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Base-promoted new C-C bond formation: an expedient route for the preparation of thiazolo- and imidazolo-pyridinones via Michael addition

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ABSTRACT

Base-catalyzed one-pot cyclocondensation reactions of acryloyl and cinnamoyl chlorides with β-nitroenamine derivatives have been performed under mild conditions and target 7-substituted thiazolo-[3,2-*a*] or imidazolo-[1,2-*a*]pyridin-5-one derivatives were prepared successfully in moderate to good yields. The cyclization reactions may proceed via Michael addition followed by iminoketene-amide tautomerization in view of the products formed.

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1. Introduction

One-pot cyclisations offer some benefits over sequential addition-cyclisation such as greater efficiency and more rapid reactions, less waste-production and greater atom economy. One-pot annulation reactions of enamines with suitable nucleophiles or electrophiles have been extensively studied over the past three decades for the preparation of functionalized heterocyclic systems.[1] However, there are few reports in the literature[2] on intermolecular annulation reactions of heterocyclic enamines bearing electron-withdrawing groups with α,β-unsaturated compounds to produce *N*-containing fused heterocycles , especially thiazolo or imidazolo-2-pyridone derivatives, in a one-pot fashion. This is due to their bisnucleophilicity, they give annulation products with different electrophiles, reacting via the carbon at a β-position to nitrogen and at the -NH group by the effect of electron-withdrawing groups on the double bond (push-pull system).[3]

Fused *N*-heterocyclic compounds (especially those containing 2-pyridone residues) produced in these cyclisations would be easily converted into biologically important natural products such as saxitoxin and camptothecin (Figure 1).[4] Moreover, the thiazolo[3,2-*a*]pyridinone structure is the key part of pilicide-based antibiotic derivatives (Figure 1) which constitute compounds targeting virulence in Gram negative bacteria.[5]

Thiazolopyridinones and imidazolopyridinones have shown a wide variety of biological activities including antihypertensive, antihepatic, antiviral, antifungal, vasodilatory and some insecticidal properties.[6-7]

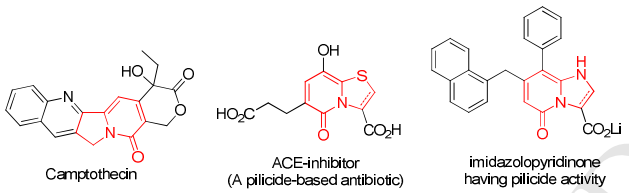
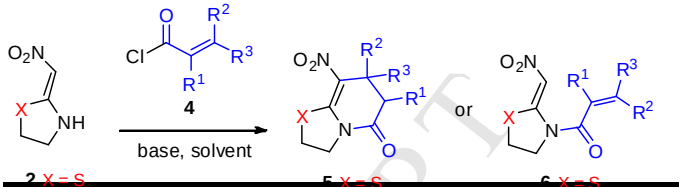


Figure 1. Examples of 2-pyridone or thiazolo- (or imidazolo-) pyridinone containing natural products and bioloically active compounds

Recently, thiazolopyridin-2-ones have been prepared by starting from 2*H*- or 2-alkyl-substituted Δ^2-thiazolines and Meldrum's acid derivatives or by using 2-piperidinethione under a modified Eschenmoser sulfur contraction reaction with DBU in moderate yields. However, tetrahydroimidazolo pyridinones were prepared in moderate to good yield through a multicomponent Michael cyclisation of β-nitroketeneaminal, aldehydes, and Meldrum's acid.[5a,8] In similar fashion, the preparation of some thiazolo (or imidazolo)pyridinone carboxylic acids by the azaannulation of itaconic anhydride with α-nitro-*N*,*S* and -*N*,*N*-ketene acetals and the preparation of imidazolopyridinones by annulation of 2-(ethoxycarbonyl methylene)tetrahydroimidazoles with different 1,3-bis-electrophiles have been found as good examples in recent literature.[9] Besides, imidazo[1,2-*a*]pyridinones can be prepared by either one-pot four-component condensation reaction of ethane-1,2-diamine, 1,1-bis(methylthio)-2-nitroethene, aldehydes, and activated methylene compounds in moderate yields or by stepwise cyclisation of α,β-unsaturated esters with 2-(nitromethylene)imidazolidine in good yields.[10] Even though the last example[10a] demonstrates preparation of imidazolo[1,2-*a*]pyridinones, it's a very limited study which contains only one example and the reaction is slow. Also, the method requires more than one step to obtain the annulation product. Conversely, in the context of our interest in one-pot ring closure reactions with suitable Michael donors and our trials to find a very efficient method using a suitable Lewis base catalyst, we envisaged that heterocyclic secondary enamines, (2-nitromethylene) thiazolidine **2** or imidazolidine **3** may react with suitable Michael acceptors similar to those found in the literature.[8-10] For this purpose, both heterocyclic nitroenamines **2**,**3** were prepared very efficiently from the reaction of 1,1-bis(methylthio)-2-nitroethene **1** with 1,2-ethylenediamine or 2-mercaptoethylamine.[11,12]



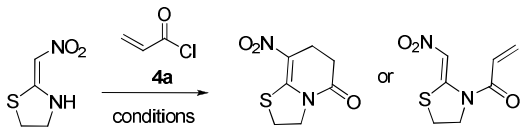
Scheme 1. General method for the preparation of thiazolo(imidazolo)pyridinones **5**,**7** and *N*-enoyl-(2-nitro methylene)thiazolidines (or imidazolidines) **6**,**8**

Here, we report a base-catalyzed one-pot aza-Michael annulation of derivatives **2** and **3** with acryloyl and cinnamic acid chlorides **4** under very mild basic conditions, which affords tetrahydrothiazolo[3,2-*a*]pyridinones **5** or tetrahydro-imidazolo[1,2-*a*]pyridinones **7** (Scheme 1) by a new and simple methodology. Besides, some uncyclised Michael addition products (derivatives of **6** and **8**) were obtained in a few reactions (Scheme 1).

2. Results and Discussion

Our initial experiments using **2** and **4a** in different solvents and conditions with different bases were focused to find the optimal reaction conditions for the cyclisations. So, we have tried a variety of bases and Lewis bases to determine their effects on the cyclisations (Table 1). First of all, no desired products (**5a** or **6a**) formed without using a base (entries 1-2).

