Hypervalent iodine(III)-mediated oxidation of aldoximes to *N*-acetoxy or *N*-hydroxy amides†

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Treatment of various aliphatic and aromatic aldoximes with the hypervalent iodine(III) reagents (diacetoxyiodo)benzene (DIB) or Koser's reagent [hydroxy(tosyloxy)iodo]benzene (HTIB) gave, respectively, *N*-acetoxy or *N*-hydroxy amides in good yields rather than the expected nitrile oxide dimerised product oxadiazole-*N*-oxides reported to be formed with other oxidising and hypervalent iodine reagents. The acetate or the hydroxyl group of DIB or HTIB attacks on the aryl/alkylnitrile oxides formed *in situ*, which, upon intramolecular rearrangement, gave the expected *N*-acetoxy or *N*-hydroxy amides.

Introduction

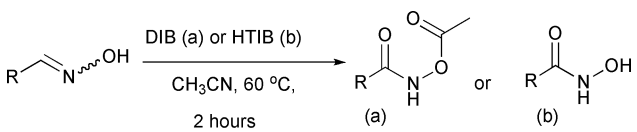
The importance of hypervalent iodine reagents in recent years is reflected by the plethora of publications and reviews.[1] Due to the low toxicity, ready availability, easy handling, clean transformation and above all, mild reaction conditions, hypervalent iodine reagents have attracted a great deal of interest in modern synthetic organic chemistry.[1] The oxidising ability of non-metallic hypervalent iodine reagents is similar to toxic metallic lead-, mercury- and thallium-based reagents. Its mild oxidising properties have been used for the oxidation of nitrogen-containing compounds such as oximes, hydrazones and acid hydrazides. Hypervalent iodine-mediated oxidative cleavage of ketoximes,[2a] hydrazones [2b] and *N*′,*N*′-dialkylhydrazides[2c] to the parent ketone and acids/esters have been studied. Unlike ketoxime, where the oxidation product is regeneration of parent ketone,[2a] the oxidation product of aldoxime is either regeneration of parent aldehyde or formation of nitrile oxide, depending on the nature of the oxidising agent employed.[2d,e] Nitrile oxides are valuable intermediates in organic synthesis.[3] 1,3-Dipolar cycloaddition reactions using nitrile oxides are versatile methods for the preparation of synthetically useful intermediates such as isoxazolines and isoxazoles.[4]

N-Acetoxy benzamides (*O*-acetyl hydroxamates) and *O*-tosyl hydroxamates are important candidates for classical Lossen rearrangements.[5] Generally, the *N*-acetoxy amides are prepared by the acylation of hydroxamic acids.[6a,b] Lately, the preparation of *O*-acyl/*O*-benzoyl hydroxamates has been reported *via* a polymer-supported reagent.[6c] The main drawback of these reported procedures is the formation of a mixture of *O*-acyl and *N*-acyl hydroxamate, resulting in a low yield of the desired *O*-acylated product.

The hydroxamic acid functionality is present in a number of biologically active molecules with antibacterial, antifungal, anti-inflammatory, anti-asthmatic, and anticancer properties.[7] Several methods have been reported with varying degrees of success for the preparation of hydroxamic acids. The reported methods include amidation of esters using hydroxylamine,[8] a nucleophilic displacement of carboxylates linked to an oxime resin,[9] amidation of carboxylic acids with hydroxylamine using various coupling reagents,[10] amidation of *N*-acyloxazolidinones with hydroxylamines using samarium triflate,[11] reaction of esters with *O*-benzyl hydroxylamine[12] and the Angelini–Rimini reaction on a solid support,[13] *etc*. Most of the reported methods use strong basic conditions, complicated experimental procedures, high reaction temperatures and tedious purification methods, which limit their synthetic utility when applied on a large scale.

Results and discussion

Aromatic aldoximes are invariably oxidised to aryl nitrile oxides with various oxidising agents such as NaOCl,[3] $Pb(OAc)_4$,[14a] NBS,[14b] 1-chlorobenzotriazole,[14c] Magtrieve™ (CrO_2),[14d] chloramine-T[14e] and $PhICl_2$.[14f] However, aryl nitrile oxides are not very stable and immediately dimerise to oxadiazole-*N*-oxide derivatives. We have been interested in hypervalent iodine-mediated oxidative desulfurization reactions.[15] During the course of (diacetoxyiodo)benzene (DIB)-mediated oxidation of aromatic aldoximes, we observed the formation of *N*-acetoxy benzamide (**a**) (Scheme 1). When the same reaction was performed using Koser's reagent [hydroxy(tosyloxy)iodo]benzene (HTIB), the product obtained was *N*-hydroxy benzamide (**b**) (Scheme 1).



Scheme 1 Reaction of aldoximes with DIB or HTIB.

