Note

Synthesis of Indazolones via Friedel-Crafts Cyclization of Blocked (Masked) N-Isocyanates

Eslam Basiouny Elkaeed, Jing An, and Andre Martin Beauchemin

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01607 • Publication Date (Web): 22 Aug 2017

Synthesis of Indazolones via Friedel-Crafts Cyclization of Blocked (Masked) *N*-Isocyanates

Eslam B. Elkaeed,[ab] Jing An,[a] André M. Beauchemin[a]*

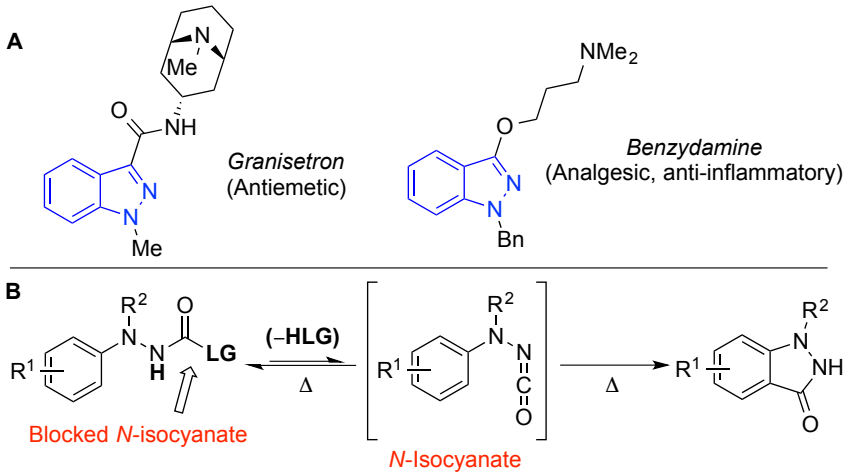
a) Centre for Catalysis Research and Innovation, Department of Chemistry and Biomolecular Sciences, University of Ottawa, 10 Marie-Curie, Ottawa, ON, K1N 6N5, Canada.

b) Department of Organic Chemistry, Faculty of Pharmacy, Al-Azhar University, Cairo 11884, Egypt.

ABSTRACT: Nitrogen-substituted isocyanates (*N*-isocyanates) are rare amphoteric reagents with high, but underdeveloped synthetic potential. Herein, we study the formation of indazolones by Friedel-Crafts cyclization of *N*-isocyanates using blocked (masked) *N*-isocyanate precursors: the effect of the masking group and the reaction scope have been delineated. Substrate synthesis has also been improved using a reported copper-catalyzed coupling of arylbismuth (V) reagents that is compatible with the hemilabile OPh blocking group.

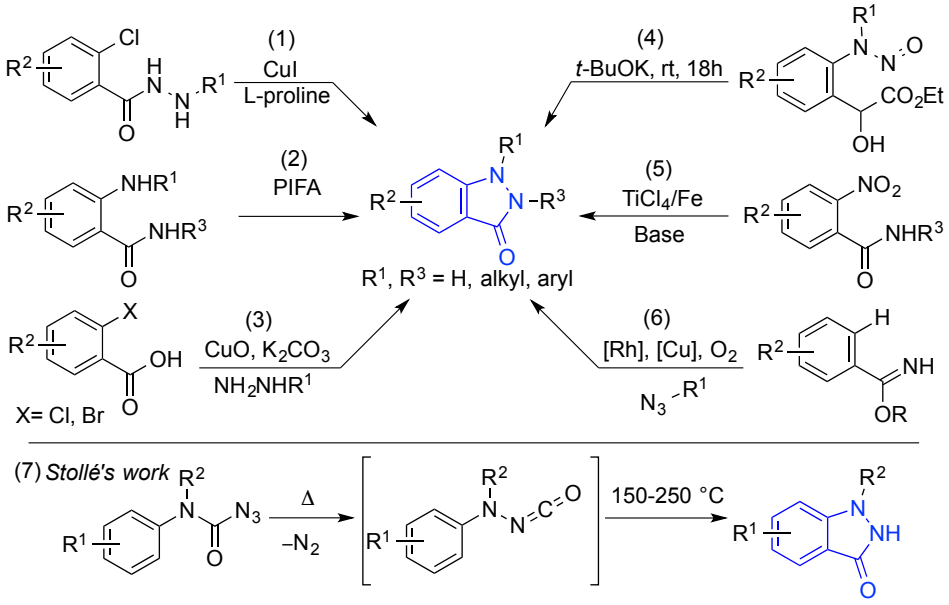
The development of new synthetic methods to form nitrogen heterocycles continues to attract significant interest, and this is stimulated by their importance as core subunits of pharmaceuticals and agrochemicals. In this context, *C*-substituted isocyanates are common building blocks (>100,000 publications and patents in the literature) and are often used in heterocyclic synthesis. In contrast, synthetic applications of nitrogen-substituted isocyanates (*N*-isocyanates) are rare,[1] despite the presence of the NNCO motif in over 50 agrochemicals and pharmaceuticals.[2] This scarcity is likely due to the amphotericity of these reactive intermediates, which contain both a nucleophile and a potent electrophile in their structure, resulting in a tendency to dimerize even at –40 °C.[1] To pursue new reactivity of *N*-isocyanates in cycloadditions[3] and cascade reactions,[4] we have recently developed an approach relying on blocked[5] (masked) *N*-isocyanate reagents, which suppresses side reactions through controlled release of *N*-isocyanates either upon heating or using a base as catalyst. Given the importance of indazole and indazolone-derived cores (**Scheme 1A**),[6] and the use of indazolones in medicinal chemistry including in anticancer,[6a] anti-inflammatory,[7] antitumor,[8] analgesic,[9] antiviral,[10] antihyperglycemic,[11] antipsychotic[12] and antihyperlipidemic[13] efforts, we were drawn to indazolones as synthetic targets. Herein, a systematic investigation of their synthesis through Friedel-Crafts cyclizations is presented, featuring the use of hydrazine derivatives as *N*-isocyanate precursors (**Scheme 1B**).

Scheme 1. (A) Examples of indazole and indazolone derivatives used as pharmaceuticals. (B) This work: synthesis of indazolones from blocked (masked) *N*-isocyanates



Many synthetic approaches have been developed to form indazolones (**Scheme 2**), including (1) CuI/proline-catalyzed intramolecular C–N bond formation of 2-chloro-benzoichydrazides,[14] (2) PIFA-mediated formation of *N*- acylnitrenium intermediates, followed by intramolecular trapping by the amine,[15] (3) CuO-catalyzed coupling of 2-haloarylcarboxylic acids with methylhydrazine,[16] (4) intramolecular [2+2] cycloaddition of ketene and *N*-nitroso compounds,[17] (5) cyclization of *N*-aryl-*o*-nitrobenzamides through a low-valent titanium reagent[18] and (6) Rh-catalyzed C-H activation/C-N bond formation and Cu-catalyzed N-N bond formation between arylimidates and azides.[19] These methods are complementary given the need to access various substitution patterns; however most methods rely on disubstituted aromatic starting materials.

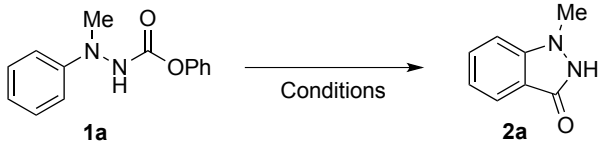
Scheme 2. Selected approaches to form indazolones



In addition, there is the pioneering work of Stollé and co-workers, who reported in 1927 the thermolysis of *N*,*N*-disubstituted carbamoyl azides to form indazolones (4 examples).[20] This key precedent showed that *N*,*N*-diaryl and *N*-alkyl-*N*-aryl carbamoyl azides undergo a thermal aza-Curtius rearrangement, yielding the desired indazolone products after cyclization of the *N*-aryl-*N*-isocyanates [(7), **Scheme 2**]. However, for two difficult cyclizations, significant amounts of *N*-isocyanate dimer by-products were also isolated.[21] This prior work, and its reinvestigation by others[22] offered a rare opportunity to compare the reactivity of *N*-isocyanates with that of their blocked (masked) *N*-isocyanate precursors. In addition, an alternative route would address the safety and scalability issues inherently associated with the use of azide precursors.

Given the versatility of phenol as a blocking (masking) group for other synthetic applications of *N*-isocyanates,[1c] phenyl carbazate **1a** was selected as the model substrate for optimization of the reaction conditions (**Table 1**).

Table 1. Optimization of reaction conditions[a]



1a **2a**

entry	T (°C)	additive	conc (M)	solvent	t (h)	yield[b] (%)
1	150	-	0.1	$PhCF_3$	2	48
2	165	-	0.1	$PhCF_3$	2	81
3	165	-	0.5	$PhCF_3$	2	66
4	165	-	0.05	$PhCF_3$	2	85
5	180	-	0.1	$PhCF_3$	3	>99 (79)[c]
6	180[d]	-	0.05	diglyme	3	50
7	180[d]	-	0.05	$PhCF_3$	3	80
8	180[d]	-	0.05	*o*-xylene	3	80
9	180[d]	-	0.05	*o*-$C_6H_4Cl_2$	3	81
10	180[d]	-	0.05	PhCl	3	83
11	180	Acetic acid[e]	0.05	PhCl	3	73
12	180	Et_3N[e]	0.05	PhCl	3	66
13	180	Citric acid[e]	0.05	PhCl	3	6

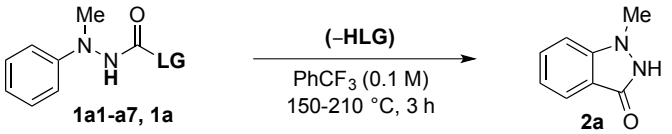
[a] All reactions were carried out in sealed microwave vials unless specified. [b] NMR yield based on 1,3,5-

trimethoxybenzene as internal standard. [c] Isolated yield [d] Conventional heating (oil bath). [e] 1 equiv of the additive was used.