Table 1. Optimisation of reaction conditions



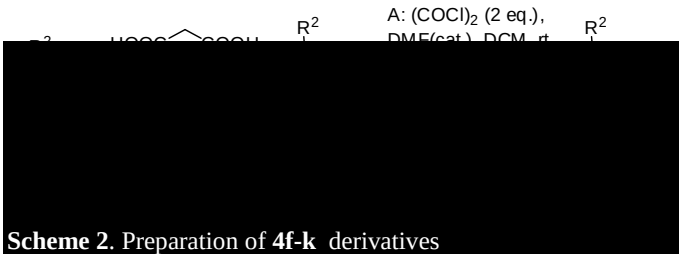
Entry	Bases (equiv.)[b]	Conditions	Yield (%)[c] 5a	6a
1	No base	DCM, r.t., 5 h	_[a]	_[a]
2	No base	CH_3CN, reflux, 3 h	_[a]	_[a]
3	pyridine (2 eq.)	DCM, r.t., 3 h	_	23
4	pyridine (2 eq.)	CH_3CN, reflux, 2 h	_	15
5	Et_3N (2.2 eq)	DCM, r.t., 4 h	21	36
6	Et_3N (2.5 eq)	CH_3CN, reflux, 2 h	_	25
7	piperidine (1.5 eq.)	CH_3CN, reflux, 2 h	_	53
8	CH_3NH_2 (2.0 eq.)	DCM, reflux, 3 h	_[a]	_[a]
9	DBU (2.0 eq.)	CH_3CN, reflux, 2 h	_	32
10	i-Pr_2NEt (1.5 eq.)	DCM, r.t., 8 h	_	48
12	$Ca(OH)_2$ (2.0 eq.)	DCM, r.t., 4 h	48	34
13	Cs_2CO_3 (2.0 eq.)	CH_3CN, r.t., 3 h	_	25
14	Cs_2CO_3 (1.2 eq.)	CH_3CN, reflux, 2 h	18	40
15	**K_2CO_3 (2.0 eq.)**	**DCM, r.t., 3 h**	**90**	_
16	K_2CO_3 (2.0 eq.)	CH_3CN, reflux, 3 h	50	_

[a] None of this product formed. [b] Equivalents of bases respect to nitroenamine. [c]All yields were calculated after purification by flash chromatography.

While most of the amine bases showed poor or no activity to induce the cyclisation (entries 3-10), inorganic bases were

moderately active and facilitated the formation of cyclisation products (entries 12-16). However, addition of 2.2 equiv of Et_3N in DCM at room temperature led to formation of products **5a** in 21% and **6a** in 36% yields (entry 5). In the presence of $Ca(OH)_2$, better yields were obtained for formation of product **5a** (entry 12). Addition of Cs_2CO_3 was only effective at reflux, giving the products in low yields (entry 14). We were then pleased to find that use of 2 equiv of K_2CO_3 in DCM gave the cyclisation product **5a** in excellent yields (90%) at room temperature with no **6a** formation observed (entry 15). However, a low yield of **5a** was obtained when the same mixture was refluxed in acetonitrile (entry 16).

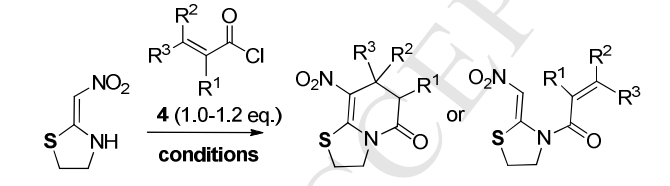
After finding the optimized conditions for the model reaction, we first studied the Michael cyclisations of some commercially available acryloyl chlorides **4a-b**, **4d-e** and cinnamoyl chloride **4c** with **2** (Table 2). Thiazolopyridinones **5a-c** were obtained in good yields (entries 1-4) using K_2CO_3 or Cs_2CO_3 at room temperature or at reflux. Also, some cinnamic acid chlorides **4f-k** were prepared in excellent yields (95-100%) by literature methods[13] (Scheme 2) and reacted with **2** (Table 2, entries 8-13).



Scheme 2. Preparation of **4f-k** derivatives

The title compounds **5g-j** have been obtained in moderate to good yields (entries 9-12) using mostly K_2CO_3 in CH_3CN at reflux. However, only using Cs_2CO_3 at 25 °C was effective in the formation of **5f** (entry 8), the use of K_2CO_3 did not lead any product formation either at room temperature or at reflux. The reaction of **4k** with **2** did not give any cyclisation or other product. The molecular structure of **5a** was determined by X-ray single crystal analysis (Figure 2).[14]

Table 2. Formation of thiazolopyridinones **5** and *N*-enoyl-(2-nitromethylene)thiazolidines **6**



2 (1.0 eq.) **5** **6**

Entry	Substrate	Conditions	Product	Yield (%) [a]
1	**4a**	A	**5a**	90
2	**4b**	B	**5b**	79
3		C		35
4	**4c**	C	**5c**	89
5	**4d**	B	**6d**	62
6		C		70
7	**4e**	C	**6e**	61
8	**4f**	C	**5f**	67
9	**4g**	B	**5g**	58
10	**4h**	B	**5h**	79
11	**4i**	B	**5i**	57
12	**4j**	B	**5j**	69
13	**4k**	B	– [b]	– [b]

Conditions: **A**: K_2CO_3 (2.0 eq.), 25˚C, DCM, 3-16h; **B**: K_2CO_3 (2.0 eq.), 80˚C, CH_3CN, 4-36h; **C**: Cs_2CO_3(1.0-2.0 eq.), 25˚C, CH_3CN, 1.5-16h;
[a] Yields after isolation by flash chromatography using hexane:ethyl acetate mixtures. [b] No product was observed in TLC.

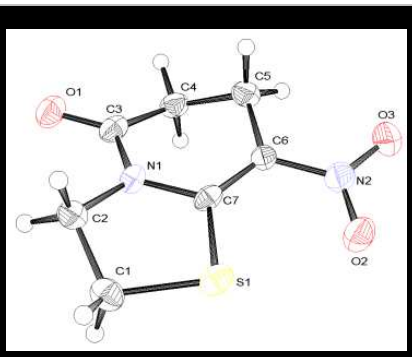
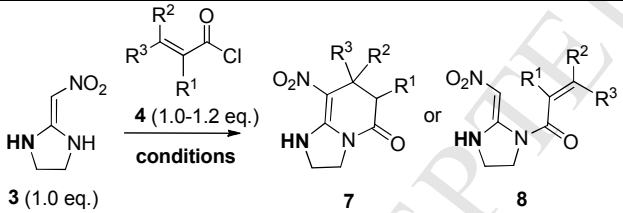


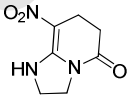
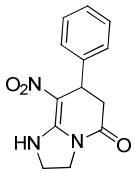
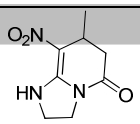
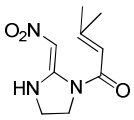
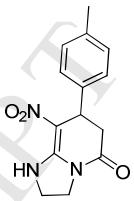
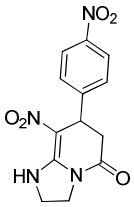
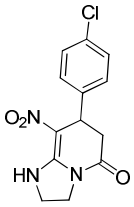
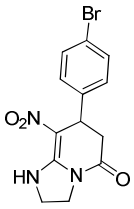
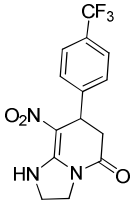
Figure 2. X-ray structure of **5a**

