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EXPERIMENTAL PAPER

N,O-Benzyl Protection of Structurally Varied Amines and Phenols Using Wells-Dawson Heteropolyacid Catalyst

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In the last two decades, the investigation of green chemistry processes[1] in the protection/deprotection[2–3] of functional groups has received much attention. Acylation[4–7] of amine and hydroxyl groups is among the most used protective strategies in organic synthesis. In the same vein, benzoylation[8] is used for the *N*-protection of amino acids via the widely-used Schotten-Bauman procedure.[9] The benzoyl (Bz) group is one of the most attractive protecting groups for amines, alcohols and phenols: this group is stable under hydrogenolysis conditions; it can be easily introduced using such bases as pyridine, TEA, or DMAP;[10] and it can be removed by hydrolysis.[11] There are a number of reagents available for the benzoylation of amine and hydroxyl groups, including *N*-benzoyltetrazole,[12] benzoyl cyanide,[13] benzoic anhydride,[14] 2-benzoylthio-1-methylpyridinium chloride[15] and benzoyl chloride. This last is widely used because of its ready availability and low cost.

Benzolyation is a well-known reaction in classical organic chemistry. Among some of the newer methods, a number of procedures have been developed for benzoylation using acidic[16–17] or basic[18–19] conditions. Benzoylation of primary amines has even been described without the use of any solvent or alkali.[20] A catalyst-free and solvent-free procedure using ultrasound irradiation was also reported.[21] No matter whether the methods are classical or more up-to-date, many of them have such limitations as highly basic conditions, long reaction times, low yields of products, environmental pollution caused by toxic reagents and solvents, or the use of expensive catalysts.

In the furtherance of our research focused on efficient and reusable catalysts in organic chemistry[22–23] and the development of green synthetic methods for protection of amine and hydroxyl groups,[24–30] we have attempted to use Wells-Dawson heteropolyacids (HPAs) as catalysts. HPAs have been demonstrated to be efficient and reusable catalysts. They possess unique physico-chemical properties, such as super-acidity, high thermal and chemical stability, the ability to accept and release electrons and high proton mobility, as well as the concomitant possibility of varying their acidities and oxidizing potentials.[31–32]

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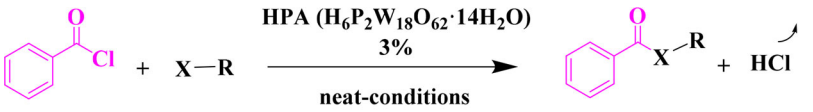

Bz-Cl (1) (2) *N*-Bz, *O*-Bz products 3(a-x)

(3a): X=NH_2, R=CH_2Ph; (3b): X=NH_2, R=CH_2CH_2Ph;
(3c): X=NH_2, R=$CH(CH_3)Ph$; (3d): X=NH_2, R=Ph-*p*-OMe;
(3e): X=NH_2, R=Ph-*m*-F; (3f): X=NH_2, R=Ph-*p*-NO_2;
(3g): X=NH_2, R=Pyr; (3h): X=NH_2, R=thiazole;
(3i): X=NH_2, R=$C(CH_3)_3$; (3j): X=NH_2, R=$CH_2CH_2CH_3$;
(3k): X=NH_2, R=$CH_2CH_2CH_2CH_3$; (3l): X=NH_2, R=C_6H_{11};
(3m): X=NH, R=C_5H_{10}; (3n): X=NH, R=C_4H_8NPh;
(3o): X=OH, R=Ph; (3p): X=OH, R=Ph-*p*-OH;
(3q): X=OH, R=Ph-*p*-Br; (3r): X=OH, R=Ph-*p*-OMe;
(3s): X=NH_2, R=CH_2CH_2OH; (3t): X=NH_2, R=Ph-*o*-OH;
(3u): X=NH_2, R=$CH(C_4H_9)COOMe$; (3v): X=NH_2, R=$CH_2(Ph)COOMe$;
(3w): X=NH_2, R= SO_2NHCH_2Ph;
(3x): X=NH_2, R=$CONH_2$

Scheme 1. Benzoylation reactions using HPA.

