 mL toluene and 2 eq. BF3*OEt_2 were added sequentially. The mixture was heated with stirring to 75°C for 10 minutes and then quenched by the addition of 2 mL conc. NH_3. The organic phase was extracted with 3 X 10 mL DCM, which was dried over $MgSO_4$, taken up on silica gel, and purified chromatographically pentane : ether (9 : 1) to yield the product(s).

v. Microwave cyclisation of hydroxylamines at 100°C

In a 5 mL MW glass 5 mol % $[Cu(CH_3CN)_4PF_6$, 1 eq. hydroxylamine and 1 mL toluene were added sequentially. The mixture was heated with stirring to 100°C for 10 minutes and then quenched by the addition of 2 mL conc. NH_3. The organic phase was extracted with 3 X 10 mL DCM, which was dried over $MgSO_4$, taken up on silica gel, and purified chromatographically pentane : ether (9 : 1) to yield the product(s).

2. p-Nitrodibenzoyl Peroxide



In a 750 mL beaker equipped with mechanical stirrer, thermometer, and drip funnel Sodium peroxide (10 g, 128 mmol) was added in portions to Water (100 ml) at 0°C to give a white suspension and stirred for 10 minutes.

p-Nitrobenzoyl Chloride (37 g, 199 mmol) was dissolved in Toluene (100 ml) and added dropwise to the water suspension at 0°C over 30 min, and the reaction mixture stirred for a further 90 minutes.

The reaction mixture was filtered through a Büchnerfunnel, washed with 200 mL ice cold water, and recrystallized from 500 mL toluene at preheated to 80°C, and filtered warm. The filtrate was left to stand overnight to dry, then removed to a flask and further dried over oil pump vacuum until the weight remained constant.

Yield: 28.83 g (87 mmol, 87%)

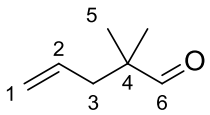
^{1}H NMR (400 MHz, CDCl3) δ = ppm 8.26-8.29 (m, 8H), 8.39-8.41 (m, 8H).

^{13}C-NMR (50 MHz, CDCl3): δ = 161.08 (C-1), 151.38 (C-5), 131.12 (C-4), 130.61 (C-2), 124.12 (C-3).

Synthesis performed in accordance with lit procedure [43].

NMR data agrees with literature data. from [44].

3. 2,2-dimethylpent-4-enal



Isobutyraldehyde and allyl alcohol were freshly distilled.

In a 1 L 3 neck round-bottomed flask, equipped with thermometer and reflux condenser on top of a dean stark trap, p-toluenesulfonic acid monohydrate (0.25 g, 1.314 mmol), isobutyraldehyde (108 g, 1.5 mol), and allyl alcohol (68.0 ml, 1 mol) in p-cymene (200 grams) were combined to give a colorless solution.

The mixture was heated to reflux for 48 hours during which time the solution turned light orange. 20 mL water was collected in the water trap and removed, after which the reflux condenser was replaced with a distillation cooler. The mixture was heated to 120°C to remove remaining reactants and cooled. Then ca. 70 cm of vigrou column was inserted and the distillation continued at 200 mbar, with the fraction between 76 and 90°C being collected, raw yield 92.6g (contains isobutyraldehyde and p-cymene as impurities).

Distilled raw yield over ca. 40 cm vigrou column, collecting fraction from 97 to 103°C.

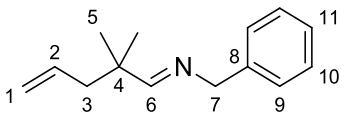
Yield: 74.4 g (0.663 mol, 64%)

1H NMR (200 MHz, CDCl3) δ = ppm 1.10 (s, 6H), 2.22 (d, *J* = 7.12 Hz, 2H), 5.11 (m, 2H), 5.7 (ddd, *J* = 7.53, 15.84, 18.77 Hz, 1H), 9.5 (s, 1H).

13C-NMR (50 MHz, CDCl3): δ = 20.98 (C-5), 41.27 (C-3), 45.54 (C-4), 118.26 (C-1), 132.97 (C-2), 205.67 (C-6).

NMR data agrees with data from [45].

4. (E)-N-(2,2-dimethylpent-4-en-1-ylidene)-1-phenylmethanamine



In a 500 mL round-bottomed flask 2,2-dimethylpent-4-enal (50.17 g, 447 mmol) and $MgSO_4$ (26.9 g, 224 mmol) were combined in DCM (300 mL) to form a white suspension, cooled to 0°C.

Benzylamine was added drop wise (48.9 ml, 447 mmol), and let stand overnight at RT. Removed $MgSO_4$ by filtration and DCM via rotary evaporator. Used product (light yellow oily substance) in next step without further purification, contained DCM.

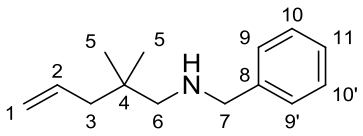
Yield: 79.0 g (392 mmol, 88%)

^{1}H NMR (400 MHz, CDCl3) δ = 1.10 (s, 6H, H-5), 2.21 (d, *J* = 7.40 Hz, 2H, H-3), 4.58 (s, 2H, H-7), 5.08-4.97 (m, 2H, H-1), 5.78 (tdd, *J* = 14.87, 11.57, 7.40, 7.40 Hz, 1H, H-2), 7.37-7.18 (m, 5H, H-9, 10, 11), 7.64 (s, 1H, H-6).

^{13}C-NMR (100 MHz, CDCl3): δ = 172.64 (C-6), 139.59 (C-8), 134.61 (C-2), 128.33 (C-9/10), 127.62 (C-9/10), 126.73 (C-11), 117.51 (C-1), 64.66 (C-7), 44.70 (C-3), 39.25 (C-4), 24.64 (C-5).

NMR data agrees with data from[46].

5. N-benzyl-2,2-dimethylpent-4-en-1-amine



In a 500 mL round-bottomed flask (E)-N-(2,2-dimethylpent-4-en-1-ylidene)-1-phenylmethanamine (78.993 g, 392 mmol) was dissolved in MeOH (200 mL) to give a colorless solution, and cooled to 0°C.

$NaBH_4$ (7.42 g, 196 mmol) was added in portions. Let reaction warm to room temperature and stirred overnight.

Hydrolyzed with 50 mL 20 % NaOH, stirred for 30 minutes, then added 100 mL diethyl ether, and separated phases. Extracted aq. phase with DCM (3 X 100 mL), washed org. phase with sat. NaCl solution (3 X 50 mL), dried over $MgSO_4$, removed solvent via rotary evaporator.

Distilled crude product (yellow oil) to obtain a clear liquid, bp: 159°C @ 50 mbar.

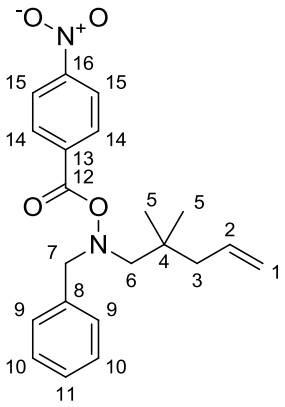
Yield: 68.5 g (377 mmol, 71%)

^{1}H NMR (400 MHz, CDCl3) δ = 0.89 (s, 6H, H-5), 1.34-1.03 (m, 1H, N-H), 2.02 (d, *J* = 7.50 Hz, 1H, H-3), 2.36 (s, 2H, H-6), 3.78 (s, 2H, H-7), 5.00 (dd, *J* = 13.71, 1.21 Hz, 2H, H-1), 5.86-5.72 (m, 1H, H-1), 7.36-7.19 (m, 5H, H-9, 10, 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 141.01 (C-8), 135.60 (C-2), 128.26 (C-9/10), 127.94 (C-9/10), 126.72 (C-11), 116.73 (C-1), 59.68 (C-7), 54.69 (C-6), 44.63 (C-3), 34.35 (C-4), 25.51 (C-5).

NMR data agrees with data from[47].

6. N-benzyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 1.44 g (2.91 mmol, 71%)

^{1}H NMR (400 MHz, CDCl3) δ = 0.85 (s, 6H, H-5), 1.99 (d, *J* = 7.45 Hz, 1H, H-3), 2.83 (s, 2H, H-6), 4.16 (s, 2H, H-7), 4.92 (ddd, *J* = 16.93, 6.25, 1.73 Hz, 2H, H-2), 5.66 (tdd, *J* = 17.60, 10.19, 7.45, 7.45 Hz, 1H, H-1), 7.43-7.24 (m, 5H, H-9, 10, 11), 8.19 (dd, *J* = 62.19, 8.95 Hz, 4H, H-14,15).

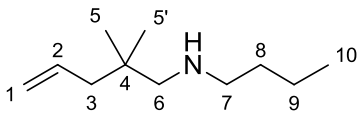
^{13}C-NMR (100 MHz, CDCl3): δ = 163.04 (C-12), 150.47 (C-16), 135.41 (C-2), 135.03 (C-8/13), 134.88 (C-8/13), 130.42 (C-14), 129.95 (C-9/10), 128.34 (C-9/10), 127.93 (C-11), 123.60 (C-15), 117.36 (C-1), 67.02 (C-7), 65.27 (C-6), 44.88 (C-3), 34.55 (C-4), 25.83 (C-5).

CHN:

calc.	C:	68.46	H:	6.57	N:	7.60
anal.	C:	68.29	H:	6.58	N:	7.60

HRMS (ESI): m/z calculated for $C_{21}H_{24}N_2NaO_4^+$: 391.1628; found: 391.1627

7. N-butyl-2,2-dimethylpent-4-en-1-amine



In a 250 mL round-bottomed flask 2,2-dimethylpent-4-enal (1 g, 8.92 mmol) and butan-1-amine (0.652 g, 8.92 mmol) were dissolved in DCM (100 mL) to give a colorless solution, cooled to 0°C. Sodium triacetoxyborohydride (2.83 g, 13.37 mmol) was added portion wise, and the reaction mixture was left to warm to RT and stir over night.

The reaction was quenched by addition of 20% NaOH, stirred for 30 min, sep. phases, extracted aq. phase with DCM (3 X 20 mL), dried over MgSO4, filtered, took up on silica gel. chromatographed 3:1.

NMR indicates clean product.

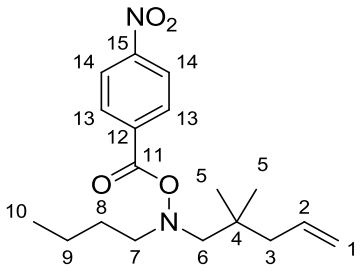
Yield: 1.24 g (7.32 mmol, 82%)

^{1}H NMR (400 MHz, CDCl3) δ = 0.82 (s, 6H, H-5, 5’), 0.84 (t, 3H, J = 7.3 Hz, 3H, H-10), 1.14 -1.39 (m, 5H, H-8, 9, N), 1.93 (d, *J* = 7.49 Hz, 2H, H3), 2.28 (s, 2H, H-6), 2.49 -2-52 (m, 2H, H-7), 4.92-4.96 (m, 2H, H-1), 5.72 – 5-78 (m, 1H, H-2).

^{13}C-NMR (100 MHz, CDCl3): δ = 135.61 (C-2), 116.677 (C-1), 60.5 (C-7), 50.72 (C-6), 44.79 (C-3), 34.21 (C-4), 32.24 (C-8), 25.53 (C-5, 5’), 20.48 (C-9), 14.04 (C-10).

NMR data agrees with data from [25, 28].

8. N-butyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 1g (2.99 mmol, 63%)

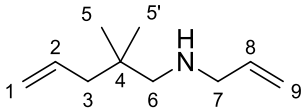
^{1}H NMR (400 MHz, CDCl3): δ = 0.99-0.85 (m, 9H, H-1, H-10), 1.41 (qd, *J* = 14.24, 6.99, 6.99, 6.97 Hz, 2H, H-9), 1.53 (td, *J* = 14.60, 7.09, 7.09 Hz, 2H, H-8), 2.07 (d, *J* = 7.43 Hz, 2H, H-3), 2.83 (s, 2H, H-6), 3.05-2.96 (m, 2H, H-7), 5.08-4.93 (m, 2H,H-1), 5.80 (tdd, *J* = 17.70, 10.30, 7.45, 7.45 Hz, 1H,H-2), 8.23 (dd, *J* = 46.20, 8.95 Hz, 4H, H-13, 14).

^{13}C-NMR (100 MHz, CDCl3): δ = 163.36 (C-11), 150.49 (C-15), 135.14 (C-2), 134.97 (C-12), 130.54 (C-14), 123.60 (C-13), 117.47 (C-1), 68.58 (C-6), 61.47 (C-7), 45.10 (C-3), 34.61 (C-4), 28.74 (C-8), 25.87 (C-9), 20.38 (C-5), 13.96 (C-10).

CHN:

calc.	C:	64.65	H:	7.84	N:	8.38
anal.	C:	63.72	H:	8.35	N:	8.35

9. N-allyl-2,2-dimethylpent-4-en-1-amine



In a 250 mL round-bottomed flask allylamine (0.669 mL, 8.92 mmol) and 2,2-dimethylpent-4-enal (1 g, 8.92 mmol) in DCM (100 mL) to give a colorless solution. Sodium triacetoxyborohydride (2.83 g, 13.37 mmol) was added portion wise, the reaction mixture was let warm to RT and stirred overnight.

The reaction was quenched by addition of 20% NaOH, stirred for 30 min, sep. phases, extracted aq. phase with DCM (3 X 20 mL), dried over MgSO4, filtered, took up on silica gel. chromatographed 3:1.

NMR indicates clean product.

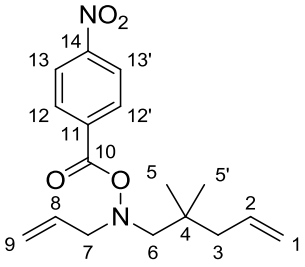
Yield: 1.1 g (7.18 mmol, 81%)

^{1}H NMR (200 MHz, CDCl3) δ = 0.89 (s, 6H, H-5, 5'), 0.99 (s, 1H, N-H), 2.01 (dt, *J* = 7.42, 1.03 Hz, 2H, H-3), 2.35 (s, 2H, H-6), 3.23 (dt, *J* = 5.93, 1.42 Hz, 2H), 4.93-5.22 (m, 4H, H-1, 9), 5.70-6.01 (m, 2H, H-2, 8).

^{13}C-NMR (100 MHz, CDCl3): δ = 137.37 (C-8), 135.45 (C-2), 116.72 (C-9), 115.43 (C-1), 59.72 (C-7), 53.25 (C-6), 44.67 (C-3), 34.16 (C-4), 25.45 (C-5).

NMR data agrees with data from [25, 28].

10. N-allyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 1.45 g (4.56 mmol, 70%)

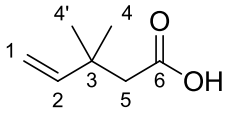
^{1}H NMR (400 MHz, CDCl3): δ = 0.92 (s, 6H, H-5, H-5’), 2.07 (d, *J* = 7.44 Hz, 2H, H-3), 2.85 (s, 2H, H-6), 3.67 (d, *J* = 6.75 Hz, 2H, H-7), 5.07-4.96 (m, 2H, H-2), 5.24-5.17 (m, 2H, H-7), 5.80 (tdd, *J* = 17.66, 10.27, 7.46, 7.46 Hz, 2H, H-1), 6.02 (tdd, *J* = 16.99, 10.19, 6.75, 6.75 Hz, 2H, H-8), 8.22 (dd, *J* = 52.03, 8.92 Hz, 4H, H-12, 13, 12’, 13’).

^{13}C-NMR (100 MHz, CDCl3): δ = 163.26 (C-10), 150.50 (C-14), 135.01 (C-11), 134.89 (C-2), 132.48 (C-8), 130.48 (C-13, 13’), 123.60 (C-12, 12’), 119.84 (C-9), 117.52 (C-1), 67.65 (C-6), 64.52 (C-7), 45.04 (C-3), 34.61 (C-4), 25.84 (C-5, 5’).

CHN:

calc.	C:	64.13	H:	6.97	N:	8.80
anal.	C:	63.74	H:	6.95	N:	8.81

11. Synthesis of 3,3-dimethylpent-4-enoic acid



In a 250 mL round-bottomed flask 4-nitrobenzoic acid (0.970 g, 5.81 mmol), trimethyl orthoacetate (69.7 g, 581 mmol), and 3-methylbut-2-en-1-ol (50 g, 581 mmol) were combined to give a colorless solution. The reaction mixture was heated, starting at 90°C and going slowly to 140°C over 3 hours and held at this temperature for 2 more hours till ca. 1.6 eq. of MeOH were distilled off and no further MeOH was forthcoming after further addition of 4-nitrobenzoic acid.

At this point 40 grams of KOH dissolved in 200 mL MeOH was added, refluxed for 5 hours, and then the majority of MeOH was removed via distillation. The semisolid suspension was acidified with conc. HCl to a pH of ~1, the phases separated and the aq. phase extracted with t-BME. The combined organic phases were dried over $MgSO_4$, then the solvent was removed via rotary evaporation, and further by oil pump.

The crude product was distilled to yield a clear liquid, bp : 57°C, oil pump vacuum.

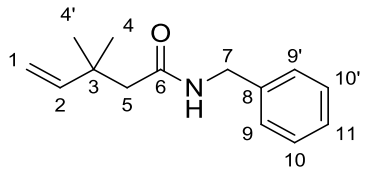
Yield: 25.47g (199 mmol, 34.2% over two steps)

^{1}H NMR (400 MHz, CDCl3): δ = 1.16 (s, 6H, H-4, H-4'), 2.34 (s, 2H, H-5), 5.91-4.92 (m, 2H, H-2), 5.91 (dd, *J* = 17.44, 10.70 Hz, 1H, H-1), 11.03 (s, 1H, O-H).

^{13}C-NMR (100 MHz, CDCl3): δ = 178.36 (C-6), 146.49 (C-2), 111.12 (C-1), 46.60 (C-5), 36.01 (C-3), 26.88 (C-4).

NMR data agrees with data from [48].

12. N-benzyl-3,3-dimethylpent-4-enamide



In a 250 mL round-bottomed flask benzylamine (2.508 g, 23.41 mmol) and 3,3-dimethylpent-4-enoic acid (3 g, 23.41 mmol) were dissolved in DCM (100 mL), and cooled to 0°C to give a colorless solution. DMAP (0.286 g, 2.341 mmol) and DCC (5.80 g, 28.1 mmol) dissolved in DCM (10 mL) were added to reaction mixture, and stirred overnight at RT.

The reaction mixture was filtered, solvent removed, and purified via silica gel chromatography pentane : diethyl ether (5:1, 2:1, 1:1) to yield the product as a clear liquid with slight urea impurity.

Yield: 3.11g (14.31 mmol, 61.1%)

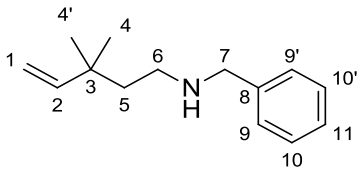
^{1}H NMR (400 MHz, CDCl3): δ =1.07 (s, 6H, H-4. 4’), 2.15 (s, 2H, H-5), 4.33 (d, *J* = 5.66 Hz, 2H, H-7), 4.90 (dd, *J* = 2.88, 0.97 Hz, 1H, H-2), 4.93 (dd, *J* = 9.73, 0.96 Hz, 1H, H-2), 5.76 (s, 1H, N-H), 5.83 (dd, *J* = 17.46, 10.71 Hz, 1H, H-2), 7.30-7.16 (m, 5H, H-9, 10, 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 170.90 (C-6), 147.27 (C-2), 138.38 (C-8), 128.66 (C-9/10), 127.90 (C-9/10), 127.46 (C-11), 111.68 (C-1), 49.47 (C-7), 43.58 (C-5), 27.00 (C-3), 36.41 (C-4, 4’).

