Silica-supported barium chloride (SiO_2–$BaCl_2$) — Efficient and heterogeneous catalyst for the environmentally friendly preparation of *N*,*N*′-alkylidene bisamides under solvent-free conditions

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Abstract: A series of *N*,*N*′-alkylidene bisamides were prepared via a green and environmentally friendly synthetic protocol from the reaction of phenyl acetylene or hex-1-yne, aromatic aldehyde, and benzamide or acetamide. Silica-supported barium chloride (SiO_2–$BaCl_2$) catalyzes the process of the reaction. The prepared catalysts were characterized by X-ray diffraction, and the products were obtained with high conversions and yields.

Key words: SiO_2–$BaCl_2$, heterogeneous catalyst, environmentally friendly synthesis, *N*,*N*′-alkylidene bisamides.

Résumé : On a préparé une série de *N*,*N*′-alkylidène bisamides par un protocole de synthèse écologique impliquant la réaction du phénylacétylène ou de l'hex-1-yne, d'un aldéhyde aromatique et du benzamide ou de l'acétamide. Du chlorure de baryum déposé sur de la silice (SiO_2–$BaCl_2$) catalyse la réaction. Les catalyseurs préparés ont été caractérisés par diffraction des rayons-X et les produits ont été obtenus avec des taux de conversion et des rendements élevés.

Mots-clés : SiO_2–$BaCl_2$, catalyse hétérogène, synthèse écologique, *N*,*N*′-alkylidène bisamides.

[Traduit par la Rédaction]

Introduction

The development of simple, efficient, and environmentally benign chemical processes or methodologies for widely used pharmacophores from readily available reagents and catalysts are the major challenges for chemists throughout the world.[1] To plan and manage chemical reactions with "green" experimental protocol is an enormous challenge that chemists have to confront to improve the quality of the environment for present and future generations.[2] Over the past, chemists have been aware of the environmental implications of their chemistry. Nowadays, they are trying to develop new synthetic methods, reaction conditions, and uses of chemicals that reduce risks to humans and the environment. Organic solvents are high on the list of damaging chemicals because they are employed in huge amounts and are usually volatile liquids that are difficult to store.[3]

One important aspect of clean technology is the use of environmentally friendly catalysts — typically a solid catalyst that can be recovered easily when the reaction is complete. Heterogeneous organic reactions have proven useful to chemists in the laboratory as well as in an industrial context. These reactions are affected by the reagents immobilized on the porous solid supports and have advantages over the conventional solution-phase reactions because of the good dispersion of active reagent sites, associated selectivity, and easier work-up.[3]

Compounds bearing amide and bisamide groups are important intermediates in organic synthesis, since these groups can be easily transformed into other functionalities (such as *gem*-diaminoalkyl and aminoalkyl groups) and are of considerable interest in the synthesis of pharmacological materials such as peptidomimetic compounds.[4] Therefore, preparation of amides has attracted considerable attention in the past and in recent years.

The common approach for the synthesis of bisamides is the direct reaction of aldehydes with the corresponding amides or nitriles.[5–10]

In this paper various acidic catalysts such as sulfuric acid (85%; also as solvent),[5] sulfonic acid,[6] triflic acid,[8] sulfamic acid,[10a] or chlorosulfonic acid[10b] were examined.

Considering that most of the organic reagents involved in fine chemical synthesis are sensitive to harsh conditions, it is desirable to choose catalysts that can catalyze organic transformations under mild conditions.

The aim of the present protocol was to summarize the data for the one-pot preparation of *N*,*N*′-alkylidene bisamide derivatives in high yield using a three-component condensation of an alkyne, aromatic aldehydes, and amides in the presence

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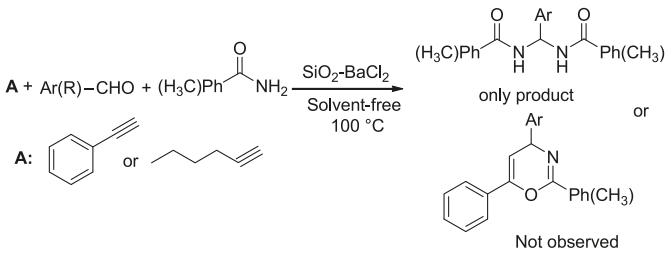
Scheme 1.



of silica-supported barium chloride (SiO_2–$BaCl_2$) as the catalyst under thermal, solvent-free conditions (Scheme 1).

