A convenient and efficient protocol for the synthesis of symmetrical *N,N′*-alkylidine bisamides by sulfamic acid under solvent-free conditions

Nagarajan Panneer Selvam, Sundar Saranya, and Paramasivan T. Perumal

Abstract: A simple and convenient approach to the synthesis of symmetrical *N,N′*-alkylidine bisamides is described. Aromatic and aliphatic nitriles react with aromatic aldehydes in the presence of sulfamic acid to give the corresponding bisamides in moderate yields.

Key words: alkylidine bisamides, nitrile, sulfamic acid.

Résumé : On a mis au point une méthode simple et pratique de réaliser la synthèse de *N,N′*-alkylidinebisamides symétriques. Les nitriles aliphatiques et aromatiques réagissent avec les aldéhydes aromatiques, en présence d'acide sulfamique, pour conduire à la formation des bisamides correspondants avec des rendements modérés.

Mots-clés : alkylidinebisamides, nitrile, acide sulfamique.

[Traduit par la Rédaction]

Introduction

The amidation of organic compounds using nitriles is a very useful tool in organic chemistry, as amide moieties are important constituents of many biologically significant compounds. In the last years, retro-amide links have successfully been incorporated in the synthesis of retro-inverso peptide analogues, such as enkephalinamide (1), substance P (2), somatosatin (3), or gastrin (4). Residues with retro-amide links are also the basic units of some aliphatic polyamides (nylons) (5), which are closely related to fibrous proteins. Specifically, bisamides are key fragments for the introduction of gem-iminoalkyl residues in retro-inverso pseudo peptide derivatives (6) by treating the corresponding amide with iodobenzene bistrifluoroacetate (7). In this regard, bisamides are of considerable interest in the synthesis of peptidomimetic compounds (5).

Result and discussion

Magat et al. (8) reported the synthesis of bisamides using sulfuric acid in good yields. However, this method suffers from few disadvantages, such as the use of 85% sulphuric acid (solvent) and the scope of the reaction was limited to few aldehydes only. Hence, the development of highly expedient protocol with wide applicability is necessary for their syntheses.

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N.P. Selvam, S. Saranya, and P.T. Perumal.[1] Organic Chemistry Division, Central Leather Research Institute, Chennai 600020, India.

[1]Corresponding author (e-mail: ptperumal@gmail.com).

The increasing demands of environmental legislation have been prompting the chemical industry to minimize or preferably eliminate waste production in chemical manufacture (9). During the last few years, sulfamic acid has emerged as a substitute for conventional acidic catalysts. Sulfamic acid has been used as an efficient heterogeneous catalyst for acid-catalyzed reactions (10), Biginelli condensation (11), Beckmann rearrangement (12), inter- and intra-molecular imino Diels–Alder reactions (13), and Pechmann condensations (14). The distinctive catalytic features and intrinsic Zwitter ionic property of sulfamic acid are very different from conventional acidic catalysts. This has encouraged us to investigate further the application of sulfamic acid in carbon–carbon and carbon–hetero atom bond-forming reactions.

Recently, we reported the synthesis of acetamidophenols (15) from aldehydes, β-naphthols and acetonitrile via modified Ritter-type protocol catalyzed by anhyd. ceric sulphate. Encouraged by these results, we also extented the protocol by replacing β-naphthols with activated substituted benzenes, like anisole, toluene, and so forth. Interestingly, we observed that anisole or toluene was not involved in the reaction, while the aldehyde reacted with acetonitrile in the presence of anhyd. ceric sulfate, yielding symmetrical bisacetamides as the major product (Scheme 1).

However, this methodology suffers from few limitations; the reaction was not complete even after refluxing for 24 h, and it requires stoichiometric amount of catalyst. Hence, to overcome these limitations, we focused on an efficient and eco-benign protocol for the synthesis of bisamides.

In the present study, we report a highly efficient method for the synthesis of biologically valuable bisamides from aromatic aldehydes with a series of nitriles using sulfamic acid in moderate yields (Scheme 2).