Based on the conditions reported in the original work by Stollé using carbamoyl azides (~140 °C, refluxing xylene)[20] and in its reinvestigation by Reichen (~207 °C, refluxing tetralin),[22] initial cyclization attempts with carbazate **1a** involved heating at 150 °C (**Table 1**). Since only a modest 48% yield was obtained (entry 1), subsequent attempts involved heating at higher temperatures (entries 2-5). As expected, the use of more dilute solutions led to improved yields at 165 °C (entries 3-4), likely by minimizing dimerization of the *N*-isocyanate intermediate, which is a known side-reaction.[1] Gratifyingly, quantitative conversion was observed at 180 °C (0.1 M, entry 5), allowing isolation of the desired indazolone **2a** in a 79% yield. While heating was typically performed using a microwave reactor, this reactivity also proceeded well upon conventional heating. Using these conditions, solvent effects could be probed in several high-boiling solvents (entries 6-10). Only the reaction in diglyme proved less efficient (entry 6), and the other aromatic solvents led to better results (80-83% yield, entries 7-10). The selection of $PhCF_3$ over the other solvents was made on the basis of its low cost and ease of solvent evaporation. Finally, the effect of several additives was investigated (e.g., entries 11-13). It was found that the addition of either acids or bases did not improve the reaction yield or efficiency; moreover citric acid almost suppressed the reactivity (6% yield).[4e] The use of both Brønsted [TsOH, MsOH, $(PhO)_2PO_2H$] and Lewis acids ($AlCl_3$, $TiCl_4$, $BF_3{\cdot}OEt_2$) was also explored to facilitate the process; unfortunately these trials were unsuccessful.

Reasoning that the nature of the blocking group would also have an impact on reaction efficiency, several hydrazine derivatives were synthesized to allow a thorough comparison. Substrates with various leaving groups (**1a1-a7, 1a**), including alcohols, phenol, thiols and amines could then be heated at 150 °C, 180 °C and 210 °C to probe their ability to serve as *N*-isocyanate precursors and form indazolones (**Table 2**).

Table 2. Survey of leaving groups



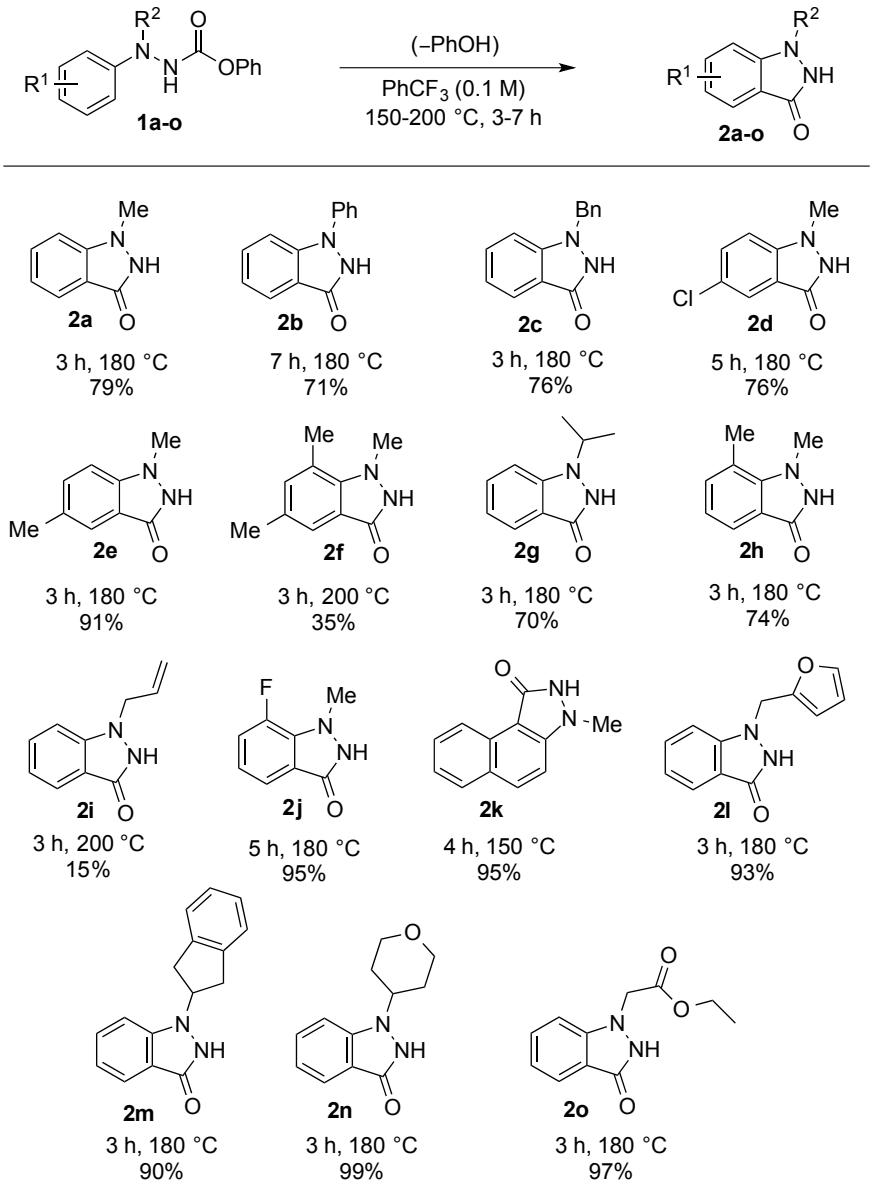
entry	**LG**	yield[a] (%) (% unreacted SM)[b] 150 °C	180 °C	210 °C
1	O*t*-Bu (**1a1**)	0 (100)	29 (63)	43 (28)
2	OMe (**1a2**)	0 (100)	0 (100)	0 (100)
3	NHPh (**1a3**)	0 (100)	8 (78)	60 (25)
4	SEt (**1a4**)	20 (70)	70 (5)	70 (0)
5	SPh (**1a5**)	35 (20)	73 (4)	56 (0)
6	OCH_2CF_3 (**1a6**)	0 (100)	34 (66)	80 (16)
7	N(*i*-Pr)$_2$ (**1a7**)	25 (40)	82 (16)	75 (25)
8	OPh (**1a**)	45 (40)	**>97 (0)**	95 (0)

[a] NMR yield based on 1,3,5-trimethoxybenzene as internal standard. [b] Amount of unreacted starting material determined using the internal standard.

Several reactivity trends were observed from this survey of different leaving (blocking) groups on the *N*-isocyanate precursor (**Table 2**). The results indicated that the reaction can proceed in yields around 70% using different groups, with several of them providing high reactivity at 180 °C under microwave heating (PhOH, EtSH, PhSH and *i*-Pr_2NH). Interestingly, the use of PhOH not only afforded higher yields, but the yield did not vary significantly at a higher temperature (210 °C) in contrast to what was observed for other groups such as PhSH and *i*-Pr_2NH (entries 5, 7). While this observation warrants further studies, it can be explained by the ability of phenol to reversibly add to the *N*-isocyanate under the reaction conditions, in contrast to some groups that would act as "irreversible" leaving groups either due to reduced nucleophilicity (PhSH) or steric hindrance (*i*-Pr_2NH). From these studies, it appeared that the optimal procedure for the preparation of indazolones involves the use of the corresponding phenyl carbazates in $PhCF_3$ (0.1 M), and heating at 180 °C. The reactivity trends above are consistent with the Friedel-Crafts cyclization being the rate determining step, occurring efficiently only above 150 °C; related precursors (LG = OPh) are known to form *N*-isocyanate at ca. 80-100 °C.[4a,b]

In order to investigate the scope of this cyclization reaction, a series of carbazates (**1a-o**) were synthesized according to a 5-step literature procedure (**1a-k**) or one step procedure (**1l-o**) (see Supporting Information for details).[4d] These substrates could then be subjected to the optimized conditions to determine the reaction scope, which had not been fully delineated by Stollé or Reichen using carbamoyl azides.[20,22] The results are presented in **Table 3**.

Table 3. Substrate scope for indazolone formation using phenyl carbazates as *N*-isocyanate precursors[a]

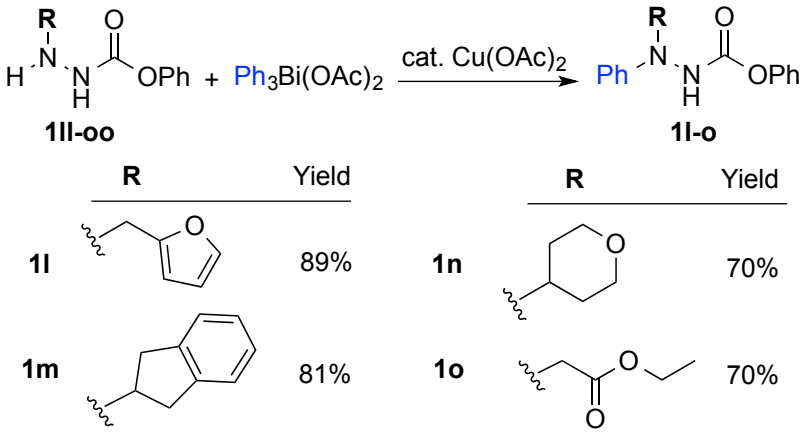


[a] All reactions were carried out in sealed microwave vials. Isolated yields are shown.

