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Iodine-catalyzed Diazenylation with Arylhydrazine hydrochlorides in air

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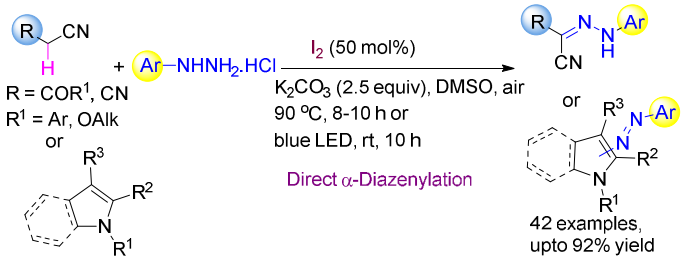


ABSTRACT. A mild approach to diazenylation of active methylene compounds and *N*-heterocyclic compounds with arylhydrazine hydrochlorides in the presence of iodine under basic aerobic conditions was developed. The reaction could be executed either under heating or in the presence of blue LED light, though later condition was found to be relatively efficient. Presumably, the aryldiazene produced by oxidation of arylhydrazine hydrochloride acts as nitrogen scavenger of the radical intermediate

generated from the active methylene compound in the presence of iodine to produce the diazo compounds. Scope and limitations of the protocol are presented.

KEYWORDS. Diazo compound, Iodine, diazenylation, Arylhydrazine hydrochloride, diazene, air,

Introduction

Azo compounds are of profound importance due to their applications in organic synthesis, chemical industry and biological systems.[1,2] They are used as radical reaction initiator, as ligands of metal complexes, dyes and pigments, therapeutic agents, materials, metallo-assemblies and sensors, food additives and in textiles. In addition, the potential of azo compounds to act as drug carrier for site specific delivery particularly to colon wherein bacterial extracellular azoreductase catalyzes the reduction to produce the therapeutically active amine is reported too.[3] Given such significance, their chemistry has received immense attention. Often, the synthesis of diazo compounds is realized by coupling of the diazo salts, Wills coupling of nitroso and nitro compounds with aromatic amines and Wallach rearrangement of azoxy derivatives.[4] Some of the recently reported methods also include catalytic reduction of aromatic nitro compounds,[5] oxidation of anilines,[6] and dehydrogenation of arylhydrazine.[7] Notably however, to overcome the limitations of the reported strategies and avoid excessive use of diazonium salts, innovative milder options for diazenylations have been reported recently. Luo and co-workers[8] disclosed $Sc(OTf)_3$-catalyzed diazenylation of 1,3-carbonyls using triazene whereas Cao et al. and Zhang et al. achieved diazenylation of indole and pyrazole, respectively with triazene in the presence of ionic liquids (Fig. 1).[9-10] Very recently, Jiang et al. disclosed silver salt-mediated gem-difluoromethylenation of the nitrogen center of aryldiazonium salts for preparing diazenyl derivatives.[11] Remarkably all these methods proceeded via the intermediacy of aryldiazonium ions which are also known to serve as precursors to arylhydrazines via reduction.[12] Heinrich et al. disclosed that the aryldiazonum salt under the influence of $SnCl_2$ in HCl leads to aryldiazene which

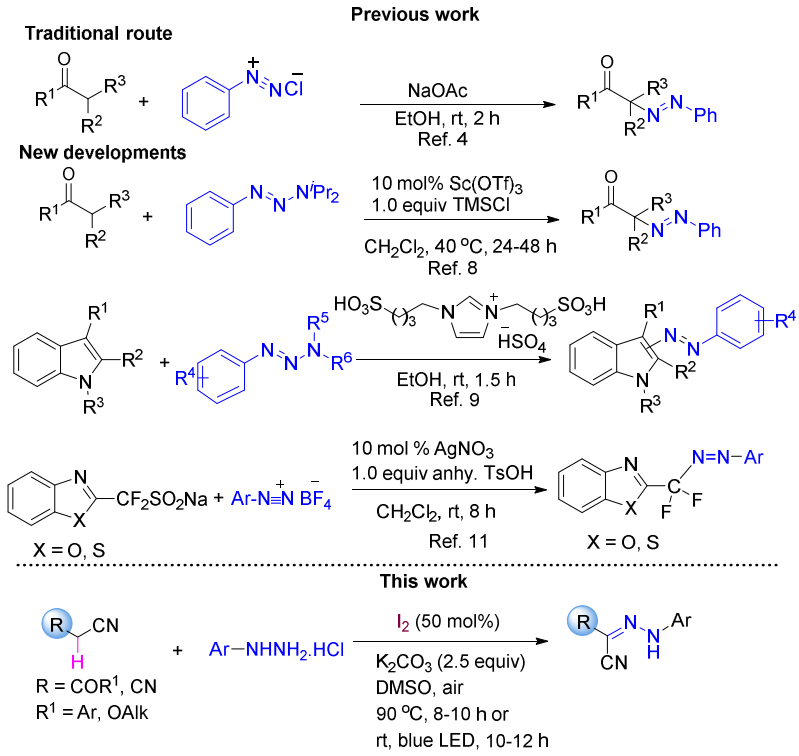
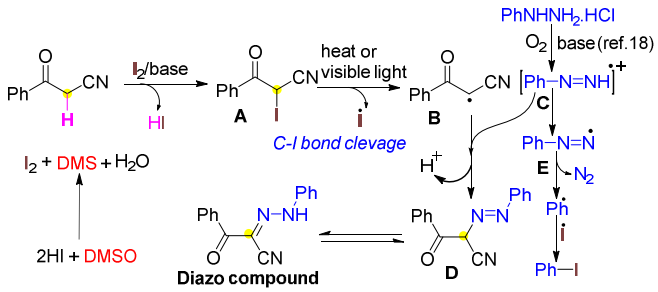


Figure 1. Strategies for diazenylation

disproportionate to arylhydrazine hydrochloride.[13] Conversely, the oxidation of phenylhydrazine results into phenyl radical via unstable phenyldiazene intermediate[14] which has the potential to act as nitrogen radical scavenger to effect diazenylation. Heinrich et al. even accomplished carbodiazenylation of olefin by phenylhydrazine in the presence of CAN albiet in 12% yield.[15] Recently, Zhu and co-workers reported that the visible light photoredox catalysis-promoted oxidation of methylhydrazine furnished diazene which added to Michael acceptors for obtaining pyrazoles but phenylhydrazine under identical conditions gave benzophenone.[16] Perhaps, lack of attempts to use arylhydrazine for diazenylation may be attributed to its unstable nature in air. In contrast, the air stable arylhydrazine hydrochloride via oxygen-mediated oxidation afforded the aryldiazene which is immediately transformed to the aryl radical under basic medium.[15] With this background and in our interest in iodine-mediated reactions,[17] we sought to investigate the potential of arylhydrazine hydrochlorides as the aryldiazene source for diazenylation of active methylene compounds in the presence of iodine under air. We reasoned that the radical intermediate **B** generated from the active methylene compound in the presence of iodine

Scheme 1. Proposed route for diazenylation of active methylene compounds via arylhydrazine hydrochloride

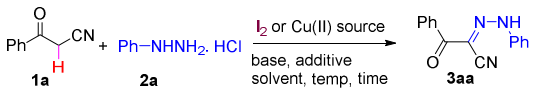


could be scavenged by the aryldiazene cation radical **C** to furnish **D** as outlined in Scheme 1.[18] However, the possibility of reaction proceeding via Japp-Klingenmann type ionic process to yield identical compound cannot be ruled out.[19]

Results and Discussion

To probe the envisaged objective, in a pilot experiment we examined the reaction between benzoylacetonitrile **1a** and phenylhydrazine hydrochloride **2a** in the presence of iodine (100 mol%), K_2CO_3 (2.0 equiv) and hydrogen peroxide (2.0 equiv) in DMSO as medium under heating at 90 ^oC. The reaction was completed in 8 h to offer a complex mixture of product from which the major product isolated in 35 % yield was established to be the desired azo compound **3aa** (see Table 1)**.** The melting point and spectral data of **3aa** was in alignment with the literature.[20] Hence we considered optimizing the reaction to obtain **3aa** in superior yield. Further evaluation demonstrated that though performing the reaction in the presence of TBHP enhanced the yield to 42%, carrying out the reaction in the absence of any external oxidant and under air gave **3aa** in 55% yield. Screening different amounts of K_2CO_3 revealed that 2.5 equiv. gave the product in best yield of 64%. Subsequently, the reaction was investigated in the presence of alternative iodine source including NIS, TBAI but herein **3aa** was isolated in relatively lower yields. Titrating the amount of iodine in the reaction revealed that 50 mol% of iodine was optimal to produce **3aa** in 82% yield. The reaction failed when performed in the absence of iodine inferring that it is necessary for the reaction. The reaction was unsuccessful under nitrogen atmosphere suggesting that aerobic conditions are required for the success of this reaction. Since the

