Solvent and catalyst free *N*-formylations of amines at ambient condition: Exploring the usability of aromatic formates as *N*-formylating agents

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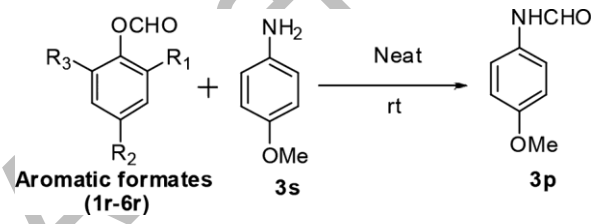
Abstract

A solvent and catalyst free *N*-formylation protocol has been developed for amines (**1s-21s**) where aromatic formates (**1r-6r**) were used as the *N*-formylating agents. The amine substrates include both primary and secondary aromatic amines (**1s-19s**) as well as aliphatic amine (**20s**) and a primary amide (**21s**). Structures of both the aromatic formate and amine components strongly influenced the rate of the reaction and yield of the *N*-formamide products. The reaction condition is mild and easy to operate. This protocol can be done smoothly under ambient condition and gives high yield of formamide products. Furthermore, the present method can not be applied for the formylation of thiol group (**22s**). This signifies its possible use for the chemoselective *N*-formylation of amine in presence of thiol functionality.



KEYWORDS: *N*-formylation, Aromatic formates, Amines.

INTRODUCTION

N-formylation reaction is often regarded as the key step in the synthesis of plethora of important organic precursors, intermediates, reagents and bioactive compounds.[1-6] Various amines undergo *N*-formylations leading to different types of formamide derivatives and structure of these compounds controls their usefulness in a specific organic reaction. Formamides are used as the precursors in the synthesis of formamidines and isocyanides. [1-2, 6-8] These compounds are being used as the synthetic intermediates for the preparation of bioactive heterocyclic compounds. [2, 9, 10] Being Lewis basic in nature, formamides find application as catalyst in the allylation **[11]** and hydrosilylation **[12]** of carbonyl compounds. Moreover, chiral formamides are being used in the asymmetric allylation of aldehyde functionalities. [13] *N*-formylation reaction is also extensively used in the organic synthesis (e.g. in the peptide synthesis) to protect the amino group. [14] Apart from these, one of the most well known applications of formamides is their use as the reagent in the Vilsmeir formylation reaction.[15] Furthermore, formamides are extensively used as solvents in various cases.[16]

So the development of easy, environment friendly and cost effective synthetic methods for the synthesis of task-specific formamides is a highly cherished goal for the synthetic organic chemists and over the years, researchers have developed a number of *N*-formylation methods. Mixed anhydrides (e.g. acetic formic anhydride [17]) are the most extensively used formylating agents. But these types of reagents are moisture sensitive and decomposed to acetic acid and carbon monoxide on storage.[2] Besides this, use of activated formic acid/DCC or EDCI, .[18, 19] chloral [20] and various solid-supported reagents [21] are quite common as *N*-formylation reagents. However, these reagents are

not free from the drawbacks like high hygroscopic nature, toxicity and high cost. On the other hand, various formates e.g. ammonium formates [20], cyanomethyl formate [22], 2,2,2-trifluoroethyl formate [23] and other aliphatic formates are often used as the source of formyl group in *N*-formylation reactions. In addition to these, ethyl or phenyl formate often serves as a promising alternative but longer reaction time and heating at high temperature are necessary for the completion of the *N*-formylation reactions.[2, 24] H.L. Yale reported the use of phenyl formate as the *N*-formylation agent at very low temperature.[25] But in that reported work[25] , phenyl formate used was not be separated from the starting phenol substrate and other impurities were also present in it.

