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SYNTHESIS OF HIGHLY SUBSTITUTED NITROPYRROLIDINES, NITROPYRROLIZINES AND NITROPYRROLES *VIA* MULTICOMPONENT-MULTISTEP SEQUENCES WITHIN A FLOW REACTOR

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Abstract – We expand upon recent results concerning dipolar cycloaddition reactions of unstabilized azomethine ylids with nitro alkenes to generate 3-nitropyrrolidines *via* a flow chemistry sequence. This new work describes the development of a three-component coupling reaction between glycine esters, aldehydes and nitro alkenes. In order to further demonstrate the utility of flow technology in concert with heterogeneous reagents and scavengers for complex reaction sequences an in-line oxidation resulting in the conversion of tetra-substituted pyrrolidines to their pyrrole congeners has been developed.

‡This paper is dedicated to Prof. Albert Eschenmoser on the occasion of his 85th birthday and in acknowledgement of his many outstanding contributions to chemistry.

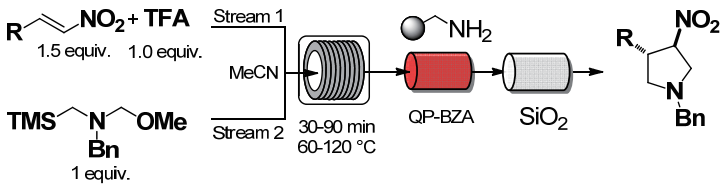
INTRODUCTION

A necessary requirement for modern drug discovery programs is the flexible and rapid access to a large number of diverse functionalized building blocks.[1] These core structures are commonly heterocyclic motifs which are obtained *via* a large range of robust chemical transformations. Furthermore, the heterocyclic frameworks provide readily tunable interactions with biogenic targets to assist optimal binding data from screening.[2] Amongst these heterocyclic structures the pyrrolidine ring has particular medicinal relevance. It is not only present in many peptide mimetics, but can also be found in numerous

drug substances such as levetiracetam[3] and vildagliptin[4] and other drug candidates including novel PDE9,[5] factor Xa,[6] rho kinase[7] and AKT kinase[8] inhibitors. In addition, the pyrrole unit is present in many of the best selling drugs exemplified by lipitor[9] and sutent.[10] Based on this evidence we set out to prepare a series of highly functionalized 3-nitropyrrolidines by means of dipolar cycloaddition chemistry between nitro alkenes and azomethine ylids using flow microreactor technology.[11] Following our previous experience in this rapidly developing area we anticipated that improved heat and mass transfer (control of mixing and exotherms),[12] safe use of hazardous reagents within the contained reactor system[13] and increased reproducibility when scaling up reactions from milligram to gram operations can be expected.[14] The use of in-line purification techniques provided by pre-packed columns of immobilized scavengers or phase separation methods furthermore facilitates isolation of pure products following solvent removal.[15]

RESULTS AND DISCUSSION

During initial experiments towards the flow synthesis of 3-nitropyrrolidines we employed commercially available *N*-(methoxymethyl)-*N*-(trimethylsilyl)benzylamine reagent as the reactive dipole precursor activated upon treatment with an acid catalyst. We used the previously described Vapourtec R2+/R4 system[16] where the reagent was dissolved in MeCN (1.0 equiv., 0.5 M) and loaded into one of the two sample injection loops. This was then combined with a second stream containing the appropriate nitro alkene (1.0-1.5 equiv., 0.5-0.75 M, in MeCN) and TFA (1.0 equiv., 0.5 M, in MeCN) within a T-mixing unit. Upon passage of this combined reaction mixture through a heated flow coil (CFC, 10 mL volume, 30-90 min residence time, 60-120 °C) the *in situ* generated dipole reacted with the olefinic counterpart to give the desired 3-nitropyrrolidine product. The excess of the nitro alkene, which was used to drive the reaction to completion within a short residence time, was removed by directing the output of the reactor coil through a glass column filled with immobilized benzylamine (QP-BZA,[17] ~3 equiv.) facilitating scavenging *via* a conjugate addition.



Scheme 1. General flow reactor set-up for the synthesis of 3-nitropyrrolidines

To further purify the reaction stream removing colored impurities, a plug of silica gel was placed at the outlet of the flow stream. Using these conditions the quick assembly of a number of differently substituted 3-nitropyrrolidines was achieved in good yields and purities after solvent removal only (Figure 1).

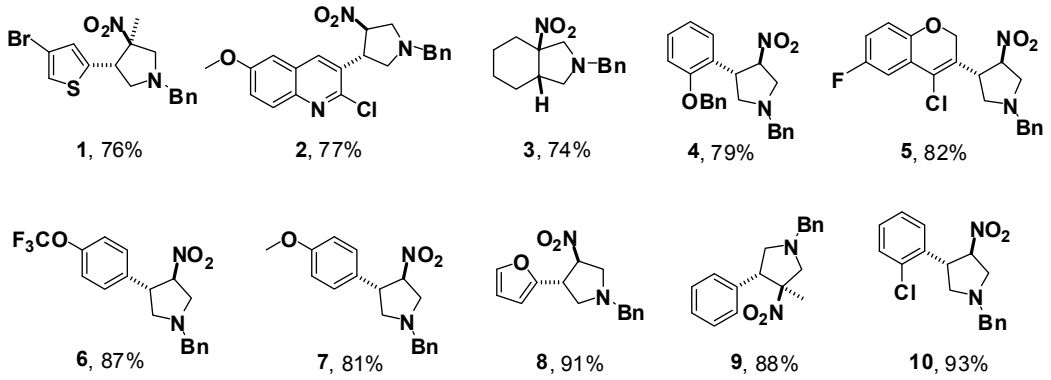


Figure 1. 3-Nitropyrrolidines prepared *via* the TFA-method

While we were able to access all these interesting structures there was a need for an improved procedure since the overall reaction time was prolonged owing to the increased affinity of the pyrrolidine products to the BZA-scavenger due to formation of TFA salts. As an alternative procedure we prepared a fluoride ion exchange monolithic cartridge as described in a previous study.[18] These ion-exchange monoliths represent not only cheap and readily prepared polymer-supports, they are also characterized by better flow parameters (high surface to volume ratio, no solvent-dependant swelling characteristics) and increased functional loadings when compared to commercial bead format resins. In addition, the use of an immobilized fluoride source circumvents potential precipitation problems that can occur during the flow process and obviates the need for TFA as an initiator for the dipole generation. These factors alleviate many of the safety concerns associate with scale-up.

In order to evaluate the fluoride monolith we used a similar reaction set-up to the one previously described where two streams of starting materials (stream 1: nitro alkene 1.0-1.5 equiv.; stream 2: *N*-(methoxymethyl)-*N*-(trimethylsilyl)benzylamine 1.0 equiv., both in MeCN) were mixed at a T-piece and directed into the monolithic cartridge which served as the reactor. A number of the previously generated 3-nitropyrrolidines (TFA method) was obtained in improved yield and purity using lower temperatures (Figure 2). Moreover, the overall reaction times could be reduced by 30 minutes as no binding to the BZA scavenging system was observed. These positive results meant that the range of substrates could also be rapidly extended to utilize acrylates, vinyl sulfones and vinyl phosphonates as dipolarophiles.

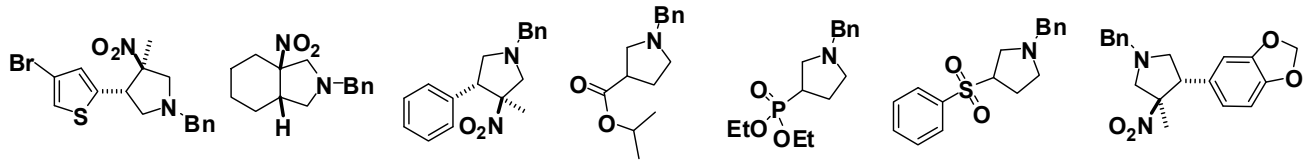
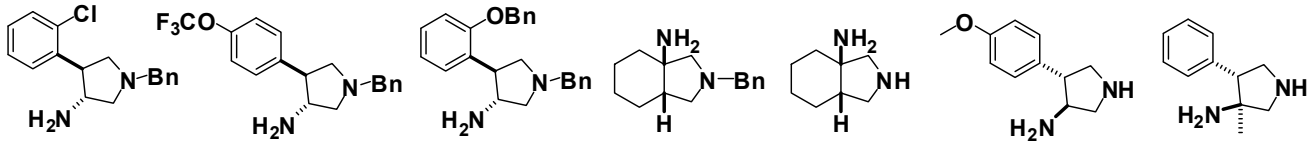


Figure 2. 3-Nitropyrrolidines prepared using a fluoride-monolith

Intrigued by these two orthogonally differentiated nitrogen moieties presented in the 3-nitropyrrolidines we furthermore investigated their chemoselective reduction and homolysis. The substrates (dissolved in EtOH/EtOAC 1:1; 0.1 equiv. HOAc) were passed through the H-Cube flow hydrogenator[19] firstly using a Raney-nickel containing cartridge. Upon premixing the on-board generated hydrogen gas (full hydrogen mode) and subsequent flow through the Raney-nickel cartridge (10 bar, 60 °C) a selective reduction of the nitro functionality was achieved to afford 3-aminopyrrolidines (Figure 3; compounds **15**, **16**, **17**, **18**) in very high yields. Additionally, when using a 10% Pd on charcoal cartridge in the flow reactor the reduction of the nitro group was observed together with simultaneous debenzylation of the inputs giving good yields of the corresponding diamines (Figure 3; compounds **19**, **20**, **21**). The products of these reactions can be elaborated by further reaction with acylating or sulfonylating agents, the results of which will be reported at a later date.[20]



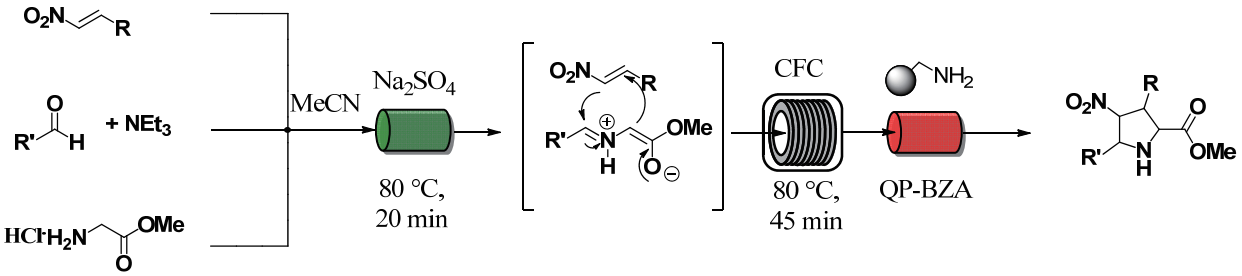
15, 95% **16**, 97% **17**, 93% **18**, 97% **19**, 90% **20**, 97% **21**, 95%

Figure 3. H-Cube hydrogenation of 3-nitropyrrolidines

With these results in hand we wished to expand on the pyrrolidine scaffold by incorporating greater diversity in the chemical transformation. We chose therefore to make use of stabilized azomethine ylids derived from readily available glycine imines, which in turn are accessible by condensation of glycine esters with various aldehydes. The use of such glycine imines in the cycloaddition with electron-deficient alkenes has been investigated previously in batch mode leading to various diastereomerically or enantiomerically enriched pyrrolidines through the application of various metal salts such as silver or lithium[21] or chiral auxillaries[22] and metal complexes such as Ag-(*S*)-QUINAP,[23] Cu^{I}-Segphos[24] and Pd-phosphoramidite.[25]

