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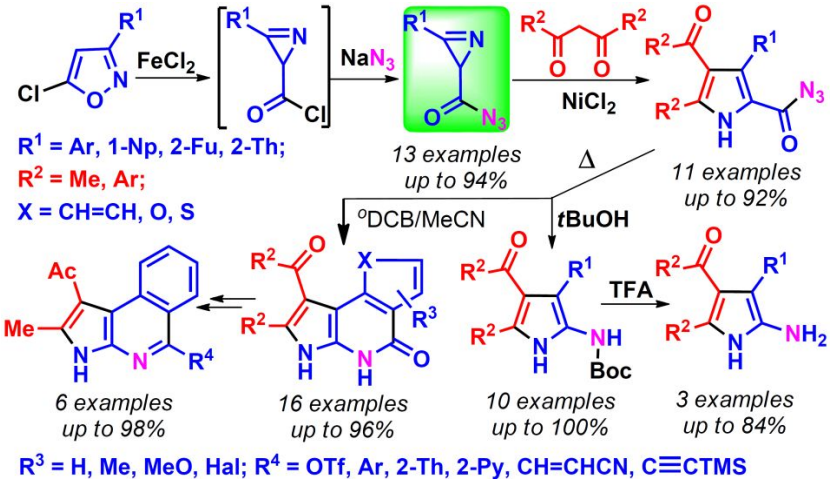
2*H*-Azirine-2-carbonyl Azides: Preparation and Use as N-Heterocyclic Building Blocks

*Liya D. Funt, Yulia V. Krivolapova, Olesya V. Khoroshilova, Mikhail S. Novikov, Alexander F. Khlebnikov**

Saint Petersburg State University, Institute of Chemistry, 7/9 Universitetskaya nab., St. Petersburg 199034, Russia

*E-mail: a.khlebnikov@spbu.ru.



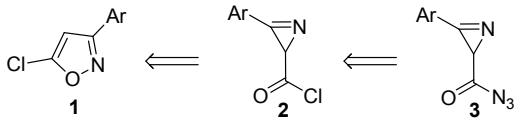
ABSTRACT: 2*H*-Azirine-2-carbonyl azides, new reactive heterocyclic building blocks, were synthesized in high yield by the reaction of sodium azide with 2*H*-azirine-2-carbonyl chlorides, generated by Fe(II)-catalyzed isomerization of 5-chloroisoxazoles. 2-(Azidocarbonyl)-1*H*-pyrroles, prepared by the Ni(II)-catalyzed reaction of 2-(azidocarbonyl)-2*H*-azirines with 1,3-diketones easily undergo the Curtius rearrangement in boiling *t*BuOH to give Boc-protected α-aminopyrroles in high yield. Heating of 2-(azidocarbonyl)-1*H*-pyrroles for a short time in inert solvents leads to the high yield formation of benzo- and hetero-fused 1*H*-pyrrolo[2,3-*b*]pyridin-6(7*H*)-ones, which are formed via a 6π electrocyclization involving the vicinal aryl or hetaryl substituent and the N=C bond of isocyanate, generated by the Curtius rearrangement of the azidocarbonyl group. The Pd-catalyzed cross-coupling reaction of 1-acetyl-2-methyl-3*H*-pyrrolo[2,3-*c*]isoquinolin-5-yl triflate, easily

prepared from the corresponding pyrroloisoquinolone, leads to variously 5-substituted 3*H*-pyrrolo[2,3-*c*]isoquinolines in excellent yields.

Introduction

Acyl azides are known as versatile reagents for the synthesis of heterocycles and natural products.[1,2] The most important reaction of these acyl azides is the Curtius rearrangement leading to isocyanates. The latter can be hydrolyzed to the corresponding amines or used in further reactions, in particular in various cyclizations leading to azaheterocycles.[1,2] A combination of the acyl azide group with strained small rings provides synthetic building blocks with increased potential by utilizing the reactivity of both components. Examples of such are azidocarbonylcyclopropanes[3] and azidocarbonyloxiranes.[4] We speculated that 2*H*-azirine-2-carbonyl azides **3** could serve as valuable synthetic building blocks for the implementation of orthogonal reactivity, since both the azirine[5] and carbonyl azide[1, 2] moieties can be activated in completely different ways using various catalysts and reaction conditions. Recently we found conditions for the generation of the unstable 2*H*-azirine-2-carbonyl chlorides **2** by Fe(II)-catalysed isomerization[6] of 5-chloroisoxazoles **1** and supposed that the use of this isomerization would allow the synthesis of 2*H*-azirine-2-carbonyl azides by the reaction of chlorides **2** with sodium azide (Scheme 1).[7] The aim of this work is, therefore, to develop a synthetic method for the preparation of 2*H*-azirine-2-carbonyl azides and to investigate their orthogonal reactivity.

Scheme 1. Retrosynthetic Scheme for the Preparation of 2*H*-Azirine-2-carbonyl Azides 3 via Isomerization of Chloroisoxazoles 1

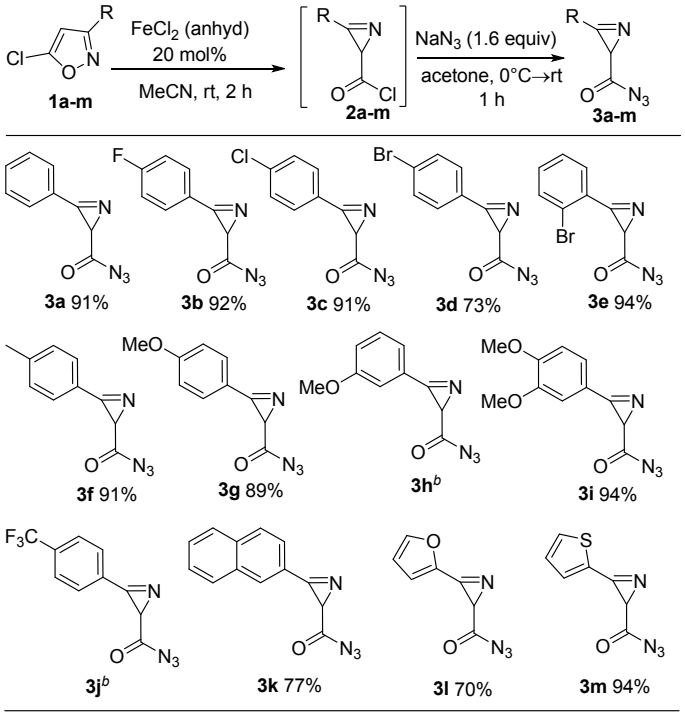


Results and discussion

3-Phenyl-2*H*-azirine-2-carbonyl chloride **2a**, generated by the Fe(II)-catalyzed isomerization of 5-chloro-3-phenylizoxazole **1a** according to the earlier described procedure,[6c] was reacted with 1 equiv of sodium azide in acetone to give target 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** in 56% yield. An

increase in the amount of NaN_3 to 1.6 equiv improved the yield of azide **3a** to 91%. In order to evaluate the scope of the reaction substituted isoxazoles **1a-m** were reacted with catalytic amounts of anhydrous $FeCl_2$ and then with sodium azide under the optimized conditions mentioned above. We failed to isolate pure samples of azides **3h** and **3j** due to their low stability, and these compounds were used in further reactions without prior isolation. Meanwhile azides **3a-g, i, k-m** with various *p*-, *m*- and *o*-substituted aryl and hetaryl groups were prepared mostly in excellent yields (Table 1). An attempt to perform the reaction with 5-chloro-4-(4-nitrophenyl)isoxazole failed, possibly due to specific reactions of the nitro-group, promoted by $FeCl_2$, leading to complete tarring of the reaction mixture at the 3-(4-nitrophenyl)-2*H*-azirine-2-carbonyl chloride preparation step. All new compounds were characterized by ^1H, ^{13}C NMR and HRMS. The structure of azide **3d** was confirmed by X-ray analysis (see the Supporting Information). Azides **3a-g, i, k-m** are non-hygroscopic crystalline solids, which are stable under an air atmosphere for a long time at rt.

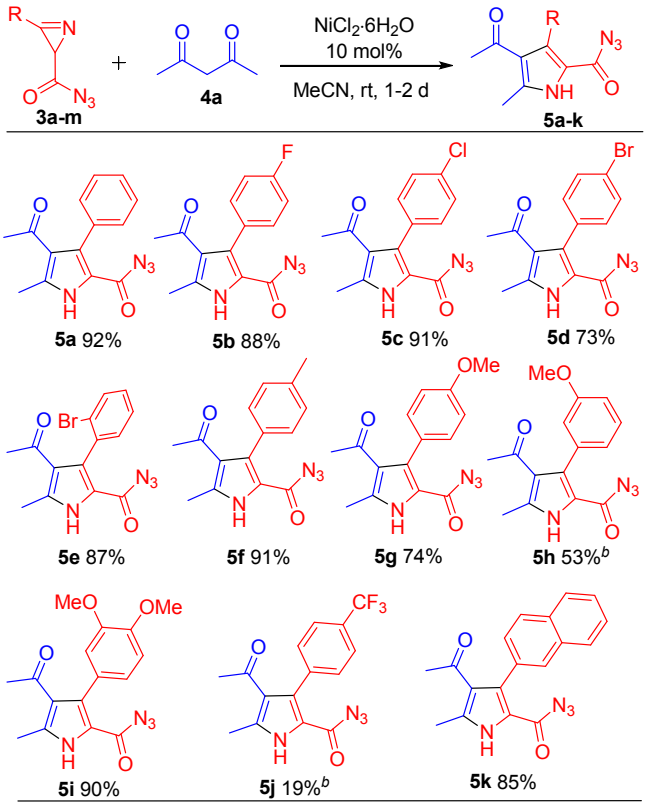
Table 1. Synthesis of 3-Aryl/hetaryl-2*H*-Azirine-2-carbonyl Azides 3a-m[a]



[a] Isolated yields. [b] Not isolated in pure form.

Attempts to carry out the Curtius rearrangement of azides **3** under various conditions to obtain 2-amino-2*H*-azirines failed. Heating azide **3a** in MeOH or *tert*-BuOH in order to obtain the corresponding azirin-2-ylcarbamate led to extensive tarring. On the other hand, the reactions of the azirine moiety of compounds **3** with the retention of the azidocarbonyl group turned out to be much more successful. Thus, the Ni(II)-catalyzed reaction of azides **3** with acetyl acetone **4a** under the conditions similar to those used for the reaction of azirine-2-carboxylic acid derivatives[6b, 8] provides 2-(azidocarbonyl)pyrroles **5** in good to excellent yields (Table 2).

Table 2. Synthesis of 4-Acetyl-3-aryl-5-methyl-1*H*-pyrrole-2-carbonyl Azide 5a-k[a]

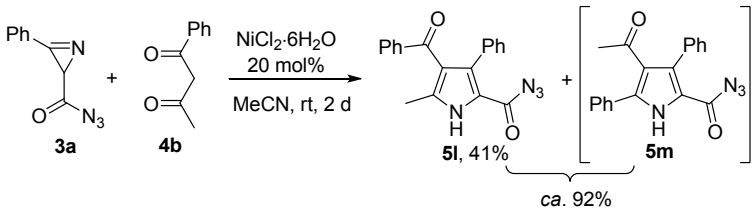


[a] Isolated yields. [b] For 3 step, starting from isoxazole **1**.

Pyrroles **5h** and **5j** were prepared without intermediate isolation of azides **3h** and **3j**. The structure of azide **5d** was confirmed by X-ray analysis (see the Supporting Information). The Ni(II)-catalyzed reaction of azide **3a** with benzoylacetone **4b** gave a *ca*. 1:1 mixture (^{1}H NMR) of regioisomers **5l** and **5m** in *ca*. 92% (Scheme 2). 2-(Azidocarbonyl)pyrrole **5l** was isolated in pure form by chromatography, in contrast to isomer **5m**, which turned out to be unstable like other pyrroles **5** with

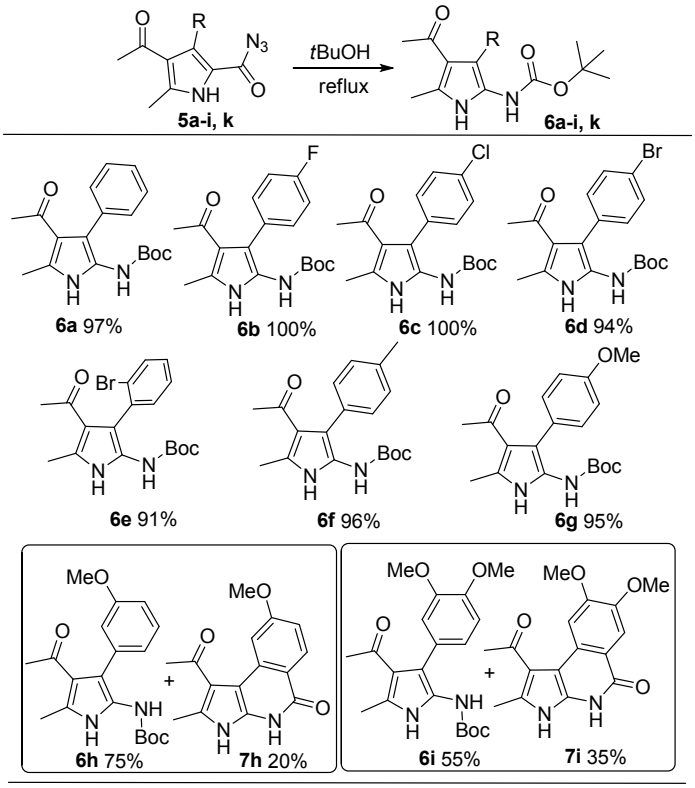
an aryl substituent in the 5 position (*vide infra*). Ethyl acetoacetate did not react with azide **3a** under the same reaction conditions.

Scheme 2. Reaction of Azide 3a with Nonsymmetrical 1,3-Diketone



In contrast to azirine-2-carbonyl azides **3**, 1*H*-pyrrole-2-carbonyl azide**s 5a-i, k** easily undergo the Curtius rearrangement in boiling *tert*-BuOH to give Boc-protected α-aminopyrroles **6a-i,k** (Table 3).