Gratifyingly, the scope of this indazolone synthesis using blocked (masked) β*N*-aryl-*N*-isocyanate precursors proved quite general (**Table 3**). This method accommodates both β*N*-alkyl and -aryl substituted phenyl carbazates. The bulkier and inductively electron-withdrawing phenyl group (entry **2b**) needed a longer reaction time (7 h) while the methyl, benzyl and isopropyl derivatives behaved similarly with average yield around 75% after a short reaction time (3 h, entries **2a**, **2c** and **2g**). As expected for a Friedel-Crafts reaction, aromatic carbazates with weakly activating substituents showed better reactivity than those with weakly deactivating groups: 4-methyl and 2-methyl-phenycarbazates afforded **2e** and **2h** in 91% and 74% yields (3 h), while 4-chloro and 2-fluoro-phenylcarbazate needed 5 h to give 76% and 95% yields (entries **2d**, **2j**). Higher reaction temperatures were needed to achieve cyclization to form the 2,4-dimethyl-substituted (**2f**) and *N*-allyl (**2i**) indazolones, but the yields remained relatively low which indicates that subtle changes can result in reduced yields. Conversely, the reaction was successful with a naphthalene derivative (entry **2k**), providing an excellent yield (95%) at a lower reaction temperature (150 °C). Moreover, the reaction tolerated the presence of heterocyclic substituents, forming products including furan (**2l**) and a cyclic ether (**2n**) ring systems. The reaction also proceeded uneventfully in the presence of an ester functional group (entry **2o**). Finally, it is also worth noting that Stollé reported that heating *N*-methyl-*o*-tolyl carbamoyl azide to form **2h** proceeded in 28% yield, and that 13% of a *N*-isocyanate dimer was also isolated.[20a] In contrast, formation of **2h** proceeded efficiently from upon heating the phenyl carbazate precursor **1h** (74% yield), suggesting that this new procedure may be advantageous for difficult cyclizations.[23]

With a broadly applicable indazolone synthesis developed using aromatic carbazates as *N*-isocyanate precursors, we felt that one aspect of the process could benefit from more practicality: substrate synthesis. As indicated previously, several substrates (carbazates **1a-k**) were prepared in 5 steps according to the general procedure in the literature.[4d] Seeking to facilitate substrate preparation from *N*-alkyl carbazates, we were drawn to the reports by Mäeorg and Ragnarsson that pentavalent organobismuth (V) compounds can act as aryl donors in the presence of copper salts.[24] This procedure allowed for a chemoselective arylation the β nitrogen atom using $Ph_3Bi(OAc)_2$ and catalytic amount of $Cu(OAc)_2$ at room temperature (**Scheme 3**), thus providing an efficient access to β-*N*,*N*-disubstituted phenyl carbazates. While previous reports showed that this arylation strategy worked well with robust derivatives (LG = O*t*-Bu, OBn, etc.),[24,25] we were pleased that the hemilabile OPh substituent did not act as a leaving group under the reaction conditions. This suggests that this strategy could be used for the synthesis of other *N*-isocyanate precursors.

Scheme 3. Arylation of phenyl carbazates using a pentavalent bismuth reagent[a]



[a] Conditions: Carbazates **1ll-oo** (1 equiv), anhydrous $Cu(OAc)_2$ (0.05 equiv), $Ph_3Bi(OAc)_2$ (2 equiv), stirred at room temperature in CH_2Cl_2 (0.2 M) for 15 min-12 h. Isolated yields are shown.

In summary, we have developed a methodology that provides ready access to indazolones from variety of carbazates acting as masked *N*-isocyanate precursors. This study avoids the use of carbamoyl azides to form the *N*-isocyanate reactive intermediates, and studied the outcome of the reaction for various blocking groups to identify phenol as the optimal *N*-isocyanate blocking group. The development of other reactivity of *N*-isocyanates is ongoing and will be reported in due course.

EXPERIMENTAL SECTION

General Information. All commercially available materials were used without further purification unless otherwise noted. Solvents for reactions were obtained from solvent system or or dried over 4Å molecular sieves. Microwave reactions were performed using a Biotage Initiator Eight microwave reactor and microwave vials. Reactions were monitored by analytical thin layer chromatography (TLC), using aluminum-backed plates, cut to size. TLC visualization was achieved by UV light followed by staining with a potassium permanganate solution and heating. Flash column chromatography was carried out using 40-63 μm silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded on 300 MHz and 400 MHz spectrometers at ambient temperature, except where noted. Spectral data is reported in ppm using solvent as the reference. ^{1}H NMR: $CDCl_3$ (7.26 ppm), DMSO-d_6 (2.50 ppm). ^{13}C NMR: $CDCl_3$ (77.16 ppm), DMSO-d_6 (39.52 ppm). ^{1}H NMR data was reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet), coupling constants (*J*) in Hz, and integration. ^{13}C NMR was reported indicating information from DEPT experiments. Infrared (IR) spectra were obtained as thin films or as neat solids on FTIR instruments. High resolution mass spectroscopy (HRMS) was performed by magnetic sector electron impact (EI) or Q-TOF electrospray ionization (ESI).

Carbazates **1a-e**,[4d] **1ll-nn**[26] and $Ph_3Bi(OAc)_2$[6,7] are known compounds and were prepared following literature procedures.

***tert*-Butyl 2-methyl-2-phenylhydrazine-1-carboxylate (1a1).** To a round bottom flask charged with stirrer and a solution of 1-methyl-1-phenylhydrazine (**1**, 0.366 g, 3.00 mmol, 1 equiv) in CH_2Cl_2 (0.5 M) was added Boc_2O (0.785 g, 3.60 mmol, 1.2 equiv) at 0 °C. Then the reaction was

refluxed for 12 hours. The mixture was allowed to cool down to room temperature, concentrated and the residue was purified by flash chromatography (hexanes/CH_2Cl_2 = 1:3 ~ 0:1) to afford *tert*-butyl 2-methyl-2-phenylhydrazine-1-carboxylate (**1a1**, 0.450 g, 68% yield) as a yellowish white solid; mp 98-100 °C. TLC Rf = 0.64 in CH_2Cl_2. ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.23 - 7.36 (m, 2 H) 6.81 - 6.94 (m, 3 H) 3.21 (s, 3 H) 1.54 (s, 9 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8 (C), 149.8 (C), 129.0 (CH), 119.2 (CH), 112.6 (CH), 80.8 (C), 40.8 (CH_3), 28.2 (CH_3). IR (neat) 3249, 2982, 2813, 1700, 1598, 1496, 1275, 1157, 1122 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{12}H_{18}N_2O_2$ $[M]^+$: 222.1368. Found: 222.1357.

Methyl 2-methyl-2-phenylhydrazine-1-carboxylate (1a2). To a round bottom flask charged with stirrer and a solution of 1-methyl-1-phenylhydrazine (**1**, 0.366 g, 3.00 mmol, 1 equiv) in CH_2Cl_2 (0.5 M) were added pyridine (0.237 g, 3.00 mmol, 1 equiv) and methyl chloroformate (0.310 g, 3.30 mmol, 1.1 equiv) at 0 °C. Then the reaction was stirred at room temperature for 2 hours. The mixture was concentrated and the residue was dissolved in water and extracted three times with diethyl ether. The organic layers were combined, washed with brine, dried over Na_2SO_4. After filtration, the solvent was concentrated and the residue was purified by flash chromatography (hexanes/CH_2Cl_2 = 3:7 ~ 0:1) to afford methyl 2-methyl-2-phenylhydrazine-1-carboxylate (**1a2,** 0.340 g, 63% yield) as yellow oil. TLC Rf = 0.35 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 - 7.68 (m, 2H), 7.16 - 7.26 (m, 3H), 4.12 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5 (C), 149.7 (C), 129.2 (CH), 119.7 (CH), 113.1 (CH), 52.6 (CH_3), 40.9 (CH_3). IR (neat) 3267, 2954, 1710, 1599, 1496, 1447, 1218, 1116, 1064 cm^{-1}. HRMS (EI): Exact mass calcd for $C_9H_{12}N_2O_2$ $[M]^+$: 180.0899. Found: 180.0899.

General procedure 1 (substrates 1a3-a7). The substrates were prepared from phenyl carbazate **1a** and the appropriate nucleophile, in a modification of a literature procedure.[4a] A round bottom flask was charged with a stir bar, phenyl 2-methyl-2-phenylhydrazine-1-carboxylate (**1a,** 1 equiv), a nucleophile (1-2 equiv), DBU (20 mol%) and THF (0.3 M). The mixture was refluxed for the specified time, concentrated, and purified by flash column chromatography to afford the desired product.

2-Methyl-*N*,2-diphenylhydrazine-1-carboxamide (1a3). Synthesized according to general procedure **1** using **1a** (0.484 g, 2.00 mmol, 1 equiv), aniline (0.102 g, 2.20 mmol, 1.1 equiv), DBU (0.060 g, 0.40 mmol), and THF (6.6 mL), reflux overnight. The title compound was purified by column chromatography (hexanes/EtOAc = 5:1) to give a white solid (0.315 g, 65%); mp 155-157 °C. TLC Rf = 0.4 in 33% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.78 (br s, 1 H) 7.45 - 7.52 (m, 2 H) 7.26 - 7.39 (m, 4 H) 6.99 - 7.11 (m, 4 H) 6.27 (s, 1 H) 3.22 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5 (C), 149.8 (C), 137.9 (C), 129.4 (CH), 128.9 (CH), 123.3 (CH), 121.8 (CH), 119.4 (CH), 114.7 (CH), 42.7 (CH_3). IR (neat) 3321, 3234, 1670, 1590, 1413, 1402, 1323, 1229 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{14}H_{15}N_3O$ $[M]^+$: 241.1215. Found: 241.12193.