Results and discussion

Hung et al.[11] reported that the condensation of phenyl acetylene, aromatic aldehyde, and urea with acetic acid / trifluoroacetic acid as the catalyst and acetonitrile as the solvent lead to the formation of 4*H*-[1,3]oxazines. In continuation of this theme, we are trying to develop new synthetic methods, reaction conditions, and uses of heterogeneous catalysts that reduce risks to humans and the environment. Thus, the reaction of phenyl acetylene, benzaldehydes, and benzamide in the presence of a catalytic amount of SiO_2–$BaCl_2$ as the catalyst under thermal, solvent-free conditions was investigated (Scheme 1). As can be seen from Scheme 1 we did not observe 2-phenyl(methyl)-4*H*-1,3-oxazine derivatives, and a series of *N*,*N*′-alkylidene bisamides formed.

Within our plan to investigate the structures of bisamide and needing an alkyne or a catalyst for the formation of bisamides, the reaction including benzaldehyde, benzamide, and a catalytic amount of SiO_2–$BaCl_2$ under heating at 100 °C failed to give the correlative product in the absence of phenyl acetylene, which indicated that phenyl acetylene plays an important role in the reaction (Scheme 2). Chromatographic studies (TLC) confirmed that the alkyne was completely disappearing when the product was formed.

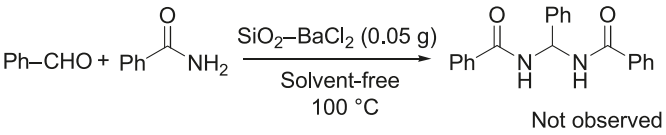
As a result the mentioned reaction failed to give any products in the absence of the catalyst.

To improve the yield and optimize the reaction conditions, the reaction was carried out using phenyl acetylene, benzaldehyde, and benzamide in the presence of SiO_2–$BaCl_2$ as the catalyst (Scheme 3). Initially, the effect of temperature on the rate of the reaction was investigated (Table 1). At 80 °C, the reaction proceeded smoothly and almost complete conversion of the product was observed. A further increase in temperature to 100 °C increased the rate of the reaction. Therefore, the reaction temperature was kept at 100 °C (giving a short reaction time and high yield).

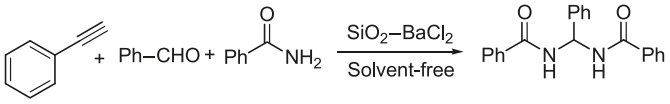
We then tried to optimize the amount of catalyst for this reaction. It should be noted that 0.025 g of SiO_2–$BaCl_2$ was efficient enough to catalyze the reaction, and increasing the amount of catalyst did not significantly improve the yield (Table 1). Finally, an optimimal set of conditions was achieved using 0.025 g of SiO_2–$BaCl_2$ as the catalyst and 100 °C. The results are summarized in Table 1.

Using these optimized reaction conditions, the scope and efficiency of these procedures were explored for the synthesis of a wide variety of substituted bisamides (Scheme 1). The results are summarized in Table 2.

Scheme 2.



Scheme 3.



As expected, this reaction proceeded smoothly, and the desired products were obtained in good to excellent yields. A series of aromatic aldehydes with either electron-donating or electron-withdrawing groups attaching to aromatic rings were investigated (Table 1, entries 1–9). However, when aromatic aldehydes with electron-withdrawing groups (such as nitro-) were reactants, the reaction time was shorter than that with electron-donating groups (such as methoxy-). Although meta- and para-substituted aromatic aldehydes gave good results, ortho-substituted aromatic aldehydes (such as 2-nitrobenzadehyde) gave lower yields and longer reaction times because of the steric effects. These good results were also obtained in the case of the hex-1-yne (Table 1, entries 14 and 15).

As a result the reaction of butyraldehyde with phenyl acetylene and benzamide failed to give any product (Table 1, entry 10).

Encouraged by the results obtained with benzamide, we turned our attention to acetamide (Table 1). As shown in Table 1, the reactions of phenyl acetylene and aryl aldehyde with acetamide under the mentioned reaction conditions progressed smoothly but with longer reaction times, and the desired products were obtained in good yields. (Table 1, entries 11 and 12). However, ortho-substituted aromatic aldehydes (such as 2-nitrobenzadehyde) failed to give any product (Table 1, entry 13).