Table 1. Optimization of the Reaction Conditions for diazenylaion with phenylhydrazine hydrochloride[a]



entry	reagent (mol%)	solvent	base (equiv)/ oxidant (equiv) or light	temp. (^{o}C)	time (h)	**3aa** yield (%)[b]
1	I_2 (100)	DMSO	K_2CO_3 (2.0)/ H_2O_2 (2.0)	90	8	35
2	I_2 (100)	DMSO	K_2CO_3 (2.0)/ TBHP (2.0)	90	8	42
3	I_2 (100)	DMSO	K_2CO_3 (2.0)	90	8	55
4	I_2 (100)	DMSO	K_2CO_3 (2.5)	90	8	64
5	I_2 (100)	DMSO	K_2CO_3 (3.0)	90	8	64
6	NIS (100)	DMSO	K_2CO_3 (2.5)	90	12	60
7	NBS (100)	DMSO	K_2CO_3 (2.5)	90	12	48
8	TBAI (100)	DMSO	K_2CO_3 (2.5)	90	12	30
9	$CuBr_2$ (10)	DMSO	K_2CO_3 (2.5)	90	12	24
10	I_2 (50)	DMSO	K_2CO_3 (2.5)	90	8	82
11	I_2 (30)	DMSO	K_2CO_3 (2.5)	90	10	57c
12	I_2 (0)	DMSO	K_2CO_3 (2.5)	90	10	No reaction
13[c,d]	I_2 (50)	DMSO	K_2CO_3 (2.5)	90	8	0
14[d]	I_2 (50)	DMSO	K_2CO_3 (2.5)/ white light	rt	24	trace
15	I_2 (50)	DMSO	K_2CO_3 (2.5)/ blue LED	rt	10	88
16[d]	I_2 (50)	EtOAc	K_2CO_3 (2.5)/ blue LED	rt	12	65
17[d]	I_2 (50)	MeCN	K_2CO_3 (2.5)/ blue LED	rt	12	47
18[d]	I_2 (50)	DMSO	Cs_2CO_3 (2.5)/ blue LED	rt	12	43
19[d]	I_2 (50)	DMSO	KOH (2.5)/ blue LED	rt	12	21

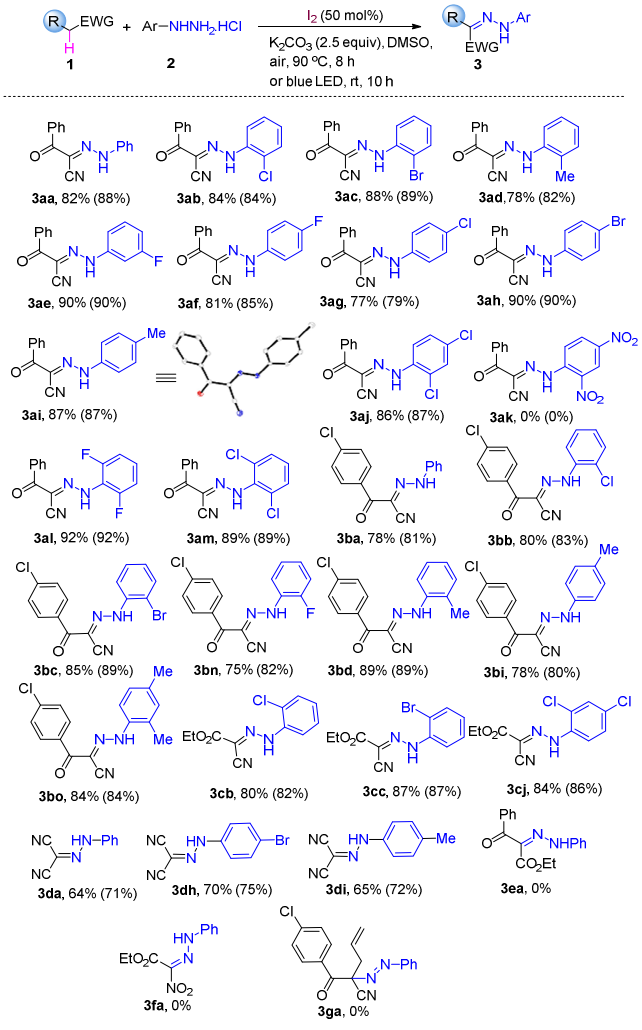
[a]All reactions were carried out using **1a** (0.1 g, 1.26 mmol), **2a** (0.095 g, 1.2 equiv), DMSO (3 mL) in air. [b]Isolated yields after column chromatography. [c]Reaction performed under nitrogen atmosphere. [d]Starting **1a** was recovered from the reaction mixture

visible light promotes homolytic carbon-iodine bond fission resulting into radical species,[21] we investigated the reaction in the presence of visible light. Although white light failed to initiate the reaction, we were delighted to note that under blue light (λ = 455 nm) the reaction was completed in 10

h to furnish **3aa** was in 88% isolated yield. Changing the solvent to MeCN or EtOAc, however was found to be detrimental to the formation of the product. Replacing K_2CO_3 with either Cs_2CO_3 or KOH gave **3aa** in lower yields. Therefore, the optimized condition identified from the study was treating **1a** with **2a** in the presence of iodine (50 mol%) and K_2CO_3 (2.5 equiv) in DMSO as medium either under heating at 90 ^oC or in blue light at room temperature under air.

With the optimized conditions in hand we tested the generality of protocol by employing different active methylene compounds and arylhydrazine hydrochlorides and the results are summarized in Scheme 2. In the first set of reaction the benzoylacetonitrile **1a** was treated with several substituted

Scheme 2. Scope of diazenylation of active methylene compounds with arylhydrazine hydrochlorides



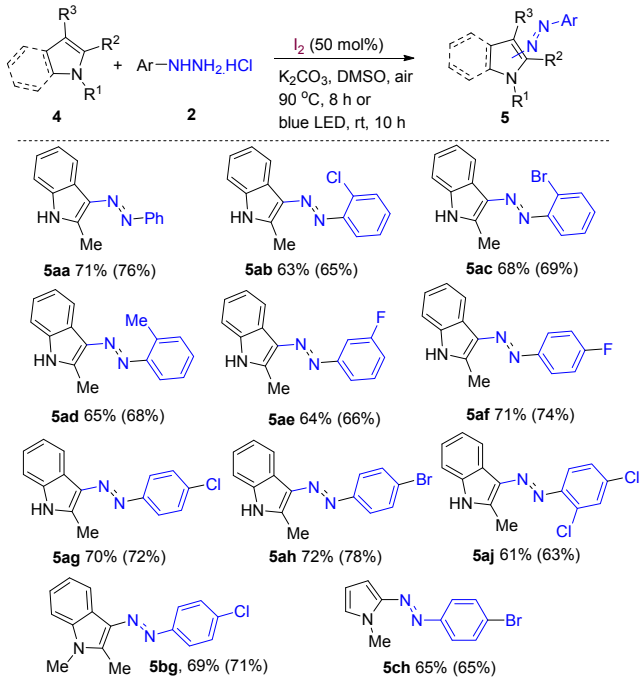
[a]All reactions were carried out at 0.1 g scale. Yields in bracket are the ones from reaction under blue LED.

phenylhydrazine hydrochlorides under heating and we discovered that nearly all substrates, except for 2,4-dinitrophenylhydrazine hydrochloride **(2k)**, afforded the corresponding azo-compounds **3ab-3aj** in 77-90% yields. As evident from the NMR spectral data recorded in $CDCl_3$ all products displayed azo-hydrazone tautomerism.[8] Nonetheless, the structure of the products was unambiguously secured by the X-ray diffraction analysis of **3ai**. For the reaction with 2,4-dinitrophenylhydrazine hydrochloride instead of isolating the expected azo derivative **3ak**, we isolated 1-iodo-2,4-dinitrobenzene suggesting that nitrogen was eliminated from the diazene leading to 2,4-dinitrophenyl radical. Subsequently we evaluated these reactions under the blue light and found that all reactions smoothly furnished **3ab-3aj** in identical or better yields. Next reactions of 3-(4-chlorophenyl)-3-oxopropanenitrile **(1b)** with different hydrazine hydrochlorides **(2a-d,i,n,o)** were probed under heating and light and the respective products **(3a-d,i,n,o)** were isolated in excellent yields. Alternatively, reactions of ethylcyanoacetate **(3c)** and malononitrile **(3d)** with different hydrazine hydrochlorides were successful resulting into the corresponding azo-derivatives. However, the reactions of ethyl 3-oxo-3-phenylpropanoate **(3e)** and ethyl nitroacetate **(3f)** with phenylhydrazine hydrochloride were unsuccessful. Perhaps the respective radical species formed from these substrates are less stable leading to the failure of the protocol.[22] Moreover, treating 2-benzoylpent-4-enenitrile **(3g)** with phenylhydrazine hydrochloride under the optimized condition was also unsuccessful to give the desired product. Finally, the scalability of the protocol was evaluated by treating 1.0 g of **1a** with **2g** to obtain the product **3ag** in 76% yield.