***S*-Ethyl 2-methyl-2-phenylhydrazine-1-carbothioate (1a4).** Synthesized according to general procedure **1** using **1a** (0.484 g, 2.00 mmol, 1.0 equiv), ethanethiol (0.186 g, 3.00 mmol, 1.5 equiv), DBU (0.060 g, 0.40 mmol), and THF (6.6 mL), reflux for 2 hours. The title compound was purified by column chromatography (hexanes/EtOAc = 8:1) to give a white solid (0.270 g, 64%); mp 109-110 °C. TLC Rf = 0.71 in 33% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 - 7.35 (m,

2H), 6.87 - 7.03 (m, 4H), 3.17 (s, 3H), 2.84 (q, J = 7.4 Hz, 2H), 1.29 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6 (C), 148.5 (C), 128.9 (CH), 120.6 (CH), 113.4 (CH), 41.2 (CH_3), 22.8 (CH_2), 14.6 (CH_3). IR (neat) 3159, 3047, 2968, 2893, 2801, 1640, 1597, 1493, 1450, 1200 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{10}H_{14}N_2OS$ $[M]^+$: 210.08268. Found: 210.08368.

***S*-Phenyl 2-methyl-2-phenylhydrazine-1-carbothioate (1a5).** Synthesized according to general procedure **1** using **1a** (0.363 g, 1.50 mmol, 1 equiv), thiophenol (0.330 g, 3.00 mmol, 2 equiv), DBU (0.045 g, 0.30 mmol), and THF (5 mL), reflux for 5 hours. The title compound was purified by column chromatography (hexanes/CH_2Cl_2 = 1:9 ~ 0:1) to give a white solid (0.320 g, 83%)%); mp 169-170 °C. TLC Rf = 0.46 in CH_2Cl_2. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 - 7.57 (m, 2H), 7.32 - 7.45 (m, 5H), 7.03 (d, J = 6.7 Hz, 4H), 3.25 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8 (C), 148.4 (C), 135.1 (C), 129.0 (CH), 128.8 (CH), 128.6 (CH), 128.0 (CH), 121.1 (CH), 113.8 (CH), 41.6 (CH_3). IR (neat) 3164, 3065, 2876, 1667, 1597, 1496, 1439, 1266, 1113, 704 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{14}H_{14}N_2OS$ $[M]^+$: 258.0827. Found: 258.08027.

2,2,2-Trifluoroethyl 2-methyl-2-phenylhydrazine-1-carboxylate (1a6). Synthesized according to general procedure **1** using **1a** (0.242 g, 1.00 mmol, 1 equiv), 2,2,2-trifluoroethanol (0.150 g, 1.50 mmol, 1.5 equiv), DBU (0.030 g, 0.20 mmol), and THF (3.3 mL), reflux for 12 hours. The title compound was purified by column chromatography (hexanes/CH_2Cl_2 = 1:1) to give a white solid (0.186 g, 75%); mp 103-104 °C. TLC Rf = 0.57 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 - 7.35 (m, 2H), 6.79 - 7.00 (m, 4H), 4.53 (q, $J_{H\text{-}F}$ = 8.4 Hz, 2H), 3.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8 (C), 149.1 (C), 129.2 (CH), 120.3 (CH), 113.1 (C), 112.6 (CH), 61.0 (q, $J_{C,F}$ = 37 Hz, CH_2), 40.8 (CH_3). IR (neat) 3272, 2963, 2885, 1730, 1598, 1505, 1453, 1281, 1213, 1119 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{10}H_{11}F_3N_2O_2$ $[M]^+$: 248.0773. Found: 248.0760.

***N*,*N*-Diisopropyl-2-methyl-2-phenylhydrazine-1-carboxamide (1a7).** Synthesized according to general procedure **1** using **1a** (0.242 g, 1.00 mmol, 1 equiv), diisopropylamine (0.111 g, 1.10 mmol, 1.1 equiv), DBU (0.030 g, 0.20 mmol), and THF (3.3 mL), reflux for 12 hours. The title compound was purified by column chromatography (CH_2Cl_2) to give a white solid (0.127 g, 55%); mp 122-124 °C. TLC Rf = 0.25 in CH_2Cl_2. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (dd, J = 1.5, 7.3 Hz, 2H), 6.82 - 6.93 (m, 3H), 6.18 (br s, 1H), 3.96 (sept., J = 6.9 Hz, 2H), 3.26 (s, 3H), 1.36 (d, J = 6.7 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7 (C), 150.4 (C), 129.0 (CH), 118.8 (CH), 112.5 (CH), 45.7 (CH), 41.4 (CH_3), 21.4 (CH_3). IR (neat) 3371, 2970, 1635, 1599, 1376, 1289 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{14}H_{23}N_3O$ $[M]^+$: 249.1841. Found: 249.1842.

General Procedure 2. Carbazates **1f-k** were prepared according to a 5-step sequence. **2A:** To a solution of *o*-tolylhydrazine hydrochloride (**A**, 2.00 g, 16.3 mmol, 1 equiv) in MeOH (0.2 M) were added triethylamine (3.31 g, 32.7 mmol, 2 equiv) and $(Boc)_2O$ (3.93 g, 18.0 mmol, 1.1 equiv) at 0 °C. Then the reaction was stirred at room temperature for 3 hours. The mixture was concentrated and the residue was dissolved in EtOAc. The mixture was washed with water and brine, dried over Na_2SO_4. After filtration, the solvent was concentrated and the residue was purified by flash chromatography (hexanes/CH_2Cl_2 = 1:1 ~ 0:1) to afford *tert*-butyl 2-(*o*-tolyl)hydrazine-1-carboxylate (**B**, 1.60 g, 44% yield) as a white solid.

General Procedure 2B: To a solution of *tert*-butyl 2-(*o*-tolyl)hydrazine-1-carboxylate (**B**, 1.57 g, 7.09 mmol, 1.0 equiv) in CH_2Cl_2 (0.2 M) were added pyridine (1.12 g, 14.1 mmol, 2.0 equiv) and NBS (1.38 g, 7.80 mmol, 1.1 equiv) at 0 °C. Then the reaction was stirred at room temperature for 20 minutes. The mixture was concentrated and the residue was purified by flash chromatography (hexanes/EtOAc = 17:1) to afford *tert*-butyl 2-(*o*-tolyl)diazene-1-carboxylate (**C**, 1.41 g, 90% yield) as an orange oil.

General Procedure 2C: To a mixture of *tert*-butyl 2-(*o*-tolyl)diazene-1-carboxylate (**C**, 1.41 g, 6.41 mmol, 1.0 equiv) in THF (0.1 M) at –100 °C was added MeMgBr (3 M in Et_2O, 2.13 mL, 1.0 equiv) under argon. Then the reaction was stirred at –100 °C for 20 minutes. The reaction was quenched with sat. aq. NH_4Cl. Then the mixture was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4. After filtration, the solvent was concentrated to give *tert*-butyl 2-methyl-2-(*o*-tolyl)hydrazine-1-carboxylate (**D**) as a yellow oil, which was used in the next step without further purification.

General Procedure 2D: To a mixture of *tert*-butyl 2-methyl-2-(*o*-tolyl)hydrazine-1-carboxylate (**D**, 1.49 g, 6.34 mmol, 1.0 equiv) in CH_2Cl_2 (0.5 M) was added TFA (3.61 g, 31.7 mmol, 5.0 equiv). Then the reaction was stirred at room temperature for 2 hours. The mixture was concentrated to give 1-methyl-1-(*o*-tolyl)hydrazine (**E**) as a TFA salt, which was used in the next step without further purification.

General Procedure 2E: To a mixture of 1-methyl-1-(*o*-tolyl)hydrazine (**E**, TFA salt, 0.340 g, 1.36 mmol, 1.0 equiv) and pyridine (0.215 g, 2.72 mmol, 2.0 equiv) in CH_2Cl_2 (0.2 M) at 0 °C was added phenyl chloroformate (0.212 g, 1.36 mmol, 1.0 equiv). Then the reaction was stirred at room temperature for 2 hours. The mixture was concentrated and the residue was dissolved in EtOAc (50 mL). After extraction, the organic phase was washed with water (25 mL), brine (25 mL), dried over Na_2SO_4. After filtration, the solvent was concentrated and the residue was purified by flash chromatography (hexanes/EtOAc = 15:1) to afford phenyl 2-methyl-2-(*o*-tolyl)hydrazine-1-carboxylate (**1h,** 0.203 g, 58% yield over 3 steps) as a white solid.

Phenyl 2-(2,4-dimethylphenyl)-2-methylhydrazine-1-carboxylate (1f). Synthesized according to general procedure **2A-E** using (2,4-dimethylphenyl)hydrazine hydrochloride (2.00 g, 11.6 mmol). The title compound was purified by column chromatography (hexanes/EtOAc = 12:1) to give **1f** (0.469 g, 15% over 5 steps) as a white solid; mp 113-115 °C. TLC Rf = 0.61 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 - 7.42 (m, 2H), 7.07 - 7.26 (m, 4H), 6.94 - 7.07 (m, 2H), 3.15 (s, 3H), 2.39 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4 (C), 151.0 (C), 146.2 (C), 134.4 (C), 132.7 (CH), 132.4 (CH), 129.5 (CH), 127.0 (CH), 125.7 (C), 121.7 (CH), 118.6 (CH), 43.3 (CH_3), 21.0 (CH_3), 18.6 (CH_3). IR (neat) 3194, 3026, 2803, 1720, 1551, 1489, 1253, 1202 cn^{-1}. HRMS (EI): Exact mass calcd for $C_{16}H_{18}N_2O_2$ $[M]^+$: 270.1368. Found: 270.1373.

Phenyl 2-isopropyl-2-phenylhydrazine-1-carboxylate (1g). Synthesized according to general procedure **2B-E** using *tert*-butyl 2-phenylhydrazine-1-carboxylate (0.500 g, 2.40 mmol) and isopropylmagmesium bromide (2.40 mmol). The title compound was purified by column chromatography (hexanes/EtOAc = 15:1~10:1) to give **1g** (0.149 g, 23% over 4 steps) as a white

solid. TLC Rf = 0.41 in 10% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 - 7.44 (m, 4H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.81 - 7.01 (m, 3H), 6.47 (br s, 1H), 4.16 - 4.32 (m, 1H), 1.24 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6 (C), 150.4 (C), 147.7 (C), 129.0 (CH), 125.1 (CH), 121.2 (CH), 120.9 (CH), 119.7 (CH), 113.7 (CH), 113.5 (CH), 50.8 (CH_3). HRMS (EI): Exact mass calcd for $C_{16}H_{18}N_2O_2$ $[M]^+$: 270.1368. Found: 270.1364.