Certainly, each of these methods have some merits but they are also not free from the drawbacks like complicated synthesis of the *N*-formylating reagents and thermal instability of these *N*-formylating reagents, formation of undesired by-products, prolong reaction time and high temperature.[1-3,5-6] Moreover, the nature of the catalyst and solvent often the control the outcome of the *N*-formylation reaction. [5-6]

In the present work, we have synthesized and isolated in pure form a series of aromatic formates (**1r-6r**) (fig.1) according to the method previously developed by us **[26]** and explored their efficacy in the *N*-formylation of a series of primary and secondary amines (both aromatic and aliphatic) and also a primary amide type of compound under solvent and catalyst free condition at ambient temperature.

These formylating agents are easy to synthesize (scheme 1) and they are not thermally unstable or hygroscopic which made them suitable as *N*-formylating agents. However,

best result (in terms of yield and reaction time) was obtained with *p*-chlorophenyl formate (**3r**) as the *N*-formylating agent (scheme 2). We have also studied the role of solvent on the reaction time/rate and yield of the *N*-formylated products synthesized by the present protocol.

RESULT AND DISCUSSION

Several combinations of aromatic formates (**1r-6r**) and aromatic amines (**1s-21s**) were tried to optimize the reaction condition. However, to test the efficacy of the six aromatic formates (**1r-6r**) towards *N*-formylation reaction, we have used *p*-methoxy aniline (**3s**) as the model substrate. Results are displayed in Table 1. Best result (in terms of reaction time and yield) was obtained when *p*-chlorophenyl formate (**3r**) was used as the *N*-formylating reagent and the substrate was *p*-methoxy aniline (**3s**) (scheme 2) (Table 1). The plausible mechanistic pathway is very simple as shown in scheme 3.

Apart from **3r**, *p*-bromophenyl formate (**4r**) was also found to be effective for the *N*-formylation of the substrate, **3s** (table 1). It is evident from scheme 3 that the carbonyl group of aromatic formates behaves as the electrophilic centre whereas amines act as the nucleophilic centre. The electrophilicity of the carbonyl C-centre of aromatic formates is high when it has an electron withdrawing substituents like Cl/Br. On the other hand, electron donating group on the aromatic nucleus enhances the nucleophilicity of amine functionality. This ultimately facilitates the *N*-formylation reaction as observed under the present protocol. Cl/Br has weak resonance dipole but the electronegativity dipole (electron withdrawing effect) for Cl is higher than that of Br. In the present case, this

phenomenon may be responsible for the better efficacy of *p*-chlorophenyl formate (**3r**) as *N*-formylating agent than *p*-bromophenyl formate (**4r**). However, besides the presence of electron withdrawing group on the aromatic nucleus, steric hindrance can be another controlling factor towards the reactivity of aromatic formates (as in the case **5r** and **6r**) and comparatively low yield and longer reaction time were observed in these cases (table 1).

To further optimize the reaction condition regarding the effect of solvent on the yield and reaction completion time, we have performed the same reaction [using *p*-Methoxy aniline (**3s**) (1 mmol) and *p*-chlorophenyl formate (**3r**) (1 mmol) as model substrate and reagent respectively] in the presence of different polar and non-polar solvents and the results are shown in table 2.

Present protocol was found to be most suitable under solvent-free condition with respect to the maximum % yield of **3p** and minimum reaction completion time. However, better % yield and shorter reaction time was observed in case of non-polar solvents in comparison to the polar solvent systems (table 2). Later, we have extended this standardized and optimized procedure towards the other combination of substrates and *p*-chlorophenyl formate (**3r)** as the *N*-formylating reagent and same trend was observed.

It is note-worthy that *p*-chlorophenyl formate (**3r**) showed considerably good yield with other aromatic amines as shown in table 3 under the same reaction condition. Total 21 formamide derivatives (**1p-21p**) were synthesized and isolated in pure form under the

present work (table 3). The synthesized products were characterized with the help of spectroscopic and other analytical data (detail is given in the supplementary information).