Initially, we carried out the reaction of 4-nitrobenzaldehyde in acetonitrile using various catalysts for the synthesis of bisacetamides (Scheme 3). After systematic screening

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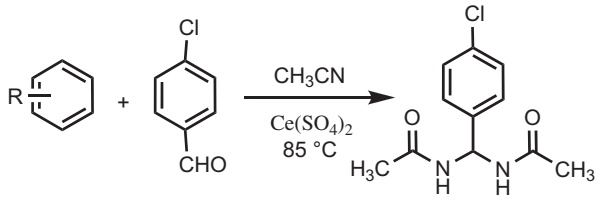
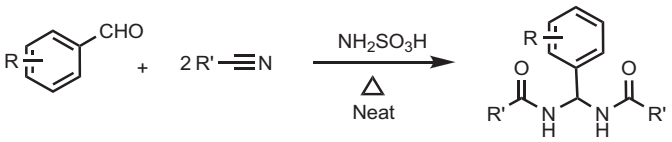
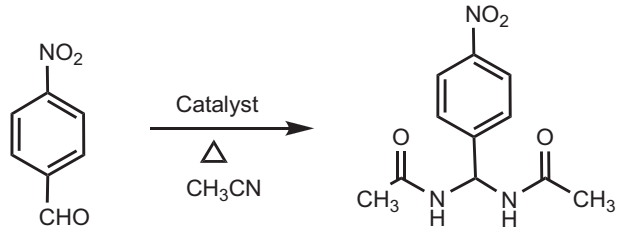
Scheme 1.



Scheme 2.



Scheme 3.



(Table 1), sulfamic acid was found to be the catalyst of choice. Similarly, the mole ratio of sulfamic acid was studied and found 50 mol% of sulfamic acid to be optimum.

We extended our protocol with various substituted aromatic nitriles. In the course of our study, we investigated the reaction of 3-nitrobenzaldehyde and 2-chlorobenzonitrile with sulfamic acid using various solvents for the synthesis of bisamides (Scheme 4), and found that solvent-free condition was the best for the conversion. The results are listed in Table 2.

The reaction was carried out with aldehyde (10 mmol) and nitrile (22 mmol) in the presence of sulfamic acid (50 mol%) and heated at 125 °C under solvent-free condition. This protocol is remarkably simple and requires non-hazardous reagents or inert atmosphere.

A mechanistic rationale portraying the probable sequence of events is given in Scheme 5. The substrate scope of the reaction under the optimized condition was investigated, and the results are summarized in Table 3. The reaction was amenable to wide variations in nitriles. The reaction went smoothly with aromatic aldehydes containing electron-withdrawing groups, while no product formation was seen with electron-rich aldehydes and aliphatic aldehydes. However, in the case of terephthalaldehyde, mono bis-amide was formed, wherein only one aldehydic group was involved in the reaction with nitrile (Table 3, entry 5).

Conclusion

Clearly, the results show that the sulfamic-acid-catalyzed protocol provides an efficient tool for the synthesis of *N*,*N*′-alkylidine symmetrical bisamides under relatively mild conditions. In conclusion, we have developed a green approach to the synthesis of symmetrical bisamides that requires neither harsh conditions nor hazardous acids. The present protocol offers several advantages, including clean and simple reaction procedure, isolation of products by crystallization without employing purification methods like column chromatography, use of an eco-friendly catalyst, and solvent-free conditions, which make it an attractive method for the synthesis of *N*,*N*′-alkylidine symmetrical bisamides.

Table 1. Screening of catalysts.

Entry	Catalyst (1 equiv.)	Time (h)	Yield[a] (%)
1	Anhyd. $Ce(SO_4)_2$	24	48
2	$InCl_3$	48	0
3	$BiCl_3$	48	0
4	$SnCl_2{\cdot}2H_2O$	48	0
5	Sulfamic acid	20	65
6	K10 montmorillonite	48	0
7	$H_3PW_{12}O_{40}$	48	5

[a]Isolated yield.