Phenyl 2-methyl-2-(*o*-tolyl)hydrazine-1-carboxylate (1h). Synthesized according to general procedure **2A-E**. The title compound was purified by column chromatography (hexanes/EtOAc = 15:1) to give **1h** (0.203 g, 19% yield over 5 steps) as a white solid; mp 101-102 °C. TLC Rf = 0.24 in 7% EtOAc/hexanes. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 - 7.39 (m, 2H), 7.18 - 7.25 (m, 4H), 7.01 - 7.18 (m, 3H), 6.68 (br s, 1H), 3.18 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1 (C), 150.7 (C), 148.3 (C), 131.5 (CH), 129.3 (CH), 126.2 (CH), 125.4 (C), 124.5 (CH), 121.4 (CH), 118.3 (CH), 42.8 (CH_3), 18.6 (CH_3). IR (neat) 3197, 2960, 2884, 1721, 1594, 1507, 1243, 1201 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{15}H_{16}N_2O_2$ $[M]^+$: 256.1212. Found: 256.1227.

Phenyl 2-allyl-2-phenylhydrazine-1-carboxylate (1i). Synthesized according to general procedure **2B-E** using *tert*-butyl 2-phenylhydrazine-1-carboxylate (0.500 g, 2.40 mmol) and allylmagnesium bromide (2.40 mmol). The title compound was purified by column chromatography (hexanes/EtOAc = 15:1) to give **1i** (0.137 g, 27% over 4 steps) as a white solid. TLC Rf = 0.54 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.98 (s, 1H), 7.39 - 7.45 (m, 2H), 7.15 - 7.28 (m, 5H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 5.88 - 6.06 (m, 1H), 5.37 (dd, *J* = 1.6, 17.2 Hz, 1H), 5.21 - 5.28 (m, 1H), 4.13 (d, *J* = 5.6 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.0 (C), 151.5 (C), 149.6 (C), 134.6 (CH), 130.3 (CH), 129.8 (CH), 126.1 (CH), 122.5 (CH), 119.6 (CH), 118.6 (CH_2), 113.6 (CH), 55.8 (CH_2). IR (neat) 3250, 1716, 1595, 1494, 1385, 1248, 1198, 1069, 1024 cm^{-1}. HRMS (ESI): Exact mass calcd for $C_{16}H_{16}N_2O_2$ $[M]^+$: 268.1212. Found: 268.1235.

Phenyl 2-(2-fluorophenyl)-2-methylhydrazine-1-carboxylate (1j). Synthesized according to general procedure **2A-E** using (2-fluorophenyl)hydrazine hydrochloride (2.00 g, 12.3 mmol). The title compound was crystallized from (hexanes/EtOAc = 10:1) to give **1j** (1.71 g, 53% over 5 steps) as a white solid; mp 134-135 °C. TLC Rf = 0.35 in 20% EtOAc/hexanes. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.04 - 7.20 (m, 5H), 6.97 (t, *J* = 8.0 Hz, 1H), 3.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.7 (C), 153.2 (C), 150.4 (C), 137.9 (C), 129.1 (CH), 125.0 (CH), 124.2 (CH), 122.2 (CH), 121.3 (CH), 117.8 (CH), 116.2 (CH), 42.3 (CH_3). IR (neat) 3214, 3026, 2997, 1722, 1596, 1489, 1249, 1212 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{14}H_{13}FN_2O_2$ $[M]^+$: 260.0961. Found: 260.0979.

Phenyl 2-methyl-2-(naphthalen-2-yl)hydrazine-1-carboxylate (1k). Synthesized according to general procedure **2A-E** using naphthalen-2-ylhydrazine hydrochloride (2.00 g, 10.3 mmol). The title compound was purified by column chromatography (hexanes/EtOAc = 13:1~6:1) to give **1k** (0.480 g, 16% over 5 steps) as a white solid; mp 190-192 °C. TLC Rf = 0.43 in 20% EtOAc/hexanes. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.20 (s, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 7.77 (dd, *J* = 2.8, 8.1 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 3H), 7.18 - 7.33 (m, 5H), 7.17 (s, 1H), 3.27 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.1 (C), 150.7 (C), 147.7 (C), 134.2 (C), 129.4 (C), 128.7 (CH), 127.6 (CH), 127.4 (CH), 126.5 (CH), 126.4 (CH), 125.4 (CH), 122.8 (CH), 121.7 (CH),

115.8 (CH), 106.6 (CH), 40.5 (CH_3). IR (neat) 3223, 2980, 2878, 1736, 1629, 1599, 1478, 1299 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{18}H_{16}N_2O_2$ $[M]^+$: 292.1212. Found: 292.1242.

Phenyl 2-(2-ethoxy-2-oxoethyl)hydrazine-1-carboxylate (1oo). Synthesized according to a reported general procedure,[25] by stirring *O*-phenyl carbazate (2.46 g, 16.1 mmol) and ethyl 2-oxoacetate (1.65 g, 16.1 mmol). The crude reaction was diluted in 2:1 MeOH:AcOH (0.2 M) and $NaBH_3CN$ (3.05 g, 48.6 mmol) was added and allowed to stir for 16 h. The title compound was purified by column chromatography (10% EtOAc/CH_2Cl_2) to yield an amorphous white solid (1.52 g, 40%); mp 110-113 °C. TLC Rf = 0.21 in 10% EtOAc/CH_2Cl_2. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (br s, 1H), 7.38 (t, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 5.10 (br s, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.59 (d, *J* = 4.7 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.4 (C), 155.0 (C), 150.8 (C), 129.3 (CH), 125.0 (CH), 121.6 (CH), 60.1 (CH_2), 51.9 (CH_2), 14.1 (CH_3). IR (film) 3283, 3217, 3094, 2988, 1742, 1717, 1550, 1491, 1427, 1379, 1197 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{11}H_{14}N_2O_4$ $[M]^+$: 238.0954. Found: 238.0947.

General Procedure 3 for the synthesis of carbazates 1l-o:[24] To a solution of carbazates **1ll-oo** in CH_2Cl_2 (0.2 M), 0.05 equiv of anhydrous $Cu(OAc)_2$ was added, followed by 2 equiv of $Ph_3Bi(OAc)_2$. The reaction was stirred at room temperature for 15 min-12 h. After completion the solids were removed by filtration, the filtrate was concentrated under reduced pressure and purified by column chromatography to afford the desired product.

Phenyl 2-(furan-2-ylmethyl)-2-phenylhydrazine-1-carboxylate (1l). Synthesized according to general procedure **3** using phenyl 2-(furan-2-ylmethyl)hydrazine-1-carboxylate (**1ll**, 0.139 g, 0.600 mmol), stirring for 1 h. The title compound was purified by column chromatography (hexanes/EtOAc =5:1) to give **1l** (0.165 g, 89%) as a white solid; mp 177-179 °C. TLC Rf = 0.32 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.98 (s, 1H), 7.66 (t, *J* = 1.2 Hz, 1H), 7.37 - 7.44 (m, 2H), 7.26 (t, *J* = 8.0 Hz, 3H), 7.13 (d, *J* = 7.7 Hz, 2H), 6.98 (d, *J* = 8.1 Hz, 2H), 6.79 - 6.85 (m, 1H), 6.45 (d, *J* = 1.4 Hz, 2H), 4.67 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.7 (C), 150.6 (C), 150.1 (C), 148.0 (C), 142.7 (CH), 129.3 (CH), 129.2 (CH), 125.6 (CH), 121.3 (CH), 120.5 (CH), 113.7 (CH), 110.4 (CH), 109.4 (CH), 49.0 (CH_2). IR (neat) 3264, 2980, 1720, 1593, 1491, 1266, 1211 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{18}H_{16}N_2O_3$ $[M]^+$: 308.1161. Found: 308.1153.

Phenyl 2-(2,3-dihydro-1*H*-inden-2-yl)-2-phenylhydrazine-1-carboxylate (1m). Synthesized according to general procedure **3** using phenyl 2-(2,3-dihydro-1*H*-inden-2-yl)hydrazine-1-carboxylate (**1mm**, 0.160 g, 0.600 mmol), stirring for 7 h. The title compound was purified by column chromatography (hexanes/EtOAc = 7:1) to give **1m** (0.166 g, 81%) as a white solid; mp 214-216 °C. TLC Rf = 0.43 in 13% EtOAc/hexanes. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.35 - 7.43 (m, 2H), 7.20 - 7.34 (m, 5H), 7.13 - 7.19 (m, 2H), 7.08 (d, *J* = 7.5 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.80 - 6.89 (m, 1H), 4.99 (quin, *J* = 7.5 Hz, 1H), 3.18 (d, *J* = 8.0 Hz, 4H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.1 (C), 150.7 (C), 148.6 (C), 141.2 (C), 129.4 (CH), 129.1 (CH), 126.3 (CH), 125.3 (CH), 124.4 (CH), 121.6 (CH), 119.2 (CH), 113.8 (CH), 59.9 (CH), 35.7 (CH_2). IR (neat) 3276, 2950, 1723, 1592, 1490, 1242, 1198 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{22}H_{20}N_2O_2$ $[M]^+$: 344.1525. Found: 344.1493.