Results shown in the above table point out that the present *N*-formylation protocol is effective for wide varieties of amines ranging from aromatic amines (both primary and secondary) (**1s-19s**) as well as aliphatic amine (**20s**) to a primary amide type of functionality (**21s**). Moreover, to study the structural effect of the substrates on the rate of the reaction, we have selected aromatic amine substrates having electron donating and electron withdrawing substituents at *o,m* and *p* positions of its aromatic ring.

A detailed scrutiny of the results (table 3) points towards some interesting facts as discussed here. Present protocol was found to be more effective (in terms of % yield and reaction completion time) for both the primary and secondary aromatic amines (**1s-19s**) than the aliphatic amine (**20s**) or the amide **(21s**) substrates. Aromatic amines having both the electron donating or electron withdrawing substituent can be *N*-formylated by the present method. However, slight difference in their reactivity was observed. Presence of electron donating substituent on the aromatic ring of the amine was found to be a favorable factor as it increases the nucleophilicity of the amine group which ultimately facilitates the reaction rate. This effect was found to be maximum when there is a -OMe group at *p*-position of the aromatic ring with respect to the $-NH_2$ group as it is observed in the case of **3s**. Longer reaction time was noticed in the case of substrates having electron withdrawing group at *o*- or *p*-positions as in the cases of **11s**, **13s**, **14s** and **15s** (table 3). However, presence of electron withdrawing group at *m*-position do not show

that much influence on the reaction pathway as it is evidenced in the case of **12s**. Electron withdrawing substituents can deactivate the amine substrate by decreasing its nucleophilicity and slower reaction rate was observed. Fused ring primary aromatic amine (**17s, 18s**) and heterocyclic aromatic primary amine (**16s**) also showed good response towards the present protocol. Primary amide group like that present in **21s** was also *N*-formylated by *p*-chlorophenyl formate (**3r**) under the present reaction condition but as the amine part is deactivated due to the electron withdrawing effect of amide carbonyl group, a very long reaction completion time was observed. Halogen substituted aromatic amines (**5s** and **6s**) can also be *N*-formylated by the present method and we have been able to get crystal structure of the product, *N*-(4-bromophenyl)formamide (**6p**) as shown in fig.2.

Present method was not found to be effective in the formylation of thiol group as in the case of (**22s**). This further opens up the possibility of the application of this method in the chemoselective *N*-formylation in presence of thiol group.

CONCLUSION

We have developed a solvent and catalyst free *N*-formylation protocol for amine type of compounds (**1s-21s**) using aromatic formates (**1r-6r**) as the *N*-formylating agents. The reaction condition is mild, easy to operate and it occurs smoothly under ambient condition giving high yield of formamide derivatives of the corresponding amine substrate. The present method is applicable to wide varieties of amine substrates ranging from aromatic amines (both primary and secondary) (**1s-19s**) as well as aliphatic amine

(**20s**) to a primary amide type of functionality (**21s**). Aromatic amines having electron donating or electron withdrawing substituent can be *N*-formylated by the present method. However in all the cases, *p*-chlorophenyl formate (**3r**) was found to most suitable *N*-formylating agent in terms of minimum reaction completion time and maximum yield of the *N*-formamide product and best result was obtained when *p*-methoxy aniline (**3s**) (1 mmol) (model substrate) and *p*-chlorophenyl formate (**3r)** (1 mmol) (model reagent) were reacted under neat and catalyst free conditions. Furthermore, the present method could not be applied for the formylation of thiol group (**22s**) which signifies the possibility of chemoselective *N*-formylation of amine in presence of thiol group by the present method. All the *N*-formamide products were characterized on the basis of physico-chemical and spectroscopic data. The structure of product *N*-(4-bromophenyl) formamide (6p) was further confirmed by X-ray crystallography study (Fig. 2)**.** [27]

EXPERIMENTAL

Analytical Data For Selected Compounds: *N-(4-Methoxyphenyl) Formamide (3p)* **[27, 28]**