To explain the formation of bisamides via the one-pot multicomponent reaction, we have proposed a plausible reaction mechanism, which is illustrated in Scheme 4. Firstly, the interaction of aldehyde with an empty π orbital of the Lewis acid occurs to form a cation intermediate. Therefore, the formation of **A** resulting from the cyclocondensation of an activated aldehyde with phenyl acetylene is established. The second step is the addition of amide to **A** to yield β-amido ketones (**B**) that protonate and convert to the bisamide as the product by an attack of the amide (Scheme 4).

Conclusion

In conclusion, a rapid and environmentally benign protocol for the preparation of *N*,*N*′-alkylidene bisamides in a one-pot procedure wasn developed. The work-up procedure is very clear-cut; that is, the products were isolated and purified by simple filtration and crystallization from aqueous ethanol (or diethyl ether). Our protocol avoids the use of dry media during the reaction process, making it superior to the reactions that use solvent.

Table 1. Preparation of *N*,*N*′-alkylidene bisamide derivatives.

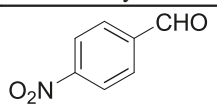
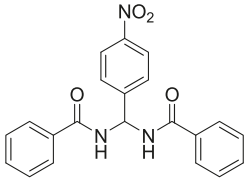
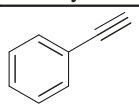
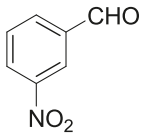
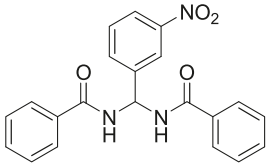
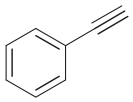
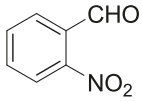
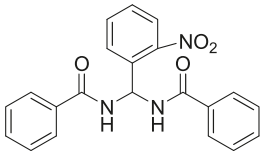
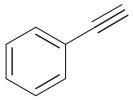
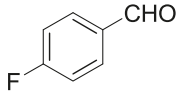
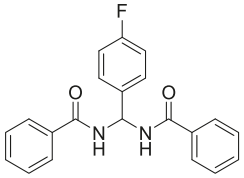
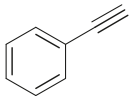
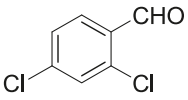
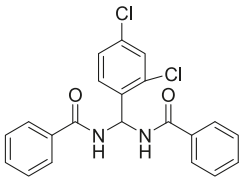
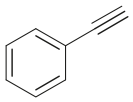
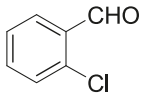
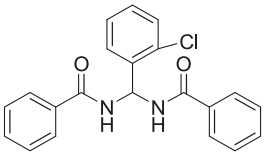
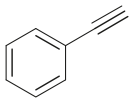
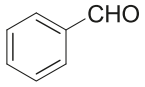
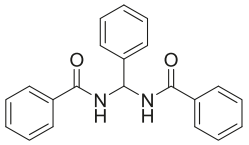
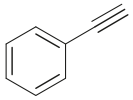
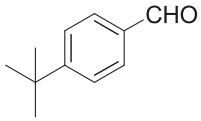
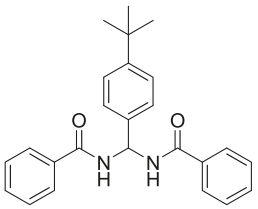
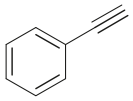
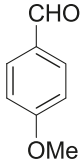
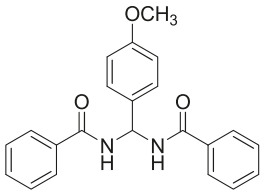
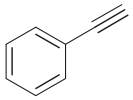
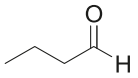
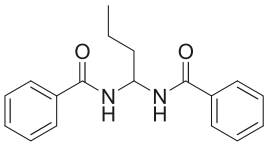
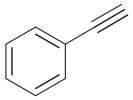
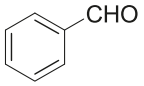
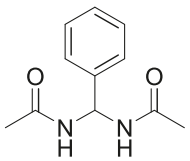
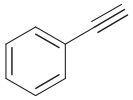
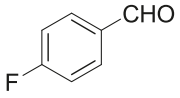
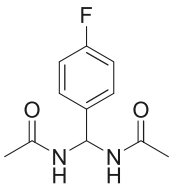
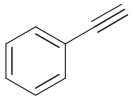
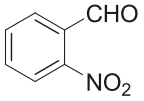
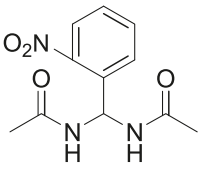
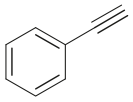
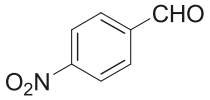
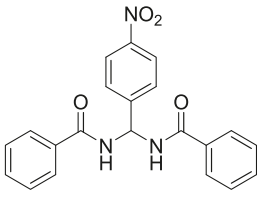
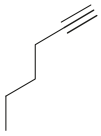
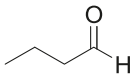
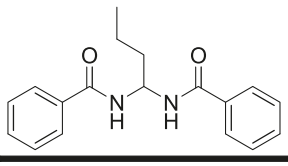
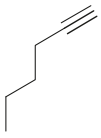
Entry	Aldehyde	Amide	Alkyne	Time (min)	Yield (%)[a]	mp (°C) [lit. mp][ref]
1				90	91	260–262 [265–267][5d]
2				100	79	235–237
3				230	71	256–258
4				160	85	203–205
5				150	89	195–197 [190–192][5e]
6				130	69	242–244
7				120	74	236–238 [237–238][5d]
8				310	67	212–214
9				300	71	227–229 [232–234][5d]