HRMS (EI): m/z calculated for C14H19NO: 217.1467 found: 217.1459

NMR data agrees with data from [49].

13. N-benzyl-3,3-dimethylpent-4-en-1-amine



In a 250 mL round-bottomed flask LAH (2.026 g, 53.4 mmol) was added to dry THF (75 mL) to give a grey suspension, and cooled to 0°C. N-benzyl-3,3-dimethylpent-4-enamide (2.9 g, 13.35 mmol) dissolved in dry THF (75 mL) was added drop wise over 10 minutes at 0°C, let warm to RT and refluxed overnight.

The reaction was diluted with diethyl ether, hydrolyzed with 2 mL H_2O, 2 mL 20% NaOH, and 6 mL H_2O at 0°C. The organic phase was decanted off, and the aq. phase extracted with 3 X 50 mL ether, dried over $MgSO_4$, filtered, and purified over a silica plug.

Yield: 2.16g (10.6 mmol, 79%)

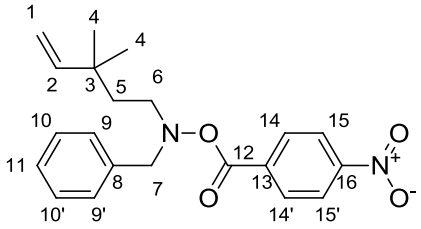
^{1}H NMR (400 MHz, CDCl3): δ = 0.93 (s, 6H, H-4, H-4'), 1.13-1.32 (m, 1H, N-H), 1.49-1.41 (m, 2H, H-5), 2.57-2.47 (m, 2H, H-6), 3.69 (s, 2H, H-7), 4.83 (dd, *J* = 14.11, 2.24 Hz, 2H, H-2), 5.72 (dd, *J* = 17.77, 10.43 Hz, 1H, H-1), 7.14-7.26 (m, 5H, H-9, 9', 10, 10', 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 148.16 (C-2), 140.51 (C-8), 128.39 (C-9/10, C9'/10'), 128.10 (C-9/10, C9'/10'), 126.87 (C-11), 110.50 (C-1), 54.28 (C-7), 45.74 (C-6), 42.69 (C-5), 35.97 (C-3), 27.00 (C-4).

HRMS (EI): m/z calculated for C14H21N: 203.1674 found: 203.1666

NMR data agrees with data from [50].

14. N-benzyl-N-(3,3-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 1.25g (3.38 mmol, 69%)

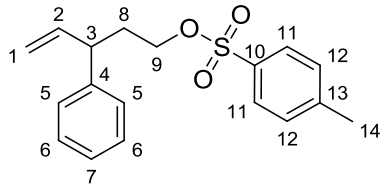
^{1}H NMR (400 MHz, CDCl3): δ = 0.93 (s, 6H, H-4, H-4’), 1.54-1.63 (m, 2H, H-5), 2.91-3.02 (m, 2H, H-6), 4.09 (s, 2H, H-7), 4.85 (ddd, *J* = 12.31, 7.82, 1.15 Hz, 2H, H-1), 5.67 (dd, *J* = 17.36, 10.83 Hz, 1H, H-2), 7.14-7.31 (m, 5H, H-9, 9’, 10, 10’, 11), 8.06 (dd, *J* = 80.30, 8.87 Hz, 4H, H-14, 14’, 15, 15’).

^{13}C-NMR (100 MHz, CDCl3): δ = 163.37 (C-12), 150.47 (C-16), 147.29 (C-2), 135.41 (C-8), 134.68 (C-8), 130.46 (C-14), 129.49 (C-9), 128.38 (C-10), 127.86 (C-11), 123.53 (C-15), 111.25 (C-1), 63.84 (C-7), 55.52 (C-6), 38.78 (C-5), 35.79 (C-3), 26.91 (C-4).

CHN:

calc.	C:	68.46	H:	6.57	N:	7.60
anal.	C:	68.61	H:	6.63	N:	7.55

15. 3-phenylpent-4-en-1-yl 4-methylbenzenesulfonate



In a 50 mL round-bottomed flask 3-phenylpent-4-en-1-ol (2 g, 12.33 mmol) and p-toluenesulfonyl chloride (7.05 g, 37.0 mmol) were dissolved in DCM (50 mL) at 0°C to give a colorless solution. Pyridine (3.99 ml, 49.3 mmol) was added drop wise at 0°C, and the reaction stirred till TLC indicated the alcohol was consumed.

The reaction mixture was washed with water (20 mL), 2 N HCl (20 mL), sat. $NaHCO_3$ (20 mL), water (20 mL), dried over $MgSO_4$, and the solvent removed via rotary evaporation. The crude product was chromatographed over silica gel with pentane : ether (10:1) to give the product as a white solid.

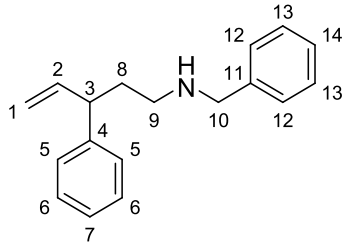
Yield: 3.2g (10.1 mmol, 82%)

^{1}H NMR (400 MHz, CDCl3): δ = 2.14-1.91 (m, 2H, H-8), 2.44 (s, 3H, H-14), 3.38 (q, *J* = 7.60, 7.60, 7.59 Hz, 1H, H-3), 3.89-4.05 (m, 2H, H-9), 4.99 (tdd, *J* = 18.39, 17.11, 1.22, 1.22 Hz, 2H, H-1), 5.84 (ddd, *J* = 17.11, 14.60, 8.32 Hz, 1H, H-1), 7.11-7.02 (m, 2H, H-11), 7.37-7.13 (m, 5H, H-5, 6, 7), 7.74-7.79 (m, 2H, H-12).

^{13}C-NMR (100 MHz, CDCl3): δ = 144.74 (C-4/10/13), 142.39 (C-4/10/13), 140.40 (C-4/10/13), 133.04 (C- 2), 129.85 (C-5/6/11/12), 128.66 (C-5/6/11/12), 128.46 (C-5/6/11/12), 127.93 (C-5/6/11/12), 127.50 (C-5/6/11/12), 126.65 (C-7), 115.22 (C-1), 68.47 (C-9), 45.39 (C-3), 34.15 (C-8), 21.66 (C-14).

NMR data agrees with data from [51].

16. N-benzyl-3-phenylpent-4-en-1-amine



In a 50 mL round-bottomed flask 3-phenylpent-4-en-1-yl 4-methylbenzenesulfonate (3.2 g, 10.11 mmol) and benzylamine (11.05 ml, 101 mmol) were combined to give a colorless solution, and heated to 70°C overnight.

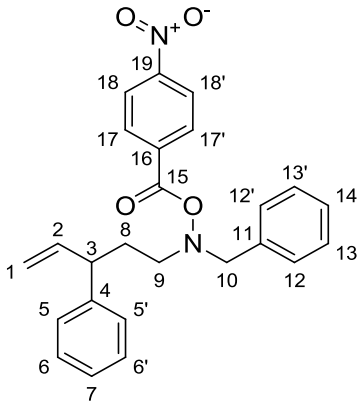
When TLC indicated the reaction had come to completion excess benzylamine was removed via oil pump vacuum, and the residue chromatographed with pentane : t-BME (20:1, 10:1, 5:1) to yield the product as a clear liquid.

Yield: 1.19g (4.73 mmol, 47%)

^{1}H NMR (400 MHz, CDCl3): δ = 1.25 (s, 1H, N-H), 1.87 -1.98 (m, 2H, H-8), 2.53-2.67 (m, 2H, H-9), 3.37 (q, *J* = 7.54, 7.54, 7.54 Hz, 1H, H-3), 3.72 (s, 2H, H-10), 4.97-5.09 (m, 2H, H-1), 5.95 (ddd, *J* = 17.55, 10.25, 7.58 Hz, 1H, H-2), 7.17-7.32 (m., 10H, H-5, 5',6 ,6' ,7, 12, 12', 13, 13', 14).

^{13}C-NMR (100 MHz, CDCl3): δ =35.54 (C-8), 47.46 (C-3), 47.71 (C-9), 54.01 (C-10), 114.14 (C-1), 126.26 (C-7/14), 126.85 (C-7/14), 127.55 (C-5/6/12/13), 128.06 (C-5/6/12/13), 128.35 (C-5/6/12/13), 128.49 (C-5/6/12/13), 140.49 (C-2), 142.02 (C-4/11), 144.02 (C-4/11).

17. N-benzyl-O-(4-nitrobenzoyl)-N-(3-phenylpent-4-en-1-yl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 1.72g (4.13 mmol, 91%)

^{1}H NMR (400 MHz, CDCl3): δ = 1.84-2.02 (m, 2H, H-8), 2.87-3.02 (m, 3H, H-9), 3.42 (q, J = 7.53, 7.52, 7.52 Hz, 1H, H-3), 4.01-4.11 (m, 2H, H-10), 4.90-4.97 (m, 2H, H-1), 5.84 (ddd, *J* = 16.95, 10.46, 7.68 Hz, 1H, H-1), 7.05-7.32 (m, 10H, H-5, 5', 6, 6', 7, 12, 12', 13, 13', 14), 8.05 (dd, *J* = 80.10, 8.86 Hz, 4H, H-17, 17', 18, 18').

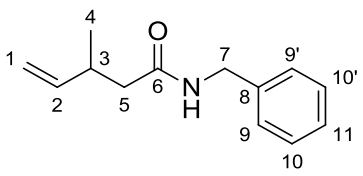
^{13}C-NMR (100 MHz, CDCl3): δ = 163.34 (C-15), 150.48 (C-19), 143.52 (C-4), 141.39 (C-X11), 135.33 (C-16), 134.66 (C-2), 130.48 (C-5/5',6/6', 12/12',13/13', 17/17',18/18'), 129.55 (C-5/5',6/6', 12/12',13/13', 17/17',18/18'), 128.56 (C-5/5',6/6', 12/12',13/13', 17/17',18/18'), 128.39 (C-5/5',6/6', 12/12',13/13', 17/17',18/18'), 127.89 (C-5/5',6/6', 12/12',13/13', 17/17',18/18'), 127.59 (C-5/5',6/6', 12/12',13/13', 17/17',18/18'), 126.43 (C-7/14), 123.54 (C-7/14), 114.71 (C-1), 63.98 (C-10), 56.83 (C-9), 47.18 (C-3), 32.462 (C-8).

CHN:

calc.	C:	72.10	H:	5.81	N:	6.73
anal.	C:	71.99	H:	5.76	N:	6.80

HRMS (ESI): m/z calculated for C14H21NNa: 439.1634 found: 439.1635

18. N-benzyl-3-methylpent-4-enamide



In a 100 mL round-bottomed flask 3-methylpent-4-enoic acid (2 g, 17.52 mmol) was dissolved in DCM (50 mL) to give a colorless solution. CDI (2.84 g, 17.52 mmol) was added portion wise, with heavy evervesance. After the CO_2 development ceased benzylamine (2.039 ml, 18.66 mmol) was added. This solution was stirred for 1 hour.

The reaction mixture was washed with water (3 X 30 mL), dried over $MgOS_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (2:1) to yield a white solid.

Yield: 2.80g (13.77 mmol, 79%)

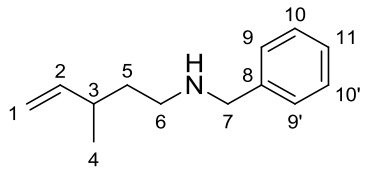
^{1}H NMR (400 MHz, CDCl3): δ = 0.99 (d, *J* = 6.77 Hz, 3H, H-4), 2.13 (ddd, *J* = 38.14, 14.06, 7.25 Hz, 2H, H-5), 2.65 (td, *J* = 13.96, 6.98, 6.98 Hz, 1H, H-3), 4.35 (d, *J* = 5.69 Hz, 2H, H-7), 4.93 (tdd, *J* = 23.88, 10.32, 1.31, 1.31 Hz, 2H, H-1), 5.70 (ddd, *J* = 17.28, 10.34, 7.01 Hz, 1H, H-2), 5.82 (s, 1H, N-H), 7.30-7.14 (m, 5H, H-9, 9', 10, 10', 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 171.64 (C-6), 142.78 (C-2), 138.33 (C-8/11), 128.68 (C-9/9' or 10/10') 127.84 (C-9/9' or 10/10'), 127.49 (C-8/11), 113.59 (C-1), 43.80 (C-7), 43.58 (C-5), 34.85 (C-3), 19.75 (C-4).

CHN:

calc.	C:	76.81	H:	8.43	N:	6.89
anal.	C:	76.82	H:	8.53	N:	6.84

19. N-benzyl-3-methylpent-4-en-1-amine



In a 250 mL round-bottomed flask LAH (0.747 g, 19.68 mmol) was added to dry THF (50 mL) to give a grey suspension at 0°C. N-benzyl-3-methylpent-4-enamide (2.0 g, 9.84 mmol) was dissolved in dry THF (50 mL) and added drop wise over 10 minutes at 0°C, let warm to RT and refluxed overnight.

The reaction was diluted with diethyl ether, hydrolyzed with 0.7 mL H_2O, 0.7 mL 20% NaOH, and 2.4 mL H_2O at 0°C. Then some MgSO4 was added, and the mixture stirred for 15 minutes. The mixture was filtered over a silica plug, and purified by chromatography with pentane : diethyl ether (5:1) to yield product as a clear oil.

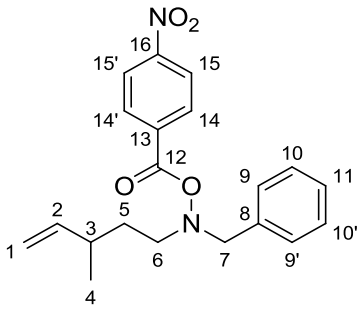
Yield: 0.935g (4.94 mmol, 50%)

^{1}H NMR (400 MHz, CDCl3): δ = 0.92 (d, J = 6.75 Hz, 3H, H-4), 1.44 (dd, *J* = 14.68, 7.17 Hz, 3H, N-H, H-5), 2.14 (td, *J* = 13.99, 6.98, 6.98 Hz, 1H, H-3), 2. 51-2. 60 (m, 2H, H-6), 3.70 (s, 2H, H-7), 4.79-4.92 (m, 2H, H-1), 5.55-5.68 (m, 1H, H-2), 7.12-7.29 (m, 5H, H-9, -9', 10, 10', 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 144.36 (C-2), 140.43 (C-8), 128.40(C-10, 10'), 128.15(C-9, 9'), 126.91(C-11), 112.79(C-1), 54.12(C-6), 47.46(C-7), 36.77(C-5), 36.04(C-3), 20.41(C-4).

NMR data agrees with data from [47].

20. N-benzyl-N-(3-methylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



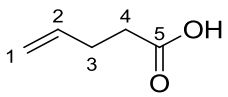
Prepared in accordance with general procedure i.

Yield: 1.72g (4.13 mmol, 91%)

^{1}H NMR (400 MHz, CDCl3): δ = 0.92 (d, *J* = 6.76 Hz, 3H, H-4), 1.46-1.63 (m, 2H, H-5), 2.14-2.28 (m, 1H, H-3), 2.92-3.07 (m, 2H, H-6), 4.03-4.17 (m, 2H, H-7), 4.85 (t, *J* = 13.33, 13.33 Hz, 2H, H-1), 5.52-5.61 (m, 2H, H-2), 7.14-7.33 (m, 5H, H-9,9',10,10',11) ,8.07 (dd, *J* = 76.25, 8.93 Hz, 4H, H-14,14',15,15').

^{13}C-NMR (100 MHz, CDCl3): δ = 163.37 (C-12), 150.47 (C-16), 143.66 (C-2), 135.43 (C-13), 134.71 (C-8), 130.46 129.49 128.34 127.86 123.54 (C-9, 9', 10, 10', 11, 14, 14', 15, 15'), 63.83 (C-7), 57.04 (C-6), 35.87 (C-3), 33.45 (C-5), 20.4 (C-4).

21. Pent-4-enoic acid



In a 250 mL round-bottomed flask allyl alcohol (20 g, 344 mmol), trimethyl orthoacetate (62.1 g, 517 mmol), and p-toluenesulfonic acid monohydrate (0.33 g, 1.73 mmol) were combined to give a brown solution. This was slowly heated to 140°C over 4 hours, and held there for 2 hours. After no more distillate was observed, the reaction was cooled to RT.

At this point MeOH (100 mL) and NaOH (27.5 g, 689 mmol) were added, and the mixture was heated to reflux for 12 hours, then let cool to RT.

The reaction mixture was acidified with conc. HCl, the phases separated, and the aq. phase extracted with DCM (3 X 50 mL), dried over $MgSO_4$, solvent removed via rotary evaporation, and the crude product distilled via 10 cm vigrou column, to yield a clear liquid.

bp: 85°C @ 100mbar.

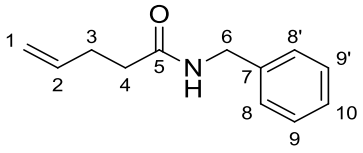
Yield: 13.16g (131 mmol, 38% over 2 steps)

^{1}H NMR (400 MHz, CDCl3): δ = 2.37 – 2.43 (m, 2H, H-3), 2.47 – 2.51 (C-4), 5.03 – 5.13 (m, 2H, H-1), 5.85 (tdd, *J* = 16.41, 10.25, 6.24, 1H, H-2) 11.7 (s, 1H, COOH).

^{13}C-NMR (100 MHz, CDCl3): δ = 28.5 (C-4), 33.5 (C-3), 115.7 (C-1), 136.3 (C-2), 179.7 (C-5).

NMR data agrees with data from [52].

22. N-benzylpent-4-enamide



In a 100 mL round-bottomed flask pent-4-enoic acid (2 g, 19.98 mmol) was dissolved in DCM (50 mL) to give a colorless solution. CDI (3.24 g, 19.98 mmol) was added portion wise, with heavy evervesance. When the CO_2 development had ceased, benzylamine (2.2 mL, 20.0 mmol) was added. The reaction mixture was stirred at room temperature for one hour.

The reaction mixture was washed with water (3 X 30 mL), dried over $MgOS_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (2:1) to yield a white solid.

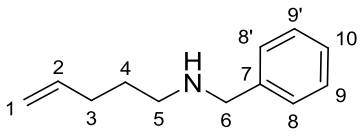
Yield: 2.85g (15.06 mmol, 75%)

^{1}H NMR (400 MHz, CDCl3): δ = 2.18 – 2.27 (m, 2H, H-3), 2.31 - 2.39 (m, 2H, H-4), 4.35 (d, *J* = 5.71 Hz, 2H, H-6), 4.96 (dddd, *J* = 10.06, 3.82, 2.90, 1.37 Hz, 2H, H-1), 5.75 (tdd, *J* = 16.81, 10.21, 6.44, 6.44 Hz, 1H, H-2), 5.84 (s, 1H, N-H), 7.13 – 7.32 (m, 5H, 8, 8’, 9, 9’, 10).

^{13}C-NMR (100 MHz, CDCl3): δ = 172.14 (C-5), 138.32 (C-7), 137.01 (C-2), 128.70 (C-9/9’) 127.83 (C-8/8’), 127.51 (C-10), 115.67 (C-1), 43.59 (C-6), 35.84 (C-4), 29.63 (C-3).

NMR data agrees with data from [53].

23. N-benzylpent-4-en-1-amine



In a 250 mL round-bottomed flask LAH (1.143 g, 30.1 mmol) was suspended in dry THF (60 mL), at 0°C, to give a grey suspension. N-benzylpent-4-enamide (2.85 g, 15.06 mmol) dissolved in THF (40 mL) was added drop wise, at 0°C. The mixture was heated to reflux until TLC indicated amide conversion to the amine was complete.