Yield-99 %,(149.6 mg), M.P. (^{o}C) 78-82, LCMS ($M+H^{+}$)-152. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.25 (s, 1H), 7.36 (d, 1H, *J* =8.8 Hz), 6.95 (d, 1H, *J* =8.8 Hz), 6.78-6.83 (m, 2H, *J* =8.8 Hz), 3.73(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.55, 114.22, 114.91, 121.70, 121.81, 130.21, 158.91, 163.25. IR (KBr): 3262, 3058, 2893, 2834, 2544, 2313, 2047, 1885, 1687, 1609, 1534, 1403, 1306, 1237, 1168 cm^{-1}. Elemental analysis (%), Calcd for $C_8H_9NO_2$: C, 63.56; H, 6.00; N, 9.27. Found. C, 63.76; H, 5.89; N, 9.39.

N-(4-Bromophenyl) Formamide (6p) [27, 28]

Yield-98%, (196 mg), M.P.(^{o}C) 117-121, LCMS (M-H^{+})-198. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.40 (s, 1H), 8.39 (s, 1H), 7.41-7.51 (m, 2H), 6.98-6.02 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 118.21, 120.27, 121.56, 132.03, 132.73, 135.89 162.48. IR (KBr): 3288, 3050, 2872, 2681, 2363, 1894, 1673, 1595, 1534, 1393, 1248, 1181 cm^{-1}. Elemental analysis (%), Calcd for C_7H_6BrNO: C, 42.03; H, 3.02; N, 7.00. Found. C, 42.29; H, 2.98; N, 7.21.

Single crystal X-ray crystallography for (6p): Empirical formula= C_7H_6BrNO, Fw = 200.03, T = 296 K, Orthorhombic, space group =P b c a, Hall group = - P 2ac 2ab ,a =10.789(2)A^{0} , b = 9.8239(18) A^{0} , c = 13.878(3) A^{0}, α = 90, β = 90 γ = 90, V = 1470.9(5), Z = 8, Dx = 1.807 g/cm^{-3}, λ (MoKa) = 0.71073 A^{0}, μ = 5.513 mm^{-1}, F000 = 784.0, F000' = 782.10. θ_{max} =25.00 , R = 0.0574(849) , wR2 = 0.1575(1298), S = 1.098, Bond precision: C- C = 0.0088 A^{0} , h,k,l_{max}=12,11,16 . N_{ref} =1299, N_{par}= 91. Crystallographic data for the structures of 6p reported in the present work have been deposited at the Cambridge Crystallographic Data Centre with CCDC No.1035596.

N,N-Diphenylformamide (19p) [28, 29]

Yield-98%, (193.3 mg), M.P. (^{o}C**)** 66-68, LCMS (M+H^{+})-198. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.60 (s, 1H), 7.30-7.35 (m, 4H), 7.18-7.24 (m, 4H), 7.09-7.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 126.13, 126.89, 127.06, 129.20, 161.77. . IR (KBr): 3313, 3059, 2852, 2355, 1686, 1535, 1593, 1490, 1337, 1264, 1134 cm^{-1}.

Elemental analysis (%), Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found. C, 79.31; H, 5.64; N, 7.23.

N-Benzylformamide (20p) [27]

Yield-90 %, (121.6 mg), M.P. (^oC) 46-48, LCMS ($M+H^+$)-136. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (s, 1H), 7.25-7.39 (m, 6H), 4.48 (d, 2H, *J* =6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.73, 110.04, 121.07, 121.11, 124.29, 147.88, 158.78. IR (KBr): 3293, 3045, 2866, 2758, 2353, 1960, 1676, 1535, 1525, 1546, 1397, 1233, 1081 cm^{-1}. Elemental analysis (%), Calcd for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36. Found. C, 71.21; H, 6.64; N, 10.46.