Having studied the scope of the protocol with active methylene substrates, we turned our attention towards investigating the suitability of the protocol for *N*-heterocyclic compounds **(4a-b)**. Treating 2-methylindole **(4a)** with different phenyl hydrazine hydrochlorides **(2a-h,j)** under heating afforded the respective products **5aa-5ah,5aj** in 61-72% yields but when identical reactions were performed under blue light, **5aa-5ah,5aj** were isolated in improved yield (Scheme 3). Likewise, reactions of **4b** and **4c** with **2g** and **2h** gave the corresponding azo-derivative **5bg** and **5ch**, respectively both under heating and blue light. The scalability of the protocol was investigated by subjecting 1.0 g **4a** to reaction with 4-

bromophenylhydrazine hydrochloride **(2h)** under heating, which resulted into the corresponding product **5ah** without any attenuation of yield.

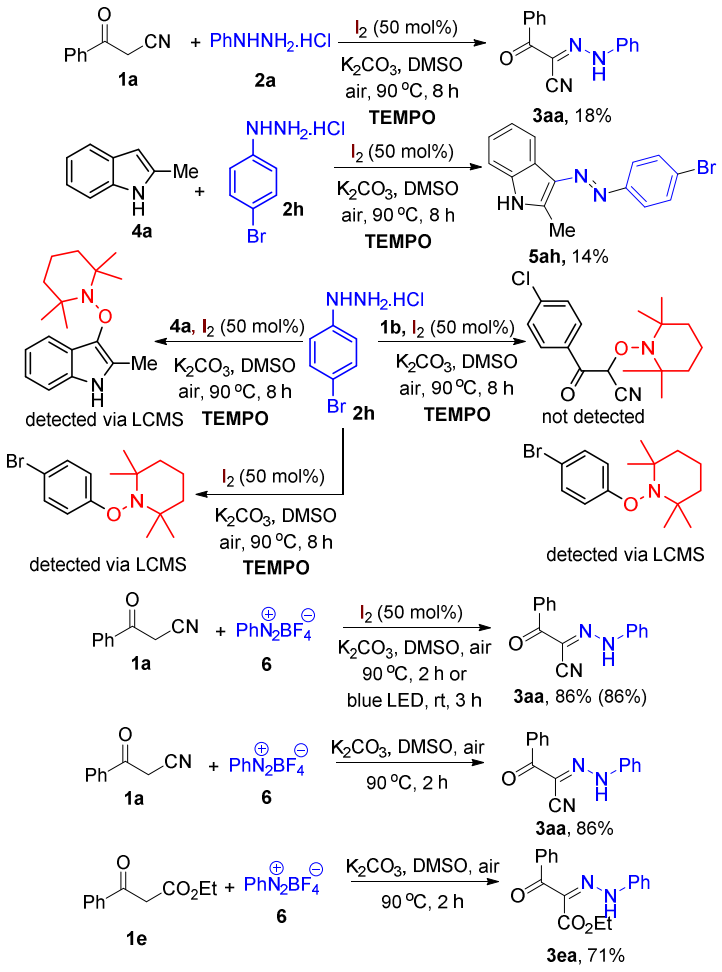
Scheme 3. Scope of diazenylation of *N*-heterocyclic compounds with arylhydrazine hydrochlorides[a]



[a]All reactions were performed at 0.1 g scale.

As stated earlier, the reaction following an ionic process via intermediacy of diazonium ion generated upon oxidation of phenyl hydrazine hydrochloride under the influence of iodine is possible too. The diazonum ion would attack the nucleophlic centre in benzoylacetonitrile to furnish the observed product. Therefore, to investigate the plausible mechanism, several control experiments were performed. The reactions between **1a** and **2a** and **4a** and **2h** were evaluated under the optimized conditions in the presence of TEMPO which gave the product **3aa** and **5ah** in 18% and 14% isolated yields, respectively thereby suggesting a radical pathway (Scheme 4). Next the reaction of 4-bromophenylhydrazine hydrochloride **(2h)** was carried out with **1b** and **4a**, respectively in the presence of TEMPO and the products were analyzed via LCMS. Although we could not detect the presence of the radical generated from **1b** via LCMS, the presence of the adduct of TEMPO with the radical generated from **4a** was observed during the analysis (see SI)**.** Conversely, when **2h** was independently treated with TEMPO under the optimized conditions, the adduct of TEMPO with 4-bromophenyl radical was observed during

Scheme 4. Control experiments

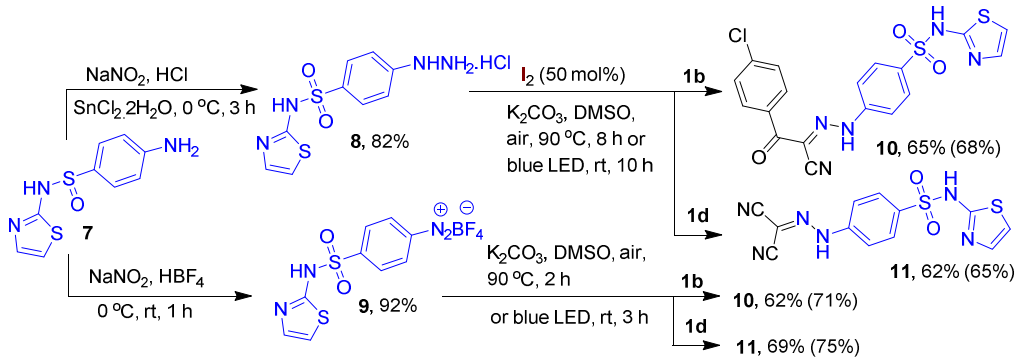


the LCMS analysis. Based on the NMR experiment using trimethoxybenzene as internal standard the yield of this adduct was calculated to be 27%. Next, to study the ionic process a reaction between the diazonium salt **(6)** and benzoylacetonitrile was performed under the optimized conditions which afforded **3aa** in 86% yield.[11,23] Notably, this reaction was completed in 2 h as compared to 10 h required with phenylhydrazine hydrochloride. Repeating this reaction in the absence of iodine too offered **3aa** in identical yield ascertaining the progress of this reaction via an ionic route. In another control experiment, treating **1e** with **6** resulted into the corresponding product **3ea** (71%) which was not formed during the reaction of **1e** and **2a**. Finally, for verifying the presence of aryldiazonium ion in the developed protocol if any, β-naphthol was added to the reaction of **1a** with **2a** under the optimized conditions.[23] However, we failed to detect the azo-coupling product 1-phenylazonaphthalen-2-ol in the reaction mixture. These control experiments suggested that diazenylation with diazonium salt follow the

traditional ionic route while phenylhydrazine hydrochloride produced the azo derivatives via the intermediacy of diazene.

To demonstrate the utility of the protocol, we transformed a sulfathiazole drug **7** into its hydrazine hydrochloride salt **8** and treated it with **1b** and **1d** independently to afford **10** and **11** in 62 and 69% yields, respectively (Scheme 5). Compounds **10** and **11** were obtained in relatively improved yields, when the reactions were performed under blue LED light. To ascertain the structure of the isolated

Scheme 5. Synthetic utility of protocol with hydrazine hydrochloride salt of sulfathiazole product unambiguously, we transformed **7** into its tetrafluoroborate salt **9** and treated it with **1b** and **1d** in the presence of a base both under heating and in the presence of blue light source. The products **10** and **11**, respectively isolated were identical to the products obtained from the hydrazine hydrochloride **8**.