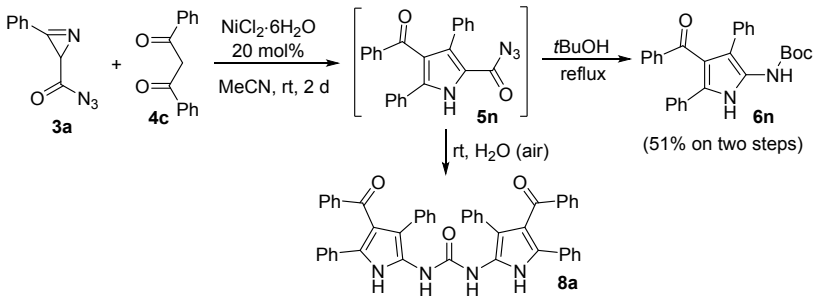
Table 3. Synthesis of Boc-Protected α-Aminopyrroles 6a-i, k[a]



[a] Isolated yields.

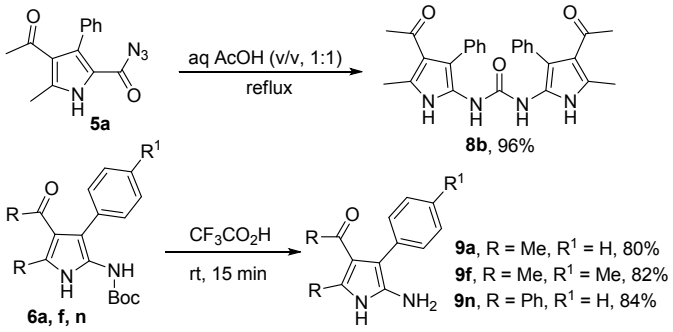
4-Benzoyl-substituted azidocarbonylpyrrole **5n** was synthesized by the Ni(II)-catalyzed reaction of azide **3a** with dibenzoylmethane **4c**, but due to its instability, it was not fully characterized. It easily decomposed when kept in air at rt to give urea **8a**. Heating crude azidocarbonylpyrrole **5n** in *tert*-BuOH led to Boc-protected α-aminopyrrole **6n** in 59% yield (Scheme 3).

Scheme 3. Synthesis of α-Aminopyrrole 6n



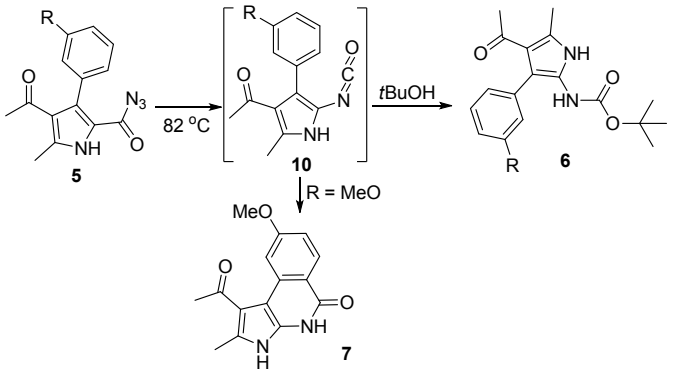
Heating of azide **5a** in boiling aq AcOH (v/v, 1:1), in an attempt to prepare unprotected α-aminopyrrole **9a**, led to the quantitative formation of urea **8b** (Scheme 3). α-Aminopyrroles **9** can be prepared, however, by deprotection of *N*-Boc-aminopyroles **6** using TFA (Scheme 4).

Scheme 4. Synthesis of Urea 8b and Unprotected α-Aminopyrroles 9a and 9f



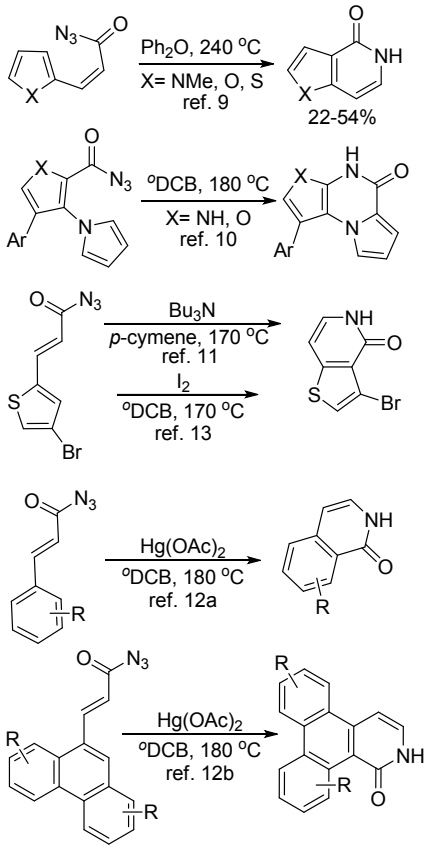
It was found that azidocarbonylpyrroles **5h** and **5i**, containing an *m*-MeO-substituted phenyl group under Curtius rearrangement conditions, afforded, in addition to Boc-protected α-aminopyrroles **6h** and **6i**, 3,4-dihydro-5*H*-pyrrolo[2,3-*c*]isoquinolin-5-ones **7h** and **7i** as byproducts. (Table 3). Compounds **7** are most likely the products of the electrocyclization of the intermediate isocyanates **10** (Scheme 5).

Scheme 5. Transformations of Intermediate isocyanates



[6π]-Electrocyclization involving the N=C bond of the isocyanates, generated via the Curtius rearrangement, with formation of fused pyridin-2(1*H*)-ones derivatives, occurs normally at high temperatures: 240 °C in diphenyl ether,[9] 180 °C in *o*-dichlorobenzene (*o*DCB),[10] 170 °C in *p*-cymene,[11] 180 °C in *o*DCB in the presence of $Hg(OAc)_2$ as a catalyst,[12] 170 °C in *o*DCB in the presence of I_2 as a catalyst.[13] The mentioned electrophilic cyclization is characteristic of electron-rich azoles (Scheme 6).[9-11, 13] When a substituted phenyl ring is involved in the cyclization, a donor substituent accelerates the reaction.[12a]

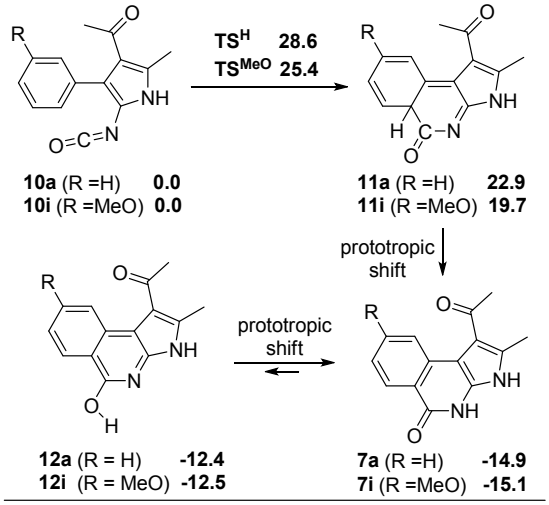
Scheme 6. [6π]-Electrocyclization Involving the N=C bond of the Isocyanates



We speculated, therefore, that the electron-donating *m*-MeO group in the 3-aryl substituent of pyrroles **5** plays a crucial role in facilitating their electrophilic cyclization into compounds **7** and thus the cyclization of intermediate isocycanates **10h** and **10i** can occur already at 82 °C.

To check this hypothesis a calculation of model isocyanates **10a** and **10i** and the transition states (TS) for their 1,6-π-cyclization were performed at the DFT B3LYP/6-311+G(d,p) level (PCM model for *o*DCB) (Scheme 7, for details of the calculations see the Supporting information).

Scheme 7. Relative Gibbs Free Energies of Isocyanates 10a and 10i and the Transition States (TS) for Their 1,6-π-Cyclization at the DFT B3LYP/6-311+G(d,p) level [a]

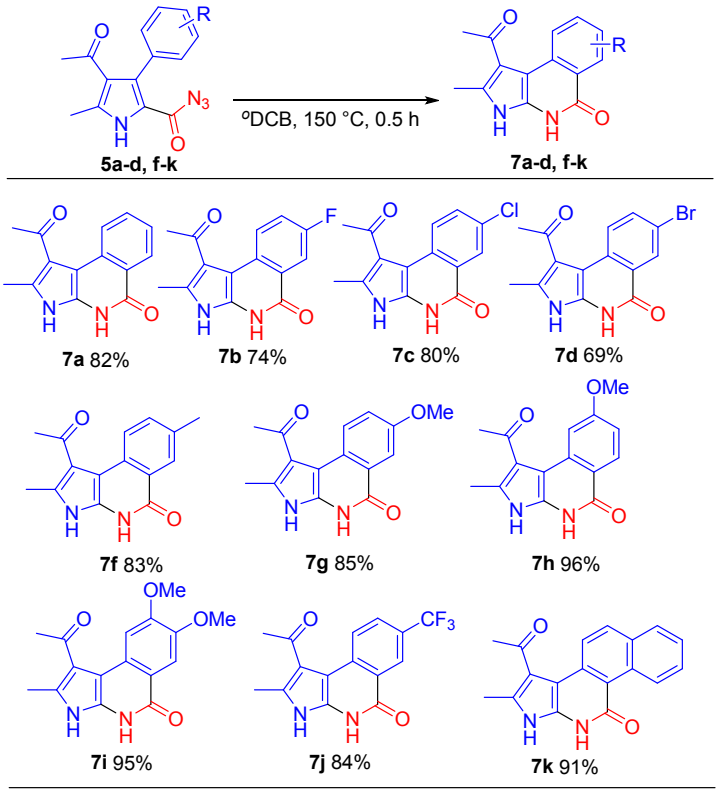


[a] In kcal/mol, 298 K, PCM model for *o*DCB.

According to the calculations, the barrier for the cyclization of the MeO-substituted compound **10i** is lower by 3.2 kcal/mol than the barrier for the cyclization of the unsubstituted compound **10a**. The value of the energy barrier for the cyclization of 25.4 kcal/mol indicates why the cyclization of compound **10i** can occur already at 82 °C. The value of the energy barrier for the cyclization of the unsubstituted analog **10a** (28.6 kcal/mol) means that this cyclization would occur at higher temperature, but obviously lower than the boiling point of *o*DCB. One more conclusion follows from the calculation: the pyridone tautomer of product **7** is much more stable than pyridol tautomer **12**. Based on this analysis, it was decided to search for conditions for the high yield transformation of acyl azides **5** into 5*H*-pyrrolo[2,3-*c*]isoquinolin-5-one derivatives **7**, which, to the best of our knowledge, have not yet been synthesized.

It was found that heating a ^{o}DCB solution of synthesized azides **5** (Table 2) at 150 °C for 0.5 h without any catalyst is sufficient to obtain 5*H*-pyrrolo[2,3-*c*]isoquinolin-5-ones **7** in high yields (Table 4). Moreover no chromatographic purification is required to isolate these products from their reaction mixtures.

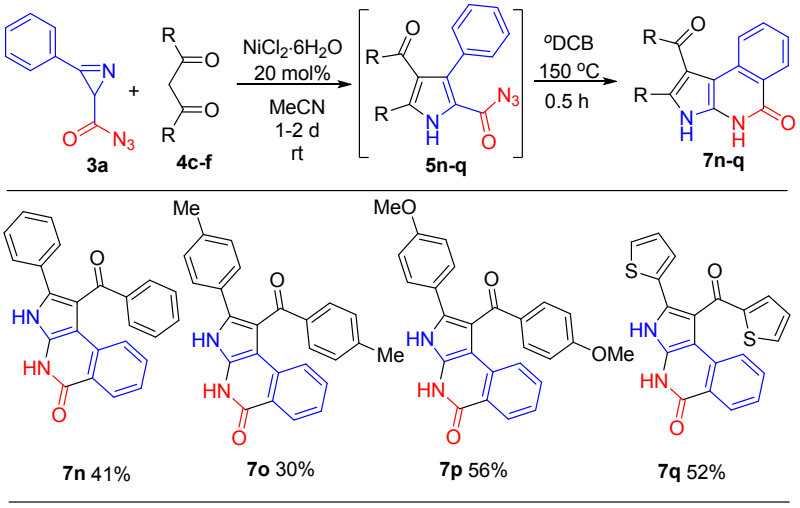
Table 4. Synthesis of 5*H*-Pyrrolo[2,3-*c*]isoquinolin-5-one Derivatives 7a-d, f-k[a]



[a] Isolated yields.

Some unstable azidocarbonylpyrroles **5**, without prior isolation from the reaction mixtures of azidocarbonylazirines **3** with diketones **4**, were rearranged to 5*H*-pyrrolo[2,3-*c*]isoquinolin-5-one derivatives **7** (Table 5). The structure of compound **7n** was confirmed by X-ray analysis (see the Supporting Information).

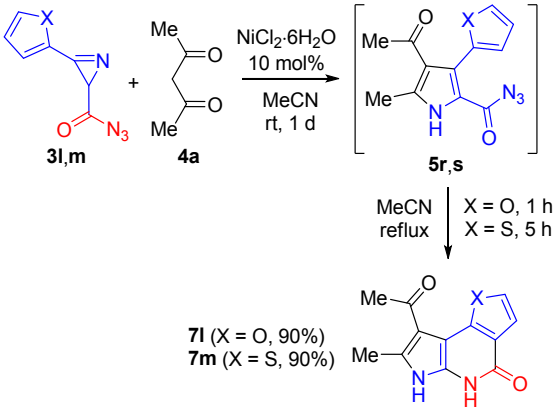
Table 5. Synthesis of 5*H*-Pyrrolo[2,3-*c*]isoquinolin-5-one Derivatives 7o-q[a]



[a] Isolated yields on two steps.

The cyclizations of isocyanates, derived from azidocarbonylpyrroles **5r** and **5s**, involving an electron rich furan and thiophene ring, proceed so easily that it is possible to perform these transformations in boiling acetonitrile (Scheme 8).