Table 1. (*concluded*).

Entry	Aldehyde	Amide	Alkyne	Time (min)	Yield (%)[a]	mp (°C) [lit. mp][ref]
10				240	—	—
11				360	69	251–253
12				280	76	257–259
13				300	—	—
14				60	82	244–246
15				10	76	210–212

[a]Isolated yields.

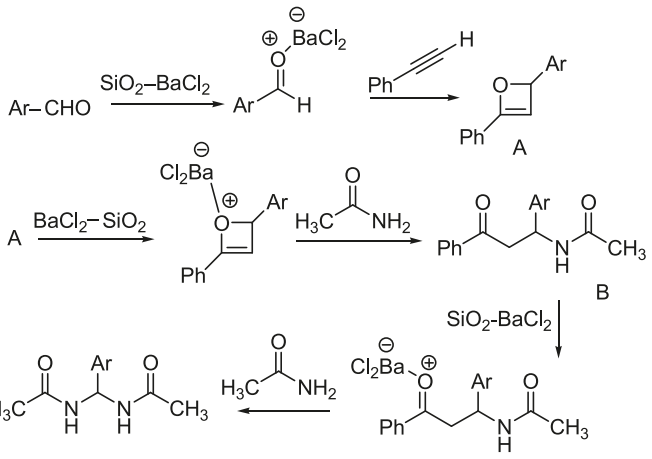
Table 2. Optimization amount of SiO_2–$BaCl_2$ and reaction temperatures.

Entry	Catalyst (g)	*T* (°C)	Time (min)	Yield (%)[a]
1	0.025	rt	300	—
2	0.025	80	450	55
3	0.1	100	180	62
4	0.05	100	170	73
5	0.025	100	120	74
6	0.01	100	160	60

Note: rt, room temperature.

[a]Isolated yield (based on phenyl acetylene (1 mmol), benzaldehyde (1.1 mmol), and benzamide (2.5 mmol)).

Scheme 4. Proposed mechanism for the formation of *N*,*N*′-alkylidene bisamides.



Experimental

All reagents were purchased from Merck and Sigma-Aldrich and used without further purification. All yields refer to isolated products after purification based on the amount of aldehyde. Products were characterized by comparison of spectroscopic data (IR and ^{1}H NMR spectra) and melting points with authentic samples. The NMR spectra were recorded on a Bruker Avance DPX 300 MHz instrument. The

spectra were measured in DMSO-d_6 relative to TMS (0.00 ppm). IR spectra were recorded on a PerkinElmer 781 spectrophotometer. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica gel polygram SIL G/UV 254 plates.