Reaction mixture was cooled in an ice bath, and hydrolyzed with 1.2 mL water, 1.2 mL 20% NaOH, 3.6 mL water, and stirred for 15 min. A small amount of $MgSO_4$ was added to the mixture and stirred for an additional 15 min. The reaction mixture was then filtered over a silica plug, and the solvent removed, yielding the product as a clear liquid.

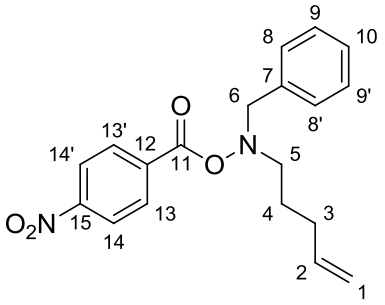
Yield: 2.50g (14.26 mmol, 95%)

^{1}H NMR (400 MHz, CDCl3): δ = 1.44 (s, 1H, N-H), 1.53 (td, *J* = 14.72, 7.38, 7.38 Hz, 2H, H-4), 2.02 (dd, *J* = 14.75, 6.87 Hz, 2H, H-3), 2.52-2.61 (m, 2H, H-5), 3.70 (s, 2H, H-6), 4.90 (dddd, *J* = 10.20, 4.22, 3.28, 1.43 Hz, 2H, H-1), 5.73 (tdd, *J* = 16.92, 10.18, 6.66, 6.66 Hz, 1H, H-1), 7.12-7.29 (m, 5H, H-8, 8', 9, 9', 10).

^{13}C-NMR (100 MHz, CDCl3): δ = 140.51 (C-7), 138.52 (C-2), 128.40 (C-9/9') 128.13 (C-8/8'), 126.91 (C-10), 114.66 (C-1), 54.058 (C-5), 48.92 (C-6), 31.58 (C-3), 29.63 (C-4).

NMR data agrees with data from [54].

24. N-benzyl-O-(4-nitrobenzoyl)-N-(pent-4-en-1-yl)hydroxylamine



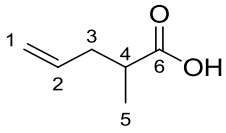
Prepared in accordance with general procedure i.

Yield: 3.50g (10.28 mmol, 71%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.64 (m, 2H, H-4), 2.08 (q, *J* = 7.14, 7.14, 7.08 Hz, 2H, H-3), 2.93 - 3.05 (m, 2H, H-5), 4.11 (s, 2H, H-6), 4.82 - 4.97 (m, 2H, H-1), 5.69 (tdd, *J* = 16.92, 10.19, 6.67, 6.67 Hz, 1H, H-2), 7.13-7.35 (m, 5H, H-8, 8’, 9, 9’, 10), 8.06 (dd, *J* = 72.74, 8.92 Hz, 4H, H-13, 13’, 14, 14’).

^{13}C-NMR (100 MHz, CDCl3): δ = 140.51 (C-7), 138.52 (C-2), 128.40 (C-9/9’) 128.13 (C-8/8’), 126.91 (C-10), 114.66 (C-1), 54.058 (C-5), 48.92 (C-6), 31.58 (C-3), 29.63 (C-4).

25. 2-methylpent-4-enoic acid



In a 25 mL microwave glass equipped with heating element and stir bar allyl alcohol (4.0 g, 68.9 mmol), triethyl orthopropionate (14.57 g, 83 mmol), and p-toluenesulfonic acid monohydrate (0.131 g, 0.689 mmol) were mixed to give a brown solution. This was heated to 165°C, max 15 bar, for 2 hours.

Dissolved reaction mixture in 100 mL MeOH, added NaOH (5.51 g, 138 mmol) and heated to reflux overnight. Cooled to RT, acidified with conc. HCl, separated phases and extracted aq. phase with t-BME (3 X 50 mL). Dried combined org. phases over $MgSO_4$, removed solvent via rotary evaporation, and cleaned product via distillation.

bp: 110°C @ 50 mbar

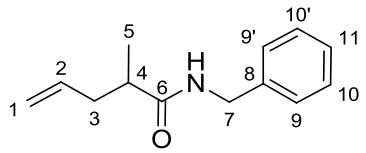
Yield: 2.06g (18.05 mmol, 26%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.19 (d, *J* = 6.95 Hz, 3H, H-5), 2.21 (td, *J* = 14.16, 7.14, 7.14 Hz, 1H, H-3), 2.45 (td, *J* = 13.64, 6.73, 6.73 Hz, 1H, H-3),2.50-2.62 (m, 1H, H-4), 5.17-4.99 (m, 2H, H-1), 5.77 (tdd, *J* = 17.09, 10.15, 7.00, 7.00 Hz, 1H, H-2), 11.66 (s, 1H, COOH).

^{13}C-NMR (100 MHz, CDCl3): δ = 16.3 (C-5), 37.5 (C-4), 39.1 (C-3), 117.2 (C-1), 135.4 (C-2), 182.2 (C-6).

NMR data agrees with data from [55].

26. N-benzyl-2-methylpent-4-enamide



In a 100 mL round-bottomed flask 2-methylpent-4-enoic acid (3.63 g, 31.8 mmol) was dissolved in DCM (50 mL) to give a colorless solution. CDI (5.16 g, 31.8 mmol) was added portion wise, with heavy evervesance. When the CO_2 development had ceased, benzylamine (3.82 mL, 35 mmol) was added. The reaction mixture was stirred at RT for one hour.

The reaction mixture was washed with water (3 X 30 mL), dried over $MgOS_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (2:1) to yield a white solid.

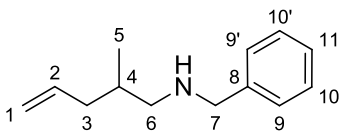
Yield: 2.94g (14.48 mmol, 46%)

^{1}H NMR (400 MHz, CDCl3): δ = 1.07-1.11 (m, 3H, H-5), 2.08 (td, *J* = 13.62, 6.85, 6.85 Hz, 1H, H-3), 2.17-2.27 (m, 1H, H-4), 2.34 (td, *J* = 13.85, 7.03, 7.03 Hz, 1H, H-3), 4.26-4.40 (m, 2H, H-7), 4.91-5.03 (m, 2H, H-1), 5.67 (tdd, *J* = 17.13, 10.12, 7.01, 7.01 Hz, 1H, H-2), 5.95 (s, 1H, N-H), 7.14-7.30 (m, 5H, H-9, 9', 10, 10', 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.43 (C-5), 38.4 (C-3), 41.2 (C-4), 43.4 (C-7), 116.9 (C-1), 127.43 (C-11), 127.77 (C-10, 10'), 128.66 (C-9, 9'), 135.85 (C-2), 138.46 (C-8), 175.71 (C-6).

NMR data agrees with data from [56].

27. N-benzyl-2-methylpent-4-en-1-amine



In a 250 mL round-bottomed flask LAH (1.624 g, 42.8 mmol) was added to THF (70 mL) to give a grey suspension, and cooled to 0°C. N-benzyl-2-methylpent-4-enamide (2.90 g, 14.27 mmol), dissolved in ca. THF (30 mL) was added drop wise. The reaction mixture was heated to reflux overnight.

Cooled to 0°C, added 1.6 mL water, 1.6 mL NaOH, 4.8 mL water, stirred for 30 min, added some $MgSO_4$, stirred for 30 min, filtered over silica plug. The raw product NMR shows slight THF impurities, used substance without further purification in next step.

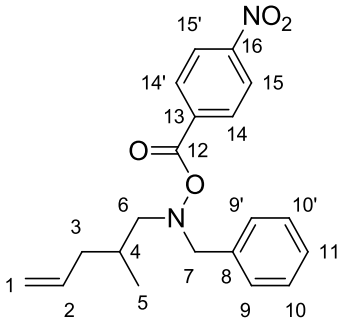
Yield: 2.65g (14.00 mmol, 98%)

^{1}H NMR (400 MHz, CDCl3): δ = 0.79 (d, *J* = 6.70 Hz, 3H, H-5), 1.57-162 (m, 1H, H-3), 1.75-1.89 (m, 1H, H-4, N-H), 1.99-2.06 (m, 1H, H-3), 2.37 (ddd, *J* = 50.90, 11.65, 6.64 Hz, 2H, H-6) , 3.56-3.72 (m, 2H, H-7), 4.80-4.96 (m, 2H, H-1), 5.60-5.70 (m, 1H, H-2),7.09-7.22 (m, 5H, H-9. 9'. 10, 10', 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.43 (C-5), 33.15 (C-4), 39.42 (C-3), 54.1 (C-6), 55.39 (C-7), 115.91 (C-1), 126.9 (C-11), 128.1 (C-9, 9', 10, 10'), 128.39 (C-9, 9', 10, 10'), 137.14 (C-2), 140.52 (C-8).

NMR data agrees with data from [57].

28. N-benzyl-N-(2-methylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



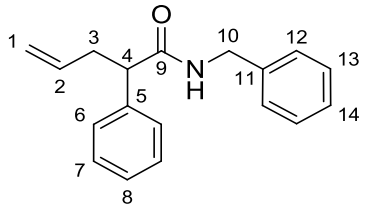
Prepared in accordance with general procedure i.

Yield: 3.66g (10.32 mmol, 71%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 0.91 (d, *J* = 6.70 Hz, 3H, H-5), 1.63-1.76 (m, 1H, H-3), 1.82-1.94 (m, 1H, H-3), 2.13-2.31 (m, 2H, H-4), 2.69 – 2.89 (m, 2H, H-6), 4.11 (s, 2H, H-7), 4.85-4.98 (m, 2H, H-1), 5.65 (tdd, *J* = 17.27, 10.37, 7.18 Hz, 1H, H-2), 7.16 – 7-35 (m, 5H, H-9, 10, 11), 8.08 (dd, *J* = 73.22, 8.95 Hz, 2H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.86 (C-5), 31.24 (C-4), 38.94 (C-3), 64.03 (C-6), 64.19 (C-7), 116.35 (C-1), 123.5, 127.79, 128.35, 129.39, 130.42 (C-9, 9', 10, 10', 11, 14, 14', 15, 15'), 134.82, 135.56, 136.46 (C-2,8,13), 150.42 (C-16), 163.13 (C-12).

29. N-benzyl-2-phenylpent-4-enamide



In a 100 mL round-bottomed flask 2-phenylpent-4-enoic acid (2.44 g, 13.85 mmol) was dissolved in DCM (50 mL) to give a colorless solution. CDI (2.25 g, 13.85 mmol) was added portion wise, with heavy evervesance. When the CO_2 development had ceased, benzylamine (1.664 ml, 15.23 mmol) was added. The reaction mixture was stirred at RT for one hour.

The reaction mixture was washed with water (3 X 30 mL), dried over $MgOS_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (1:1) to yield a white solid.

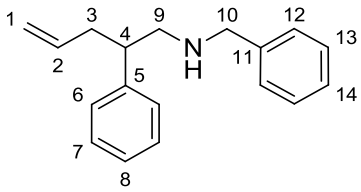
Yield: 2.56g (9.65 mmol, 70%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 2.78 (tdd, *J* = 7.45, 14.50, 163.49 Hz, 2H, H-3), 3.45 – 3.53 (m, 1H, H-4), 4.34 – 4.49 (m, 2H, H-10), 4.99 – 5.11 (m, 2H, H-1), 5.70 – 5.80 (m, 2H, H-2, N), 7.16 – 7.38 (m, 10H, H-6, 7, 8, 12, 13, 14).

^{13}C-NMR (100 MHz, CDCl3): δ = 37.3 (C-3), 43.5 (C-4), 53.2 (C-10), 116.8 (C-1), 127.3, 127.5, 127.9, 128.6, 128.8 (C-6, 7, 8, 12, 13, 14), 135.8 (C-2), 138.2 (C-5), 139.3 (C-11).

NMR data agrees with data from [58].

30. N-benzyl-2-phenylpent-4-en-1-amine



In a 250 mL round-bottomed flask LAH (1.373 g, 36.2 mmol) was suspended in THF (100mL and cooled to 0°C. N-benzyl-2-phenylpent-4-enamide (2.4 g, 9.04 mmol) dissolved in 30 mL THF was added drop wise, after which the reaction mixture was heated to reflux for 12 hours.

Cooled to 0°C, added 1.4 mL water, 1.4 mL of 20% NaOH, 4.1 mL of water, and some $MgSO_4$. Filtered over a silica plug, then chromatographed over silica gel with pentane : diethyl ether (1:1) to yield a clear oil.

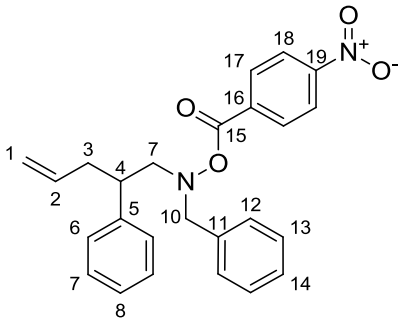
Yield: 0.81g (3.20 mmol, 35%)

^{1}H NMR (400 MHz, CDCl3): δ = 1.76 – 2.01 (m, 2H, H-4, N-H), 2.24 – 2.38 (m, 2H, H-3), 2.81-2.89 (m, 2H, H-9), 3.67 (q, *J* = 13.42, 13.42, 13.42 Hz, 2H, H-10), 4.84-4.97 (m, 2H, H-1), 5.59 (tdd, *J* = 17.05, 10.12, 7.01, Hz, 1H, H-2), 7.10-7.25 (m, 10H, H-6, 7, 8, 12, 13, 14).

^{13}C-NMR (100 MHz, CDCl3): δ = 39.0 (C-3), 45.7 (C-4), 53.6 (C-10), 54.1 (C-9), 116.2 (C-1), 126.6, 126.9 (C-8, 14), 127.8, 128.1, 128.4, 128.6 (C-6, 7, 12, 13), 136.5 (C-2), 139.8 (C-11), 143.1 (C-5).

NMR data agrees with data from [59].

31. N-benzyl-O-(4-nitrobenzoyl)-N-(2-phenylpent-4-en-1-yl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 0.633g (1.52 mmol, 48%)

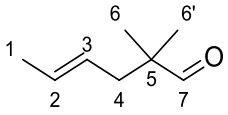
^{1}H NMR (400 MHz, *CDCl3*): δ = 2.49 (dtd, *J* = 22.05, 14.40, 14.14, 7.56 Hz, 2H, H-3), 2.98 (qd, *J* = 13.25, 6.66, 6.59, 6.59 Hz, 1H, H-4), 3.29 (d, *J* = 6.72 Hz, 2H, H-7), 4.16 (s, 2H, H-10), 4.86 – 4.96 (m, 2H, H-1), 5.59 (tdd, *J* = 17.09, 10.14, 7.07, 7.07 Hz, 1H, H-1), 6.99 – 7.40 (m, 10H, H-6, 7, 8, 12, 13, 14), 7.81 (d, *J* = 8.87 Hz, 2H, H-17/18), 8.16 (d, *J* = 8.90 Hz, 2H, H-17/18).

^{13}C-NMR (100 MHz, CDCl3): δ = 38.8 (C-3), 44.2 (C-4), 63.0 (C-7), 64.0 (C-10), 116.7 (C-1), 123.3 (Ar-H), 126.3 (Ar-H), 127.7 (Ar-H), 127.9 (Ar-H), 128.4 (Ar-H), 128.4 (Ar-H), 129.6 (Ar-H),130.4 (Ar-H), 134.5 (C-5/11), 135.2 (C-5/11), 136.1 (C-2), 143.1 (C-16), 150.3 (C-19), 163.0 (C-15).

CHN:

calc.	C:	72.10	H:	5.81	N:	6.73
anal.	C:	72.22	H:	5.78	N:	6.96

32. (E)-2,2-dimethylhex-4-enal



In a 250 mL round-bottomed flask equipped with reflux condenser and dean stark trap but-3-en-2-ol (20 g, 277 mmol), isobutyraldehyde (30 g, 416 mmol), and p-toluenesulfonic acid monohydrate (0,1 g, 0,526 mmol) were dissolved in toluene (75 mL), and refluxed overnight. When no more water separated from the reaction, the toluene was distilled off, and the product distilled under vacuum.

Bp.: 135°C, 70 mbar

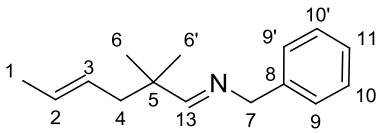
Yield: 21.46g (170 mmol, 61%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 0.96 (s, 6H, H-6, 6'), 1.58 (ddd, *J* = 6.41, 2.48, 1.11 Hz, 3H, H-1), 2.03-2.11 (m, 2H, H-4), 5.21-5.29 (m, 1H, H-3), 5.37-5.46 (m, 1H, H-2), 9.40 (s, 1H, H-7).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.92 (C-1), 21.13 (C-6, 6'), 40.33 (C-4), 45.97 (C-5), 125.44 (C-2), 129.04 (C-3), 206.35 (C-7).

NMR data agrees with data from [60].

33. (E)-N-((E)-2,2-dimethylhex-4-en-1-ylidene)-1-phenylmethanamine



In a 250 mL round-bottomed flask (E)-2,2-dimethylhex-4-enal (5 g, 39.6 mmol), p-toluenesulfonic acid monohydrate (0.1 g, 0.526 mmol), and $MgSO_4$ (2.385 g, 19.81 mmol) in DCM (75 mL) to give a white suspension, cooled to 0°C. Benzylamine (4.25 g, 39.6 mmol) in DCM (25 mL) was added. Let stir at RT over 72 hours.

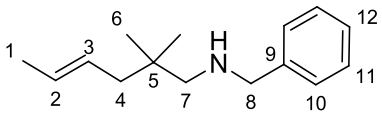
Removed $MgSO_4$ via filtration, and DCM via rotary evaporation.

Yield: 7.9g, (36.7 mmol, 93%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.00 (s, 6H, H-6, 6'), 1.56-1.59 (m, 3H, H-1), 2.05 (d, *J* = 6.07 Hz, 2H, H-4), 4.51 (s, 2H, H-7), 5.28-5.42 (m, 2H, H-2, 3), 7.12-7.36 (m, 5H, H-9, 9', 10, 10', 11), 7.55 (s, 1H, H-13).

^{13}C-NMR (100 MHz, CDCl3): δ = 18.0 (C-1), 24.6 (C-6, 6'), 39.5 (C-5), 43.6 (C-4), 64.7 (C-7), 126.7 (C-2), 127.0 (C-11), 127.7 (C-9/10), 128.02 (C-3), 128.3 (C-9/10), 139.6 (C-8), 172.2 (C-13).

34. (E)-N-benzyl-2,2-dimethylhex-4-en-1-amine



In a 250 mL round-bottomed flask (E)-N-((E)-2,2-dimethylhex-4-en-1-ylidene)-1-phenylmethanamine (3 g, 13.93 mmol) was dissolved in MeOH (100 mL) to give a colorless solution, and cooled to 0°C. $NaBH_4$ (0.3 g, 7.93 mmol) was added. The reaction mixture was let warm to RT and stirred overnight.

Hydrolyzed with 50 mL 20 % NaOH, stirred for 30 minutes, then added 100 mL diethyl ether, and separated phases. Extracted aq. phase with DCM (3 X 100 mL), washed org. phase with sat. NaCl solution (3 X 50 mL), dried over $MgSO_4$, removed solvent via rotary evaporator.

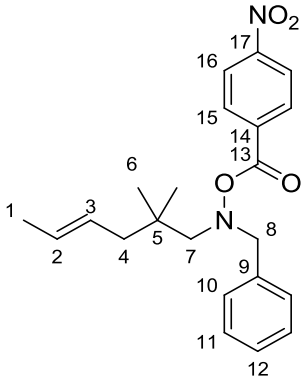
Yield: 2.01g, (9.25 mmol, 66%)

^{1}H NMR (400 MHz, *CDCl3*): δ =0,80 (s, 6H, H-6), 1.55 (d, J = 4.45, 3H, H-1), 1.85 (d, J = 5.11, 2H, H-4), 2.28 (s, 2H, H-7), 2.48 (s, 1H, N-H), 3.76 (s, 2H, H-8), 5.29 – 5.33 (m, 2H, H-2, 3), 7.15 – 7.28 (m, 5H, H-10, 11, 12).