When benzaldehyde oxime (**1**) (1 equiv.) was reacted with (diacetoxyiodo)benzene (DIB) (1.1 equiv.) in acetonitrile at 60 °C, *N*-acetoxy benzamide (**1a**) was obtained in 78% isolated yield rather than the expected benzonitrile oxide or its dimerised product. This observation is in sharp contrast to the observation

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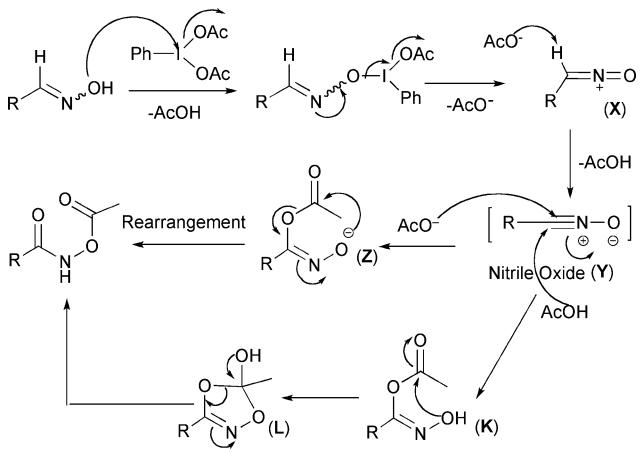
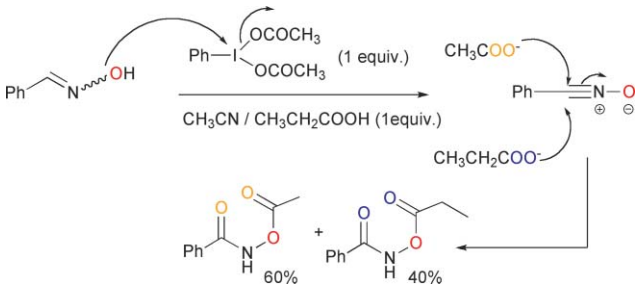
made by Das *et al.*,[16a] where in a CH_2Cl_2 medium and in the absence of any alkenes, the nitrile oxide dimerised product is speculated. The difference between the observation Das *et al.*[16a] and ours is the use of different organic solvents. In order to ascertain the role of the solvent, the reaction was carried out in various organic solvents such as CH_3CN, $CHCl_3$, CH_2Cl_2, THF, MeOH, toluene and DMSO. The isolated yields of (**1a**) after 2 h were 78, 70, 58, 50, 51, 35 and ~7%, respectively. In the CH_2Cl_2 solvent, the product **1a** was obtained in 58% isolated yield along with a mixture of other side products. However, in THF, MeOH, toluene and DMSO, the reaction gave an unclean reaction mixture. Thus, CH_3CN was found to be the most suitable solvent giving good yield of *N*-acetoxy amide.

Although the starting aldoxime **1** was a diastereomeric (*syn*- and *anti*-) mixture, both gave the same product *N*-acetoxy benzamide (**1a**). Alkyl/aryl aldoxime, when treated with heavy metal oxidants such as $Pb(OAc)_4$,[14a] is reported to form nitrile oxide along with other products. In this oxidation, the *anti*-aldoxime proceeds *via* an iminoxy radical path, whereas the *syn*-aldoxime reacts in concerted path giving nitrile oxide.[14a] A (diacetoxyiodo)benzene (DIB)-mediated nitrile oxide formation from aldoxime has been proposed by Das *et al.*[16a] According to this mechanism, the first step is the nucleophilic displacement of one of the acetate groups of DIB by an aldoxime oxygen. This is then followed by the formation of intermediate (**X**), which, upon deprotonation, gives nitrile oxide (**Y**) (Scheme 2). Nitrile oxide (**Y**), which is reported to be the intermediate for this kind of reaction,[16a,b] is attacked by the *in situ* liberated acetate ion from DIB, giving acylated intermediate (**Z**). The intermediate (**Z**), upon intramolecular rearrangement, gave the expected *N*-acetoxy arylamide. Alternatively, attack of nitrile oxide (**Y**) by an acetic acid gives intermediate (**K**), which in turn generates a tetrahedral intermediate (**L**) leading to the expected *N*-acetoxy amide.



Scheme 2 Mechanism for the formation of *N*-acetoxy amides.

When the reaction was carried out in the presence of one equivalent of propionic acid, *N*-acetoxy benzamide (**1a**) along with *N*-propionyloxy benzamide (**1c**) were obtained in the ratio 60 : 40.[17] The formation of *N*-propionyloxy benzamide (**1c**) proves the intermolecular attack of acetate or propionate on benzonitrile oxide (Scheme 3), thus ruling out the possibility of a radical-type mechanism as has been proposed using $Pb(OAc)_4$.[14a]



Scheme 3 Intermolecular nature of the mechanism.

When the DIB-mediated oxidation of aromatic aldoxime was conducted in the presence of an activated alkene, methyl acrylate, in dicloromethane, there was no formation of *N*-acetoxy benzamide, but isoxazoline was isolated as the sole product an observation consistent with the literature.[16a] It is also reported that oxidation of aldoxime with iodosyl arene forms the dimerised product of nitrile oxide, oxadiazole-*N*-oxide, which has been isolated and well characterised.[16b] Therefore, it is clear that in the absence of an activated alkene the dimerisation of the intermediate nitrile oxide solely depends on the presence or absence of external nucleophiles. In the presence of a suitable external nucleophiles, such as acetate or hydroxy, the intermediate nitrile oxides undergo oxidative rearrangement to produce the corresponding *N*-acetoxy amides or *N*-hydroxy-amides without forming any dimerised product.