Experimental

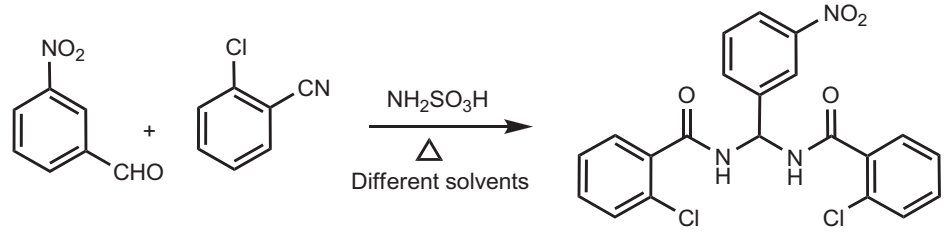
General

Glassware was dried in a hot-air oven prior to use. 2-(Trifluoromethyl)benzonitrile and benzonitrile were purchased from Lancaster Research Chemicals. All other reagents were purchased from S. D. Fine. Chem. Limited and used as received. Acetonitrile was distilled from CaH_2 under nitrogen and stored over 4 Å molecular sieves. DMSO-d_6 was purchased from Aldrich. IR measurements were done as KBr pellets for solids using PerkinElmer Spectrum RXI FTIR. The ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 with JEOL 500 MHz high-resolution NMR spectrometer. DMSO-d_6 was used as the solvent for the NMR spectral measurements, and the spectra were recorded in ppm with TMS as internal standards. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), multiplet (m), and broad (br). Mass spectra were recorded by using an Electrospray Ionization Method with Thermo Fennigan Mass spectrometer. Melting points were determined in capillary tubes and are uncorrected. Analytical TLC was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2 mm thickness (Macherey–Nagel, Germany). Elemental analysis data were recorded using Thermo Finnigan FLASH EA 1112 CHN analyzer. Column Chromatography was carried out using 100–200 mesh silica gel.

Representative procedure for the synthesis of *N*,*N*′-alkylidine bisamides

A mixture of aldehyde (10 mmol), nitrile (22 mmol), and sulfamic acid (5 mmol) was stirred at 125 °C for the appropriate time as mentioned in Table 3. When acetonitrile (taken in excess, 10 mL) was used, the reaction was carried out at 85 °C. After the completion of the reaction (as monitored by TLC), ethanol:water (8:2 mL) was added, and the reaction mixture was refluxed for 20 min and allowed to stay overnight. The solid obtained was filtered and dried.

Scheme 4.



Scheme 5.

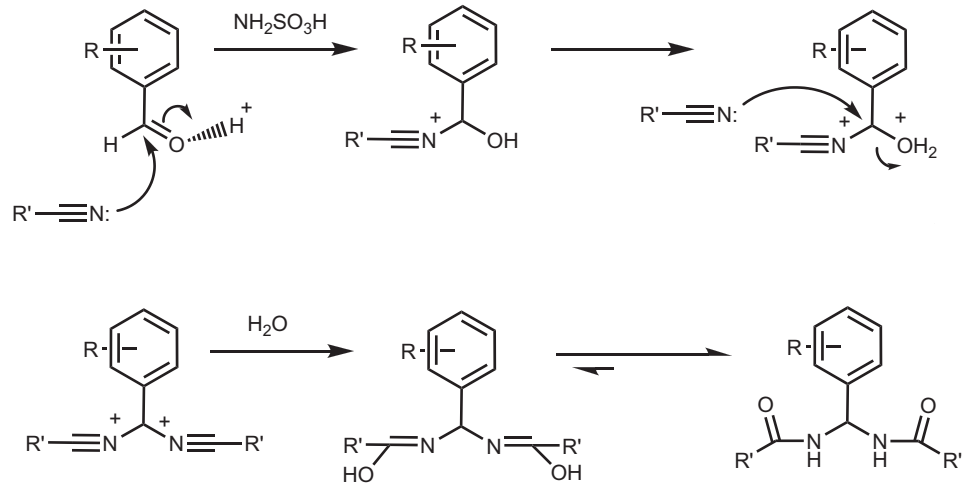


Table 2. Solvent-effect study.