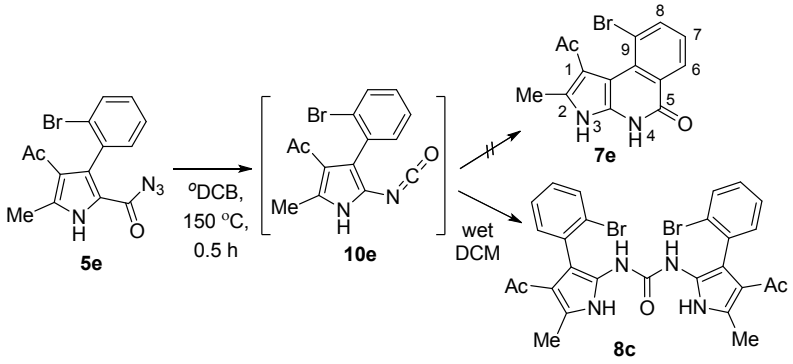
Scheme 8. Synthesis of Compounds 7l, m



Moreover, preparation of these new heterocyclic backbones, 5,6-dihydro-4*H*-furo[2,3-*d*]pyrrolo[2,3-*b*]pyridin-4-one and 5,6-dihydro-4*H*-pyrrolo[2,3-*b*]thieno[2,3-*d*]pyridin-4-one, can be implemented as one-pot process in up to 90% yield over two steps. Thus, various 1,2,7,8-substituted 3*H*-pyrrolo[2,3-*c*]isoquinolin-5(4*H*)-ones and their benzo[*g*] and hetero-analogs can be prepared from the

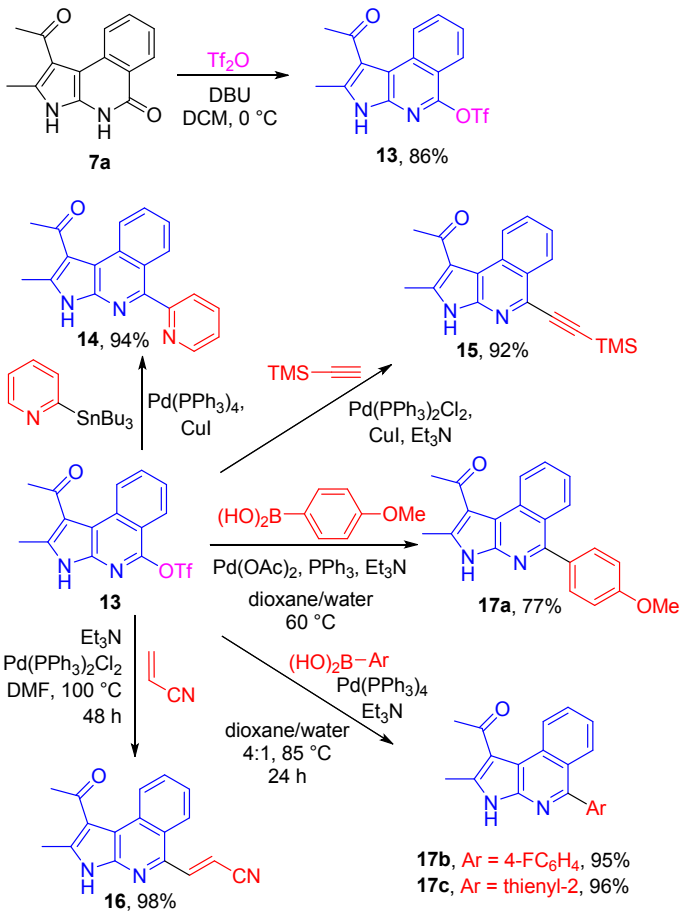
appropriate 2-(azidocarbonyl)-2*H*-azirines **3**. However, 2-aryl-2-(azidocarbonyl)-2*H*-azirines with *ortho*-substituted aryl ring cannot be used for the preparation of 9-substituted derivatives, probably due to steric hindrance, preventing the isocyanate **10e** adopting the conformation required for cyclization. Thus, heating of azidocarbonylpyrrole **5e** does not lead to pyrroloisoquinolinone **7e**, although it is obvious that the formation of isocyanate **10e** does occur, since the treatment of the reaction mixture with wet DCM gave urea **8c** (Scheme 9).

Scheme 9. Transformation of Azidocarbonyl Pyrrole 5e



It is easy to introduce a substituent into the 5 position of the pyrrolo[2,3-*c*]isoquinoline skeleton via *O*-triflation of 3*H*-pyrrolo[2,3-*c*]isoquinolin-5(4*H*)-one **7**, followed by various cross-coupling reactions. The reaction of compound **7a** with triflic anhydride in the presence of DBU afforded triflate **13** in 86% yield (Scheme 10). The structure of **13** was confirmed by X-ray analysis (see Supporting Information). The Stille reaction of triflate **13** with 2-(tributylstannyl)pyridine afforded the modified 2,2'-bipyridyl ligand **14** in 94% yield. The Sonogashira reaction of **13** with ethynyltrimethylsilane gave 5-ethynyl-substituted 3*H*-pyrrolo[2,3-*c*]isoquinoline **15** in 92% yield. The Heck reaction of triflate **13** with acrylonitrile led to 5-(2-cyanovinyl)-substituted 3*H*-pyrrolo[2,3-*c*]isoquinoline **16** in 98% yield and its Suzuki reaction with boronic acids afforded 5-aryl-substituted 3*H*-pyrrolo[2,3-*c*]isoquinolines **17a-c** in 77-95% yield.

Scheme 10. Synthesis of Triflate 13 and Its Cross-Coupling Reactions



In conclusion: a synthetic method was developed for the high yielding preparation of 2*H*-azirine-2-carbonyl azides through reaction of sodium azide with 2*H*-azirine-2-carbonyl chlorides, generated by Fe(II)-catalyzed isomerization of 5-chloroisoxazoles. Attempts to prepare 2-amino-2*H*-azirines by the Curtius rearrangement of 2-(azidocarbonyl)-2*H*-azirines under various conditions were unsuccessful. However, 2-(azidocarbonyl)-1*H*-pyrroles, prepared by the Ni(II)-catalyzed reaction of 2-(azidocarbonyl)-2*H*-azirines with 1,3-diketones, easily undergo the Curtius rearrangement in boiling *t*BuOH to give Boc-protected α-aminopyrroles in high yield and these could be deprotected by TFA. Short-term heating of 3-aryl-2-(azidocarbonyl)-1*H*-pyrroles in *o*-dichlorobenzene at 150 °C leads to the high yield formation of substituted 3*H*-pyrrolo[2,3-*c*]isoquinolin-5(4*H*)-ones via a [6π]-electrocyclization of isocyanates, generated by the Curtius rearrangement. The cyclizations of

activated 3-methoxyphenyl, furyl and thienyl groups occur already at 82 °C. Thus, various 1,2,7,8-substituted 3*H*-pyrrolo[2,3-*c*]isoquinolin-5(4*H*)-ones and their benzo[*g*] and hetero analogs can be prepared from the appropriate 2-(azidocarbonyl)-2*H*-azirines. The Pd-catalyzed cross-coupling reaction of 1-acetyl-2-methyl-3*H*-pyrrolo[2,3-*c*]isoquinolin-5-yl triflate, easily prepared from the corresponding pyrroloisoquinolone, lead to variously 5-substituted 3*H*-pyrrolo[2,3-*c*]isoquinolines in excellent yields.

EXPERIMENTAL SECTION

General Information and Methods. Melting points were determined on a melting point apparatus. ^{1}H (400 MHz), ^{13}C (100 and 125 MHz) and ^{19}F (376 and 470 MHz) NMR spectra were recorded on a NMR spectrometer in $CDCl_3$ or DMSO-d_6. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane (TMS δ = 0.00). ^{1}H NMR spectra were calibrated to the residual peak of $CHCl_3$ (7.26 ppm) or DMSO-d_5 (2.50 ppm). For all new compounds, ^{13}C{^{1}H} and ^{13}C DEPT-135 spectra were recorded and calibrated according to the peak of $CDCl_3$ (77.00 ppm) or DMSO-d_6 (39.51 ppm). ^{19}F NMR spectra were calibrated according to a $CFCl_3$ external standard (δ = 0 ppm). Electrospray ionization (ESI) mass spectra were recorded on a mass spectrometer, HRMS-ESI-QTOF, electrospray ionization. Single crystal X-ray data were collected by means of diffractometer. Crystallographic data for the structures **3d**, **5d**, **7n** and **13** (CCDC 1956380, 1956383, 1956381 and 1956382 correspondingly) have been deposited with the Cambridge Crystallographic Data Centre. Thin-layer chromatography (TLC) was conducted on aluminum sheets with 0.2 mm silica gel with fluorescent indicator.

3-Aryl/heteryl-5-chloroimidazoles **1a-d, f-h, k, m**,[14] **1e**[15] were prepared according to the published procedures. Physical and spectral data of 5-chloroisoxazoles **1a**, **c**, **d**, **f-h**, **k**,[16] **1b**,[17] **1e**,[15] **1l**, **m**,[6b] were in agreement with previously reported values.

*CAUTION: Although azides **3** and **5** were found to be safe in our hands, they are potentially explosive and should be handled with care.*

*5-Chloro-3-(3,4-dimethoxyphenyl)isoxazole (**1i**).* Compound **1i** was prepared following the published procedure[6a] from 3-(3,4-dimethoxyphenyl)isoxazol-5(4*H*)-one (2.5 g, 11.31 mmol), $POCl_3$ (17.36 g, 113.12 mmol, 10 equiv) and Et_3N (913 mg, 9.04 mmol, 0.6 equiv) in 1.84 g (68% yield, after flash chromatography on silica gel using hexanes/EtOAc (5:1 v/v) as eluent) as a beige solid: mp 68-70 °C (hexane/ EtOAc). ^1H NMR ($CDCl_3$, 400 MHz): δ 3.93 s (2H), 3.94 s (3H), 6.44 s (1H), 6.93 d (1H, J = 8.3 Hz), 7.24 dd (1H, J = 8.3, 2.0 Hz), 7.36 d (1H, J = 1.9 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 55.9 (CH_3), 56.0 (CH_3), 99.4 (CH), 108.9 (CH), 111.1 (CH), 120.0 (CH), 120.8 (C), 149.4 (C), 151.1 (C), 154.8 (C), 163.9 (C).). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{11}H_{10}ClNNaO_3^+$ 262.0241; Found 262.0249.

*5-Chloro-3-(4-(trifluoromethyl)phenyl)isoxazole (**1j**).* Compound **1j** was prepared following the published procedure[6a] from 3-(4-(trifluoromethyl)phenyl)isoxazol-5(4*H*)-one (1.84 g, 8.05 mmol), $POCl_3$ (12.35 g, 80.52 mmol, 10 equiv) and Et_3N (488 mg, 4.83 mmol, 0.6 equiv) in 1.72 g (86% yield, after flash chromatography on silica gel using hexanes/EtOAc (5:1 v/v) as eluent) as a beige solid: mp 93-95 °C (hexane/ EtOAc). ^1H NMR ($CDCl_3$, 400 MHz): δ 6.53 (s, 1H), 7.68-7.79 (m, 2H), 7.85-7.96 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 99.8 (CH), 123.9 (q, J_{C-F} = 270.6 Hz, q), 126.2 (q, J_{C-F} = 3.7 Hz, CH), 127.2 (CH), 131.8 (C), 132.6 (q, J_{C-F} = 33.0 Hz, C), 156.0 (C), 163.2 (C). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_6ClF_3NO^+$ 248.0085; Found 248.0085.

General Procedure A for the Preparation of 2*H*-Azirine-2-carbonyl azides (3a-m).

Anhydrous iron(II) chloride (1.40 mmol, 20 mol%) was added to a solution of 5-chloroisoxazole **1** (7.00 mmol, 1 equiv) in dry acetonitrile (50 mL) under argon atmosphere and the reaction mixture was stirred for around 2 h (TLC control). After the reaction was completed, the solvent was evaporated, the residue was diluted with dry diethyl ether (50 mL) and the precipitated iron chloride

was filtered off through Celite. The ether was also evaporated, anhydrous acetone (40 mL) was added and the resulting solution was cooled to 0 °C in an ice bath. Sodium azide (0.011 mol, 1.6 equiv) was added and the reaction mixture was stirred for additional 20 minutes at 0 °C and then for 1 h at rt. After the reaction was completed, the solvent was evaporated and the residue was partitioned between water and dichloromethane, water layer was extracted three times with dichloromethane, the combined organic phases were washed with water, dried over Na_2SO_4, filtered, concentrated in vacuo and the residue was purified by column chromatography on silica gel (hexanes or petroleum ether/ethyl acetate, 3:1 v/v).

*3-Phenyl-2H-azirine-2-carbonyl azide (**3a**)*. Compound **3a** was prepared following general procedure A from 5-chloro-3-phenylisoxazole **1a** (1.26 g, 7.00 mmol), $FeCl_2$ (178 mg, 1.40 mmol) and NaN_3 (729 mg, 0.011 mol) in 1.19 g (91% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a beige solid: mp 56-58 °C (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.87 (s, 1H), 7.57-7.63 (m, 2H), 7.65-7.71 (m, 1H), 7.86-7.92 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 32.1 (CH), 121.7 (C), 129.6 (CH), 130.7 (CH), 134.4 (CH), 158.1 (C), 178.7 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_9H_6N_4NaO^+$ 209.0434; Found 209.0435.

*3-(4-Fluorophenyl)-2H-azirine-2-carbonyl azide (**3b**)*. Compound **3b** was prepared following general procedure A from 5-chloro-3-(4-fluorophenyl)isoxazole **1b** (850 mg, 4.33 mmol), $FeCl_2$ (110 mg, 0.87 mmol) and NaN_3 (448 mg, 6.89 mmol) in 810 mg (92% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a beige solid: mp 59-60 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.87 (s, 1H), 7.25-7.34 (m, 2H), 7.86-7.98 (m, 2H). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz): δ -101.54. ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 32.2 (CH), 117.3 d (CH, $J_{C\text{-}F}$ = 22.9 Hz), 118.2 d (C, $J_{C\text{-}F}$ = 3.5 Hz), 133.3 d (CH, $J_{C\text{-}F}$ = 9.7 Hz), 157.1 (C), 166.4 d (C, $J_{C\text{-}F}$ = 258.1 Hz), 178.5 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_9H_5FN_4NaO^+$ 227.0340; Found 227.0345.

*3-(4-Chlorophenyl)-2H-azirine-2-carbonyl azide (**3c**)*. Compound **3c** was prepared following general procedure ***A*** from 5-chloro-3-(4-chlorophenyl)isoxazole **1c** (642 mg, 3.00 mmol), $FeCl_2$ (76 mg, 0.60 mmol) and NaN_3 (312 mg, 4.80 mmol) in 602 mg (91% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as beige solid: mp 96-98 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.87 (s, 1H), 7.55-7.63 (m, 2H), 7.80-7.88 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 32.2 (CH), 120.3 (C), 130.1 (CH), 131.9 (CH), 141.1 (C), 157.5 (C), 178.4 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_9H_5ClN_4NaO^+$ 243.0044; Found 243.0036.

*3-(4-Bromophenyl)-2H-azirine-2-carbonyl azide (**3d**)*. Compound **3d** was prepared following general procedure A from 3-(4-bromophenyl)-5-chloroisoxazole **1d** (864 mg, 3.34 mmol), $FeCl_2$ (85 mg, 0.67 mmol) and NaN_3 (262 mg, 4.02 mmol) in 650 mg (73% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent and recrystallization from benzene) as a beige solid: mp 110-112 ºC (benzene). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.88 (s, 1H), 7.72-7.79 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 32.2 (CH), 120.7 (C), 129.7 (C), 131.9 (CH), 133.1 (CH), 157.7 (C), 178.4 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_9H_5{}^{79}BrN_4NaO^+$ 286.9539; Found 286.9548.