Due to their immense synthetic importance of *N*-acetoxy amide, we applied this strategy to various aldoxime for the construction of *N*-acetoxy amide. Various aromatic aldoximes containing electron donating groups (**2–3**) as well as electron withdrawing groups (**4–9**) gave their corresponding *N*-acetoxy benzamide (**2a–9a**) in good yields (Table 1) when reacted with DIB in acetonitrile at 60 °C within 2 h. The structure of *N*-acetoxy-2,6-dichloro benzamide (**9a**) has been confirmed by crystal X-ray crystallography (Fig. 1).

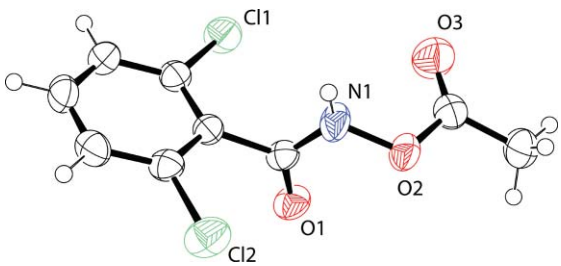


Fig. 1 ORTEP view of **9a** with atom-numbering scheme.

Furthermore, the method was successfully extended to the synthesis of a variety of aliphatic *N*-acetoxy amides (**10a–13a**) from their corresponding aliphatic aldoximes (**10–13**). It was observed that aliphatic aldoximes were more reactive than aromatic aldoximes. For aliphatic aldoximes (**10–13**), complete conversion took 30 min compared to 2 h for the aromatic aldoxime. Substrates containing both electron donating as well as electron withdrawing groups in the aromatic ring react efficiently (Table 1). In a competing reaction, when an equimolar mixture of 4-methylbenzaldehyde oxime (**2**) and 4-nitrobenzaldehyde oxime (**8**) was reacted with 1 equiv. of DIB, the ratio of the acetoxy products **2a** and **8a** formed after 2 h was 3 : 1. This demonstrates the faster reactivity for the substrates with an electron donating group compared to

Table 1 Preparation of *N*-acetoxy amide[a]

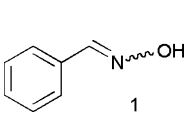
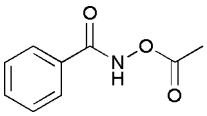
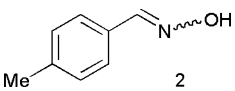
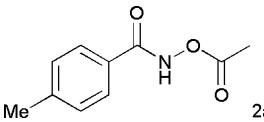
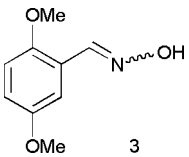
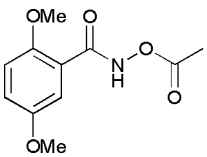
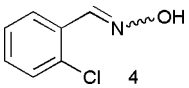
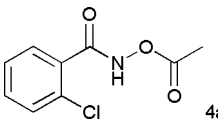
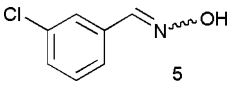
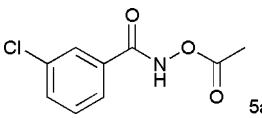
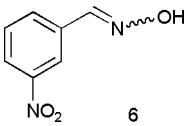
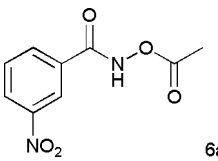
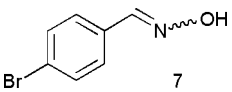
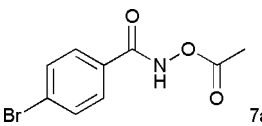
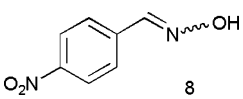
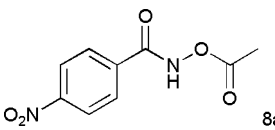
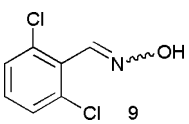
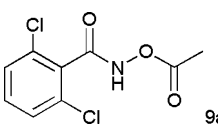
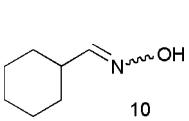
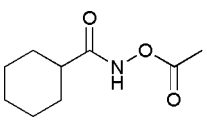
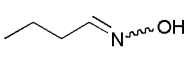
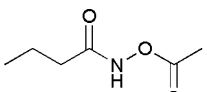
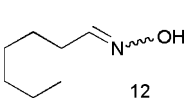
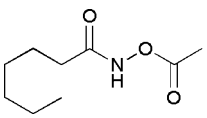
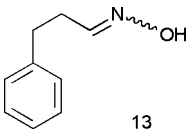
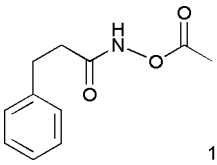
Substrate	Product[b]	Yield (%)[c]
 1	 1a	78
 2	 2a	83
 3	 3a	74
 4	 4a	81
 5	 5a	77
 6	 6a	69
 7	 7a	76
 8	 8a	79
 9	 9a	86
 10	 10a	75
 11	 11a	61
 12	 12a	66