However, as these routes[26] call for extended reaction times (equivalent to many hours or days) and usually include the handling and generation of solid materials, which are not deemed to be ideal for continuous flow processing, we decided to adapt the reported procedures to a more practical method. In addition, we wanted to interlink the individual steps of imine formation and dipolar cycloaddition by means of a telescoped sequence. In order to achieve this we prepared stock solutions containing β-nitrostyrene, benzaldehyde, glycine methylester hydrochloride and triethylamine all dissolved in MeCN. Each of these solutions was then introduced into a sample loop mounted on the flow reactor and directed into a heated glass column filled with anhydrous sodium sulfate or magnesium sulfate (typically held at

60-80 °C) to promote the imine formation. Upon exiting the drying column the reaction mixture was directed into a convection flow coil (CFC, 10 mL PFA) heated at 80-100 °C where the cycloaddition between the nitro alkene and the *in situ* formed stabilized azomethine ylid takes place (Scheme 2). Pleasingly, we found that residence times of 20 min in the dehydrating column and 45 min in the CFC reactor were sufficient to obtain the tetra-substituted nitro-pyrrolidine products in yields greater than 70% after in-line work-up with the aforementioned benzylamine scavenger (QP-BZA) had removed residual starting materials. NMR-analysis of this material direct from the reactor revealed that a mixture of typically three diastereoisomers was formed under thermal conditions albeit with complete regioselective control. This result is consistent with previous reports.[27]



Scheme 2. Flow microreactor set-up for the three-component coupling towards nitro-pyrrolidines

Although, these reaction parameters allowed for the rapid generation of the desired nitropyrrolidine products we were not able to establish conditions to prepare these structures in a diastereomerically pure form, despite screening different temperatures, reaction times and also utilizing silver or lithium salts (AgOAc, AgO, LiCl) dispersed on sodium sulfate. Additionally, we observed the formation of a fourth diastereoisomer by thermally induced epimerization of the stereocenter next to the nitro-functionality as evidenced by X-ray analysis of compound **22** (Figure 4). As the epimerization occurred under the standard conditions, i.e. during the 60-90 min in the flow system at a temperature of 80 °C, we anticipate that epimerization accounts for one diastereoisomer being formed in the synthesis of other tetra-substituted nitropyrrolidines.

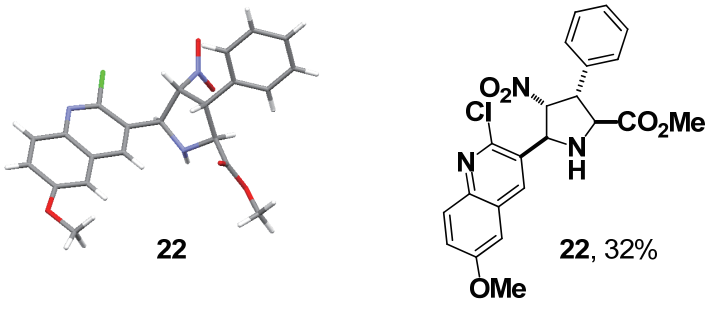


Figure 4. Epimerization for 3-nitropyrrolidine product **22** under thermal conditions

In a further extension of this work we wished to not only alter the aldehyde and nitro alkene inputs, but to also introduce a further point of diversity by modifying the amino acid derived component. For this reason we chose to use L-proline methyl ester as a readily available alternative to the glycine ester giving rise to nitropyrrolizine systems which hold interest as novel peptide mimetic structures. Noteworthy, when applying the previous flow conditions to the multi-component coupling with L-proline methyl ester we obtained the desired nitropyrrolizine product not only in high yield and purity, but also with good diastereoselectivity. Careful NMR-analysis on the reaction products still indicated the presence of three diastereoisomers, however this time in a 10:1:1 ratio as opposed to a 1:1:1 ratio as seen before. Using nOe experiments we were able to deduce the relative stereochemistry of the major diastereoisomer, which was later confirmed by X-ray analysis on some of the corresponding HCl-salts (Figure 5). The formation of the HCl-salt was achieved by adding stoichiometric amounts of HCl (4 M in dioxane) to the product stream and was found useful not only to obtain single crystals of the nitropyrrolizine product, but also allowed isolation of a solid material for subsequent storage of these intermediates.

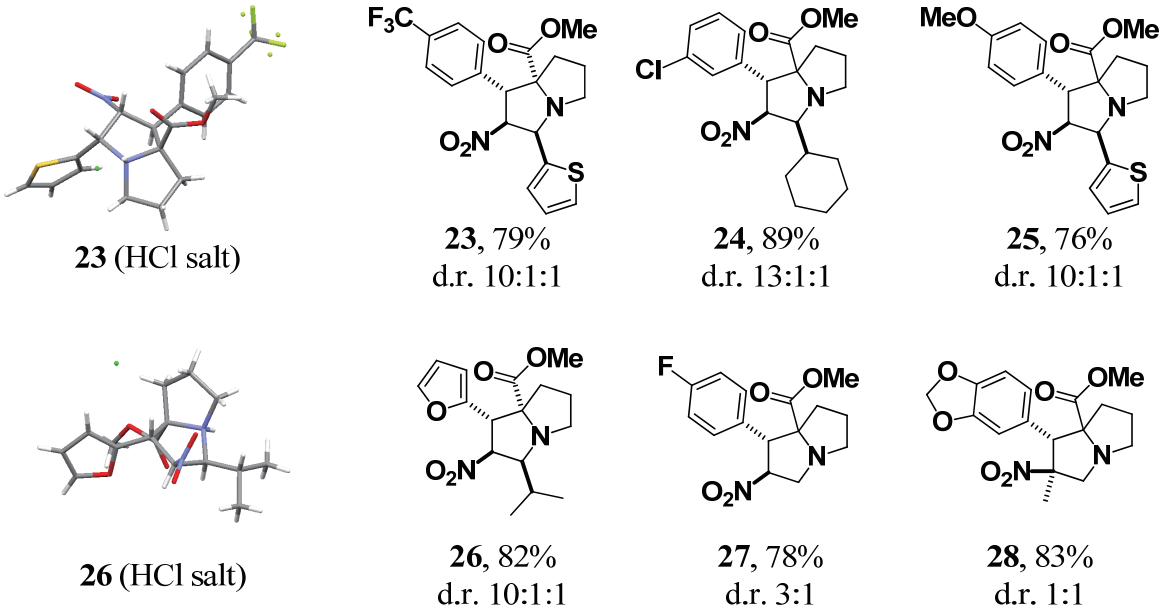
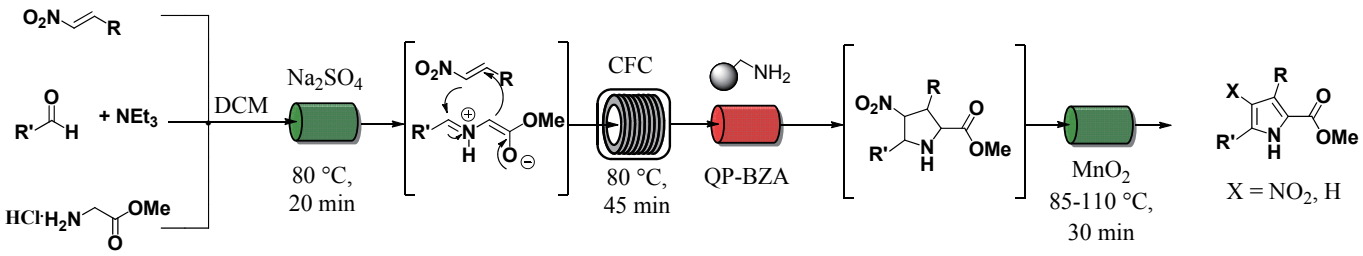


Figure 5. Structures of nitropyrrolizines prepared

Interestingly, when we investigated the synthesis of pyrrolizines using paraformaldehyde, which was performed as one-pot microwave reaction due to the insolubility of paraformaldehyde, (45 minutes at 80 °C) as aldehyde input we observed lower diastereomeric excesses (**27**) and in the case of the quarternary nitro derivative **28** a 1:1 mixture of both diastereoisomers highlighting the importance of bulkier substituents in order to obtain good diastereoselectivity.

Although only a small number of these interesting nitropyrrolizines was prepared both the yields as well as the diastereomeric ratios seem to be fairly consistent for various inputs. We believe that these compounds will gain some interest especially as they can be converted into novel amino acid derivatives by reduction of the nitro group.

Recently, a number of 3,5-diarylpyrrole-2-carboxylates has been described as members of a new sub-class of histone-deacetylase inhibitors displaying antitumor activity both *in vitro* and *in vivo*.[28] Consequently, we set out to extend our flow sequence by performing the final aromatization step from the 3-nitropyrrolidines to the corresponding pyrrole derivatives by means of a telescoped oxidation reaction. In order to conduct this oxidation from the pyrrolidine to the pyrrole a number of heterogeneous oxidants was investigated by placing them into a glass column situated at the end of the flow stream. Surprisingly, oxidants such as CrO_2 (Magtrieve®) and NiO_2 did not generate any of the desired pyrrole product, nevertheless we found that activated MnO_2 (either from commercial sources or freshly prepared[29]) at elevated temperatures (85-110 °C) afforded clean conversion to the corresponding pyrroles. We also found that MeCN was not a suitable solvent in this case as the high temperatures in the MnO_2 column led to solvent break-down forming acetamide as a hydrolysis product. However, when performing the multi-step sequence in dichloromethane (Scheme 3) no drop in conversion or purity of the resulting pyrrole products was observed. Consequently, this flow protocol allowed us to conduct a multi-component flow sequence involving imine formation, ylid-formation, dipolar cycloaddition and the final oxidation as a single concerted operation.