Finally, we investigated the compatibility of aliphatic hydrazine salt with the protocol by treating methylhydrazine sulphate with **1a** under the optimized conditions but the reaction was unsuccessful.

Conclusions

In summary, we have illustrated a mild approach to diazenylation of active methylene compounds and *N*-heterocyclic compounds with arylhydrazine hydrochloride in the presence of iodine and base under aerobic conditions. It is proposed that the reaction proceed via the intermediacy of diazene rather than the ionic mechanism and therefore it provides a new alternative to diazenylation reaction. The protocol was however found to be limited to active methylene compounds bearing at least one nitrile group. Nonetheless, commercially available cheap starting materials, simple reaction conditions in the presence of air make it an attractive option for diazenylation.

Experimental

General. Unless otherwise stated all reactions were performed in non-dry glassware under an air atmosphere and were monitored by thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates. After elution, plate was visualized under UV illumination at 254 nm for UV active materials. The melting points were recorded on a hot stage apparatus and are uncorrected. IR spectra were recorded using a FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 or 500 MHz spectrometers with $CDCl_3$ or DMSO-d^6 as solvent, using TMS as an internal standard (chemical shifts in δ ppm). Peak multiplicities of ^{1}H-NMR signals were designated as s (singlet), brs (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), m (multiplet) etc. Coupling constants (*J*) are in Hz. The LC-ESI-MS were recorded on triple quadrupole Mass spectrometer. Column chromatography was performed using silica gel (100-200 mesh). Analytical grade solvents for the column chromatography were used as received. Commercial grade reagents and solvents were purchased from different commercial sources and used without further purification. The yields were calculated based on the nitriles or *N*-heterocycles as the starting material. The yields within the bracket are the ones from the reaction performed via Method B. The products originating from substrate **1a** and **1b** exist in azo-hydrazo (keto-enol) tautomeric forms and in the solution equilibrium is tilted to enol form (major tautomer, 70%) and therefore the NMR characterization data is in the enol form.

General procedure for the synthesis of azo derivatives 3,5,10-11 as exemplified for the synthesis of 3aa.

Method A. To a stirred solution of 3-oxo-3-phenylpropanenitrile **1a** (0.1 g, 0.69 mmol) in DMSO (3 mL) was added I_2 (0.09 g, 0.34 mmol) at room temperature. After a delay of 15 minutes, phenyl hydrazine hydrochloride **2a** (0.12 g, 0.83 mmol) and K_2CO_3 (0.24 g, 1.72 mmol) were added and the resulting mixture was heated at 90 ^{o}C for 8 h under aerobic condition. After completion of the reaction (as monitored by TLC), the solvent was removed under vacuum and the reaction was quenched with saturated thiosuphate solution (25 mL) and subsequently extracted with EtOAc (2 x 20 mL). The

organic layers were pooled, dried over anhyd. Na_2SO_4 and evaporated to yield the crude material that was purified via silica gel column chromatography using hexanes/ EtOAc (9:1, v/v) as eluent to afford **2a** (0.140 g, 82%) as a yellow solid.

Method B. To a solution of **1a** (0.1 g, 0.69 mmol) in DMSO (3 mL) were added I_2 (0.09 g, 0.34 mmol), phenyl hydrazine hydrochloride (0.12 g, 0.83 mmol) and K_2CO_3 (0.24 g, 1.72 mmol) and the reaction was continued for 10 h under the blue LED (λ = 455 nm) light at room temperature. After completion of the reaction mixture was processed as stated above to furnish 0.150 g (88%) of **2a** as a yellow solid.

(*E*)-2-Oxo-*N*',2-diphenylacetohydrazonoyl cyanide (**3aa**).[20] Mp: 136-138 ^oC [Lit. 134-136 ^oC]; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1695, 2224, 3251 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, J = 7.7 Hz, 1H), 7.48-7.58 (m, 4H), 7.66 (d, J = 7.0 Hz, 1H), 7.86 (d, J = 8.7 Hz, 1H), 8.00-8.06 (m, 3H), 15.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.7, 115.3, 116.8, 117.9, 121.4, 123.3, 125.8, 127.2, 127.4, 128.3, 128.7, 129.0, 129.3, 129.4, 129.8, 130.1, 132.9, 133.3, 135.7, 136.0, 138.1, 140.5, 140.6, 186.1, 187.7 ppm. MS (ESI+): *m/z* = 250.1 ESI-HR-MS calcd. for $C_{15}H_{12}N_3O$ (M^++H): 250.0980, found: 250.0982.

^1H NMR (400 MHz, DMSO-d^6): δ = 7.39 (d, J = 4.0 Hz, 4H), 7.55 (d, J = 7.7 Hz, 2H), 7.64 (d, J= 7.2 Hz, 2H), 7.88 (d, J = 7.5 Hz, 2H), 12.37 (s, 1H).

(*E*)-*N*'-(2-Chlorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3ab**). Yield: 84% (84%) (0.163 g from 0.1 g); a yellow solid; mp: 125-127 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1685, 2217, 3260 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.12 (d, J = 8.8 Hz, 1H), 7.26-7.35 (m, 3H), 7.43-7.48 (m, 2H), 7.52-7.58 (m, 1H), 7.91 (m, 2H), 15.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.9, 110.6, 111.8, 112.2, 116.9, 117.5, 117.6, 126.2, 127.7, 128.3, 128.7, 129.0, 129.2, 130.1, 133.1, 133.1, 133.1, 133.6, 135.4., 135.81, 137.5, 138.7, 185.7, 188.3 ppm. MS (ESI+): *m/z* = 284.0. ESI-HR-MS calcd. for $C_{15}H_{11}ClN_3O$ (M^++H): 284.0591, found: 284.0594.

(*E*)-*N*'-(2-Bromophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3ac**). Yield: 88% (89%) (0.198 g from 0.1 g); a yellow solid, mp: 124-126 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr)

ν_{max}: 1689, 2210, 3281 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.02-7.10 (m, 1H), 7.30-7.38 (m, 2H), 7.42-7.45 (m, 2H), 7.52-7.55 (m, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 15.19 (s, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.9, 117.6, 127.9, 128.7, 129.1, 130.2, 131.5, 133.1 ppm. MS (ESI+): *m/z* = 328.0. ESI-HR-MS calcd. for $C_{15}H_{11}BrN_3O$ (M^++H): 328.0085, found: 328.0085.

(*E*)-2-Oxo-2-phenyl-*N*'-o-tolylacetohydrazonoyl cyanide (**3ad**). Yield: 78% (82%) (0.141 g from 0.1 g); a yellow solid, mp: 136-138 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1679, 2231, 3273 cm^{-1}. ^1H NMR (400 MHz, , $CDCl_3$): δ = 2.39 (s, 3H), 7.10-7.18 (m, 2H), 7.24-7.33 (m, 1H), 7.42-7.47 (m, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.92-7.97 (m, 2H), 15.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9, 111.3, 115.8, 118.0, 125.1, 127.0, 127.8, 128.3, 128.6, 128.7, 130.1, 131.1, 133.3, 136.1, 138.9, 188.7 ppm. MS (ESI+): *m/z* = 264.1. ESI-HR-MS calcd. for $C_{16}H_{14}N_3O$ (M^++H): 264.1137, found: 264.1138.

(*E*)-*N*'-(3-Fluorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3ae**). Yield: 90% (90%) (0.165 g from 0.1 g); a yellow solid, mp: 140-142 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1683, 2227, 3249 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.80-6.96 (m, 2H), 7.19-7.35 (m, 2H), 7.44-7.58 (m, 3H) 7.92 (d, *J* = 7.5 Hz, 2H), 15.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 103.3, 103.5, 103.9, 104.1, 110.1, 111.4, 111.6, 111.7, 112.5 (d, *J* = 21 Hz), 113.9 (d, *J* = 21.7 Hz), 116.0, 117.5, 128.3, 128.6, 128.7, 130.1, 131.1, 131.2, 131.2, 131.3, 133.4 (d, *J* = 48 Hz), 135.6 (d, *J* = 31.14 Hz), 142.13, 142.2, 142.3, 163.7 (d, *J* = 247.3 Hz), 186.0, 188.8 ppm. MS (ESI+): *m/z* = 268.1. ESI-HR-MS calcd. for $C_{15}H_{11}FN_3O$ (M^++H): 268.0886, found: 268.0889.