N-Formylbenzamide (21p) [30]

Yield-90%, (134.2 mg), M.P. (^oC) 108-110, LCMS ($M+H^+$)-150. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 10.39 (s, 1H), 9.44 (d, 1H, *J* =9.6 Hz), 8.05 (d, 1H, *J* =7.5 Hz), 7.69 (t, 1H, *J* =7.2 Hz),), 7.58(t, 2H, *J* =7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 128.15, 128.98, 129.06, 131.07, 133.95, 164.93, 166.77. IR (KBr): 3313, 3059, 2852, 2355, 1686, 1535, 1593, 1490, 1337, 1264, 1134 cm^{-1}. Elemental analysis (%), Calcd for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found. C, 64.39; H, 4.64; N, 9.53.

SUPPLEMENTAL MATERIAL

General experimental, characterization data of *N*-formylated products and related references, ^1H and ^{13}C NMR, LC-MS and IR Spectra of *N*-formylated products can be accessed on the publisher's website.

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REFERENCES

[1] Kim, J.-G.; Jang, D. O. *Synlett* **2010**, 14, 2093-2096.

[2] Hosseini-Sarvari, M.; Sharghi, H. *J. Org. Chem.* **2006**, 71, 6652-6654.

[3] Yang, D.; Jeon, H. B. *Bull. Korean Chem. Soc.* **2010**, 31, 1424-1426

[4] Bahari, S.; Mohammadi-Aghdam, B.; Sajadi, S. M.; Zeidali, F. *Bull. Korean Chem. Soc.* **2012**, 33, 2251-2253.

[5] Lv, H.; Xing, Q.; Yue, C.; Lei, Z.; Li, F. *Chem. Commun.* **2016**, 52, 6545-6548.

[6] Akbari, J.; Hekmati, M.; Sheykhan, M.; Heydari, A. ARKIVOC (XI) **2009**, 11, 123-129.

[7] Han, Y.; Cai, L. *Tetrahedron Lett.* **1997**, 38, 5423-5426.

[8] Schöllkopf, U. *Angew. Chem. Int. Ed. Engl.* **1977**, 16, 339-348.

[9] Chen, B.C.; Bednarz, M. S.; Zhao, R.; Sundeen, J. E.; Chen, P.; Shen, Z.; Skoumbourdis, A. P.; Barrish, J. C. *Tetrahedron Lett.* **2000**, 41, 5453-5456.

[10] Kakehi, A.; Ito, S.; Hayashi, S.; Fujii, T. *Bull. Chem. Soc. Jpn*. 1995, 68, 3573-3580.

[11] Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, 59, 6620-6628.

[12] Kobayashi, S.; Yasuda, M.; Hachiya, I. *Chem. Lett.* **1996**, 25, 407-408.

[13] Iseki, K.; Mizuno, S.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron* **1999**, 55, 977-988.

[14] Martinez, J.; Laur, J. *Synthesis* **1982**, 979-981.

[15] Downie, I. M.; Earle, M. J.; Heaney, H.; Shuhaibar, K. F. *Tetrahedron* **1993**, 49, 4015-4034.

[16] Tlili, A.; Blondiaux, E.; Frogneux, X.; Cantat, T. *Green Chem*. **2015**, 17, 157-168.

[17] Strazzolini, P.; Giumanini, A. G.; Cauci, S. *Tetrahedron* **1990**, 46, 1081-1118.

[18] Waki, J.; Meienhofer, J. *J. Org. Chem.* **1977**, 42, 2019-2020.

[19] Chen, F. M. F.; Benoiton, N. L. *Synthesis* **1979**, 9, 709-710.

[20] Blicke, F. F.; Lu, C.-J. *J. Am. Chem. Soc.* **1952**, 74, 3933-3934.

[21] Desai, B.; Danks, T. N.; Wagner, G. *Tetrahedron Lett.* **2005**, 46, 955-957.

[22] Sheehan, J. C.; Yang, D. D. H. *J. Am. Chem. Soc.* **1958**, 80, 1154-1158.

[23] Flöresheimer, A.; Kula, M. *Monatsh. Chem*. **1988**, 119, 1323-1331.

[24] Schmidhammer, H.; Brossi, A. *Can. J. Chem.* **1982**, 60, 3055-3060.

[25] Yale, H. *J. Org. Chem.* **1971**, 36, 3238-3240.