Our success in the formation of derivatives **5** using compound **2** through Michael addition by this one-step transformation prompted us to investigate the behaviour of 2-(nitromethylene)imidazoline **3** with compounds **4a-k** (Table 3). Perhaps surprisingly, no cyclisation product **7** was obtained in the reaction of **3** with **4a** in the presence of K_2CO_3 (or Cs_2CO_3) (entry 1). However, the title compound **7a** was obtained in excellent yield (96%) using 2 equiv of Et_3N in CH_3CN at reflux (entry 2). Suprisingly, the reaction of **4b** with **3** was unsuccessful in giving either product **7b** or **8b** (entry 3), but the reaction of **4d** with **3** did give the expected cyclisation product **7d** in good yield (entry 6). This contrast between the reactions of **2** and **3** with compounds **4b** and **4d** might be explained by the mechanistic difference in their cyclisation reactions (see schemes 3 and 5). However, **4e** with **3** afforded only addition product **8e** in excellent yields (entry 7). The reactions of cinnamic acid chlorides **4c** and **4f-j** with **3** afforded the expected cyclisation products **7c** and **7f-j** in the presence of triethylamine in good yields (entry 5 and entries 8-12).

Table 3. Formation of imidazolopyridinones **7** and *N*-enoyl-(2-nitromethylene)imidazolidines **8**



3 (1.0 eq.) **7** **8**

Entry	Substrate	Conditions	Product	Yield(%)[a]
1	**4a**	A, C	–[b]	–[b]
2	**4a**	D	 **7a**	96
3	**4b**	B, D	–[b]	–[b]
4	**4c**	B	 **7c**	–[b]
5		D		89[c]
6	**4d**	D	 **7d**	74
7	**4e**	D	 **8e**	95
8	**4f**	D	 **7f**	68
9	**4g**	D	 **7g**	60
10	**4h**	D	 **7h**	76
11	**4i**	D	 **7i**	58
12	**4j**	D	 **7j**	72
13	**4k**	D	–[b]	–[b]

Conditions: **A**: K_2CO_3 (2.0 eq.), 25 ˚C, DCM, 3-16 h; **B**: K_2CO_3 (2.0 eq.), 80 ˚C, CH_3CN, 4-36 h; **C**: Cs_2CO_3 (1.0-2.0 eq.), 25 ˚C, CH_3CN, 1.5-16 h; **D**: Et_3N (2.0 eq.), 80 ˚C, CH_3CN, 2-24 h.

[a] Yields after isolation by flash chromatography using ethyl acetate. [b] No product was observed in TLC. [c] Purified by recrystallization from ethyl acetate.

We propose a plausible mechanism for the formation of thiazolo derivatives **5** in Scheme 3. First, in the presence of K_2CO_3 or Cs_2CO_3, **2** gives a nitronic acid salt intermediate by tautomerization. Then, Michael addition through the β-C atom of **4** with the nitronic acid gives an imino-ketene intermediate. Then

follows an acylation of the imine nitrogen and a second tautomerization step, resulting in ring closure reactions affording thiazolopyridinones **5**.

Scheme 3. Plausible mechanism for the formation of **5**

However, uncyclised addition products **6d-e** have been obtained by the reactions of compound **2** with **4d-e** in moderate yields under similar conditions (Table 2, entries 5-7). Since crotonoyl (**4d**) and 3,3-dimethylacryloyl (**4e**) chlorides have alkyl group(s) on the end of double bond, they are poor Michael acceptors and this may prevent the cyclisation. Alternatively, they may form by loss of a proton next to the C=O on **5d-e** and retrocyclisation via an allenyl nitronate and tautomerism (Scheme 4). The structure of **6d** was demonstrated by X-ray crystallography (Figure 3).[14]

Scheme 4. Ring-opening mechanism for the formation of **6d-e**

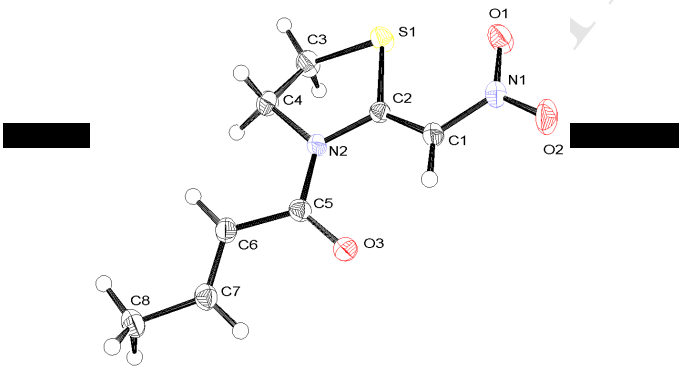
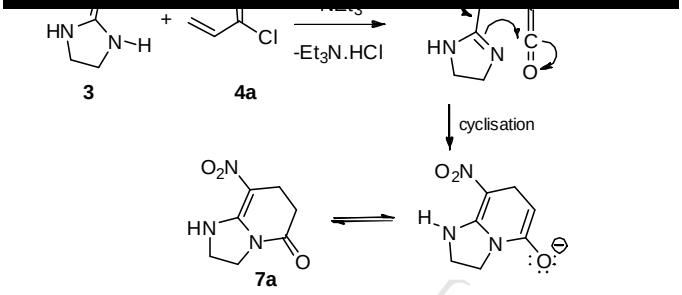


Figure 3. X-ray structure of **6d**

Likewise, we can propose a similar mechanism for the formation of derivatives **7**. First, in the presence of triethylamine, Michael addition through the β-C atom of **4a** with compound **3** gives an imino-ketene intermediate which undergoes an intramolecular cyclisation with a final tautomerization affording the title compound **7a** (Scheme 5).



Scheme 5. Proposed mechanism for the formation of **7a**

3. Conclusions

In summary, we have described a practical, rapid and very efficient one-pot protocol for the preparation of thiazolo[3,2-*a*]- and imidazolo[1,2-*a*]-pyridinones in good yields through the reactions of 2-(nitromethylene)thiazolidine (or imidazolidine) with β-substituted acryloyl chlorides using homogenous or heterogenous bases under mild conditions. Since various biologically important molecules containing thiazolo (or imidazolo) pyridinone cores are of interest in a pharmaceutical context, our synthetic process would provide a new contribution to the preparation of industrially relevant molecules. Besides, further applications of this method are underway in our laboratories for the synthesis of analogous heterocycles.