Table 1 *(Contd.)*

Substrate	Product[b]	Yield (%)[c]
 13	 13a	69

[a] Reactions were monitored by TLC. [b] Confirmed by IR, and ^{1}H and ^{13}C NMR. [c] Isolated yield. For aromatic substrates **1–9** the reaction time was 2 h, and for aliphatic substrates **10–13** the reaction time was 0.5 h.

the substrates with an electron withdrawing group. In a similar competing reaction between an aliphatic aldoxime (**11**) and an aromatic aldoxime (**1**), the ratio of the acetoxy product **11a** and **1a** formed after 2 h was 4 : 1, exhibiting the faster reactivity of the aliphatic aldoxime compared to the aromatic aldoxime.

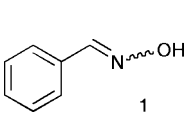
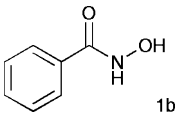
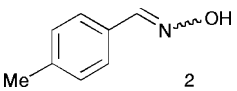
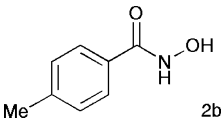
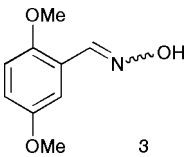
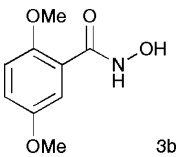
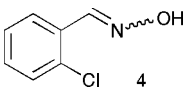
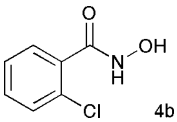
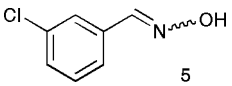
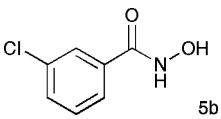
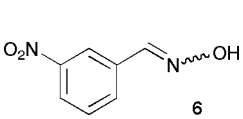
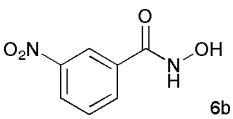
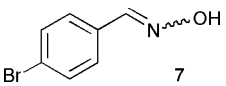
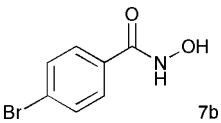
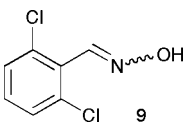
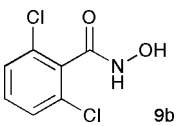
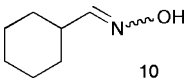
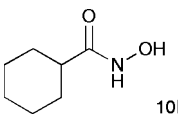
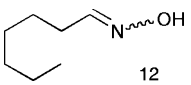
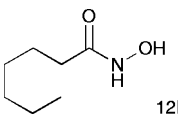
When another hypervalent iodine(III) reagent [hydroxy- (tosyloxy)iodo]benzene (HTIB, Koser's Reagent) was used as the oxidising agent instead of DIB for the oxidation of benzaldehyde oxime (**1**), *N*-hydroxybenzamide (**1b**) was isolated as the sole product. Here, the –OH nucleophile (generated from the reagent, HTIB) attacks the intermediate benzonitrile oxide (Scheme 2), forming *N*-hydroxy benzamide (**1b**). This reaction works better in a chloroform medium compared to an acetonitrile medium.

Hydroxamic acids bearing various substituents on the aromatic ring (**1b–9b**) can be efficiently prepared from the corresponding benzaldehyde oximes (**1–9**), as shown in Table 2. Here again, aliphatic aldoximes **10** and **12** were successfully converted to their corresponding hydroxamic acids **10b** and **12b** in a shorter time (30 min). Although quantitative conversion to hydroxamic acids for both aromatic and aliphatic compounds from the parent aldoximes were observed by GC/TLC, the isolated yields were modest. This is because of the difficulties in separating the water soluble product and byproduct *p*-toluenesulfonic acid (generated from reagent HTIB). Several extraction and chromatographic techniques were adopted but efficient separation could not be achieved. The yield in the table refers to the pure isolated product only. Similar purification difficulties were encountered by others and have been overcome by attaching the reagent on a solid support.[13]

Conclusion

In conclusion, the oxidation of both aromatic and aliphatic aldoximes with hypervalent iodine(III) reagents DIB or HTIB gave the corresponding *N*-acetoxy and *N*-hydroxy amides in good yields, rather than the expected nitrile oxide dimerised products oxadiazole-*N*-oxides reported with other oxidising agents. A plausible mechanism for this transformation involves acetate attack on the intermediate aryl/alkyl nitrile oxides, which, upon rearrangement, gave the expected *N*-acetoxy amides. Thus, using this approach, various *N*-acetoxy and *N*-hydroxy amides can be prepared conveniently from their aldoximes.

