Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201500914

Transformation of Contact-Explosives Primary Amines and Iodine(III) into a Successful Chemical Reaction under Solvent-Free Ball Milling Conditions

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Received: September 29, 2015; Published online: December 9, 2015

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201500914.

Abstract: Any synthetic transformation using contact-explosives primary amines and hypervalent iodine(III) (phenyliodine diacetate) in constrained media (extreme conditions) is practically impossible. Herein, we report a method of controlling the explosion into a successful chemical reaction using the acid-salt $NaHSO_4$. As a proof-of-concept, we considered mechanochemical (ball-milling) cross dehydrogenative coupling (CDC) reaction for the amidation of aldehydes *via* C–H activation. An isothermal titration calorimetric (ITC) study was helpful to understand the enthalpy changes during the reactions before and after addition of $NaHSO_4$.

Keywords: ball milling; cross dehydrogenative coupling (CDC) reaction; contact explosive; hypervalent iodine; phenyliodine diacetate (PIDA)

Introduction

The behavior of a chemical system is known to be controlled by the environment. In 1867, to reduce safety problems when transporting nitroglycerine, Alfred Nobel mixed an absorbent clay 'Kieselguhr' with nitroglycerine to diminish the sensitivity.[1] Encapsulation within a cavity of a container molecule, is known to prevent oligomerization of a reactive species like cyclotrisiloxane[2] or cyclobutadiene.[3] Also, we reported with Nitschke that white phosphorus was air-stable upon incarceration within a tetrahedral metallo-supramolecular capsule.[4] The iodine-ammonia combination is known as a *contact explosive*[5] in constrained media. Similarly, hypervalent iodine compounds, as oxidizers,[6] form charge transfer complexes with fuel-amines[7] and cause highly exothermic reactions. Under solvent-free conditions (constrained media) the reactants experience maximum possible contacts among themselves and create an extreme situation for contact-explosives. Therefore, a violent exothermic reaction takes place for hypervalent iodine(III) reagents and electron-rich amines under solvent-free conditions. To the best of our knowledge, no synthetic applications using hypervalent iodine(III) reagents and primary amines in a constrained media have been reported as yet.

Recently, ball-milling mechanochemistry[8] has gained significant interest as an alternative technology in organic synthesis.[9] This mechanochemical methodology has huge significance to green processes, is time efficient, environmentally benign and has shown to be economical. Towards quantitative conversion, less by-products and minimum purification bring extra importance to this method.[10] The mechanochemical syntheses of small organic molecules,[9b,10c] including hypervalent iodine-mediated synthesis[11] are well explored.

Results and Discussion

We report here a mechanochemical cross dehydrogenative coupling (CDC)[12] for the oxidative amidation[13] of aryl aldehydes *via* C–H activation[14] using phenyliodine diacetate (PIDA)[15] and benzylamines. The acid-salt sodium bisulfate ($NaHSO_4$) was used to control the reactivity of the contact-explosive (Figure 1).

The CDC reaction has proven to be a powerful and atom-economic approach for C–N bond construction. Making a C–N bond is an important transformation in organic synthesis as it constitutes the structural backbone of proteins and peptides through amide linkages. Common methods for oxidative amidation involve: coupling of carboxylic acids and amines in

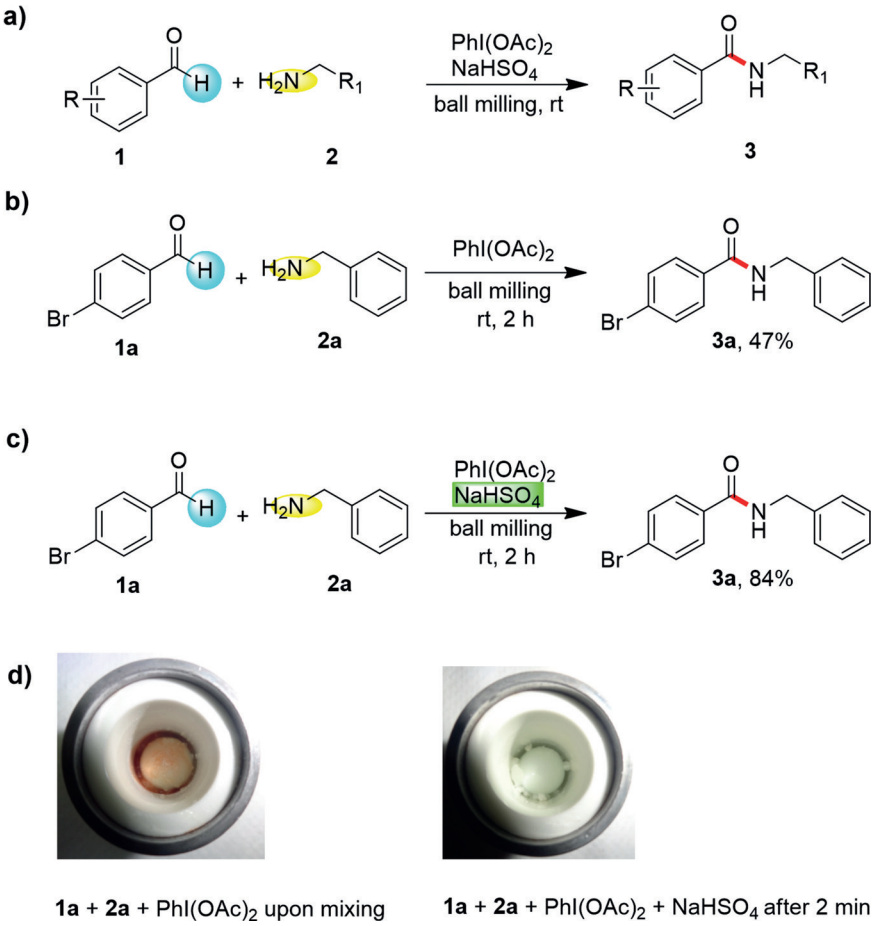


Figure 1. Mechanochemical cross dehydrogenative coupling (CDC); newly formed bond is shown as a red-thick line. a) This work. b) Uncontrollable reaction in the absence of $NaHSO_4$. c) $NaHSO_4$-mediated explosion-free and successful reaction. d) Photographs of reaction mixture after explosion (*left*) and subsequent to making it explosion-free (*right*).

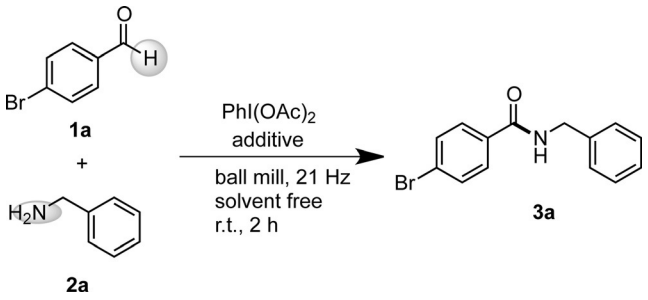
the presence of a coupling agent,[16] acylation of amines with activated carboxylic acids, etc.[17] Recently we reported the metal- and solvent-free oxidative amidation of aldehydes with *N*-chloramines *via* C–H activation under neat and ball-milling conditions using TBAI (tetrabutyl ammonium iodide)-TBHP (*tert*-butyl hydroperoxide) combinations.[18]

For C–N bond construction, hypervalent iodine compounds are also considered as useful reagents.[19] However, an immediate explosion was observed and the reaction mixture became brownish during the mixing of benzaldehydes, benzylamines and PIDA under solvent-free ball-milling conditions (*Caution!!* see Experimental Section) (Figure 1d, *left*). Consequently, it was found that acetic acid generated (from PIDA) could control the reactivity of the amine through protonation and a 47% yield of the amide was obtained (Figure 1b). The same reaction was found to be explosion free in the presence of externally-added acetic acid (yield 41%, Table 1). Likewise, use of an acid-salt such as $NaHSO_4$ (Figure 1c) as additive afforded an 84% yield of **3a**.

Table 1 represents the optimization of the reaction conditions. Mechanochemical CDC for the synthesis of *N*-benzyl-4-bromobenzamide (**3a**) was done successfully using 4-bromobenzaldehyde (1.0 equiv., **1a**), benzylamine (1.1 equiv., **2a**), PIDA (2.0 equiv.) and $NaHSO_4$ (2.0 equiv.). During optimization, the progress of the reaction was monitored using thin layer chromatography (TLC) or ^{1}H NMR (see the Supporting Information).