In this paper, we report an alternative green method for the *N*-Bz and *O*-Bz protection of amines, phenols, aminoesters, aminoalcohols, ureas and sulfonamides using an HPA ($H_6P_2W_{18}O_{62}\cdot14H_2O$) (Scheme 1). It is worth noting that our method is solvent-free and thus adheres to a key green chemistry principle.

Firstly, in order to optimize the amount of the catalyst, the benzoylation of benzylamine was carried out varying the amount of catalyst under solvent-free conditions at room temperature. The reaction was monitored by TLC and was stopped when the amine disappeared. The results show that the use of 3 mol% resulted in the highest yield (93%) (Table 1).

On the basis of the above results, to extend the generality of the reaction, this procedure was applied to structurally varied amines. The benzoylation of primary and secondary, aliphatic and aromatic amines afforded their corresponding *N*-Bz protected derivatives within 1-5 min in 66-93% yields (mean 77%). In the case of aromatic amines, the nature of the aryl substituent does not have a significant influence on the reaction time and the yields of the reaction (Scheme 1 and Table 2).

With the optimal conditions (3 mol% of $H_6P_2W_{18}O_{62}\cdot14H_2O$, room temperature and solvent-free), we evaluated the applicability of this protocol to the protection of hydroxyl groups. The corresponding benzoyl esters were obtained within a maximum of 9 min with excellent yields (89-96%). Benzoylation of 4-hydroxyphenol led selectively to the mono *O*-benzoylation (**3p**). In the benzoylation of hydroxyl groups, we also observed that the aryl substituents on the aromatic ring do not have much effect on the reaction times and the yields.

Using our protocol, benzoylation was carried out on two β-amino alcohols, namely, ethanolamine and *O*-aminophenol. In each case, the *N*-Bz protected derivatives were obtained in good yields (79 and 78% respectively) in 8 min. Thus our method showed good chemoselectivity (compounds **3s**, **3t**). Benzoylation of *S*-α-aminoesters under the

Table 1. Optimization of the amount of the catalyst.

Catalyst (mol)	t (°C)	Times (min)	Yields (%)
1.5%	rt	5	54
3%	rt	7	62
3%	rt	3	93
4%	rt	5	93

Table 2. Catalyzed *N*- and *O*-Benzoylation.

Entry	Product	Time(min)	Yield(%)	mp (°C)(lit mp[reference])
1	**3a**[20]	3	93	105-106 (105[20])
2	**3b**	3	82	120-123 (-)
3	**3c**	4	79	100-101 (-)
4	**3d**[20]	2	81	153-155 (153-154[20])
5	**3e**	2	86	140-142 (-)
6	**3f**[20]	3	70	155-156 (156[20])
7	**3g**[20]	5	69	208-209 (208-209[20])
8	**3h**[20]	4	66	150-153 (150[20])
9	**3i**	2	74	85-87 (-)
10	**3j**	2	81	69-71 (-)
11	**3k**	3	72	92-95 (-)
12	**3l**[20]	2	79	147-148 (147-148[20])
13	**3m**[21]	2	77	75-79 (-)
14	**3n**[21]	1	74	95-97 (-)
15	**3o**	9	96	120-123 (-)
16	**3p**	7	89	153-158 (-)
17	**3q**	6	90	170-171 (-)
18	**3r**	4	91	166-170 (-)
19	**3s**	8	79	149-153 (-)
20	**3t**[21]	8	78	151-152 (-)
21	**3u**	2	94	130-135 (-)
22	**3v**	2	89	148-149 (-)
23	**3w**	7	75	160-166 (-)
24	**3x**	2	94	97-100 (-)

same reaction conditions was obtained after just a few minutes in excellent yields (**3u** (94%), **3v** (89%)). Selective reactivity in a sulfonamide was tested, and the results showed that the benzoylation occurred only at the less highly substituted nitrogen atom.