Table 2 Preparation of *N*-hydroxy amides[a]

Substrate	Product[b]	Yield (%)[c]
 1	 1b	76
 2	 2b	81
 3	 3b	73
 4	 4b	83
 5	 5b	74
 6	 6b	72
 7	 7b	70
 9	 9b	78
 10	 10b	62
 12	 12b	68

[a] Reactions were monitored by TLC. [b] Confirmed by IR, and ^{1}H and ^{13}C NMR. [c] Isolated yield. For aromatic substrates **1–9** the reaction time was 2 h, and for aliphatic substrates **10–12** the reaction time was 0.5 h

Experimental

General remarks

Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. Reaction progress was monitored by TLC using Merck silica gel 60 F_{254} (0.25 mm) with detection by UV or iodine. Chromatography was performed using Merck silica gel (60–120) mesh size with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian FT-400 MHz instrument using TMS as an internal standard. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, b = broad, coupling constant *J* (Hz). Elemental analyses were carried out on a Perkin–Elmer 2400 automatic carbon, hydrogen and nitrogen analyzer. Melting points were recorded on Buchi B-545 melting point apparatus and are uncorrected. IR spectra were recorded in KBr or neat on a Nicolet Impact 410 spectrophotometer. The crystal structure was recorded on Bruker Smart APEX-II CCD diffractometer. Mass data were obtained with a WATERS MS system, Q-tof premier and data analyzed using Mass Lynx4.1.

General experimental procedure

General procedure for preparation of *N*-acetoxy benzamide (1a) from benzaldehyde oxime (1). DIB (708 mg, 2.2 mmol) was added to a stirred solution of benzaldehyde oxime **1** (242 mg, 2 mmol) in acetonitrile at room temperature, portion wise over a period of 10 min. A white precipitate started to separate out during this period. After the complete addition of DIB, the reaction mixture was heated at 60 °C for 2 h (30 min for aliphatic substrates) and conversion to the corresponding *N*-acetoxy benzamide **1a** was monitored by TLC. At the end of the reaction, the reaction mixture becomes a clear solution. The organic layer was concentrated and admixed with ethyl acetate (15 mL). The ethyl acetate layer was washed with water (5 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified through a short column of silica gel to afford the pure product **1a**.

General procedure for preparation of *N*-hydroxy-benzamide (1b) from benzaldehyde oxime (1). HTIB (862 mg, 2.2 mmol) was added to a stirred solution of benzaldehyde oxime **1** (242 mg, 2 mmol) in chloroform at room temperature, in portion wise manner over a period of 10 min. After the complete addition of HTIB, the reaction mixture was heated at 60 °C for 2 h (30 min for aliphatic substrates), and conversion to the corresponding *N*-hydroxy benzamide **1b** was confirmed by TLC. The organic layer was concentrated and admixed with ethyl acetate (15 mL). The ethyl acetate layer was washed with 10% HCl water solution (5 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified through a short column of silica gel to afford the pure product **1b**.

The identities of the known compounds **1a**, **2a** and **5a**,[6c] **6a**,[18a] **8a**,[6b] **12a**,[14a] **13a**,[18d] **1b**,[9b] **2b**,[17] **4b** and **5b**[18b] **6b**,[18c] **7b**,[9b] **10b**,[12a] and **12b**[13] were confirmed by comparison of their spectral data with the reported ones. The physical and spectroscopic data of the others synthesised compounds are given below.

***N*-Acetoxy benzamide (1a)[6c].** mp: 126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.29 (s, 3H), 7.46 (t, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.82 (d, J = 7.6 Hz, 2H), 9.63 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.5, 127.7, 128.9, 130.7, 132.9, 166.5,

169.3; IR (KBr): 3151, 2961, 1793, 1650, 1531, 1366, 1198, 1021, 896, 695 cm^{-1}. MS (ESI): 180.07 (MH^+).

***N*-Acetoxy-4-methyl-benzamide (2a)[6c].** mp: 133–135 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.28 (s, 3H), 2.41 (s, 3H), 7.25 (d, $J = 8.0$ Hz, 2H), 7.71 (d, $J = 8.0$ Hz, 2H), 9.64 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.5, 21.7, 127.7, 127.9, 129.6, 143.6, 166.6, 169.4; IR (KBr): 3180, 2949, 2851, 1794, 1660, 1651, 1488, 1302, 1176, 1017, 906, 851, 753, 602 cm^{-1}; Elemental analysis: $C_{10}H_{11}NO_3$ (193.20): calcd C, 62.17; H, 5.74; N, 7.25. found: C, 62.15; H, 5.79; N, 7.24.

***N*-Acetoxy-2,5-dimethoxy-benzamide (3a).** Gummy; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.22 (s, 3H), 3.74 (s, 3H), 3.89 (s, 3H), 6.87 (d, $J = 8.8$ Hz, 1H), 6.98 (dd, $J_1 = 3.2$ Hz, $J_2 = 3.6$ Hz, 1H), 7.62 (d, $J = 3.2$ Hz, 1H), 11.18 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.5, 55.9, 56.9, 113.1, 115.5, 119.2, 120.6, 151.6, 154.1, 163.1, 168.6; IR (KBr): 3307, 2946, 2839, 1790, 1668, 1496, 1464, 1283, 1217, 1185, 1042, 815, 736 cm^{-1}; Elemental analysis: $C_{11}H_{13}NO_5$ (239.23): calcd C, 55.23; H, 5.48; N, 5.85. found: C, 55.23; H, 5.46; N, 5.84.