^{13}C-NMR (100 MHz, CDCl3): δ =18.0 (C-1), 25.6 (C-6), 34.4 (C-4), 43.2 (C-5), 54.4 (C-7), 59.2 (C-8), 126.9 (C-2), 127.3 (C-12), 127.7 (C-3), 128.2 (C-10/11), 128.3 (C-10/11), 140.3 (C-9).

NMR data agrees with data from [61].

35. (E)-N-benzyl-N-(2,2-dimethylhex-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



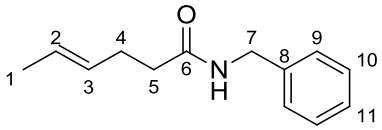
Prepared in accordance with general procedure i.

Yield: 1.35g (3.53 mmol, 77%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 0.75 (s, 6H, H-6), 1.5 (d, *J* = 5.05 Hz, 3H, H-1), 1.8 (d, *J* = 6.27 Hz, 2H, H-4), 2.74 (s, 2H, H-7), 4.08 (s, 2H, H-8), 5.11 – 5.26 (m, 2H, H-2, 3), 7.21 – 7.37 (m, 5H, H-10, 11, 12), 8.12 (dd, *J* = 61.73, 8.93, 4H, H-15, 16).

^{13}C-NMR (100 MHz, CDCl3): δ = 18.0 (C-1), 25.9 (C-6), 34.7 (C-5), 43.5 (C-4), 65.3 (C-7), 66.9 (C-8), 123.6, 127.2, 127.8, 127.9, 130.4, 135.1, 135.5 (C-2, 3, 9, 10, 11, 12, 14, 15, 16), 150.5 (C-17), 163.1 (C-13).

36. (E)-N-benzylhex-4-enamide



In a 100 mL round-bottomed flask (E)-hex-4-enoic acid (1.8 g, 15.77 mmol) was dissolved in DCM (50mL) to give a colorless solution. CDI (2.56 g, 15.77 mmol) was added portion wise, with heavy evervesance. When the CO_2 development had ceased, benzylamine (2.067 mL, 18.92 mmol) was added. The reaction mixture was stirred at RT for one hour.

The reaction mixture was washed with water (3 X 30 mL), dried over $MgOS_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (4:1) to yield a white solid.

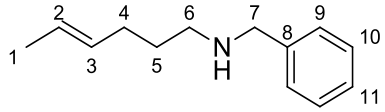
Yield: 1.68g (8.26 mmol, 52%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.53 – 1.56 (m, 3H, H-1), 2.15 – 2.27 (m, 4H, H-4, 5), 4.3 (d, *J* = 5.7 Hz, 2H, H-7), 5.29 – 5.44 (m, 2H, H-2, 3), 5.99 (s, 1H, N-H), 7.16 – 7.26 (m, H-9, 10, 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.9 (C-1), 28.6 (C-4), 36.5 (C-5), 43.5 (C-7), 126.4, 127.4, 127,8, 128.7, 129.5 (C-2, 3, 9, 10, 11), 138.4 (C-8), 172.5 (C-6).

NMR data agrees with data from [62].

37. (E)-N-benzylhex-4-en-1-amine



In a 250 mL round-bottomed flask LAH (0.629 g, 16.57 mmol) was suspended in THF (75 mL) to give a grey suspension, and cooled to 0°C. (E)-N-benzylhex-4-enamide (1.684 g, 8.28 mmol) dissolved in THF (50 mL) was added drop wise, and then the reaction mixture heated to reflux overnight.

The reaction was cooled to 0°C, and hydrolyzed by the addition of 0.63 mL water, 0.63 mL of 20% NaOH, and 1.89 mL water. It was then dried with some $MgSO_4$, filtered over a silica plug, and used without further purification.

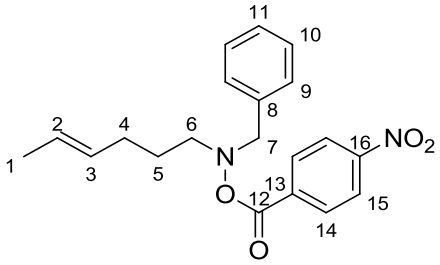
Yield: 0.62g (3.13 mmol, 38%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.46 – 1.57 (m, 6H, H-1, 5, N), 1.92 – 1.97 (m, 2H, H-4), 2.6 (t, *J* = 7.28 Hz, 2H, H-6), 3.71 (s, 2H, H-7), 5.33 – 5.36 (m, 2H, H-2, 3), 7.15 – 7.27 (m, 5H, H-9, 10, 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.9 (C-1), 29.8 (C-5), 30.4 (C-4), 48.9 (C-6), 54.0 (C-7), 125.2, 126.9, 128.2, 128.7, 130.9, 140.4 (C-2, 3, 8, 9, 10, 11).

NMR data agrees with data from [63].

38. (E)-N-benzyl-N-(hex-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



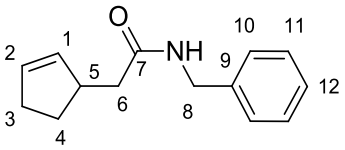
Prepared in accordance with general procedure i.

Yield: 0.74 g (2.09 mmol, 66%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.53 – 1.63 (m, 5H, H-1, 5), 1.97 – 2.02 (m, 2H, H-4), 2.96 – 2.99 (m, 2H, H-6), 4.11 (s, 2H, H-7), 5.30 – 5.32 (m, 2H, H-2, 3), 7.19 – 7.33 (m, 5H, H-9, 10, 11), 8.08 (dd, *J* = 75.65, 8.92, 4H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.9 (C-1), 26.8 (C-5), 29.9 (C-4), 58.2 (C-6), 63.8 (C-7), 123.5, 125.8, 127.9, 128.4, 129.5, 130.2, 130.5, 134.8, 135.5 (C-2, 3, 8, 9, 10, 11, 13, 14, 15), 150.5 (C-16), 163.4 (C-12).

39. N-benzyl-2-(cyclopent-2-en-1-yl)acetamide



In a 250 mL round-bottomed flask 2-(cyclopent-2-en-1-yl)acetic acid (3 g, 23.78 mmol) and CDI (3.86 g, 23.78 mmol) in were dissolved in DCM (50 mL) to give a colorless solution. After the completion of CO_2 evolution, benzylamine (2.86 ml, 26.2 mmol) was added. This reaction mixture was stirred for one hour at RT.

The reaction mixture was washed with water (3 X 30 mL), dried over $MgOS_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (4:1) to yield a white solid.

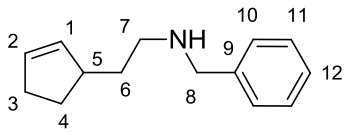
Yield: 3.32g (15.42 mmol, 65%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.40 (tdd, *J* = 6.32, 8.77, 12.8 Hz, 1H, H-5), 2.02 – 2.29 (m, 5H, H-3, 4, 6), 3.04 – 3.12 (m, 1H, H-3, 4, 6), 4.38 (d, *J* = 5.41, 2H, H-8), 5.59 – 5.62 (m, 1H, H-2), 5.68 – 5.71 (m, 1H, H-1), 5.82 (s, 1H, N-H), 7.19 – 7.29 (m, 5H, H-10, 11, 12).

^{13}C-NMR (100 MHz, CDCl3): δ = 29.6 (C-4), 31.9 (C-3), 42.6 (C-5), 42.8 (C-6), 43.6 (C-8), 127.5 (C-12), 127.8 (C-10/11), 128.7 (C-10/11), 131.6 (C-2), 133.8 (C-1), 138.3 (C-9), 172.2 (C-7).

NMR data agrees with data from [64].

40. N-benzyl-2-(cyclopent-2-en-1-yl)ethanamine



In a 250 mL round-bottomed flask LAH (0.353 g, 9.29 mmol) was suspended in dry diethyl ether (50 mL) to give a grey suspension, which was cooled to 0°C. To this suspension was added drop wise N-benzyl-2-(cyclopent-2-en-1-yl)acetamide (2 g, 9.29 mmol) dissolved in Diethyl ether (50 mL). The reaction mixture was then refluxed overnight.

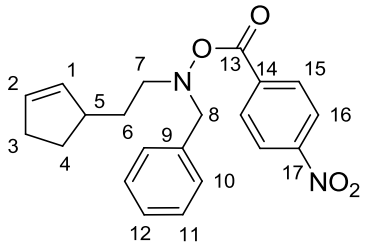
The reaction was hydrolyzed by the addition of 0.35 mL water, then 0.35 mL 20% NaOH, and finally 1.05 mL water. This was stirred till the suspension turned a fluffy white, at which point some $MgSO_4$ was added and stirred for an additional hour. The crude product was purified over a silica gel slug and solvent removed under reduced pressure.

Yield: 1.52g (7.55 mmol, 81%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.29 – 1.48 (m, 3H), 1.52 – 1.60 (m, 1H) 1.92 – 2.00 (m, 1H), 2.14 – 2.31 (m, 2H), 2.53 – 2.67 (m, 3H), 3.72 (s, 2H, H-8).

^{13}C-NMR (100 MHz, CDCl3): δ = 29.9 (C-4), 31.9 (C-3), 36.4 (C-6), 43.5 (C-5), 48.1 (C-7), 54.1 (C-8), 126.9 (C-12), 128.1 (C-10/11), 128.4 (C-10/11), 130.5 (C-2), 134.9 (C-1), 140.4 (C-9).
NMR data agrees with data from [64].

41. N-benzyl-N-(2-(cyclopent-2-en-1-yl)ethyl)-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 2.17g (5.92 mmol, 78%)

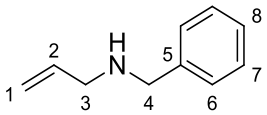
^{1}H NMR (400 MHz, *CDCl3*): δ = 1.39 (tdd, *J* = 12.94, 8.96, 6.54, 6.54 1H, H-4), 1.54 – 1.84 (m, 2H, H-6), 2.18 – 2.40 (m, 1H, H-4), 1.95 – 2.12 (m, 2H, H-3), 2.76 (dp, *J* = 8.40, 8.40, 8.40, 8.35, 2.21 Hz, 1H, H-5) 3.04 – 3.18 (m, 2h, H-7), 4.20 (s, 2H, H-8), 5.63 (ddd, *J* = 5.81, 4.06, 1.98 Hz, 1H, H-1), 5.72 (dt, *J* = 4.35, 4.35, 2.13 Hz, 1H, H-2), 7.36 – 7.46 (m, 2H, H-10/11/12), 7.21 – 7.35 (m, 3H, H-10/11/12), 8.05 (d, *J* = 8.82, 2H, H-15/16), 8.24 (d, *J* = 8.82, 2H, H-15/16).

^{13}C-NMR (100 MHz, CDCl3): δ = 29.7 (C-4), 31.9 (C-3), 32.9 (C-6), 43.3 (C-5), 57.4 (C-7), 63.7 (C-8), 123.5 (C-15/16), 127.9 (C-12), 128.4 & 129.5 (C-10, 11), 130.5 (C-15/16), 130.9 (C-2), 134.2 (C-1), 134.7 (C-9), 135.5 (C-14), 150.4 (C-17), 163.3 (C-13).

CHN:

calc.	C:	68.84	H:	6.05	N:	7,65
anal.	C:	68.55	H:	6.10	N:	7.64

42. N-benzylprop-2-en-1-amine



In a 100 mL round-bottomed flask allylamine (0.707 mL, 9.42 mmol) and benzaldehyde (0.955 mL, 9.42 mmol) were dissolved in DCM (40 ml) to give a colorless solution and cooled to 0°C. Sodium triacetoxyborohydride (3.00 g, 14.13 mmol) was added portionwise, and the reaction mixture stirred overnight.

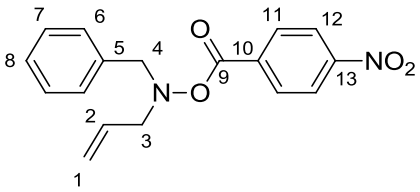
The reaction was quenched by addition of 20% NaOH, stirred for 30 min, sep. phases, extracted aq. phase with DCM (3 X 20 mL), dried over $MgSO_4$, filtered, took up on silica gel. chromatographed 3:1.

Yield: 0.90 g (6.09 mmol, 65%)

^{1}H NMR (400 MHz, CDCl3) δ = 1.67 (s, 1H, N-H), 3.28 (td, *J* = 5.98, 1.38, 1.38 Hz, 2H, H-3), 3.80 (s, 2H, H-4), 5.07 – 5.26 (m, 2H, H-1), 5.94 (tdd, *J* = 16.25, 10.25, 5.97, 5.97 Hz, 1H, H-2), 7.23 – 7.35 (m, 5H, H-6, 7, 8).

^{13}C-NMR (100 MHz, CDCl3): δ = 51.7 (C-3), 53.3 (C-4), 116.1 (C-1), 126.9 (C-8), 128.2, 128.4 (C-6, 7), 136.7 (C-2), 140.2 (C-5).
NMR data agrees with data from [65].

43. N-allyl-N-benzyl-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 1.38 g (4.42 mmol, 75%)

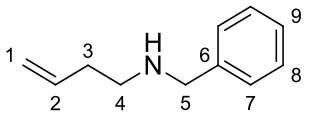
^{1}H NMR (400 MHz, *CDCl3*): δ = 3.73 (d, *J* = 6.57 Hz, 2H, H-3), 4.21 (s, 2H, H-4), 5.17 – 5.34 (m, 2H, H-1), 6.05 (tdd, *J* = 16.89, 10.20, 6.61, 6.61 Hz, 1H, H-2), 7.21 – 7.35 (m, 3H, H-6, 7, 8), 7.36 – 7.46 (m, 2H, H-6, 7, 8), 7.99 – 8.07 (m, 2H, H-11, 12), 8.17 – 8.28 (m, 2H, H-11, 12).

^{13}C-NMR (100 MHz, CDCl3): δ = 61.7 (C-3), 62.8 (C-4), 119.9 (C-1), 123.5 (C-11/12), 127.9 (C-8), 128.4, 129.4 (C-6, 7) 130.4 (C-11/12), 132.4 (C-2), 134.7, 135.3 (C-5, 10), 150.4 (C-13), 163.2 (C-9).

CHN:

calc.	C:	65.38	H:	5.16	N:	8.97
anal.	C:	64.79	H:	5.08	N:	8.94

44. N-benzylbut-3-en-1-amine



In a 25 mL round-bottomed flask benzylamine (2.43 mL, 22.22 mmol) was heated to 90°C. To this was added 4-bromo-1-butene (0.752 mL, 7.41 mmol) drop wise, and stirred for three hours.

The reaction mixture was cooled to RT, diluted with diethylether and washed with water (3 X 25 mL). The raw product was purified via distillation over a vigreux column.

bp: 105°C @ 7 mbar

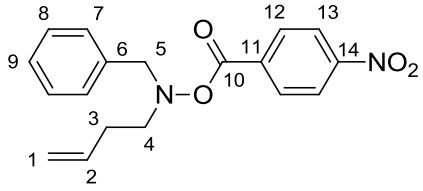
Yield: 0.79 g (4.90 mmol, 66%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 2.28 (q, *J* = 6.86, 6.83, 6.83 Hz, 2H, H-3), 2.70 (t, *J* = 6.83 Hz, 2H, H-4), 3.79 (s, 2H, H-5), 4.99 – 5.13 (m, 2H, H-1), 5.78 (tdd, *J* = 17.07, 10.18, 6.85, 6.85 Hz, 1H, H-2), 7.21 – 7.34 (m, 5H, H-7, 8, 9).

^{13}C-NMR (100 MHz, CDCl3): δ = 34.3 (C-3), 48.3 (C-4), 53.9 (C-5), 116.3 (C-1), 126.9 (C-9), 128.1, 128.4 (C-7, 8), 136.5 (C-2), 140.4 (C-6).

NMR data agrees with data from [66].

45. N-benzyl-N-(but-3-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



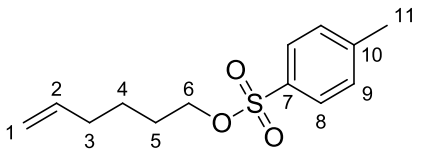
Prepared in accordance with general procedure i.

Yield: 0.36 g (1.36 mmol, 52%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 2.40 (dd, *J* = 14.54, 6.98 Hz, 2H, H-3), 3.09 – 3.20 (m, 2H, H-4), 4.21 (s, 2H, H-5), 5.03 (ddd, *J* = 13.68, 11.68, 1.52 Hz, 2H, H-1), 5.83 (tdd, *J* = 17.00, 10.21, 6.73, 6.73 Hz, 1H, H-2), 7.22 – 7.34 (m, 3H, H-7, 8, 9), 7.36 – 7.46 (m, 2H, H-7, 8, 9), 8.04 – 8.07 (m, 2H, H-12, 13), 8.23 – 8.26 (m, 2H, H-12, 13).

^{13}C-NMR (100 MHz, CDCl3): δ = 31.5 (C-3), 58.0 (C-4), 63.8 (C-5), 116.4 (C-1), 123.5 (C-11/12), 127.9 (C-9), 128.4, 129.5 (C-8, 7), 130.5 (C-11/12), 134.7 (C-11), 135.2 (C-6), 135.3 (C-2), 150.5 (C-14), 163.3 (C-10).

46. Hex-5-en-1-yl 4-methylbenzenesulfonate



In a 50 mL round-bottomed flask hex-5-en-1-ol (1.0 g, 9.98 mmol) and p-toluenesulfonyl chloride (2.86 g, 14.98 mmol) were dissolved in pyridine (25 mL) at 0°C to give a yellow solution, which was then stirred overnight at RT.

The reaction mixture was poured onto ice cold conc. HCl (100 mL) and extracted with diethyl ether (3 X 50 mL), dried over $MgSO_4$, and taken up on silica gel. The crude product was chromatographed with pentane : diethyl ether (5:1) to yield a white solid.

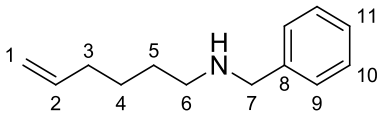
Yield: 0.77g (3.04 mmol, 30%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.37 – 1.45 (m, 2H, H-5), 1.62 – 1.67 (m, 2H, H-4), 1.98 – 2.03 (m, 2H, H-3), 2.45 (s, 3H, H-11), 4.03 (t, *J* = 6.45 Hz, 2H, H-6), 4.93 – 4.98 (m, 2H, H-1), 5.72 (tdd, *J* = 16.97, 10.24, 6.67, 6.67 Hz, 1H, H-2), 7.35 (d, *J* = 7.97 Hz, 2H, H-8, 9), 7.79 (d, *J* = 8.31 Hz, 2H, H-8, 9).

^{13}C-NMR (100 MHz, CDCl3): δ = 21.6 (C-11), 24.5 (C-4), 28.2 (C-5), 32.9 (C-3), 70.4 (C-6), 115.1 (C-1), 127.9, 129.8 (C-8, 9), 133.2 (C-2), 137.9 (C-10), 144.7 (C-7).

NMR data agrees with data from [67].

47. N-benzylhex-5-en-1-amine



In a 50 mL round-bottomed flask hex-5-en-1-yl 4-methylbenzenesulfonate (0.772g, 3.04 mmol) was dissolved in benzylamine (16.58 mL, 152 mmol) to give a colorless solution. This reaction mixture was stirred at reflux overnight.