No bis-*N,N'*-Bz formation was observed. The mono-*N*-protected sulfonamide was synthesized in good yield (**3w** (75%)). Similarly, in the case of the benzoylation of urea, only the mono *N*-Bz derivative was observed (**3x**, 94%). We infer that the use of the HPA in these reactions productively emphasizes the expected nucleophilicity of the sites benzoylated.

In conclusion, our alternative protocol offers free-solvent conditions, excellent yields and short reaction times, as well as regioselectivity and chemoselectivity. It is our hope that the procedure will find expanded use; for example, it may be suitable for peptide and nucleotide chemistry.

Experimental section

Commercially available chemicals were used without further purification. All reactions were monitored by thin layer chromatography (TLC) on silica Merck 60 F254 precoated aluminium plates. Melting points were determined in open capillary tubes on an electro-thermal apparatus and uncorrected. Mass spectra were recorded on a SHIMADZU QP 1100 Ex mass spectrometer. IR spectra were recorded on a Perkin-Elmer FT-600 spectrometer. Microanalysis data were obtained on an Elementar Analyzer (Euro E.A. 3000-V3.0-single-2007). ^{1}H NMR and ^{13}C NMR were recorded with a Bruker spectrometer at 300 and 75 MHz, respectively using $CDCl_3$ as solvent. Chemical shifts are reported in δ units (ppm) with tetramethylsilane (TMS) as a reference. All coupling constants (J) are reported in Hertz.

Preparation of Catalyst ($H_6P_2W_{18}O_{62}\cdot 14H_2O$)

The catalyst was prepared by a polycondensation of tungstate ions under acidic conditions in order to form the saturated heteropolyanion $K_6P_2W_{18}O_{62}\cdot 12H_2O$, followed by an extraction with ether in the presence of hydrochloric acid to get the acid form ($H_6P_2W_{18}O_{62}\cdot 14H_2O$).[33–34] The IR spectrum of the acid Wells-Dawson compound $H_6P_2W_{18}O_{62}\cdot 14H_2O$ shows the appropriate bands of W-O at 962, 914 and 769 cm^{-1} and P-O at 1090 cm^{-1} respectively. The ^{31}P NMR shifts were determined for a 0.001 M solution of polyanion in D_2O solution and were referenced to H_3PO_4 (85%). We confirmed the purity of the product readily by phosphorus NMR; the single resonance peak at δ=-12.44 ppm revealed a virtually pure product. In the present work, we found that it could be recovered at the end of the reaction by simple filtration, leaving the way open to recycling of the catalyst.

Typical benzoylation procedure

The procedure was done in a well-ventilated hood. In a 10 mL flask, benzoyl chloride (1 mmol, 0.16 ml) was added to the appropriate amine or phenol (1 mmol) and the mixture was stirred at room temperature in the presence of 0.003 g $H_6P_2W_{18}O_{62}\cdot 14H_2O$ as catalyst under solvent-free conditions for the appropriate time. During the reaction, the formation of hydrogen chloride gas was observed. After completion of the reaction (as monitored by TLC), diethyl ether (8 mL) was added, and the products were obtained by

filtration. The products were then recrystallized from *n*-hexane/diethyl ether to give the *N*-Bz and *O*-Bz derivatives in the yields specified in Table 2.

N-Benzylbenzamide (3a)

White solid, mp 105-106 °C (lit mp 105 °C[20]), Rf 0.55 (DCM/MeOH(9/1)). IR: (KBr, cm^{-1}) 3315 (NH), 1640 (C = O), 1579 (C = C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60-7.54 (m, 3H), 7.38 (d, J = 6.9 Hz, 3H), 7.14-7.03 (m, 5H), 3.95 (s, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.57, 139.90, 134.74, 132.61, 131.21, 131.02, 127.31, 127.20, 125.13, 125.09, 123.59, 123.42. MSEI (m/z) 212.1 $[M+H]^+$.

Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.62; H, 6.42; N, 6.95.

N-Phenethylbenzamide (3b)

White solid, mp 120-123 °C, Rf 0.56 (DCM/MeOH (9/1)). IR: (KBr, cm^{-1}) 3430 (NH), 1632 (C = O), 1452 (C-N). MSEI (m/z) 226.1 $[M+H]^+$.

Anal. Calcd for $C_{14}H_{13}NO$: C, 79.97; H, 6.71; N, 6.22. Found: 79.92; H, 6.75; N, 6.17

N-(1-Phenylethyl)benzamide (3c)

White solid, mp 100-101 °C, Rf 0.55 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3355 (NH), 1634 (C = O), 1519 (C = C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27-7.07 (m, 6H), 7.05-7.00 (m, 4H), 5.01 (q, J_1=9.9 Hz, J_2=9.6 Hz, 1H), 1.82 (d, J = 11.4 Hz, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.23, 140.30, 135.42, 132.01, 128.01, 127.90, 126.67, 126.22, 123.55, 121.95, 121.88, 54.21, 20.15. MSEI (m/z) 226.1 $[M+H]^+$.

Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.82; H, 6.52; N, 6.05.

N-(3-Fluorophenyl)benzamide (3e)

White solid, mp 140-142 °C, Rf 0.54 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3347 (NH), 1661 (C = O), 1437 (C-N). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 6.8Hz, 2H), 7.39-7.36 (m, 3H), 7.36 (s, 1H), 7.35-7.30 (m, 5H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.79, 164.29, 161.86, 139.52, 139.41, 134.62, 132.11, 130.21, 130.12, 128.89, 127.03, 115.38, 115.35, 111.41, 111.20, 107.81, 107.55. MSEI (m/z) 215.1 $[M]^+$.

Anal. Calcd for $C_{13}H_{10}NOF$: C, 72.55; H, 4.68; N, 6.51. Found: C, 72.92; H, 4.82; N, 6.35.

N-(Thiazol-2-yl)benzamide (3h)

White solid, mp 150-153 °C (lit mp 150 °C[20]), Rf 0.50 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3259 (NH), 1697 (C = O), 1555(C = C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 6.9 Hz, 2H), 7.66-6.49 (m, 3H), 7.00 (d, J = 3.6 Hz, 1H), 6.93 (d, J = 3.6 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.34, 162.09, 134.28, 132.04, 131.32, 128.21, 128.04, 127.92, 127.89, 110.49. MSEI (m/z) 205.1 $[M+H]^+$.

Anal. Calcd for $C_{10}H_8N_2OS$: C, 58.81; H, 3.95; N, 13.72. Found: C, 58.92; H, 3.82; N, 13.95.

N-(tert-Butyl)benzamide (3i)

White solid, mp 85-87 °C, Rf 0.51 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3330 (NH), 1695 (C = O), 1446(C-N). ^1H NMR (300 MHz, $CDCl_3$) δ 7.81-7.26 (m, 4H), 7.04-6.87 (m, 1H), 3.90 (s, 9H).

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.51; H, 8.58; N, 7.96.

N-Propylbenzamide (3j)

White solid, mp 69-71 °C, Rf 0.52 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3314 (NH), 1696 (C = O), 1450 (C-N). ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 6.0 Hz, 2H), 7.43-7.26 (m, 1H), 3.61 (t, J_1=3.0 Hz, J_2=6.0 Hz, 3H), 2.10-1.80 (m, 2H), 0.94 (t, J_1=6.0 Hz, J_2=9.0 Hz, 3H).

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.51; H, 8.08; N, 8.61.