Scheme 3. Multistep flow set-up towards nitropyrrole products

Interestingly, analysis by both LC-MS and NMR-spectroscopy indicated two different pyrrole species were which were identified as the expected 3-nitropyrrole and its *des*-nitro derivative (Figure 6) which presumably forms upon formal elimination of nitrous acid as opposed to hydrogen. These results are consistent with previous literature reports.[27,30] The two pyrroles were readily separated using an automated Biotage SP2 chromatography system allowing for independent characterisation.[31]

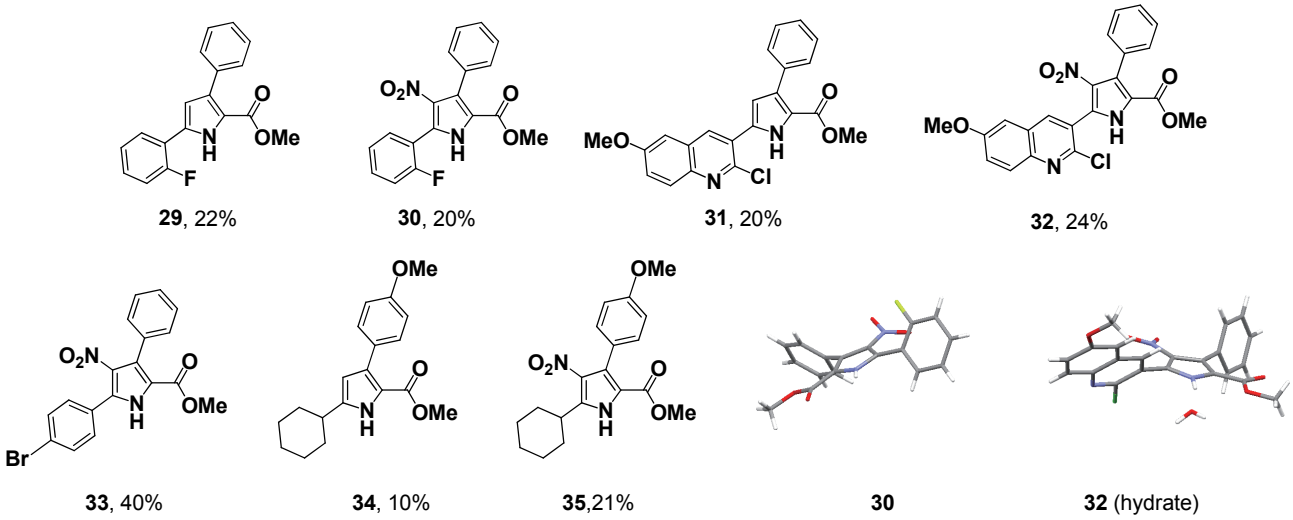


Figure 6. Structures of 1*H*-pyrroles prepared by multi-step flow synthesis

One limitation of using manganese dioxide as a heterogeneous oxidant for the conversion of nitropyrrolidines to the corresponding pyrroles is the only moderate recovery of material despite the starting material being fully converted to the desired product. Unfortunately, we were not able to obtain more than a 50-60% isolated yield for this second step. In addition we did not find any evidence for formation of byproducts, even when washing the MnO_2-cartridge with more polar solvents such as acetone or methanol. We ascribe this finding to the very large surface area of the MnO_2 particles leading to a high affinity for organic substrates, similar to that seen when charcoal is used as a support material in certain cases.[32]

Despite this issue the system can be applied to various substrates with success. The process tolerates different heteroaromatic structures giving the desired pyrroles in reasonable yields albeit in very high purity.

In summary, new flow chemistry processes have been established to prepare a variety of 3-nitropyrrolidines and nitropyrrolizines *via* dipolar cycloaddition reactions. These valuable building blocks were subsequently subjected to flow-mediated diversification protocols either *via* reduction pathways or by oxidation to the corresponding pyrroles. Overall, these investigations demonstrate how new multi-component multistep flow processes can be developed and applied to pharmaceutically relevant heterocyclic structures clearly highlighting the further value of these flow devices in chemical synthesis programs.

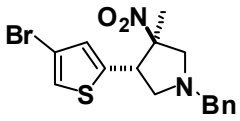
EXPERIMENTAL

Unless otherwise stated reaction solutions were prepared in MeCN or DCM in 20 mL glass vials. ^{1}H-NMR spectra were recorded on a Bruker Avance DPX-400 or DPX-600 spectrometer with residual $CHCl_3$ as the internal reference ($CHCl_3$ δ_H = 7.26 ppm). ^{13}C-NMR spectra were also recorded in $CDCl_3$ on the same spectrometers with the central peak of the residual solvent as the internal reference (δ_C = 77.0 ppm). COSY, DEPT 135, HMQC, HMBC and nOe spectroscopic techniques were used to aid the assignment of signals in the ^{13}C-NMR spectra. Infrared spectra were recorded neat on a Perkin-Elmer Spectrum One FT-IR spectrometer. Letters in the parentheses refer to relative absorbency of the peak: w, weak, < 40% of the main peak; m, medium, 41-74% of the main peak; s, strong, >74% of the main peak. LC-MS analysis was performed on an Agilent HP 1100 chromatograph (Luna Max RP column) attached to an HPLC/MSD mass spectrometer. Elution was carried out using a reversed-phase gradient of MeCN/water with both solvents containing 0.1% formic acid. The gradient is described in Table 1. For HRMS a LCT Premier Micromass spectrometer was used.

Table 1. LC-MS conditions

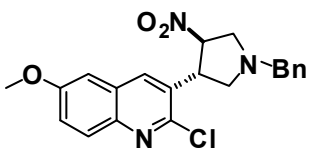
Time/ min	MeCN/ %	Flow rate/ mL/min
0.00	5	1.0
3.00	95	1.0
5.00	95	1.0
5.50	5	1.0
8.00	5	1.0

1-Benzyl-4-(4-bromothiophene-2-yl)-3-methyl-3-nitropyrrolidine, 1:



Yield: 76%, t_{Ret} = 4.97 min, m/z = 381.0 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.27-7.37 (5H, m), 7.15 (1H, s), 6.93 (1H, s), 4.46 (1H, t, *J* = 7.2 Hz), 3.77 (1H, d, *J* = 11.4 Hz), 3.71 (2H, s), 3.28 (1H, dd, *J* = 9.0, 9.6 Hz), 2.72 (1H, dd, *J* = 9.0, 9.6 Hz), 2.65 (1H, d, *J* = 11.4 Hz), 1.38 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 141.8 (C), 137.7 (C), 129.5 (CH), 128.5 (2CH), 128.4 (2CH), 127.4 (CH), 122.6 (CH), 109.4 (C), 95.9 (C), 63.7 (CH_2), 59.4 (CH_2), 59.1 (CH_2), 47.4 (CH), 23.1 (CH_3). IR (neat) ν = 2799.3 (w), 1694.3 (w), 1539.2 (s), 1452.6 (m), 1341.9 (m), 1189.9 (m), 1142.5 (m), 1108.4 (m), 1074.2 (m), 1027.9 (m), 855.7 (m), 833.3 (m), 737.4 (s), 698.4 (s) cm^{-1}. HRMS calculated for $C_{16}H_{18}N_2O_2SBr$ 381.0272, found: 381.0283.

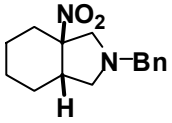
3-(1-Benzyl-4-nitropyrrolidin-3-yl)-2-chloro-6-methoxyquinoline, 2:



Yield: 77%, t_{Ret} = 4.58 min, m/z = 398.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.08 (1H, s), 7.88 (1H, d, *J* = 9.0 Hz), 7.30-7.40 (6H, m), 7.02 (1H, d, *J* = 3.0 Hz), 5.13 (1H, ddd, J = 3.6, 7.8, 12.0 Hz), 4.51 (1H, ddd, *J* = 3.6, 7.8, 12.0 Hz), 3.94 (3H, s), 3.82 (1H, d, *J* = 12.6 Hz), 3.75 (1H, d, *J* = 12.6 Hz), 3.46 (1H, dd, *J* = 7.8, 10.8 Hz), 3.29 (1H, dd, *J* = 7.8, 9.0 Hz), 3.24 (1H, dd, *J* = 4.8, 10.8 Hz), 3.02 (1H, dd, *J* = 4.8, 9.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 158.4 (C), 147.6 (C), 142.8 (C), 137.7 (C), 136.0 (CH), 132.2 (C), 129.6 (CH), 128.7 (2CH), 128.6 (2CH), 128.3 (C), 127.5 (CH), 123.3 (CH), 104.9 (CH), 89.2 (CH), 59.1 (CH_2), 58.5 (CH_2), 58.4 (CH_2), 55.6 (CH_3), 45.9 (CH). IR

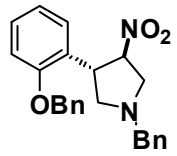
(neat) ν = 1666.7 (m), 1622.2 (m), 1591.3 (m), 1549.9 (s), 1495.6 (s), 1453.1 (m), 1346.9 (s), 1230.1 (s), 1166.3 (s), 1046.9 (s), 1026.3 (s), 911.7 (m), 828.8 (s), 731.1 (s), 699.7 (s) cm^{-1}. HRMS calculated for $C_{21}H_{21}ClN_3O_3$ 398.1271, found: 398.1279.

2-Benzyl-3a-nitrooctahydro-1*H*-isoindole, 3:



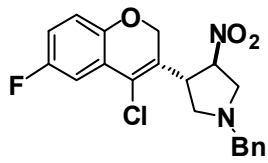
Yield: 74%, t_{Ret} = 3.60 min, m/z = 261.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.23-7.35 (5H, m), 3.74 (1H, d, *J* = 13.2 Hz), 3.70 (1H, d, *J* = 13.2 Hz), 3.39 (1H, d, *J* = 10.8 Hz), 2.92-3.05 (3H, m), 2.56 (1H, dd, *J* = 4.8, 9.0 Hz), 2.12-2.17 (1H, m), 2.06-2.11 (1H, m), 1.84-1.90 (1H, m), 1.55-1.60 (2H, m), 1.47-1.53 (1H, m), 1.43 (2H, t, *J* = 7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 139.6 (C), 128.4 (2CH), 128.3 (2CH), 127.0 (CH), 95.4 (C), 60.5 (CH_2), 59.8 (CH_2), 57.4 (CH_2), 40.5 (CH), 32.0 (CH_2), 27.1 (CH_2), 21.6 (CH_2), 21.5 (CH_2). IR (neat) ν = 2930.4 (m), 2863.3 (m), 2797.3 (w), 1671.9 (w), 1535.3 (s), 1495.0 (m), 1452.6 (m), 1366.0 (m), 1345.1 (m), 1247.8 (m), 1156.9 (m), 1072.7 (m), 1027.9 (m), 854.4 (s), 737.6 (s), 698.0 (s) cm^{-1}. HRMS calculated for $C_{15}H_{21}N_2O_2$ 261.1603, found: 261.1599.

1-Benzyl-3-(2-(benzyloxy)phenyl)-4-nitropyrrolidine, 4:



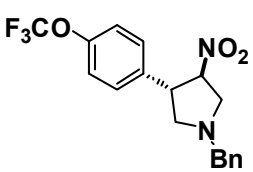
Yield: 79%, t_{Ret} = 4.57 min, m/z = 389.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.40-7.50 (5H, m), 7.33-7.38 (4H, m), 7.28-7.32 (3H, m), 6.90-7.05 (2H, m), 5.13 (1H, ddd, *J* = 2.4, 4.8, 7.2 Hz), 5.10 (1H, d, *J* = 11.4 Hz), 5.07 (1H, d, *J* = 11.4 Hz), 4.29 (1H, dt, *J* = 4.8, 7.8 Hz), 3.70 (1H, d, *J* = 12.6 Hz), 3.55 (1H, d, *J* = 12.6 Hz), 3.32 (1H, dd, *J* = 2.4, 11.8 Hz), 3.24 (1H, t, *J* = 9.0 Hz), 2.80 (2H, t, *J* = 9.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 156.3 (C), 138.2 (C), 136.3 (C), 129.5 (CH), 128.8 (CH), 128.7 (2CH), 128.6 (CH), 128.4 (2CH), 128.3 (2CH), 128.1 (2CH), 127.9 (C), 127.2 (CH), 121.1 (CH), 112.0 (CH), 90.0 (CH), 70.4 (CH_2), 59.3 (CH_2), 58.6 (CH_2), 58.2 (CH_2), 46.0 (CH). IR (neat) ν = 2919.6 (w), 2807.2 (w), 1601.4 (w), 1544.4 (s), 1493.5 (m), 1452.2 (m), 1372.5 (m), 1292.9 (m), 1236.1 (s), 1120.1 (m), 1009.2 (m), 909.7 (m), 748.8 (s), 732.7 (s), 696.2 (s) cm^{-1}. HRMS calculated for $C_{24}H_{25}N_2O_3$ 389.1865, found: 389.1847.