***N*-Acetoxy-2-chloro-benzamide (4a).** mp: 99–101 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.29 (s, 3H), 7.36 (m, 1H), 7.44 (m, 2H), 7.71 (d, $J = 7.2$ Hz, 1H), 9.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.4, 127.2, 130.5, 130.6, 131.2, 131.6, 132.5, 164.1, 168.6; IR (KBr): 3140, 2951, 2824, 1797, 1651, 1531, 1435, 1365, 1189, 1022, 901, 755, 638 cm^{-1}; Elemental analysis: $C_9H_8ClNO_3$ (213.62): calcd C, 50.60; H, 3.77; N, 6.56. found: C, 50.61; H, 3.77; N, 6.50.

***N*-Acetoxy-3-chloro-benzamide (5a)[6c].** mp: 100–102 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.28 (s, 3H), 7.38 (t, $J = 8.0$ Hz, 1H), 7.53 (d, $J = 7.6$ Hz, 1H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.80 (s, 1H), 9.90 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.5, 125.7, 127.9, 130.3, 132.4, 132.9, 135.2, 165.2, 169.2; IR (KBr): 3147, 2955, 2824, 1798, 1651, 1533, 1188, 1027, 915, 751 cm^{-1}; Elemental analysis: $C_9H_8ClNO_3$ (213.62): calcd C, 50.60; H, 3.77; N, 6.56. found: C, 50.58; H, 3.79; N, 6.53.

***N*-Acetoxy-3-nitro-benzamide (6a)[18a].** mp: 146–148 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 2.29 (s, 3H), 7.68 (t, $J = 8.0$ Hz, 1H), 8.29 (d, $J = 7.2$ Hz, 1H), 8.39 (d, $J = 7.2$ Hz, 1H), 8.81 (s, 1H), 12.29 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 18.4, 122.7, 126.6, 129.7, 132.7, 134.1, 147.9, 163.0, 168.7; IR (KBr): 3148, 2958, 1798, 1661, 1524, 1352, 1185, 1027, 857, 844, 737, 680 cm^{-1}; Elemental analysis: $C_9H_8N_2O_5$ (224.17): calcd C, 48.22; H, 3.60; N, 12.50. found: C, 48.22; H, 3.63; N, 12.45.

***N*-Acetoxy-4-bromo-benzamide (7a).** mp: 126–128 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.27 (s, 3H), 7.57 (d, $J = 8.4$ Hz, 2H), 7.66 (d, $J = 8.4$ Hz, 2H), 9.84 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.5, 127.9, 129.2, 129.6, 132.3, 165.7, 169.3; IR (KBr): 3194, 2938, 1789, 1662, 1588, 1479, 1196, 1069, 1011, 909, 841, 750, 514 cm^{-1}; Elemental analysis: $C_9H_8BrNO_3$ (258.07): calcd C, 41.89; H, 3.12; N, 5.43. found: C, 41.92; H, 3.14; N, 5.40.

***N*-Acetoxy-4-nitro-benzamide (8a)[6b].** mp: 189–191 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 2.29 (s, 3H), 8.09 (d, $J = 8.4$ Hz, 2H), 8.28 (d, $J = 8.4$ Hz, 2H), 12.11 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 18.4, 123.5, 129.2, 136.9, 149.9, 163.6, 168.7; IR (KBr): 3154, 2971, 1795, 1660, 1603, 1524, 1352, 1297, 1187, 1107, 1029, 1012, 850, 725, 588 cm^{-1}; Elemental analysis: $C_9H_8N_2O_5$ (224.17) requires C, 48.22; H, 3.60; N, 12.50. found: C, 48.25; H, 3.57; N, 12.47.

***N*-Acetoxy-2,6-dichloro-benzamide (9a).** mp: 162–164 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 2.26 (s, 3H), 7.35 (m, 5H), 12.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 18.1, 127.7, 131.2, 132.6, 133.0, 160.5, 167.8; IR (KBr): 3149, 2995, 2809, 1798, 1661, 1524, 1434, 1191, 1026, 910, 792, 561 cm^{-1}; Elemental analysis: $C_9H_7Cl_2NO_3$ (248.06) requires C, 43.58, H, 2.84, N, 5.65. found: C, 43.59; H, 2.81; N, 5.63.

Cyclohexanecarboxylic acid acetoxy-amide (10a). mp: 85–87 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.27 (m, 3H), 1.53 (m, 2H), 1.69 (m, 1H), 1.82 (m, 5H), 2.23 (s, 3H), 9.08 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.4, 25.60, 25.63, 29.3, 42.3, 169.0, 174.6; IR (KBr): 3175, 2856, 1798, 1667, 1520, 1450, 1370, 1189, 1019, 961, 857, 761, 589 cm^{-1}; Elemental analysis: $C_9H_{15}NO_3$ (185.22) requires C, 58.36, H, 8.16, N, 7.56. found: C, 58.38; H, 8.11; N, 7.52.