Entry	Solvent	Temperature	Yield[a] (%)
1	1,2-Dichloroethane	Reflux	34
2	1,2-Dichlorobenzene	Reflux	Trace
3	PhMe	Reflux	22
4	Xylene	Reflux	48
5	Neat	125 °C	68

[a]Isolated yield.

N-[acetylamino-(4-nitrophenyl)methyl]-acetamide (Table 3, entry 1)

Pale brownish yellow solid. Yield: 65%, mp: 270–272 °C (Lit. 272 °C) (16). IR ν_{max}: 3270, 3107, 1672, 1518, 1352, 1194, 1094, 824 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ: 1.85 (s, 6H), 6.53 (t, 1H, J = 7.65 Hz), 7.54 (d, 2H, J = 8.4 Hz), 8.17 (d, 2H, J = 9.15 Hz), 8.70 (d, 2H, J = 7.5 Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 22.94, 57.45, 123.99, 128.28, 147.41, 148.36, 169.53. MS (ESI): 251 (M^+). Anal. calcd. for $C_{11}H_{13}N_3O_4$: C 52.59, H 5.22, N 16.73. Found: C 52.68, H 5.15, N 16.67%.

N-[acetylamino-(4-chlorophenyl)methyl]-acetamide (Table 3, entry 2)

White solid. Yield: 60%, mp: 258–260 °C (Lit. 260–261 °C) (17). IR ν_{max} KBr: 3271, 3123, 1670, 1093, 1529, 1370 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ: 1.83 (s, 6H), 6.42 (t, 1H, J = 8.05 Hz), 7.28 (d, 2H, J = 8.6 Hz), 7.37 (d, 2H, J = 8.6 Hz), 8.52 (d, 2H, J = 8.05 Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 22.96, 57.33, 128.73, 128.80, 132.66, 139.87, 169.35. LR-MS (EI^+): 240 (M^+). Anal. calcd. for $C_{11}H_{13}N_2O_2Cl$: C 54.89, H 5.44, N 11.64. Found: C 54.86; H 5.42; N,11.62%.

N-[acetylamino-(3-nitrophenyl)methyl]-acetamide (Table 3, entry 3)

White solid. Yield: 68%, mp: 256–257 °C (Lit 256–257 °C) (18). IR ν_{max}: 3275, 3118, 2369, 1665, 1561, 1529, 1350, 1272, 1095, 764 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ: 1.86 (s, 6H), 6.53 (t, 1H, J = 7.45Hz), 7.62 (t, 1H, J = 8.05Hz), 7.74 (d, 1H, J = 7.45Hz), 8.14 (s, 2H, br), 8.71 (d, 2H, J = 7.45Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 98, 57.45, 121.47, 123.16, 130.50, 133.99, 143.22, 148.31, 169.49. MS (ESI): 251(M^+). Anal. calcd. for $C_{11}H_{13}N_3O_4$: C 52.59, H 5.22, N 16.73. Found: C 52.65, H 5.18, N 16.68%.

N-[acetylamino-(2-nitrophenyl)methyl]-acetamide (Table 3, entry 4)

Reddish brown solid. Yield: 60%, mp: 231–232 °C (Lit. 231–232 °C) (19). IR ν_{max}: 3273, 1668, 1526, 1359, 1097, 776 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ: 1.79 (s, 6H), 6.82 (t, 1H, J = 7.65 Hz), 7.69 (t, 3H, J = 6.9 Hz), 7.88 (d, 1H, J = 8.4 Hz), 8.62 (d, 2H, J = 7.65 Hz, D_2O exchangeable).^{13}C NMR (125 MHz, DMSO-d_6) δ: 22.74, 54.83, 124.80, 128.92, 129.69, 133.60, 134.61, 148.81, 169.29. MS (ESI): 251 (M^+). Anal. calcd. for $C_{11}H_{13}N_3O_4$: C 52.59, H 5.22, N 16.73. Found: C 52.40, H 5.26, N 16.70%.

N-[(acetylamino)(4-formylphenyl)methyl]acetamide (Table 3, entry 5)

Off white solid. Yield: 40%, mp: 258–260 °C. IR ν_{max}: 3261, 3116, 1665, 1560, 1373, 1094, 802 cm^{-1}. ^1H NMR

Table 3. Results of the reactions under the optimized conditions.