1-Benzyl-3-(4-chloro-6-fluoro-*2H*-chromen-3-yl)-4-nitropyrrolidine, 5:



Yield: 82%, t_{Ret} = 5.64 min, m/z = 389.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.28-7.38 (6H, m), 7.18 (1H, dd, *J* = 3.0, 9.0 Hz), 6.89 (1H, dt, *J* = 3.0, 8.4 Hz), 6.79 (1H, dd, *J* = 4.8, 9.0 Hz), 4.90 (1H, dt, *J* = 5.4, 7.8 Hz), 4.84 (1H, d, *J* = 14.4 Hz), 4.79 (1H, d, *J* = 14.4 Hz), 4.27 (1H, dt, *J* = 4.8, 7.8 Hz), 3.73 (1H, d, *J* = 12.6 Hz), 3.66 (1H, d, *J* = 12.6 Hz), 3.29 (1H, dd, *J* = 7.8, 10.2 Hz), 3.11 (1H, dd, *J* = 5.4, 10.8 Hz), 3.00 (1H, dd, *J* = 8.4, 9.6 Hz), 2.69 (1H, dd, *J* = 4.8, 9.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 157.7 (C, d, *J* = 238 Hz), 149.7 (C), 137.4 (C), 128.9 (C), 128.6 (2CH), 128.5 (2CH), 127.6 (CH), 125.1 (C), 122.9 (C), 116.7 (CH), 116.6 (CH), 111.8 (CH, d, *J* = 26 Hz), 87.1 (CH), 66.6 (CH_2), 59.0 (CH_2), 58.0 (CH_2), 56.0 (CH_2), 44.9 (CH). IR (neat) ν = 2808.7 (w), 1551.6 (s), 1487.3 (s), 1454.3 (m), 1432.2 (m), 1373.0 (m), 1334.6 (m), 1280.0 (m), 1249.8 (m), 1160.6 (s), 1068.9 (m), 1029.1 (s), 982.7 (m), 911.6 (m), 868.3 (m), 817.6 (s), 733.7 (s), 699.0 (s) cm^{-1}. HRMS calculated for $C_{20}H_{19}ClFN_2O_3$ 389.1068, found: 389.1074.

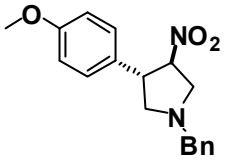
1-Benzyl-3-nitro-4-(4-trifluoromethoxy)-phenyl)pyrrolidine, 6:



Yield: 87%, t_{Ret} = 4.40 min, m/z = 367.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.34-7.38 (6H, m), 7.28-7.32 (1H, m), 7.21 (2H, d, *J* = 7.8 Hz), 4.91 (1H, dt, *J* = 4.8, 7.8 Hz), 4.04 (1H, dt, *J* = 6.6, 7.2 Hz), 3.76 (1H, d, *J* = 13.2 Hz), 3.72 (1H, d, *J* = 13.2 Hz), 3.38 (1H, dd, *J* = 4.2, 10.8 Hz), 3.27 (1H, t, *J* = 8.4 Hz), 3.18 (1H, dd, *J* = 7.8, 10.8 Hz), 2.72 (1H, dd, *J* = 6.6, 9.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 148.5 (C), 139.6 (C), 137.7 (C), 128.9 (2CH), 128.6 (CH), 128.5 (2CH), 127.4 (2CH), 121.4 (2CH), 120.5 (CF_3, q, *J* = 255 Hz), 90.9 (CH), 60.4 (CH_2), 59.2 (CH_2), 58.1 (CH_2), 48.5 (CH). IR (neat) ν = 2803.3 (w), 1549.6 (s), 1510.7 (m), 1454.7 (w), 1374.1 (w), 1341.3 (w), 1254.9 (s), 1215.2 (s), 1161.3

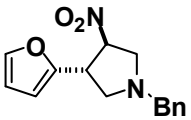
(s), 1110.3 (m), 1019.6 (m), 849.8 (m), 735.3 (m), 699.7 (m) cm^{-1}. HRMS calculated for $C_{18}H_{18}F_3N_2O_3$ 367.1270, found: 367.1277.

1-Benzyl-3-(4-methoxyphenyl)-4-nitropyrrolidine, 7:



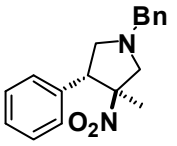
Yield: 81%, t_{Ret} = 4.16 min, m/z = 313.2 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.25-7.37 (5H, m), 7.22 (2H, d, *J* = 8.4 Hz), 6.88 (2H, d, *J* = 8.4 Hz), 4.90 (1H, dt, *J* = 4.8, 7.2 Hz), 3.96 (1H, q, *J* = 6.6 Hz), 3.80 (3H, s), 3.72 (2H, app. q, *J* = 12.6 Hz), 3.40 (1H, dd, *J* = 3.6, 10.8 Hz), 3.27 (1H, t, *J* = 8.7 Hz), 3.09 (1H, dd, *J* = 7.8, 10.8 Hz), 2.66 (1H, dd, *J* = 7.5, 9.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 158.9 (C), 137.9 (C), 132.6 (C), 128.6 (2CH), 128.5 (2x2CH), 127.4 (CH), 114.3 (2CH), 91.4 (CH), 60.8 (CH_2), 59.3 (CH_2), 58.2 (CH_2), 55.3 (CH_3), 48.7 (CH). IR (neat) ν = 2916.4 (w), 2805.1 (w), 1611.7 (w), 1546.7 (s), 1513.9 (s), 1454.0 (m), 1372.6 (m), 1304.7 (m), 1248.7 (s), 1179.0 (s), 1030.7 (s), 829.7 (s), 733.7 (s), 700.2 (s) cm^{-1}. HRMS calculated for $C_{18}H_{20}N_2O_3$ 313.1552, found: 313.1549.

1-Benzyl-3(furan2-yl)-4-nitropyrrolidine, 8:



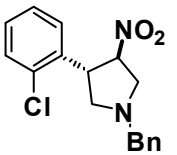
Yield: 91%, t_{Ret} = 3.77 min, m/z = 273.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.37 (1H, d, *J* = 1.2 Hz), 7.30-7.38 (4H, m), 7.29 (1H, app. sextet, *J* = 4.2 Hz), 6.33 (1H, dd, *J* = 1.8, 3.0 Hz), 6.19 (1H, d, *J* = 3.0 Hz), 5.00 (1H, ddd, *J* = 3.6, 5.4, 7.8 Hz), 4.21 (1H, dt, *J* = 5.4, 8.4 Hz), 3.73 (1H, d, *J* = 13.2 Hz), 3.68 (1H, d, *J* = 13.2 Hz), 3.50 (1H, dd, *J* = 3.0, 11.4 Hz), 3.30 (1H, t, *J* = 8.4 Hz), 2.96 (1H, dd, *J* = 7.2 , 11.4 Hz), 2.64 (1H, t, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 152.5 (C), 142.3 (C), 137.7 (C), 128.6 (2CH), 128.5 (2CH), 127.4 (CH), 110.5 (CH), 106.6 (CH), 88.3 (CH), 59.0 (CH_2), 57.8 (CH_2), 57.7 (CH_2), 42.6 (CH). IR (neat) ν = 2802.7 (w), 1548.1 (s), 1495.9 (m), 1454.4 (m), 1371.2 (m), 1327.6 (m), 1148.3 (m), 1074.3 (m), 1010.9 (m), 884.2 (w), 810.9 (w), 738.9 (s), 700.4 (m) cm^{-1}. HRMS calculated for $C_{15}H_{17}N_2O_3$ 273.1239, found: 273.1237.

1-Benzyl-3-methyl-3-nitro-4-phenylpyrrolidine, 9:



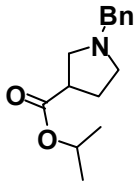
Yield: 88%, t_{Ret} = 4.26 min, m/z = 297.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.27-7.47 (m, 10 H), 4.27 (1H, t, *J* = 7.2 Hz), 3.77 (1H, d, *J* = 13.2 Hz), 3.74 (1H, d, *J* = 10.8 Hz), 3.72 (1H, d, *J* = 13.2 Hz), 3.27 (1H, t, *J* = 9.0 Hz), 2.90 (1H, dd, *J* = 7.9, 9.6 Hz), 2.69 (1H, d, *J* = 10.8 Hz), 1.25 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 138.0 (C), 130.0 (CH), 129.1 (2CH), 128.9 (CH), 128.5 (2x2CH), 128.4 (2CH), 127.4 (C), 96.2 (C), 64.7 (CH_2), 59.5 (CH_2), 58.9 (CH_2), 51.2 (CH), 23.50 (CH_3). IR (neat) ν = 2919.7 (w), 2801.3 (w), 1537.2 (s), 1495.4 (m), 1453.1 (m), 1388.3 (m), 1322.7 (s), 1110.9 (w), 1028.8 (w), 980.8 (w), 870.1 (m), 854.7 (m), 757.1 (m), 740.6 (m), 699.2 (s) cm^{-1}. HRMS calculated for $C_{18}H_{21}N_2O_2$ 297.1603, found: 297.1603.

1-Benzyl-3-(2-chlorophenyl)-4-nitropyrrolidine, 10:



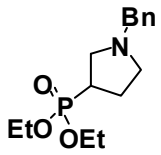
Yield: 93%, t_{Ret} = 4.45 min, m/z = 317.1 ($M+H^+$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.43 (1H, d, *J* = 7.2 Hz), 7.38 (1H, d, *J* = 7.2 Hz), 7.32-7.36 (4H, m), 7.26-7.30 (2H, m), 7.21 (1H, t, *J* = 7.2 Hz), 5.03 (1H, dt, *J* = 4.2, 7.8 Hz), 4.52 (1H, dt, *J* = 4.8, 7.8 Hz), 3.76 (1H, d, *J* = 12.6 Hz), 3.72 (1H, d, *J* = 12.6 Hz), 3.23-3.33 (3H, m), 2.84 (1H, dd, *J* = 6.0, 9.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 138.1 (C), 137.9 (C), 133.9 (C), 129.9 (CH), 128.7 (CH), 128.6 (2CH), 128.5 (2CH), 128.4 (2CH), 127.4 (CH), 90.1 (CH), 59.3 (CH_2), 59.2 (CH_2), 58.5 (CH_2), 45.9 (CH). IR (neat) ν = 2800.8 (w), 1670.8 (m), 1549.8 (s), 1495.3 (m), 1476.3 (m), 1453.7 (m), 1371.5 (m), 1131.1 (m), 1039.3 (m), 755.8 (s), 700.7 (s) cm^{-1}. HRMS calculated for $C_{17}H_{18}N_2O_2Cl$ 317.1057, found: 317.1057.