4. Experimental

4.1. General information

All reactions were carried out at room temperature without excluding air and stirred magnetically. β-Nitroenamines[11-12] and cinnamic acid chlorides[13] were synthesized prior to use following literature procedures. ^{1}H and ^{13}C NMR (400 or 300 MHz for proton and 100 or 75 MHz for carbon, respectively) spectra were recorded either in $CDCl_3$ or in DMSO-d_6 at ambient temperature. Infrared spectra were recorded on a FT-IR Spectrometer (KBr pellet or NaCl discs) and a FT-IR Spectormeter with ATR (Attenuated Total Reflectance) system. High resolution mass spectra (HRMS) of compounds were obtained on an orthogonal acceleration-TOF mass spectrometer and a FTMS (4.7T) mass spectrometer. Melting points were determined with a Meltemp apparatus without corrections. TLC was done using precoated plates with fluorescent indicator (Merck 5735) and plates were visualized by exposure to ultraviolet light or with the stain solution of permanganate and iodine chamber.
Reagents and solvents were purchased as reagent grade and were used without further purification. Flash column chromatography was performed over silica gel (Merck, 230-400 Mesh ASTM) and the eluent was a mixture of ethyl acetate (EA) and hexanes (H) or only ethyl acetate.

4.2. General procedure for preparation of thiazolo[3,2-*a*]pyridin-5-one(s) 5 or *N*-enoyl-(2-nitromethylene) thiazolidines 6.

A solution of heterocyclic nitroenamine **2** (0.5 mmol) and β-substituted acryloyl chloride **4** (0.6 mmol) in CH_2Cl_2 (20 mL) was stirred for 5 minutes, then K_2CO_3 (1 mmol) was added. The reaction mixture was stirred for 3 hours at 25 ^{o}C and checked regularly by TLC. After consumption of compound **2**, the reaction was stopped and undissolved solid was removed by filtration. The remaining solution was evaporated to afford yellow crystalline solid. The crude product was purified by using

flash chromatography on silica gel, (50% hexane/ethyl acetate) to give desired product **5** or **6**.

4.2.1. 8-Nitro-6,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridin-5(3*H*)-one (5a). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), acryloyl chloride **4a** (50µL, 55 mg, 0.6 mmol) and K_2CO_3 (138 mg, 1 mmol) were stirred in CH_2Cl_2 (20 mL) at 25 ^oC for 3 hours and purified by flash chromatography (50% ethyl acetate/hexane) to afford **5a** (90 mg, 90%) as yellow-greenish crystals, m.p. 190-191 ˚C; R_f: (33% hexane/ethyl acetate) 0.70; ν_{max} (KBr) 2922 (C-H), 2852, 1701 (amide C=O), 1577 (C=C-NO_2), 1369, 1274, 1180, 1089, 1035, 819, 740 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 4.12 (2H, t, *J* 7.6 Hz), 3.27 (2H, t, *J* 8.0 Hz), 2.96 (2H, t, *J* 7.6 Hz), 2.72 (2H, t, *J* 8.0 Hz); δ_C (100 MHz, DMSO-d_6, Me_4Si) 21.6, 28.8, 30.7, 49.0, 123.4, 156.2, 167.2; *m/z* (TOF-MS ES^+) 201 (100, MH^+), 189 (18), 181 (2), 55 (2%); HRMS (ESI^+): MH^+, found 201.0329. $C_7H_9N_2O_3S$ requires 201.0334.

4.2.2. 7-Methyl-8-nitro-6,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridin-5(3*H*)-one (5b). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), methacryloyl chloride **4b** (59µL, 63 mg, 0.6 mmol) and K_2CO_3 (138 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for overnight and purified by flash chromatography (50% ethyl acetate/hexane) to afford **5b** (85 mg, 79%) as orange-yellow crystals, m.p. 170-172 ˚C; R_f: (50% ethyl acetate/hexane) 0.65; ν_{max} (KBr) 2974 (C-H), 2916, 1701 (amide C=O), 1581 (C=C-NO_2), 1371, 1313, 1292, 1234, 1184, 1062, 995, 877, 717 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 4.42 (1H, pentet, *J* 6.0 Hz), 4.11 (1H, m), 3.35 (1H, q, *J* 6.0 Hz), 3.21 - 3.27 (2H, m), 2.67 - 2.85 (2H, m), 1.34 (3H, d, *J* 6.6 Hz); δ_C (75 MHz, $CDCl_3$, Me_4Si) 15.4, 28.7, 29.3, 35.4, 49.0, 122.7, 155.7, 170.2; *m/z* (TOF-MS AP^+) 215 (100, MH^+), 198 (80), 183 (15), 159 (25%); HRMS (AP^+): MH^+, found 215.0495. $C_8H_{11}N_2O_3S$ requires 215.0490.

4.2.3. 8-Nitro-7-phenyl-6,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridin-5(3*H*)-one (5c). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), cinnamoyl chloride **4c** (83 mg, 0.5 mmol) and Cs_2CO_3 (163 mg, 0.5 mmol) were stirred in CH_3CN (25 mL) at 25 ^oC for overnight and purified by flash chromatography (33% ethyl acetate/hexane) to afford **5c** (123 mg, 89%) as yellow powder, m.p. 155-157 ˚C; R_f: (50% ethyl acetate/hexane) 0.47; ν_{max} (KBr) 3063 (arom. C-H), 2922 (C-H), 2854, 1703 (amide C=O), 1579 (C=C-NO_2), 1450, 1371, 1278, 1226, 1157, 1091, 952, 844, 700 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.26 - 7.34 (3H, m, Ph), 7.13 (2H, d, *J* 8.1 Hz, Ph), 4.76 (1H, dd, *J* 8.1, 1.2 Hz), 4.63 (1H, ddd, *J* 14.7, 6.9, 4.5 Hz), 4.00 (1H, dt, *J* 11.7, 9.3 Hz), 3.25 - 3.35 (2H, m), 3.17 (1H, dd, *J* 16.8, 8.1 Hz), 2.97 (1H, dd, *J* 16.8, 1.8 Hz); δ_C (75 MHz, $CDCl_3$, Me_4Si) 28.6, 38.1, 38.8, 48.9, 126.2, 127.8, 129.1, 129.2, 139.5(C=C-NO_2), 156.5, 166.2 (C=O); *m/z* (TOF-MS APCI) 277 (100, MH^+), 260 (40), 243 (8), 215 (8), 181 (1%); HRMS (APCI): MH^+, found 277.0653. $C_{13}H_{13}N_2O_3S$ requires 277.0647.