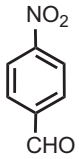
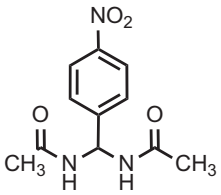
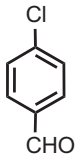
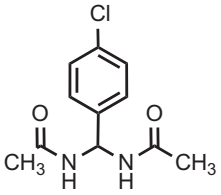
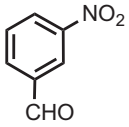
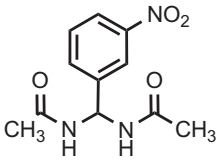
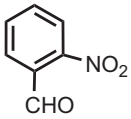
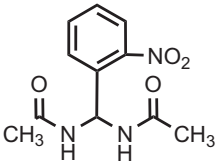
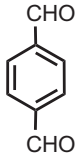
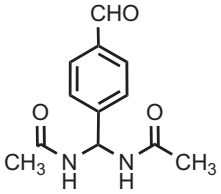
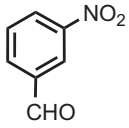
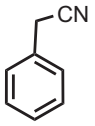
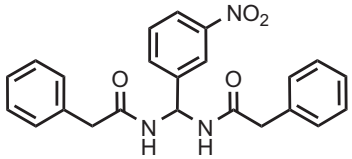
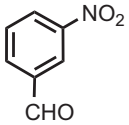
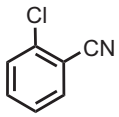
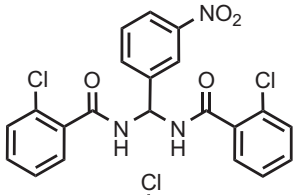
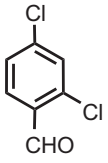
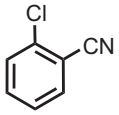
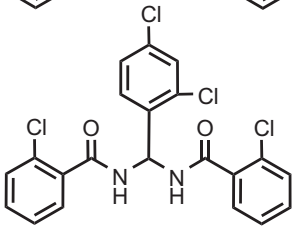
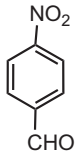
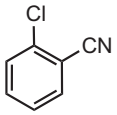
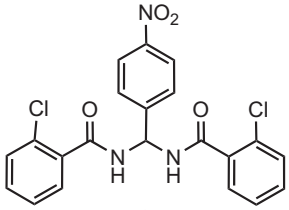
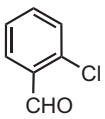
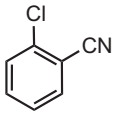
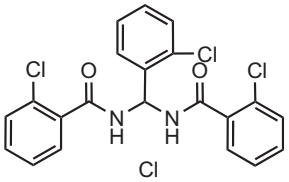
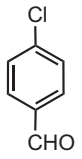
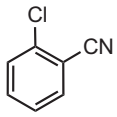
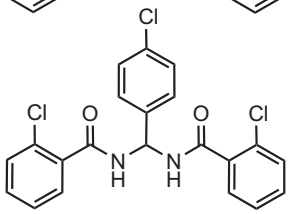
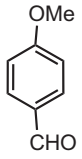
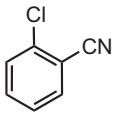
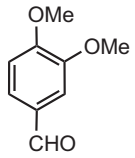
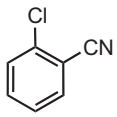
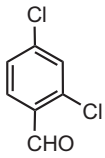
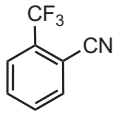
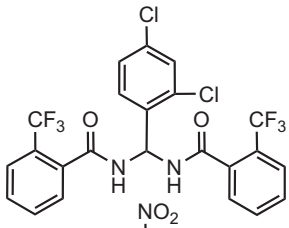
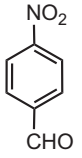
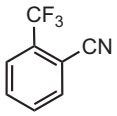
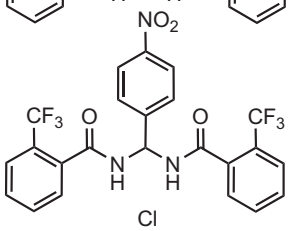
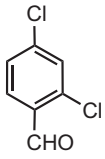
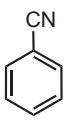
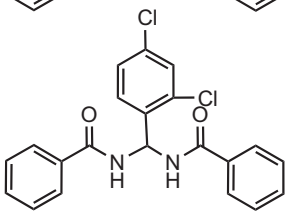
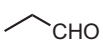
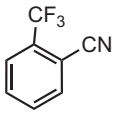
Entry	Aldehyde	Nitrile	Product[a]	Time (h)	Mp (Ref.)	Yield (%)[b]
1		CH_3CN		20	270–272 °C (Lit. 272 °C)[16]	65
2		CH_3CN		20	258–260 °C (Lit. 260–261 °C)[17]	60
3		CH_3CN		18	256–257 °C (Lit. 256–257 °C)[18]	68
4		CH_3CN		18	231–232 °C (Lit. 231–232 °C)[19]	60
5		CH_3CN		24	258–260 °C	40
6				5	214–215 °C (Lit. 216 °C)[20]	65
7				6	212–214 °C	68
8				4	202–204 °C	65