Isopropyl-1-benzylpyrrolidine-3-carboxylate, 11:



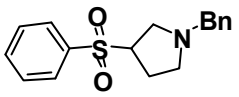
Yield: 86%, t_{Ret} = 2.45 min, m/z = 248.2 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.22-7.35 (5H, m), 5.00 (1H, app. quin., *J* = 6.0 Hz), 3.65 (1H, d, *J* = 13.2 Hz), 3.61 (1H, d, *J* = 13.2 Hz), 2.99 (1H, app. quin., *J* = 7.8 Hz), 2.91 (1H, t, *J* = 9.0 Hz), 2.70-2.75 (1H, m), 2.61 (1H, dd, *J* = 7.2, 9.0 Hz), 2.51 (1H, q, *J* = 8.4 Hz), 2.05-2.12 (2H, m), 1.23 (3H, d, *J* = 6.0 Hz), 1.22 (3H, d, *J* = 6.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 174.6 (C), 138.9 (C), 128.7 (2CH), 128.2 (2CH), 127.0 (CH), 67.7 (CH), 60.1 (CH_2), 56.7 (CH_2), 53.8 (CH_2), 42.3 (CH), 27.6 (CH_2), 21.8 (CH_3), 21.7 (CH_3). IR (neat) ν = 2978.1 (m), 2790.3 (m), 1727.8 (s), 1494.7 (m), 1453.4 (m), 1373.5 (m), 1193.9 (s), 1174.6 (s), 1108.6 (s), 911.1 (m), 855.9 (m), 739.5 (m), 699.7 (s) cm^{-1}. HRMS calculated for $C_{15}H_{22}NO_2Na$ 248.1645, found: 248.1643.

Diethyl-1-benzylpyrrolidin-3-ylphosphonate, 12:



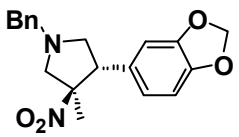
Yield: 92%, t_{Ret} = 2.92 min, m/z = 298.3 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.25-7.36 (5H, m), 4.07-4.13 (4H, m), 3.63 (2H, s), 2.93-2.99 (1H, m), 2.80-2.84 (1H, m), 2.51-2.55 (2H, m), 2.42 (1H, q, *J* = 8.4 Hz), 2.04-2.09 (2H, m), 1.31 (6H, t, *J* = 6.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 138.8 (C), 128.7 (2CH), 128.2 (2CH), 127.0 (CH), 61.7 ($2CH_2$, m), 59.9 (CH_2), 54.2 (CH_2), 53.8 (CH_2, d, *J* = 6.3 Hz), 33.7 (CH, d, *J* = 148 Hz), 25.2 (CH_2, d, *J* = 3.0 Hz), 16.4 ($2CH_3$, m); ^{31}P-NMR (162 MHz, $CDCl_3$): δ/ppm 33.2 (s). IR (neat) ν = 2978.7 (w), 2795.4 (w), 1670.4 (w), 1538.9 (w), 1495.2 (w), 1453.8 (w), 1391.0 (w), 1349.9 (w), 1231.4 (m), 1051.9 (s), 1021.6 (s), 956.9 (s), 850.2 (m), 788.4 (m), 741.8 (s), 698.7 (s) cm^{-1}. HRMS calculated for $C_{15}H_{25}NO_3P$ 298.1572, found: 298.1587.

1-Benzyl-3-(phenylsulfonyl)pyrrolidine, 13:



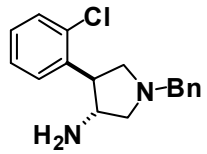
Yield: 83%, t_{Ret} = 2.55 min, m/z = 302.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.89 (2H, d, *J* = 7.2 Hz), 7.66 (1H, t, *J* = 7.2 Hz), 7.56 (2H, t, *J* = 7.2 Hz), 7.28-7.32 (2H, m), 7.25-7.28 (3H, m), 3.76-3.79 (1H, m), 3.71 (1H, d, *J* = 12.6 Hz), 3.66 (1H, d, *J* = 12.6 Hz), 3.02 (1H, br. s), 2.91-2.96 (1H, m), 2.83 (1H, br. s), 2.64 (1H, q, *J* = 7.8 Hz), 2.30-2.34 (1H, m), 2.15 (1H, dt, *J* = 7.8, 17.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 138.3 (C), 133.8 (C), 129.3 (2CH), 128.8 (2CH), 128.5 (2CH), 128.4 (2CH), 127.6 (C+CH), 62.4 (CH), 59.4 (CH_2), 53.4 (CH_2), 53.2 (CH_2), 25.8 (CH_2). IR (neat) ν = 2800.2 (w), 1675.2 (w), 1446.6 (m), 1305.1 (s), 1290.0 (s), 1144.3 (s), 1085.7 (s), 921.7 (m), 732.1 (s), 689.4 (s) cm^{-1}. HRMS calculated for $C_{17}H_{20}NO_2S$ 302.1215, found: 302.1228.

4-(Benzo[*d*][1,3]dioxol-5-yl)-1-benzyl-3-methyl-3-nitropyrrolidine, 14:



Yield: 87%, t_{Ret} = 3.83 min, m/z = 341.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.32-7.38 (4H, m), 7.27-7.29 (1H, m), 6.88 (1H, s), 6.74-6.80 (2H, m), 5.96 (2H, s), 4.16 (1H, t, *J* = 7.2 Hz), 3.74 (1H, d, *J* = 13.2 Hz), 3.67-3.73 (2H, m), 3.21 (1H, dd, *J* = 8.4 Hz), 2.83 (1H, dd, *J* = 7.2, 9.0 Hz), 2.67 (1H, d, *J* = 10.8 Hz), 1.27 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 147.8 (C), 146.9 (C), 138.1 (C), 131.6 (C), 128.5 (2CH), 128.4 (2CH), 127.3 (CH), 122.4 (CH), 109.2 (CH), 108.1 (CH), 101.1 (CH_2), 96.3 (C), 64.5 (CH_2), 59.5 (CH_2), 59.1 (CH_2), 51.6 (CH), 23.4 (CH_3). IR (neat) ν = 2907.7 (w), 2804.0 (w), 1538.3 (s), 1504.3 (s), 1490.3 (s), 1444.6 (m), 1378.7 (w), 1344.3 (w), 1250.6 (m), 1237.0 (m), 1105.3 (w), 1038.5 (s), 933.9 (m), 858.9 (m), 811.1 (w), 739.3 (m), 700.1 (m) cm^{-1}. HRMS calculated for $C_{19}H_{21}N_2O_4$ 341.1501, found: 341.1510.

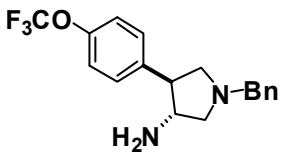
1-Benzyl-4-(2-chlorophenyl)pyrrolidine-3-amine, 15:



Yield: 95%, t_{Ret} = 3.67 min, m/z = 287.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.44 (1H, dd, *J* = 1.2, 7.8 Hz), 7.30-7.36 (5H, m), 7.22-7.26 (2H, m), 7.12 (1H, dt, *J* = 1.2, 7.8 Hz), 3.72 (1H, d, *J* = 12.6 Hz), 3.64 (1H, d, *J* = 12.6 Hz), 3.50-3.57 (2H, m), 3.12 (1H, dd, *J* = 6.6, 9.6 Hz), 3.08 (1H, dd, *J* = 8.1, 9.6 Hz), 2.70 (1H, dd, *J* = 5.4, 9.6

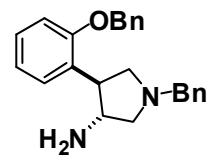
Hz), 2.42-2.49 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 141.2 (C), 138.6 (C), 133.9 (C), 129.3 (CH), 128.8 (2CH), 128.3 (2CH), 128.2 (CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 62.9 (CH_2), 60.3 (CH_2), 60.1 (CH_2), 59.8 (CH), 50.6 (CH). IR (neat) ν = 2909.9 (w), 2791.2 (m), 1671.9 (m), 1569.1 (m), 1494.9 (m), 1474.6 (m), 1453.0 (m), 1439.8 (m), 1377.8 (m), 1339.5 (m), 1259.4 (m), 1126.5 (m), 1034.1 (m), 858.8 (m), 751.2 (s), 699.2 (s) cm^{-1}. HRMS calculated for $C_{17}H_{20}N_2Cl$ 287.1315, found: 287.1322.

1-Benzyl-4-(4-(trifluoromethoxy)phenyl)pyrrolidine-3-amine, 16:



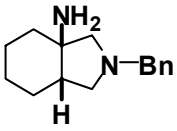
Yield: 97%, t_{Ret} = 4.35 min, m/z = 337.1 (M+H$^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.29-7.36 (5H, m), 7.24-7.27 (2H, m), 7.14 (2H, d, *J* = 7.8 Hz), 3.70 (1H, d, *J* = 13.2 Hz), 3.64 (1H, d, *J* = 13.2 Hz), 3.44 (1H, q, *J* = 6.6 Hz), 3.09 (1H, app. t, *J* = 9.0 Hz), 3.02 (1H, dd, J = 7.8, 9.6 Hz), 2.93 (1H, q, *J* = 7.2 Hz), 2.64 (1H, dd, *J* = 7.8, 9.0 Hz), 2.54 (1H, dd, *J* = 6.0, 9.6 Hz), 2.18 (2H, br. s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 147.8 (C), 142.3 (C), 138.7 (C), 128.7 (2x2CH), 128.3 (2CH), 127.0 (CH), 121.0 (2CH), 120.5 (CF_3, q, *J* = 255 Hz) 63.5 (CH_2), 61.3 (CH_2), 60.3 (CH_2), 60.2 (CH), 54.5 (CH). IR (neat) ν = 2793.3 (w), 1508.7 (m), 1453.9 (w), 1254.5 (s), 1219.4 (s), 1156.3 (s), 1019.4 (m), 919.9 (m), 846.9 (m), 810.1 (m), 737.6 (m), 698.7 (s), 677.0 (m) cm^{-1}. HRMS calculated for $C_{18}H_{20}F_3N_2O$ 337.1528, found: 337.1521.

1-Benzyl-4-(2-(benzyloxy)phenyl)pyrrolidin-3-amine, 17:



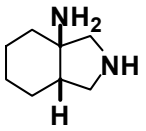
Yield: 93%, t_{Ret} = 3.54 min, m/z = 359.2 (M+H$^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.40-7.44 (4H, m), 7.18-7.38 (8H, m), 6.91 (1H, d, *J* = 7.8 Hz), 6.88 (1H, t, *J* = 7.8 Hz), 5.88 (2H, br. s), 5.06 (1H, d, *J* = 13.2 Hz), 5.04 (1H, d, *J* = 13.2 Hz), 3.83 (1H, br. s), 3.67 (1H, d, *J* = 13.2 Hz), 3.59 (1H, d, *J* = 13.2 Hz), 3.51-3.54 (1H, m), 3.27 (1H, t, *J* = 9.0 Hz), 3.01-3.05 (1H, m), 2.88-2.94 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 156.2 (C), 136.6 (C), 129.9 (CH), 129.5 (2CH), 129.0 (2CH), 128.7 (CH), 128.7 (2CH), 128.6 (CH), 128.4 (2CH), 128.3 (CH), 126.9 (2C), 121.6 (CH), 111.9 (CH), 70.4 (CH_2), 59.4 (CH_2), 58.9 (CH_2), 57.0 (CH_2), 56.3 (CH), 50.5 (CH). IR (neat) ν = 2700-3250 (br.), 1600.4 (m), 1585.6 (m), 1493.4 (m), 1451.8 (m), 1377.6 (m), 1237.3 (m), 1120.5 (m), 1007.9 (s), 911.6 (m), 853.8 (m), 748.7 (s), 734.4 (s), 697.3 (s) cm^{-1}. HRMS calculated for $C_{24}H_{27}N_2O$ 359.2123, found: 359.2118.