Preparation of SiO_2–$BaCl_2$

In a 250 mL flask, barium chloride dihydrate ($BaCl_2 \cdot 2H_2O$, 1 g) was dissolved in water (50 mL) and silica gel (10 g) (Silica gel 60 for column chromatography, 230 mesh) was added to this mixture, which was vigorously stirred under rotary evaporation until the water was completely evaporated. This powder was kept in an oven at 100 °C for 1 h to give the active catalyst.

X-ray diffraction (XRD)

Powder X-ray diffraction measurements were performed using a D_8 Advance diffractometer made by Bruker AXS, Germany. Scans were taken with a 2θ step size of 0.02 and a counting time of 1.0 s using a Cu Kα radiation source generated at 40 kV and 30 mA. Specimens for XRD were prepared by compaction into a glass-backed aluminum sample holder. Data were collected over a 2 u range from 48° to 70°, and phases were identified by matching experimental patterns to entries in the Diffract^{plus} version 6.0 indexing software. The fresh catalyst was characterized by XRD and its pattern is presented in Fig. 1. As shown in Fig. 1, the actual phases were silicon oxide (silica) – SiO_2 (cubic) and $BaCl_2$.

General procedure for the synthesis of *N*,*N*′-alkylidene bisamides

To a mixture of aryl aldehyde (1.1 mmol), benzamide or acetamide (2.5 mmol), and phenyl acetylene or hex-1-yne (1 mmol) was added SiO_2–$BaCl_2$ (0.025 g) and the mixture was heated at 100 °C in an oil bath for the appropriate time (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, the mass was cooled to 25 °C, and the mixture was dissolved in boiling ethanol. The catalyst was removed by simple filtration. The solvent was concentrated and the solid product was purified by a recrystallization procedure in the appropriate solvent (ethanol 40% or diethyl ether).

All products were characterized by IR, ^{1}H NMR, and ^{13}C NMR spectra.

N-Benzoylamino(4-nitrophenyl)methyl benzamide (Table 1, entry 1)

IR (KBr, cm^{-1}): 3264, 3085, 3028, 2963, 1650, 1633, 1608, 1579, 1548, 1486, 1345, 1295, 1277, 1201, 1143, 1083, 1055, 875, 852, 794, 718, 695. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.08 (t, J = 7.3 Hz, 1H), 7.47–7.60 (m, 6H), 7.75 (d, J = 8.6 Hz, 2H), 7.93 (d, J = 7.1 Hz, 4H), 8.26 (d, J = 8.7 Hz, 2H), 9.22 (d, J = 7.4 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 59.4, 124.4, 128.5, 128.9, 129.2, 132.6, 134.4, 147.9, 148.4, 166.8. Anal. calcd for $C_{21}H_{17}N_3O_4$ (%): C 67.19, H 4.56, N 11.19; found: C 67.36, H 4.60, N 11.26.

N-Benzoylamino(3-nitrophenyl)methyl benzamide (Table 1, entry 2)

IR (KBr, cm^{-1}): 3313, 3259, 3086, 2969, 1649, 1602, 1581, 1534, 1505, 1340, 1271, 1211, 1140, 1054, 873, 736, 716. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.11 (t, J = 7.3 Hz, 1H), 7.47–7.60 (m, 6H), 7.71 (t, J = 7.9 Hz, 1H), 7.94–7.96 (m, 5H), 8.21 (d, J = 8.1 Hz, 2H), 8.36 (s1, H), 9.27 (d, J = 7.3 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 59.5, 122.3, 123.6, 128.5, 129.2, 130.8, 132.6, 134.4, 134.6, 143.3, 148.7, 166.8. Anal. calcd for $C_{21}H_{17}N_3O_4$ (%): C 67.19, H 4.56, N 11.19; found: C 67.32, H 4.65, N 11.29.

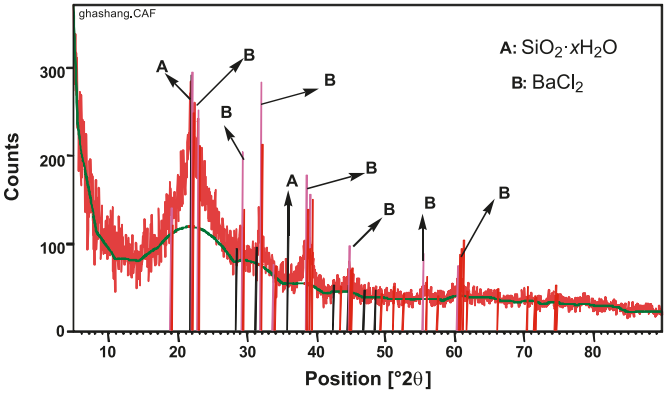


Fig. 1. X-ray diffraction (XRD) pattern of SiO_2–$BaCl_2$.