*3-(2-Bromophenyl)-2H-azirine-2-carbonyl azide (**3e**)*. Compound **3e** was prepared following general procedure A from 3-(2-bromophenyl)-5-chloroisoxazole **1e** (1.02 g, 3.94 mmol), $FeCl_2$ (100 mg, 0.79 mmol) and NaN_3 (409 mg, 6.30 mmol) in 977 mg (94% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a beige solid: mp 68-70 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.94 (s, 1H), 7.47-7.58 (m, 2H), 7.74-7.81 (m, 1H), 7.83-7.92 (m, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 33.4 (CH), 122.4 (C), 126.0 (C), 128.2 (CH), 133.6 (CH), 134.4 (CH), 135.2 (CH), 158.6 (C), 178.4 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_9H_5{}^{79}BrN_4NaO^+$ 286.9539; Found 286.9533.

*3-(p-Tolyl)-2H-azirine-2-carbonyl azide (**3f**)*. Compound **3f** was prepared following general procedure A from 5-chloro-3-(*p*-tolyl)isoxazole **1f** (830 mg, 4.29 mmol), $FeCl_2$ (109 mg, 0.86 mmol) and NaN_3 (446 mg, 6.87 mmol) in 781 mg (91% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a beige solid: mp 86-87 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.48 (s, 3H), 2.83 (s, 1H), 7.34-7.44 (m, 2H), 7.74-7.80 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 22.1 (CH_3), 32.0 (CH), 118.9 (C), 130.4 (CH), 130.8 (CH), 145.7 (C), 157.6 (C), 178.9 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{10}H_8N_4NaO^+$ 223.0590; Found 223.0591.

*3-(4-Methoxyphenyl)-2H-azirine-2-carbonyl azide (**3g**)*. Compound **3g** was prepared following general procedure A from 5-chloro-3-(4-methoxyphenyl)isoxazole **1g** (841 mg, 4.02 mmol), $FeCl_2$ (102 mg, 0.80 mmol) and NaN_3 (418 mg, 6.42 mmol) in 768 mg (89% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 106-107 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.81 (s, 1H), 3.91 (s, 3H), 7.05-7.12 (m, 2H), 7.79-7.86 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 32.0 (CH), 55.8 (CH_3), 113.9 (C), 115.2 (CH), 132.9 (CH), 156.6 (C), 164.5 (C), 179.1 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{10}H_8N_4NaO_2^+$ 239.0539; Found 239.0532.

*3-(3,4-Dimethoxyphenyl)-2H-azirine-2-carbonyl azide (**3i**)*. Compound **3i** was prepared following general procedure A from 5-chloro-3-(3,4-dimethoxyphenyl)isoxazole **1i** (1.745 g, 7.29 mmol), $FeCl_2$ (185 mg, 1.46 mmol) and NaN_3 (758 mg, 11.66 mmol) in 1.68 g (94% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 84-86 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.84 (s, 1H), 3.97 (s, 3H), 3.98 (s, 3H), 7.03 (d, J = 8.2 Hz, 1H), 7.40 (d, J = 1.9 Hz, 1H), 7.43 (dd, J = 8.2, 1.9 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 32.3 (CH), 56.3 (CH_3), 56.4 (CH_3), 111.3 (CH), 111.8 (CH), 114.0 (C), 125.9 (CH), 150.0 (C), 154.3 (C), 157.0 (C), 179.0 (C). HRMS (ESI) *m/z*: $[M + Ag]^+$ Calcd for $C_{11}H_{10}{}^{107}AgN_4O_3^+$ 352.9798; Found 352.9798.

*3-(Naphthalen-2-yl)-2H-azirine-2-carbonyl azide (**3k**).* Compound **3k** was prepared following general procedure A from 5-chloro-3-(naphthalen-2-yl)isoxazole **1k** (300 mg, 1.31 mmol), $FeCl_2$ (33 mg, 0.26 mmol) and NaN_3 (136 mg, 2.09 mmol) in 238 mg (77% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a beige solid: mp 97-99 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.96 (s, 1H), 7.57-7.74 (m, 2H), 7.90-8.10 (m, 4H), 8.32 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 32.4 (CH), 119.0 (C), 124.9 (CH), 127.7 (CH), 128.3 (CH), 129.4 (CH), 129.5 (CH), 129.8 (CH), 132.8 (C), 133.4 (CH), 136.1 (C), 158.2 (C), 178.8 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_8N_4NaO^+$ 259.0590; Found 259.0588.

*3-(Furan-2-yl)-2H-azirine-2-carbonyl azide (**3l**).* Compound **3l** was prepared following general procedure A from 5-chloro-3-(furan-2-yl)isoxazole **1l** (267 mg, 1.58 mmol), $FeCl_2$ (40 mg, 0.32 mmol) and NaN_3 (164 mg, 2.52 mmol) in 194 mg (70% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a beige solid: mp 87-89 ºC (hexane/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.86 (s, 3H), 6.71 (dd, J = 3.6, 1.8 Hz, 1H), 7.30 (dd, J = 3.6, 0.5 Hz, 1H), 7.86 (dd, J = 1.8, 0.5 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 31.7 (CH), 113.3 (CH), 122.5 (CH), 138.8 (C), 147.9 (C), 149.8 (CH), 178.1 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_7H_4N_4NaO_2^+$ 199.0226; Found 199.0222.

*3-(Thiophen-2-yl)-2H-azirine-2-carbonyl azide (**3m**).* Compound **3m** (855 mg, 94%) was prepared following general procedure A from 5-chloro-3-(thiophen-2-yl)isoxazole **1m** (884 mg, 4.76 mmol), $FeCl_2$ (121 mg, 0.95 mmol) and NaN_3 (495 mg, 7.62 mmol) in 855 mg (94% yield, after flash chromatography on silica gel using hexanes/EtOAc (3:1 v/v) as eluent) as a brown solid: mp 47-49 ºC (hexanes/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.89 (s, 1H), 7.30 (dd, J = 5.0, 3.8 Hz, 1H), 7.73 (dd, J = 3.8, 1.1 Hz, 1H), 7.92 (dd, J = 5.0, 1.1 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 32.8 (CH), 123.9 (C), 128.8 (CH), 136.1 (CH), 136.3 (CH), 151.3 (C), 178.3 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_7H_4N_4NaOS^+$ 214.9998; Found 214.9990.

General Procedure B for the Preparation of 1*H*-Pyrrole-2-carbonyl azides (5a-k).

1,3-Diketone **4** (1.60 mmol, 1.05 equiv) and $NiCl_2 \cdot 6H_2O$ (0.15 mmol, 10 mol%) were added to a solution of azirine **3** (1.52 mmol, 1 equiv) in acetonitrile (5 mL) and the resulting mixture was stirred at rt to the completion of the reaction (monitored by TLC, 1-2 d). After the reaction was over, the product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1 v/v). Poorly soluble compounds such as **5d** and **5g** could be purified by filtration from the reaction mixture and washing with acetonitrile and water.

*4-Acetyl-5-methyl-3-phenyl-1H-pyrrole-2-carbonyl azide (**5a**)*. Compound **5a** was prepared following general procedure B from 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (283 mg, 1.52 mmol), acetylacetone **4a** (160 mg, 1.60 mmol) and $NiCl_2 \cdot 6H_2O$ (36 mg, 0.15 mmol) in 375 mg (92% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 116-117 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.78 (s, 3H), 2.59 (s, 3H), 7.27-7.33 (m, 2H), 7.38-7.46 (m, 3H), 9.39 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 30.8 (CH_3), 119.3 (C), 124.8 (C), 128.2 (CH), 128.2 (CH), 130.1 (CH), 134.5 (C), 134.7 (C), 141.0 (C), 164.9 (C), 196.6 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{14}H_{11}N_4O_2^-$ 267.0887; Found 267.0874.

*4-Acetyl-3-(4-fluorophenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5b**)*. Compound **5b** was prepared following general procedure B from 3-(4-fluorophenyl)-2*H*-azirine-2-carbonyl azide **3b** (400 mg, 1.96 mmol), acetylacetone **4a** (206 mg, 2.06 mmol) and $NiCl_2 \cdot 6H_2O$ (47 mg, 0.20 mmol) in 495 mg (88% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 118-119 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.81 (s, 3H), 2.59 (s, 3H), 7.06-7.18 (m, 2H), 7.22-7.32 (m, 2H), 9.69 (s, 1H). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz): δ -113.62. ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 30.9 (CH_3), 115.3 (d, $J_{C\text{-}F}$ = 21.6 Hz, CH), 119.5 (C), 124.8 (C), 130.4 (d, $J_{C\text{-}F}$ = 3.8 Hz, C), 131.8 (d, $J_{C\text{-}F}$ = 7.9 Hz, CH), 133.5

(C), 141.2 (C), 162.8 (d, J_{C-F} = 247.8 Hz, C), 164.9 (C), 196.2 (C). HRMS (ESI) m/z: [M - H]$^-$ Calcd for $C_{14}H_{10}FN_4O_2^-$ 285.0793; Found 285.0793.

*4-Acetyl-3-(4-chlorophenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5c**)*. Compound **5c** was prepared following general procedure B from 3-(4-chlorophenyl)-2*H*-azirine-2-carbonyl azide **3c** (250 mg, 1.13 mmol), acetylacetone **4a** (119 mg, 1.19 mmol) and $NiCl_2 \cdot 6H_2O$ (27 mg, 0.11 mmol) in 303 mg (91% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 124-125 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.82 (s, 3H), 2.58 (s, 3H), 7.20-7.27 (m, 2H), 7.36-7.46 (m, 2H), 9.37 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 31.0 (CH_3), 119.4 (C), 124.7 (C), 128.5 (CH), 131.5 (CH), 133.0 (C), 133.2 (C), 134.4 (C), 141.1 (C), 164.8 (C), 196.1 (C). HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{14}H_{11}ClN_4NaO_2^+$ 325.0463; Found 325.0455.

*4-Acetyl-3-(4-bromophenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5d**)*. Compound **5d** was prepared following general procedure B from 3-(4-bromophenyl)-2*H*-azirine-2-carbonyl azide **3d** (165 mg, 0.62 mmol), acetylacetone **4a** (66 mg, 0.66 mmol) and $NiCl_2 \cdot 6H_2O$ (15 mg, 0.06 mmol) in 158 mg (73% yield) as a colorless solid: mp 129-130 ºC (MeCN). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.82 (s, 3H), 2.58 (s, 3H), 7.10-7.23 (m, 2H), 7.47-7.65 (m, 2H), 9.35 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 31.0 (CH_3), 119.3 (C), 122.6 (C), 124.7 (C), 131.4 (CH), 131.8 (CH), 133.1 (C), 133.5 (C), 141.0 (C), 164.7 (C), 196.1 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{14}H_{10}{}^{79}BrN_4O_2^-$ 344.9993; Found 344.9994.

*4-Acetyl-3-(2-bromophenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5e**)*. Compound **5e** was prepared following general procedure B from 3-(2-bromophenyl)-2*H*-azirine-2-carbonyl azide **3e** (300 mg, 1.13 mmol), acetylacetone **4a** (119 мг, 1.19 mmol) and $NiCl_2 \cdot 6H_2O$ (27 mg, 0.11 mmol) in 341 mg (87% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 118-119 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz):

δ 1.82 (s, 3H), 2.63 (s, 3H), 7.23-7.33 (m, 2H), 7.34-7.43 (m, 1H), 7.64-7.72 (m, 1H), 9.51 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 15.0 (CH_3), 30.1 (CH_3), 119.4 (C), 123.8 (C), 124.7 (C), 127.3 (CH), 129.9 (CH), 131.6 (CH), 132.7 (CH), 132.9 (C), 136.1 (C), 141.6 (C), 164.7 (C), 195.6 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{11}{}^{79}BrN_4NaO_2^+$ 368.9958; Found 368.9950.

*4-Acetyl-5-methyl-3-(p-tolyl)-1H-pyrrole-2-carbonyl azide (**5f**)*. Compound **5f** was prepared following general procedure B from 3-(*p*-tolyl)-2*H*-azirine-2-carbonyl azide **3f** (150 mg, 0.75 mmol), acetylacetone **4a** (79 mg, 0.79 mmol) and $NiCl_2{\cdot}6H_2O$ (18 mg, 0.08 mmol) in 193 mg (91% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 119-120 ºC (petroleum ether/EtOAc). ^1H NMR ($CDCl_3$, 400 MHz): δ 1.80 (s, 3H), 2.42 (s, 3H), 2.58 (s, 3H), 7.09-7.19 (m, 2H), 7.20-7.32 (m, 2H), 9.39 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 21.5 (CH_3), 30.8 (CH_3), 119.3 (C), 124.9 (C), 128.9 (CH), 130.0 (CH), 131.3 (C), 134.9 (C), 138.0 (C), 141.0 (C), 164.9 (C), 196.8 (C). HRMS (ESI) *m/z*: $[M + H]^-$ Calcd for $C_{15}H_{15}N_4O_2$+ 283.1190; Found 283.1201.

*4-Acetyl-3-(4-methoxyphenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5g**)*. Compound **5g** was prepared following general procedure **B** from 3-(4-methoxyphenyl)-2*H*-azirine-2-carbonyl azide **3g** (150 mg, 0.69 mmol), acetylacetone **4a** (73 mg, 0.73 mmol) and $NiCl_2{\cdot}6H_2O$ (16 mg, 0.07 mmol) in 152 mg (74% yield) as a colorless solid: mp 100-101 ºC (MeCN). ^1H NMR ($CDCl_3$, 400 MHz): δ 1.81 (s, 3H), 2.57 (s, 3H), 3.87 (s, 3H), 6.92-7.00 (m, 2H), 7.17-7.24 (m, 2H), 9.37 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 30.8 (CH_3), 55.4 (CH_3), 113.7 (CH), 119.3 (C), 124.9 (C), 126.4 (C), 131.3 (CH), 134.6 (C), 140.9 (C), 159.6 (C), 164.8 (C), 196.8 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{15}H_{14}N_4NaO_3^+$ 321.0958; Found 321.0959.