The excess benzylamine was removed via distillation, and the semisolid crude product dissolved in DCM. This was washed with water (3 X 50 mL), dried over $MgSO_4$, taken up on silica gel, and chromatographed with pentane : diethyl ether 3:1, 0:1, to yield a clear liquid.

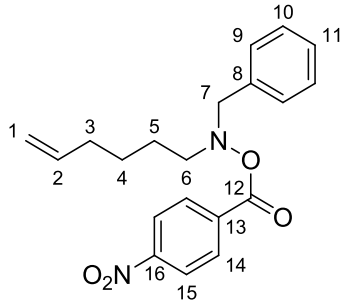
Yield: 0.42g (2.21 mmol, 73%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.21 (s, 1H, N-H), 1.37-1.65 (m, 4H, H-4, 5), 2.05 (dd, *J* = 14.18, 7.05 Hz, 2H, H-3), 2.58 – 2.68 (m, 2H, H-6), 3.78 (s, 2H, H-7), 4.90 – 5.04 (m, 2H, H-1), 5.80 (tdd, *J* = 16.91, 10.16, 6.67, 6.67 Hz, 1H, H-2), 7.20 – 7.28 (m, 1H, H-9, 10, 11), 7.30 – 7.34 (m, 4H, H-9, 10, 11).

^{13}C-NMR (100 MHz, CDCl3): δ = 26.7 (C-4), 29.6 (C-5), 33.7 (C-3), 49.3 (C-7), 54.1 (C-6), 114.4 (C-1), 126.9 (C-11), 128.1, 128.4 (C-9, 10), 138.8 (C-2), 140.6 (C-8).

NMR data agrees with data from [65].

48. N-benzyl-N-(hex-5-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine



Prepared in accordance with general procedure i.

Yield: 0.56 g (1.59 mmol, 77%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.45 – 1.52 (m, 2H, H-4), 1.56 – 1.67 (m, 2H, H-5), 2.04 (dd, *J* = 14.33, 7.04 Hz, 2H, H-3), 3.01 – 3.12 (m, 2H, H-6), 4.19 (s, 2H, H-7), 4.87 – 5.01 (m, 2H, H-1), 5.76 (tdd, *J* = 16.92, 10.17, 6.66, 6.66 Hz, 1H, H-2), 7.22 – 7.34 (m, 3H, H-9, 10, 11), 7.36 – 7.46 (m, 2H, H-9, 10, 11), 8.00 – 8.10 (m, 2H, H-14, 15), 8.19 – 8.29 (m, 2H, H-14, 15).

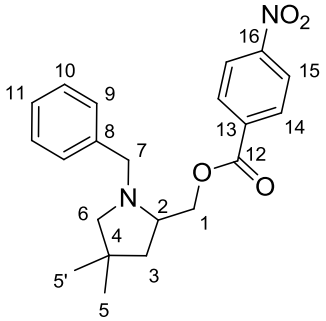
^{13}C-NMR (100 MHz, CDCl3): δ = 26.31, 26.34 (C-4, 5), 33.4 (C-3), 58.5 (C-6), 63.7 (C-7), 114.7 (C-1), 123.5 (C-14/15), 127.9 (C-11), 128.4, 129.5 (C-9, 10), 130.4 (C-14, 15), 134.7 (C-8), 135.4 (C-13), 138.4 (C-2), 150.5 (C-16), 163.3 (C-12).

CHN:

calc.	C:	67.78	H:	6.26	N:	7.90
anal.	C:	67.41	H:	6.18	N:	7.96

4. Cyclisation of Hydroxylamines

    1. (1-Benzyl-4,4-dimethylpyrrolidin-2yl)methyl 4-nitrobenzoate



Prepared in accordance with general procedure ii & iv.

Yield: 0.106 g (0.288 mmol, 73%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.04 (s, 3H, H-5/5'), 1.11 (s, 3H, H-5/5'), 1.60 (dd, *J* = 12.79, 6.99 Hz, 1H, H-3), 1.88 (dd, *J* = 12.84, 8.89 Hz, 1H, H-1), 2.13 (d, *J* = 9.08 Hz, 1H, H-6), 2.69 (d, *J* = 9.06 Hz, 1H, H-6), 3.08 (tdd, *J* = 8.93, 6.90, 5.33, 5.33 Hz, 1H, H-2), 3.41 (d, *J* = 13.39 Hz, 1H, H-7), 4.15 (d, *J* = 13.39, 1H, H-7), 4.37 – 4.47 (m, 2H, H-1), 7.17 – 7.35 (m, 5H, H-9, 10, 11), 8.19 (d, *J* = 8.97 Hz, 2H, H-14, 15), 8.27 (d, *J* = 8.95, 2H, H-14, 15).

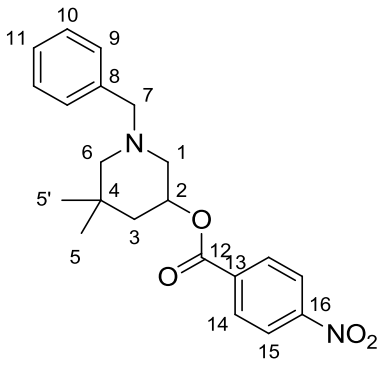
^{13}C-NMR (100 MHz, CDCl3): δ = 28.3 (C-5), 29.6 (C-5'), 36.6 (C-4), 43.8 (C-3), 59.2 (C-7), 62.7 (C-2), 68.0 (C-6), 68.3 (C-1), 123.6 (C-14/15), 126.8 (C-11), 128.2, 128.4 (C-9, 10), 130.7 (C-14/15), 135.8 (C-8), 139.8 (C-13), 150.5 (C-16), 164.7 (C-12).

CHN:

calc.	C:	68.46	H:	6.57	N:	7.60
anal.	C:	68.31	H:	6.57	N:	7.61

HRMS (ESI): m/z calculated for $C_{21}H_{24}N_2NaO_4^+$: 391.1628; found: 391.1627

2. 1-benzyl-5,5-dimethylpiperidin-3-yl 4-nitrobenzoate



Prepared in accordance with general procedure iii & v.

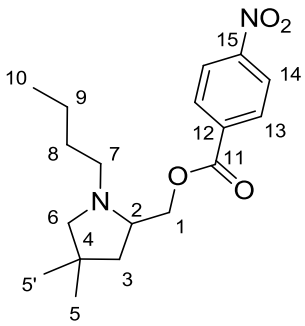
Yield: 0.218 g (0.059 mmol, 15%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.00 (s, 3H, H-5), 1.10 (s, 3H, H-5'), 1.38 (dd, *J* = 12.40, 9.74 Hz, 1H, H-3), 1.85 (dd, *J* = 12.63, 4.50 Hz, 1H, H-3), 1.94 (d, *J* = 11.02 Hz, 1H, H-7), 2.20 (t, *J* = 9.51, 9.51 Hz, 1H, H-1), 2.34 (d, *J* = 11.04 Hz, 1H, H-7), 3.02 (dd, *J* = 10.13, 3.21 Hz, 1H, H-1), 3.55 (q, *J* = 13.49, 13.49, 13.49 Hz, 2H, H-6), 5.29 (qd, *J* = 13.63, 4.48, 4.48, 4.48 Hz, 1H, H-2), 7.19 – 7.39 (m, 5H, H-9, 10, 11), 8.18 (d, *J* = 8.77 Hz, 2H, H-14, 15), 8.27 (d, *J* = 9.01 Hz, 2H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ =26.3 (C-5), 29.0 (C-5'), 32.0 (C-4), 42.6 (C-3), 57.3 (C-6), 62.5 (C-7), 64.9 (C-1), 70.6 (C-2), 123.5 (C-14/15), 127.0 (C-11), 128.3, 128.6 (C-9, 10), 130.7 (C-14/15), 136.0 (C-8), 138.6 (C-13), 150.5 (C-16), 164.0 (C-12).

HRMS (ESI): m/z calculated for $C_{21}H_{24}N_2NaO_4^+$: 391.1628; found: 391.1627

3. (1-Butyl-4,4-dimethylpyrrolidin-2-yl)methyl 4-nitrobenzoate



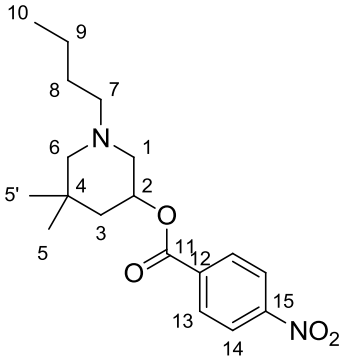
Prepared in accordance with general procedure ii & iv.

Yield: 0.125 g (0.374 mmol, 62%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 0.82 (t, *J* = 7.27, 7.27 Hz, 3H, H-10), 0.99 (s, 3H, H-5), 1.07 (s, 3H, H-5'), 1.13 – 1.42 (m, 4H, H-8, 9), 1.46 (dd, *J* = 12.76, 7.29 Hz, 1H, H-3), 1.75 (dd, *J* = 12.77, 8.60 Hz, 1H, H-3), 2.03 (d, *J* = 9.04 Hz, 1H, H-6), 2.16 – 2.27 (m, 1H, H-7), 2.72 – 2.91 (m, 3H, H-2, 6, 7), 4,29 (ddd, *J* = 17.06, 11.01, 5.55 Hz, 2H, H-1), 8.13 (d, *J* = 8.95 Hz, 2H, H-13/14), 8.22 (d, *J* = 8.94 Hz, 2H, H-13/14).

^{13}C-NMR (100 MHz, CDCl3): δ = 14.0 (C-10), 20.6 (C-9), 28.6, 29.7 (C-5, 5'), 30.9 (C-8), 36.6 (C-4), 43.7 (C-3), 55.2 (C-7), 63.1 (C-2), 67.9 (C-6), 68.6 (C-1), 123.5, 130.7 (C-13, 14), 135.8 (C-12), 150.5 (C-15), 164.6 (C-11).

4. 1-butyl-5,5-dimethylpiperidin-3-yl 4-nitrobenzoate



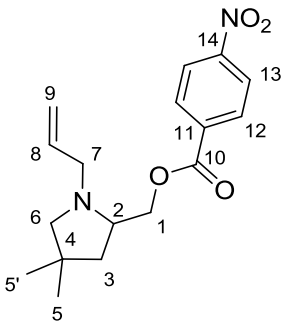
Prepared in accordance with general procedure iii & v.

Yield: 0.018 g (0.054 mmol, 9%)

^{1}H NMR (400 MHz, *CDCl3*): δ =0.7-2.7 (m, 15H, H-3,5,5',8,9,10), 2.7-3.1 (m, 4H, H-6,7), 4.2-4.4 (m, 1H, H-2), 5.0-5.2 (m, 2H, H-1), 8.0-8.3 (m, 4H, H-13, 14).

^{13}C-NMR (100 MHz, CDCl3): δ = 14.0 (C-10), 20.5 (C-9), 26.4 (C-8), 28.9 (C-4), 29.2, 31.9 (C-5, 5'), 42.6 (C-3), 57.5, 57.9 (C-6, 7), 62.0 (C-1), 70.8 (C-2), 123.5, 130.7 (C-13, 14), 135.9 (C-12), 150.5 (C-15), 164.0 (C-11).

5. (1-allyl-4,4-dimethylpyrrolidin-2-yl)methyl 4-nitrobenzoate



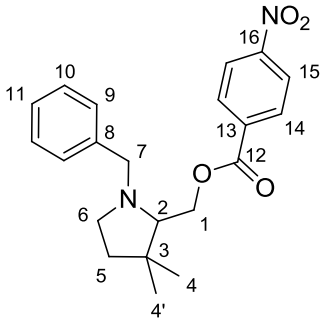
Prepared in accordance with general procedure ii & iv.

Yield: 0.100 g (0.314 mmol, 54%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.04 (s, 3H, H-5/5'), 1.11 (s, 3H, H-5/5'), 1.60 (dd, *J* = 12.79, 6.99 Hz, 1H, H-3), 1.88 (dd, *J* = 12.84, 8.89 Hz, 1H, H-1), 2.13 (d, *J* = 9.08 Hz, 1H, H-6), 2.89 (d, *J* = 9.06 Hz, 1H, H-6), 3.05 (tdd, *J* = 8.93, 6.90, 5.33, 5.33 Hz, 1H, H-2), 3.52 (d, *J* = 13.39 Hz, 1H, H-7), 4.30 (d, *J* = 13.39, 1H, H-7), 5,01 – 5.32 (m, 2H, H-9), 5.77 – 6.00 (m, 1H, H-8), 8.27 (d, *J* = 8.95, 2H, H-12, 13).

^{13}C-NMR (100 MHz, CDCl3): δ = 28.5 (C-5), 29.6 (C-5'), 36.5 (C-4), 43.9 (C-3), 58.1 (C-7), 62.2 (C-2), 68.0 (C-6), 68.5 (C-1), 116.7 (C-9), 123.6 (C-12/13), 130.7 (C-12/13), 136.0 (C-8), 150.5 (C-16), 164.7 (C-12).

6. (1-benzyl-3,3-dimethylpyrrolidin-2-yl)methyl 4-nitrobenzoate



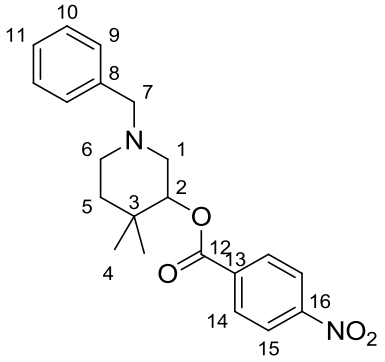
Prepared in accordance with general procedure ii & iv.

Yield: 0.09 g (0.244 mmol, 43%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.04 (s, 6H, H-4, 4'), 1.46 – 1.62 (m, 2H, H-5), 2.28 (dd, *J* = 17.22, 8.44 Hz, 1H, H-6), 2.59 (t, *J* = 5.39, 5.39 Hz, 1H, H-2), 2.86 (t, *J* = 10.16, 10.16 Hz, 1H, H-6), 3.43 (d, *J* = 13.39 Hz, 1H, H-7), 4.11 (d, *J* = 13.40 Hz, 1H, H-7), 4.36 (ddd, *J* = 40.01, 11.45, 5.59 Hz, 2H, H-1), 7.09 – 7.30 (m, 5H, H-9, 10, 11), 8.10 (d, *J* = 8.92 Hz, 2H, H-14, 15), 8.19 (d, *J* = 8.91 Hz, 2H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ =24.14 (C-4), 28.85 (C-4'), 39.4 (C-5), 40.6 (C-3), 51.4 (C-6), 59.9 (C-7), 66.8 (C-1), 71.1 (C-2), 123.6 (C-14/15), 126.9 (C-11), 128.3, 128.5 (C- 9, 10), 130.7 (C-14/15), 135.7 (C-8), 139.7 (C-13), 150.5 (C-16), 164.6 (C-12).

7. 1-benzyl-4,4-dimethylpiperidin-3-yl 4-nitrobenzoate



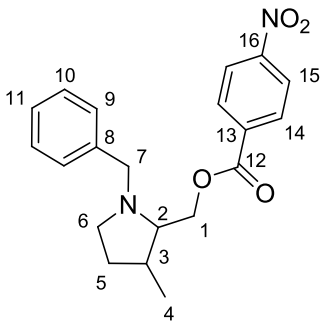
Prepared in accordance with general procedure iii & v.

Yield: 0.029 g (0.079 mmol, 15%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.05 (s, 6H, H-4), 1.47 – 1.62 (m, 2H, H-5), 2.30 (d, J = 8.04 Hz, 1H, H-6), 2.60 (s, 1H, H-2), 2.88 (s, 1H, H-6), 3.45 (d, J = 13.10 Hz, 1H, H-7), 4.12 (d, J = 13.38 Hz, 1H, H-7), 4.26 – 4.48 (m, 1H, H-1), 7.10 – 7.33 (m, 5H, H-9, 10, 11), 8.10 (d, J = 8.90 Hz, 2H, H-14, 15), 8.20 (d, J = 8.95 Hz, 2H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ = 24.1 (C-4/4’), 28.8 (C-4/4’), 39.4 (C-5), 40.5 (C-3), 51.3 (C-6), 59.8 (C-7), 66.7 (C-1), 71.1 (C-2), 123.6 (C-14/15), 126.9 (C-11), 128.2, 128.5 (C-9, 10), 130.6 (C-14/15), 135.6 (C-13), 139.6 (C-8), 150.5 (C-16), 164.6 (C-12).

8. (1-benzyl-3-methylpyrrolidin-2-yl)methyl 4-nitrobenzoate



Prepared in accordance with general procedure ii & iv.

Yield: 0.07 g (0.198 mmol, 50%)

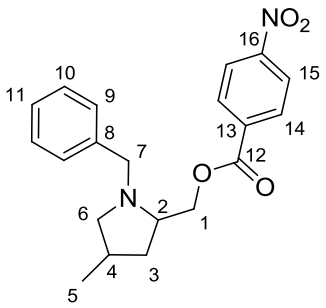
^{1}H NMR (400 MHz, *CDCl3*): δ =1.03 (d, *J* = 6.89 Hz, 3H, H-4), 1.23 – 1.35 (m, 1H, H-5), 1.88 – 1.98 (m, 1H, H-5), 2.03 – 2.12 (m, 1H, H-3), 2.31 (dd, *J* = 16.95, 9.18 Hz, 1H, H-6), 2.44 (dd, *J* = 11.18, 5.11 Hz, 1H, H-2), 2.80 – 2.88 (m, 1H, H-6), 3.37 (d, *J* = 13.10 Hz, 1H, H-7), 4.08 (d, *J* = 13.10 Hz, 1H, H-7), 4.36 (ddd, *J* = 36.15, 11.39, 5.07 Hz, 2H, H-1), 7.10 – 7.29 (m, 5H, H-9, 10, 11), 8.09 – 8.13 (m, 2H, H-14, 15), 8.18 – 8.21 (m, 2H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ = 20.0 (C-4), 31.3 (C-5), 36.3 (C-3), 52.6 (C-6), 59.6 (C-7), 67.3 (C- 1), 70.3 (C-2), 123.5 (C-14/15), 126.9 (C-11), 128.2, 128.6 (C-9, 10), 130.6 (C-14/15), 135.6 (C-13), 139.4 (C-8), 150.4 (C-16), 164.6 (C-12).

The erythro/threo mixture could not be separated, and the ^{1}H signals were covered and not able to be analyzed. Following are the isolable ^{13}C signals.

^{13}C-NMR (100 MHz, CDCl3): δ = 17.9 (C-4), 32.8 (C-5), 35.3 (C-3), 52.9 (C-6), 59.7 (C-7), 123.4 (C-14/15), 127.1 (C-11), 128.5 (C-9, 10), 130.57 (C-14/15), 135.7 (C-13), 164.5 (C-12).

9. (1-benzyl-4-methylpyrrolidin-2-yl)methyl 4-nitrobenzoate



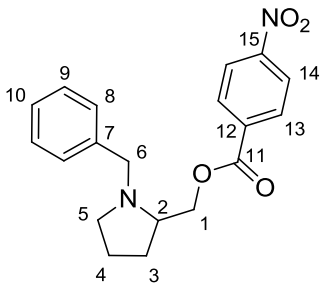
Prepared in accordance with general procedure ii & iv.

Yield: 0.079 g (0.223 mmol, 48%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 0.96 (d, *J* = 6.57 Hz, 3H, H-5), 1.21 – 1.42 (m, 1H, H-3), 2.04 – 2.28 (m, 2H, H-3, 4), 2.39 – 2.61 (m, 2H, H-6), 2.90 – 3.06 (m, 1H, H-2), 3.39 (d, *J* = 13.36, 1H, H-7), 4.02 (d, *J* = 13.39 Hz, 1H, H-7), 4.33 (d, *J* = 5.35 Hz, 2H, H-1), 7.05 – 7.36 (m, 5H, H-9, 10, 11), 8.08 – 8.13 (m, 2H, H-14, 15), 8.18 – 8.20 (m, 2H, H-14, 15).