Table 3 (*concluded*).

Entry	Aldehyde	Nitrile	Product[a]	Time (h)	Mp (Ref.)	Yield (%)[b]
9				8	244–246 °C	60
10				6	223–226 °C	63
11				6	225–226 °C	68
12			No product	24	–	–
13			No product	24	–	–
14				6	244–246 °C	45
15				6	233–234 °C	60
16				8	190–192 °C	42
17			no product	24	–	-

[a]The products were characterized by IR, NMR, mass spectroscopy, and combustion analyses and compared with authentic samples.
[b]Isolated yields

(500 MHz, DMSO-d_6) δ: 1.84 (s, 6H), 6.51 (t, 1H, J = 7.65 Hz), 7.49 (d, 2H, J = 8.4Hz), 7.86 (d, 2H, J = 8.4 Hz), 8.71 (d, 2H, J = 7.65 Hz, D_2O exchangeable), 9.96 (s, 1H).^{13}C NMR (125 MHz, DMSO-d_6) δ: 22.98, 57.69, 127.67, 130.12, 136.07, 147.56, 169.36, 193.33. MS (ESI): 234 (M^+). Anal. calcd. for $C_{12}H_{14}N_2O_3$: C 61.53, H 6.02, N 11.96. Found: C 61.42, H 5.96, N 11.85%.

2-Phenyl-N-{(3-nitrophenyl)[(phenylacetyl)amino]methyl}acetamide (Table 3, entry 6)

Pale yellow solid. Yield: 65%, mp: 214–215 °C (Lit 216 °C) (16). IR ν_{max}: 3285, 3026, 1668, 1555, 1514, 1348, 704 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.49 (s, 4H), 6.54 (t, 1H, J = 7.8 Hz), 7.21 (m, 10H), 7.52 (d, 2H, J = 8.4 Hz), 8.17 (d, 2H, J = 8.4Hz), 8.97 (d, 2H, J = 7.95 Hz, D_2O exchangeable).^{13}C NMR (125 MHz, DMSO-d_6) δ: 42.39, 57.66, 124.02, 126.97, 128.16, 128.77, 129.60, 136.45, 147.46, 148.15, 170.35. MS (ESI): 403 (M^+). Anal. calcd. for $C_{23}H_{21}N_3O_4$: C 68.47, H 5.25, N 10.42. Found: C 68.30, H 5.20, N 10.38%.