Phenyl 2-phenyl-2-(tetrahydro-2*H*-pyran-4-yl)hydrazine-1-carboxylate (1n). Synthesized according to general procedure **3** using phenyl 2-(tetrahydro-2*H*-pyran-4-yl)hydrazine-1-carboxylate (**1nn**, 0.141 g, 0.600 mmol), stirring for 5 h. The title compound was purified by column chromatography (hexanes/EtOAc = 5:2) to give **1n** (0.131 g, 70%) as a white solid; mp 192-193 °C. TLC Rf = 0.31 in 15% EtOAc/hexanes. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s, 1H), 7.40 - 7.44 (m, 2H), 7.24 - 7.28 (m, 3H), 7.20 (dd, J = 0.9, 8.5 Hz, 2H), 6.94 (d, J = 7.8 Hz, 2H), 6.77 - 6.81 (m, 1H), 4.09 (t, J = 7.6 Hz, 1H), 3.93 (d, J = 11.2 Hz, 2H), 3.45 (dd, J = 7.5, 18.3 Hz, 2H), 1.70 (br s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6 (C), 150.3 (C), 147.0 (C), 129.1 (CH), 129.0 (CH), 125.3 (CH), 120.9 (CH), 120.1 (CH), 113.7 (CH), 67.0 (CH_2), 56.4 (CH), 28.6 (CH_2). IR (neat) 3273, 2955, 2828, 1730, 1593, 1490, 1287, 1214 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{18}H_{20}N_2O_3$ $[M]^+$: 312.1474. Found: 312.1471.

Phenyl 2-(2-ethoxy-2-oxoethyl)-2-phenylhydrazine-1 carboxylate (1o). Synthesized according to general procedure **3** using phenyl 2-(2-ethoxy-2-oxoethyl)hydrazine-1-carboxylate (**1oo**, 0.238 g, 1.00 mmol), stirring for 12 h. The title compound was purified by column chromatography (hexanes/EtOAc = 4:1) to give **1o** (0.220 g, 70%) as a yellow oil. TLC Rf = 0.22 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (br s, 1H), 7.23 - 7.48 (m, 7H), 6.90 - 7.03 (m, 3H), 4.42 (br s, 2H), 4.27 (q, J = 7.2 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9 (C), 153.4 (C), 150.2 (C), 147.3 (C), 128.9 (2xCH), 125.2 (CH), 120.8 (CH), 120.4 (CH), 112.8 (CH), 61.0 (CH_2), 53.3 (CH_2), 13.7 (CH_3). IR (neat) 3293, 2981, 2937, 1727, 1598, 1493, 1373, 1179 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{17}H_{18}N_2O_4$ $[M]^+$: 314.12666. Found: 314.12646.

General Procedure 4: A microwave vial was charged with a stir bar. The carbazate **1a-o** and α,α,α-trifluorotoluene (0.1 M) were added. The vial was capped and heated in a microwave reactor for 3−7 hours at 150−200 °C. The reaction was cooled and the mixture was concentrated under reduced pressure. The residue was purified either by crystallization or flash chromatography on silica gel.

General Procedure for Conventional Heating: A sealed pressure tube was charged with a stir bar. The carbazate **1a** (0.1 mmol) and the solvent (0.05 M) were added. The vial was capped and heated in wax bath for 3 hours at 180 °C. The reaction was cooled, the solvent was removed under reduced pressure and the NMR yield was determined using 1,3,5-trimethoxybenzene as internal standard.

1-Methyl-1,2-dihydro-3*H*-indazol-3-one (2a). Synthesized according to general procedure **4** using phenyl 2-methyl-2-phenylhydrazine-1-carboxylate (**1a**, 0.048 g) for 3 hours at 180 °C. The residue was purified by column chromatography (hexanes/EtOAc = 2:1) to give **2a** (0.020 g, 79%) as a white solid; mp 154-156 °C. TLC Rf = 0.37 in 33% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.0 Hz, 1H), 7.46 (ddd, J = 1.1, 7.0, 8.4 Hz, 1H), 7.24 (d, J = 8.5 Hz, 1H), 7.07 - 7.14 (m, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4 (C), 142.1 (C), 128.6 (CH), 121.1 (CH), 119.3 (C), 112.6 (CH), 108.7 (CH), 34.8 (CH_3). IR (neat) 2942, 2543, 1616, 1580, 1537, 1445, 1307, 1288, 1178, 1009 cm^{-1}. HRMS (EI): Exact mass calcd for $C_8H_8N_2O$ $[M]^+$: 148.0637. Found: 148. 0652.

1-Phenyl-1,2-dihydro-3*H*-indazol-3-one (2b). Synthesized according to general procedure **4** using phenyl 2,2-diphenylhydrazine-1-carboxylate (**1b**, 0.091 g) for 7 hours at 180 °C. The residue was purified by column chromatography (hexanes/EtOAc = 2:1) to give **2b** (0.045 g, 71%) as a white solid; mp 222-224 °C. TLC Rf = 0.37 in 33% EtOAc/hexanes. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77 (dd, J = 3.7, 8.4 Hz, 2H), 7.69 (d, J = 7.5 Hz, 2H), 7.49 - 7.55 (m, 2H), 7.43 - 7.48 (m, 1H), 7.23 - 7.29 (m, 1H), 7.16 (t, J = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 156.3 (C), 140.2 (C), 139.2 (C), 129.5 (CH), 128.3 (CH), 124.7 (CH), 120.6 (CH), 120.5 (CH), 120.3 (C), 114.8 (CH), 110.3 (CH). IR (neat) 2960, 2578, 1619, 1592, 1444, 1309, 1233 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{13}H_{10}N_2O$ $[M]^+$: 210.0793. Found: 210.0796.

1-Benzyl-1,2-dihydro-3*H*-indazol-3-one (2c). Synthesized according to general procedure **4** using phenyl 2-benzyl-2-phenylhydrazine-1-carboxylate (**1c**, 0.063 g) for 3 hours at 180 °C. The residue was crystallized from toluene to give **2c** (0.034 g, 76%) as a white solid; mp 181-182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 1H), 7.40 (ddd, J = 1.1, 7.0, 8.4 Hz, 1H), 7.26 - 7.34 (m, 5H), 7.22 (d, J = 8.6 Hz, 1H), 7.09 (ddd, J = 0.7, 7.1, 7.9 Hz, 1H), 5.34 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8 (C), 141.8 (C), 136.5 (C), 128.8 (CH), 128.7 (CH), 127.8 (CH), 127.4 (CH), 121.4 (CH), 119.6 (C), 113.3 (CH), 109.2 (CH), 52.4 (CH_2). IR (neat) 2965, 2543, 1617, 1585, 1443, 1321, 1140 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{14}H_{12}N_2O$ $[M]^+$: 224.0950. Found: 224.0951.

5-Chloro-1-methyl-1,2-dihydro-3*H*-indazol-3-one (2d). Synthesized according to general procedure **4** using phenyl 2-(4-chlorophenyl)-2 methylhydrazine-1-carboxylate (**1d**, 0.110 g) for 5 hours at 180 °C. The residue was crystallized from CH_2Cl_2 to give **2d** (0.055 g, 76%) as a white solid; mp 245-246 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 1.8 Hz, 1H), 7.39 (dd, J = 1.4, 9.0 Hz, 1H), 7.17 (d, J = 9.0 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2 (C), 140.3 (C), 129.3 (CH), 124.9 (C), 120.3 (C), 113.0 (CH), 109.9 (CH), 34.9 (CH_3). IR (neat) 2981, 2547, 1617, 1583, 1555, 1472, 1294, 1257, 1040 cm^{-1}. HRMS (EI): Exact mass calcd for $C_8H_7ClN_2O$ $[M]^+$: 182.0247. Found: 182.0227.

1,5-Dimethyl-1,2-dihydro-3*H*-indazol-3-one (2e). Synthesized according to general procedure **4** using phenyl 2-methyl-2-(*p*-tolyl)hydrazine-1-carboxylate (**1e**, 0.102 g) for 3 hours at 180 °C. The residue was purified by column chromatography (CH_2Cl_2/MeOH = 99:1) to give **2e** (0.059 g, 91%) as a white solid; mp 202-203 °C. TLC Rf = 0.42 in 95% CH_2Cl_2/MeOH. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.29 (d, J = 4.1 Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 3.82 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.3 (C), 141.3 (C), 130.7 (CH), 128.8 (C), 120.2 (C), 113.0 (CH), 108.6 (CH), 35.0 (CH_3), 21.1 (CH_3). IR (neat) 2914, 2569, 1626, 1524, 1393, 1279, 1239, 1047 cm^{-1}. HRMS (EI): Exact mass calcd for $C_9H_{10}N_2O$ $[M]^+$: 162.07931. Found: 162.07655.

1,5,7-Trimethyl-1,2-dihydro-3*H*-indazol-3-one (2f). Synthesized according to general procedure **4** using phenyl 2-(2,4-dimethylphenyl)-2-methylhydrazine-1-carboxylate (**1f**, 0.135 g) for 3 hours at 200 °C. The residue was purified by column chromatography (hexanes/EtOAc = 2:1 ~ 1:1) to give **2f** (0.031 g, 35%) as a white solid; mp 177-179 °C. TLC Rf = 0.25 in 33% EtOAc/hexanes. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.02 (s, 1H), 3.88 (s, 3H), 2.60 (s, 3H), 2.39 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5 (C), 142.3 (C), 132.8 (CH), 129.7 (CH), 120.3 (C), 118.2 (C), 115.0 (C), 38.1 (CH_3), 20.5 (CH_3), 18.6 (CH_3). IR (neat) 2968, 2586, 1662,

1531, 1451, 1272, 1223, 1019 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{10}H_{12}N_2O$ $[M]^+$: 176.0950. Found: 176.0959.