N-Benzoylamino(2-nitrophenyl)methyl benzamide (Table 1, entry 3)

IR (KBr, cm^{-1}): 3275, 3073, 3030, 1648, 1610, 1531, 1481, 1347, 1274, 1189, 1146, 1086, 1059, 854, 796, 703. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.41–7.61 (m, 8H), 7.76–7.81 (m, 2H), 7.91 (d, J = 7.0 Hz, 4H), 7.98 (d, J = 8.1 Hz, 1H), 9.19 (d, J = 6.9 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 56.7, 125.3, 128.6, 129.1, 129.7, 130.1, 132.5, 133.9, 134.4, 134.6, 149.4, 166.9. Anal calcd for $C_{21}H_{17}N_3O_4$ (%): C 67.19, H 4.56, N 11.19; found: C 67.26, H 4.63, N 11.24.

N-Benzoylamino(4-fluorophenyl)methyl benzamide (Table 1, entry 4)

IR (KBr, cm^{-1}): 3277, 3065, 3026, 1643, 1521, 1480, 1350, 1275, 1141, 1072, 1037, 800, 753, 699. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.19 (t, J = 6.9 Hz, 1H), 7.36–7.69 (m, 10H), 7.94 (d, J = 7.2 Hz, 4H), 9.11 (d, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 58.1, 127.9, 128.2, 128.5, 129.0, 129.3, 129.6, 130.3, 130.4, 132.4, 133.4, 134.7, 138.2, 166.6. Anal. calcd for $C_{21}H_{17}FN_2O_2$ (%): C 72.40, H 4.92, N 8.04; found: C 72.49, H 4.98, N 8.11.

N-Benzoylamino(2,4-dichlorophenyl)methyl benzamide (Table 1, entry 5)

IR (KBr, cm^{-1}): 3290, 3214, 3066, 3028, 1639, 1602, 1579, 1543, 1514, 1364, 1330, 1261, 1145, 1078, 1043, 860, 827, 744, 698. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.14 (t, J = 6.8 Hz, 1H), 7.45–7.68 (m, 9H), 7.93 (d, J = 7.1 Hz, 4H), 9.13 (d, J = 6.8 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 57.9, 128.0, 128.5, 129.1, 129.7, 130.7, 132.4, 134.1, 134.4, 134.6, 137.4, 166.7. Anal. calcd for $C_{21}H_{16}Cl_2N_2O_2$ (%): C 63.17, H 4.04, N 7.02; found: C 63.19, H 4.08, N 7.05.

N-Benzoylamino(2-chlorophenyl)methyl benzamide (Table 1, entry 6)

IR (KBr, cm^{-1}): 3280, 3092, 1649, 1547, 1506, 1343, 1274, 1228, 1146, 1062, 830, 790, 703. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.01 (t, J = 7.5 Hz, 1H), 7.18–7.24 (m, 2H), 7.46–7.59 (m, 8H), 7.91 (d, J = 7.1 Hz, 4H), 9.05 (d, J = 7.6 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 58.1, 117.3, 117.7, 128.3, 129.2, 129.5, 129.8, 132.5, 134.6, 137.5, 164.1, 166.5. Anal. calcd for $C_{21}H_{17}ClN_2O_2$ (%): C 69.14, H 4.70, N 7.68: found: C 69.19, H 4.81, N 7.72.

N-Benzoylamino(phenyl)methyl benzamide (Table 1, entry 7)

IR (KBr, cm^{-1}): 3285, 3088, 1651, 1543, 1497, 1342, 1269, 1137, 1047, 875, 802, 702. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 7.05 (t, J = 7.7 Hz, 1H), 7.29–7.58 (m, 11H), 7.92 (d, J = 7.1 Hz, 4H), 9.03 (d, J = 7.7 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 59.6, 127.4, 128.4, 128.5, 129.2, 132.5, 134.7, 141.1, 166.5. Anal. calcd for $C_{21}H_{18}N_2O_2$ (%): C 76.34, H 5.49, N 8.48; found: C 76.39, H 5.55, N 8.51.