^{13}C-NMR (100 MHz, CDCl3): δ = 20.6 (C-5), 30.6 (C-4), 37.6 (C-3), 59.3 (C-7), 61.3(C-6), 63.0 (C-2), 68.2 (C-1), 123.4 (C-14/15), 126.8 (C-11), 128.2, 128.4 (C-9, 10), 128.6 (C-13), 130.6 (C-14/15), 135.6 (C-8), 150.4 (C-16), 164.5 (C-12).

10. (1-benzylpyrrolidin-2-yl)methyl 4-nitrobenzoate



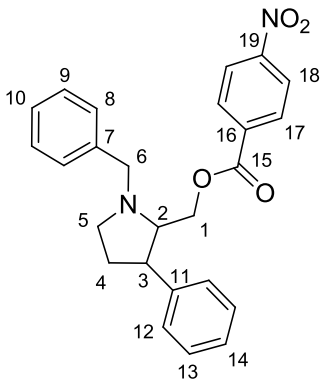
Prepared in accordance with general procedure ii & iv.

Yield: 0.132 g (0.388 mmol, 51%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.65 – 1.75 (m, 3H, H-3, 4), 1.92 – 2.00 (1H, H-3), 2.21 – 2.27 (1H, H-5), 2.87 – 2.96 (2H, H-2, 5), 3.42 (d, *J* = 13.1 Hz, 1H, H-6), 4.03 (d, *J* = 13.1 Hz, 1H, H-6), 4.27 (d, *J* = 5.52 Hz, 2H, H-1), 7.13 – 7.26 (m, 5H, H-8, 9, 10), 8.10 (d, *J* = 8.95 Hz, 2H, H-13, 14), 8.19 (d, *J* = 8.94 Hz, 2H, H-13, 14).

^{13}C-NMR (100 MHz, CDCl3): δ =23.2 (C-4), 28.6 (C-3), 54.5 (C-5), 59.5 (C-6), 62.0 (C-2), 68.3 (C-1), 123.6 (C-13/14), 127.0 (C-10), 128.3, 128.7 (C-8, 9), 130.7 (C-13/14), 135.7 (C-7), 139.3 (C-12), 150.5 (C-15), 164.7 (C-11).

11. (1-benzyl-3-phenylpyrrolidin-2-yl)methyl 4-nitrobenzoate



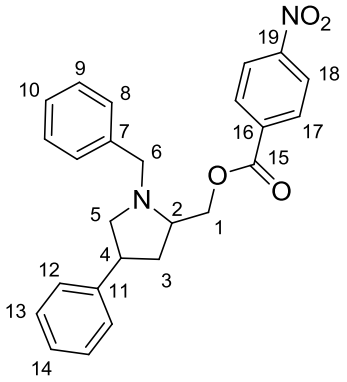
Prepared in accordance with general procedure ii & iv.

Yield: 0.032 g (0.077 mmol, 28%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.79 – 1.87 (m, 1H, H-4), 2.19 – 2.28 (m, 1H, H-4), 2.55 – 2.65 (m, 1H, H-5), 2.99 – 3.12 (m, 2H, H-2, 5), 3.19 (d, *J* = 7.45 Hz, 1H, H-3), 3.49 – 3.57 (m, 1H, H-6), 4.16 (d, *J* = 12.86 Hz, 1H, H-6), 4.38 – 4.47 (m, 2H, H-1), 7.13 – 7.31 (m, 10H, H-8, 9, 10, 12, 13, 14), 7.82 (d, *J* = 8.65 Hz, 2H, H-17, 18), 8.11 (d, *J* = 8.87 Hz, 2H, H-17, 18).

^{13}C-NMR (100 MHz, CDCl3): δ =32.5 (C-4), 49.2 (C-3), 53.6 (C-5), 59.0 (C-6), 66.7 (C-1), 70.2 (C-2), 123.4 (C-17/18), 126.5 (C-X), 127.1 (C-X), 127.8, 128.4, 128.7, 128.7 (C-8, 9, 12, 13), 130.7 (C-17/18), 135.4 (C-16), 139.2 (C-11), 144.0 (C-7), 150.4 (C-19), 164.5 (C-15).

12. (1-benzyl-4-phenylpyrrolidin-2-yl)methyl 4-nitrobenzoate



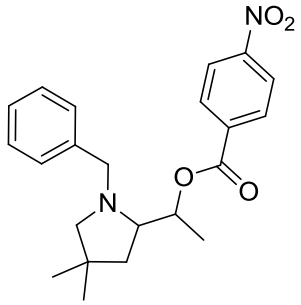
Prepared in accordance with general procedure ii & iv.

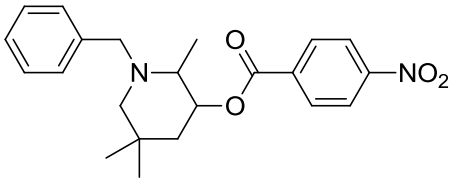
Yield: 0.047 g (0.113 mmol, 29%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.83 – 1.96 (m, 1H, H-3), 2.59 (ddd, *J* = 12.88, 8.56, 7.57 Hz, 1H, H-3), 2.80 (dd, *J* = 10.15, 8.18 Hz, 1H, H-5), 3.04 – 3.12 (m, 1H, H-5), 3.16 (ddd, *J* = 13.39, 8.68, 4.99 Hz, 1H, H-2), 3.31 (dq, *J* = 8.11, 8.10, 8.10, 4.98 Hz, 1H, H-4), 3.50 (d, *J* = 13.27 Hz, 1H, H-6), 4.20 (d, *J* = 13.27 Hz, 1H, H-6), 4.48 (ddd, *J* = 32.79, 11.28, 4.98 Hz, 2H, H-1), 7.11 – 7.43 (m, 10H, H-8, 9, 10, 12, 13, 14), 8.13 (d, *J* = 8.93 Hz, 2H, H-17, 18), 8.25 (d, *J* = 8.94 Hz, 2H, H-17, 18).

^{13}C-NMR (100 MHz, CDCl3): δ = 38.52 (C-3), 41.39 (C-4), 59.45 (C-6), 61.20 (C-5), 63.43 (C-2), 67.36 (C-1), 123.57 (C-17/18), 126.2, 127.0, 127.1, 128.3, 128.45, 128.51, 130.8 (C-8, 9, 10, 12, 13, 14), 135.6, 139.5, 145.7 (C-7, 11, 16), 150.5 (C-19), 164.6 (C-15).

13. 1-(1-benzyl-4,4-dimethylpyrrolidin-2-yl)ethyl 4-nitrobenzoate





Prepared in accordance with general procedure ii, iii, iv & v.

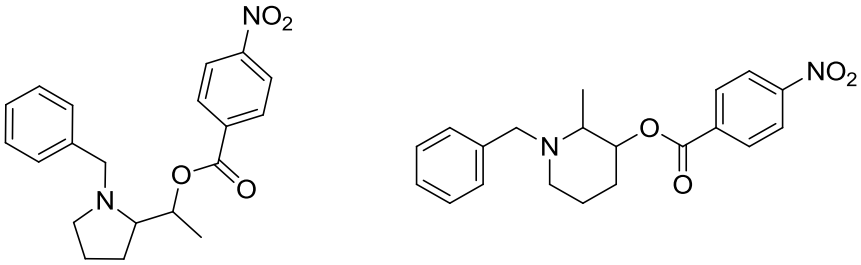
The individual products were not isolable. There is also no indication of a main product, but a mixture of erythro/threo product, and maybe 6 ring. Due to this problem the NMR spectrum peaks were not able to be correlated with specific atoms and are listed just as peaks.

Yield: 0.073 g (0.191 mmol, 73%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 0.83, 0.87, 0.94, 0.955, 0.963, 0.99, 1.00, 1.01, 1.06, 1.11, 1.14, 1.15, 1.18, 1.21, 1.305, 1.309, 1.321, 1.324, 1.54, 1.561, 1.565, 1.598, 1.91, 1.94, 2.26, 2.27, 2.29, 3.13, 3.17, 3.50, 3.53, 3.59, 3.62, 5.31, 5.32, 5.33, 5.34, 5.35, 5.36, 7.15 – 7.31 (m, Aromatic H), 8.03 – 8.23 (m, Aromatic H).

^{13}C-NMR (100 MHz, CDCl3): δ = 26.6, 26.9, 28.8, 29.0, 29.1, 31.2, 31.8, 36.6, 38.1, 55.4, 57.5, 58.5, 123.4, 123.5, 125.3, 126.6, 126.7, 126.9, 127.9, 128.09, 128.15, 128.19, 128.26, 128.36, 129.0, 130.5, 130.6, 130.7, 136.1, 139.6, 139.7, 150.4, 163.9.

14. 1-(1-benzylpyrrolidin-2-yl)ethyl 4-nitrobenzoate



Prepared in accordance with general procedure ii, iii, iv & v.

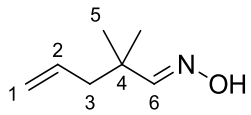
Yield: 0.031 g (0.088 mmol, 45%)

The individual products were not isolable. There is also no indication of a main product, but a mixture of erythro/threo product, and maybe 6 ring. Due to this problem the NMR spectrum peaks were not able to be correlated with specific atoms and are listed just as peaks.

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.33, 1.55 – 1.70, 1.75 – 1.95, 2.06 – 2.15, 2.66 – 2.80, 3.23, 4.14, 5.73, 7.10 – 7.30 (m, Aromatic H), 8.10 – 8.21 (m, Aromatic H).

^{13}C-NMR (100 MHz, CDCl3): δ = 16.8, 23.2, 25.9, 54.4, 59.2, 67.1, 72.1, 123.5, 126.8, 128.1, 128.6, 130.6, 136.4, 139.6, 150.4, 164.2.

5. Molecules for other attempts at oxyamination
    1. (E)-2,2-dimethylpent-4-enal oxime



Dissolved hydroxylamine hydrochloride (2.97 g, 42.8 mmol) in 4 mL of water and NaOH (1.07 g, 26.8 mmol) in 3 mL of water. Combined solutions in 13 mL EtOH. 2,2-dimethylpent-4-enal were dissolved in 75 mL EtOH and added to first solution. The mixture was let stand overnight.

The reaction was diluted with 50 mL water and 150 mL of t-BME. The phases separated, and the aq. phase extracted with t-BME (3 X 50 mL), dried over $MgSO_4$, solvent removed via rotary evaporation.

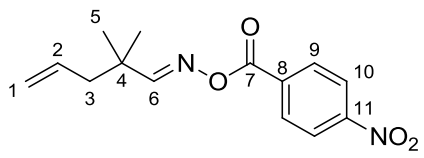
The crude product was distilled over a 10 cm vigreux column to yield a clear liquid, bp : 57°C,

Yield: 3.22 g (25.3 mmol, 71%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.02 (s, 6H, H-5), 2.09 (d, *J* = 7.37 Hz, 2H, H-3), 5.05-4.93 (m, 2H, H-1), 5.69 (tdd, *J* = 17.57, 10.26, 7.39, 7.39 Hz, 1H, H-2), 7.27 (s, 1H, H-6).

^{13}C-NMR (100 MHz, CDCl3): δ = 25.0 (C-5), 36.6 (C-3), 45.2 (C-4), 118.1 (C-1), 133.9 (C-2), 158.6 (C-6).

2. (E)-2,2-dimethylpent-4-enal O-(4-nitrobenzoyl) oxime



Dissolved (E)-2,2-dimethylpent-4-enal oxime (0.5 g, 3.93 mmol) and triethylamine (0.6 g, 5.9 mmol) in DCM (25 mL), cooled to 0°C. Added p-nitrobenzoyl chloride (0.802 g, 4.32 mmol) dissolved in DCM (20 mL) dropwise, maintaining T at 0°C. Let come to RT and stirred overnight.

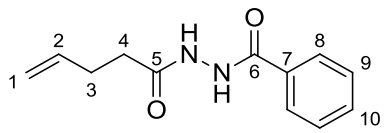
Quenched reaction with water (50 mL), separated phases, washed org. phase with water (3 X 25 mL), dried org. phase over $MgSO_4$, solvent removed via rotary evaporation, took up on silica gel, and chromatographed with pentane : diethyl ether 1:1, to yield a white solid.

Yield: 0.9g (3.26 mmol, 83%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.18 (s, 6H, H-5), 2.23 (d, *J* = 7.39 Hz, 2H, H-3), 4.99 – 5.12 (m, 2H, H-1), 5.75 (tdd, *J* = 17.57, 10.25, 7.41, 7.41 Hz, 1H, H-2), 7.76 (s, 1H, N-H), 8.17 (d, *J* = 8.88 Hz, 2H, H-9, 10), 8.24 (d, *J* = 8.86 Hz, 2H, H-9, 10).

^{13}C-NMR (100 MHz, CDCl3): δ = 24.7 (C-5), 37.8 (C-4), 44.8 (C-3), 118.8 (C-1), 123.6 (C-10), 130.7 (C-9), 133.1 (C-2), 134.4 (C-8), 150.6 (C-11), 162.2 (C-7), 167.2 (C-6).

3. N'-(pent-4-enoyl)benzohydrazide



Dissolved pent-4-enoic acid (2.73 g, 27.3 mmol) in 30 mL DCM. CDI (4.42 g, 27.3 mmol) was added portion wise, with heavy evervesance. After the CO_2 development ceased benzohydrazide was added. Let stir for 5 h.

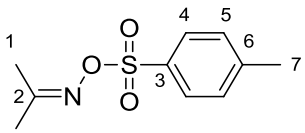
Added water (25 mL), separated phases, washed org. phase with water (3 X 25 mL), dried over $MgSO_4$, solvent removed via rotary evaporation, took up on silica gel, and chromatographed with pentane : ethylacetate 1:1, to yield a white solid.

Yield: 3.94 g (18.05 mmol, 66%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 2.23 – 2.38 (m, 4H, H-3, 4), 4.86 – 5.01 (m, 2H, H-1), 5.64 – 5.77 (m, 1H, H-2), 7.28 (t, *J* = 7.72, 7.72 Hz, 2H, H-8, 9, 10), 7.41 (t, *J* = 7.44, 7.41 Hz, 1H, H- 8, 9, 10), 7.71 – 7.80 (m, 2H, H-8, 9, 10), 9.85 (s, CNH), 10.13 (s, CNH).

^{13}C-NMR (100 MHz, CDCl3): δ =29.3 (C-3), 33.2 (C-4), 115.8 (C-1), 127.4, 128.6 (C-8, 9), 131.2 (C-10), 132.3 (C-8), 136.5 (C-2), 164.8 (C-5), 170.6 (C-6).

4. Propan-2-on-tosilate-oxime



In a 100 mL round-bottomed flask propan-2-one oxime (0.93 g, 12.72 mmol) was dissolved in DCM (50 ml) to give a colorless solution. Triethylamine (2.66 ml, 19.09 mmol) was added, and the solution was cooled to 0°C. P-toluenesulfonyl chloride (2.426 g, 12.72 mmol) dissolved in DCM (50 ml) was added dropwise over 30 min. This solution was stirred at 0°C for 3 h.

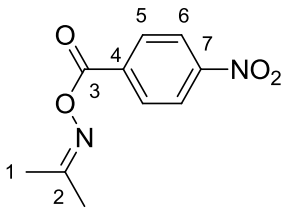
Quenched reaction with water (50 mL), separated phases, washed organic phase with water (3 X 50 mL), dried over $MgSO_4$, removed solvent via rotary evaporation, and took up on silica gel, purified via chromatography, pentane : diethylether 1:1, to obtain the pure product as a white solid.

Yield: 1.27 g (5.59 mmol, 44%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 1.85 (s, 3H, H-1), 1.90 (s, 3H, H-1’), 2.38 (s, 3H, H-7), 7.26 (d, *J* = 8.41 Hz, 2H, H-4, 5), 7.79 (d, *J* = 8.29 Hz, 2H, H-4, 5).

^{13}C-NMR (100 MHz, CDCl3): δ = 16.9 (C-1), 21.71 (C-1’, 7), 21.73 (C-1’, 7), 128.8 (C-4), 129.6 (C-5), 132.9 (C-6), 144.8 (C-3), 164.9 (C-2).

5. Propan-2-one O-(4-nitrobenzoyl) oxime



In a 100 mL round-bottomed flask propan-2-one oxime (1.0 g, 13.68 mmol) was dissolved in DCM (50 ml) to give a colorless solution. Triethylamine (2.86 ml, 20.52 mmol) was added, and the solution was cooled to 0°C. P-nitrobenzoyl chloride (2.539 g, 13.68 mmol) dissolved in DCM (50 ml) was added dropwise over 30 min. This solution was stirred at 0°C for 3 h.

Quenched reaction with water (50 mL), separated phases, washed organic phase with water (3 X 50 mL), dried over $MgSO_4$, removed solvent via rotary evaporation, and took up on silica gel, purified via chromatography, pentane : diethylether 1:1, to obtain the pure product as a white solid.

Yield: 2.61 g (11.75 mmol, 86%)

^{1}H NMR (400 MHz, *CDCl3*): δ = 2.17 (d, *J* = 1.82 Hz, 6H, H-1, 1‘), 8.25 (d, *J* = 8.95 Hz, 2H, H-5, 6), 8.33 (d, *J* = 8.94 Hz, 2H, H-5, 6).

^{13}C-NMR (100 MHz, CDCl3): δ = 17.3 (C-1), 22.1 (C-1’), 123.7 (C-5), 120.7 (C-6), 134.7 (C-4), 150.6 (C-7), 162.1 (C-2), 165.7 (C-3)

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Appendix

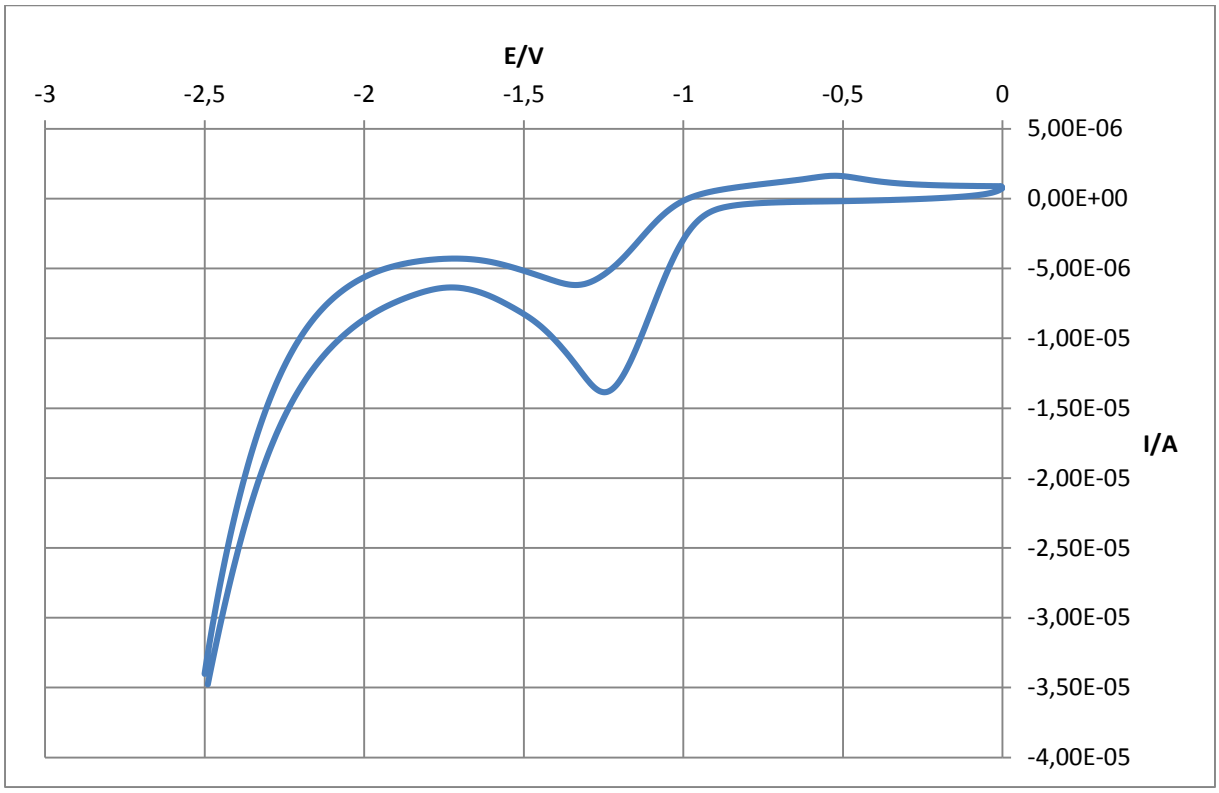

Figure A.1 Cyclovoltammogram of 1, *O*-acetyl-*N*,*N*-diethylhydroxylamine.