[26] Shaikh, B.; Ali, M. A.; Chatterjee , A.; Alam, M. N.; Das, S.; Mandal, D.; Begum, N. A. *Synth. Commun* . **2016**, 46, 692-700.

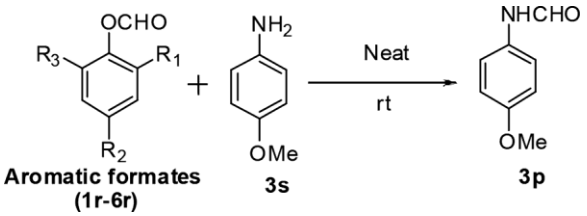
[27] Das, B.; Krishnaiah, M.; Balasubramanyam, P.; Veeranjaneyulu, B.; Kumar, D. N. *Tetrahedron Lett*. **2008**, 49, 2225-2227.

[28] Zhao, Z.; Ge, G.; Li, W.; Guo, X.; Wang, G. *Chin. J. Catal.* **2016**, 37, 644–670.

[29] Sajadi, S. M.; Maham, M.; Rezaei, A. *Lett. Org. Chem.* **2014**, 45, 49-54.

[30] Brahmachari, B.; Laskar, S.; *Tetrahedron Lett*. **2010**, 51, 2319–2322.

Table 1: Optimization towards the selection of aromatic formates as the *N*-formylating reagent for *p*-methoxy aniline (**3s**), selected as model the substrate [a].



Aromatic formates (1r-6r) **3s** **3p**

Entry	Reagent	Time	Yield (%)[b]
1	**1r**	1 hr	99
2	**2r**	2 hr	99
3	**3r**	30 min	99
4	**4r**	40min	99
5	**5r**	8 hr	94
6	**6r**	24 hr	93

[a] Reaction condition: *p*-Methoxy aniline (**3s**) (1 mmol) (model substrate) and various aromatic formates (1 mmol) under neat condition.

[b] Isolated yields.

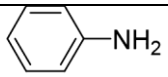
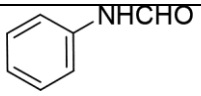
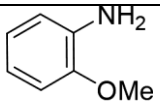
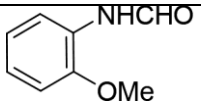
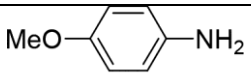
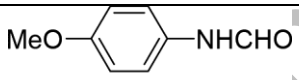
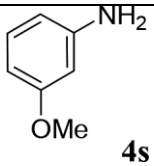
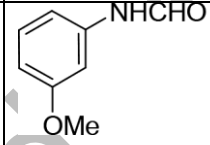
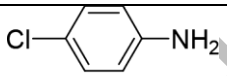
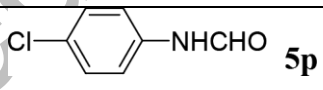
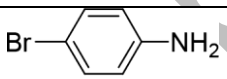
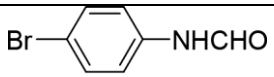
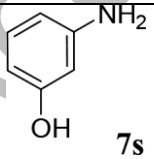
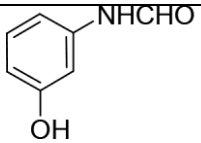
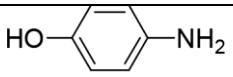
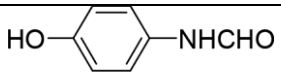
Table 2: Optimization of reaction condition (neat/solvent)[a].