N-Benzoylamino(4-(1,1-dimethylethyl)phenyl)methyl benzamide (Table 1, entry 8)

IR (KBr, cm^{-1}): 3271, 3060, 2965, 1646, 1601, 1579, 1555, 1511, 1352, 1271, 1136, 1075, 871, 833, 710. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 1.29 (s, 9H), 7.03 (t, J = 7.6 Hz, 1H), 7.36–7.58 (m, 10H), 7.93 (d, J = 7.8 Hz, 4H), 9.02 (d, J = 7.7 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 32.0, 35.1, 59.4, 125.9, 127.1, 128.1, 128.4, 129.2, 132.4, 134.7, 138.3, 166.4. Anal. calcd for $C_{25}H_{26}N_2O_2$ (%): C 77.69, H 6.78, N 7.25; found: C 77.80, H 6.89, N 7.29.

N-Benzoylamino(4-methoxyphenyl)methyl benzamide (Table 1, entry 9)

IR (KBr, cm^{-1}): 3273, 3068, 2958, 1648, 1546, 1511, 1280, 1249, 1177, 1065, 815, 765, 703. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 3.74 (s, 3H), 6.93–6.99 (m, 3H), 7.39–7.55 (m, 8H), 7.91 (d, J = 7.3 Hz, 4H), 8.97 (d, J = 7.3 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 56.0, 59.3, 114.5, 128.3, 128.6, 129.2, 132.4, 133.3, 134.8, 159.7, 166.3. Anal. calcd for $C_{22}H_{20}N_2O_3$ (%): C 73.32, H 5.59, N 7.77; found: C 73.37, H 5.65, N 7.89.

N-Acetylamino(phenyl)methyl acetamide (Table 1, entry 11)

IR (KBr, cm^{-1}): 3278, 3119, 3060, 3029, 2932, 1663, 1563, 1517, 1371, 1273, 1094, 848, 749, 696. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 1.86 (s, 6H), 6.52 (t, J = 7.8 Hz, 1H), 7.26–7.38 (m, 5H), 8.57 (d, J = 7.8 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 23.3, 58.1, 127.2, 128.4, 129.1, 141.4, 169.4. Anal. calcd for $C_{11}H_{14}N_2O_2$ (%): C 64.06, H 6.84, N 13.58; found: C 64.16, H 6.91, N 13.66.

N-Acetylamino(4-fluorophenyl)methyl acetamide (Table 1, entry 12)

IR (KBr, cm^{-1}): 3276, 3124, 3016, 2957, 1665, 1555, 1515, 1369, 1237, 1093, 1028, 861, 823. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 1.86 (s, 6H), 6.48 (t, J = 7.7 Hz, 1H), 7.19 (t, J = 8.8 Hz, 2H), 7.32–7.37 (dd, J = 5.6, 8.4 Hz, 2H), 8.53 (d, J = 7.7 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 23.3, 57.6, 115.7, 116.0, 129.2, 129.3, 137.5, 137.6, 160.8, 164.0, 169.4. Anal. calcd for $C_{11}H_{13}FN_2O_2$ (%): C 58.92, H 5.84, N 12.49: found: C 59.01, H 5.95, N 12.56.

N-Acetylamino(4-nitrophenyl)methyl acetamide (Table 1, entry 14)

IR (KBr, cm^{-1}): 3270, 3116, 2999, 2949, 1670, 1605, 1563, 1518, 1353, 1273, 1089, 1017, 852, 825, 772. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 1.88 (s, 6H), 6.56 (t, J = 7.7 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 8.23 (d, J = 8.5 Hz, 2H), 8.71 (d, J = 7.6 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 23.3, 57.8, 124.3, 128.6, 147.8, 148.7, 169.7. Anal. calcd for $C_{11}H_{13}N_3O_4$ (%): C 52.59, H 5.22, N 16.73; found: C 52.63, H 5.30, N 16.83.