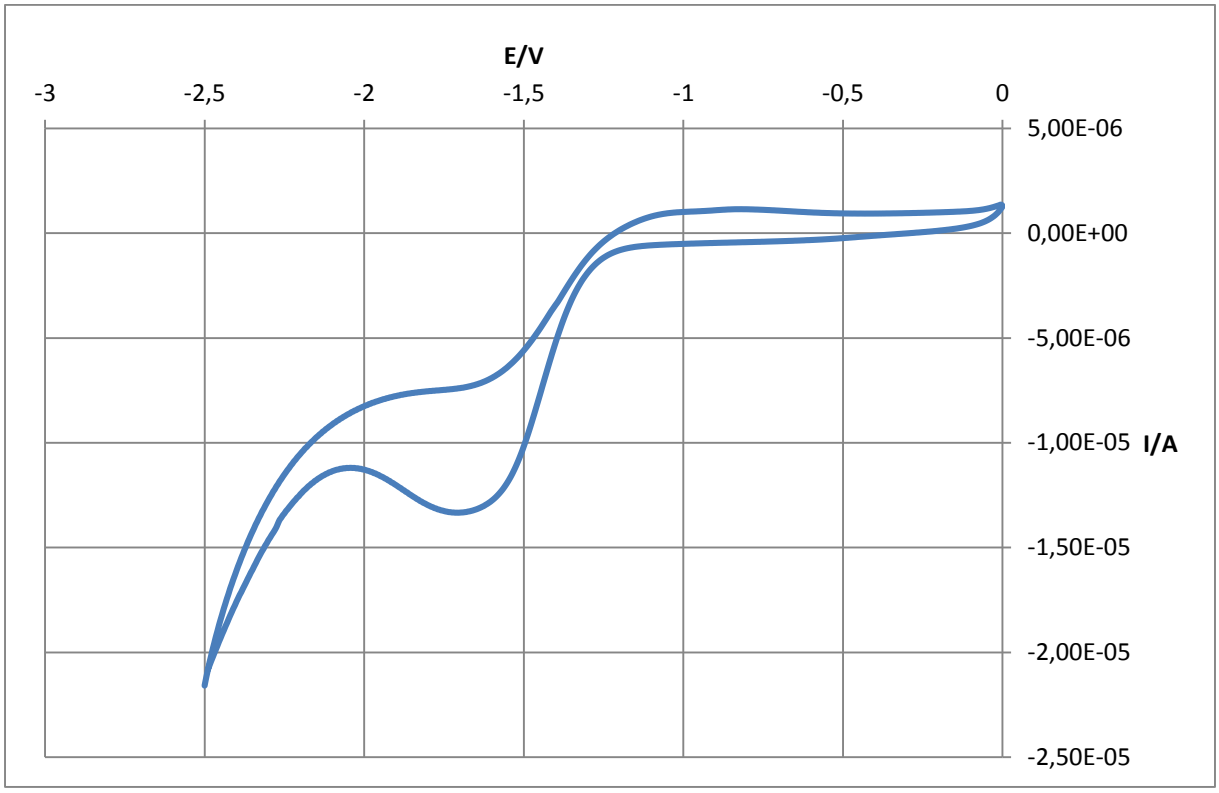

Figure A.2 Cyclovoltammogram of 2, *O*-benzoyl-*N*,*N*-diethylhydroxylamine

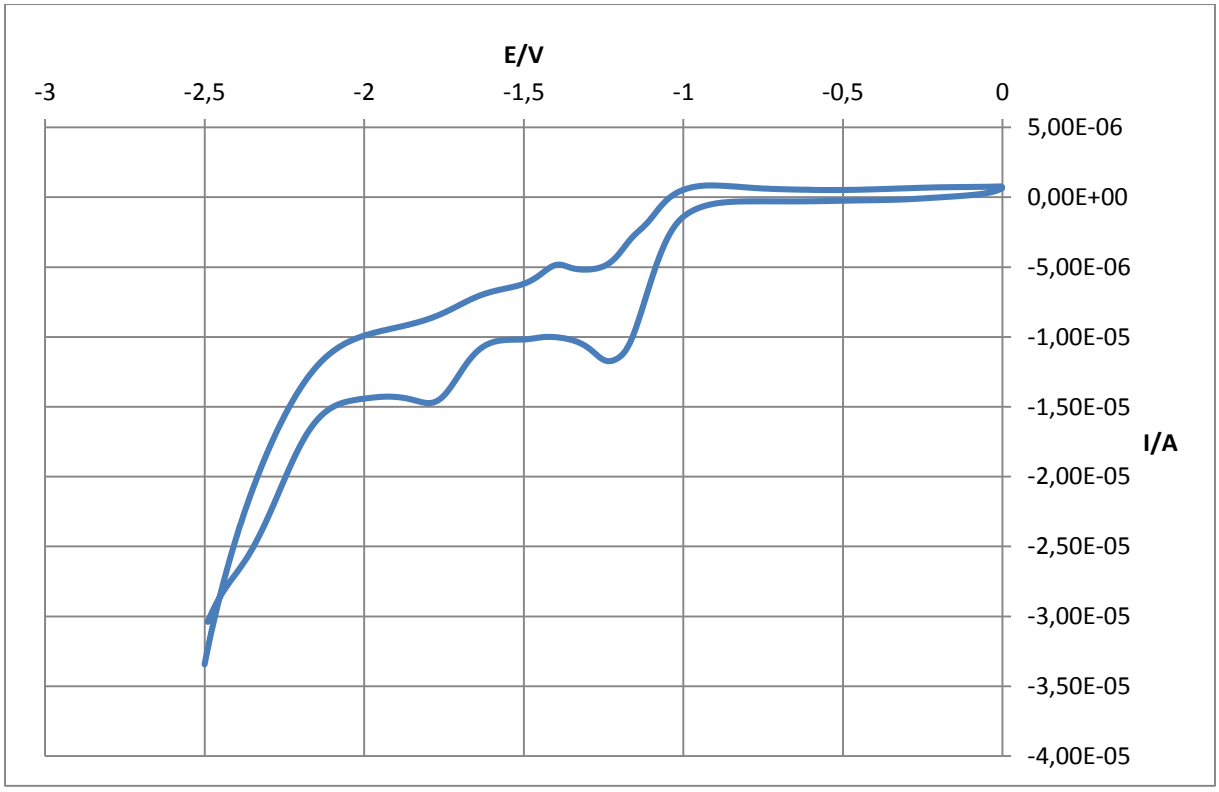

Figure A.3 Cyclovoltammogram of 3, *N*,*N*-diethyl-*O*-(4-nitrobenzoyl)hydroxylamine

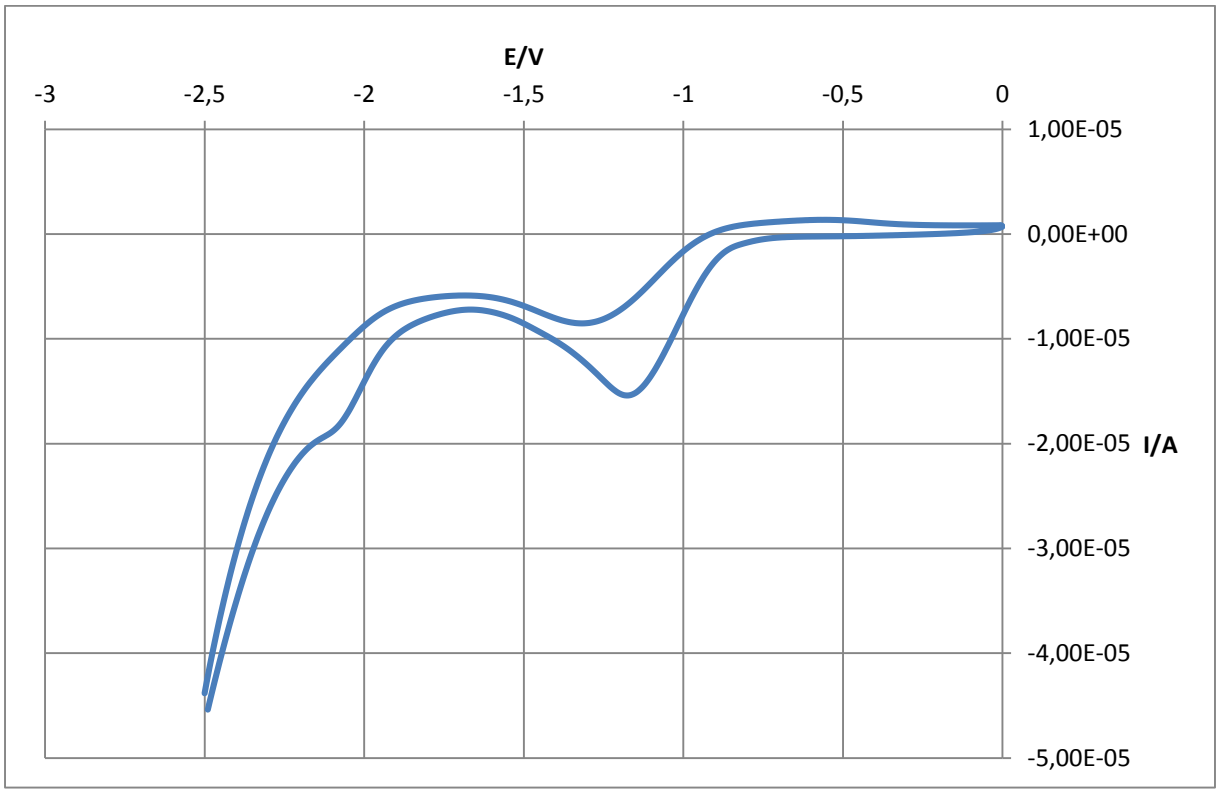

Figure A.4 Cyclovoltammogram of 4, *N*,*N*-diethyl-*O*-picolinoylhydroxylamine

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JLU Giessen - Inst. für Org. Chemie

AK Göttlich

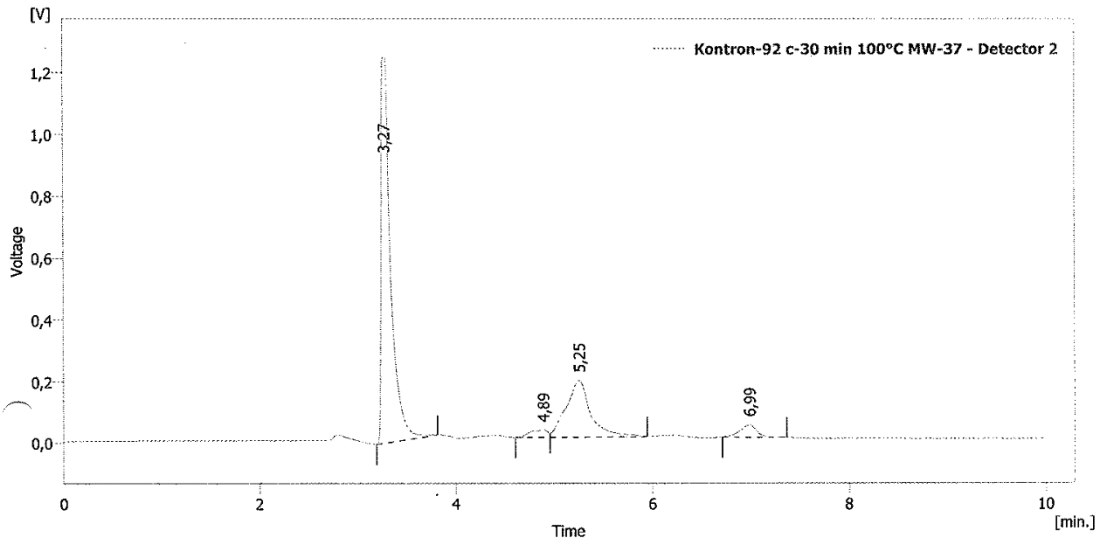
Chromatogram Info:

File Name	:	D:\Daten\Kontron\Data\Kontron-92 c-30 min 100°C MW-37.PRM	File Created	:	29.08.2011 10:45:53
Origin	:	Acquired	Acquired Date	:	29.08.2011 10:45:53
Project	:	D:\Daten\Projects\Kontron.PRJ	By	:	BAS

Sample Info:

Sample ID	:	92 c	Amount	:	0
Sample	:	30 min 100°C MW	ISTD Amount	:	0
Inj. Volume [mL]	:	0,02	Dilution	:	1

Column	:	SI-60	Detection	:	UV 254 nm
Mobile Phase	:	n-Hexane/tBME	Temperature	:	RT
Flow Rate	:	1.0 mL/min	Pressure	:	10 bar
Note	:	Flow = 1 mL/min 0.00 A 95 B 5 10.0 A 80 B 20 11.0 A 95 B 5 16.4 ENDE			



Result Table (Uncal - Kontron-92 c-30 min 100°C MW-37 - Detector 2)

	Reten. Time [min]	Compound Name	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
2	4,887		304,136	24,484	7,7	9,8	0,24
3	5,253		3203,901	184,086	80,7	73,8	0,24
4	6,987		463,617	40,864	11,7	16,4	0,18
	Total		3971,655	249,434	100,0	100,0	

Figure A.5 Chromatogram showing RT of X-5, X-10 & X-11

N-benzyl-N-(2,2-dimethylpent-4-en-1-yl)-O-(4-nitrobenzoyl)hydroxylamine

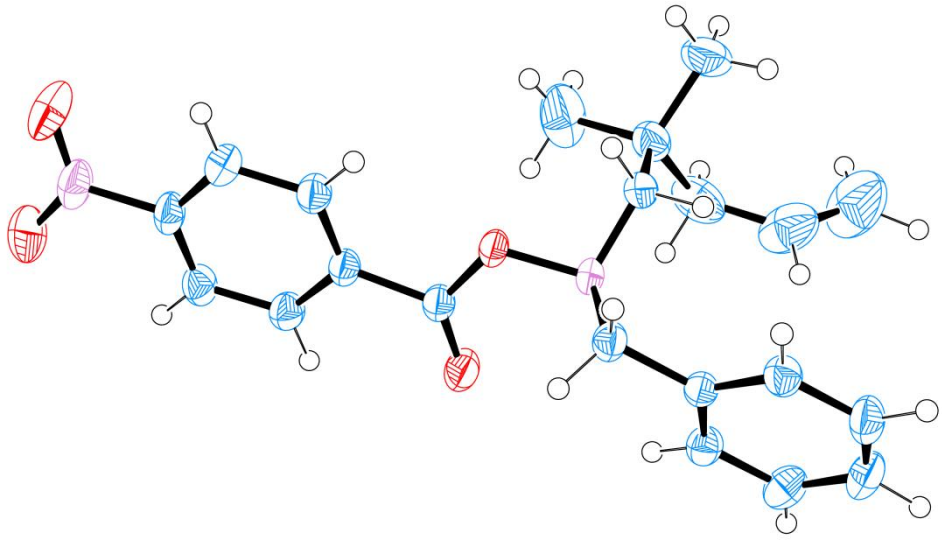


Table 1. Crystal data and structure refinement for goettlich12011.

Identification code	goettlich12011
Empirical formula	C21 H24 N2 O4
Formula weight	368.42
Temperature	190 K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.6860(15) Å alpha = 77.59(3) °
	b = 11.765(2) Å beta = 80.67(3) °
	c = 11.930(2) Å gamma = 72.64(3) °
Volume	1000.0(3) Å ^{3}
Z, Calculated density	2, 1.224 Mg/m^3
Absorption coefficient	0.085 mm^{-1}
F(000)	392
Crystal size	3.50 x 0.55 x 0.70 mm
Theta range for data collection	1.76 to 27.43 °
Limiting indices	-9<=h<=9, -15<=k<=15, -15<=l<=15
Reflections collected / unique	20719 / 4552 [R(int) = 0.0711]
Completeness to theta = 27.43	99.8 %
Absorption correction	semi empirical
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4552 / 0 / 340
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0493, wR2 = 0.1343
R indices (all data)	R1 = 0.0616, wR2 = 0.1443
Largest diff. peak and hole	0.254 and -0.326 e.A^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for goettlich12011. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	-3628(4)	3214(4)	5332(3)	106(1)
C(2)	-2229(3)	3126(3)	4541(2)	75(1)
C(3)	-525(3)	2115(2)	4582(2)	59(1)
C(4)	1260(2)	2417(1)	4684(1)	41(1)
C(5)	1030(3)	2979(2)	5761(1)	54(1)
C(6)	2813(4)	1243(2)	4786(2)	77(1)
C(7)	1687(2)	3357(1)	3650(1)	32(1)
C(8)	1621(2)	4032(1)	1570(1)	32(1)
C(9)	-411(2)	4578(1)	1515(1)	28(1)
C(10)	-1291(2)	5718(1)	1774(1)	34(1)
C(11)	-3176(2)	6195(1)	1739(1)	42(1)
C(12)	-4180(2)	5526(1)	1443(1)	44(1)
C(13)	-3316(2)	4391(1)	1176(1)	41(1)
C(14)	-1437(2)	3916(1)	1211(1)	34(1)
C(15)	4197(2)	1473(1)	1716(1)	30(1)
C(16)	6166(2)	735(1)	1683(1)	29(1)
C(17)	7489(2)	1033(1)	2144(1)	33(1)
C(18)	9301(2)	330(1)	2053(1)	36(1)
C(19)	9719(2)	-653(1)	1505(1)	34(1)
C(20)	8438(2)	-971(1)	1040(1)	36(1)
C(21)	6638(2)	-268(1)	1141(1)	35(1)
N(1)	1909(1)	2981(1)	2523(1)	29(1)
N(2)	11633(2)	-1420(1)	1411(1)	44(1)
O(1)	3879(1)	2335(1)	2366(1)	31(1)
O(2)	3078(1)	1323(1)	1213(1)	45(1)
O(3)	12705(2)	-1268(1)	1975(1)	63(1)
O(4)	12037(2)	-2171(1)	775(1)	68(1)

Table 3. Bond lengths [Å] and angles [°] for goettlich12011.