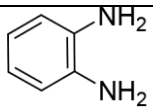
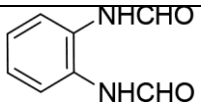
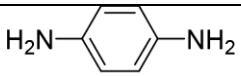
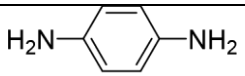
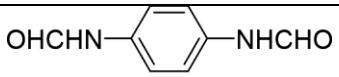
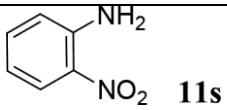
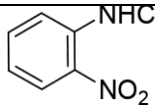
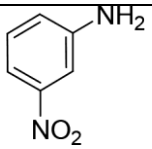
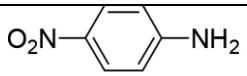
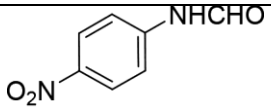
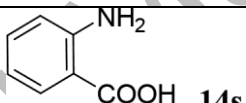
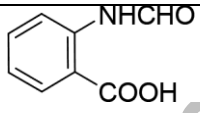
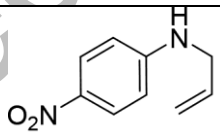
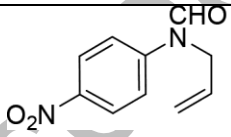
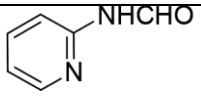
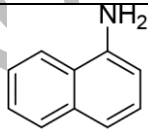
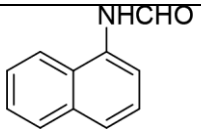
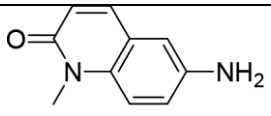
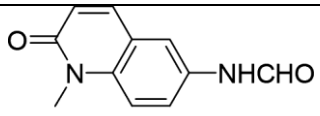
Entry No.	Solvent	Time	Yield[b] (%)
1	Neat	30 min	99
2	Hexane	1.5 hr	97
3	p-Xylene	1.5 hr	97
4	Toluene	1.5 hr	97
5	DCM	1.5 hr	96
6	Ethanol	3.5 hr	94
7	Methanol	3.5 hr	93
8	DMF	6.0 hr	88
9	DMSO	6.5 hr	83
10	Water	4.0 hr	81

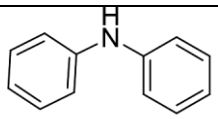
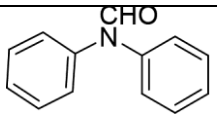
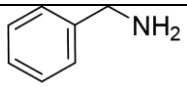
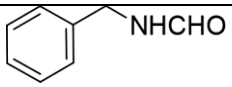
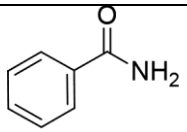
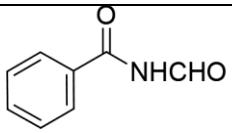
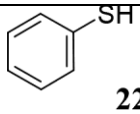
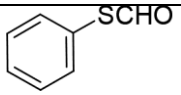
[a] Reaction condition: *p*-Methoxy aniline (**3s**) (1 mmol) (model substrate) and *p*-chlorophenyl formate (**3r)** (1 mmol) (model reagent) were reacted under neat condition as well as in presence of solvent (3 ml) to get the product, *N*-(4-methoxyphenyl)formamide (**3p**).

[b] Isolated yields.

Table 3. Synthesis of *N*-formyl amine derivatives using *p*-chlorophenyl formate (3r) as the *N*-formylating reagent under solvent and catalyst free condition.[a]

Entry	Substrate	Product	Time	Yield (%)[b]	M.P. (^{o}C)
1	 **1s**	 **1p**	3 hr	95	47-49
2	 **2s**	 **2p**	1 hr	99	80-82
3	 **3s**	 **3p**	30 min	99	78-82
4	 **4s**	 **4p**	2 hr	97	45-48
5	 **5s**	 **5p**	2 hr	98	100-102
6	 **6s**	 **6p**	2.5 hr	98	117-121
7	 **7s**	 **7p**	2.5 hr	97	104-106
8	 **8s**	 **8p**	3 hr	95	132-136