N-Butylbenzamide (3k)

White solid, mp 92-95 °C, Rf 0.50 (DCM-MeOH (9/1)). ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 6.0 Hz, 2H), 7.61 (d, J = 6.0 Hz, 2H), 7.43-7.31 (m, 1H), 3.21 (t, J_1=6.0 Hz, J_2=9.0 Hz, 2H), 1.54-1.26 (m, 4H), 0.93 (t, J_1=6.0 Hz, J_2=9.0 Hz, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.28, 134.49, 128.21, 128.04, 127.92, 127.89, 18.65, 19.34, 10.49.

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.49; H, 8.60; N, 7.81.

N-Cyclohexylbenzamide (3l)

White solid, mp 147-148 °C (lit mp 147-148 °C[20]), Rf 0.55 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3292 (NH), 1640 (C = O), 1544 (C = C). ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 3.2Hz, 2H), 7.82 (s, 1H), 7.61 (t, J = 4.9Hz, 1H), 7.42 (t, J = 4.2Hz, 2H), 3.63 (m, 1H), 2.32 (m, 4H), 1.74 (m, 4H), 1.42 (m, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 166.0, 130.2, 128.7, 119.5, 119.1, 47.6, 37.3, 25.9, 24.2. MSEI (m/z) 204.1 $[M+H]^+$.

Anal. Calcd for $C_{13}H_{16}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.90; H, 8.59; N, 6.55.

Phenyl (piperidin-1-yl)methanone (3m)[21]

White solid, mp 75-79 °C, Rf 0.48 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3293 (NH), 1652 (C = O), 1492 (C = C).

Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.11; H, 8.06; N, 7.31.

Phenyl (4-phenylpiperazin-1-yl)methanone (3n)

White solid, mp 95-97 °C, Rf 0.52 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3451 (NH), 1631 (C = O), 1599 (C = C). ^1H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 2H), 7.70 (m, 2H), 7.50 (m, 2H), 7.11 (t, J_1=14.7 Hz, J_2=15.3 Hz, 2H), 6.75 (d, J = 3.9 Hz, 2H), 3.53 (t, J_1=3 Hz, J_2=1.5 Hz, 4H), 3.05 (t, J_1=3.9 Hz, J_2=7.2 Hz, 4H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.50, 149.32, 139.20, 129.32, 129.03, 128.54, 128.22, 127.98,

127.75, 126.70, 120.83, 114.41, 114.20, 54.21, 54.02, 50.40, 50.35. MSEI (m/z) 267.1 $[M]^+$.

Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.92; H, 6.89; N, 10.35.

Phenyl benzoate (3o)

White solid, mp 120-123 °C, Rf 0.55 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 1728 (C = O), 1489 (C = C).^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, J = 3.6 Hz, 2H), 8.15 (t, J_1=5.4 Hz, J_2=5.1 Hz, 2H), 7.68 (t, J_1=3.9 Hz, J_2=3.0 Hz, 1H), 7.48-7.19 (m, 5H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.55, 148.89, 133.81, 132.66, 132.42, 130.45, 130.22, 128.54, 128.34, 127.92, 127.82, 123.25, 123.02, 117.82. MSEI (m/z) 199.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.71; H, 5.13.

4-Hydroxyphenyl benzoate (3p)

White solid, mp 153-158 °C, Rf 0.54 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3261 (OH), 1701 (C = O). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (t, J = 5.2 Hz, 2H), 7.26 (t, J = 14.8 Hz, 1H), 7.07-7.04 (m, 5H), 5.27 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.65, 156.78, 151.70, 133.81, 130.28, 130.21, 129.34, 128.65, 113.74, 113.39, 109.44. MSEI (m/z) 214.1 $[M]^+$.

Anal. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71. Found: C, 72.95; H, 4.65.

4-Bromophenyl benzoate (3q)

White solid, mp 170-171 °C, Rf 0.50 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 1732 (C = O), 1486 (C = C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, J = 3.6 Hz, 2H), 7.68-7.33 (m, 5H), 7.22 (d, J = 6.9 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.31, 148.01, 133.89, 132.72, 132.56, 130.45, 130.22, 128.54, 128.34, 127.92, 127.89, 123.25, 118.93. MSEI (m/z) 277.1 $[M]^+$.