C(1)-C(2)	1.306(3)
C(2)-C(3)	1.482(3)
C(3)-C(4)	1.545(2)
C(4)-C(6)	1.529(2)
C(4)-C(5)	1.530(2)
C(4)-C(7)	1.534(2)
C(7)-N(1)	1.4723(16)
C(8)-N(1)	1.4779(17)
C(8)-C(9)	1.5072(17)
C(9)-C(10)	1.3862(18)

C(9)-C(14)	1.3931(18)
C(10)-C(11)	1.393(2)
C(11)-C(12)	1.382(2)
C(12)-C(13)	1.382(2)
C(13)-C(14)	1.3884(19)
C(15)-O(2)	1.1979(16)
C(15)-O(1)	1.3486(15)
C(15)-C(16)	1.5021(17)
C(16)-C(17)	1.3906(18)
C(16)-C(21)	1.3929(18)
C(17)-C(18)	1.3919(18)
C(18)-C(19)	1.380(2)
C(19)-C(20)	1.379(2)
C(19)-N(2)	1.4795(17)
C(20)-C(21)	1.3852(19)
N(1)-O(1)	1.4787(13)
N(2)-O(3)	1.2177(18)
N(2)-O(4)	1.2250(18)
C(1)-C(2)-C(3)	125.1(3)
C(2)-C(3)-C(4)	117.06(17)
C(6)-C(4)-C(5)	109.48(17)
C(6)-C(4)-C(7)	111.60(14)
C(5)-C(4)-C(7)	106.63(13)
C(6)-C(4)-C(3)	108.44(18)
C(5)-C(4)-C(3)	109.76(14)
C(7)-C(4)-C(3)	110.92(13)
N(1)-C(7)-C(4)	114.35(11)
N(1)-C(8)-C(9)	108.63(10)
C(10)-C(9)-C(14)	119.05(11)
C(10)-C(9)-C(8)	121.66(12)
C(14)-C(9)-C(8)	119.29(11)
C(9)-C(10)-C(11)	120.66(13)
C(12)-C(11)-C(10)	119.72(13)
C(13)-C(12)-C(11)	120.15(13)
C(12)-C(13)-C(14)	120.10(13)
C(13)-C(14)-C(9)	120.31(12)
O(2)-C(15)-O(1)	124.99(11)
O(2)-C(15)-C(16)	124.14(11)
O(1)-C(15)-C(16)	110.85(10)
C(17)-C(16)-C(21)	120.49(11)
C(17)-C(16)-C(15)	122.77(11)
C(21)-C(16)-C(15)	116.73(11)
C(16)-C(17)-C(18)	119.84(12)
C(19)-C(18)-C(17)	118.06(13)
C(20)-C(19)-C(18)	123.43(12)
C(20)-C(19)-N(2)	117.62(12)
C(18)-C(19)-N(2)	118.95(13)
C(19)-C(20)-C(21)	117.95(12)
C(20)-C(21)-C(16)	120.23(12)
C(7)-N(1)-C(8)	111.68(10)
C(7)-N(1)-O(1)	103.54(9)
C(8)-N(1)-O(1)	105.66(9)

O(3)-N(2)-O(4)	124.18(12)
O(3)-N(2)-C(19)	117.89(13)
O(4)-N(2)-C(19)	117.92(13)
C(15)-O(1)-N(1)	111.85(9)

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for goettlich12011. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U11 + ... + 2 h k a^* b^* U^{12}]$

	U11	U22	U33	U23	U13	U12
C(1)	56(1)	144(3)	96(2)	13(2)	4(1)	-23(2)
C(2)	53(1)	110(2)	62(1)	9(1)	-10(1)	-35(1)
C(3)	76(1)	69(1)	42(1)	-15(1)	9(1)	-39(1)
C(4)	45(1)	39(1)	32(1)	-5(1)	-2(1)	-3(1)
C(5)	63(1)	71(1)	32(1)	-12(1)	-5(1)	-20(1)
C(6)	86(2)	50(1)	57(1)	13(1)	9(1)	14(1)
C(7)	31(1)	31(1)	31(1)	-9(1)	-5(1)	-2(1)
C(8)	25(1)	33(1)	32(1)	-3(1)	0(1)	-5(1)
C(9)	26(1)	29(1)	24(1)	-1(1)	-1(1)	-4(1)
C(10)	35(1)	31(1)	35(1)	-7(1)	-3(1)	-6(1)
C(11)	37(1)	32(1)	47(1)	-7(1)	0(1)	3(1)
C(12)	26(1)	43(1)	51(1)	3(1)	-4(1)	-1(1)
C(13)	34(1)	41(1)	49(1)	0(1)	-10(1)	-13(1)
C(14)	34(1)	28(1)	37(1)	-4(1)	-5(1)	-5(1)
C(15)	26(1)	30(1)	33(1)	-9(1)	-3(1)	-4(1)
C(16)	25(1)	28(1)	31(1)	-4(1)	-1(1)	-3(1)
C(17)	28(1)	32(1)	38(1)	-10(1)	-3(1)	-5(1)
C(18)	27(1)	38(1)	43(1)	-5(1)	-6(1)	-6(1)
C(19)	26(1)	30(1)	35(1)	2(1)	2(1)	1(1)
C(20)	36(1)	29(1)	39(1)	-8(1)	-1(1)	-1(1)
C(21)	32(1)	32(1)	38(1)	-9(1)	-5(1)	-4(1)
N(1)	21(1)	31(1)	31(1)	-8(1)	-2(1)	2(1)
N(2)	29(1)	37(1)	52(1)	2(1)	-1(1)	1(1)
O(1)	21(1)	33(1)	38(1)	-13(1)	-5(1)	1(1)
O(2)	29(1)	50(1)	60(1)	-28(1)	-11(1)	-1(1)
O(3)	31(1)	55(1)	95(1)	-9(1)	-15(1)	1(1)
O(4)	48(1)	61(1)	78(1)	-28(1)	-2(1)	19(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for goettlich12011.

	x	y	z	U(eq)
H(1)	-3560(40)	2500(30)	6020(30)	110(9)
H(2)	-4810(50)	3950(30)	5220(30)	135(11)
H(3)	-2380(40)	3780(30)	3820(20)	107(9)
H(4)	-710(30)	1510(20)	5200(20)	84(7)
H(5)	-370(30)	1820(20)	3860(20)	76(6)
H(6)	30(30)	3740(20)	5746(18)	70(6)
H(7)	650(30)	2420(20)	6496(19)	72(6)
H(8)	2140(40)	3120(20)	5860(20)	85(7)
H(9)	2590(40)	710(30)	5510(30)	104(8)
H(10)	3990(40)	1470(20)	4810(20)	89(8)
H(11)	2900(30)	800(20)	4140(20)	80(7)
H(12)	2790(20)	3571(14)	3761(14)	40(4)
H(13)	640(20)	4093(13)	3617(12)	30(3)
H(14)	2190(20)	4650(15)	1672(14)	40(4)
H(15)	2200(20)	3745(13)	836(13)	33(4)
H(16)	-580(20)	6178(15)	1983(14)	44(4)
H(17)	-3790(30)	6976(19)	1927(16)	58(5)
H(18)	-5480(30)	5837(17)	1388(16)	58(5)
H(19)	-4030(30)	3930(17)	975(16)	56(5)
H(20)	-820(20)	3137(16)	1054(14)	40(4)
H(21)	7190(20)	1723(15)	2490(13)	38(4)
H(22)	10190(30)	525(16)	2365(15)	53(5)
H(23)	8780(20)	-1677(17)	660(16)	52(5)
H(24)	5680(20)	-465(16)	816(15)	51(5)

(1-benzylpyrrolidin-2-yl)methyl 4-nitrobenzoate Hydrochloride

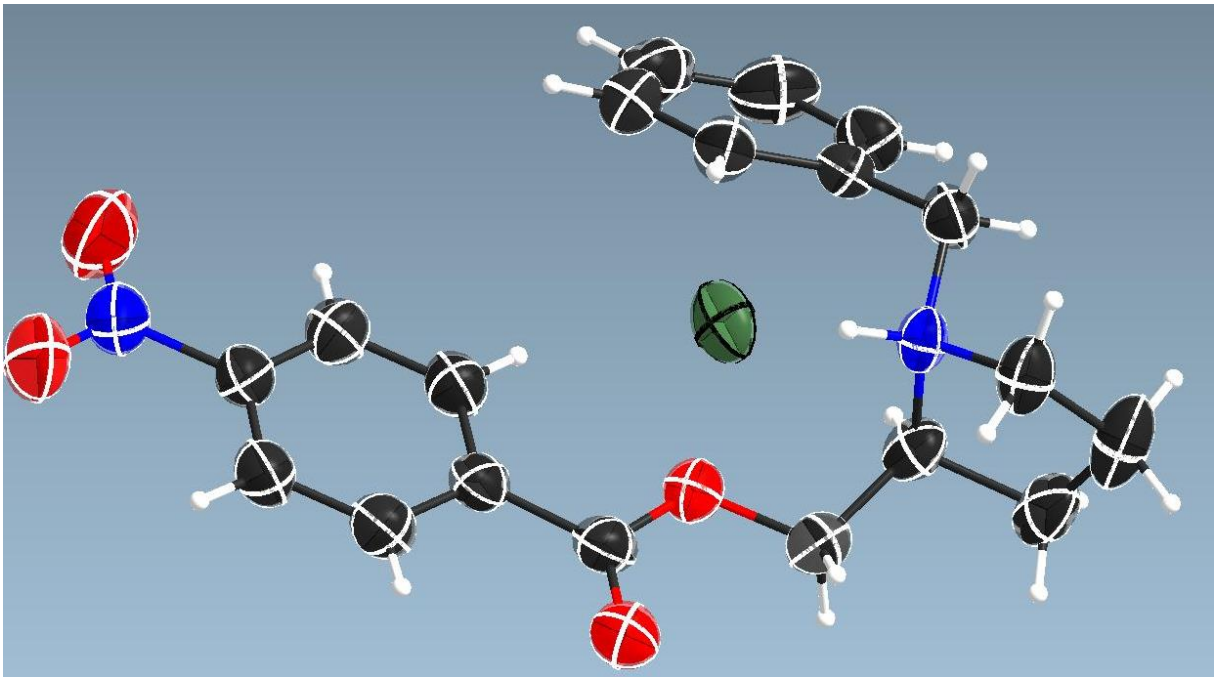


Table 1. Crystal data and structure refinement for goettlich12016.

Identification code	goettlich12016
Empirical formula	C19 H21 Cl N2 O4
Formula weight	376.83
Temperature	299(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.4170(15) Å alpha = 99.87(3)°
	b = 8.1060(16) Å beta = 96.17(3)°
	c = 15.864(3) Å gamma = 95.03(3)°
Volume	928.7(3) A^3
Z, Calculated density	2, 1.348 Mg/m^3
Absorption coefficient	0.232 mm^{-1}
F(000)	396
Crystal size	0.55 x 0.15 x 0.12 mm
Theta range for data collection	2.57 to 27.48°
Limiting indices	-8<=h<=9, -9<=k<=10, -19<=l<=20
Reflections collected / unique	7606 / 4057 [R(int) = 0.0845]
Completeness to theta = 27.48	95.1 %
Absorption correction	Semi-empirical
Max. and min. transmission	1.09430 and 0.88572
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4057 / 0 / 319
Goodness-of-fit on F^2	1.010
Final R indices [I>2sigma(I)]	R1 = 0.0506, wR2 = 0.1300
R indices (all data)	R1 = 0.1014, wR2 = 0.1800
Largest diff. peak and hole	0.219 and -0.292 e. $Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for goettlich12016. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Cl(1)	2264(1)	8035(1)	8998(1)	64(1)
O(1)	-3998(4)	6923(4)	4887(2)	111(1)
N(1)	-2374(4)	7413(4)	4969(2)	71(1)
C(2)	-1139(4)	6751(3)	5593(2)	56(1)
N(2)	6314(3)	7700(3)	8999(1)	44(1)
O(2)	-1727(4)	8447(4)	4581(2)	98(1)
C(3)	678(4)	7313(4)	5705(2)	61(1)
O(3)	1786(3)	3663(3)	7725(2)	78(1)
C(4)	1833(4)	6696(4)	6284(2)	58(1)
O(4)	4075(2)	5469(2)	7493(1)	52(1)
C(5)	1152(4)	5508(3)	6739(2)	50(1)
C(6)	-696(4)	4954(4)	6600(2)	58(1)
C(7)	2330(4)	4777(3)	7370(2)	53(1)
C(8)	5241(4)	4862(4)	8133(2)	59(1)
C(9)	6861(4)	6135(3)	8464(2)	52(1)
C(10)	6549(4)	7400(5)	9920(2)	59(1)
C(11)	8225(5)	6498(6)	9982(2)	78(1)
C(12)	8192(4)	5425(5)	9089(3)	69(1)
C(13)	7426(4)	9283(4)	8910(2)	52(1)
C(14)	7103(3)	9734(3)	8037(2)	47(1)
C(15)	5369(4)	9990(4)	7674(2)	58(1)
C(16)	5125(5)	10482(4)	6887(2)	69(1)
C(17)	6575(6)	10758(4)	6450(2)	73(1)
C(18)	8289(6)	10524(4)	6791(2)	73(1)
C(19)	8553(5)	10008(4)	7577(2)	59(1)
C(1)	-1865(4)	5571(4)	6030(2)	62(1)

Table 3. Bond lengths [A] and angles [deg] for goettlich12016.

O(1)-N(1)	1.220(4)
N(1)-O(2)	1.217(4)
N(1)-C(2)	1.476(4)
C(2)-C(3)	1.367(4)
C(2)-C(1)	1.380(4)
N(2)-C(13)	1.500(4)
N(2)-C(9)	1.513(3)
N(2)-C(10)	1.516(3)
C(3)-C(4)	1.375(4)
O(3)-C(7)	1.207(3)
C(4)-C(5)	1.390(4)
O(4)-C(7)	1.345(3)
O(4)-C(8)	1.442(3)
C(5)-C(6)	1.387(4)
C(5)-C(7)	1.491(4)
C(6)-C(1)	1.372(4)
C(8)-C(9)	1.499(4)
C(9)-C(12)	1.540(4)
C(10)-C(11)	1.499(5)
C(11)-C(12)	1.527(5)
C(13)-C(14)	1.493(4)
C(14)-C(19)	1.386(4)
C(14)-C(15)	1.398(4)
C(15)-C(16)	1.374(4)
C(16)-C(17)	1.363(5)
C(17)-C(18)	1.369(6)
C(18)-C(19)	1.381(5)
O(2)-N(1)-O(1)	123.6(3)
O(2)-N(1)-C(2)	118.3(3)
O(1)-N(1)-C(2)	118.1(3)
C(3)-C(2)-C(1)	122.6(3)
C(3)-C(2)-N(1)	118.8(3)
C(1)-C(2)-N(1)	118.5(3)
C(13)-N(2)-C(9)	113.1(2)
C(13)-N(2)-C(10)	111.4(2)
C(9)-N(2)-C(10)	105.1(2)
C(2)-C(3)-C(4)	119.0(3)
C(3)-C(4)-C(5)	120.1(3)
C(7)-O(4)-C(8)	114.8(2)
C(6)-C(5)-C(4)	119.3(3)
C(6)-C(5)-C(7)	117.8(3)
C(4)-C(5)-C(7)	122.8(3)
C(1)-C(6)-C(5)	121.2(3)
O(3)-C(7)-O(4)	123.3(3)
O(3)-C(7)-C(5)	123.7(3)
O(4)-C(7)-C(5)	113.0(2)
O(4)-C(8)-C(9)	109.5(2)
C(8)-C(9)-N(2)	111.2(2)
C(8)-C(9)-C(12)	109.7(3)

N(2)-C(9)-C(12)	104.9(2)
C(11)-C(10)-N(2)	104.4(2)
C(10)-C(11)-C(12)	104.8(3)
C(11)-C(12)-C(9)	107.1(3)
C(14)-C(13)-N(2)	113.7(2)
C(19)-C(14)-C(15)	117.6(3)
C(19)-C(14)-C(13)	120.3(3)
C(15)-C(14)-C(13)	122.0(3)
C(16)-C(15)-C(14)	120.8(3)
C(17)-C(16)-C(15)	120.5(3)
C(16)-C(17)-C(18)	120.0(3)
C(17)-C(18)-C(19)	120.2(3)
C(18)-C(19)-C(14)	120.9(3)
C(6)-C(1)-C(2)	117.8(3)

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for goettlich12016. The anisotropic displacement factor exponent takes the form: $-2\,pi^2\,[\,h^2\,a^{*2}\,U^{11} + ... + 2\,h\,k\,a^*\,b^*\,U^{12}\,]$

	U11	U22	U33	U23	U13	U12
Cl(1)	37(1)	82(1)	70(1)	-1(1)	10(1)	8(1)
O(1)	77(2)	104(2)	145(3)	44(2)	-42(2)	-6(2)
N(1)	76(2)	65(2)	65(2)	7(1)	-13(1)	11(1)
C(2)	64(2)	50(2)	50(2)	4(1)	-5(1)	7(1)
N(2)	32(1)	55(1)	47(1)	12(1)	2(1)	7(1)
O(2)	102(2)	111(2)	87(2)	46(2)	-5(2)	17(2)
C(3)	67(2)	60(2)	56(2)	16(2)	0(1)	-1(2)
O(3)	74(2)	66(1)	89(2)	27(1)	-14(1)	-12(1)
C(4)	54(2)	59(2)	58(2)	7(1)	-1(1)	-2(1)
O(4)	54(1)	54(1)	48(1)	12(1)	2(1)	5(1)
C(5)	61(2)	43(1)	43(1)	2(1)	2(1)	2(1)
C(6)	60(2)	56(2)	56(2)	7(1)	5(1)	-3(1)
C(7)	64(2)	43(1)	48(1)	4(1)	3(1)	-2(1)
C(8)	61(2)	52(2)	67(2)	19(2)	2(1)	9(1)
C(9)	44(1)	54(2)	61(2)	13(1)	10(1)	17(1)
C(10)	51(2)	81(2)	51(2)	25(2)	5(1)	11(2)
C(11)	54(2)	119(3)	76(2)	53(2)	6(2)	22(2)
C(12)	42(2)	71(2)	100(3)	34(2)	3(2)	16(2)
C(13)	43(2)	56(2)	53(2)	4(1)	-4(1)	1(1)
C(14)	47(1)	39(1)	52(1)	4(1)	-1(1)	0(1)
C(15)	50(2)	61(2)	64(2)	22(2)	0(1)	2(1)
C(16)	72(2)	60(2)	74(2)	23(2)	-13(2)	2(2)
C(17)	108(3)	56(2)	56(2)	17(2)	5(2)	6(2)
C(18)	93(3)	62(2)	73(2)	22(2)	34(2)	6(2)
C(19)	53(2)	60(2)	66(2)	14(1)	11(2)	4(1)
C(1)	53(2)	60(2)	65(2)	4(2)	-6(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for goettlich12016.

	x	y	z	U(eq)
H(1)	-3130(50)	5210(40)	5940(20)	70(9)
H(2)	-1110(40)	4210(40)	6910(20)	70(10)
H(3)	4510(40)	4570(40)	8650(20)	75(9)
H(4)	4430(40)	9790(40)	8030(20)	63(8)
H(5)	7720(50)	4330(50)	9110(20)	83(11)
H(6)	9290(50)	7310(40)	10060(20)	82(11)
H(7)	7160(40)	10100(40)	9414(19)	61(8)
H(8)	9630(40)	9870(30)	7804(18)	49(8)
H(9)	9270(50)	10680(50)	6530(30)	96(13)
H(10)	6330(50)	11120(40)	5890(20)	85(10)
H(11)	4010(50)	10680(40)	6650(20)	75(10)
H(12)	1100(50)	8030(40)	5420(20)	73(10)
H(13)	3060(40)	7060(40)	6360(20)	67(9)
H(14)	5730(40)	3810(40)	7850(20)	73(9)
H(15)	9310(50)	5460(40)	8870(20)	90(11)
H(16)	7370(40)	6470(40)	8030(20)	71(10)
H(17)	8220(50)	5750(50)	10400(30)	110(14)
H(18)	5460(50)	6660(40)	9970(20)	71(9)
H(20)	8560(50)	9120(40)	9120(20)	66(9)
H(21)	5140(40)	7820(30)	8830(17)	52(7)
H(19)	6580(40)	8460(40)	10310(20)	63(9)