Amide derivatives were obtained in good to excellent yields (Figure 2) under the optimized conditions. Higher yields of amides were observed with the aromatic aldehydes containing electron-withdrawing (**3a–3c**, **3f–3o**, **3q–3s**, **3u–3x**, **3z** and **3aa**) than electron-donating groups (**3d**, **3e**, **3t**, **3y**). Amides from halogen-substituted benzaldehydes (**3a**, **3f**, **3h**, **3j**, **3n**, **3o**, **3r** and **3w**) were also isolated in convincing yields. Accordingly, various amines like benzylamine (**3a–h**, **3o**,**p**), 4-fluorobenzylamine (**3i–k** and **3aa**), 2-phenylethanamine (**3q–u**), 2-chlorobenzylamine (**3l–n**) and [3,5-bis(trifluoromethyl)phenyl]methanamine (**3v–z**) derivatives also facilitated excellent yields of the

Table 1. Optimization of reaction condition for the synthesis of **3a** as shown in Figure 1.[a]



Entry	PIDA (equiv.)	Additive (equiv.)	Yield [%]
1	1.1	$NaHSO_4$ (1)	44
2	2.0	$NaHSO_4$ (2)	84 (67)
3	1.1	NaH_2PO_4 (1)	15
4	1.1	NaCl (1)	Trace
5	1.1	$NaHCO_3$ (1.2)	23
6	2	KH_2PO_4 (2)	19
7	2	AcOH (2)	41
8	2	H_2SO_4 (2)	11
9	2	PTSA (2)	<5
10	2	TBAHS (2)	~5

[a] Reactions were performed with 1.0 equiv. of **1a** and 1.1 equiv. of **2a**.
[b] Yields (based on recovered aldehydes after chromatographic purification) are shown.

amides. In addition, reactions were performed under solvent-free conditions and therefore highly volatile aliphatic amines were not considered for this study.

Control experiments (Figure 3) were performed to shed some light on the mechanism of the reaction. Reaction of 4-nitrobenzaldehyde (**1b**) with a secondary amine (dibenzylamine, **4**) led to corresponding amide in 13% yield (Figure 3 a) and the majority of the aldehydes remained unreacted. More reactive secondary amines possibly destroyed PIDA and the reaction became uncontrollable using $NaHSO_4$. Oligomeric iodosylbenzene sulfate **6** $[(PhIO)_3SO_3)]_n$[20] is known to be synthesized from grinding of PIDA with $NaHSO_4$.[21] Mechanochemical milling of **6** and imine **5** (synthesized separately from **1a** and **2a**) did not result in any amide (Figure 3b). Separately, **1a**, **2a** and **6** under ball-milling also led to explosions (*Caution!!*) (Figure 3d). More examples of unsuccessful one-pot milling reactions were: (i) imine **5**, PIDA, $NaHSO_4$ and K_2CO_3 (14%, Figure 3c), (ii) imine **5** and PIDA (0%, Figure 3e) because PIDA was unable to perform oxo transfer reactions, and (iii) **5**, $NaHSO_4$ and PIDA (5%, Figure 3f). From these observations, it was rationalized that the iodosylbenzene sulfate **6** $[(PhIO)_3SO_3)]_n$ was not the active reagent and imine **5** was not the intermediate[22] for this transformation. Expectedly, the oxidative amidation proceeded *via* a hemiaminal intermediate (Figure 4a).[23]

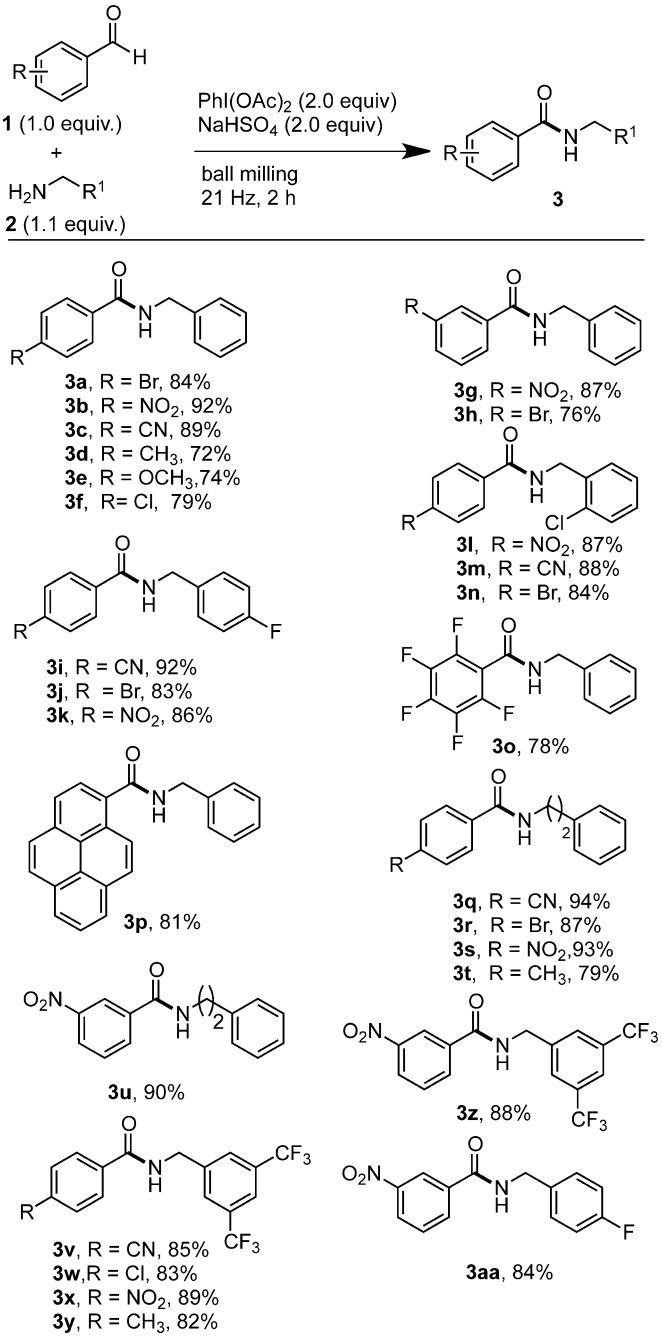


Figure 2. Compound identification numbers and yields are shown for the synthesized compounds.

The role of $NaHSO_4$ towards the successful and explosion-free mechanochemical CDC reactions was clarified. The acid-salt $NaHSO_4$ is widely used in the poultry industry to decrease basic-ammonia and bacterial levels in litter.[24] In aqueous solution, $NaHSO_4$ acts as a medium-strong acid. A solution of 1.0 M $NaHSO_4$ in water shows pH <1.0 and the bisulfate anion has a pK_a value of ~1.99. The pK_a of benzylamine is 9.38 (through dissociation of $-NH^+$) and