4.2.4. 8-Nitro-7-p-tolyl-6,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridin-5(3*H*)-one (5f). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), *p*-methylcinnamoyl chloride **4f** (90 mg, 0.5 mmol) and Cs_2CO_3 (326 mg, 1 mmol) were stirred in CH_3CN (25 mL) at 25 ^oC for overnight and purified by flash chromatography (50% ethyl acetate/hexane) to afford **5f** (97 mg, 67%) as yellow powder, m.p. 213-214 ˚C; R_f: (33% hexane/ethyl acetate) 0.67; ν_{max} (KBr) 3016 (arom.CH), 2916 (C-H), 2852, 1701 (amide C=O), 1581 (C=C-NO_2), 1444, 1367, 1282, 1226, 1192, 1087, 950, 848, 723 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.11 (2H, d, *J* 8.1 Hz), 7.01 (2H, d, *J* 8.1 Hz), 4.72 (1H, dd, *J* 7.8, 1.2 Hz), 4.62 (1H, ddd, *J* 11.7, 7.2, 4.5 Hz), 3.99 (1H, dt, *J* 12.0, 9.3 Hz), 3.24- 3.30 (2H, m), 3.15 (1H, dd, *J* 16.5, 8.1 Hz), 2.95 (1H, dd, *J* 16.5, 1.5 Hz), 2.31 (3H, s, -CH_3); δ_C (75 MHz, $CDCl_3$, Me_4Si) 21.0 (-CH_3), 28.6, 37.7, 38.8, 48.8, 126.1, 129.8, 136.4, 137.5, 148.4 (C=C-NO_2), 156.4, 166.4 (C=O); *m/z* (TOF-MS ES^+) 291 (100, MH^+), 239 (40), 196 (10), 140 (30), 102 (90%); HRMS (ESI^+): MH^+, found 291.0802. $C_{14}H_{15}N_2O_3S$ requires 291.0803.

4.2.5. 8-Nitro-7-(4-nitrophenyl)-6,7-dihydro-2*H*-thiazolo[3,2-*a*] pyridin-5(3*H*)-one (5g). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), *p*-nitrocinnamoyl chloride **4g** (106 mg, 0.5 mmol) and K_2CO_3 (138 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for overnight and purified by flash chromatography (50% ethyl acetate/hexane) to afford **5g** (93 mg, 58%) as yellow powder, m.p. 204-206 ˚C; R_f: (33% hexane/ethyl acetate) 0.20; ν_{max} (KBr) 3074 (arom. C-H), 2906 (C-H), 2848, 1707 (amide C=O), 1572 (C=C-NO_2), 1450, 1348, 1284, 1228, 1188, 1157, 1087, 949, 856, 703 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.20 (2H, d, *J* 8.6 Hz), 7.32 (2H, d, *J* 9.0 Hz), 4.87 (1H, d, *J* 7.5 Hz), 4.64 (1H, ddd, *J* 11.7, 6.3, 5.1 Hz), 4.06 (1H, dt, *J* 12.0, 9.3 Hz), 3.30 - 3.36 (2H, m), 3.25 (1H, dd, *J* 16.8, 8.4 Hz), 2.97 (1H, dd, *J* 16.8, 1.6 Hz); δ_C (75 MHz, $CDCl_3$, Me_4Si) 28.7, 38.1, 38.2, 49.1, 100.0, 124.5, 127.4, 146.8, 147.5, (C=C-NO_2), 157.3, 165.3 (C=O); *m/z* (TOF-MS ES^+) 322 (55, MH^+), 239 (95), 196 (8), 140 (30), 102 (93%); HRMS (ESI^+): MH^+, found 322.0486. $C_{13}H_{12}N_3O_5S$ requires 322.0498.

4.2.6. 7-(4-Chlorophenyl)-8-nitro-6,7-dihydro-2*H*-thiazolo [3,2-*a*]pyridin-5(3*H*)-one (5h). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), *p*-chlorocinnamoyl chloride **4h** (100.5 mg, 0.5 mmol) and K_2CO_3 (138 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 6 hours and purified by flash chromatography (50% ethyl acetate/hexane) to afford **5h** (122 mg, 79%) as white solid, m.p. 162 ˚C (decomp.); R_f: (50% ethyl acetate/hexane) 0.82; ν_{max} (KBr) 3053 (arom. C-H), 2983 (C-H), 2916, 1701 (amide C=O), 1570 (C=C-NO_2), 1438, 1282, 1226, 1147, 1109, 950, 848, 736 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.28 (2H, d, *J* 8.1 Hz), 7.06 (2H, d, *J* 8.4 Hz), 4.73 (1H, dd, *J* 8.1, 1.5 Hz), 4.62 (1H, ddd, *J* 12.0, 6.9, 4.8 Hz), 4.01 (1H, dt, *J* 11.7, 9.3 Hz), 3.26 -3.31 (2H, m), 3.17 (1H, dd, *J* 16.8, 8.1 Hz), 2.93 (1H, dd, *J* 16.8, 1.5); δ_C (75 MHz, $CDCl_3$, Me_4Si) 28.6, 37.6, 38.6, 48.9, 127.7, 129.3, 133.7, 138.0, 144.7, 156.7, 165.9 (C=O); *m/z* (TOF-MS ES^+) 311 (100, MH^+), 239 (30), 196 (8), 140 (25), 102 (65%); HRMS (ESI^+): MH^+, found 311.0250. $C_{13}H_{12}ClN_2O_3S$ requires 311.0257.

4.2.7. 7-(4-Bromophenyl)-8-nitro-6,7-dihydro-2*H*-thiazolo [3,2-*a*]pyridin-5(3*H*)-one (5i). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), *p*-bromocinnamoyl chloride **4i** (122.5 mg, 0.5 mmol) and K_2CO_3 (138 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 4 hours and purified by flash chromatography (50% ethyl acetate/hexane) to afford **5i** (100 mg, 57%) as yellow crystals, m.p. 145 ˚C (decomp.); R_f: (50% ethyl acetate/hexane) 0.63; ν_{max} (KBr) 3053 (arom. C-H), 2929 (C-H), 2858, 1701 (amide C=O), 1581 (C=C-NO_2), 1450, 1282, 1226, 1192, 1157, 1087, 952, 844, 763 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.42 (2H, d, *J* 8.4 Hz), 6.99 (2H, d, *J* 8.4 Hz), 4.71 (1H, dd, *J* 6.9, 0.9 Hz), 4.61 (1H, ddd, *J* 11.7, 6.6, 4.5 Hz), 3.99 (1H, dt, *J* 12.0, 9.3 Hz), 3.24 - 3.31 (2H, m), 3.16 (1H, dd, *J* 16.5, 8.1 Hz), 2.92 (1H, dd, *J* 13.5, 1.5 Hz); δ_C (75 MHz, $CDCl_3$, Me_4Si) 28.6, 37.7, 38.5, 48.9, 121.8, 125.5, 128.0, 132.3, 138.5 (C=C-NO_2), 156.8, 165.9 (C=O); *m/z* (TOF-MS ES^+) 354 (50, MH^+), 301 (25), 266(50), 239 (45), 140

(30), 102 (100%); HRMS (ESI^+): MH^+, found 354.9746. $C_{13}H_{12}BrN_2O_3S$ requires 354.9752.

4.2.8. 8-Nitro-7-(4-(trifluoromethyl)phenyl)-6,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridin-5(3*H*)-one (5j). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), *p*-trifluoromethylcinnamoyl chloride **4j** (117 mg, 0.5 mmol) and K_2CO_3 (138 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for overnight and purified by flash chromatography (33% hexane/ethyl acetate) to afford **5j** (118 mg, 69%) as white crystals, m.p. 148-149 ˚C; R_f: (50% ethyl acetate/hexane) 0.70; ν_{max} (ATR-mode) 3051 (arom. C-H), 2897 (C-H), 1701 (amide C=O), 1581 (C=C-NO_2), 1448, 1369, 1284, 1226, 1192, 1157, 1085, 950, 837, 727 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.10 (2H, dd, *J* 9.0, 5.4 Hz), 7.00 (2H, t, *J* 8.6 Hz), 4.75 (1H, dd, *J* 8.1, 1.5 Hz), 4.63 (1H, ddd, *J* 11.6, 6.8, 4.4 Hz), 4.01 (1H, dt, *J* 12.0, 9.6 Hz), 3.26 - 3.32 (2H, m), 3.17 (1H, dd, *J* 16.5, 8.1 Hz), 2.94 (1H, dd, *J* 16.8, 1.6 Hz); δ_C (75 MHz, $CDCl_3$, Me_4Si) 28.4, 37.2, 38.5, 48.6, 115.6, 115.9, 125.6, 127.6, 135.0, 156.4, 160.3, 163.5, 165.7 (C=O); *m/z* (TOF-MS ES^+) 295 (100, MH^+-CF_2), 239 (40), 196 (5), 140 (20), 102 (60%); HRMS (ESI^+): MH^+, found 295.0539. $C_{13}H_{12}FN_2O_3S$ requires 295.0553.

4.2.9. 2-(Nitromethylene)thiazolidin-3-yl)but-2-en-1-one (6d). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), crotonoyl chloride **4d** (58µL, 63 mg, 0.6 mmol) and Cs_2CO_3 (163 mg, 0.5 mmol) were stirred in CH_3CN (25 mL) at 25 ^oC for 1.5 hour or K_2CO_3 (138 mg, 1 mmol) in CH_3CN (25 mL) at reflux for 16 hours and purified by flash chromatography (25% ethyl acetate/hexane) to afford **6d** (80 mg, 70%) as yellow crystals, m.p. 112-114 ˚C; R_f: (50% ethyl acetate/hexane) 0.42; ν_{max} (KBr) 3174 (C=$CHNO_2$), 2960 (C-H), 2937, 1685 (C=$C(CH_3)_2$, 1629(C=C-NO_2), 1533, 1453, 1388, 1321, 1290, 1203, 1176, 1101, 1012, 956, 779, 665 cm^{-1}; δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.42 (1H, s, C=$CHNO_2$), 7.15 (1H, septet, *J* 7.2 Hz), 6.26 (1H, dq, *J* 15.0, 1.5 Hz), 4.30 (3H, t, *J* 7.2 Hz), 3.15 (3H, t, *J* 7.2 Hz), 2.00 (3H, dd, *J* 6.9, 1.6 Hz); δ_C (75 MHz, $CDCl_3$, Me_4Si) 18.6, 27.7, 52.4, 122.8, 148.1, 158.6, 164.5; *m/z* (TOF-MS AP^+) 215 (15, MH^+), 170 (8), 129 (15), 95.0 (12), 83.0 (100%); HRMS (AP^+): MH^+, found 215.0490. $C_8H_{11}N_2O_3S$ requires 215.0490.

4.2.10. 3-Methyl-1-(2-(nitromethylene)thiazolidin-3-yl)but-2-en-1-one (6e). Following the general procedure, heterocyclic nitroenamine **2** (73.0 mg, 0.5 mmol), 3,3-dimethylacryloyl chloride **4e** (55 µL,59 mg, 0.5 mmol) and Cs_2CO_3 (163 mg, 0.5 mmol) were stirred in CH_3CN (25 mL) at 25 ^oC for overnight and purified by flash chromatography (33% ethyl acetate/hexane) to afford **6e** (70 mg, 61%) as pale yellow crystals, m.p. 98-99 ˚C; R_f: (50% ethyl acetate/hexane) 0.54; ν_{max} (KBr) 3174 (C=$CHNO_2$), 2941 (C-H), 2916, 1685 (C=O), 1631 (C=$C(CH_3)_2$, 1545 (C=C-NO_2), 1444, 1365, 1323, 1232, 1165, 1143, 1062, 864, 777, 665 cm^{-1}; δ_H (400 MHz, $CDCl_3$, Me_4Si) 8.43 (1H, s, C=$CHNO_2$), 5.93 (1H, t, *J* 1.2 Hz), 4.26 (3H, t, *J* 7.2 Hz), 3.12 (3H, t, *J* 14.8 Hz), 2.13 (3H, d, *J* 1.2 Hz), 1.99 (3H, d, *J* 1.2 Hz); δ_C (100 MHz, $CDCl_3$, Me_4Si) 21.2, 27.8, 27.9, 52.9, 117.6, 121.9, 158.7, 159.1, 165.2; *m/z* (TOF-MS AP^+) 229 (100, MH^+), 215 (8), 173 (25), 156 (60%); HRMS (AP^+): MH^+, found 229.0641. $C_9H_{13}N_2O_3S$ requires 229.0647.

4.3. General procedure for preparation of tetrahydroimidazo[1,2-*a*]pyridin-5-one(s) 7 or *N*-enoyl-(2-nitromethylene) imidazolidines 8.

A solution of heterocyclic nitroenamine **3** (0.5 mmol) and β-substituted acryloyl chloride **4** (0.6 mmol) in CH_3CN (25 mL) was stirred for 5 minutes, then triethylamine (1 mmol) was added. The reaction mixture was refluxed in CH_3CN for 3.5 hours and the completion of reaction was contolled by TLC. The reaction was stopped and the solvent was rotary evaporated to dryness. 20 mL of water was added into remaining crude product and stirred for 15 min at room temperature. The organic part was extracted using ethyl acetate (3x15 mL) and combined organic layers were dried over anhydrous $MgSO_4$ and filtered. Remaining brown solution was evaporated and the crude product was purified by using flash chromatography on silica gel, using ethyl acetate, to give desired product **7** or **8**.

4.3.1. 8-Nitro-2,3,6,7-tetrahydroimidazo[1,2-*a*]pyridin-5(1*H*)-one (7a). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), acryloyl chloride **4a** (50µL, 55 mg, 0.6 mmol) and Et_3N (68 µL, 50 mg, 0.5 mmol) were stirred in CH_3CN (25 mL) at reflux for 3.5 hours and purified by flash chromatography (ethyl acetate) to afford **7a** (88 mg, 96%) as yellowish-white powder, m.p. 208 ˚C (decomp.); R_f: (ethyl acetate) 0.10; ν_{max} (KBr) 3355 (N-H), 2956 (C-H), 2918, 1701 (C=O), 1647 (C=C-NO_2), 1489, 1400, 1350, 1315, 1286, 1217, 1174, 1147, 1022, 933, 661, 555 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.59 (1H, s, -NH), 3.85 (2H, t, *J* 7.6 Hz), 3.72 (2H, t, *J* 7.2 Hz), 2.82 (2H, t, *J* 8.0 Hz), 2.61 (2H, t, *J* 7.6 Hz); δ_C (100 MHz, DMSO-d_6, Me_4Si) 20.9, 31.0, 43.1, 43.8, 103.8, 153.2, 168.8; *m/z* (TOF-MS ES^+) 184 (100, MH^+), 173 (35), 167 (5%); HRMS (ESI^+): MH^+, found 184.0724. $C_7H_{10}N_3O_3$ requires 184.0722.

4.3.2. 8-Nitro--7-phenyl-2,3,6,7-tetrahydroimidazo[1,2-*a*] pyridin-5(1*H*)-one (7c). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), cinnamoyl chloride **4c** (83 mg, 0.5 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 4 hours and purified by flash chromatography (ethyl acetate) to afford **7c** (114 mg, 88%) as yellow powder, m.p. 228-229 ˚C; R_f: (ethyl acetate) 0.43; ν_{max} (KBr) 3279 (N-H), 3026 (arom. CH), 2922 (C-H), 1697 (C=O), 1631 (C=C-NO_2), 1485, 1444, 1284, 1213, 1180, 1143, 1028, 937,756, 698 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.73 (1H, s, -NH), 7.29 (2H, t, *J* 7.2 Hz), 7.22 (1H, t, *J* 6.8 Hz), 7.15 (2H, d, *J* 7.2 Hz), 4.54 (1H, d, *J* 6.8 Hz), 3.76 - 3.96 (4H, m), 3.21 (1H, dd, *J* 15.6, 8.0 Hz), 2.58 (1H, d, *J* 15.6 Hz); δ_C (100 MHz, DMSO-d_6, Me_4Si) 37.8, 40.8, 43.2, 44.1, 106.8, 127.0, 127.5, 129.3, 143.1, 153.3, 168.0; *m/z* (TOF-MS ES^+) 260 (100, MH^+), 231.5 (30), 203.0 (12), 167 (5%); HRMS (ESI^+): MH^+, found 260.1028. $C_{13}H_{14}N_3O_3$ requires 260.1035.

4.3.3. 7-Methyl-8-nitro-2,3,6,7-tetrahydroimidazo[1,2-*a*] pyridin-5(1*H*)-one (7d). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), crotonoyl chloride **4d** (58µL, 63 mg, 0.6 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 3.5 hours and purified by flash chromatography (ethyl acetate) to afford **7d** (72 mg, 74%) as yellowish-white solid, m.p. 186-187 ˚C; R_f: (ethyl acetate) 0.30; ν_{max} (KBr) 3347 (N-H), 2956 (C-H), 2924, 2854, 1701 (C=O), 1631 (C=C-NO_2), 1485, 1450, 1348, 1309, 1286, 1172, 1147, 1030, 935, 765, 665 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.53 (1H, s, -NH), 3.80 - 3.93 (3H, m), 3.70 - 3.74 (2H, m), 2.86 (1H, dd, *J* 16.4, 6.8 Hz), 2.34 (1H, dd, *J* 16.8, 2.0 Hz), 1.00 (3H, d, *J* 6.4 Hz); δ_C (100 MHz, DMSO-d_6, Me_4Si) 18.9, 27.6, 38.8, 43.1, 43.9, 108.8, 152.5, 168.4; *m/z* (TOF-MS ES^+) 196 (40, M^+-H), 187(5%); HRMS (ESI^-): M^+-H, found 196.0729. $C_8H_{10}N_3O_3$ requires 196.0722.

4.3.4. 8-Nitro-7-p-tolyl-2,3,6,7-tetrahydroimidazo[1,2-*a*]pyridin-5 (1*H*)-one (7f). Following the general procedure,

heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), *p*-methylcinnamoyl chloride **4f** (90 mg, 0.5 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 3 hours and purified by flash chromatography (ethyl acetate) to afford **7f** (93 mg, 68%) as white powder, m.p. 275 ˚C (decomp.); R_f: (ethyl acetate) 0.33; ν_{max} (KBr) 3358 (N-H), 2920 (C-H), 2852, 1701 (C=O), 1620 (C=C-NO_2), 1444, 1344, 1325, 1282, 1213, 1180, 1143, 1028, 810, 767, 665 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.71 (1H, s, -NH), 7.09 (2H, d, *J* 8.4 Hz), 7.02 (2H, t, *J* 7.6 Hz), 4.49 (1H, d, *J* 6.8 Hz), 3.75 - 3.97 (4H, m), 3.18 (1H, dd, *J* 16.8, 7.6 Hz), 2.58 (1H, d, *J* 16.4 Hz), 2.24 (3H, s); δ_C (100 MHz, DMSO-d_6, Me_4Si) 20.4, 30.2, 36.6, 42.4, 43.3, 106.2, 126.1, 129.1, 135.8, 139.2, 152.5, 167.3; *m/z* (TOF-MS ES^+) 274 (100, MH^+), 238 (10), 218.0 (5), 161 (2%); HRMS (ESI^+): MH^+, found 274.1183. $C_{14}H_{16}N_3O_3$ requires 274.1192.

4.3.5. 8-Nitro-7-(4-nitrophenyl)-2,3,6,7-tetrahydroimidazo [1,2-*a*]pyridin-5(1*H*)-one (7g). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), *p*-nitrocinnamoyl chloride **4g** (106 mg, 0.5 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 2 hours and purified by flash chromatography (ethyl acetate) to afford **7g** (92 mg, 60%) as yellow powder, m.p. 208 ˚C (decomp.); R_f: (ethyl acetate) 0.30; ν_{max} (KBr) 3358 (N-H), 3072, 2983(C-H), 2926, 1707 (C=O), 1639 (C=C-NO_2), 1597 (-NO_2), 1491, 1452, 1344, 1313, 1286, 1174, 1147, 1026, 933, 856, 771, 665 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.81 (1H, s, -NH), 8.15 (2H, d, *J* 8.4 Hz), 7.47 (2H, d, *J* 8.4 Hz), 4.71 (1H, d, *J* 7.6 Hz), 3.78 - 3.97 (4H, m), 3.29 (1H, dd, *J* 16.8, 8.4 Hz), 2.62 (1H, d, *J* 16.4 Hz); δ_C (100 MHz, DMSO-d_6, Me_4Si) 30.2, 37.1, 42.5, 43.5, 105.2, 123.7, 127.8, 146.4, 150.2, 152.5, 166.7; *m/z* (TOF-MS ES^+) 305 (100, MH^+), 254(45), 225.0 (20), 123 (2%); HRMS (ESI^+): MH^+, found 305.0883. $C_{13}H_{13}N_4O_5$ requires 305.0886.