Anal. Calcd for $C_{13}H_9O_2Br$: C, 56.35; H, 3.27. Found: C, 56.55; H, 3.12.

4-Methoxyphenyl benzoate (3r)

White solid, mp 166-170 °C, Rf 0.50 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 1712 (C = O), 1496 (C = C). MSEI (m/z) 228.1 $[M]^+$.

Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.62; H, 5.36.

N-(2-Hydroxyethyl)benzamide (3s)

White solid, mp 149-153 °C, Rf 0.51 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3244 (OH), 3045 (NH), 1614 (C = O), 1520 (C = C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.2 Hz, 2H), 7.45 (t, J_1=7.5 Hz, J_2=7.2 Hz, 1H), 7.36 (t, J_1=7.8 Hz, J_2=7.2 Hz, 2H), 7.05 (s, 1H), 3.76 (t, J_1=4.8 Hz, J_2=5.4 Hz, 2H), 3.55 (t, J_1=4.8 Hz, J_2=5.4 Hz, 2H), 3.02 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.28, 132.04, 128.28, 128.04, 127.92, 127.89, 63.43, 47.90. MSEI (m/z) 166.1 $[M]^+$.

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.63; H, 6.59; N, 8.55.

N-(2-Hydroxyphenyl) benzamide (3t)[21]

White solid, mp 151-152 °C, Rf 0.46 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3523 (OH), 3277 (NH), 1617 (C = O).

Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.18; H, 5.27; N, 6.60.

Methyl benzoylphenylalaninate (3u)

White solid, mp 130-135 °C, Rf 0.61 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3262 (NH), 1727 (C = O), 1603 (C = O). MSEI (m/z) 284.3 $[M+1]^+$.

Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05, N, 4.49. Found: C, 72.02; H, 6.12, N, 4.52.

Methyl benzoylleucinate (3v)

White solid, mp 148-149 °C, Rf 0.63 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3356 (NH), 1727 (C = O), 1687 (C = O). MSEI (m/z) 250.1 $[M+1]^+$.

Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68, N, 5.62. Found: C, 67.39; H, 7.71 N, 5.64.

N-[[(Phenylmethyl)amino]sulfonyl]benzamide (3w)

White solid, mp 164-166 °C, Rf 0.50 (DCM-MeOH (9/1)). IR (KBr, cm^{-1}): 3274 (NH), 1677 (C = O), 1425 (C-N). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (s, NH, 1H), 7.86 (d, J = 1.5 Hz, 2H), 7.64-7.58 (m, 1H), 7.47 (t, J_1=6.3 Hz, J_2=7.2 Hz, 2H), 7.33-7.20 (m, 5H), 5.75 (s, NH, 1H), 4.29 (s, 2H).^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.73, 143.43, 134.94, 132.04, 128.39, 128.21, 128.15, 128.13, 127.93, 127.89, 126.53, 126.42, 126.29, 43.24. MSEI (m/z) 290.3 $[M]^+$.

Anal. Calcd for $C_{14}H_{14}N_2O_3S$: C, 57.92; H, 4.86; N, 9.65. Found: C, 58.03; H, 4.94; N, 9.55.

N-Carbamoylbenzamide (3x)

White solid, mp 97-100 °C, Rf 0.45 (DCM/MeOH (9/1)). IR (KBr, cm^{-1}): 3377 (NH), 3290 (NH), 1645 (C = O), 1541 (C = C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, NH, 1H), 7.64 (d, J = 1.5 Hz, 2H), 7.61 (t, J_1=1.8 Hz, J_2=2.1 Hz, 1H), 7.59 (t, J_1=1.2 Hz, J_2=1.2 Hz, 2H), 5.49 (s, NH, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.47, 133.39, 129.09, 127.44. MSEI (m/z) 165.1 $[M+H]^+$.

Anal. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.09. Found: C, 58.64; H, 4.98; N, 16.91

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