***N*-Acetoxy-butyramide (11a).** Oily; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.97 (t, 3H, $J = 7.6$ Hz), 1.69 (m, 2H), 2.20 (s, 3H), 2.22 (m, 2H), 10.37 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.5, 13.9, 18.2, 18.7, 34.5, 168.7, 171.5; IR (KBr): 3196, 2878, 1797, 1669, 1505, 1464, 1369, 1181, 1029, 853, 748 cm^{-1}; Elemental analysis: $C_6H_{11}NO_3$ (145.16) requires C, 49.65, H, 7.64, N, 9.65. found: C, 49.61; H, 7.63; N, 9.68.

Heptanoic acid acetoxy-amide (12a)[14a]. mp: 80–82 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (t, $J = 6.4$ Hz, 3H), 1.30 (m, 6H), 1.67 (m, 2H), 2.21 (s, 3H), 2.24 (m, 2H), 9.47 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.8, 18.4, 22.6, 25.3, 28.9, 31.6, 32.9, 168.9, 171.5; IR (KBr): 3156, 2859, 1791, 1658, 1533, 1418, 1378, 1192, 1042, 852, 565 cm^{-1}; Elemental analysis: $C_9H_{17}NO_3$ (187.24) requires C, 57.73; H, 9.15; N, 7.48. found: C, 57.70; H, 9.18; N, 7.48.

***N*-Acetoxy-3-phenyl-propionamide (13a)[18d].** mp: 64–66 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.18 (s, 3H), 2.25 (t, $J = 7.6$ Hz, 2H), 2.99 (t, $J = 7.6$ Hz, 2H), 7.21 (m, 3H), 7.28 (m, 2H), 9.20 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.4, 31.2, 34.7, 126.7, 128.6, 128.8, 140.4, 168.9, 170.7; IR (KBr): 3148, 2961, 1790, 1667, 1497, 1453, 1368, 1176, 1063, 1017, 858, 747, 700, 560 cm^{-1}; Elemental analysis: $C_{11}H_{13}NO_3$ (207.23) requires C, 63.76; H, 6.32; N, 6.76. found: C, 63.75; H, 6.35; N, 6.71.

***N*-Hydroxy benzamide (1b)[9b].** mp: 124 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 7.17 (m, 2H), 7.24 (t, $J = 7.2$ Hz, 1H), 7.57 (d, $J = 8.0$ Hz, 2H), 10.9 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 126.8, 128.1, 131.1, 131.8, 165.2; IR (KBr): 3300, 2753, 1645, 1613, 1563, 1453, 1435, 1163, 1022, 898, 690 cm^{-1}; MS (ESI): 138.06 (MH^+).

***N*-Hydroxy-4-methyl-benzamide (2b)[17].** mp: 145–147 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm) 2.37 (s, 3H), 7.21 (d, $J = 7.6$ Hz, 2H), 7.71 (d, $J = 7.6$ Hz, 2H), 8.72 (br s, 1H), 11.05 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 21.2, 127.2, 129.2, 141.8, 165.8; IR (KBr): 3296, 2760, 1648, 1565, 1508, 1374, 1309, 1161, 1037, 902, 839, 738, 538 cm^{-1};

Elemental analysis: $C_8H_9NO_2$ (151.16): calcd C, 63.57; H, 6.00; N, 9.27. found: C, 63.52; H, 6.10; N, 9.20.

***N*-Hydroxy-2,5-dimethoxy-benzamide (3b).** Gummy; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 3.80 (s, 3H), 3.92 (s, 3H), 6.90 (d, J = 9.2 Hz, 1H), 7.00 (dd, J_1 = 3.2 Hz, J_2 = 2.8 Hz, 1H), 7.70 (d, J = 3.2 Hz, 1H), 10.50 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 56.0, 56.6, 112.8, 115.2, 118.8, 119.8, 151.5, 154.0, 163.7; IR (KBr): 3305, 2944, 2837, 1645, 1607, 1495, 1282, 1218, 1179, 1043, 813, 735 cm^{-1}; Elemental analysis: $C_9H_{11}NO_4$ (197.19): calcd C, 54.82; H, 5.62; N, 7.10. found: C, 54.80; H, 5.57; N, 7.15.

2-Chloro-*N*-hydroxy-benzamide (4b)[18b]. mp: 150 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 6.28 (br s, 1H), 7.30 (m, 1H), 7.38 (m, 2H), 7.49 (m, 1H), 10.50 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 126.6, 129.5, 129.8, 131.1, 131.4, 133.1, 164.3; IR (KBr): 3228, 1632, 1594, 1543, 1474, 1321, 1172, 907, 750, 724, 649 cm^{-1}; Elemental analysis: $C_7H_6ClNO_2$ (171.58): calcd C, 49.00; H, 3.52; N, 8.16. found: C, 48.97; H, 3.51; N, 8.14.