4.3.6. 7-(4-Chlorophenyl)-8-nitro-2,3,6,7-tetrahydroimidazo [1,2-*a*]pyridin-5(1*H*)-one (7h). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), *p*-chlorocinnamoyl chloride **4h** (100.5 mg, 0.5 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 5 hours and purified by flash chromatography (ethyl acetate) to afford **7h** (112 mg, 76%) as white powder, m.p. 250 ˚C (decomp.); R_f: (ethyl acetate) 0.83; ν_{max} (KBr) 3219 (N-H), 2922 (C-H), 2852, 1701 (C=O), 1620 (C=C-NO_2), 1485, 1448, 1369, 1344, 1319, 1282, 1215, 1180, 1143, 1028, 933, 819, 767, 665 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.72 (1H, s, -NH), 7.31 (2H, d, *J* 8.4 Hz), 7.15 (2H, d, *J* 8.4 Hz), 4.52 (1H, d, *J* 6.8 Hz), 3.73 - 3.92 (4H, m), 3.18 (1H, dd, *J* 16.8, 8.0 Hz), 2.54 (1H, dd, *J* 16.8, 1.6 Hz); δ_C (100 MHz, DMSO-d_6, Me_4Si) 37.3, 39.5, 43.3, 44.2, 106.5, 129.0, 129.2, 132.1, 142.1, 153.2, 167.8; *m/z* (TOF-MS ES^+) 294 (100, MH^+), 248.0 (5), 220.0 (2), 156 (1%); HRMS (ESI^+): MH^+, found 294.0631. $C_{13}H_{13}ClN_3O_3$ requires 294.0645.

4.3.7. 7-(4-Bromophenyl)-8-nitro-2,3,6,7-tetrahydroimidazo [1,2-*a*]pyridin-5(1*H*)-one (7i). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), *p*-bromocinnamoyl chloride **4i** (122.5 mg, 0.5 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 24 hours and purified by flash chromatography (ethyl acetate) to afford **7i** (98 mg, 58%) as yellow powder, m.p. 200 ˚C (decomp.); R_f: (ethyl acetate) 0.10; ν_{max} (ATR-mode) 3219 (N-H), 2953 (C-H), 2922, 2854, 1699 (C=O), 1622 (C=C-NO_2), 1485, 1446, 1371, 1342, 1317, 1280, 1213, 1180, 1145, 1028, 964, 821, 767, 642 cm^{-1}; δ_H (300 MHz, DMSO-d_6, Me_4Si) 9.74 (1H, s, -NH), 7.48 (2H, d, *J* 8.4 Hz), 7.12 (2H, d, *J* 8.4 Hz), 4.52 (1H, d, *J* 6.6 Hz), 3.77 - 3.97 (4H, m), 3.21 (1H, dd, *J* 16.8, 8.1 Hz), 2.57 (1H, dd, *J* 16.5, 1.5 Hz); δ_C (75 MHz, DMSO-d_6, Me_4Si) 32.0, 37.1, 43.1, 43.9, 106.3, 120.3, 129.1, 131.9, 142.3, 153.0, 167.5; *m/z* (TOF-MS ES^+) 338 (100, MH^+), 239.0 (10), 140.0 (5), 102 (15%); HRMS (ESI^+): MH^+, found 338.0128. $C_{13}H_{13}BrN_3O_3$ requires 338.0140.

4.3.8. 8-Nitro-7-(4-(trifluoromethyl)phenyl)-2,3,6,7-tetra hydroimidazo[1,2-*a*]pyridin-5(1*H*)-one (7j). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), *p*-trifluoromethylcinnamoyl chloride **4j** (117 mg, 0.5 mmol) and Et_3N (135 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 24 hours and purified by flash chromatography (ethyl acetate) to afford **7j** (118 mg, 72%) as white crystals, m.p. 255-256 ˚C; R_f: (ethyl acetate) 0.10; ν_{max} (ATR-mode) 3246 (N-H), 2922(C-H), 2854, 1703 (C=O), 1622 (C=C-NO_2), 1508, 1485, 1446, 1342, 1315, 1284, 1180, 1143, 1028, 939, 837, 767, 686 cm^{-1}; δ_H (300 MHz, DMSO-d_6, Me_4Si) 9.71 (1H, s, -NH), 7.19 (2H, td, *J* 5.1, 2.5 Hz), 7.10 (2H, t, *J* 9.0 Hz), 4.54 (1H, d, *J* 7.2 Hz), 3.75 - 3.96 (4H, m), 3.20 (1H, dd, *J* 16.5, 7.8 Hz), 2.56 (1H, dd, *J* 16.5, 0.9 Hz); δ_C (75 MHz, DMSO-d_6, Me_4Si) 36.9, 43.0, 43.9, 106.6, 115.6, 115.9, 128.7, 139.0, 153.0, 159.9, 163.1, 167.7; *m/z* (TOF-MS ES^+) 278 (100, MH^+-CF_2), 239.0 (20), 140.0 (10), 102.1 (40%); HRMS (ESI^+): MH^+-CF_2, found 278.0937. $C_{13}H_{13}FN_3O_3$ requires 278.0941.

4.3.9. 3-Methyl-1-(2-(nitromethylene)imidazolidin-1-yl)but-2-en-1-one (8e). Following the general procedure, heterocyclic nitroenamine **3** (64.5 mg, 0.5 mmol), 3,3-dimethylacryloyl chloride **4e** (68 µL,71 mg, 0.6 mmol) and Et_3N (139 µL, 101 mg, 1 mmol) were stirred in CH_3CN (25 mL) at reflux for 5.5 hours and purified by flash chromatography (33% hexane/ethyl acetate) to afford **8e** (100 mg, 95%) as yellow solid, m.p. 171-172 ˚C; R_f: (50% ethyl acetate/hexane) 0.75; ν_{max} (ATR-mode) 3253 (-NH), 3178 (C=$CHNO_2$), 2922 (C-H), 2859, 1739(C=O), 1683 (C=$C(Me)_2$), 1585 (C=C-NO_2), 1436, 1355, 1307, 1205, 1182, 1126, 1083, 1051, 958, 823, 765, 684 cm^{-1}; δ_H (400 MHz, DMSO-d_6, Me_4Si) 9.65 (1H, s, -NH), 7.78 (1H, s, C=$CHNO_2$), 6.03 (1H, s, C=CHCO), 4.06 (2H, t, *J* 8.4), 3.65 (2H, t, *J* 8.4), 2.02 (3H, s), 1.90 (3H, s); δ_C (100 MHz, DMSO-d_6, Me_4Si) 20.2, 26.9, 42.4, 45.9, 101.4, 116.9, 154.5, 156.6, 165.0 (C=O); *m/z* (TOF-MS ES^+) 212 (100, MH^+), 190 (1), 130 (5%); HRMS (ESI^+): MH^+, found 212.1030. $C_9H_{14}N_3O_3$ requires 212.1035.

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