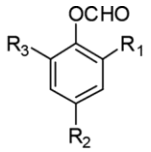
9	 **9s**	 **9p**	2 hr	98	156-158
10	 **10s**	 **10s**	2 hr	98	154-156
11	 **10p**	 **11s**	10 hr	90	120-124
12	 **11p**	 **12s**	4 hr	93	126-128
13	 **12p**	 **13s**	12 hr	92	186-188
14	 **13p**	 **14s**	14 hr	93	164-166
15	 **14p**	 **15s**	16 hr	90	75-78
16	 **15p**	 **16p**	3 hr	97	78-80
17	 **17s**	 **17p**	5 hr	97	136-138
18	 **18s**	 **18p**	6 hr	97	202-206

19	 **19s**	 **19p**	2 hr	98	66-68
20	 **20s**	 **20p**	3.5 hr	90	46-48
21	 **21s**	 **21p**	24 hr	90	108-110
22	 **22s**	 **22p**	24 hr	0	-

[a] Reaction condition: Amine substrates (**1s-21s**) or thiophenol (**22s**) (1 mmol) and *p*-chlorophenyl formate (**3r)** (1 mmol) (model *N*-formylating reagent) were reacted under neat condition.

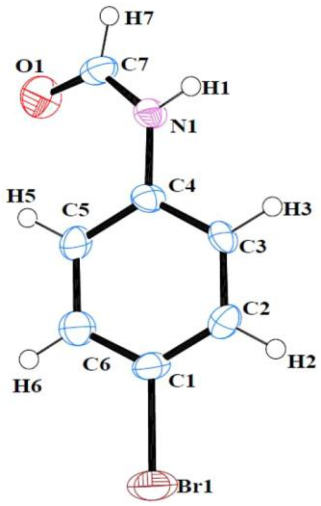
[b] Isolated yields.

Figure 1: Aromatic formates used as *N*-formylating agents

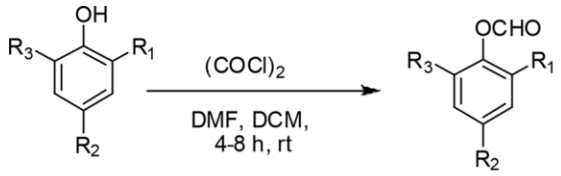


1r. R_1= R_2= R_3=H: Phenyl formate
2r. R_1= R_3=H, R_2=Me: *p*-Methylphenyl formate
3r. R_1= R_3=H, R_2=Cl: *p*-Chlorophenyl formate
4r. R_1= R_3=H, R_2=Br: *p*-Bromophenyl formate
5r. R_1= R_3=Me, R_2=H: 2,6-Dimethylphenyl formate
6r. R_1= ^{t}Bu, R_2=OMe, R_3=H: 2-tert-Butyl-4-methoxyphenyl formate

Figure 2. Single crystal X-ray diffraction structure of *N*-(4-bromophenyl) formamide (6p) [27]

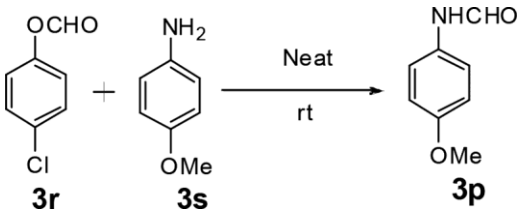


Scheme 1. Synthesis of aromatic formates used as *N*-formylating agents [26].



1r. R_1= R_2= R_3=H: Phenyl formate
2r. R_1= R_3=H, R_2=Me: *p*-Methylphenyl formate
3r. R_1= R_3=H,R_2=Cl:*p*-Chlorophenyl formate
4r. R_1= R_3=H, R_2=Br: *p*-Bromophenyl formate
5r. R_1= R_3=Me, R_2=H: 2,6-Dimethylphenyl formate
6r. R_1=^{t}Bu, R_2=OMe, R_3=H: 2-tert-Butyl-4-methoxyphenyl formate

Scheme 2. *N*-formylation of 4-methoxyaniline (3s) using 4-chlorophenyl formate (3r) as *N*-formylating agent at ambient temperature and under solvent and catalyst free condition.



Scheme 3: Plausible mechanistic pathway of the *N*-formylations of amines by aromatic formates.