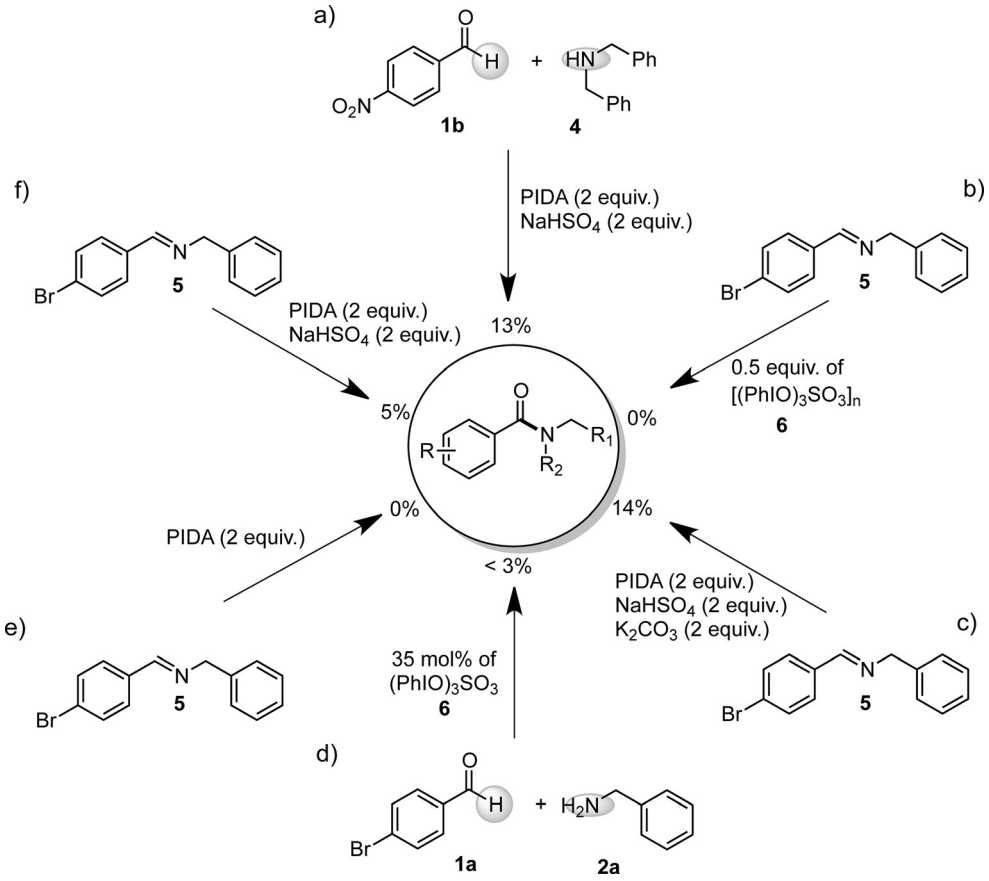


Figure 3. a)–f) Control experiments to understand the mechanism of the reaction.

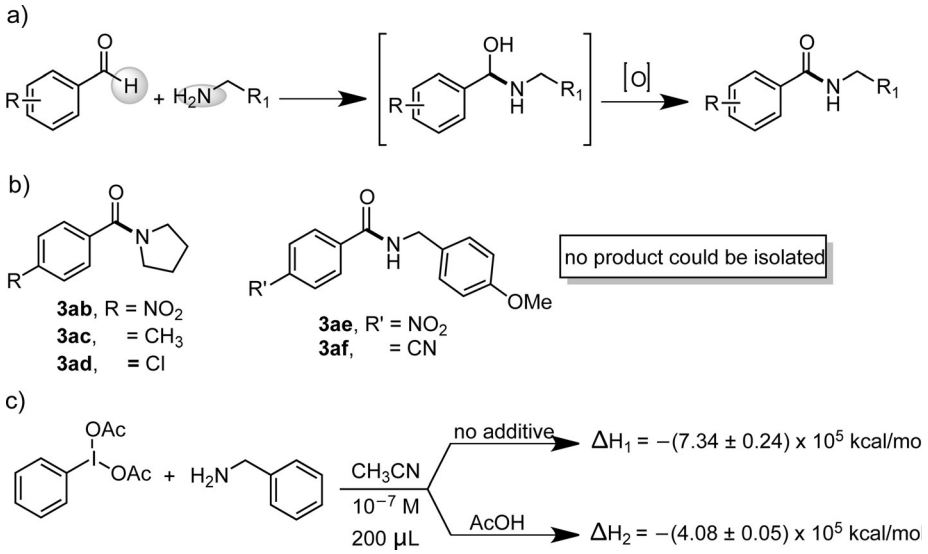


Figure 4. a) Plausible mechanism for the CDC reaction. b) Unsuccessful amidation under optimized conditions. c) Determination of enthalpy changes from the reaction of benzylamine and PIDA, both in the absence and the presence of acetic acid (AcOH).

comparable to that of ammonia (9.21).[25] Ammonia generally reacts with $NaHSO_4$ to form salts.[24]

$$2\ NaHSO_4 + 2\ NH_4OH \rightarrow (NH_4)_2SO_4 + Na_2SO_4 + 2\ H_2O$$

Similarly, $NaHSO_4$ may form an acid-base complex with basic amines to realize the explosion-free oxidative amidation. Also, in the presence of concentrated H_2SO_4, benzylamine did not react with either alde-

hyde or PIDA. The stronger protic acid H_2SO_4 (pK_a: −10) could completely deactivate the amine upon $-NH^+$ protonation. However, using the weaker organic acid *p*-toluenesulfonic acid (pK_a: −2.8), the amide (**3a**) was isolated in <5% yield. Pyrrolidine (pK_a: 11.27 conjugate acid in water) and 4-methoxybenzylamine are stronger bases than benzylamine and the explosion could not be controlled using $NaHSO_4$. Accordingly, no amidation products were isolated using pyrrolidine or 4-methoxybenzylamine (**3ab–3af**, Figure 4b). Also, a gram-scale synthesis of amide was done successfully using the proposed methodology (see large-scale synthesis paragraph in the Experimental Section).

An isothermal titration calorimetric analysis (ITC, see the Supporting Information) analysis (see also isothermal titration calorimetric (ITC) study in the Experimental Section) was performed to estimate the enthalpy of the reaction (ΔH) from the reaction of PIDA and benzylamine in acetonitrile both in the absence (ΔH_1) and in the presence (ΔH_2) of acetic acid (Figure 4c). The acetic acid could control the reaction and $\Delta\Delta H$ ($\Delta H_1 - \Delta H_2$) of the reaction was 3.26×10^5 kcal mol^{-1}.

Amidation reactions using primary amines and iodine(III) reported by Tiwari and co-workers were done in an ionic liquid.[22] Higher concentrations of primary amine destroyed PIDA during fast addition and that resulted in poor yields of amides. A two-fold increase in the yield of amide was achieved upon dropwise addition of amine with constant stirring to the PIDA solution in ionic liquids. The high polarity of ionic liquids and the high-dilution effect, cooperatively, could stop the immediate explosion of primary amines and iodine(III). However, in this work under solvent-free ball-milling conditions the maximum possible concentration puts the system under high stress and thus it could lead to uncontrollable oxidation more easily. As a result an explosion was observed immediately in the absence of $NaHSO_4$.

Conclusions

In summary, the present work describes an unprecedented approach in which either an acid or acid-salt ($NaHSO_4$) could transform an explosive reaction mixture into a successful chemical reaction. A concept is proposed in which, by selecting appropriate conditions, it is now possible to perform a highly exothermic reaction in the ambient laboratory atmosphere. We anticipate that stopping an explosion of the contact-explosives primary amines-phenyliodine diacetate system and the safety benefits of using them are substantial: (i) a new research area can be initiated using this concept; (ii) this approach could be used directly to diffuse dangerous chemical weapons; (iii) the environment can be protected through the sequestration of hazardous substances. This study also highlights the progress of C–H bond activation chemistry for the formation of amides and should find wide application in the context of both natural product synthesis and pharmaceuticals using mechanochemistry.

Experimental Section

General Methods

The ball milling (21 Hz) experiments were performed in the open atmosphere. Column chromatographic purifications of compounds were done using silica-gel (mesh 100–200) and hexane-ethyl acetate mixtures as eluent, unless otherwise mentioned. NMR spectra were recorded on a 400 MHz instrument at 25 °C. The chemical shift values are reported in parts per million (ppm) and referred to the residual chloroform (7.26 ppm for ^{1}H and 77.16 for ^{13}C) and deuterium oxide (4.79 ppm for ^{1}H). The peak patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets; br s, broad singlet. The coupling constants (*J*) are reported in hertz (Hz). High-resolution mass spectrometry (HR-MS) was conducted on an ESI-TOF (time of flight) mass spectrometer. The isothermal titration calorimetric (ITC) experiment was performed in a MicroCal iTC200 isothermal titration calorimeter. Infrared spectral data are reported in wavenumber (cm^{-1}). Melting points of the compounds were determined using a digital melting point apparatus and are uncorrected.

Caution: When PIDA and primary amines were mixed under solvent-free conditions, an immediate explosion was observed. In the presence of $NaHSO_4$, no explosion was observed under similar conditions. Still, general safety concerns in the laboratory should be carefully exercised and it is highly recommended that all reactions should be carried out in a well-ventilated fume hood behind a blast shield.

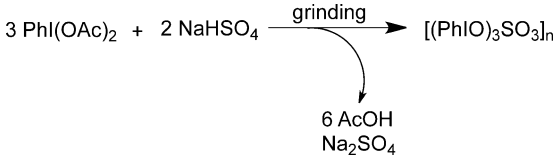
Large Scale Synthesis

The recommended loading of the reactant materials should be less than one third of the jar volume. In a 25-mL stainless steel milling jar, two balls (15 mm dia), PIDA (1.74 g, 5.4 mmol), $NaHSO_4$ (746 mg, 5.4 mmol), 4-bromobenzaldehyde (500 mg, 2.7 mmol) and benzylamine (324 μL, 2.9 mmol) were added sequentially and milled for 2 h. Work-up and subsequent purification (see the Suppoorting Information) led to 4-bromobenzaldehyde (**1a**; yield: 167 mg) and product **3a**; yield: 406 mg (78%).