N-Benzoylamino butyl benzamide (Table 1, entry 15)

IR (KBr, cm^{-1}): 3237, 3106, 2966, 2927, 1648, 1557, 1518, 1483, 1365, 1333, 1288, 1134, 1079, 1053, 995, 844, 809, 764. ^1H NMR (300 MHz, DMSO-d_6, ppm) δ: 0.93 (t, J = 7.3 Hz, 3H), 1.37 (six, J = 7.4 Hz, 2H), 1.82 (q, J = 7.6 Hz, 2H), 5.88 (quin, J = 7.4 Hz, 1H), 7.43–7.55 (m, 6H), 7.86 (d, J = 7.0 Hz, 4H), 8.57 (d, J = 7.6 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ: 14.5, 19.3, 37.2, 57.7, 128.2, 129.1, 132.2, 135.1, 166.4. Anal. calcd for $C_{18}H_{20}N_2O_2$ (%): C 72.95, H 6.80, N 9.45; found: C 73.00, H 6.89, N 9.55.

Acknowledgments

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References

(1) (a) Bannwarth, W.; Hinzen, B. *Combinatorial Chemistry: From Theory to Application;* Wiley/VCH: Weinheim, 2006; (b) Laszlo, P. *Preparative Chemistry Using Supported Reagents;* Academic Press, Inc.: San Diego, 1987; (c) Smith, K. *Solid Supports and Catalyst in Organic Synthesis;* Ellis Horwood: Chichester, UK, 1992.

(2) (a) Corma, A. *Curr. Opin. Solid State Mater. Sci.* **1997** *2* (1), 63. doi:10.1016/S1359-0286(97)80107-6;; (b) Tanaka, K.; Kaupp, G. *Solvent-free Organic Synthesis;* Wiley-VCH: Weinheim, 2009.

(3) (a) Varma, R. S. *Green Chem.* **1999** *1* (1), 43. doi:10.1039/a808223e;; (b) Anastasas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice;* Oxford University Press: New York, 1988; (c) Shaterian, H. R.; Ghashang, M.; Feyzi, M. *Appl. Catal. A Gen.* **2008** *345* (2), 128. doi:10.1016/j.apcata.2008.04.032;; (d) Shaterian, H. R.; Ghashang, M.; Hassankhani, A. *Dyes Pigments* **2008** *76* (2), 564. doi:10.1016/j.dyepig.2006.11.004.

(4) (a) Dingermann, T. Steinhilber, D.; Folkers, G. In *Molecular Biology in Medicinal Chemistry;* Wiley-VCH: Weinheim, 2004; (b) Shen, A. Y.; Tsai, C. T.; Chen, C. L. *Eur. J. Med. Chem.* **1999** *34* (10), 877. doi:10.1016/S0223-5234(99)00204-4;; (c) Shaterian, H. R.; Hosseinian, A.; Ghashang, M. *Can. J. Chem.* **2008** *86* (5), 376. doi:10.1139/V08-013.

(5) Magat, E. E.; Faris, B. F.; Reith, J. E.; Salisbury, L. F. *J. Am. Chem. Soc.* **1951** *73* (3), 1028. doi:10.1021/ja01147a042.

(6) Zhu, S.; Xu, G.; Chu, Q.; Xu, Y.; Qui, C. *J. Fluor. Chem.* **1999** *93* (1), 69. doi:10.1016/S0022-1139(98)00286-3.
(7) Pernak, J.; Błazej, M.; Józef, W. *Synthesis* **1994** *1994* (12), 1415. doi:10.1055/s-1994-25705.
(8) Herrera Fernández, A.; Martínez Alvarez, R.; Morales Abajo, T. *Synthesis* **1996** *1996* (11), 1299. doi:10.1055/s-1996-4385.
(9) Selvam, N. P.; Saranya, S.; Perumal, P. T. *Can. J. Chem.* **2008** *86* (1), 32. doi:10.1139/V07-134.
(10) (a) Anary-Abbasinejad, M.; Mosslemin, M.; Hassanabadi, A.; Safa, S. T. *Synth. Commun.* **2010** *40* (15), 2209. doi:10.1080/00397910903219617;; (b) Anary-Abbasinejad, M.; Mosslemin, M. H.; Hassanabadi, A. *J Chem. Res.* **2009** *2009* (4), 218. doi:10.3184/030823409X435937.
(11) Huang, S.; Pan, Y.; Zhu, Y.; Wu, A. *Org. Lett.* **2005** *7* (17), 3797. doi:10.1021/ol051458e.