2-Benzyloctahydro-1*H*-isoindole-*3a*-amine, 18:



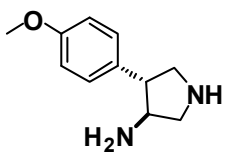
Yield: 97%, t_{Ret} = 0.41 min, m/z 231.2 (M+H$^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.33-7.28 (4H, m), 7.22 (1H, t, *J* = 6.6 Hz), 3.75 (1H, d, *J* = 13.2 Hz), 3.72 (1H, d, *J* = 13.2 Hz), 3.01 (1H, dd, *J* = 7.8, 9.0 Hz), 2.75 (1H, s, *J* = 9.0 Hz), 2.51 (1H, dd, *J* = 5.4, 9.6 Hz), 2.47 (1H, d, *J* = 9.0 Hz), 1.75-1.83 (2H, m), 1.60-1.73 (3H, m), 1.48-1.55 (2H, m), 1.37-1.45 (2H, m), 1.27-1.35 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 139.8 (C), 128.5 (2CH), 128.1 (2CH), 126.7 (CH), 65.4 (CH_2), 61.0 (CH_2), 57.8 (CH_2), 57.7 (C), 45.9 (CH), 34.6 (CH_2), 27.4 (CH_2), 22.7 (CH_2), 22.1 (CH_2). IR (neat) ν = 2923.2 (m), 2854.1 (m), 2785.7 (m), 1602.7 (m), 1494.8 (m), 1451.2 (m), 1311.94 (w), 1214.1 (w), 1150.2 (m), 1071.9 (m), 1028.1 (m), 833.1 (m), 736.5 (s), 697.7 (s) cm^{-1}. HRMS calculated for $C_{15}H_{23}N_2$ 231.1861, found: 231.1858.

Octahydro-1*H*-isoindol-3a-amine, 19:



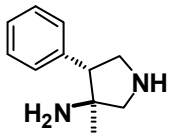
Yield: 90%, t_{Ret} = 0.41 min, m/z = 141.0 (M+H$^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 3.25 (1H, dd, *J* = 7.2, 10.2 Hz), 2.99 (1H, d, *J* = 10.8 Hz), 2.78 (1H, dd, *J* = 4.8, 10.2 Hz), 2.59 (1H, d, *J* = 10.8 Hz), 1.20-1.75 (12H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 58.4 (C), 57.6 (CH_2), 50.7 (CH_2), 46.3 (CH), 34.4 (CH_2), 27.0 (CH_2), 23.2 (CH_2), 22.7 (CH_2). IR (neat) ν = 3000-3400 (br.), 2925.3 (s), 2854.5 (m), 1655.7 (m), 1447.4 (m), 1259.4 (m), 1065.8 (m), 1019.1 (m), 795.6 (s), 729.2 (s), 700.2 (s) cm^{-1}. HRMS calculated for $C_8H_{17}N_2$ 141.1388, found: 141.1386.

4-(4-Methoxyphenyl)pyrrolidin-3-amine, 20:



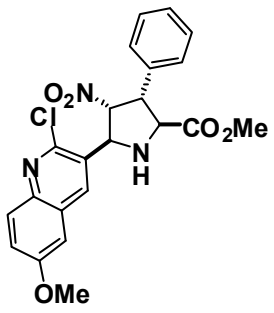
Yield: 93%, t_{Ret} = 0.51 min, m/z = 193.1 ($M+H^+$). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 7.17 (2H, d, *J* = 8.7 Hz), 6.87 (2H, d, *J* = 8.7 Hz), 3.84 (3H, br. s), 3.78 (3H, s), 3.60-3.42 (3H, m), 3.15 (1H, t, *J* = 15.0 Hz), 2.97-2.86 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 158.9 (C), 130.6 (C), 128.5 (2CH), 114.4 (2CH), 59.2 (CH_3), 55.3 (CH), 53.3 (CH), 52.3 (CH_2), 51.3 (CH_2). IR (neat) ν = 2800-3500 (br.), 2923.7 (m), 1610.3 (m), 1582.2 (m), 1512.8 (s), 1441.0 (m), 1247.0 (s), 1179.5 (s), 1111.7 (m), 1031.9 (s), 831.8 (m), 757.5 (m), 704.0 (m) cm^{-1}. HRMS calculated for $C_{11}H_{17}N_2O$ 193.1341, found: 193.1347.

3-Methyl-4-phenylpyrrolidin-3-amine, 21:



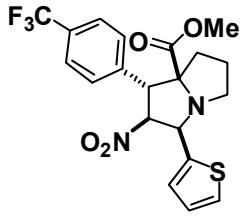
Yield: 95%, t_{Ret} = 0.31 min, m/z = 177.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.35 (2H, t, *J* = 7.2 Hz), 7.29 (1H, t, *J* = 7.2 Hz), 7.24 (2H, d, *J* = 7.2 Hz), 4.12 (3 H, br. s), 3.75 (1H, dd, *J* = 8.4, 12.0 Hz), 3.54 (1H, dd, *J* = 8.4, 12.0 Hz), 3.22 (1H, t, *J* = 7.8 Hz), 3.17 (1H, d, *J* = 12.6 Hz), 3.13 (1H, d, *J* = 12.6 Hz), 0.95 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 137.2 (C), 128.6 (2CH), 128.1 (2CH), 127.5 (CH), 60.6 (C), 57.0 (CH_2), 55.8 (CH), 48.8 (CH_2), 23.3 (CH_3). IR (neat) ν = 2900-3400 (br.), 1650.3 (m), 1555.4 (m), 1454.1 (m), 1403.6 (m), 1275.7 (m), 1260.9 (m), 764.6 (s), 750.1 (s), 702.8 (m) cm^{-1}. HRMS calculated for $C_{11}H_{17}N_2$ 177.1392, found: 177.1398.

Methyl-5-(2-chloro-6-methoxyquinolin-3-yl)-3-nitro-4-phenylpyrrolidine-2-carboxylate, 22:



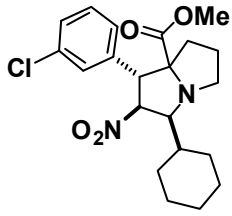
Yield: 32%, t_{Ret} = 4.76 min, m/z 442.2 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.87 (1H, s), 7.94 (1H, d, *J* = 9.0 Hz), 7.41 (1H, dd, *J* = 3.0, 9.0 Hz), 7.30-7.33 (3H, m), 7.21 (1H, d, *J* = 3.0 Hz), 7.18 (2H, d, *J* = 7.2 Hz), 5.47 (1H, s), 5.16 (1H, d, *J* = 6.6 Hz), 4.95 (1H, d, *J* = 11.4 Hz), 3.96 (4H, m), 3.77 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 173.2 (C), 158.5 (C), 146.0 (C), 143.3 (C), 137.6 (CH), 132.7 (C), 132.5 (C), 129.5 (CH), 129.0 (2CH), 128.7 (CH), 128.5 (C), 128.2 (2CH), 127.8 (CH), 105.6 (CH), 95.7 (CH), 62.8 (CH), 62.2 (CH), 55.7 (CH_3), 52.6 (CH), 50.9 (CH_3). IR (neat) ν = 1739.6 (m), 1622.2 (m), 1591.5 (s), 1548.9 (s), 1497.2 (s), 1348.2 (m), 1227.9 (s), 1162.0 (m), 1047.3 (m), 832.2 (m), 736.5 (m), 698.7 (m) cm^{-1}. HRMS calculated for $C_{22}H_{21}N_3O_5Cl$ 442.1170, found: 442.1188; X-ray data: CCDC 782326; space group Pbca; Unit cell parameters: a = 19.6970(2) Å, b = 9.3719(1) Å, c = 22.1754(3) Å, α = 90 °, β = 90 °, γ = 90 °.

Methyl-2-nitro-3-(thiophen-2-yl)-1-(4-(trifluoromethyl)phenyl)hexahydro-1*H*-pyrrolizine-7a-carboxylate, 23:



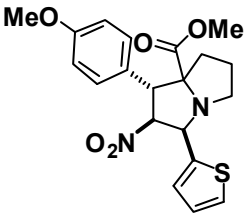
Yield: 79%, t_{Ret} = 5.18 min, m/z 441.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.59 (2H, d, *J* = 7.8 Hz), 7.32-7.38 (3H, m), 7.05 (1H, d, *J* = 2.4 Hz), 7.02 (1H, t, *J* = 4.2 Hz), 6.38 (1H, dd, *J* = 7.8, 11.4 Hz), 5.61 (1H, d, *J* = 7.8 Hz), 4.42 (1H, d, *J* = 11.4 Hz), 3.38 (3H, s), 2.94 (1H, dt, *J* = 7.8, 9.0 Hz), 2.76-2.81 (2H, m), 2.15-2.19 (1H, m), 2.01-2.07 (1H, m), 1.90-2.00 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 173.4 (C), 138.2 (C), 137.3 (C), 130.3 (C, q, *J* = 34 Hz), 129.8 (CH), 128.3 (C, q, *J* = 267 Hz), 127.6 (2CH), 127.1 (CH), 127.0 (CH), 125.7 (2CH, q, *J* = 3 Hz), 90.9 (CH), 79.8 (C), 61.9 (CH), 53.1 (CH), 52.0 (CH_3), 46.1 (CH_2), 34.8 (CH_2), 27.6 (CH_2). IR (neat) ν = 1731.8 (m), 1621.4 (w), 1549.2 (s), 1433.8 (w), 1371.5 (w), 1324.6 (s), 1165.1 (s), 1118.0 (s), 1067.1 (s), 1017.6 (m), 910.1 (m), 838.3 (m), 728.2 (m), 705.3 (s) cm^{-1}. HRMS calculated for $C_{20}H_{20}N_2O_4F_3S$ 441.1096, found: 441.1075; X-ray data: CCDC 782329; space group P2(1)/n; Unit cell parameters: a = 12.3233(2) Å, b = 13.7686(2) Å, c = 14.1185(2) Å, α = 90 °, β = 114.309(1) °, γ = 90 °.

Methyl-1-(3-chlorophenyl)-3-cyclohexyl-2-nitrohexahydro-1*H*-pyrrolizine-7a-carboxylate, 24:



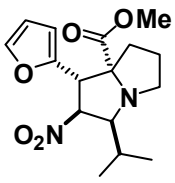
Yield: 89%, t_{Ret} = 5.07 min, m/z 407.2 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.20-7.25 (2H, m), 7.10 (1H, s), 6.99 (1H, d, *J* = 6.6 Hz), 4.17 (1H, dd, *J* = 7.2, 10.8 Hz), 3.83 (1H, d, *J* = 6.0 Hz), 3.44 (1H, dd, *J* = 7.8, 14.4 Hz), 3.25 (3H, s), 3.15 (1H, dd, *J* = 7.8, 15.6 Hz), 2.40-2.50 (1H, m), 2.19-2.28 (2H, m), 2.09 (1H, d, *J* = 12.0 Hz), 1.88-1.93 (1H, m), 1.63-1.72 (6H, m), 1.21-1.35 (4H, m), 1.11 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 172.4 (C), 138.6 (C), 134.6 (C), 129.9 (CH), 128.0 (CH), 127.7 (CH), 125.8 (CH), 98.0 (CH), 83.4 (C), 73.1 (CH), 63.3 (CH), 51.5 (CH_3), 47.0 (CH_2), 37.3 (CH), 34.0 (CH_2), 32.2 (CH_2), 30.9 (CH_2), 26.3 (CH_2), 25.7 (CH_2), 25.5 (CH_2), 22.7 (CH_2), . IR (neat) ν = 2925.7 (m), 2853.4 (m), 1732.9 (s), 1545.2 (s), 1449.6 (m), 1432.9 (m), 1336.0 (m), 1281.6 (m), 1227.6 (m), 1194.8 (m), 1152.1 (m), 1114.1 (m), 1082.9 (m), 1061.8 (m), 781.7 (m), 729.8 (m), 694.0 (s) cm^{-1}. HRMS calculated for $C_{21}H_{27}N_2O_4Cl$ 407.1738, found: 407.1750.

Methyl-2-nitro-3-(thiophen-2-yl)-1-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine-7a-carboxylate, 25:



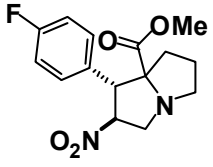
Yield: 76%, t_{Ret} = 5.18 min, m/z 441.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.33 (1H, d, *J* = 4.8 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 7.03 (1H, d, *J* = 3.0 Hz), 6.99 (1H, t, *J* = 4.2 Hz), 6.84 (2H, d, *J* = 8.4 Hz), 6.31 (1H, dd, *J* = 8.4, 12.0 Hz), 5.60 (1H, d, *J* = 7.8 Hz), 4.31 (1H, d, *J* = 11.4 Hz), 3.77 (3H, s), 3.40 (3H, s), 2.92 (1H, dt, *J* = 7.2, 9.0 Hz), 2.72-2.80 (2H, m), 2.10-2.17 (1H, m), 1.95-2.00 (1H, m), 1.86-1.93 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 173.9 (C), 159.3 (C), 137.7 (C), 129.6 (CH), 128.2 (2CH), 127.0 (CH), 126.9 (CH), 125.8 (C), 114.2 (2CH), 91.3 (CH), 80.0 (C), 62.0 (CH), 55.2 (CH_3), 52.8 (CH), 52.0 (CH_3), 46.3 (CH_2), 34.8 (CH_2), 27.6 (CH_2). IR (neat) ν = 2952.2 (w), 1730.2 (m), 1612.4 (w), 1547.5 (s), 1514.4 (s), 1441.1 (m), 1370.5 (m), 1303.7 (m), 1250.6 (s), 1179.3 (s), 1120.4 (m), 1030.6 (s), 834.9 (s) 703.6 (s) cm^{-1}. HRMS calculated for $C_{20}H_{23}N_2O_5S$ 441.1096, found: 441.1075.

Methyl-1-(furan-2-yl)-3-isopropyl-2-nitrohexahydro-1*H*-pyrrolizine-7a-carboxylate, 26:



Yield: 82%, t_{Ret} = 4.47 min, m/z 323.2 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.32 (1H, s), 6.31 (1H, s), 6.18 (1H, d, *J* = 3.0 Hz), 5.48 (1H, t, *J* = 6.6 Hz), 3.97-4.05 (2H, m), 3.45 (3H, s), 3.39-3.44 (1H, m), 3.18 (1H, q, *J* = 7.8 Hz), 2.52 (1H, dt, *J* = 8.4, 13.2 Hz), 2.33 (1H, ddd, *J* = 5.4, 8.4, 13.2 Hz), 2.15-2.23 (1H, m), 1.92-2.05 (2H, m), 1.20 (3H, d, *J* = 6.0 Hz), 1.03 (3H, d, *J* = 6.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 172.1 (C), 149.9 (C), 142.4 (CH), 110.6 (CH), 107.5 (CH), 96.2 (CH), 81.4 (C), 73.9 (CH), 56.0 (CH), 52.2 (CH_3), 46.9 (CH_2), 33.8 (CH_2), 27.8 (CH), 22.7 (CH_2), 22.3 (CH_3), 20.7 (CH_3). IR (neat) ν = 2953.8 (w), 2877.6 (w), 1736.5 (s), 1547.9 (s), 1370.7 (m), 1336.5 (m), 1233.1 (m), 1148.7 (m), 1080.9 (m), 1066.9 (m), 1012.4 (m), 913.4 (m), 735.7 (s) cm^{-1}. HRMS calculated for $C_{16}H_{23}N_2O_5$ 323.1607, found: 323.1603; X-ray data: CCDC 782330; space group P2(1)/c; Unit cell parameters: a = 7.83550(1) Å, b = 12.8006(2) Å, c = 17.5169(3) Å, α = 90 °, β = 99.445(1) °, γ = 90 °.

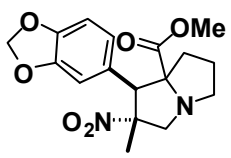
Methyl 1-(4-fluorophenyl)-2-nitrohexahydro-1*H*-pyrrolizine-7a-carboxylate, 27:



Yield: 78%, t_{Ret} = 4.36 min, m/z 309.2 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.24 (2H, dd, *J* = 5.4, 8.4 Hz), 6.97 (2H, app. t, *J* = 9.0 Hz), 5.73 (1H, d, *J* = 10.2 Hz), 4.00 (1H, dt, *J* = 7.2, 10.8 Hz), 3.79 (3H, s), 3.27-3.30 (1H, m), 3.24 (1H, t, *J* = 12.6 Hz), 3.17 (1H, dd, *J* = 7.2, 12.6 Hz), 2.72-2.78 (1H, m), 2.32 (1H, dd, *J* = 6.0, 12.6 Hz), 1.76-1.97 (2H, m), 1.55 (1H, dt, *J* = 7.2, 12.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 173.3 (C), 162.1 (C, d, *J* = 240 Hz), 132.1 (C), 129.1 (2CH, d, *J* = 8 Hz), 115.7 (2CH, d, *J* = 14 Hz), 96.0 (CH), 77.8 (C), 58.4 (CH_2), 56.9 (CH_2), 53.2 (CH_3), 42.3 (CH), 32.0 (CH_2), 26.2 (CH_2). IR (neat) ν = 2956.1 (w), 2876.5 (w), 1731.9 (s), 1606.2 (w), 1546.1 (s), 1511.6 (s), 1369.9 (m), 1272.6 (m), 1224.3 (s), 1161.7 (s), 1013.7 (m), 835.7 (s), 718.6 (m) cm^{-1}. HRMS calculated for $C_{15}H_{18}N_2O_4F$,

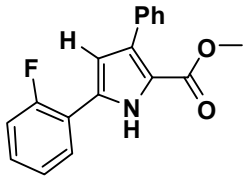
309.1239 found: 309.1243.

Methyl-1-(benzo[*d*][1,3]dioxol-5-yl)-2-methyl-2-nitrohexahydro-1*H*-pyrrolizine-7a-carboxylate, 28:



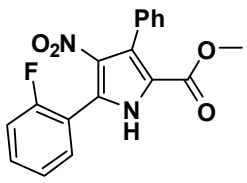
Yield: 83%, t_{Ret} = 3.95 min, m/z 349.1 ($M+H^+$). Diastereoisomer 1: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 6.72-6.75 (2H, m), 6.69 (1H, d, *J* = 8.4 Hz), 5.93 (2H, d, *J* = 3.6 Hz), 4.11 (1H, dd, *J* = 7.8, 10.8 Hz), 3.81 (3H, s), 3.66 (1H, d, *J* = 4.2 Hz), 3.64 (1H, d, *J* = 7.2 Hz), 3.27 (1H, t, *J* = 7.2 Hz), 3.00 (1H, ddd, *J* = 5.4, 7.8, 10.8 Hz), 2.65 (1H, dd, *J* = 7.2, 13.2 Hz), 2.03-2.10 (1H, m), 1.88-1.98 (1H, m), 1.48 (3H, s), 1.45-1.49 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 174.0 (C), 147.9 (C), 147.6 (C), 126.7 (C), 122.8 (CH), 109.2 (CH), 108.3 (CH), 101.2 (CH_2), 97.9 (C), 86.0 (C), 57.6 (CH_2), 57.3 (CH), 55.1 (CH_2), 53.1 (CH_3), 31.0 (CH_2), 28.4 (CH_2), 19.4 (CH_3). Diastereoisomer 2: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 6.73 (1H, d, *J* = 8.4 Hz), 6.71 (1H, s), 6.67 (1H, d, *J* = 8.4 Hz), 5.92 (2H, d, *J* = 4.8 Hz), 4.40 (1H, dd, *J* = 7.8, 12.0 Hz), 3.79 (3H, s), 3.59 (1H, t, *J* = 12.0 Hz), 3.42 (1H, t, *J* = 7.8 Hz), 3.10 (1H, dd, *J* = 7.8, 12.0 Hz), 2.81 (1H, ddd, *J* = 5.4, 9.6, 15.0 Hz), 2.37 (1H, dd, *J* = 6.0, 12.6 Hz), 1.95-2.02 (1H, m), 1.91-1.94 (1H, m), 1.84-1.88 (1H, m), 1.63 (1H, ddd, *J* = 5.4, 11.4, 16.8 Hz), 1.39 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 173.0 (C), 147.8 (C), 147.2 (C), 127.5 (C), 122.2 (CH), 109.1 (CH), 108.3 (CH), 101.1 (CH_2), 98.8 (C), 83.1 (C), 57.6 (CH_2), 56.3 (CH_2), 52.6 (CH_3), 47.6 (CH), 34.9 (CH_2), 25.2 (CH_2), 18.6 (CH_3). IR (neat) ν = 2949.9 (w), 2874.6 (w), 1729.9 (s), 1539.6 (s), 1504.9 (m), 1488.3 (s), 1442.7 (s), 1390.4 (m), 1350.0 (w), 1306.1 (w), 1255.8 (s), 1234.3 (s), 1167.6 (s), 1036.2 (s), 930.9 (s), 864.9 (m), 814.7 (m), 731.4 (m) cm^{-1}. HRMS calculated for $C_{17}H_{21}N_2O_6$, 349.1400 found: 349.1384.

Methyl-5-(2-fluorophenyl)-3-phenyl-1*H*-pyrrole-2-carboxylate, 29:



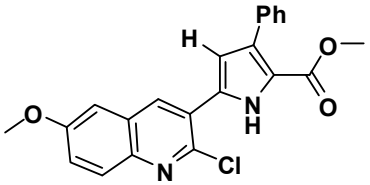
Yield: 22%, t_{Ret} = 5.06 min, m/z = 318.2 ($M+Na^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 9.73 (1H, br. s), 7.67 (1H, ddd, *J* = 1.3, 7.8, 7.8 Hz), 7.62-7.60 (2H, m), 7.41 (2H, pt, *J* = 7.6 Hz), 7.34 (1H, pt, *J* = 7.4 Hz), 7.29 (1H, dd, *J* = 13.2, 6.0 Hz), 7.23-7.16 (2H, m), 6.75 (1H, d, *J* = 2.9 Hz), 3.82 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 161.3 (C), 159.3 (C, d, *J* = 247 Hz), 134.9 (C), 133.0 (C), 130.2 (C, d, *J* = 2 Hz), 129.6 (2CH), 129.2 (CH, d, *J* = 9 Hz), 128.0 (2CH), 127.5 (CH, d, *J* = 4 Hz), 127.3 (CH), 125.0 (CH, d, *J* = 3 Hz), 118.8 (C, d, *J* = 11 Hz), 118.6 (C, d, *J* = 2 Hz), 116.7 (CH, d, *J* = 23 Hz), 111.6 (CH, d, *J* = 2 Hz), 51.6 (CH_3). IR (neat) ν = 3462 (bw), 3287 (bw), 2985 (m), 1715 (s), 1687 (s), 1492 (m), 1471 (s), 1453 (s), 1234 (s), 1124 (m), 1107 (m), 1067 (m), 1009 (m), 946 (w), 817 (m), 761 (s), 698 (m) cm^{-1}. HRMS calculated for $C_{18}H_{15}NO_2F^+$ 296.1081, found: 296.1070.

Methy-5-(2-fluorophenyl)-4-nitro-3-phenyl-1*H*-pyrrole-2-carboxylate, 30:



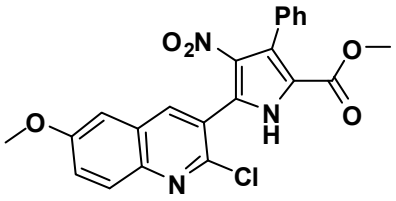
Yield: 20%, t_{Ret} = 4.78 min, m/z = 339.1 ($M-H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 10.21 (1H, br. s), 7.54 (1H, t, *J* = 7.3 Hz), 7.49-7.45 (1H, m), 7.41-7.36 (5H, m), 7.26 (1H, dd, *J* = 6.9, 8.1 Hz), 7.20 (1H, t, *J* = 9.2 Hz), 3.54 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 161.3 (C), 160.1 (C, d, *J* = 251 Hz), 134.6 (C), 132.1 (CH, d, *J* = 9 Hz), 131.0 (C), 130.9 (CH), 129.9 (2CH), 128.6 (C), 128. (CH), 127.8 (2CH), 127.4 (C), 124.5 (CH, d, *J* = 4 Hz), 119.1 (C), 117.2 (C, d, *J* = 14 Hz), 116.3 (CH, d, *J* = 22 Hz), 52.2 (CH_3). IR (neat) ν = 3258 (w), 2955 (w), 1677 (s), 1621 (w), 1584 (w), 1560 (w), 1496 (s), 1449 (s), 1409 (m), 1365 (m), 1338 (m), 1298 (s), 1279 (s), 1236 (m), 1206 (m), 1168 (w), 1104 (w), 1033 (w), 945 (s), 912 (w), 859 (m), 814 (m), 757 (s), 738 (s), 697 (s) cm^{-1}. HRMS calculated for $C_{18}H_{14}N_2O_4F^+$ 341.0938 found: 341.0936. X-ray data: CCDC782327; space group P2(1)/n; Unit cell parameters: a = 14.1489 Å, b = 11.6603 Å, c = 19.3413 Å, α = 90°, β = 100.28°, γ = 90°.

Methyl-5-(2-chloro-6-methoxyquinolin-3-yl)-3-phenyl-1*H*-pyrrole-2-carboxylate, 31:



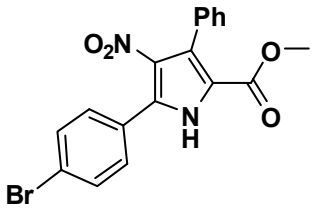
Yield: 20%, t_{Ret} = 5.30 min, m/z = 393.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 9.91 (1H, br. s), 8.25 (1H, s), 7.92 (1H, d, *J* = 9.2 Hz), 7.62 (2H, d, *J* = 7.2 Hz), 7.43-7.40 (2H, m), 7.39 (1H, dd, *J* = 2.7, 9.2 Hz), 7.37-7.35 (1H, m), 7.08 (1H, d, *J* = 2.7 Hz), 6.01 (1H, d, *J* = 3.1 Hz), 3.94 (3H, s), 3.82 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 161.2 (C), 158.7 (C), 144.2 (C), 142.7 (C), 136.3 (CH), 134.5 (C), 132.8 (C), 130.4 (C), 129.7 (CH), 129.4 (2CH), 128.2 (C), 127.9 (2CH), 127.3 (CH), 124.4 (C), 123.8 (CH), 119.1 (C), 114.0 (CH), 104.8 (CH), 55.6 (CH_3), 51.6 (CH_3); IR (neat) ν = 3292 (m), 2949 (w), 1662 (s), 1621 (m), 1604 (w), 1562 (w), 1496 (m), 1480 (m), 1455 (m), 1364 (w), 1346 (s), 1279 (s), 1206 (m), 1165 (m), 1138 (m), 1036 (s), 1006 (w), 957 (w), 909 (w), 827 (m), 809 (m), 763 (s), 699 (s) cm^{-1}. HRMS calculated for $C_{22}H_{18}N_2O_3Cl^+$ 393.1006, found: 393.1005.

Methyl-5-(2-chloro-6-methoxyquinolin-3-yl)-4-nitro-3-phenyl-1*H*-pyrrole-2-carboxylate, 32:



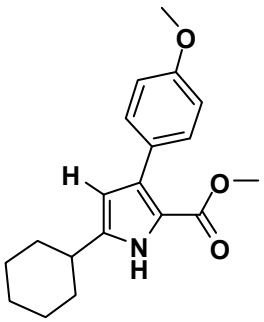
Yield: 24%, t_{Ret} = 5.07 min, m/z = 438.1 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 10.31 (1H, br. s), 8.16 (1H, s), 7.94 (1H, d, *J* = 9.2 Hz), 7.46-7.38 (6H, m), 7.03 (1H, d, *J* = 2.3 Hz), 3.93 (3H, s), 3.53 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 160.9 (C), 158.7 (C), 146.2 (C), 143.7 (C), 139.2 (CH), 134.6 (C), 130.6 (C), 130.1 (C), 129.9 (2CH), 129.8 (CH), 128.2 (CH), 127.7 (2CH), 127.2 (CH), 127.1 (C), 124.7 (CH), 123.0 (C); 119.3 (C), 105.3 (CH), 55.7 (CH_3), 52.1 (CH_3); IR (neat) ν = 3676 (w), 2988 (s), 2901 (s), 1705 (w), 1620 (w), 1495 (m), 1451 (m), 1404 (m), 1354 (m), 1275 (m), 1228 (s), 1159 (w), 1079 (s), 1066 (s), 907 (w), 834 (m), 725 (m), 696 (m) cm^{-1}. HRMS calculated for $C_{22}H_{17}N_3O_5Cl^+$ 438.0857, found: 438.0855. X-ray data: CCDC 782328; space group P-1; Unit cell parameters: a = 9.5144 Å, b = 9.6002 Å, c = 12.5135 Å, α = 75.501°, β = 86.354°, γ = 75.572°.

Methyl 5-(4-bromophenyl)-4-nitro-3-phenyl-1*H*-pyrrole-2-carboxylate, 33:



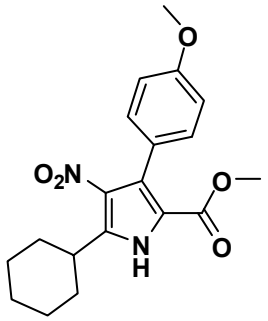
Yield: 40%, t_{Ret} = 5.15 min, m/z = 423.0 ($M+Na^+$). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 9.79 (1H, br. s), 7.62 (2H, d, *J* = 8.5 Hz), 7.48 (2H, d, *J* = 8.5 Hz), 7.42-7.40 (3H, m), 7.36-7.34 (2H, m), 3.61 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 161.2 (C), 133.5 (C), 132.1 (2CH), 131.0 (C), 130.7 (2CH), 129.8 (2CH), 128.3 (CH), 127.9 (2CH), 127.8 (C), 127.7 (C), 124.8 (C), 118.8 (C), 52.2 (CH_3); IR (neat) ν = 3355 (w), 3314 (w), 3171 (w), 2924 (w), 1708 (m), 1683 (s), 1658 (s), 1619 (s), 1563 (m), 1492 (s), 1449 (m), 1384 (m), 1358 (s), 1197 (m), 1101 (m), 1068 (s), 1010 (s), 951 (w), 843 (m), 831 (m), 765 (s), 699 (s) cm^{-1}. HRMS calculated for $C_{18}H_{14}N_2O_4Br$ 401.0137, found: 401.0152.

Methyl 5-cyclohexyl-3-(4-methoxyphenyl)-1H-pyrrole-2-carboxylate, 34:



Yield: 21%, t_{Ret} = 5.20 min, m/z = 314.2 ($M+H^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.84 (1H, br. s), 7.50 (2H, d, *J* = 8.5 Hz), 6.91 (2H, d, *J* = 8.5 Hz), 6.05 (1H, d, *J* = 2.7 Hz), 3.84 (3H, s), 3.76 (3H, s), 2.61-2.58 (1H, m), 2.03 (2H, d, *J* = 11.3 Hz), 1.84 (2H, d, *J* = 12.3 Hz), 1.74 (1H, d, *J* = 12.2 Hz), 1.46-1.35 (4H, m), 1.29-1.23 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 161.5 (C), 158.7 (C), 142.5 (C), 132.5 (C), 130.4 (2CH), 127.9 (C), 115.4 (C), 113.2 (2CH), 108.3 (CH), 55.2 (CH_3), 51.0 (CH_3), 36.8 (CH), 32.7 ($2CH_2$), 26.1 ($2CH_2$), 25.9 (CH_2). IR (neat) ν = 3307 (w), 2926 (m), 2851 (w), 1664 (s), 1611 (w), 1523 (s), 1449 (s), 1364 (w), 1246 (s), 1177 (s); 1100 (m), 908 (m), 835 (m), 806 (m), 731 (s) cm^{-1}. HRMS calculated for $C_{19}H_{24}NO_3$ 314.1756, found: 314.1758.

Methyl 5-cyclohexyl-3-(4-methoxyphenyl)-4-nitro-1H-pyrrole-2-carboxylate, 35:



Yield: 10%, t_{Ret} = 5.05 min, m/z = 381.19 ($M+Na^+$). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 9.09 (1H, br. s). 7.23 (2H, d, *J* = 8.6 Hz), 6.92 (2H, d, *J* = 8.6 Hz), 3.85 (3H, s), 3.69 (3H, s), 3.47 (1H, tt, *J* = 2.84, 11.7 Hz), 2.11 (2H, d, *J* = 11.7 Hz), 1.90 (2H, d, *J* = 13.1 Hz), 1.82 (1H, d, *J* = 13.1 Hz), 1.52-1.46 (2H, m), 1.41 (2H, ddd, *J* = 2.4, 12.1, 15.2 Hz), 1.27-1.25 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 160.9 (C), 159.2 (C), 142.7 (C), 131.0 (2CH), 127.3 (C), 123.4 (C), 116.9 (C), 113.1 (2CH), 55.2 (CH_3), 51.9 (CH_3), 36.1 (CH), 31.6 ($2CH_2$), 26.1 ($2CH_2$), 25.8 (CH_2). IR (neat) ν = 3295 (w), 2930 (m), 2854 (w), 1695 (s), 1613 (w), 1528 (m), 1493 (s), 1446 (s), 1358 (s), 1245 (s), 1176 (m), 1096 (w), 1034 (m), 909 (m), 846 (m), 830 (m), 782 (m), 729 (s) cm^{-1}. HRMS calculated for $C_{19}H_{23}N_2O_5$ 359.1607, found: 359.1617.

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