3-Chloro-*N*-hydroxy-benzamide (5b)[18b]. mp: 169–171 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 7.46 (m, 2H), 7.72 (d, J = 7.2 Hz, 1H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 124.4, 126.1, 129.1, 130.1, 132.7, 133.2, 162.6; IR (KBr): 3295, 2758, 1655, 1621, 1564, 1474, 1173, 1047, 796, 747, 726, 673, 530 cm^{-1}; Elemental analysis: $C_7H_6ClNO_2$ (171.58): calcd C, 49.00; H, 3.52; N, 8.16. found: C, 49.08; H, 3.50; N, 8.08.

***N*-Hydroxy-3-nitro-benzamide (6b)[18c].** mp: 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 7.64 (t, J = 8.0 Hz, 1H), 8.23 (d, J = 8.00 Hz, 1H), 8.32 (d, J = 7.6 Hz, 1H), 8.75 (s, 1H), 11.67 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 122.1, 125.6, 129.5, 133.2, 133.7, 147.9, 162.6; IR (KBr): 3375, 3178, 1670, 1656, 1619, 1521, 1350, 1172, 1035, 933, 715, 671 cm^{-1}; Elemental analysis: $C_7H_6N_2O_4$ (182.14): calcd C, 46.16; H, 3.32; N, 15.38. found: C, 46.18; H, 3.31; N, 15.27.

4-Bromo-*N*-hydroxy-benzamide (7b)[9b]. mp: 184–186 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 3.10 (br s, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 11.25 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 125.3, 128.5, 129.5, 131.1, 163.7; IR (KBr): 3294, 3065, 2754, 1646, 1614, 1591, 1483, 1433, 1329, 1075, 843, 742, 525 cm^{-1}; Elemental analysis: $C_7H_6BrNO_2$ (216.04): calcd C, 38.92; H, 2.80; N, 6.48. found: C, 38.85; H, 2.83; N, 6.46.

2,6-Dichloro-*N*-hydroxybenzamide (9b). mp: 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 4.30 (br s, 1H), 7.32 (m, 4H), 10.79 (br s, 1H);^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 127.4, 130.5, 132.6, 133.4, 160.9; IR (KBr): 3227, 3031, 2905, 1630, 1580, 1524, 1433, 1310, 1194, 1098, 1025, 901, 804, 780, 467 cm^{-1}; Elemental analysis: $C_7H_5Cl_2NO_2$ (206.03) requires C, 40.81; H, 2.45; N, 6.80. found: C, 40.81; H, 2.41; N, 6.78.

***N*-Hydroxycyclohexanecarboxamide (10b)[12a].** mp: 120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.25 (m, 3H), 1.47 (m, 2H), 1.69 (m, 1H), 1.80 (m, 4H), 2.08 (m, 1H), 8.37 (br s, 1H);^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 25.4, 28.6, 29.0, 41.7, 174.0; IR (KBr): 3296, 2852, 1632, 1541, 1449, 1142, 1060, 963, 808, 753, 663, 617 cm^{-1}; Elemental analysis: $C_7H_{13}NO_2$ (143.18) requires C, 58.72; H, 9.15; N, 9.78. found: C, 58.77; H, 9.18; N, 9.76.

***N*-Hydroxyheptanamide (12b)[13].** mp: 72–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.84 (t, J = 6.0 Hz, 3H), 1.18 (m, 6H), 1.47 (m, 2H), 2.01 (m, 2H), 9.50 (br s, 1H);^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ (ppm) 14.1, 22.7, 25.7, 29.3, 29.8, 31.7, 171.7; IR (KBr): 3250, 2857, 1644, 1467, 1401, 1176, 1125, 1037, 1011, 816, 690, 615, 570 cm^{-1}; Elemental analysis: $C_7H_{15}NO_2$ (145.20) requires C, 57.90; H, 10.41; N, 9.65. found: C, 57.93; H, 10.40; N, 9.61.

Crystal data for 9a. $C_9H_7Cl_2NO_3$ M = 248.06, monoclinic, space group $P2_1/c$, a = 9.8316(4), b = 12.1236(5), c = 8.8033(3) Å, α = 90.00, β = 92.170(2), γ = 90.00°, V = 1048.55(7) Å^3, T = 298(2) K, Z = 4, μ(Mo-Kα) = 0.71073 Å, colourless block, crystal dimensions 0.50 × 0.30 × 0.20 mm, crystal density 1.571. Full matrix least squares based on F^2 gave R_1 = 0.0299 and wR_2 = 0.0753 for 1655 ($I \geq 2\sigma(I)$), GOF = 1.046 for 141 parameters. CCDC 744680.†

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17 The ratio of the two products (**1a**) and (**1c**) was determined by ^{1}H NMR. Spectral data of the mixture of products: *N*-acetoxy benzamide (**1a**) + *N*-propionyloxy benzamide (**1c**) (60 : 40): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.25 (t, J = 7.6 Hz, 1H), 2.28 (s, 3H), 2.57 (m, 2H), 7.43–8.16 (m, 10H), 9.76 (br s, 1H); IR (KBr): 3152, 2952, 2813, 1793, 1769, 1653, 1579, 1487, 1241, 1179, 1021, 897, 694 cm^{-1}.

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