Isothermal Titration Calorimetric (ITC) Study

In acetonitrile, 200 μL of 2.08×10^{-7} M solution of benzylamine were titrated with 1.36×10^{-7} M of PIDA solution. Using 0.5 μL per titration, 40 titrations were performed.

Synthesis of Oligomeric Iodosylbenzene Sulfate $[(PhIO)_3SO_3]_n$ (6)[26]



Phenyliodine diacetate (400 mg, 1.24 mmol) was added to $NaHSO_4 \cdot H_2O$ (176 mg, 1.03 mmol) in an agate mortar. Then the mixture was ground for 10 min and the resulting mass was transferred to a beaker and dissolved in 5 mL of water. After 5 min, a clear yellow solution was formed and allowed to settle for 2 h. After that the yellow precipitate was filtered off and washed with cold water and dried to afford a yellow crystalline compound (yield: 135 mg). The filtrate was left for slow evaporation and an additional 92 mg of compound **6** was isolated; total yield: 227 mg (74%). ^{1}H NMR (400 MHz, D_2O): $\delta = 8.09$ (d, $J = 8$ Hz, 2H), 7.71 (t, $J = 7.5$ Hz, 1H), 7.55 (t, $J = 7.8$ Hz, 2H); ^{13}C NMR (100 MHz, D_2O): $\delta = 134.3$, 133.1, 131.5, 123.5.

General Procedure for the Preparation of Amides under Ball-Milling

In a 10-mL stainless steel milling jar, benzylamine (65 μL, 0.59 mmol) was added to the mixture of 4-bromobenzaldehyde (100 mg, 0.54 mmol), PIDA (348 mg, 1 mmol), $NaHSO_4$ (149 mg, 1 mmol) and one grinding ball (15 mm diameter, stainless steel). The progress of the reaction under milling conditions was monitored by thin layer chromatography (TLC) or ^{1}H NMR. After completion of the reaction, the mixture was dissolved in dichloromethane and the product (*N*-benzyl-4-bromobenzamide) was purified by column chromatography. Isolated materials: 20 mg of 4-bromobenzaldehyde (**1a**) were recovered as unreacted material together with **3a**; yield: 105 mg (84% based on recovered **1a**).

The isolated yields given below (after column chromatography) were calculated based on recovered starting material. However, in parenthesis the yields are calculated based on aldehydes used for the reaction.

***N*-Benzyl-4-bromobenzamide (3a):** $R_f = 0.30$ (ethyl acetate/hexane = 1:4); white solid; yield: 84% (73 mg, 67%); mp 155–159 °C (lit.[27] 160–162 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.66$ (d, $J = 8$ Hz, 2H), 7.56 (d, $J = 8$ Hz, 2H), 7.35–7.31 (m, 5H), 6.42 (br s, 1H), 4.63 (d, $J = 8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.5$, 138.0, 133.3, 131.9, 129.0, 128.7, 128.1, 127.9, 126.4, 44.4; IR (KBr): $\tilde{\nu} = 3308$ (m), 3081 (s), 2919 (s), 2848 (s), 1640 (m), 1548 (m), 1416 (s), 1256 (s), 847 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z =$ 290.0176, calcd. for $C_{14}H_{13}BrNO$ ($M+H^+$): 290.0175.

***N*-Benzyl-4-nitrobenzamide (3b):** $R_f = 0.32$ (ethyl acetate/hexane = 1:4); white solid; yield: 92% (87 mg, 73%); mp 141–144 °C (lit.[28] 142 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.26 (d, $J = 8$ Hz, 2H), 7.94 (d, $J = 8$ Hz, 2H), 7.37–7.34 (m, 5H), 6.60 (br s, 1H), 4.65 (d, $J = 8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.4$, 149.7, 140.0, 137.5, 129.0, 128.3, 128.1, 128.1, 123.9, 44.6; IR (KBr): $\tilde{\nu} = 3280$ (m), 2922 (m), 2839 (s), 1633 (m), 1597 (m), 1515 (m), 1345 (m), 1105 (s), 870 (s), 697 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z =$ 257.0924, calcd. for $C_{14}H_{13}N_2O_3$ ($M+H^+$): 257.0921.

***N*-Benzyl-4-cyanobenzamide (3c):** $R_f = 0.32$ (ethyl acetate/hexane = 1:4); white solid; yield: 89% (89 mg, 71%); mp 154–156 °C (lit.[29] 150–151 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.87$ (d, $J = 8$ Hz, 2H), 7.69 (d, $J = 8$ Hz, 2H), 7.37–7.29 (m, 5H), 6.67 (br s, 1H), 4.62 (d, $J = 4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.7$, 138.3, 137.6, 132.5, 129.0, 128.0, 128.0, 127.8, 118.0, 115.2, 44.4; IR (KBr) $\tilde{\nu} = 3316$ (w), 2923 (s), 2218 (s), 1643 (m), 1550 (s), 1422 (s), 1311 (s), 864 (s), 721 (s) cm^{-1}; IR (KBr): $\tilde{\nu} = 3315$ (w), 3090 (s), 3064 (s), 3028 (s), 2923 (s), 2231 (s), 1644 (s), 1547 (m), 1496 (m), 1286 (m), 857 (m), 697 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z =$ 237.1041, calcd. for $C_{15}H_{13}N_2O$ ($M+H^+$): 237.1022.

***N*-benzyl-4-methylbenzamide (3d):** $R_f = 0.40$ (ethyl acetate/hexane = 1:4); white solid; yield: 72% (77 mg, 59%); mp 133–136 °C (lit.[27] 131–134 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.69$ (d, $J = 8.1$ Hz, 6H), 7.37–7.27 (m, 16H), 7.21 (d, $J = 8.0$ Hz, 6H), 6.58 (s, 3H), 4.61 (d, $J = 5.6$ Hz, 7H), 2.39 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 167.43$, 142.02, 138.47, 131.63, 129.31, 128.83, 128.65, 127.97, 127.65, 127.61, 127.10, 77.48, 77.16, 76.84, 44.12, 21.53; IR (KBr): $\tilde{\nu} = 3311$ (m), 3085 (s), 3054 (s), 3028 (s), 1639 (m), 1546 (m), 1420 (s), 1323 (s), 1058 (s), 841 (s), 721 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 226.1247$, calcd. for $C_{15}H_{16}NO$ ($M+H^+$): 226.1226.

***N*-Benzyl-4-methoxybenzamide (3e):** $R_f = 0.20$ (ethyl acetate/hexane = 1:4); white solid; yield: 74% (69 mg, 56%); mp 118–121 °C (lit.[30] 124–126 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.76$ (d, $J = 8$ Hz, 2H), 7.40–7.28 (m, 5H), 6.92 (d, $J = 8$ Hz, 2H), 6.31 (br s, 1H), 4.64 (d, $J = 8$ Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.9$, 162.3, 138.5, 128.9, 128.9, 128.0, 127.7, 126.7, 113.9, 55.5, 44.2; IR (KBr): $\tilde{\nu} = 3521$ (w), 3295 (m), 3054 (s), 1633 (m), 1537 (m), 1505 (s), 1256 (s), 846 (m), 726 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z = 242.1198$, calcd. for $C_{15}H_{16}NO_2$ ($M+H^+$): 242.1176.

***N*-Benzyl-4-chlorobenzamide (3f):** $R_f = 0.25$ (ethyl acetate/hexane = 1:4); white solid; yield: 79% (76 mg, 62%); mp 157–162 °C (lit.[27] 163–166 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.79$ (d, $J = 8$ Hz, 2H), 7.43 (d, $J = 8$ Hz, 2H), 7.37–7.27 (m, 5H), 6.51 (br s, 1H), 4.645 (d, $J = 4$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 167.5$, 138.2, 134.4, 131.6, 128.9, 128.7, 128.0, 127.7, 127.1, 44.2; IR (KBr): $\tilde{\nu} = 3324$ (m), 3059 (s), 3030 (s), 2928 (s), 1643 (s), 1603 (s), 1576 (s), 1542 (m), 1452 (s), 1418 (s), 1312 (s), 1259 (s), 1028 (s), 727 (s), 694 (m), 666 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 246.0672$, calcd. for $C_{14}H_{13}ClNO$ ($M+H^+$): 246.0686.