*4-Acetyl-3-(3-methoxyphenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5h**)*. Compound **5h** was prepared following general procedure B from crude 3-(3-methoxyphenyl)-2*H*-azirine-2-carbonyl azide **3h** (which in its turn was prepared following general procedure A from 350 mg (1.67

mmol) of 5-chloro-3-(3-methoxyphenyl)isoxazole **1h**, 42 mg (0.33 mmol), $FeCl_2$ and 174 mg (2.67 mmol) NaN_3), acetylacetone **4a** (129 мг, 1.29 mmol) and $NiCl_2 \cdot 6H_2O$ (29 mg, 0.12 mmol) in 264 mg (53% yield for two steps, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 118-120 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.83 (s, 3H), 2.58 (s, 3H), 3.83 (s, 3H), 6.80-6.85 (m, 1H), 6.86-6.91 (m, 1H), 6.92-6.98 (m, 1H), 7.33 (t, J = 8.0 Hz, 1H), 9.36 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 30.6 (CH_3), 55.4 (CH_3), 113.6 (CH), 116.0 (CH), 119.2 (C), 122.7 (CH), 124.7 (C), 129.2 (CH), 134.4 (C), 135.8 (C), 141.1 (C), 159.4 (C), 165.0 (C), 196.6 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{15}H_{14}N_4NaO_3^+$ 321.0958; Found 321.0946.

*4-Acetyl-3-(3,4-dimethoxyphenyl)-5-methyl-1H-pyrrole-2-carbonyl azide (**5i**).* Compound **5i** was prepared following general procedure B from 3-(3,4-dimethoxyphenyl)-2*H*-azirine-2-carbonyl azide **3i** (281 mg, 1.14 mmol), acetylacetone **4a** (120 mg, 1.20 mmol) and $NiCl_2 \cdot 6H_2O$ (27 mg, 0.11 mmol) in 336 mg (90% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 129-131 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.84 (s, 3H), 2.57 (s, 3H), 3.88 (s, 3H), 3.94 (s, 3H), 6.80 (d, J = 1.8 Hz, 1H), 6.85 (dd, J = 8.2, 1.8 Hz, 1H), 6.93 (d, J = 8.2 Hz, 1H), 9.29 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.6 (CH_3), 30.6 (CH_3), 55.9 (CH_3), 56.1 (CH_3), 110.9 (CH), 113.5 (CH), 119.3 (C), 122.7 (CH), 124.9 (C), 126.6 (C), 134.5 (C), 140.8 (C), 148.7 (C), 149.1 (C), 164.8 (C), 196.8 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{16}N_4NaO_4+^+$ 351.1064; Found 351.1064.

*4-Acetyl-5-methyl-3-(4-(trifluoromethyl)phenyl)-1H-pyrrole-2-carbonyl azide (**5j**).* Compound **5j** was prepared following general procedure B from crude 3-(4-(trifluoromethyl)phenyl)-2*H*-azirine-2-carbonyl azide **3j** (which in its turn was prepared following general procedure A from 433 mg (1.75 mmol) of 5-chloro-3-(4-(trifluoromethyl)phenyl)isoxazole **1j**, 44 mg (0.35 mmol) $FeCl_2$ and 182 mg (2.80 mmol) NaN_3), acetylacetone **4a** (55 мг, 0.55 mmol) and $NiCl_2 \cdot 6H_2O$ (12 mg, 0.05

mmol) in 110 mg (19% yield for two steps, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 129-131 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.79 (s, 3H), 2.60 (s, 3H), 7.35-7.52 (m, 2H), 7.65-7.77 (m, 2H), 9.42 (s, 1H). ^{19}F{^{1}H} NMR (DMSO-d_6, 376 MHz): δ -60.85. ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.8 (CH_3), 30.5 (CH_3), 118.7 (C), 123.7 (C), 124.3 (q, $J_{C\text{-}F}$ = 270.3 Hz, C), 124.4 (q, $J_{C\text{-}F}$ = 3.7 Hz, CH), 127.9 (q, $J_{C\text{-}F}$ = 31.5 Hz, C), 130.9 (CH), 132.2 (C), 139.3 (C), 140.9 (C), 163.1 (C), 194.1 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{15}H_{10}F_3N_4O_2^-$ 335.0761; Found 335.0763.

*4-Acetyl-5-methyl-3-(naphthalen-2-yl)-1H-pyrrole-2-carbonyl azide (**5k**).* Compound **5k** was prepared following general procedure B from 3-(naphthalen-2-yl)-2*H*-azirine-2-carbonyl azide **3k** (177 mg, 0.75 mmol), acetylacetone **4a** (79 mg, 0.79 mmol) and $NiCl_2{\cdot}6H_2O$ (18 mg, 0.08 mmol) in 202 mg (85% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 134-135 ºC (petroleum ether/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 3H), 3.00 (s, 3H), 7.77-7.84 (m, 1H), 7.88-7.95 (m, 2H), 8.12-8.18 (m, 1H), 8.20-8.26 (m, 1H), 8.27-8.33 (m, 2H), 10.35 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 14.7 (CH_3), 30.9 (CH_3), 119.5 (C), 125.0 (C), 126.6 (CH), 126.6 (CH), 127.7 (CH), 128.0 (CH), 128.1 (CH), 128.2 (CH), 129.2 (CH), 132.0 (C), 133.0 (C), 133.1 (C), 134.5 (C), 141.1 (C), 165.0 (C), 196.6 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{14}N_4NaO_2^+$ 341.1009; Found 341.1010.

*4-Benzoyl-5-methyl-3-phenyl-1H-pyrrole-2-carbonyl azide (**5l**).* Reaction of 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (150 mg, 0.81 mmol), 1-phenylbutane-1,3-dione **4b** (137 mg, 0.85 mmol) and $NiCl_2{\cdot}6H_2O$ (19 mg, 0.08 mmol), performed following general procedure B, gave a *ca*. 1:1 mixture (^{1}H NMR) of regioisomers **5l** and **5m** 245 mg (*ca*. 92% yield). 2-(Azidocarbonyl)pyrrole **5l** was isolated in pure form by chromatography on silica gel (eluent a mixture of benzene/DCM, 5:4 v/v) in 110 mg (41% yield), in contrast to isomer **5m**, which turned out to be unstable. Compound **5l**, colorless solid: mp 106-107 ºC (benzene/DCM). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.88 s (3H), 7.35-7.40 m (2H),

7.40-7.50 m (6H), 7.52-7.60 m (2H), 9.44 s (1H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz): δ 31.4 (CH_3), 120.6 (C), 126.0 (C), 128.1 (CH), 128.3 (CH), 128.9 (CH), 128.9 (CH), 129.7 (CH), 130.3 (CH), 130.7 (C), 133.5 (C), 134.1 (C), 139.3 (C), 164.7 (C), 197.2 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{14}N_4NaO_2^+$ 353.1009; Found 353.0997.

General Procedure C for the Preparation of Carbamates (6a-i, n). A solution of azide **5** (0.93 mmol) in anhyd *t*-BuOH (10 mL) was refluxed for 1 h (monitored by TLC) using oil bath. After the reaction was complete, the solvent was evaporated and the residue was purified by flash column chromatography on silica gel (eluent a mixture of petroleum ether/EtOAc, 3:1 v/v).

*tert-Butyl (4-acetyl-5-methyl-3-phenyl-1H-pyrrol-2-yl)carbamate (**6a**)*. Compound **6a** was prepared following general procedure C from 4-acetyl-5-methyl-3-phenyl-1*H*-pyrrole-2-carbonyl azide **5a** (250 mg, 0.93 mmol) in 283 mg (97% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 177-178 ºC (petroleum ether/EtOAc). ^1H NMR (DMSO-d_6, 400 MHz): δ 1.38 (s, 9H), 1.84 (s, 3H), 2.36 (s, 3H), 7.14-7.28 (m, 3H), 7.29-7.39 (m, 2H), 8.36 (s, 1H), 11.39 (s, 1H). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz): δ 13.5 (CH_3), 28.0 (CH_3), 30.3 (CH_3), 78.6 (C), 118.9 (C), 119.5 (C), 121.3 (C), 126.2 (CH), 127.7 (CH), 129.9 (CH), 131.0 (C), 135.4 (C), 155.2 (C), 194.3 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{23}N_2O_3^+$ 315.1703; Found 315.1716.

*tert-Butyl (4-acetyl-3-(4-fluorophenyl)-5-methyl-1H-pyrrol-2-yl)carbamate (**6b**)*. Compound **6b** was prepared following general procedure C from 4-acetyl-3-(4-fluorophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5b** (323 mg, 1.20 mmol) in 400 mg (100% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 174-176 ºC (petroleum ether/EtOAc). ^1H NMR (DMSO-d_6, 400 MHz): δ 1.37 (s, 9H), 1.88 (s, 3H), 2.36 (s, 3H), 7.02-7.20 (m, 2H), 7.21-7.35 (m, 2H), 8.39 (s, 1H), 11.41 (s, 1H). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz): δ 13.6 (CH_3), 28.0 (CH_3), 30.4 (CH_3), 78.7 (C), 114.4 (d, $J_{C\text{-}F}$ = 21.0 Hz, CH),

117.8 (C), 119.4 (C), 121.6 (C), 131.2 (C), 131.6 (C), 131.7 (d, J_{C-F} = 7.9 Hz, CH), 155.2 (C), 161.0 (d, J_{C-F} = 242.6 Hz, C), 194.0 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{22}FN_2O_3^+$ 333.1609; Found 333.1617.

tert-Butyl (4-acetyl-3-(4-chlorophenyl)-5-methyl-1H-pyrrol-2-yl)carbamate ***(6c)***. Compound **6c** was prepared following general procedure C from 4-acetyl-3-(4-chlorophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5c** (300 mg, 0.99 mmol) in 344 mg (100% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 191-193 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.38 (s, 9H), 1.92 (s, 3H), 2.37 (s, 3H), 7.19-7.26 (m, 2H), 7.34-7.43 (m, 2H), 8.43 (s, 1H), 11.44 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.6 (CH_3), 28.0 (CH_3), 30.4 (CH_3), 78.8 (C), 117.5 (C), 119.3 (C), 121.7 (C), 127.6 (CH), 130.8 (C), 131.3 (C), 131.6 (CH), 134.3 (C), 155.1 (C), 193.9 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{21}ClN_2O_3Na^+$ 371.1133; Found 371.1148.

tert-Butyl (4-acetyl-3-(4-bromophenyl)-5-methyl-1H-pyrrol-2-yl)carbamate ***(6d)***. Compound **6d** was prepared following general procedure C from 4-acetyl-3-(4-bromophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5d** (53 mg, 0.15 mmol) in 57 mg (94% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 199-200 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.38 (s, 9H), 1.93 (s, 3H), 2.37 (s, 3H), 7.01-7.30 (m, 2H), 7.36-7.70 (m, 2H), 8.43 (s, 1H), 11.45 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.6 (CH_3), 28.0 (CH_3), 30.4 (CH_3), 78.8 (C), 117.5 (C), 119.3 (C), 119.4 (C), 121.7 (C), 130.5 (CH), 131.4 (C), 132.0 (CH), 134.6 (C), 155.1 (C), 193.9 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{21}{}^{79}BrN_2O_3Na^+$ 415.0628; Found 415.0611.

tert-Butyl (4-acetyl-3-(2-bromophenyl)-5-methyl-1H-pyrrol-2-yl)carbamate ***(6e)***. Compound **6e** was prepared following general procedure C from 4-acetyl-3-(2-bromophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5e** (300 mg, 0.86 mmol) in 310 mg (91% yield, after flash

chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 194-196 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.35 (s, 9H), 1.79 (s, 3H), 2.39 (s, 3H), 7.19-7.27 (m, 1H), 7.28-7.40 (m, 2H), 7.60-7.69 (m, 1H), 8.37 (m, 1H), 11.41 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.6 (CH_3), 28.0 (CH_3), 29.3 (CH_3), 78.7 (C), 116.9 (C), 119.2 (C), 121.9 (C), 125.4 (C), 127.1 (CH), 128.8 (CH), 131.0 (C), 132.1 (CH), 132.5 (CH), 136.7 (C), 154.7 (C), 193.3 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{21}{}^{79}BrN_2NaO_3^+$ 415.0628; Found 415.0632.

*tert-Butyl (4-acetyl-5-methyl-3-(p-tolyl)-1H-pyrrol-2-yl)carbamate (**6f**)*. Compound **6f** was prepared following general procedure C from 4-acetyl-5-methyl-3-(*p*-tolyl)-1*H*-pyrrole-2-carbonyl azide **5f** (320 mg, 1.13 mmol) in 356 mg (96% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 200-201 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.38 (s, 9H), 1.83 (s, 3H), 2.31 (s, 3H), 2.35 (s, 3H), 7.05-7.20 (m, 4H), 8.32 (s, 1H), 11.36 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.5 (CH_3), 20.7 (CH_3), 28.0 (CH_3), 30.3 (CH_3), 78.6 (C), 118.7 (C), 119.5 (C), 121.2 (C), 128.3 (CH), 129.8 (CH), 131.0 (C), 132.3 (C), 135.2 (C), 155.3 (C), 194.4 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{25}N_2O_3^+$ 329.1860; Found 329.1865.

*tert-Butyl (4-acetyl-3-(4-methoxyphenyl)-5-methyl-1H-pyrrol-2-yl)carbamate (**6g**)*. Compound **6g** was prepared following general procedure C from 4-acetyl-3-(4-methoxyphenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5g** (262 mg, 0.88 mmol) in 287 mg (95% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 194-196 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.38 (s, 9H), 1.83 (s, 3H), 2.35 (s, 3H), 3.76 (s, 3H), 6.84-6.95 (m, 2H), 7.10-7.19 (m, 2H), 8.32 (s, 1H), 11.34 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.5 (CH_3), 28.0 (CH_3), 30.3 (CH_3), 55.0 (CH_3), 78.6 (C),

113.2 (CH), 118.5 (C), 119.5 (C), 121.2 (C), 127.4 (C), 130.9 (C), 131.0 (CH), 155.3 (C), 157.9 (C), 194.4 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{25}N_2O_4^+$ 345.1809; Found 345.1824.

*tert-Butyl (4-acetyl-3-(3-methoxyphenyl)-5-methyl-1H-pyrrol-2-yl)carbamate (**6h**)*. Compound **6h** was prepared following general procedure C from 4-acetyl-3-(3-methoxyphenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5h** (116 mg, 0.39 mmol) in 100 mg (75% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 147-148 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.38 (s, 9H), 1.86 (s, 3H), 2.34 (s, 3H), 3.74 (s, 3H), 6.64-6.94 (m, 3H), 7.24 (t, J = 7.7 Hz, 1H), 8.37 (s, 1H), 11.39 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.4 (CH_3), 28.0 (CH_3), 30.2 (CH_3), 54.9 (CH_3), 78.7 (C), 111.9 (CH), 115.4 (CH), 118.7 (C), 119.5 (C), 121.3 (C), 122.5 (CH), 128.6 (CH), 131.0 (C), 136.7 (C), 155.2 (C), 158.8 (C), 194.4 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{24}N_2NaO_4^+$ 367.1628; Found 367.1630.

*tert-Butyl (4-acetyl-3-(3,4-dimethoxyphenyl)-5-methyl-1H-pyrrol-2-yl)carbamate (**6i**)*. Compound **6i** was prepared following general procedure C from 4-acetyl-3-(3,4-dimethoxyphenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5i** (181 mg, 0.55 mmol) in 113 mg (55% yield, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a colorless solid: mp 163-165 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.39 (s, 9H), 1.85 (s, 3H), 2.34 (s, 3H), 3.72 (s, 3H), 3.76 (s, 3H), 6.68-6.78 (m, 1H), 6.79-6.87 (m, 1H), 6.92 (d, J = 8.2 Hz, 1H), 8.33 (s, 1H), 11.35 (m, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.5 (CH_3), 28.2 (CH_3), 30.2 (CH_3), 55.3 (CH_3), 55.5 (CH_3), 78.6 (C), 111.4 (CH), 114.0 (CH), 118.7 (C), 119.5 (C), 121.1 (C), 122.3 (CH), 127.8 (C), 130.9 (C), 147.5 (C), 148.0 (C), 155.2 (C), 194.4 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{27}N_2O_5^+$ 375.1914; Found 375.1905.

*tert-Butyl (4-benzoyl-3,5-diphenyl-1H-pyrrol-2-yl)carbamate (**6n**)*. Compound **6n** was prepared following general procedure C from 4-benzoyl-3,5-diphenyl-1*H*-pyrrole-2-carbonyl azide

(which in its turn was prepared following general procedure B from 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (200 mg, 1.08 mmol), 1,3-diphenylpropane-1,3-dione **4b** (253 mg, 1.13 mmol) and $NiCl_2 \cdot 6H_2O$ (26 mg, 0.11 mmol)) in 240 mg (yield 51% for 2 steps, after flash chromatography on silica gel using petroleum ether/EtOAc (3:1 v/v) as eluent) as a pale green solid: mp 177-178 ºC (petroleum ether/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.44 (s, 9H), 7.03-7.10 (m, 1H), 7.11-7.19 (m, 5H), 7.20-7.27 (m, 4H), 7.30-7.39 (m, 3H), 7.58-7.64 (m, 2H), 8.69 (s, 1H), 11.88 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 28.3 (CH_3), 79.1 (C), 118.8 (C), 120.3 (C), 123.9 (C), 125.9 (CH), 127.2 (CH), 127.7 (CH), 127.9 (CH), 128.3 (CH), 128.4 (CH), 129.0 (CH), 129.4 (CH), 129.9 (C), 131.7 (C), 132.6 (CH), 134.2 (C), 138.7 (C), 155.5 (C), 194.2 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{28}H_{25}N_2O_3^-$ 437.1871; Found 437.1861.

*1,3-Bis(4-benzoyl-3,5-diphenyl-1H-pyrrol-2-yl)urea (**8a**)*. Compound **8a** was obtained from crude 4-benzoyl-3,5-diphenyl-1*H*-pyrrole-2-carbonyl azide **5n** (48 mg, 0.12 mmol) while standing on air for 2 weeks and purified by column chromatography on silica gel (eluent a mixture of hexanes/EtOAc, 1:1 v/v) to give 22 mg (50% yield) of pure product as a yellow solid: mp 167-169 ºC (dec., hexanes/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.07-7.13 (s, 2H), 7.14-7.20 (m, 10H), 7.21-7.28 (m, 8H), 7.31-7.40 (m, 6H), 7.62-7.69 (m, 4H), 8.41 (s, 2H), 11.75 (s, 2H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 118.6 (C), 124.5 (C), 125.7 (CH), 126.9 (CH), 127.5 (CH), 128.0 (CH), 128.0 (CH), 128.2 (CH), 128.2 (C), 129.0 (CH), 129.2 (C), 129.3 (CH), 131.5 (C), 132.4 (CH), 133.7 (C), 138.5 (C), 155.7 (C), 194.0 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{47}H_{35}N_4O_3^+$ 703.2704; Found 703.2711.

*1,3-Bis(4-acetyl-5-methyl-3-phenyl-1H-pyrrol-2-yl)urea (**8b**)*. 4-Acetyl-5-methyl-3-phenyl-1*H*-pyrrole-2-carbonyl azide **5a** (70 mg, 0.26 mmol) was dissolved in AcOH/H_2O mixture (v/v 1:1, 2 mL) and the resulting solution was refluxed for 1 h by using oil bath heating. The reaction mixture was poured into water (30 mL), neutralized with 5% $NaHCO_3$ and extracted with EtOAc

(3×20 mL). The combined organic phases were washed with water (30 mL), dried over Na_2SO_4, filtered off and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent a mixture of DCM/MeOH, 50:1 v/v) to give 58 mg (96% yield) of pure product as an ochre solid: mp 246-247 ºC (dec., DCM/MeOH). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.83 (s, 6H), 2.37 (s, 6H), 7.10-7.22 (m, 4H), 7.24-7.30 (m, 2H), 7.31-7.38 (m, 4H), 7.84 (s, 2H), 11.30 (s, 2H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.5 (CH_3), 30.3 (CH_3), 119.3 (C), 122.2 (C), 126.2 (CH), 128.0 (CH), 129.0 (C), 130.1 (CH), 130.8 (C), 135.1 (C), 155.5 (C), 194.2 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{27}N_4O_3^+$ 455.2078; Found 455.2095.

*1,3-Bis(4-acetyl-3-(2-bromophenyl)-5-methyl-1H-pyrrol-2-yl)urea (**8c**).* A solution of 4-acetyl-3-(2-bromophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5e** (259 mg, 0.75 mmol) in *o*-DCB (3 mL) was kept at 150 °C for 1 h by using oil bath heating, then the solvent was evaporated and the residue was left overnight. After that it was diluted with DCM containing traces of water, the precipitate formed was filtered off and washed with Et_2O to give pure compound **8c** in 107 mg (47% yield) as an ochre solid: mp > 182 ºC (dec., DCM). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.75 (s, 6H), 2.40 (s, 6H), 7.16-7.31 (m, 4H), 7.33-7.41 (m, 2H), 7.55-7.70 (m, 2H), 7.75 (s, 2H), 11.32 (m, 2H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.7 (CH_3), 29.4 (CH_3), 29.4 (CH_3), 118.7 (C), 118.8 (C), 122.6 (C), 125.6 (C), 127.6 (CH), 129.0 (CH), 130.8 (C), 132.2 (CH), 132.2 (CH), 132.7 (CH), 132.8 (CH), 136.3 (C), 136.3 (C), 154.2 (C), 154.5 (C), 193.1 (C). (Extra peaks in the NMR spectra are associated with hindered rotation of the *o*-bromophenyl moiety of the molecule). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{27}H_{23}{}^{79}Br_2N_4O_3^-$ 611.0142; Found 611.0119.

General Procedure D for the Preparation of Aminopyrroles (9a-c). Carbamate **6** (0.45 mmol) was stirred in CF_3COOH (2-3 mL) at rt for 0.25 h. The reaction mixture was poured into water, neutralized with 5% aq $NaHCO_3$ and extracted with EtOAc. The combined organic phases were dried

with Na_2SO_4, filtered off and concentrated in vacuo. The crude product was washed with benzene and EtOH to give pure aminopyrrole **9**.

1-(5-Amino-2-methyl-4-phenyl-1H-pyrrol-3-yl)ethan-1-one ***(9a)***. Compound **9a** was prepared following general procedure D from *tert*-butyl (4-acetyl-5-methyl-3-phenyl-1*H*-pyrrol-2-yl)carbamate **6a** (141 mg, 0.45 mmol) in 77 mg (80% yield) as a pale yellow solid: mp 214-215 ºC (EtOH). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 2.30 (s, 3H), 4.05 (s, 2H), 7.06-7.25 (m, 3H), 7.27-7.37 (m, 2H), 10.55 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.3 (CH_3), 30.3 (CH_3), 103.4 (C), 119.5 (C), 124.8 (CH), 127.5 (C), 128.0 (CH), 129.7 (CH), 133.6 (C), 136.7 (C), 194.1 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{15}N_2O^+$ 215.1179; Found 215.1171.

1-(5-Amino-2-methyl-4-(p-tolyl)-1H-pyrrol-3-yl)ethan-1-one ***(9f)***. Compound **9f** was prepared following general procedure D from *tert*-butyl (4-acetyl-5-methyl-3-(*p*-tolyl)-1*H*-pyrrol-2-yl)carbamate **6f** (250 mg, 0.76 mmol) in 142 mg (82% yield) as a pale yellow solid: mp 174-176 ºC (EtOH). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.83 (s, 3H), 2.30 (s, 6H), 3.97 (s, 2H), 6.92-7.09 (m, 2H), 7.10-7.23 (m, 2H), 10.53 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 13.3 (CH_3), 20.7 (CH_3), 30.3 (CH_3), 103.3 (C), 119.5 (C), 127.4 (C), 128.7 (CH), 129.7 (CH), 133.4 (C), 133.6 (C), 133.8 (C), 194.1 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{16}N_2NaO^+$ 251.1155; Found 251.1165.

(5-Amino-2,4-diphenyl-1H-pyrrol-3-yl)(phenyl)methanone ***(9n)***. Compound **9n** was prepared following general procedure D from *tert*-butyl (4-benzoyl-3,5-diphenyl-1*H*-pyrrol-2-yl)carbamate **6n** (238 mg, 0.54 mmol) in 155 mg (84% yield) as a red solid: mp > 160 ºC (dec., EtOH). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.58 (s, 2H), 6.93-7.01 (m, 1H), 7.05-7.30 (m, 11H), 7.31-7.38 (m, 1H), 7.60-7.75 (m, 2H), 10.92 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 105.2 (C), 118.9 (C), 124.1 (CH), 125.0 (C), 125.7 (CH), 126.3 (CH), 128.0 (CH), 128.0 (CH), 128.0 (CH), 128.2 (CH), 129.2 (CH), 132.1 (C), 132.2 (CH), 135.3 (C), 136.8 (C), 138.7 (C), 194.5 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{23}H_{17}N_2O^-$ 337.1346; Found 337.1349.

General Procedure E for the Preparation of 3,4-Dihydro-5*H*-pyrrolo[2,3-c]isoquinolin-5-ones (7a-d, f-k). A solution of 1*H*-pyrrole-2-carbonyl azide **5** (0.3-3.5 mmol) in *o*DCB (2-25 mL) was stirred at 150 °C for 0.5 h by using oil bath heating. After the reaction was complete the resulting mixture was cooled to rt, diluted with Et_2O, the precipitate was filtered off, washed with Et_2O and dried to give the pure product.

*1-Acetyl-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7a**).* Compound **7a** was prepared following general procedure E from 4-acetyl-5-methyl-3-phenyl-1*H*-pyrrole-2-carbonyl azide **5a** (955 mg, 3.56 mmol) in 705 mg (82% yield) as a colorless solid: mp > 265 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.51 (s, 3H), 2.60 (s, 3H), 7.25-7.42 (m, 1H), 7.53-7.69 (m, 1H), 8.14-8.31 (m, 1H), 8.77-8.97 (m, 1H), 11.59 (s, 1H), 12.08 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.7 (CH_3), 31.5 (CH_3), 100.9 (C), 117.9 (C), 121.7 (C), 123.5 (CH), 125.3 (CH), 127.3 (CH), 131.4 (CH), 132.7 (C), 134.3 (C), 134.7 (C), 160.5 (C), 194.6 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{12}N_2NaO_2^+$ 263.0791; Found 263.0784.

*1-Acetyl-7-fluoro-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7b**).* Compound **7b** was prepared following general procedure E from 4-acetyl-3-(4-fluorophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5b** (190 mg, 0.66 mmol) in 125 mg (74% yield) as a colorless solid: mp > 300 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.52 (s, 3H), 2.62 (s, 3H), 7.49-7.60 (m, 1H), 7.80-7.94 (m, 1H), 8.99-9.18 (m, 1H), 11.70 (s, 1H), 12.25 (s, 1H). ^{19}F{^{1}H} NMR (DMSO-d_6, 470 MHz): δ -117.80. ^{13}C{^{1}H, ^{19}F} NMR (DMSO-d_6, 125 MHz): δ 14.9 (CH_3), 31.5 (CH_3), 100.9 (C), 111.6 (CH), 117.6 (C), 119.7 (CH), 123.0 (C), 128.4 (CH), 131.2 (C), 132.4 (C), 135.4 (C), 158.7 (C), 159.6 (C), 194.4 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{14}H_{10}FN_2O_2^-$ 257.0732; Found 257.0714.

*1-Acetyl-7-chloro-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7c**).* Compound **7c** was prepared following general procedure E from 4-acetyl-3-(4-chlorophenyl)-5-

methyl-1*H*-pyrrole-2-carbonyl azide **5c** (160 mg, 0.53 mmol) in 116 mg (80% yield) as a colorless solid: mp > 270 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.52 (s, 3H), 2.62 (s, 3H), 7.66 (dd, J = 9.0, 2.5 Hz, 1H), 8.16 (d, J = 2.5 Hz, 1H), 9.01 (d, J = 8.6 Hz, 1H), 11.74 (s, 1H), 12.32 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.9 (CH_3), 31.5 (CH_3), 100.7 (C), 117.6 (C), 122.9 (C), 126.2 (CH), 127.8 (CH), 128.0 (C), 131.3 (CH), 132.9 (C), 132.9 (C), 135.7 (C), 159.4 (C), 194.4 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{14}H_{10}ClN_2O_2^-$ 273.0436; Found 273.0415.

*1-Acetyl-7-bromo-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7d**)*. Compound **7d** was prepared following general procedure E from 4-acetyl-3-(4-bromophenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5d** (104 mg, 0.30 mmol) in 66 mg (69% yield) as a colorless solid: mp > 300 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.51 (s, 3H), 2.61 (s, 3H), 7.77 (dd, J = 9.0, 2.3 Hz, 1H), 8.31 (d, J = 2.2 Hz, 1H), 8.93 (d, J = 8.6 Hz, 1H), 11.74 (s, 1H), 12.33 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.9 (CH_3), 31.5 (CH_3), 100.7 (C), 116.1 (C), 117.7 (C), 123.2 (C), 128.0 (CH), 129.3 (CH), 132.9 (C), 133.2 (C), 134.0 (CH), 135.7 (C), 159.3 (C), 194.4 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{14}H_{10}{}^{79}BrN_2O_2^-$ 316.9931; Found 316.9913.

*1-Acetyl-2,7-dimethyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7f**)*. Compound **7f** was prepared following general procedure E from 4-acetyl-5-methyl-3-(*p*-tolyl)-1*H*-pyrrole-2-carbonyl azide **5f** (145 mg, 0.51 mmol) in 109 mg (83% yield) as a colorless solid: mp > 270 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.41 (s, 3H), 2.50 (s, 3H), 2.59 (s, 3H), 7.45 (dd, J = 8.5, 1.7 Hz, 1H), 7.96-8.10 (m, 1H), 8.80 (d, J = 8.5 Hz, 1H). 11.54 (s, 1H), 11.95 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.8 (CH_3), 20.8 (CH_3), 31.5 (CH_3), 101.0 (C), 117.8 (C), 121.8 (C), 125.4 (CH), 126.9 (CH), 132.1 (C), 132.1 (C), 132.7 (CH), 132.7 (C), 134.5 (C), 160.4 (C), 194.4 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{15}H_{13}N_2O_2^-$ 253.0983; Found 253.0972.

*1-Acetyl-7-methoxy-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7g**)*. Compound **7g** was prepared following general procedure E from 4-acetyl-3-(4-methoxyphenyl)-5-

methyl-1*H*-pyrrole-2-carbonyl azide **5g** (200 mg, 0.67 mmol) in 154 mg (85% yield) as a colorless solid: mp > 270 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.50 (s, 3H), 2.60 (s, 3H), 3.84 (s, 3H), 7.27 (dd, J = 9.1, 3.0 Hz, 1H), 7.67 (d, J = 3.0 Hz, 1H), 8.93 (d, J = 9.1 Hz, 1H), 11.56 (s, 1H), 12.04 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.9 (CH_3), 31.5 (CH_3), 55.1 (CH_3), 101.2 (C), 107.9 (CH), 117.5 (C), 120.9 (CH), 122.8 (C), 127.4 (CH), 128.5 (C), 131.4 (C), 134.6 (C), 155.8 (C), 160.0 (C), 194.3 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{15}H_{13}N_2O_3^-$ 269.0932; Found 269.0923.

*1-Acetyl-8-methoxy-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7h**).* Compound **7h** was prepared following general procedure E from 4-acetyl-3-(3-methoxyphenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5h** (120 mg, 0.40 mmol) in 105 mg (96% yield) as a colorless solid: mp > 280 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.51 (s, 3H), 2.60 (s, 3H), 3.87 (s, 3H), 6.92 (dd, J = 8.9, 2.6 Hz, 1H), 8.13 (d, J = 8.8 Hz), 8.57 (d, J = 2.3 Hz, 1H), 11.55 (s, 1H), 11.86 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.9 (CH_3), 31.6 (CH_3), 55.1 (CH_3), 100.9 (C), 107.5 (CH), 112.5 (CH), 115.8 (C), 117.8 (C), 129.3 (CH), 133.0 (C), 135.0 (C), 136.3 (C), 160.3 (C), 161.7 (C), 194.5 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{15}H_{13}N_2O_3^-$ 269.0932; Found 269.0913.

*1-Acetyl-7,8-dimethoxy-2-methyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7i**).* Compound **7i** was prepared following general procedure E from 4-acetyl-3-(3,4-dimethoxyphenyl)-5-methyl-1*H*-pyrrole-2-carbonyl azide **5i** (120 mg, 0.37 mmol) in 105 mg (95% yield) as a colorless solid: mp > 290 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.51 (s, 3H), 2.62 (s, 3H), 3.84 (s, 3H), 3.90 (s, 3H), 7.61 (s, 1H), 8.78 (s, 1H), 11.56 (s, 1H), 11.90 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 15.2 (CH_3), 31.6 (CH_3), 55.2 (CH_3), 55.3 (CH_3), 101.4 (C), 107.4 (CH), 107.6 (C), 115.3 (CH), 117.3 (C), 129.9 (C), 132.1 (C), 135.2 (C), 146.3 (C), 152.1 (C), 159.6 (C), 194.3 (C). HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{16}H_{16}N_2NaO_4^+$ 323.1002; Found 323.1004.

1-Acetyl-2-methyl-7-(trifluoromethyl)-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (7j). Compound **7j** was prepared following general procedure E from 4-acetyl-5-methyl-3-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole-2-carbonyl azide **5j** (80 mg, 0.24 mmol) in 61 mg (84% yield) as a colorless solid: mp > 280 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.54 (s, 3H), 2.63 (s, 3H), 7.81-8.00 (m, 1H), 8.36-8.63 (m, 1H), 8.89-9.36 (m, 1H), 11.86 (s, 1H), 12.55 (s, 1H). ^{19}F{^{1}H} NMR (DMSO-d_6, 470 MHz): δ -60.56. ^{13}C{^{1}H,^{19}F} NMR (DMSO-d_6, 125 MHz): δ 14.8 (CH_3), 31.5 (CH_3), 100.6 (C), 117.8 (C), 121.2 (C), 123.5 (C), 124.5 (CH), 124.5 (C), 126.7 (CH), 127.1 (C), 134.2 (C), 136.2 (C), 137.0 (C), 160.1 (C), 194.5 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{15}H_{10}F_3N_2O_2^-$ 307.0700; Found 307.0697.

*3-Acetyl-2-methyl-1,11-dihydro-10H-benzo[h]pyrrolo[2,3-c]isoquinolin-10-one (7**k**)*. Compound **7k** was prepared following general procedure E from 4-acetyl-5-methyl-3-(naphthalen-2-yl)-1*H*-pyrrole-2-carbonyl azide **5k** (110 mg, 0.35 mmol) in 91 mg (91% yield) as a yellow solid: mp > 310 ºC (dec., *o*DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.57 (s, 3H), 2.63 (s, 3H), 7.89-7.99 (m, 1H), 8.04 (d, J = 9.1 Hz, 1H), 8.80 (d, J = 9.1 Hz, 1H), 10.07 (d, J = 8.0 Hz, 1H), 11.72 (s, 1H), 12.37 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 14.6 (CH_3), 31.8 (CH_3), 102.9 (C), 117.5 (C), 124.2 (CH), 124.8 (CH), 126.5 (CH), 127.2 (CH), 128.0 (CH), 130.7 (C), 131.9 (CH), 132.0 (C), 134.7 (C), 135.8 (C), 161.0 (C), 195.4 (C). HRMS (ESI) *m/z*: [M + H]$^+$ Calcd for $C_{18}H_{15}N_2O_2^+$ 291.1128; Found 291.1115.

General Procedure F for the Preparation of 3,4-Dihydro-5*H*-pyrrolo[2,3-c]isoquinolin-5-ones (7l, m). A stirring solution of azide **3l** or **3m** (0.5 mmol), acetylacetone **4a** (0.53 mmol, 1.05 equiv) and $NiCl_2{\cdot}6H_2O$ (0.05 mmol, 10 mol%) in dry acetonitrile (5 mL) was refluxed for 1 h or 5 h, respectively, by using oil bath heating. After the reaction was complete, the resulting mixture was cooled to rt, diluted with Et_2O, the precipitate was filtered off, washed with Et_2O and dried to give the pure product.

*8-Acetyl-7-methyl-5,6-dihydro-4H-furo[2,3-d]pyrrolo[2,3-b]pyridin-4-one (**7l**).* Compound **7l** was prepared following general procedure F from 3-(furan-2-yl)-2*H*-azirine-2-carbonyl azide **3l** (80 mg, 0.45 mmol), acetylacetone **4a** (48 mg, 0.48 mmol) and $NiCl_2 \cdot 6H_2O$ (6 mg, 0.05 mmol) in 94 mg (90% yield) as a colorless solid: mp > 320 ºC (dec., MeCN/Et_2O). ^1H NMR (DMSO-d_6, 400 MHz): δ 2.56 (s, 3H), 2.67 (s, 3H), 6.97 (d, J = 1.9 Hz, 1H), 7.86 (d, J = 1.9 Hz, 1H), 11.64 (s, 1H), 11.95 (s, 1H). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 13.9 (CH_3), 30.9 (CH_3), 96.9 (C), 106.1 (CH), 108.1 (C), 111.9 (C), 137.2 (C), 138.5 (C), 142.2 (CH), 154.3 (C), 155.7 (C), 192.2 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{10}N_2NaO_3^+$ 253.0584; Found 253.0584.

*8-Acetyl-7-methyl-5,6-dihydro-4H-pyrrolo[2,3-b]thieno[2,3-d]pyridin-4-one (**7m**).* Compound **7m** was prepared following general procedure F from 3-(thiophen-2-yl)-2*H*-azirine-2-carbonyl azide **3m** (100 mg, 0.52 mmol), acetylacetone **4a** (55 mg, 0.55 mmol) and $NiCl_2 \cdot 6H_2O$ (7 mg, 0.05 mmol) in 115 mg (90% yield) as a colorless solid: mp > 310 ºC (dec., MeCN/Et_2O). ^1H NMR (DMSO-d_6, 400 MHz): δ 2.48 (s, 3H), 2.66 (s, 3H), 7.35 (d, J = 5.5 Hz, 1H), 7.45 (d, J = 5.5 Hz, 1H), 11.66 (s, 1H), 11.87 (s, 1H). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 14.6 (CH_3), 30.0 (CH_3), 104.2 (C), 114.0 (C), 122.8 (CH), 123.0 (C), 123.4 (CH), 135.7 (C), 136.1 (C), 143.2 (C), 156.6 (C), 192.7 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{12}H_9N_2O_2S^-$ 245.0390; Found 245.0372.

General Procedure G for the Preparation of 3,4-Dihydro-5*H*-pyrrolo[2,3-c]isoquinolin-5-ones (7n-q). A solution of azide **3a** (0.5 mmol), diketone **4b, c** or **d** (0.53 mmol) and $NiCl_2 \cdot 6H_2O$ (0.05 mmol) in dry acetonitrile (3 mL) was stirred for 2 d. The solvent was removed in vacuo, dry ^{o}DCB (2-3 mL) was added to the residue and the mixture was stirred at 150 °C for 0.5 h by using oil bath heating. After the reaction was complete, the resulting mixture was cooled to rt, diluted with Et_2O, the precipitate was filtered off, washed with Et_2O and dried to give the pure product.

*1-Benzoyl-2-phenyl-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7n**).* Compound **7n** was prepared following general procedure G from 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (80

mg, 0.43 mmol), 1,3-diphenylpropane-1,3-dione **4b** (101 mg, 0.45 mmol) and $NiCl_2 \cdot 6H_2O$ (10 mg, 0.04 mmol) in 65 mg (41% yield) as a yellow solid: mp 296-298 ºC (^{o}DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.12-7.18 (m, 1H), 7.19-7.26 (m, 2H), 7.28-7.36 (m, 5H), 7.43-7.53 (m, 2H), 7.59-7.66 (m, 1H), 7.74-7.82 (m, 2H), 8.22-8.29 (m, 1H), 12.04 (s, 1H), 12.04 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 102.4 (C), 114.5 (C), 121.7 (C), 122.3 (CH), 123.8 (CH), 127.3 (CH), 128.0 (CH), 128.0 (CH), 128.1 (CH), 128.5 (CH), 129.5 (CH), 131.2 (C), 131.4 (C), 132.0 (CH), 133.0 (CH), 133.4 (C), 134.2 (C), 138.3 (C), 160.8 (C), 195.0 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{24}H_{15}N_2O_2^-$ 363.1139; Found 363.1121.

*1-(4-Methylbenzoyl)-2-(p-tolyl)-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7o**).* Compound **7o** was prepared following general procedure G from 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (140 mg, 0.75 mmol), 1,3-di-*p*-tolylpropane-1,3-dione **4c** (199 mg, 0.79 mmol) and $NiCl_2 \cdot 6H_2O$ (18 mg, 0.08 mmol) in 50 mg (30% yield) as a pale green solid: mp 215-217 ºC (^{o}DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.21 (s, 3H), 2.27 (s, 3H), 7.02-7.09 (m, 2H), 7.14-7.19 (m, 2H), 7.22-7.27 (m, 2H), 7.26-7.31 (m, 1H), 7.45-7.52 (m, 2H), 7.66-7.75 (m, 2H), 8.21-8.28 (m, 1H), 11.95 (s, 2H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 20.6 (CH_3), 21.1 (CH_3), 102.2 (C), 114.1 (C), 121.7 (C), 122.0 (CH), 123.7 (CH), 127.4 (CH), 128.0 (CH), 128.5 (C), 128.9 (CH), 129.2 (CH), 129.6 (CH), 130.2 (C), 132.0 (CH), 133.4 (C), 133.8 (C), 135.7 (C), 136.5 (C), 143.7 (C), 160.7 (C), 195.0 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{26}H_{20}N_2NaO_2^+$ 415.1417; Found 415.1414.

*1-(4-Methoxybenzoyl)-2-(4-methoxyphenyl)-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7p**).* Compound **7p** was prepared following general procedure G from 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (80 mg, 0.43 mmol), 1,3-bis(4-methoxyphenyl)propane-1,3-dione **4d** (128 mg, 0.45 mmol) and $NiCl_2 \cdot 6H_2O$ (10 mg, 0.04 mmol) in 102 mg (56% yield) as a pale green solid: mp 275-276 ºC (^{o}DCB). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.70 (s, 3H), 3.75 (s, 3H), 6.77-6.86 (m, 2H), 6.87-6.92 (m, 2H), 7.24-7.33 (m, 3H), 7.44-7.54 (m, 2H), 7.74-7.82 (m, 2H), 8.19-

8.30 (m, 1H), 1.83 (s, 1H), 11.96 (m, 1H). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz): δ 55.1 (CH_3), 55.4 (CH_3), 102.2 (C), 113.7 (C), 113.8 (CH), 113.9 (CH), 121.6 (C), 122.1 (CH), 123.5 (CH), 123.9 (C), 128.0 (CH), 128.9 (CH), 130.0 (C), 132.1 (C), 131.9 (CH), 131.9 (CH), 133.4 (C), 133.6 (C), 158.5 (C), 160.7 (C), 163.1 (C), 193.8 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{26}H_{19}N_2O_4^-$ 423.1350; Found 423.1338.

*2-(Thiophen-2-yl)-1-(thiophene-2-carbonyl)-3,4-dihydro-5H-pyrrolo[2,3-c]isoquinolin-5-one (**7q**)*. Compound **7q** was prepared following general procedure G from 3-phenyl-2*H*-azirine-2-carbonyl azide **3a** (80 mg, 0.43 mmol), 1,3-di(thiophen-2-yl)propane-1,3-dione **4e** (107 mg, 0.45 mmol) and $NiCl_2{\cdot}6H_2O$ (10 mg, 0.04 mmol) in 84 mg (52% yield) as an ochre solid: mp 285-287 ºC (^{o}DCB). ^1H NMR (DMSO-d_6, 400 MHz): δ 6.98-7.08 (m, 2H), 7.21-7.29 (m, 1H), 7.29-7.36 (m, 1H), 7.38-7.46 (m, 1H), 7.47-7.50 (m, 1H), 7.50-7.60 (m, 2H), 7.91-8.09 (m, 1H), 8.18-8.33 (m, 1H), 12.02 (s, 1H), 12.10 (s, 1H). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz): δ 101.9 (C), 114.7 (C), 121.8 (C), 122.0 (CH), 124.0 (CH), 124.1 (C), 126.0 (CH), 126.4 (CH), 127.4 (CH), 128.1 (CH), 128.7 (CH), 132.2 (CH), 132.7 (C), 133.9 (C), 133.9 (C), 135.3 (CH), 136.0 (CH), 145.2 (C), 160.8 (C), 186.3 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{12}N_2NaO_2S_2^+$ 399.0232; Found 399.0229.

*1-Acetyl-2-methyl-3H-pyrrolo[2,3-c]isoquinolin-5-yl trifluoromethanesulfonate (**13**)*. A suspension of 1-acetyl-2-methyl-3,4-dihydro-5*H*-pyrrolo[2,3-*c*]isoquinolin-5-one (**7a**) (300 mg, 1.25 mmol) in of anhyd DCM (10 mL) was cooled to 0 °C with ice bath and DBU (285 mg, 1.88 mmol, 1.5 equiv) was added under inert atmosphere. After 10 min of stirring, Tf_2O (394 mg, 1.88 mmol, 1.5 equiv) was added and the resulting mixture was stirred for an additional 10 min, after that poured into water, extracted three times with EtOAc; the combined organic phases were washed with sat. aq $NaHCO_3$, dried over Na_2SO_4, filtered and concentrated in vacuo. The resulting solid was washed with Et_2O to give 400 mg (86% yield) of pure product as a colorless solid: mp 237-239 ºC (dec., EtOAc). ^1H NMR (DMSO-d_6, 400 MHz): δ 2.64 (s, 3H), 2.79 (s, 3H), 7.70-7.81 (m, 1H), 7.85-

7.98 (m, 1H), 8.02-8.18 (m, 1H), 9.33-9.51 (m, 1H), 13.04 (s, 1H). $^{19}F\{^{1}H\}$ NMR (DMSO-d_6, 470 MHz): δ -72.96. $^{13}C\{^{1}H,^{19}F\}$ NMR (DMSO-d_6, 125 MHz) : δ 15.5 (CH_3), 31.7 (CH_3), 112.9 (C), 115.8 (C), 117.0 (C), 118.2 (C), 122.6 (CH), 126.4 (CH), 126.4 (CH), 131.1 (CH), 133.7 (C), 137.4 (C), 142.7 (C), 148.0 (C), 194.8 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{15}H_{10}F_3N_2O_4S^-$ 371.0319; Found 371.0294.

1-(2-Methyl-5-(pyridin-2-yl)-3H-pyrrolo[2,3-c]isoquinolin-1-yl)ethan-1-one ***(14)***. Triflate **13** (38 mg, 0.1 mmol), 2-(tributylstannyl)pyridine (99 mg, 0.27 mmol, 2.7 equiv) and CuI (4 mg, 0.02 mmol, 20 mol%) were mixed in dioxane (2 mL). The screw cap tube was flushed with argon, $Pd(PPh_3)_4$ (24 mg, 0.02 mmol, 20 mol%) was added and the mixture was stirred for 48 h at 85 °C by using oil bath heating (monitored by TLC). The solvent was evaporated and the crude product was purified by flash chromatography on silica gel (DCM/MeOH, starting from 100:1 to 20:1 v/v) to give **15** in 29 mg (94% yield) as a yellow solid: mp 242-244 °C (dec., DCM/MeOH). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.64 (s, 3H), 2.80 (s, 3H), 7.43-7.52 (m, 1H), 7.53-7.64 (m, 1H), 7.67-7.78 (m, 1H), 7.84-8.17 (m, 1H), 7.96-8.11 (m, 1H), 8.34-8.75 (m, 1H), 8.50-9.17 (m, 1H), 9.26-9.45 (m, 1H), 12.72 (s, 1H). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz): δ 15.6 (CH_3), 31.8 (CH_3), 111.9 (C), 116.7 (C), 123.3 (C), 123.4 (CH), 124.3 (CH), 125.3 (CH), 125.9 (CH), 128.2 (CH), 128.8 (CH), 131.9 (C), 137.0 (CH), 141.7 (C), 141.9 (C), 148.1 (CH), 152.1 (C), 158.3 (C), 194.9 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{16}N_3O^+$ 302.1288; Found 302.1282.

1-(2-Methyl-5-((trimethylsilyl)ethynyl)-3H-pyrrolo[2,3-c]isoquinolin-1-yl)ethan-1-one ***(15)***. Triflate **13** (38 mg, 0.1 mmol), ethynyltrimethylsilane (15 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol, 10 mol%), CuI (2 mg, 0.01 mmol, 10 mol%) and Et_3N (31 mg, 0.3 mmol, 30 mol%) were mixed in dioxane (2 mL) and heated in a screw cap tube under inert atmosphere for 1 h at 50 °C by using oil bath heating (monitored by TLC). After the reaction was complete the solvent was evaporated and the crude product was purified by flash chromatography on silica gel (eluent a mixture

of hexanes/EtOAc, 1:1 v/v) to give 30 mg (92% yield) of compound **15** as a pale yellow solid: mp 254-256 ºC (dec., hexanes/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.35 (s, 9H), 2.62 (s, 3H), 2.80 (s, 3H), 7.60-7.70 (m, 1H), 7.71-7.81 (m, 1H), 8.31-8.52 (m, 1H), 9.20-9.40 (m, 1H), 12.66 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ -0.3 (CH_3), 15.6 (CH_3), 31.7 (CH_3), 98.3 (C), 102.9 (C), 112.4 (C), 117.0 (C), 125.5 (CH), 125.7 (C), 126.3 (CH), 126.8 (CH), 129.5 (CH), 130.7 (C), 136.5 (C), 142.1 (C), 142.9 (C), 194.9 (C). HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{20}N_2NaOSi^+$ 343.1237; Found 343.1238.

*3-(1-Acetyl-2-methyl-3H-pyrrolo[2,3-c]isoquinolin-5-yl)acrylonitrile (**16**).* Triflate **13** (38 mg, 0.1 mmol), acrylonitrile (11 mg, 0.2 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol, 10 mol%) and Et_3N (31 mg, 0.3 mmol, 30 mol%) were mixed in DMF (2 mL) and heated for 48 h in a screw cap tube under inert atmosphere at 100 °C by using oil bath heating (monitored by TLC). After the reaction was complete the solvent was evaporated and the crude product was purified by flash chromatography on silica gel (eluent a mixture of hexanes/EtOAc, 1:1 v/v) to give 27 mg (98% yield) of compound **16** as a yellow solid: mp 254-256 ºC (dec., hexanes/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.63 (s, 3H), 2.80 (s, 3H), 6.78 (d, J = 15.8 Hz, 1H), 7.56-7.66 (m, 1H), 7.71-7.82 (m, 1H), 8.61 (d, J = 8.5 Hz, 1H), 8.81 (d, J = 15.8 Hz, 1H), 9.30 (d, J = 8.5 Hz, 1H), 12.81 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 15.6 (CH_3), 31.8 (CH_3), 100.1 (CH), 114.1 (C), 117.0 (C), 119.9 (C), 123.6 (C), 124.8 (CH), 125.3 (CH), 126.2 (CH), 129.1 (CH), 131.2 (C), 141.9 (C), 143.9 (C), 144.1 (C), 145.6 (CH), 195.0 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{17}H_{12}N_3O^-$ 274.0986; Found 274.0969.

*1-(5-(4-Methoxyphenyl)-2-methyl-3H-pyrrolo[2,3-c]isoquinolin-1-yl)ethan-1-one (**17a**).* Triflate **13** (38 mg, 0.1 mmol), (4-methoxyphenyl)boronic acid (23 mg, 0.15 mmol, 1.5 equiv), $Pd(OAc)_2$ (2 mg, 0.01 mmol, 10 mol%), PPh_3 (3 mg, 0.01 mmol, 10 mol%), and Et_3N (21 mg, 0.2 mmol, 2 equiv) were mixed in dioxane/water (v/v 4:1, 2 mL) and heated for 24 h in a screw cap tube under inert atmosphere at 60 °C by using oil bath heating (monitored by TLC). After the reaction was

complete the solvent was evaporated and the residue was redissolved in EtOAc and filtered through celite. The resulting solution was washed three times with 1M aq NaOH, twice with water, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (eluent a mixture of hexanes/EtOAc, 1:1 v/v) to give 26 mg (77% yield) of compound **17a** as a colorless solid: mp 261-263 ºC (dec., hexanes/EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.63 (s, 3H), 2.78 (s, 3H), 3.86 (s, 3H), 7.04-7.22 (m, 2H), 7.42-7.52 (m, 1H), 7.56-7.66 (m, 2H), 7.67-7.78 (m, 1H), 7.99-8.17 (m, 1H), 9.23-9.51 (m, 1H), 12.61 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 15.6 (CH_3), 31.7 (CH_3), 55.2 (CH_3), 110.6 (C), 113.6 (CH), 116.6 (C), 123.3 (C), 124.2 (CH), 126.2 (CH), 127.8 (CH), 128.8 (CH), 131.3 (CH), 132.0 (C), 132.0 (C), 141.1 (C), 142.1 (C), 154.7 (C), 159.3 (C), 194.8 (C). HRMS (ESI) *m/z*: [M - H]$^-$ Calcd for $C_{21}H_{17}N_2O_2^-$ 329.1296; Found 329.1284.

*1-(5-(4-Fluorophenyl)-2-methyl-3H-pyrrolo[2,3-c]isoquinolin-1-yl)ethan-1-one (**17b**).* Triflate **13** (38 mg, 0.1 mmol), (4-fluorophenyl)boronic acid (21 mg, 0.15 mmol, 1.5 equiv) and Et_3N (31 mg, 0.3 mmol, 3 equiv) were mixed in dioxane/water (v/v 4:1, 2 mL). The screw cap tube was flushed with argon, $Pd(PPh_3)_4$ (6 mg, 0.005 mmol, 5 mol%) was added and the mixture was stirred for 24 h at 85 °C by using oil bath heating (monitored by TLC). The solvent was evaporated and the residue was redissolved in EtOAc and filtered through celite. The resulting solution was washed three times with 1M aq NaOH, twice with water, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by washing with Et_2O/hexanes to give 31 mg (95%) of compound **17b** as a colorless solid: mp 288-290 °C (dec., EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.64 (s, 3H), 2.79 (s, 3H), 7.29-7.44 (m, 2H), 7.45-7.52 (m, 1H), 7.65-7.81 (m, 3H), 8.00 (d, J = 8.5 Hz, 1H), 9.37 (d, J = 8.5 Hz, 1H), 12.66 (s, 1H). ^{19}F{^{1}H} NMR (DMSO-d_6, 376 MHz): δ -113.78. ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 11.56 (CH_3), 31.7 (CH_3), 111.0 (C), 115.1 (d, $J_{C\text{-}F}$ = 21.5 Hz, CH), 116.6 (C), 123.2 (C), 124.4 (CH), 126.2 (CH), 127.5 (CH), 129.0 (CH), 131.9 (C), 132.0 (d, $J_{C\text{-}F}$

= 8.3 Hz, CH), 136.1 (d, J_{C-F} = 3.1 Hz, C), 141.4 (C), 142.0 (C), 153.8 (C), 162.1 (d, J_{C-F} = 245.2, C), 194.8 (C). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{16}FN_2O^+$ 319.1241; Found 319.1242.

1-(2-Methyl-5-(thiophen-2-yl)-3H-pyrrolo[2,3-c]isoquinolin-1-yl)ethan-1-one ***(17c)***.

Triflate **13** (38 mg, 0.1 mmol), thiophen-2-ylboronic acid (20 mg, 0.15 mmol, 1.5 equiv) and Et_3N (31 mg, 0.3 mmol, 3 equiv) were mixed in dioxane/water (v/v 4:1, 2 mL). The screw cap tube was flushed with argon, $Pd(PPh_3)_4$ (6 mg, 0.005 mmol, 5 mol%) was added and the mixture was stirred for 24 h at 85 °C by using oil bath heating (monitored by TLC). The solvent was evaporated and the residue was redissolved in EtOAc and filtered through celite. The resulting solution was washed three times with 1M aq NaOH, twice with water, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by washing with Et_2O/hexanes to give 30 mg (96%) of compound **17c** as a beige solid: mp 232-234 °C (dec., EtOAc). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.63 (s, 3H), 2.78 (s, 3H), 7.16-7.38 (m, 1H), 7.50-7.61 (m, 1H), 7.63-7.71 (m, 1H), 7.72-7.90 (m, 2H), 8.54 (d, J = 8.5 Hz, 1H), 9.36 (d, J = 8.5 Hz, 1H), 12.74 (s, 1H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): δ 15.6 (CH_3), 31.7 (CH_3), 111.2 (C), 116.7 (C), 122.6 (C), 124.9 (CH), 126.3 (CH), 127.1 (CH), 127.7 (CH), 127.8 (CH), 128.7 (CH), 129.1 (CH), 132.0 (C), 141.7 (C), 141.9 (C), 142.7 (C), 147.4 (C), 194.8 (C). HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{18}H_{13}N_2OS^-$ 305.0754; Found 305.0740.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.0000000.

X-ray diffraction experiments, NMR spectra for new compounds, computation details, and energies of compounds and their Cartesian coordinates (PDF)**.**

Crystal data for compound **3d**, **5d**, **7n** and **14** (CIF).

AUTHOR INFORMATION

ORCID

Liya D. Funt: 0000-0001-9322-4078

Yulia V. Krivolapova: 0000-0002-0965-3732

Mikhail S. Novikov: 0000-0001-5106-4723

Alexander F. Khlebnikov: 0000-0002-6100-0309

Notes

The authors declare no competing financial interest.

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