1-Isopropyl-1,2-dihydro-3*H*-indazol-3-one (2g). Synthesized according to general procedure **4** using phenyl 2-isopropyl-2-phenylhydrazine-1-carboxylate 1**g**, 0.050 g) for 3 hours at 180 °C. The residue was purified by column chromatography (CH_2Cl_2/MeOH = 98:2) to give **2g** (0.022 g, 70%) as a white solid; mp 151-152 °C. TLC Rf = 0.17 in 97% CH_2Cl_2/MeOH. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 1H), 7.38 - 7.45 (m, 1H), 7.29 (s, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 4.66 (td, *J* = 6.7, 13.5 Hz, 1H), 1.55 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8 (C), 141.0 (C), 128.1 (CH), 121.1 (CH), 118.9 (C), 112.7 (CH), 108.7 (CH), 49.7 (CH), 21.1 (CH_3). IR (neat) 2969, 2568, 1651, 1585, 1537, 1304, 1145 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{10}H_{12}N_2O$ $[M]^+$: 176.09496. Found: 176.09423.

Table 3, indazolone 2h: 1,7-Dimethyl-1,2-dihydro-3*H*-indazol-3-one (2h). Synthesized according to general procedure **4** using phenyl 2-methyl-2-(*o*-tolyl)hydrazine-1-carboxylate (**1h**, 0.128 g) for 3 hours at 180 °C. The residue was purified by column chromatography (hexanes/EtOAc = 2:1) to give **2h** (0.060 g, 74%) as a white solid; mp 217-219 °C. TLC Rf = 0.23 in 20% EtOAc/hexanes. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.8 Hz, 1H), 7.16 (td, *J* = 1.0, 7.1 Hz, 1H), 6.96 - 7.03 (m, 1H), 4.00 (s, 3H), 2.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7 (C), 142.4 (C), 130.4 (CH), 120.2 (C), 119.8 (CH), 118.9 (C), 113.9 (CH), 37.7 (CH_3), 18.8 (CH_3). IR (neat) 2922, 2556, 1612, 1527, 1430, 1311, 1194 cm^{-1}. HRMS (EI): Exact mass calcd for $C_9H_{10}N_2O$ $[M]^+$: 162.0793. Found: 162.0792.

Table 3, indazolone 2i: 1-Allyl-1,2-dihydro-3*H*-indazol-3-one (2i). Synthesized according to general procedure **4** using phenyl 2-allyl-2-phenylhydrazine-1-carboxylate (**1i**, 0.085 g) for 3 hours at 200 °C. The residue was purified by column chromatography (hexanes/EtOAc = 5:1 ~ 4:1) to give **2i** (0.008 g, 15%) as a white solid; mp 128-129 °C. TLC Rf = 0.23 in 20% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.41 - 7.48 (m, 1H), 7.24 (s, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 5.91 - 6.08 (m, 1H), 5.20 - 5.30 (m, 2H), 4.77 (d, *J* = 5.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCL_3$) δ 157.2 (C), 142.4 (C), 132.6 (CH), 129.2 (CH), 121.8 (CH), 120.0 (CH_2), 118.6 (C), 113.6 (CH), 109.5 (CH), 51.4 (CH_2). IR (neat) 2987, 2557, 1615, 1544, 1445, 1304, 1252, 1201 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{10}H_{10}N_2O$ $[M]^+$: 174.0793. Found: 174.0814.

7-Fluoro-1-methyl-1,2-dihydro-3*H*-indazol-3-one (2j). Synthesized according to general procedure **4** using phenyl 2-(2-fluorophenyl)-2-methylhydrazine-1-carboxylate (**1j**, 0.130 g) for 5 hours at 180 °C. After cooling the precipitated solid was filtered, washed with petroleum ether and allowed for air drying to give **2j** (0.079 g, 95%) as a white solid; mp 218-219 °C. TLC Rf = 0.22 in 20% EtOAc/Hexane. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 7.6, 12.2 Hz, 1H), 6.98 (dt, *J* = 4.1, 7.8 Hz, 1H), 4.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1 (C), 149.3 (C), 146.8 (C), 131.2 (CH), 119.4 (C), 116.5 (CH), 112.7 (CH), 37.0 (CH_3). IR (neat) 2947, 2573, 1549, 1445, 1309, 1222, 1151 cm^{-1}. HRMS (EI): Exact mass calcd for $C_8H_7FN_2O$ $[M]^+$: 166.05424. Found: 166.05462.

3-Methyl-2,3-dihydro-1*H*-benzo[e]indazol-1-one (2k). Synthesized according to general procedure **4** using phenyl 2-methyl-2-(naphthalen-2-yl)hydrazine-1-carboxylate (**1k**, 0.088 g) for

4 hours at 150 °C. After cooling the precipitated solid was filtered, washed with petroleum ether and allowed for air drying to give **2k** (0.057 g, 95%) as a white solid; mp 298-299 °C. TLC Rf = 0.21 in 33% EtOAc/hexanes. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 9.0 Hz, 1H), 7.56 - 7.62 (m, 2H), 7.37 - 7.42 (m, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.4 (C), 138.9 (C), 128.1 (CH), 127.9 (CH), 127.5 (CH), 127.0 (C), 123.0 (CH), 122.2 (CH), 110.8 (C), 103.7 (CH), 34.7 (CH_3). IR (neat) 2970, 2521, 1530, 1472, 1393, 1301, 1251, 1203 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{12}H_{10}N_2O$ $[M]^+$: 198.0793. Found: 198.0809.

1-(Furan-2-ylmethyl)-1,2-dihydro-3*H*-indazol-3-one (2l). Synthesized according to general procedure **4** using phenyl 2-(furan-2-ylmethyl)-2-phenylhydrazine-1-carboxylate (**1l**, 0.048 g) for 3 hours at 180 °C. The residue was purified by column chromatography (hexanes/EtOAc = 5:2) to give **2l** (0.031 g, 93%) as a white solid; mp 225-227 °C. TLC Rf = 0.23 in 30% EtOAc/hexanes. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (td, J = 1.0, 8.1 Hz, 1H), 7.42 - 7.47 (m, 1H), 7.30 - 7.38 (m, 2H), 7.12 (ddd, J = 0.8, 7.0, 8.1 Hz, 1H), 6.35 - 6.39 (m, 1H), 6.30 (dd, J = 1.9, 3.2 Hz, 1H), 5.27 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6 (C), 150.0 (C), 142.9 (C), 142.6 (CH), 129.2 (CH), 121.7 (CH), 120.2 (C), 114.0 (CH), 110.8 (CH), 109.6 (CH), 109.1 (CH), 45.7 (CH_2). IR (neat) 3090, 2969, 2576, 1621, 1586, 1421, 1321, 1225 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{12}H_{10}N_2O_2$ $[M]^+$: 214.0742. Found: 214.0738.

1-(2,3-Dihydro-1*H*-inden-2-yl)-1,2-dihydro-3*H*-indazol-3-one (2m). Synthesized according to general procedure **4** using phenyl 2-(2,3 dihydro-1*H*-inden-2-yl)-2-phenylhydrazine-1-carboxylate (**1m**, 0.040 g) for 3 hours at 180 °C. The residue was purified by column chromatography (hexanes/EtOAc = 7:2) to give **2m** (0.027 g, 90%) as a white solid; mp 220-222 °C. TLC Rf = 0.23 in 23% EtOAc/hexanes. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (td, J = 0.9, 8.0 Hz, 1H), 7.40 (ddd, J = 1.2, 7.1, 8.4 Hz, 1H), 7.27 - 7.30 (m, 2H), 7.24 (td, J = 3.3, 8.9 Hz, 3H), 7.06 - 7.11 (m, 1H), 5.28 (quin, J = 8.28 Hz, 1H), 3.48 (dd, J = 8.2, 15.9 Hz, 2H), 3.38 (dd, J = 8.2, 15.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0 (C), 142.2 (C), 140.1 (C), 128.6 (CH), 126.6 (CH), 124.3 (CH), 121.4 (CH), 119.5 (C), 113.6 (CH), 109.2 (CH), 59.2 (CH), 37.3 (CH_2). IR (neat) 2918, 2531, 1617, 1585, 1535, 1443, 1308, 1252 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{16}H_{14}N_2O$ $[M]^+$: 250.1106. Found: 250.1113.

1-(Tetrahydro-2*H*-pyran-4-yl)-1,2-dihydro-3*H*-indazol-3-one (2n). Synthesized according to general procedure **4** using phenyl 2-phenyl-2-(tetrahydro-2*H*-pyran-4-yl)hydrazine-1-carboxylate (**1n**, 0.110 g) for 3 hours at 180 °C. The residue was purified by column chromatography (hexanes/EtOAc = 3:2 ~ 1:1) to give **2n** (0.075 g, 99%) as a white solid; mp 242-244 °C. TLC Rf = 0.22 in 40% EtOAc/hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 1H), 7.31 - 7.44 (m, 1H), 7.22 (d, J = 10.3 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 4.38 (tt, J = 4.1, 11.9 Hz, 1H), 4.14 (dd, J = 4.4, 11.6 Hz, 2H), 3.49 - 3.61 (m, 2H), 2.30 (dq, J = 4.7, 12.4 Hz, 2H), 1.86 (dd, J = 2.0, 12.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCL_3$) δ 156.6 (C), 141.0 (C), 128.2 (CH), 121.4 (CH), 119.3 (C), 112.8 (CH), 108.5 (CH), 67.2 (CH_2), 54.9 (CH), 31.6 (CH_2). IR (neat) 2955, 2926, 2833, 2523, 1614, 1583, 1538, 1442, 1381, 1311, 1236, 1144, 1125 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{12}H_{14}N_2O_2$ $[M]^+$: 218.10553. Found: 218.10507.

Ethyl 2-(3-oxo-2,3-dihydro-1*H*-indazol-1-yl)acetate (2o). Synthesized according to general procedure **4** using phenyl 2-(2-ethoxy-2-oxoethyl)-2-phenylhydrazine-1-carboxylate (**1o**, 0.060 g) for 3 hours at 180 °C. After cooling the precipitated solid was filtered, washed with petroleum ether and allowed for air drying to give **2o** (0.038 g, 97%) as a white solid; mp 196-197 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (td, J = 1.0, 8.0 Hz, 1H), 7.46 (ddd, J = 1.1, 7.1, 8.4 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 7.14 (ddd, J = 0.7, 7.1, 8.0 Hz, 1H), 4.87 (s, 2H), 4.23 (q, J = 7.2 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3 (C), 158.1 (C), 143.4 (C), 129.5 (CH), 121.8 (CH), 120.5 (C), 114.2 (CH), 109.1 (CH), 62.1 (CH_2), 50.2 (CH_2), 14.4 (CH_3). IR (neat) 2982, 2932, 2550, 1740, 1621, 1590, 1553, 1447, 1309, 1201 cm^{-1}. HRMS (EI): Exact mass calcd for $C_{11}H_{12}N_2O_3$ $[M]^+$: 220.08479. Found: 220.08351.

ASSOCIATED CONTENT

NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: andre.beauchemin@uottawa.ca.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

We thank the University of Ottawa and NSERC for support of this work and the Egyptian Ministry of High Education for a scholarship E. B. E. We are grateful to Mr. Ryan Ivanovich (University of Ottawa) for useful suggestions and for sharing reagents for this project. We also thank Dr. Adel Ghiaty (Al-Azhar University) for encouragements, stimulating discussions and comments on the manuscript and supporting information.

REFERENCES

(1) General reviews on *N*-isocyanates: (a) Reichen, W. *Chem. Rev.* **1978**, *78*, 569. (b) Wentrup, C.; Finnerty, J. J.; Koch, R. *Curr. Org. Chem.* **2011**, *15*, 1745. (c) Vincent-Rocan, J.-F.; Beauchemin, A. M. *Synthesis* **2016**, *48*, 3625.

(2) Vincent-Rocan, J.-F.; Ivanovich, R. A.; Clavette, C.; Leckett, K.; Bejjani, J.; Beauchemin, A. M. *Chem. Sci.* **2016**, *7*, 315.

(3) For selected examples: (a) Clavette, C.; Gan, W.; Bongers, A.; Markiewicz, T.; Toderian, A. B.; Gorelsky, S. I.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2012**, *134*, 16111. (b) Bongers, A.; Ranasinghe, I.; Lemire, P.; Perozzo, A.; Vincent-Rocan, J.-F.; Beauchemin, A. M. *Org. Lett.* **2016**, *18*, 3778. (c) Bongers, A.; Clavette, C.; Gan, W.; Gorelsky, S. I.; Betit, L.; Lavergne, K.; Markiewicz, T.; Moon, P. J.; Das Neves, N.; Obhi, N. K.; Toderian, A. B.; Beauchemin, A. M. *J. Org. Chem.* **2017**, *82*, 1175.

(4) For selected examples: (a) Clavette, C.; Vincent Rocan, J.-F.; Beauchemin, A. M. *Angew. Chem., Int. Ed.* **2013**, *52*, 12705. (b) Vincent-Rocan, J. F.; Clavette, C.; Leckett, K.; Beauchemin, A. M. *Chem. Eur. J.* **2015**, *21*, 3886. (c) Reference 2. (d) An, J.; Alper, H.; Beauchemin, A. M. *Org. Lett.* **2016**, *18*, 3482. (e) Dahab, M. A.; Derasp, J. S.; Beauchemin, A. M. *Synlett* **2017**, *13*, 456.

(5) For reviews on blocked isocyanates, see: (a) Wicks, D. A.; Wicks, Z. W. Jr. *Prog. Org. Coat.* **1999**, *36*, 148; (b) Wicks, D. A.; Wicks, Z. W. Jr. *Prog. Org. Coat.* **2001**, *41*, 1; (c) Delebecq, E.; Pascault, J.-P.; Boutevin, B.; Ganachaud, F. *Chem. Rev.* **2013**, *113*, 80.

(6) (a) Sonpavde, G.; Hutson, T. E. *Curr. Oncol. Rep.* **2007**, *9*, 115. (b) Feyer, P.; Seegenschmiedt, M. H.; Steingraeber, M. *Support. Care Cancer* **2005**, *13*, 671. (c) Raj, T. B.; Wickham, M. H. *J. Laryngol. Otol.* **2007**, *100*, 303.

(7) Yu, W.; Guo, Z.; Orth, P.; Madison, V.; Chen, L.; Dai, C.; Feltz, R. J.; Girijavallabhan, V. M.; Kim, S. H.; Kozlowski, J. A.; Lavey, B. J.; Li, D.; Lundell, D.; Niu, X.; Piwinski, J. J.; Popovici-Muller, J.; Rizvi, R.; Rosner, K. E.; Shankar, B. B.; Shih, N. Y.; Siddiqui, M. A.; Sun, J.; Tong, L.; Umland, S.; Wong, M. K.; Yang, D. Y.; Zhou, G. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1877.

(8) Wang, H.; Han, H.; Von Hoff, D. D. *Cancer Res.* **2006**, *66*, 9722.

(9) Fletcher, S. R.; McIver, E.; Lewis, S.; Burkamp, F.; Leech, C.; Mason, G.; Boyce, S.; Morrison, D.; Richards, G.; Sutton, K.; Jones, A. B. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2872.

(10) Leis, J.; Carter, C.; US20140179637 A1: **2014**.

(11) Qian, Y.; Bolin, D.; Conde-Knape, K.; Gillespie, P.; Hayden, S.; Huang, K. S.; Olivier, A. R.; Sato, T.; Xiang, Q.; Yun, W.; Zhang, X. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 2936.

(12) Norman, M. H.; Rigdon, G. C.; Navas, F., 3rd; Cooper, B. R. *J. Med. Chem.* **1994**, *37*, 2552.

(13) Kawanishi, N.; Sugimoto, T.; Shibata, J.; Nakamura, K.; Masutani, K.; Ikuta, M.; Hirai, H. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5122.

(14) Tanimori, S.; Kobayashi, Y.; Iesaki, Y.; Ozaki, Y.; Kirihata, M. *Org. Biomol. Chem.* **2012**, *10*, 1381.

(15) Correa, A.; Tellitu, I.; Dominguez, E.; Sanmartin, R. *J. Org. Chem.* **2006**, *71*, 3501.

(16) Viña, D.; del Olmo, E.; López-Pérez, J. L.; San Feliciano, A. *Org. Lett.* **2007**, *9*, 525.

(17) Chen, J.; Chen, P.; Song, C.; Zhu, J. *Chem. Eur. J.* **2014**, *20*, 14245.

(18) Dou, G.; Shi, D. *J. Comb. Chem.* **2009**, *11*, 1073.

(19) (a) Yu, D.-G.; Suri, M.; Glorius, F. *J. Am. Chem. Soc.* **2013**, *135*, 8802. (b) Tanimori, S.; Ozaki, Y.; Iesaki, Y.; Kirihata, M. *Synlett* **2008**, 1973. (c) Shaw, A. Y.; Chen, Y.-R.; Tsai, C.-H. *Synth. Commun.* **2009**, *39*, 2647. (d) Conrad, W. E.; Fukazawa, R.; Haddadin, M. J.; Kurth, M. J. *Org. Lett.* **2011**, *13*, 3138. (e) Park, S. W.; Choi, H.; Lee, J. H.; Lee, Y. J.; Ku, J. M.; Lee, S. Y.; Nam, T. G. *Arch. Pharm. Res.* **2016**, *39*, 302.

(20) (a) Stollé, R. *J. Prakt. Chem.* **1927**, *116*, 192. (b) Stollé, R.; Nieland, H.; Merkle, M. *J. Prakt. Chem.* **1927**, *117*, 185.

(21) (a) Kurz, M.; Reichen, W. *Tetrahedron Lett.* **1978**, *19*, 1433. (b) Richter, R.; Ulrich, H.; Duchamp, D. J. *J. Org. Chem.* **1978**, *43*, 3060.

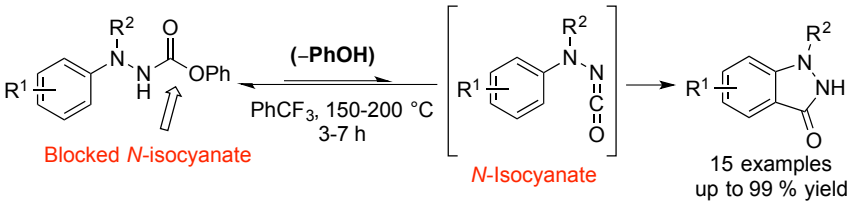
(22) Dimerization is a common side-reaction of *N*-isocyanates. For reviews, see reference 1. See also: Gaber, A.-A. M.; Wentrup, C. *J. Anal. Appl. Pyrolysis* **2017**, *125*, 258.

(23) For substrates that did not cyclize under the reaction conditions or at higher temperatures, please see the Supporting Information.

(24) (a) Finet, J. P. *Chem. Rev.* **1989**, *89*, 1487. (b) Tšubrik, O.; Mäeorg, U.; Ragnarsson, U. *Tetrahedron Lett.* **2002**, *43*, 6213. (c) Tšubrik, O.; Mäeorg, U.; Sillard, R.; Ragnarsson, U. *Tetrahedron* **2004**, *60*, 8363.

(25) Zhang, J.-Q.; Huang, G.-B.; Weng, J.; Lu, G.; Chan, A. S. C. *Org. Biomol. Chem.* **2015**, *13*, 2055.

(26) Ivanovich, R. A.; Vincent-Rocan, J. F.; Elkaeed, E. B.; Beauchemin, A. M. *Org. Lett.* **2015**, *17*, 4898.



- Use of masked *N*-Isocyanate precursors allow a general route to indazolones
- Effect of blocking (leaving) group investigated / substrate synthesis improved