2-Chloro-N-[[(2-chlorobenzoyl)amino](3-nitrophenyl)methyl]benzamide (Table 3, entry 7)

Off white solid. Yield: 68%, mp: 212–214 °C. IR ν_{max}: 3276, 1667, 1594, 1529, 1346, 1068, 738 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6 + acetone-d_6) δ: 7.54 (t, 1H, J = 8.4 Hz), 7.84 (m, 6H), 8.00 (d, 2H, J = 7.6 Hz), 8.16 (t, 1H, J = 8.4Hz), 8.48 (d, 1H, J = 7.6 Hz), 8.65 (d, 1H, J = 8.65 Hz), 8.99 (s, 1H), 9.75 (d, 2H, J = 7.65 Hz, D_2O exchangeable).^{13}C NMR (125 MHz, DMSO-d_6) δ: 58.76, 122.30, 123.43, 127.69, 130.02, 130.43, 130.55, 131.16, 131.73, 134.24, 137.06, 142.83, 148.87, 166.83. MS (ESI): 466 (M + 23) – Na adduct. Anal. calcd. for $C_{21}H_{15}N_3O_4Cl_2$: C 56.77, H 3.40, N 9.46. Found: C 56.59, H 3.46, N 9.40%.

2-Chloro-N-[[(2-chlorobenzoyl)amino](2,4-dichlorophenyl)methyl]benzamide (Table 3, entry 8)

White solid. Yield: 65%, mp: 202–204 °C. IR ν_{max}: 3287, 3084, 2959, 1665, 1546, 745 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.99 (t, 1H, J = 6.85 Hz), 7.35 (m, 11H), 9.33 (d, 2H, J = 7.65 Hz, D_2O exchangeable proton). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 56.62, 127.48, 127.76, 128.68, 129.39, 129.74, 130.15, 130.27, 130.60, 131.11, 131.58, 133.95, 136.57, 166.22. MS (ESI): 489 (M + 23) – Na adduct. Anal. calcd. for $C_{21}H_{14}N_2O_2Cl_4$: C 53.88, H 3.01, N 5.98. Found: C 53.78, H 3.07, N 5.89%.

2-Chloro-N-[[(2-chlorobenzoyl)amino](4-nitrophenyl)methyl]-benzamide (Table 3, entry 9)

Yellow solid. Yield: 60%, mp: 244–246 °C. IR ν_{max}: 3239, 1671, 1523, 1348, 1069, 743 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.95 (t, 1H, J = 7.65 Hz), 7.38 (t, 2H, J = 7.65 Hz), 7.43 (t, 2H, J = 7.65 Hz), 7.48 (t, 4H, J = 7.6Hz), 7.77 (d, 2H, J = 9.2 Hz), 8.26 (d, 2H, J = 8.4 Hz), 9.47 (d, 2H, J = 8.45 Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 58.30, 124.09, 127.58, 128.58, 129.73, 130.16, 130.59, 131.67, 136.50, 147.12, 147.68, 166.53. MS (ESI): 466 (M + 23) – Na adduct. Anal. calcd. for $C_{21}H_{15}N_3O_4Cl_2$: C 56.77, H 3.40, N 9.46. Found: C 56.70, H 3.42, N 9.50%.

2-Chloro-N-[[(2-chlorobenzoyl)amino](2-chlorophenyl)methyl]benzamide (Table 3, entry 10)

White solid. Yield: 63%, mp: 223–226 °C. IR ν_{max}: 3264, 1667, 1507, 1548, 1074, 749 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.06 (t, 1H, J = 7.65 Hz), 7.35 (m, 4H), 7.41 (t, 2H, J = 7.65 Hz), 7.45 (t, 5H, J = 7.65 Hz), 7.71 (d, 1H, J = 6.9 Hz), 9.32 (d, 2H, J = 6.9 Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 56.94, 127.44, 127.56, 128.91, 129.79, 129.94, 130.12, 130.24, 130.63, 131.49, 133.02, 136.77, 137.28, 166.14. MS (ESI): 455 (M + 23) – Na adduct. Anal. calcd. for $C_{21}H_{15}N_2O_3Cl_3$: C 58.16, H 3.49, N 6.46. Found: C 58.32, H 3.54, N 6.38%.

2-Chloro-N-[[(2-chlorobenzoyl)amino](4-chlorophenyl)methyl]benzamide (Table 3, entry 11)

White solid. Yield: 68%, mp: 225–226 °C. IR ν_{max}: 3247, 1672, 1493, 1069, 742 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.86 (t, 1H, J = 7.65Hz), 7.38 (t, 2H, J = 7.65Hz), 7.43 (m, 8H), 7.51 (d, 2H, J = 8.4Hz), 9.29 (d, 2H, J = 7.65Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 58.17, 127.53, 128.81, 129.09, 129.73, 130.13, 130.57, 131.55, 132.97, 136.74, 138.84, 166.31. MS (ESI): 455 (M + 23) – Na adduct. Anal. calcd. for $C_{21}H_{15}N_2O_3Cl_3$: C 58.16, H 3.49, N 6.46. Found: C 58.30, H 3.44, N 6.38%.