(*E*)-*N*'-(4-Fluorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3af**). Yield: 81% (85%) (0.149 g from 0.1 g); a yellow solid, mp: 145-147 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v) IR (KBr) ν_{max}: 1695, 2233, 3256 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.00-7.10 (m, 2H), 7.38-7.56 (m, 5H), 7.92 (d, *J* = 7.4 Hz, 2H), 15.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.4, 110.8, 115.7 (d, *J* = 22.6 Hz), 116.6, 116.7, 116.9, 116.9, 117.4, 117.5, 117.8, 118.4, 118.5, 122.29 (d, *J* = 7 Hz), 127.0, 128.3, 128.5, 128.7, 128.8, 130.1, 131.9, 132.9, 133.79 (d, *J* = 54 Hz), 134.7, 135.7, 135.9, 136.9, 137.0, 159.2, 160.2,

161.4 (d, J = 247.4 Hz), 165.8, 186.1, 188.1 ppm. MS (ESI+): *m/z* = 268.1. ESI-HR-MS calcd. for $C_{15}H_{11}FN_3O$ (M^++H): 268.0886, found: 268.0888.

(*E*)-*N*'-(4-Chlorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3ag**). Yield: 77% (79%) (0.150 g from 0.1 g); a yellow solid, mp: 168-170 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1682, 2221, 3248 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.16-7.25 (m, 1H), 7.40-7.48 (m, 2H), 7.53-7.58 (m, 2H), 7.66 (t, J = 7.6 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 8.03-8.06 (m, 2H), 15.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 117.0, 117.1, 117.9, 127.2, 128.3, 128.4, 128.6, 128.7, 130.0, 133.5, 135.8. ppm. MS (ESI+): *m/z* = 284.1. ESI-HR-MS calcd. for $C_{15}H_{11}ClN_3O$ (M^++H): 284.0591, found: 284.0593.

(*E*)-*N*'-(4-Bromophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3ah**). Yield: 90% (90%) (0.202 g from 0.1 g); a yellow solid, mp: 173-175 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1691, 2229, 3279 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.16 (d, J = 8.9 Hz, 1H), 7.39 (d, J = 8.9 Hz, 1H), 7.52-7.60 (m, 4H), 7.65 (t, J = 7.4 Hz, 1H), 8.00-8.02 (m, 2H), 15.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 117.3, 117.6, 118.2, 120.3, 128.3, 128.6, 128.7, 130.1, 132.9, 133.0, 133.1, 133.5, 135.8, 139.7, 188.8 ppm. MS (ESI+): *m/z* = 328.0. ESI-HR-MS calcd. for $C_{15}H_{11}BrN_3O$ (M^++H): 328.0085, found: 328.0088.

(*E*)-2-Oxo-2-phenyl-*N*'-p-tolylacetohydrazonoyl cyanide (**3ai**). Yield: 87% (87%) (0.150 g from 0.1 g); a yellow solid, mp: 153-155 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1688, 2232, 3266 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (d, J = 12.53 Hz, 3H), 7.18-7.28 (m, 3H), 7.40 (d, J = 8.3 Hz, 1H), 7.51-7.65 (m, 3H), 8.01 (t, J = 8.5 Hz 2H), 15.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 21.13, 110.2, 110.5, 114.8, 116.8, 118.1, 128.2, 128.5, 128.6, 130.1, 130.4, 130.4, 132.8, 133.2, 135.8, 136.1, 137.5, 138.2, 138.4, 186.1, 188.6 ppm. MS (ESI+): *m/z* = 264.1. ESI-HR-MS calcd. for $C_{16}H_{14}N_3O$ (M^++H): 264.1137, found: 264.1138.

(*E*)-*N*'-(2,4-Dichlorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3aj**). Yield: 86% (87%) (0.187 g from 0.1 g); a yellow solid, mp: 159-161 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1691, 2213, 3274 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30 (d, J = 7.8 Hz, 1H), 7.39-7.57 (m,

4H), 7.76 (d, J = 8.8 Hz, 1H), 7.91-7.96 (m, 2H), 15.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 117.5, 117.9, 122.7, 128.4, 128.7, 128.7, 128.8, 129.6, 130.1, 132.1, 133.7, 135.6 ppm. MS (ESI+): *m/z* = 318.0. ESI-HR-MS calcd. for $C_{15}H_{10}Cl_2N_3O$ (M^++H): 318.0201, found: 318.0202.

(*E*)-*N*'-(2,6-Difluorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3al**). Yield: 92% (92%) (0.180 g from 0.1 g); a yellow solid, mp: 135-137 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1687, 2219, 3242 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97-7.06 (m, 2H), 7.56 (t, J = 7.8 Hz, 2H), 7.64-7.68 (m, 1H),7.83-7.89 (m, 1H), 8.00-8.04 (m, 2H) 15.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 104.4, 104.6, 104.6, 104.8, 109.6, 112.3, 112.8 (d, J = 23.0 Hz), 112.9 (d, J = 23.0 Hz), 117.4, 118.2 (d, J = 8 Hz), 126.0, 128.3, 128.6, 128.7, 130.1, 133.4 (d, J = 45 Hz), 135.4, 135.7, 151.9 (d, J = 262.8 Hz), 153.2, 160.7 (d, J = 262.4 Hz) 161.9, 162.0, 185.6, 188.6 ppm. MS (ESI+): *m/z* = 286.1. ESI-HR-MS calcd. for $C_{15}H_{10}F_2N_3O$ (M^++H): 286.0792, found: 286.0794

(*E*)-*N*'-(2,6-Dichlorophenyl)-2-oxo-2-phenylacetohydrazonoyl cyanide (**3am**). Yield: 89% (89%) (0.194 g from 0.1 g); a yellow solid, mp: 158-160 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1688, 2215, 3268 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09-7.14 (m, 1H), 7.33-7.40 (m, 3H), 7.45-7.59 (m, 2H), 7.97-8.04 (m, 2H), 14.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.4, 112.3, 117.1, 118.9, 128.0, 128.1, 128.1, 128.5, 128.6, 128.7, 128.8, 129.5, 129.7, 130.3, 133.7, 134.0, 134.6, 134.8, 135.6, 185.3, 188.5 ppm. MS (ESI+): *m/z* = 318.0. ESI-HR-MS calcd. for $C_{15}H_{10}Cl_2N_3O$ (M^++H): 318.0201, found: 318.0201.

(*E*)-2-(4-Chlorophenyl)-2-oxo-*N*'-phenylacetohydrazonoyl cyanide (**3ba**). Yield: 78% (81%) (0.123g from 0.1 g); a yellow solid, mp: 181-183 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1681, 2229, 3278 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12-7.19 (m, 1H), 7.29-7.35 (m, 3H), 7.46 (s, 2H), 7.55 (d, J = 6.9 Hz, 1H), 7.82-7.96 (m, 2H), 15.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.9, 115.1, 116.0, 116.9, 118.6, 120.6, 121.7, 125.1, 128.5, 129.0, 129.2, 129.8, 129.9, 130.0, 130.2, 130.5, 131.5, 135.1, 137.6, 142.1, 146.4, ppm. MS (ESI+): *m/z* = 284.0. ESI-HR-MS calcd. for $C_{15}H_{11}ClN_3O$ (M^++H): 284.0591, found: 284.0589.

(*E*)-*N*'-(2-Chlorophenyl)-2-(4-chlorophenyl)-2-oxoacetohydrazonoyl cyanide (**3bb**). Yield: 80% (83%) (0.141 g from 0.1 g); a yellow solid; mp: 148-150 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1689, 2224, 3264 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08-7.19 (m, 1H), 7.26-7.45 (m, 4H), 7.81-7.93 (m, 3H), 15.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.6, 111.9, 116.6, 117.2, 117.5, 121.2, 122.5, 126.0, 127.5, 128.4, 128.6, 129.1, 129.9, 130.0, 130.1, 131.5, 133.7, 134.0, 136.4, 137.4, 139.7, 140.2, 184.4, 186.9 ppm. MS (ESI+): *m/z* = 318.0. ESI-HR-MS calcd. for $C_{15}H_{10}Cl_2N_3O$ (M^++H): 318.0201, found: 318.0202.

(*E*)-*N*'-(2-Bromophenyl)-2-(4-chlorophenyl)-2-oxoacetohydrazonoyl cyanide (**3bc**). Yield: 85% (89%) (0.170 g from 0.1 g); a yellow solid, mp: 139-141 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1695, 2237, 3259 cm^{-1}. ^{1}H NMR (400 MHz $CDCl_3$): δ = 7.08-7.17 (m, 1H), 7.37-7.41 (m, 1H), 7.49-7.53 (m, 2H), 7.59-7.62 (m, 1H), 7.79 (dd, J_1 = 6.9 Hz, J_2 = 1.3 Hz, 1H), 7.96-8.01 (m, 2H), 15.25 (s, 1H); ^{13}C NMR (400 MHz $CDCl_3$): δ = 109.7, 110.7, 111.8, 111.9, 115.7, 116.9, 117.5, 117.6, 119.4, 126.4, 127.9, 128.3, 128.7, 129.05, 129.1, 129.2, 130.2, 131.5, 133.1, 133.2, 133.7, 134.1, 137.0, 138.6, 139.7, 140.2, 184.4, 186.8 ppm. MS (ESI+): *m/z* = 361.8. ESI-HR-MS calcd. for $C_{15}H_{10}BrClN_3O$ (M^++H): 361.9696, found: 361.9698.

(*E*)-2-(4-Chlorophenyl)-*N*'-(2-fluorophenyl)-2-oxoacetohydrazonoyl cyanide (**3bn**). Yield: 75% (82%) (0.126 g from 0.1 g); a yellow solid; mp: 142-144 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v) IR (KBr) ν_{max}: 1676, 2219, 3273 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09-7.20 (m, 3H), 7.43 (dd, J_1 = 8.5 Hz, J_2 = 2.4, Hz 2H), 7.75-7.79 (m, 1H), 7.90 (dd, J_1 = 8.6 Hz, J_2 = 2.3 Hz, 2H), 15.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.5, 111.8, 116.0, 116.1, 116.1, 116.3, 116.8, 117.4 (d, J = 23 Hz), 125.5, 125.5, 125.6, 126.1, 127.6, 127.6, 128.7, 128.7, 129.1, 130.1, 131.5, 133.8 (d, J = 36.1 Hz), 139.7, 140.2, 150.2, 151.8 (d, J = 248.4 Hz) 152.7, 184.4, 187.1 ppm. MS (ESI+): *m/z* = 302.0. ESI-HR-MS calcd. for $C_{15}H_{10}ClFN_3O$ (M^++H): 302.0496, found: 302.0494..

(*E*)-2-(4-Chlorophenyl)-2-oxo-*N*'-o-tolylacetohydrazonoyl cyanide (**3bd**). Yield: 89% (89%) (0.147g from 0.1 g); a yellow solid, mp: 163-165 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1684, 2221, 3271 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.46 (s, 3H), 7.16 (t, J = 7.4 Hz, 1H),

7.25-7.27 (m, 1H), 7.30-7.40 (m, 2H), 7.50-7054 (m, 2H), 8.00 (t, J = 8.5 Hz, 2H), 15.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.0, 110.9, 115.7, 115.9, 117.9, 124.4, 125.7, 126.1, 127.2, 127.9, 128.0, 128.6, 129.0, 130.0, 131.1, 131.5, 131.5, 133.9, 134.3, 138.1, 138.8, 139.5, 139.9, 184.5, 187.2 ppm. MS (ESI+): *m/z* = 298.1. ESI-HR-MS calcd. for $C_{16}H_{13}ClN_3O$ (M^++H): 298.0747, found: 298.0745.

(*E*)-2-(4-Chlorophenyl)-2-oxo-*N*'-p-tolylacetohydrazonoyl cyanide (**3bi**). Yield: 78% (80%) (0.129 g from 0.1 g); a yellow solid, mp: 180-182 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1673, 2235, 3251 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27-2.32 (m, 3H), 7.06-7.19 (m, 2H), 7.31 (d, J = 8.5Hz, 1H), 7.39-7.43 (m, 3H), 7.86-7.90 (m, 2H), 15.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 21.1, 109.8, 110.3, 114.7, 115.9, 116.9, 118.0, 120.4, 123.8, 128.5, 128.6, 128.7, 129.0, 129.6, 129.8, 130.0, 130.3, 130.4, 130.5, 130.8, 131.5, 134.1, 134.4, 134.50, 136.1, 137.8, 138.1, 138.3, 139.2, 139.7, 184.8, 187.2 ppm. MS (ESI+): *m/z* = 298.1. ESI-HR-MS calcd. for $C_{16}H_{13}ClN_3O$ (M^++H): 298.0747, found: 298.0745.

(*E*)-2-(4-Chlorophenyl)-*N*'-(2,4-dimethylphenyl)-2-oxoacetohydrazonoyl cyanide (**3bo**). Yield: 84% (84%) (0.145 g from 0.1 g); a yellow solid; mp: 173-175 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1689, 2218, 3268 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.28 (s, 3H), 2.35 (s, 3H), 6.98-7.03 (m, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.3 Hz, 1H), 7.88-7.92 (m, 2H), 15.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.8, 21.1, 110.4, 115.8, 116.0, 118.1, 126.1, 128.6, 129.0, 130.0, 131.5, 131.7, 132.0, 134.4, 136.5, 137.6, 139.7, 187.2 ppm. MS (ESI+): *m/z* = 312.1. ESI-HR-MS calcd. for $C_{17}H_{15}ClN_3O$ (M^++H): 312.0904, found: 312.0902.

(*E*)-Ethyl 2-(2-(2-chlorophenyl)hydrazono)-2-cyanoacetate (**3cb**). Yield: 80% (82%) (0.177 g from 0.1 g); a yellow solid, mp: 139-141 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1716, 2236, 3261 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.44 (t, J =7.3 Hz, 3H), 4.44 (q, J =7.2 Hz, 2H), 7.31-7.17 (m, 1H), 7.36 (dd, J_1 =7.9 Hz, J_2 = 0.5 Hz 1H), 7.41 (dd, J_1 =7.4 Hz, J_2 = 1.2 Hz 1H), 7.75 (dd, J_1 =8.3 Hz, J_2 = 1.1 Hz 1H), 13.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 62.7, 106.6, 114.9,

116.3, 121.4, 126.1, 128.3, 129.7, 137.5, 162.0 ppm. MS (ESI+): *m/z* =252.1. ESI-HR-MS calcd. for $C_{11}H_{11}ClN_3O_2$ (M^++H): 252.0540, found: 252.0543.

(*E*)-Ethyl 2-(2-(2-bromophenyl)hydrazono)-2-cyanoacetate (**3cc**). Yield: 87% (87%) (0.181g from 0.1 g); a yellow solid, mp: 138-140 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1734, 2224, 3246 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (t, *J* =7.1 Hz, 3H), 4.34 (q, *J* =7.14Hz, 2H), 6.99 (t, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 13.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 62.7, 106.5, 110.7, 115.0, 116.6, 126.5, 128.9, 132.9, 138.6, 161.9 ppm. MS (ESI+): *m/z* = 296.0. ESI-HR-MS calcd. for $C_{11}H_{11}BrN_3O_2$ (M^++H): 296.0035, found: 296.0032.

(*E*)-Ethyl 2-cyano-2-(2-(2,4-dichlorophenyl)hydrazono)acetate (**3cj**). Yield: 84% (86%) (0.237 g from 0.1 g); a yellow solid, mp: 176-178 ^oC; R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1729, 2238, 3258 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, *J* =7.1 Hz, 3H), 4.43 (q, *J* =7.1 Hz, 2H), 7.33 (dd, J_1 =8.8 Hz, J_2 = 2.1 Hz 1H), 7.43 (d, *J* = 2.1 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 13.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 62.9, 107.2, 114.7, 117.1, 121.7, 128.7, 129.4, 130.9, 136.3, 161.9 ppm. MS (ESI+): *m/z* = 286.0. ESI-HR-MS calcd. for $C_{11}H_{10}Cl_2N_3O_2$ (M^++H): 286.0150, found: 286.0146.

Phenylcarbonohydrazonoyl dicyanide (**3da**). Yield: 64% (71%) (0.164 g from 0.1 g); a yellow solid, mp: 140-142 ^oC; R_f = 0.45 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 2231, 3278 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.28 (m, 1H), 7.32 (d, *J* = 7.7 Hz, 2H), 7.43 (dd, J_1 = 8.4 Hz, J_2 = 0.9 Hz, 2H), 9.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 86.5, 108.4, 112.3, 116.1, 126.8, 129.9, 139.8 ppm. MS (ESI+): *m/z* =171.1. ESI-HR-MS calcd. for $C_9H_7N_4$ (M^++H): 171.0671, found: 171.0668.

(4-Bromophenyl)carbonohydrazonoyl dicyanide (**3dh**). Yield: 70% (75%) (0.261 g from 0.1 g); a yellow solid, mp: 173-175 ^oC; R_f = 0.45 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 2246, 3267 cm^{-1}. ^1H NMR (400 MHz, DMSO-d^6): δ = 7.41 (d, *J* = 7.4 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.87, 13.05 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 90.6, 115.1, 119.5, 123.1, 123.7, 137.6, 146.1 ppm. MS (ESI+): *m/z* = 248.7. ESI-HR-MS calcd. for $C_9H_6BrN_4$ (M^++H): 248.9776, found: 248.9775.

***p*-Tolylcarbonohydrazonoyl dicyanide** (**3di**). Yield: 65% (72%) (0.181 g from 0.1 g); a yellow solid, mp: 168-170 ^{o}C; R_f = 0.45 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 2238, 3251 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d^6): δ = 2.29 (s, 3H), 7.23 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 13.47 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 20.9, 84.2, 110.5, 115.0, 116.9, 130.4, 135.9, 139.7 ppm. MS (ESI+): *m/z* =185.1. ESI-HR-MS calcd. for $C_{10}H_9N_4$ (M^++H): 185.0827, found: 185.0825.

(*E*)-2-Methyl-3-(phenyldiazenyl)-1*H*-indole (**5aa**).[9] Yield: 71% (76%) (0.127 g from 0.1 g); a yellow solid; mp: 173-175 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 2128, 3339 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.71 (s, 3H), 7.19-7.23 (m, 3H), 7.33 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.87 (d, J = 7.4 Hz, 2H) 8.21(s, 1H), 8.52 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.51, 110.8, 119.5, 121.6, 122.5, 122.9, 123.6, 128.6, 128.9, 132.8, 135.2, 143.7, 153.9 ppm. MS (ESI+): *m/z* = 236.1. ESI-HR-MS calcd. for $C_{15}H_{14}N_3$ (M^++H): 236.1188, found: 236.1186.

(*E*)-3-((2-Chlorophenyl)diazenyl)-2-methyl-1*H*-indole (**5ab**). Yield: 63% (65%) (0.129 g from 0.1 g); a yellow solid; mp: 134-136 ^{o}C R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2121, 3329 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.81 (s, 3H), 7.24-7.32 (m, 5H), 7.53 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 7.7 Hz, 1H), 8.27(s, 1H), 8.62 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 110.5, 116.9, 119.5, 122.8, 123.5, 123.9, 127.1, 129.2, 130.4, 133.8, 134.1, 135.0, 143.8, 150.0 ppm. MS (ESI+): *m/z* = 270.0. ESI-HR-MS calcd. for $C_{15}H_{13}ClN_3$ (M^++H): 270.0798, found: 270.0794.

(*E*)-3-((2-Bromophenyl)diazenyl)-2-methyl-1*H*-indole (**5ac**). Yield: 68% (69%) (0.162 g from 0.1 g); a yellow solid; mp: 178-180 ^{o}C R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2125, 3327 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.82 (s, 3H), 7.18-7.38 (m, 5H), 7.72 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 6.9 Hz, 1H), 8.30(s, 1H), 8.68 (d, J = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 110.4, 117.2, 118.4, 119.0, 119.4, 120.7, 123.0, 123.5, 123.9, 127.7, 129.5, 133.4, 143.9, 151.0 ppm. MS (ESI+): *m/z* = 314.0. ESI-HR-MS calcd. for $C_{15}H_{13}BrN_3$ (M^++H): 314.0293, found: 314.0289.

(*E*)-2-Methyl-3-(o-tolyldiazenyl)-1*H*-indole (**5ad**). Yield: 65% (68%) (0.123 g from 0.1 g); a yellow solid; mp: 119-121 ^{o}C R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2118, 3322 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.76 (s, 3H), 2.81 (s, 3H), 7.23-7.33 (m, 6H), 7.69-7.71 (m, 1H), 8.21(s, 1H),

8.46 (d, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 18.2, 110.6, 114.9, 119.5, 122.3, 122.9, 123.5, 126.3, 128.6, 131.0, 133.6, 135.1, 136.2, 152.2 ppm. MS (ESI+): *m/z* = 250.1. ESI-HR-MS calcd. for $C_{16}H_{16}N_3$ (M^++H): 250.1344, found: 250.1341.

(*E*)-3-((3-Fluorophenyl)diazenyl)-2-methyl-1*H*-indole (**5ae**). Yield: 64% (66%) (0.123 g from 0.1 g); a yellow solid; mp: 109- 111 ^oC R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2120, 3324 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.81 (s, 3H), 7.01-7.06 (m, 1H), 7.23-7.30 (m, 3H), 7.40-7.45 (m, 1H), 7.56-7.59 (m, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 8.28(s, 1H), 8.49-8.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 106.7 (d, J = 22.6 Hz), 110.6, 115.1 (d, J = 22.2 Hz), 119.4, 122.5, 123.1, 123.8, 129.9 (d, J = 8.7 Hz), 132.9, 135.1, 143.7, 155.9 (d, J = 6.8 Hz), 162.3, 164.7 ppm. MS (ESI+): *m/z* = 254.1. ESI-HR-MS calcd. for $C_{15}H_{13}FN_3$ (M^++H): 254.1094, found: 254.1089.

(*E*)-3-((4-Fuorophenyl)diazenyl)-2-methyl-1*H*-indole (**5af**). Yield: 71% (74%) (0.137 g from 0.1 g); a yellow solid; mp: 117-119 ^oC R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2118, 3326 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.79 (s, 3H), 7.15 (t, *J* = 8.4 Hz, 2H) , 7.23-7.26 (m, 3H), 7.86-7.89 (m, 2H), 8.24 (s, 1H), 8.42 (d, *J* = 7.19 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.5, 110.0, 110.5, 115.5, 115.8, 118.7 (d, J = 61.0 Hz), 120.2 (d, J = 117.6 Hz), 122.4, 122.9, 123.3 (d, J = 8.5 Hz), 123.5, 135.0, 150.7, 161.7, 164.3 ppm. MS (ESI+): *m/z* = 254.1. ESI-HR-MS calcd. for $C_{15}H_{13}FN_3$ (M^++H): 254.1094, found: 254.1091.

(*E*)-3-((4-Chlorophenyl)diazenyl)-2-methyl-1*H*-indole (**5ag**). Yield: 70% (72%) (0.143 g from 0.1 g); a yellow solid; mp: 162-164 ^oC R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2117, 3322 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.80 (s, 3H), 7.23-7.28 (m, 3H), 7.43 (d, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 8.7 Hz, 2H), 8.40(s, 1H), 8.49 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 110.6, 116.3, 119.5, 122.9, 123.0, 123.7, 129.0, 129.1, 132.9, 134.0, 135.1, 143.4, 152.7 ppm. MS (ESI+): *m/z* = 270.0. ESI-HR-MS calcd. for $C_{15}H_{13}ClN_3$ (M^++H): 270.0798, found: 270.0795.

(*E*)-3-((4-Bromophenyl)diazenyl)-2-methyl-1*H*-indole (**5ah**). Yield: 72% (78%) (0.171 g from 0.1 g); a yellow solid; mp: 198-200 ^oC R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2119, 3321 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.73 (s, 3H), 7.14-7.20 (m, 3H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J*

= 8.4 Hz, 2H), 8.23(s, 1H), 8.42 (d, J = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 110.6, 116.7, 119.5, 122.3, 122.5, 123.0, 123.2, 123.7, 132.0, 133.0, 135.1, 143.4, 153.0 ppm. MS (ESI+): *m/z* = 314.0. ESI-HR-MS calcd. for $C_{15}H_{13}BrN_3$ (M^++H): 314.0293, found: 314.0292.

(*E*)-3-((2,4-Dichlorophenyl)diazenyl)-2-methyl-1*H*-indole (**5aj**). Yield: 61% (63%) (0.140 g from 0.1 g); a yellow solid; mp: 188- 190^{o}C R_f = 0.49 (Hexanes: EtOAc, 6:4, v/v); IR (KBr) ν_{max}: 2119, 3323 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.82 (s, 3H), 7.25-7.31 (m, 4H), 7.55 (d, J = 2.2 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H), 8.31(s, 1H), 8.58 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6, 110.5, 117.7, 119.4, 122.8, 123.7, 124.0, 127.4, 130.0, 134.0, 134.2, 134.3, 135.1, 144.2, 148.6 ppm. MS (ESI+): *m/z* = 304.0. ESI-HR-MS calcd. for $C_{15}H_{12}Cl_2N_3$ (M^++H): 304.0408, found: 304.0411.

(*E*)-3-((4-Chlorophenyl)diazenyl)-1,2-dimethyl-1*H*-indole (**5bg**). Yield: 69% (71%) (0.134 g from 0.1 g); a yellow solid; mp: 136-138 ^{o}C; R_f = 0.49 (Hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 2128, cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.78 (s, 3H), 3.72 (s, 3H), 7.24-7.29 (m, 3H), 7.41 (d, J = 8.6 Hz, 2H), 7.80 (d, J = 8.6 Hz, 2H), 8.51-8.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 10.2, 29.9, 108.9, 119.0, 122.5, 122.8, 123.0, 123.3, 129.0, 132.5, 133.6, 136.9, 145.3, 152.8 ppm. MS (ESI+): *m/z* = 284.1 ESI-HR-MS calculated for $C_{16}H_{15}ClN_3$ (M^++H): 284.0955, found: 284.0951.

(*E*)-2-((4-Bromophenyl)diazenyl)-1-methyl-1*H*-pyrrole (**5ch**). Yield: 65% (65%) (0.210 g from 0.1 g); a red oil; R_f = 0.59 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 2233 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.96 (s, 3H), 6.30 (dd, J_1 = 4.2 Hz, J_2 = 2.6 Hz, 1H), 6.72 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 6.96 (s, 1H), 7.56 (d, J = 8.7 Hz, 2H), 7.67 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.4, 100.6, 110.5, 123.5, 127.4, 131.6, 132.1, 146.8, 152.9 ppm. MS (ESI+): *m/z* = 264.0. ESI-HR-MS calcd. for $C_{11}H_{11}BrN_3$ (M^++H): 264.0136, found: 264.0133.

(*E*)-2-Oxo-2-phenyl-*N*'-(4-(*N*-thiazol-2-ylsulfamoyl)phenyl)acetohydrazonoylcyanide (10). Yield: 65% (68%) (0.161 g from 0.1 g); a yellow solid, mp: 262-264 ^{o}C; R_f = 0.48 (Hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1085, 1676, 2229, 3262, 2217 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d^6): δ = 6.83 (d, J = 4.5 Hz, 1H), 7.25 (d, J = 4.5 Hz, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.5 Hz, 2H), 7.92 (d, J = 8.4 Hz, 2H), 12.71 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 108.7, 111.5, 115.3,

116.9, 128.1, 128.9, 132.3, 135.1, 137.9, 138.3, 138.5, 145.1, 186.5 ppm. MS (ESI+): *m/z* = 446.0. ESI-HR-MS calcd. for $C_{18}H_{13}ClN_5O_3S_2$ (M^++H): 446.0148, found: 446.0148.

(4-(*N*-Thiazol-2-ylsulfamoyl)phenyl)carbonohydrazonoyl dicyanide (11). Yield: 62% (65%) (0.311 g from 0.1 g); a yellow solid, mp: >300^{o}C; R_f = 0.49 (Hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1071, 1683, 2219, 3277, 2217 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d^6): δ = 6.84 (d, *J* = 4.5 Hz, 1H), 7.26 (d, *J* = 4.5 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 12.76 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 87.1, 108.8, 110.1, 114.6, 117.0, 125.0, 128.0, 139.2, 144.7, 169.3 ppm. MS (ESI+): *m/z* = 333.0. ESI-HR-MS calcd. for $C_{12}H_9N_6O_2S_2$ (M^++H): 333.0228, found: 333.0229.

Typical procedure for the synthesis of 8[24]

Sulfathiazole **(7)** (0.5 g, 1.95 mmol) was dissolved in HCl (2 mL) at 0 ^{o}C maintained by an ice bath. $NaNO_2$ (0.1 g, 1.95 mmol) was dissolved in water (2 mL) and added dropwise in to the reaction mixture under stirring. The reaction was continued for 1h after which a solution of $SnCl_2.2H_2O$ (0.9 g, 3.91 mmol) in 3 mL HCl was added dropwise at 0 ^{o}C. The reaction was continued for another 2 h after which it was extracted with 30 mL EtOAc and organic layer was discarded. The solution was basified with NaOH until it pH 7 and then extracted with EtOAc (3 X 20 mL). The organic layers were pooled, dried over anhyd. Na_2SO_4 and evaporated to obtain the crude product **8** (0.5 g, 82%) as a yellow solid.

4-Hydrazinyl-*N*-(thiazol-2-yl)benzenesulfonamide (**8**). Yield: 82% (0.5 g from 0.5 g); a yellow solid, mp: 228-230 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d^6): δ = 6.56 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 4.6 Hz, 1H), 7.18 (d, *J* = 4.6 Hz, 1H), 7.43 (d, *J* = 8.7 Hz, 2H), 9.51 (s, 1H), 10.18 (s, 2H), 12.41 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d^6): δ = 107.9, 119.0, 128.5, 137.8, 141.3, 142.9, 170.1 ppm. MS (ESI+): *m/z* = 271.0. ESI-HR-MS calcd. for $C_9H_{11}N_4O_2S_2$ (M^++H): 271.0323, found: 271.0327.

General procedure for the synthesis of 3aa, 3ea, 10, 11 from diazonium salt as exemplified for the synthesis of 3ea

To a stirred solution of ethyl 3-oxo-3-phenylpropanoate **1e** (0.1 g, 0.52 mmol) in DMSO (3 mL), phenyldiazonium salt **6** (0.24 g, 0.78 mmol) and K_2CO_3 (0.06 g, 0.62 mmol) were added to the reaction mixture and the reaction was heated at 90 ^{o}C for 2 h. After completion (as monitored by TLC), the

reaction was quenched with water (30 mL) and extracted with EtOAc (3 x 20 mL). The organic layers were pooled, dried over Na_2SO_4 and evaporated to obtain a residue. This residue was purified by column chromatography over silica gel using hexanes/ EtOAc (9:1, v/v) as eluent to afford the desired product **3ea** (0.11 g, 71%) as a yellow solid.

(*Z*)-Ethyl 3-oxo-3-phenyl-2-(2-phenylhydrazono)propanoate (**3ea**). Mp: 63-65 ^{o}C [Lit. 63-65 ^{o}C][4b] R_f = 0.49 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 1673, 1738, 3251 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (t, J = 7.1 Hz, 3H), 4.36 (q, J = 7.1 Hz, 2H), 7.05-7.09 (m, 1H), 7.15-7.17 (m, 2H), 7.27-7.31 (m, 2H), 7.42-7.47 (m, 2H), 7.53-7.57 (m, 1H), 7.92-7.94 (m, 2H), 12.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 61.4, 115.3, 124.4, 127.9, 129.5, 130.4, 132.4, 137.8, 141.9, 164.1, 189.5 ppm. MS (ESI+): *m/z* = 297.1. ESI-HR-MS calcd. for $C_{17}H_{17}N_2O_3$ (M^++H): 297.1239, found: 297.1233.

(*E*)-Ethyl 2-nitro-2-(2-phenylhydrazono)acetate (**3fa**). Yield: 73% (0.130 g from 0.1 g); a yellow solid; mp: 65-67 ^{o}C; R_f = 0.47 (Hexanes: EtOAc, 9:1, v/v); IR (KBr) ν_{max}: 2135, cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, J = 7.1 Hz, 3H), 4.43 (q, J = 7.13 Hz, 2H), 7.17-7.26 (m, 1H), 7.34-7.43 (m, 4H), 12.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 14.1, 62.9, 116.3, 125.8, 126.5, 129.7, 140.6, 159.4 ppm. MS (ESI+): *m/z* = 238.1 ESI-HR-MS calculated for $C_{10}H_{12}N_3O_4$ (M^++H): 238.0828, found: 238.0831.

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SUPPORTING INFORMATION. X-ray analysis data of **3ai** and copies of ^{1}H and ^{13}C-NMR data are provided. The CIF for **3ai** is also included. The Supporting Information is available free of charge on the ACS Publications website.

SB-JOC-SI-Diazenylation (PDF); SB-**3ai** (cif).

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