***N*-Benzyl-3-nitrobenzamide (3g):** $R_f = 0.17$ (ethyl acetate/hexane = 1:4); white solid; yield: 87% (81 mg, 68%); mp 99–102 °C (lit.[31] 95–96 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.60 (s, 1H), 8.34 (d, $J = 8$ Hz, 1H), 8.17 (d, $J = 8$ Hz, 1H), 7.63 (dt, $J = 11.7$, 6.0 Hz, 1H), 7.36–7.31 (m, 5H), 6.75, 6.65 (br s, 1H), 4.655 (d, $J = 4$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.0$, 148.3, 137.6, 136.1, 133.4, 130.0, 129.0, 128.1, 128.0, 126.2, 121.9, 44.6; IR (KBr): $\tilde{\nu} = 3301$ (w), 3086 (s), 2926 (s), 1642 (m), 1528 (m), 1349 (m), 1159 (s), 1081 (s), 909 (s), 814 (s), 699 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z = 257.0931$, calcd. for $C_{14}H_{13}N_2O_3$ ($M+H^+$): 257.0921.

***N*-Benzyl-3-bromobenzamide (3h):**[32] $R_f = 0.30$ (ethyl acetate/hexane = 1:4); white solid; yield: 76% (69 mg, 63%); mp 112–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.93$ (s,

1H), 7.71 (d, $J=8$ Hz, 1H), 7.62 (d, $J=8$ Hz, 1H), 7.38–7.27 (m, 6H), 6.43 br (s, 1H), 4.635 (d, $J=4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=166.1$, 137.9, 136.4, 134.6, 130.3, 130.3, 129.0, 128.1, 127.9, 125.7, 122.9, 44.4; IR (KBr): $\tilde{\nu}=$ 3320 (m), 3063 (s), 3028 (s), 2925 (s), 1638 (m), 1562 (m), 1542 (m), 1471 (s), 1454 (s), 1315 (s), 1071 (s), 996 (s), 894 (s), 744 (m), 698 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z=$ 290.0189, calcd. for $C_{14}H_{13}BrNO$ ($M+H^+$): 290.0175.

4-Cyano-*N*-(4-fluorobenzyl)benzamide (3i): $R_f=0.20$ (ethyl acetate/hexane = 1:4); white solid; yield: 92% (100 mg, 74%); mp 109–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.88$ (d, $J=8$ Hz, 2H), 7.72 (d, $J=8$ Hz, 2H), 7.31 (dd, $J=10$, 6 Hz, 2H), 7.03 (dd, $J=12$, 5 Hz, 2H), 6.59 (br s, 1H), 4.60 (d, $J=8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=165.7$, 162.5 (d, $^1J_{C,F}=245$ Hz), 138.2, 133.5 (d, $^4J_{C,F}=3$ Hz), 132.6, 129.8 (d, $^3J_{C,F}=8$ Hz), 127.8, 118.0, 115.9 (d, $^2J_{C,F}=21$ Hz), 115.3, 43.7; IR (KBr): $\tilde{\nu}=$3265 9 m), 3094 (m), 2922 (m), 2852 (s), 2230 (m), 1633 (m), 1556 (m), 1512 (m), 1428 (s), 1251 (s), 1220 (m), 1154 (s), 1059 (s), 861 (m), 840 (m), 807 (m), 731 (s), cm^{-1}; HR-MS (ESI-TOF): $m/z=$ 255.0925, calcd. for $C_{15}H_{12}FN_2O$ ($M+H^+$): 255.0928.

4-Bromo-*N*-(4-fluorobenzyl)benzamide (3j): $R_f=0.35$ (ethyl acetate/hexane = 1:4); white solid; yield: 83% (80 mg, 69%); mp 128–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.63$ (d, $J=8.5$ Hz, 2H), 7.53 (d, $J=8.5$ Hz, 2H), 7.28 (dd, $J=8.3$, 5.5 Hz, 2H), 7.01 (t, $J=8.6$ Hz, 2H), 6.65 (br s, 1H), 4.55 (d, $J=5.7$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=166.6$, 162.4 (d, $^1J_{C,F}=244$ Hz), 133.9 (d, $^4J_{C,F}=3$ Hz), 133.1, 131.9, 129.7 (d, $^3J_{C,F}=8$ Hz), 128.7, 126.4, 115.7 (d, $^2J_{C,F}=21$ Hz), 43.5; IR (KBr): $\tilde{\nu}=3315$ (m), 3081 (s), 1638 (m), 1548 (m), 1227 (s), 841 (s), 801 (s), 711 (s) cm^{-1}; HR-MS (ESI-TOF): m/z = 308.0099, calcd. for $C_{14}H_{12}BrFNO$ ($M+H^+$): 308.0081.

***N*-(4-Fluorobenzyl)-4-nitrobenzamide (3k):** $R_f=0.30$ (ethyl acetate/hexane = 1:4); white solid; yield: 86% (85 mg, 67%); mp 129–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.27$ (d, $J=8$ Hz, 2H), 7.94 (d, $J=8$ Hz, 2H), 7.33 (s, 2H), 7.04 (t, $J=8.1$ Hz, 2H), 6.57 (br s, 1H), 4.625 (d, $J=4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=165.4$, 162.5 (d, $^1J_{C,F}=$ 245 Hz), 149.8, 139.9, 133.4 (d, $^4J_{C,F}=3$ Hz), 129.9 (d, $^3J_{C,F}=$ 9 Hz), 128.3, 124.0, 115.9 (d, $^2J_{C,F}=22$ Hz), 43.8; IR (KBr): $\tilde{\nu}=$3271 (m), 3077 (s), 2923 (m), 2853 (m), 1644 (m), 1600 (m), 1548 (m), 1510 (m), 1349 (m), 1219 (m), 1156 (s), 1064 (s), 981 (s), 824 (m), 723 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z=275.0829$, calcd. for $C_{14}H_{12}FN_2O_3$ ($M+H^+$): 275.0826.

***N*-(2-Chlorobenzyl)-4-nitrobenzamide (3l):** $R_f=0.45$ (ethyl acetate/hexane = 1:4); white solid; yield: 87% (93 mg, 69%); mp 163–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.27$ (d, $J=$ 8 Hz, 2H), 7.93 (d, $J=8$ Hz, 2H), 7.48–7.38 (m, 2H), 7.29–7.25 (m, 2H), 6.69 (br s, 1H), 4.745 (d, $J=4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=165.3$, 149.6, 139.8, 134.9, 133.8, 130.8, 129.7, 129.5, 128.2, 127.3, 123.8, 42.5; IR (KBr): $\tilde{\nu}=$3331 (m), 3063 (s), 2920 (m), 2857 (s), 1644 (m), 1598 (m), 1523 (m), 1345 (m), 1300 (m), 1015 (s), 752 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z=291.0537$, calcd. for $C_{14}H_{12}ClN_2O_3$ ($M+H^+$): 291.0531.

***N*-(2-Chlorobenzyl)-4-cyanobenzamide (3m):** $R_f=0.30$ (ethyl acetate/hexane = 1:4); white solid; yield; 88% (92 mg, 64%); mp 132–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.87$ (d, $J=8.3$ Hz, 2H), 7.72 (d, $J=8.2$ Hz, 2H), 7.51–7.43 (m, 1H), 7.43–7.36 (m, 1H), 7.30–7.25 (m, 2H), 6.70 (s, 1H), 4.73 (d, $J=5.9$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 165.67, 138.29, 135.10, 133.94, 132.61, 130.83, 129.86, 129.55, 127.86, 127.43, 118.09, 115.36, 77.48, 77.16, 76.84, 42.54; IR (KBr): $\tilde{\nu}=3415$ (w), 2923 (s), 2848 (s), 2230 (s), 1648 (m), 1543 (s), 1288 (s), 858(s), 750 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z=271.0640$, calcd. for $C_{15}H_{12}ClN_2O$ ($M+H^+$): 271.0632.

4-Bromo-*N*-(2-chlorobenzyl)benzamide (3n): $R_f=0.37$ (ethyl acetate/hexane = 1:4); white solid; yield 84% (83 mg, 68%); mp 138–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.65$ (d, $J=8$ Hz, 2H), 7.56 (d, $J=8$ Hz, 2H), 7.46 (dd, $J=6$, 4 Hz, 1H), 7.39 (dd, $J=8$, 4 Hz, 1H), 7.27–7.24 (m, 2H), 6.56 (br s, 1H), 4.72 (d, $J=8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=166.5$, 135.4, 133.9, 133.2, 132.0, 130.7, 129.8, 129.3, 128.7, 127.4, 126.4, 42.3; IR (KBr) $\tilde{\nu}=3320$ (m), 3068 (s), 1633 (m), 1590 (s), 1539 (m), 1482 (m), 1318 (m), 1070 (s), 1009 (s), 847 (s), 749 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z=323.9794$, calcd. for $C_{14}H_{12}BrClNO$ ($M+H^+$): 323.9785.

***N*-Benzyl-2,3,4,5,6-pentafluorobenzamide (3o):** $R_f=0.45$ (ethyl acetate/hexane = 1:4); white solid; yield: 78% (63 mg, 59%); mp 215 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.38$–7.29 (m, 5H), 6.42 (br s, 1H), 4.61 (d, $J=8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=157.5$, 145.7–145.4 (m), 143.9–143.5 (m), 143.2–142.9 (m), 141.3–141.0, 139.2–138.8 (m), 136.7–136.3 (m), 129.0, 128.1, 127.8, 111.7–111.3 (m), 44.5; IR (KBr): $\tilde{\nu}=3235$ (m), 3068 (m), 2953 (m), 1652 (m), 1566 (s), 1494 (m), 1059 (s), 988 (m), 875 (s), 746 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z=302.0588$, calcd. for $C_{14}H_9F_5NO$ ($M+H^+$): 302.0599.

***N*-Benzylpyrene-1-carboxamide (3p):** $R_f=0.32$ (ethyl acetate/hexane = 1:4); white solid; yield: 81% (49 mg, 48%); mp 105 °C; 4:3 mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.57$ (dd, $J=9.2$, 3.5 Hz, 1H), 8.28–8.16 (m, 2H), 8.16–7.93 (m, 6H), 7.84–7.71 (m, 3H), 7.52–7.37 (m, 8H), 7.37–7.27 (m, 8H), 6.60 (s, 1H), 6.49 (s, 1H), 4.87–4.73 (m, 2H), 4.71–4.54 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=169.9$, 167.4, 138.3, 138.3, 134.4, 132.6, 131.6, 131.2, 130.8, 130.8, 128.9, 128.9, 128.8, 128.7, 128.6, 128.1, 128.0, 127. 8, 127.7, 127.2, 127.1, 126.4, 125.9, 125.8, 124.8, 124.6, 124.5, 124.4, 77.9, 77.2, 76.8, 44.8, 44.2; IR (KBr): $\tilde{\nu}=3288$ (m), 3063 (s), 3030 (s), 2923 (s), 1635 (m), 1537 (m), 1490 (s), 1291 (m), 848 (s), 695 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z=$ 336.1393, calcd. for $C_{24}H_{18}NO$ ($M+H^+$): 336.1383.

4-Cyano-*N*-phenethylbenzamide (3q): $R_f=0.18$ (ethyl acetate/hexane = 1:4); white solid; yield: 94% (91 mg, 68%); mp 115–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.77$ (d, $J=$ 8 Hz, 2H), 7.70 (d, $J=8$ Hz, 2H), 7.35–7.32 (m, 2H), 7.28–7.22 (m, 3H), 6.21 (br s, 1H), 3.76–3.71 (m, 2H), 2.95 (t, $J=$ 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=165.8$, 138.6, 132.5, 128.9, 128.9, 127.6, 126.9, 118.1, 115.1, 41.4, 35.6; IR (KBr): $\tilde{\nu}=3306$ (w), 3085 (s), 2923 (s), 2852 (s), 2228 (s), 1633 (m), 1543 (m), 1497 (s), 1313 (s), 857 (s), 753 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z=251.1192$, calcd. for $C_{16}H_{15}N_2O$ ($M+H^+$): 251.1178.

4-Bromo-*N*-phenethylbenzamide (3r): $R_f=0.35$ (ethyl acetate/hexane = 1:4); white solid; yield: 87% (71 mg, 62%); mp 113–116 °C (lit.[33] 143–144 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.55$ (s, 4H), 7.35–7.32 (m, 2H), 7.27–7.22 (m, 3H), 6.08 (br s, 1H), 3.71 (dd, $J=12$, 8 Hz, 2H), 2.93 (t, $J=$ 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=166.6$, 138.8, 133.5, 131.9, 131.8, 128.9, 128.5, 126.8, 126.2, 41.3, 35.7; IR (KBr): $\tilde{\nu}=3419$ (w), 2923 (s), 2848 (s), 1639 (m), 1542 (s), 1482 (s), 1317 (s), 1068 (s), 1009 (s), 755 (s) cm^{-1}; HR-MS

(ESI-TOF): $m/z = 304.0348$, calcd. for $C_{15}H_{15}BrNO$ ($M+H^+$): 304.0331.

4-Nitro-*N*-phenethylbenzamide (3s): $R_f = 0.20$ (ethyl acetate/hexane = 1:4); white solid; yield: 93% (95 mg, 76%); mp 152–156 °C (lit.[34] 151 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.24$ (d, $J = 8$ Hz, 2H), 7.83 (d, $J = 8$ Hz, 2H), 7.34–7.22 (m, 5H), 6.31 (br s, 1H), 3.74 (dd, $J = 12$, 6 Hz, 2H), 2.96 (t, $J = 6.6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.6$, 149.6, 140.3, 138.6, 128.9, 128.8, 128.1, 126.9, 123.9, 41.5, 35.5; IR (KBr): $\tilde{\nu} = 3328$ (m), 3063 (s), 2923 (s), 1643 (m), 1597 (m), 1541 (m), 1517 (m), 1452 (s), 1352 (s), 1193 (s), 867 (s), 753 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 271.1077$, calcd. for $C_{15}H_{15}N_2O_3$ ($M+H^+$): 271.1077.

4-Methyl-*N*-phenethylbenzamide (3t): $R_f = 0.25$ (ethyl acetate/hexane = 1:4); white solid; yield: 79% (99 mg, 71%); mp 82–84 °C (lit.[35] 76–77 °C); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.60$ (d, $J = 8$ Hz, 2H), 7.33 (d, $J = 8$ Hz, 2H), 7.27–7.21 (m, 5H), 6.15 (br s, 1H), 3.72 (dd, $J = 12$, 8 Hz, 2H), 2.94 (t, $J = 6.8$ Hz, 2H), 2.39 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$): $\delta = 167.5$, 141.9, 139.1, 131.9, 129.3, 128.9, 128.8, 126.9, 126.7, 41.2, 35.8, 21.5; IR (KBr): $\tilde{\nu} = 3313$ (m), 3026 (s), 2937 (s), 1637 (m), 1534 (m), 1307 (m), 1199 (s), 836 (s), 749 (s), 697 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z = 262.1211$, calcd. for $C_{16}H_{17}NNaO$ ($M+Na^+$): 262.1202.

3-Nitro-*N*-phenethylbenzamide (3u): $R_f = 0.20$ (ethyl acetate/hexane = 1:4); white solid; yield: 90% (97 mg, 78%); mp 118–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.51$ (s, 1H), 8.35 (d, $J = 8$ Hz, 1H), 8.08 (d, $J = 8$ Hz, 1H), 7.63 (t, $J = 8$ Hz, 1H), 7.32 (dt, $J = 17$, 7.8 Hz, 5H), 6.28 (br s, 1H), 3.77 (dd, $J = 12$, 6 Hz, 2H), 2.98 (t, $J = 6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.1$, 148.3, 138.6, 136.4, 133.1, 130.0, 128.9, 128.9, 126.9, 126.1, 121.8, 41.5, 35.6; IR (KBr): $\tilde{\nu} = 3305$ (m), 3085 (s), 3032 (s), 2923 (s), 1644 (m), 1530 (m), 1350 (m), 1322 (m), 906 (s), 814 (s), 719 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 271.1088$, calcd. for $C_{15}H_{15}N_2O_3$ ($M+H^+$): 271.1077.

***N*-[3,5-Bis(trifluoromethyl)benzyl]-4-cyanobenzamide (3v):** $R_f = 0.32$ (ethyl acetate/hexane = 1:4); white solid; yield: 85% (143 mg, 72%); mp 166–170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.91$ (d, $J = 8$ Hz, 2H), 7.82–7.81 (m, 3H), 7.77 (d, $J = 8$ Hz, 2H), 6.70 (br s, 1H), 4.775 (d, $J = 4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.0$, 140.5, 137.6, 132.8, 132.4 (q, $J_{C,F} = 79.5$ Hz), 128.1 (d, $J_{C,F} = 3$ Hz), 127.9, 123.3 (q, $J_{C,F} = 543$ Hz), 122.0 (q, $J_{C,F} = 7$ Hz), 117.9, 115.8, 43.5; IR (KBr): $\tilde{\nu} = 3407$ (w), 3249 (m), 3050 (s), 2920 (s), 2851 (s), 2234 (s), 1642 (m), 1543 (m), 1307 (s), 1278 (m), 1160 (s), 1116 (m), 985 (s), 703 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 373.0770$, calcd. for $C_{17}H_{11}F_6N_2O$ ($M+H^+$): 373.0770.

***N*-[3,5-Bis(trifluoromethyl)benzyl]-4-chlorobenzamide (3w):** $R_f = 0.40$ (ethyl acetate/hexane = 1:4); white solid; yield: 83% (124 mg, 65%); mp 137–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.80$ (s, 3H), 7.75 (d, $J = 8.4$ Hz, 2H), 7.44 (d, $J = 8.4$ Hz, 2H), 6.58 (s, 1H), 4.76 (d, $J = 6.0$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.7$, 140.9, 138.5, 132.3 (q, $J_{C,F} = 66$ Hz), 132.1, 129.2, 128.6, 128.0 (d, $J_{C,F} = 3$ Hz), 123.3 (q, $J_{C,F} = 542$ Hz), 121.8 (q, $J_{C,F} = 8$ Hz), 43.4; IR (KBr): $\tilde{\nu} = 3286$ (w), 3076 (m), 2927 (s), 1640 (s), 1538 (m), 1487 (m), 1278 (s), 1173 (s), 1132 (s), 845 (m), 705 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 382.0451$, calcd. for $C_{16}H_{11}ClF_6NO$ ($M+H^+$): 382.0428.

***N*-[3,5-Bis(trifluoromethyl)benzyl]-4-nitrobenzamide (3x):** $R_f = 0.27$ (ethyl acetate/hexane = 1:4); white solid; yield: 89% (133 mg, 73%); mp 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.32$ (d, $J = 8$ Hz, 2H), 7.98 (d, $J = 8$ Hz, 2H), 7.82 (s, 3H), 6.72 (br s, 1H), 4.795 (d, $J = 4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.8$, 150.1, 140.4, 139.2, 132.4 (q, $J_{C,F} = 66$ Hz), 128.4, 128.2 (d, $J_{C,F} = 3$ Hz), 123.2 (q, $J_{C,F} = 542$ Hz), 124.2, 122.0 (q, $J_{C,F} = 8$ Hz), 43.6; IR (KBr): $\tilde{\nu} = 3298$ (m), 3056 (s), 2989 (s), 2929 (s), 2851 (s), 1644 (m), 1600 (m), 1519 (m), 1352 (m), 1282 (m), 1124 (m), 985 (s), 896 (s), 870 (s), 738 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z = 393.0673$, calcd. for $C_{16}H_{11}F_6N_2O_3$ ($M+H^+$): 393.0668.

***N*-[3,5-Bis(trifluoromethyl)benzyl]-4-methylbenzamide (3y):** $R_f = 0.40$ (ethyl acetate/hexane = 1:4); white solid; yield: 82% (147 mg, 70%); mp 107–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ)7.95–7.54 (m, 5H), 7.23 (s, 2H), 6.91 (s, 1H), 4.72 (s, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 167.8$, 142.7, 141.4, 132.1 (q, $J_{C,F} = 67$ Hz), 130.9, 129.5, 127.9, 127.1, 123.3 (q, $J_{C,F} = 542$ Hz), 121.5 (q, $J_{C,F} = 7$ Hz), 43.2, 21.5; IR (KBr): $\tilde{\nu} = 3303$ (w), 3047 (s), 2934 (s), 1634 (m), 1538 (m), 1505 (m), 1380 (m), 1355 (m), 1278 (m), 1173 (m), 1133 (m), 889 (m), 837 (m), 705 (m), 682 (m) cm^{-1}; HR-MS (ESI-TOF): $m/z = 362.0986$, calcd. for $C_{17}H_{14}F_6NO$ ($M+H^+$): 362.0974.

***N*-[3,5-Bis(trifluoromethyl)benzyl]-3-nitrobenzamide (3z):** $R_f = 0.27$ (ethyl acetate/hexane = 1:4); white solid; yield: 88% (138 mg, 76%); mp 152–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.63$ (s, 1H), 8.40 (d, $J = 8$ Hz, 1H), 8.21 (d, $J = 8$ Hz, 1H), 7.83 (s, 3H), 7.69 (t, $J = 8$ Hz, 1H), 6.82 (br s, 1H), 4.805 (d, $J = 4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.3$, 148.4, 140.5, 135.3, 133.5, 132.4 (q, $J_{C,F} = 66.5$ Hz), 130.3, 128.2 (d, $J_{C,F} = 3$ Hz), 126.7, 123.3 (q, $J_{C,F} = 536$ Hz), 122.0 (q, $J_{C,F} = 10$ Hz), 43.7; IR (KBr): $\tilde{\nu} = 3315$ (w), 3087 (m), 2924 (m), 2853 (s), 1645 (m), 1531 (s), 1351 (s), 1278 (s), 1174 (m), 1133 (m), 898 (s), 705 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 393.0680$, calcd. for $C_{16}H_{11}F_6N_2O_3$ ($M+H^+$): 393.0668.

***N*-(4-Fluorobenzyl)-3-nitrobenzamide (3aa):** $R_f = 0.20$ (ethyl acetate/hexane = 1:4); white solid; yield: 84% (93 mg, 73%); mp 119–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.59$ (s, 1H), 8.36 (d, $J = 7.3$ Hz, 1H), 8.18 (d, $J = 7.1$ Hz, 1H), 7.65 (t, $J = 7.6$ Hz, 1H), 7.34 (s, 2H), 7.05 (t, $J = 7.5$ Hz, 2H), 6.57 (brs, 1H), 4.64 (d, $J = 4.4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.0$, 162.5 (d, $^1J_{C,F} = 245$ Hz), 148.3, 135.9, 133.5 (d, $^4J_{C,F} = 3$ Hz), 133.4, 130.0, 129.9 (d, $^3J_{C,F} = 8$ Hz), 126.4, 121.9, 115.9 (d, $^2J_{C,F} = 21$ Hz), 43.8; IR (KBr): $\tilde{\nu} = 3290$ (w), 3087 (s), 1640 (m), 1557 (m), 1525 (s), 1509 (s), 1350 (s), 1320 (m), 1216 (m), 1157 (s), 1095 (s), 820 (m), 673 (s) cm^{-1}; HR-MS (ESI-TOF): $m/z = 275.0829$, calcd. for $C_{14}H_{12}FN_2O_3$ ($M+H^+$): 275.0826.

Acknowledgements

We are thankful to DST (New Delhi, India), (Grant no. INT/FINLAND/P-06 and SR/S1/IC-59/2010) for financial support. TKA is thankful to UGC (India) for a fellowship.

References

[1] J. Akhavan, in: *The Chemistry of Explosives*, 2nd edn., (Ed.: J. Akhavan), The Royal Society of Chemistry, **2004**, pp 1–20.

[2] M. Yoshizawa, T. Kusukawa, M. Fujita, K. Yamaguchi, *J. Am. Chem. Soc.* **2000**, *122*, 6311–6312.

[3] D. J. Cram, M. E. Tanner, R. Thomas, *Angew. Chem.* **1991**, *103*, 1048–1051; *Angew. Chem. Int. Ed.* **1991**, *30*, 1024–1027.

[4] P. Mal, B. Breiner, K. Rissanen, J. R. Nitschke, *Science* **2009**, *324*, 1697–1699.

[5] I. Tornieporth-Oetting, T. Klapötke, *Angew. Chem.* **1990**, *102*, 726–727; *Angew. Chem. Int. Ed.* **1990**, *29*, 677–679.

[6] K. C. Nicolaou, P. S. Baran, R. Kranich, Y.-L. Zhong, K. Sugita, N. Zou, *Angew. Chem.* **2001**, *113*, 208–212; *Angew. Chem. Int. Ed.* **2001**, *40*, 202–206.

[7] O. Hassel, *Science* **1970**, *170*, 497–502.

[8] a) G.-W. Wang, *Chem. Soc. Rev.* **2013**, *42*, 7668–7700; b) P. Balaz, M. Achimovicova, M. Balaz, P. Billik, Z. Cherkezova-Zheleva, J. M. Criado, F. Delogu, E. Dutkova, E. Gaffet, F. J. Gotor, R. Kumar, I. Mitov, T. Rojac, M. Senna, A. Streletskii, K. Wieczorek-Ciurowa, *Chem. Soc. Rev.* **2013**, *42*, 7571–7637; c) T. Friščić, I. Halasz, P. J. Beldon, A. M. Belenguer, F. Adams, S. A. J. Kimber, V. Honkimäki, R. E. Dinnebier, *Nat. Chem.* **2013**, *5*, 66–73.

[9] a) S. Ley, M. O'Brien, R. Denton, *Synthesis* **2011**, 1157–1192; b) J.-L. Do, C. Mottillo, D. Tan, V. Štrukil, T. Friščić, *J. Am. Chem. Soc.* **2015**, *137*, 2476–2479; c) S. L. James, C. J. Adams, C. Bolm, D. Braga, P. Collier, T. Friscic, F. Grepioni, K. D. M. Harris, G. Hyett, W. Jones, A. Krebs, J. Mack, L. Maini, A. G. Orpen, I. P. Parkin, W. C. Shearouse, J. W. Steed, D. C. Waddell, *Chem. Soc. Rev.* **2012**, *41*, 413–447.

[10] a) C. Giri, P. K. Sahoo, R. Puttreddy, K. Rissanen, P. Mal, *Chem. Eur. J.* **2015**, *21*, 6390–6393; b) J. G. Hernandez, I. S. Butler, T. Friscic, *Chem. Sci.* **2014**, *5*, 3576–3582; c) A. Stolle, T. Szuppa, S. E. S. Leonhardt, B. Ondruschka, *Chem. Soc. Rev.* **2011**, *40*, 2317–2329; d) L. Takacs, *Chem. Soc. Rev.* **2013**, *42*, 7649.

[11] a) M. S. Yusubov, T. Wirth, *Org. Lett.* **2005**, *7*, 519–521; b) T. K. Achar, S. Maiti, P. Mal, *RSC Adv.* **2014**, *4*, 12834–12839.

[12] a) A. Studer, D. P. Curran, *Nat. Chem.* **2014**, *6*, 765–773; b) S. A. Girard, T. Knauber, C.-J. Li, *Angew. Chem.* **2014**, *126*, 76–103; *Angew. Chem. Int. Ed.* **2014**, *53*, 74–100; c) M.-L. Louillat, F. W. Patureau, *Chem. Soc. Rev.* **2014**, *43*, 901–910; d) A. F. M. Noisier, M. A. Brimble, *Chem. Rev.* **2014**, *114*, 8775–8806; e) S. Guin, S. K. Rout, A. Banerjee, S. Nandi, B. K. Patel, *Org. Lett.* **2012**, *14*, 5294–5297; f) Z. Fu, J. Lee, B. Kang, S. H. Hong, *Org. Lett.* **2012**, *14*, 6028–6031; g) W. Su, J. Yu, Z. Li, Z. Jiang, *J. Org. Chem.* **2011**, *76*, 9144–9150.

[13] a) T. Nobuta, N. Tada, A. Fujiya, A. Kariya, T. Miura, A. Itoh, *Org. Lett.* **2013**, *15*, 574–577; b) R. Vanjari, T. Guntreddi, K. N. Singh, *Org. Lett.* **2013**, *15*, 4908–4911; c) J. Gao, G.-W. Wang, *J. Org. Chem.* **2008**, *73*, 2955–2958.

[14] a) F. Collet, C. Lescot, P. Dauban, *Chem. Soc. Rev.* **2011**, *40*, 1926–1936; b) A. McNally, B. Haffemayer, B. S. L. Collins, M. J. Gaunt, *Nature* **2014**, *510*, 129–133; c) A. Sharma, J. F. Hartwig, *Nature* **2015**, *517*, 600–604; d) J. Schranck, A. Tlili, M. Beller, *Angew. Chem.* **2014**, *126*, 9580–9582; *Angew. Chem. Int. Ed.* **2014**, *53*, 9426–9428; e) J. He, S. Li, Y. Deng, H. Fu, B. N. Laforteza, J. E. Spangler, A. Homs, J.-Q. Yu, *Science* **2014**, *343*, 1216–1220; f) A. Studer, D. P. Curran, *Angew. Chem.* **2011**, *123*, 5122–5127; *Angew. Chem. Int. Ed.* **2011**, *50*, 5018–5022.

[15] a) A. P. Antonchick, R. Samanta, K. Kulikov, J. Lategahn, *Angew. Chem.* **2011**, *123*, 8764–8767; *Angew. Chem. Int. Ed.* **2011**, *50*, 8605–8608; b) V. V. Zhdankin, *ARKIVOC (Gainesville, FL, U.S.A.)* **2009**, 1–62; c) S. Maiti, P. Mal, *Adv. Synth. Catal.* **2015**, *357*, 1416–1424.

[16] E. Valeur, M. Bradley, *Chem. Soc. Rev.* **2009**, *38*, 606–631.

[17] V. R. Pattabiraman, J. W. Bode, *Nature* **2011**, *480*, 471–479.

[18] T. K. Achar, P. Mal, *J. Org. Chem.* **2015**, *80*, 666–672.

[19] a) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299–5358; b) P. Dauban, R. H. Dodd, *Synlett* **2003**, 1571–1586.

[20] I. M. Geraskin, O. Pavlova, H. M. Neu, M. S. Yusubov, V. N. Nemykin, V. V. Zhdankin, *Adv. Synth. Catal.* **2009**, *351*, 733–737.

[21] M. S. Yusubov, R. Y. Yusubova, V. N. Nemykin, A. V. Maskaev, M. R. Geraskina, A. Kirschning, V. V. Zhdankin, *Eur. J. Org. Chem.* **2012**, 5935–5942.

[22] V. Prasad, R. R. Kale, B. B. Mishra, D. Kumar, V. K. Tiwari, *Org. Lett.* **2012**, *14*, 2936–2939.

[23] C. L. Allen, J. M. J. Williams, *Chem. Soc. Rev.* **2011**, *40*, 3405–3415.

[24] H. Sun, Y. Pan, Y. Zhao, W. A. Jackson, L. M. Nuckles, I. L. Malkina, V. E. Arteaga, F. M. Mitloehner, *J. Environ. Qual.* **2008**, *37*, 608.

[25] H. K. Hall, *J. Am. Chem. Soc.* **1957**, *79*, 5441–5444.

[26] A. Y. Koposov, B. C. Netzel, M. S. Yusubov, V. N. Nemykin, A. Y. Nazarenko, V. V. Zhdankin, *Eur. J. Org. Chem.* **2007**, 4475–4478.

[27] E. Petricci, C. Mugnaini, M. Radi, F. Corelli, M. Botta, *J. Org. Chem.* **2004**, *69*, 7880–7887.

[28] H. Mahdavi, J. Amani, *Tetrahedron Lett.* **2008**, *49*, 2204–2207.

[29] D. A. Ockey, J. L. Dotson, M. E. Struble, J. T. Stults, J. H. Bourell, K. R. Clark, T. R. Gadek, *Biol. Med. Chem.* **2004**, *12*, 37–44.

[30] K. E. Fairfull-Smith, I. D. Jenkins, W. A. Loughlin, *Org. Biomol. Chem.* **2004**, *2*, 1979–1986.

[31] V. C. Agwada, *J. Chem. Eng. Data* **1982**, *27*, 479–481.

[32] T. Suzuki, M. N. A. Khan, H. Sawada, E. Imai, Y. Itoh, K. Yamatsuta, N. Tokuda, J. Takeuchi, T. Seko, H. Nakagawa, N. Miyata, *J. Med. Chem.* **2012**, *55*, 5760–5773.

[33] C. M. Boehner, D. M. Marsden, H. F. Sore, D. Norton, D. R. Spring, *Tetrahedron Lett.* **2010**, *51*, 5930–5932.

[34] Z. Hu, Y. Wang, D. Shi, H. Tan, X. Li, L. Wang, W. Zhu, Y. Cao, *Dyes Pigm.* **2010**, *86*, 166–173.

[35] D. Xing, X. Xu, L. Yang, *Synthesis* **2009**, 3399–3404.