N-((2,4-dichlorophenyl){[2-(trifluoromethyl)benzoyl]-amino}methyl)-2-(trifluoromethyl)benzamide (Table 3, entry 14)

Off white solid. Yield: 45%, mp: 244–246 °C. IR ν_{max}: 3259, 1672, 1548, 1318, 1125, 766 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.00 (t, 1H, J = 6.9 Hz), 7.49 (d, 1H, J = 8.4 Hz), 7.56 (d, 2H, J = 7.65 Hz),7.63 (m, 4H), 7.70 (t, 2H, J = 7.65 Hz), 7.76 (d, 2H, J = 7.65 Hz), 9.43 (d, 2H, J = 6.85 Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 56.56, 123.10, 125.27, 126.55, 126.79, 127.75, 129.45, 130.13, 130.57, 132.79, 133.97, 134.03, 136.08, 136.24, 166.94. MS (ESI): 557 (M + 23) – Na adduct. Anal. calcd. for $C_{23}H_{14}N_2O_2Cl_2F_6$: C 51.61, H 2.62, N 5.23. Found: C 51.75, H 2.56, N 5.17%.

N-((4-nitrophenyl){[2-(trifluoromethyl)benzoyl]-amino}methyl)-2-(trifluoromethyl)benzamide (Table 3, entry 15)

Pale yellow solid. Yield: 60%, mp: 233–234 °C. IR ν_{max}: 3259, 1669, 1530, 1349, 1315, 1126, 731 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.95 (t, 1H, J = 7.6 Hz), 7.59 (d, 2H, J = 7.65 Hz), 7.64 (t, 2H, J = 7.65 Hz), 7.69 (t, 1H, J = 7.6 Hz), 7.73 (t, 2H, J = 7.6 Hz), 7.78 (d, 2H, = 7.65 Hz), 7.91 (d, 1H, J = 7.6 Hz) 8.19 (d, 1H, J = 8.4 Hz), 8.34 (s, 1H), 9.59 (d, 2H, J = 7.65 Hz, D_2O exchangeable). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 58.18, 121.81, 123.47, 126.78, 129.33, 130.55, 130.62, 132.91, 134.06, 136.05, 141.83, 148.33, 167.25. MS (ESI): 534 (M + 23) – Na adduct. Anal. calcd. for $C_{23}H_{15}N_3O_4F_6$: C 59.23, H 3.46, N 6.01. Found: C 59.14, H 3.42, N 5.98%.

N-[(benzoylamino)(2,4-dichlorophenyl)methyl]benzamide (Table 3, entry 16)

Off white solid. Yield: 42%, mp: 190–192 °C. IR ν_{max}: 3286, 1640, 1542, 1514, 1145, 696 cm^{-1}. ^{1}H NMR

(500 MHz, DMSO-d_6) δ: 7.00 (t, 1H, J = 7.6 Hz), 7.43 (m, 5H), 7.50 (m, 2H), 7.61 (m, 2H), 7.88 (d, 4H, J = 7.6 Hz), 9.09 (d, 2H, J = 6.8Hz, D_2O exchangeable).[13]C NMR (125 MHz, DMSO-d_6) δ: 57.47, 127.73, 128.20, 128.77, 129.33, 130.36, 132.14, 133.74, 134.00, 134.16, 137.08, 166.34. MS (ESI): 399 (M^+). Anal. calcd. for $C_{21}H_{16}N_2O_2Cl_2$: C 63.17, H 4.04, N 7.02. Found: C 63.42, H 3.95, N 6.94%.[2]

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[2] Supplementary data for this article are available on the journal Web site (canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 5248. For more information on obtaining material, refer to cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml.