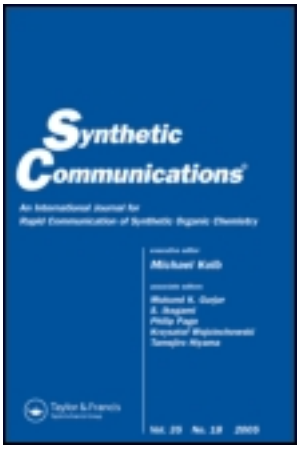

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Environmentally Friendly Preparation of Amidoalkyl Naphthols

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Environmentally Friendly Preparation of Amidoalkyl Naphthols

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Abstract: A new, facile, and cost-effective process involving the solvent-free synthesis of amidoalkyl naphthols using a three-component, one-pot condensation reaction of β-naphthol, aromatic aldehyde, and amides in the presence of $Al(H_2PO_4)_3$ as heterogeneous catalyst under thermal conditions and microwave irradiation has been described. This new approach has the advantage of consistently excellent yields and short reaction times. The catalyst has shown a very stable catalytic activity in the reaction conditions and also can be recovered and recycled.

Keywords: Aluminum *tris*(dihydrogen phosphate), amidoalkyl naphthol, heterogeneous catalyst, multicomponent reaction, solvent-free

INTRODUCTION

Solid-phase organic synthesis (SPOS) has become increasingly important in synthesizing large numbers of combinatorial and parallel compound collections.[1] Acidic catalysts have been used, mainly in industry, for producing more than 1×10^8 Mt/year of products.[2] Among acidic catalysts, the most commonly used are HF, H_2SO_4, $HClO_4$, and H_3PO_4. Solid acids have many advantages such as ease of handling and environmentally safe disposal.[3,4] Also, wastes and by-products can be minimized or avoided by developing cleaner synthetic routes.[5] Heterogeneous organic

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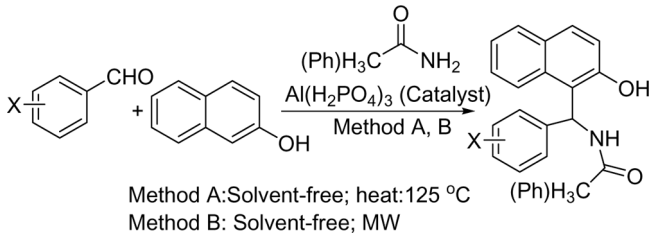
reactions have proven useful to chemists in the laboratory as well as in the industrial context. These reactions are affected by the reagents immobilized on the porous solid supports and have advantages over the conventional solution-phase reactions because of the good dispersion of active reagent sites, associated selectivity, and easier workup.[6] On the other hand, thermal and microwave-assisted solvent-free organic synthesis has attracted increasing attention by providing a much faster, simpler, and more energy-efficient technique for rapid synthesis then the conventional methods.

Compounds bearing 1,3-amino oxygenated functional groups are ubiquitous to a variety of biologically important natural products and potent drugs including a number of nucleoside antibiotics and HIV protease inhibitors, such as ritonavir and lipinavir.[7,8] In this research, we represent an advance in the context of synthetic methodology for a class of biologically important molecules; it is noteworthy that 1-amidomethyl-2-naphthols can convert to important biologically active 1-aminomethyl-2-naphthol derivatives by an amide hydrolysis reaction. The hypotensive and bradycardiac effects of these compounds have been evaluated.[7,8] Amidoalkyl naphthols have been prepared by multicomponent condensation of aryl aldehydes, 2-naphthol, and acetonitrile or amide in the presence of Lewis or Brønsted acid catalysts such as montmorillonite K-10 clay,[9] $Ce(SO_4)_2$,[10] iodine,[11] $K_5CoW_{12}O_{40}{\cdot}3H_2O$,[12] *p*-TSA,[13] sulfamic acid,[14] zirconyl(IV) chloride,[15] silica sulfuric acid,[16] and cation-exchanged resins.[17]

However, some of these catalysts suffer from drawbacks such as prolonged reaction times, low yields, toxicity, and low recovery and reusability of the catalyst. Therefore, introducing clean processes and utilizing ecofriendly and green catalysts that can be simply recycled at the end of reactions have received attention. Herein, we report a simple and efficient method for one-pot preparation of 1-amidoalkyl-2-naphthols using $Al(H_2PO_4)_3$ as catalyst by the three-component condensation (Scheme 1).



Scheme 1. One-pot preparation of 1-amidoalkyl-2-naphthols using $Al(H_2PO_4)_3$ as catalyst.

RESULTS AND DISCUSSION

To find optimum conditions, first the reaction of benzaldehyde, 2-naphthol, and acetamide in the presence of $Al(H_2PO_4)_3$ (0.05 g) as a model was performed under thermal solvent-free conditions at different temperatures in an oil bath and also in a microwave oven under different irradiation power. As can be seen from Table 1, shorter time and excellent yield were achieved at 125 °C and 450 W respectively (Table 1).

Next, to optimize the quantity of the catalyst, the reaction of benzaldehyde with 2-naphthol and acetamide was carried out using different quantities of $Al(H_2PO_4)_3$ under solvent-free thermal conditions at 125 °C (Table 2). As can be seen from Table 2, the best results were obtained using 0.075 g of the catalyst.

Thus, we prepared a range of 1-amidoalkyl-2-naphthols under optimized reaction conditions: (un)substituted benzaldehyde (1 equiv), 2-naphthol (2 equiv), and acetamide or benzamide in the presence of $Al(H_2PO_4)_3$ (0.075 g) as a catalyst under solvent-free thermal (method A) and microwave irradiation (method B) conditions (Table 3).

As summarized in Table 3, 1-amidoalkyl-2-naphthol derivatives were obtained in good to excellent yields in short reaction times without formation of any side products such as dibenzoxanthenes (Scheme 1 and Table 3). The reaction time upon microwave irradiation can be shortened considerably as compared to solvent-free thermal conditions. Aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted successfully and gave the

Table 1. Effect of temperature and MW irradiation power in the synthesis of N-[phenyl-(2-hydroxynapthalen-1-yl)-methyl] acetamide in the presence of $Al(H_2PO_4)_3$ (0.05 g) under thermal solvent-free and microwave (MW) irradiation conditions[a]

Entry	Temperature (°C)	Time	Yield (%)[b]
1	50	48 h	67
2	80	15 h	80
3	100	80 min	89
4	125	31 min	92
5	MW (1000 W)	1.5 min	55
6	MW (850 W)	2.5 min	58
7	MW (600 W)	3 min	63
8	MW (450 W)	4 min	67

[a]The molar ratio of benzaldehyde/2-naphthol/acetamide is 1/1/1.2.

[b]Yields refer to pure isolated product.

Table 2. Effect of amount of $Al(H_2PO_4)_3$ in the synthesis of N-[phenyl-(2-hydroxynapthalen-1-yl)-methyl]acetamide under thermal solvent-free conditions[a]

Entry	Catalyst (g)	Time (min)	Yield (%)[b]
1	0.05	31	92
2	0.075	21	93
3	0.1	17	90
4	0.15	15	87
5	0.2	14	85

[a]The molar ratio of benzaldehyde/2-naphthol/acetamide is 1/1/1.2.
[b]Yields refer to the pure isolated products.

products in high yields. The aromatic aldehydes with electron-withdrawing groups reacted faster than the aromatic aldehydes with electron-donating groups, as would be expected. Electron-withdrawing groups on the benzaldehyde in the *o*-QMs intermediates increase the rate of the 1,4-nucleophilic addition reaction because the alkene lowest unoccupied molecular orbital (LUMO) is at lower energy in the presence of electron-withdrawing groups compared with electron-donating groups.[18] Aliphatic aldehydes such as propionaldehyde were also examined, but the yields were trace amounts compared to aromatic aldehydes (Table 3, entry 21).

$Al(H_2PO_4)_3$ can act as a Brønsted acid and also a Lewis acid because of the empty aluminum p orbital. Although an operation process chart (OPC) of catalyst in this work is unknown, a possible mechanism is proposed in Scheme 2. The reaction of 2-naphthol with aromatic aldehydes in the presence of an acid catalyst is known to give *ortho*-quinone methides (*o*-QMs).[13] The same *o*-QMs, generated in situ, have been reacted with acetamide or benzamide via conjugate addition to form 1-amidoalkyl-2-naphthol derivatives.

To show the merit of the present work in comparison with reported results in the literature, we compared results of $Al(H_2PO_4)_3$ with montmorillonite K-10 clay,[9] $Ce(SO_4)_2$,[10] iodine,[11] and $K_5CoW_{12}O_{40}{\cdot}3H_2O$[12] in the synthesis of 1-amidomethyl-2-naphthol derivatives. As shown in Table 4, $Al(H_2PO_4)_3$ can act as an effective catalyst with respect to reaction times and yields of the obtained products. Thus, the present protocol with $Al(H_2PO_4)_3$ as catalyst is convincingly superior to the recently reported catalytic methods.

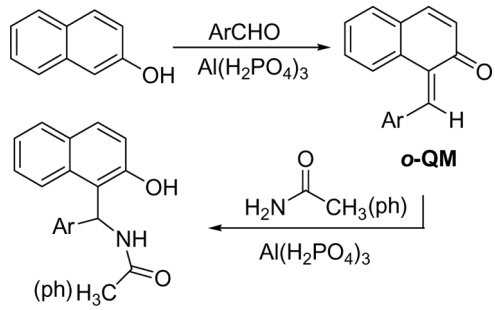
The reusability of the catalysts is an important benefit and makes them useful for commercial applications. Thus, the recovery and reusability of

Table 3. Preparation of 1-amidoalkyl-2-naphthols

Entry	Aldehyde	Amide	Method A		Method B		Mp (lit. mp)[ref]
			time (min)	Yield (%)[a]	time (min)	Yield (%)[a]	
1	3,4,5-Trimethoxybenzaldehyde	CH_3CONH_2	4 h	63	6	55	190–193 (192–194)[9]
2	Benzaldehyde	CH_3CONH_2	21	90–93[b]	4	67	245–246 (241–243)[10]
3	3,4-Dimethoxybenzaldehyde	CH_3CONH_2	26 h	55	7	60	235–237 (235–236)[10]
4	4-Chlorobenzaldehyde	CH_3CONH_2	34	89	4	69	223–225 (224–227)[10]
5	4-(N,N-Dimethylamino)benzaldehyde	CH_3CONH_2	2 h	61	8	50	123–125 (78–79)[10]
6	3-Nitrobenzaldehyde	CH_3CONH_2	17	93	3	72	241–242 (182–184)[10]
7	4-Flourobenzaldehyde	CH_3CONH_2	34	83	4	67	230–232 (209–210)[10]
8	2,4-Dichlorobenzaldehyde	CH_3CONH_2	20	91	4	73	201–203 (198–199)[10]
9	3,4,5-Trimethoxybenzaldehyde	$PhCONH_2$	2.5 h	71	5	62	234–236 (235–238)[12]
10	2-Chlorobenzaldehyde	CH_3CONH_2	22	87	4	63	213–215 (194–196)[14]
11	2-Methylbenzaldehyde	CH_3CONH_2	36	85	3	63	199–2202 (200–202)[14]
12	Benzaldehyde	$PhCONH_2$	23	91	4	67	233–235 (234–236)[14]
13	4-Methylbenzaldehyde	$PhCONH_2$	35	86	5	63	175–177 (177–178)[14]
14	4-Chlorobenzaldehyde	$PhCONH_2$	55	93	4	63	225–227 (228–230)[14]
15	3-Nitrobenzaldehyde	$PhCONH_2$	25	91	3	66	215–217 (216–217)[14]
16	4-Flourobenzaldehyde	$PhCONH_2$	43	92	3	68	191–193 (193–194)[14]
17	2,5-Dimethoxybenzaldehyde	CH_3CONH_2	15	87	8	69	251–253
18	4-Methylbenzaldehyde	CH_3CONH_2	33	87	5	69	222–223
19	4-Nitrobenzaldehyde	CH_3CONH_2	25	90	3	66	248–250
20	3-Flourobenzaldehyde	CH_3CONH_2	20	88	3	65	248–249
21	Propionaldehyde	CH_3CONH_2	60	—	9	—	—

[a]Yields refer to the pure isolated products. All known products have been reported previously in the literature and were characterized by comparison of IR and NMR spectra with authentic samples.

[b]Yield after five recoveries of the catalyst.



Scheme 2. Suggested mechanism for preparation of 1-amidoalkyl-2-naphthols.

$Al(H_2PO_4)_3$ was investigated. The recyclability of the catalyst in the reaction of benzaldehyde and 2-naphthol in the presence of $Al(H_2PO_4)_3$ was checked (Table 3, method A, entry 2). The separated catalyst can be reused after washing with acetone and drying at 100 °C. The catalyst was recovered in excellent yields and was used in the reaction five times; it showed the same activity as fresh catalyst without any loss of its activity.

In conclusion, an efficient method for synthesis of 1-amidoalkyl-2-naphthols via a three-component reaction of aryl aldehydes, 2-naphthol, and acetamide or benzamide in the presence of $Al(H_2PO_4)_3$ as effective catalyst under thermal solvent-free and microwave irradiation was described. The operational simplicity of the procedure, shorter reaction times, simple workup, environmental friendliness, excellent yield, cost-effective recovery, and reusability of the catalyst for a number of times without appreciable loss of activity are also attractive. The catalyst can

Table 4. Comparison results of $Al(H_2PO_4)_3$ with montmorillonite K-10 clay,[9] $Ce(SO_4)_2$,[10] iodine,[11] and $K_5CoW_{12}O_{40}{\cdot}3H_2O$[12] in the synthesis amidoalkyl naphthol[a]

Entry	Catalyst	Molar ratio aldehyde/ 2-naphthol (catalyst)	Conditions	Time	Yield (%)
1	$Ce(SO_4)_2$	1/1/(1 mol%)	Reflux	36 h	72
2	I_2	1/1/(5 mol%)	Solvent-free, 125 °C	5.5 h	85
3	Montmorillonite K10 clay	1/1/0.1 g	Solvent-free, 125 °C	1.5 h	89
4	$K_5CoW_{12}O_{40}\cdot 3H_2O$	1/1/0.01 g	Solvent-free, 125 °C	2 h	90
5	$Al(H_2PO_4)_3$	1/1/0.075 g	Solvent-free, 125 °C	21 min	93

[a]Based on 2-naphthol, benzaldehyde, and acetamide.

be prepared easily with readily available inexpensive reagents, which are heterogeneous and nonhazardous.

EXPERIMENTAL

All reagents were purchased from Merck and Aldrich and used without further purification. $Al(H_2PO_4)_3$ was prepared according to the reported procedure.[19,20] All yields refer to isolated products after purification. Products were characterized by comparison with authentic samples and by spectroscopy data (IR, NMR spectra). The NMR spectra were recorded on a Bruker Avance DPX 300- and 500-MHz instrument. The spectra were measured in DMSO-d_6 relative to TMS (0.00 ppm). IR spectra were recorded on a Jasco FT-IR 460-plus spectrophotometer. Mass spectra were recorded on an Agilent technologies 5973 network mass selective detector (MSD) operating at an ionization potential of 70 eV. Melting points were determined in open capillaries with a Buchi 510 melting-point apparatus. Thin-layer chromatography (TLC) was performed on silica-gel polygram SIL G/UV 254 plates.

Preparation of $Al(H_2PO_4)_3$[19,20]

The catalyst was prepared by taking a mixture of alumina (neutral) and concentrated phosphoric acid (88%) in a silica boat maintaining the molar ratio of alumina–H_3PO_4 as 1:3 and heating at 200–220 °C on a hot sand bath [Eq. (1)]. The mixture was stirred at the stipulated temperature until the swampy mass solidified, and then the temperature was reduced to around 100 °C. The whole was then placed in a vacuum desiccator and cooled to ambient temperature. The catalyst thus prepared was finally transferred and stored in an air-tight sample vial. The catalyst has been reported previously in the literature and was characterized by comparison of IR spectroscopy and the powder XRD with known samples.[19,20] [$Al(H_2PO_4)_3$: 317.84 g mol^{-1}].

$$Al_2O_3 + H_3PO_4 \xrightarrow{\text{Heat20}} Al(H_2PO_4)_3 + H_2O\uparrow \quad (1)$$

General Procedure: Preparation of Amidoalkyl Naphthols Using $Al(H_2PO_4)_3$ as Catalyst

To a mixture of 2-naphthol (4 mmol), aldehydes (4 mmol), and acetamide (4.8 mmol), $Al(H_2PO_4)_3$ (0.3 g) was added. The mixture was stirred at 125 °C in an oil bath (method A) or inserted in a microwave oven

(Samsung model KE300R) at 450 W (method B) for the appropriate time (Table 3). The reaction was followed by thin-layer chromatography (TLC). After completion, the mixture was cooled to 25 °C; then the solid material was dissolved in acetone. The catalyst was recovered by simple filtration. Then filtrate solution was evaporated under vacuum and the solid obtained was recrystallized from aqueous EtOH (20%).The spectral data of some representative amidoalkyl naphthols are given next.

N-[Phenyl-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide[10] (Table 3, Entry 2)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.95 (s, 3H), 7.10–7.19 (m, 4H), 7.21–7.25 (m, 4H), 7.33 (t, J = 7.4 Hz, 1H), 7.74 (d, J = 9.0 Hz, 1H,), 7.77 (d, J = 8.1 Hz, 1H), 7.84 (s, 1H), 8.44 (d, J = 8.4 Hz, 1H), 10.02 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 23.2, 40.3, 119.2, 119.4, 122.9, 123.8, 126.6, 126.8, 128.5, 126.8, 128.9, 129.1, 129.8, 132.8, 143.1, 153.7, 169.0 ppm; IR (KBr, cm^{-1}): 3399, 3246, 3062, 1640, 1582, 1514, 1372, 1337, 1060, 808, 742, 696, 623.

N-[(4-Chloro-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide[10] (Table 3, Entry 4)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.95 (s, 3H), 7.04 (d, J = 8.0 Hz, 1H), 7.10 (d, J = 8.5 Hz, 2H), 7.17 (d, J = 8.5 Hz, 1H), 7.18 (m, 3H), 7.32 (t, J = 7.6 Hz, 1H), 7.74 (m, 3H), 8.43 (d, J = 8.5 Hz, 1H), 10.10 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 20.5, 23.2, 48.0, 118.8, 119.1, 123.1, 126.8, 128.9, 128.5, 129.1, 129.4, 130.1, 131.2, 132.8, 142.4, 153.7, 169.7 ppm; IR (KBr, cm^{-1}): 3392, 2962, 2700, 2613, 1637, 1577, 2523, 1490, 1436, 1374, 1331, 1278, 1243, 1171, 1091, 819, 747, 588, 499.

N-[(3-Nitro-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide[10] (Table 3, Entry 6)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.01 (s, 3H), 7.17 (t, J = 8.0 Hz, 1H), 7.19 (d, J = 8.6 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.4 Hz, Hz, 1H), 7.51 (m, 2H), 7.78 (t, J = 8.6 Hz, 2H), 7.83 (br, 1H), 7.98 (m, 2H), 8.58 (d, J = 8.0 Hz, 1H), 10.16 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 23.1, 48.2, 118.3, 118.9, 120.9, 121.8, 123.2, 127.3, 123.2, 128.9, 129.2, 130.1, 130.5, 132.6, 133.4, 145.9, 148.2,

153.9, 170.3 ppm; IR (KBr, cm^{-1}): 3373, 3088, 2598, 1645, 1524, 1350, 1232, 1158, 1063, 808, 705.

N-[(4-Fluoro-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide[10] (Table 3, Entry 7)

^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 1.94$ (s, 3H), 7.01 (t, $J = 9.0$ Hz, 2H), 7.06 (d, $J = 8.1$ Hz, 1H), 7.11 (m, 2H), 7.17 (t, $J = 8.0$ Hz, 1H), 7.22 (t, $J = 7.4$ Hz, 1H), 7.31 (t, $J = 8.1$ Hz, 1H), 7.74 (m, 3H), 8.45 (d, $J = 8.5$ Hz, 1H), 10.04 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 23.1, 47.7, 115.0, 115.2, 118.9, 119.0, 122.8, 126.8, 128.2, 128.4, 128.8, 129.1, 129.8, 132.8, 139.2, 153.5, 160.2, 162.3, 169.8 ppm; IR (KBr, cm^{-1}): 3392, 2974, 1627, 1576, 1508, 1438, 1334, 1225, 1062, 823, 748, 601, 489.

N-[(2,5-Dimethoxy-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide (Table 3, Entry 17)

^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 1.88$ (s, 3H), 3.48 (s, 3H), 3.64 (s, 3H), 6.72–6.77 (m, 2H), 7.10–7.23 (m, 4H), 7.39 (s, 1H), 7.66–7.73 (m, 2H), 8.15–8.27 (m, 2H), 9.75 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 22.5, 44.4, 55.2, 55.9, 111.1, 111.9, 115.7, 118.5, 118.9, 122.0, 123.2, 125.7, 128.1, 128.6, 131.7, 132.4, 150.7, 152.7, 153.1, 168.1 ppm.; IR (KBr, cm^{-1}): 3365, 3174, 1644, 1497, 1436, 1277, 1218, 1052, 819, 727, 624.; MS: $m/z = 351$ (M^+, 17.83%), 308 (5.82%), 276 (5.87%), 262 (36.04%), 261 (100.00%), 218 (16.71%), 144 (6.60%), 115 (7.99%). Anal. calcd. for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99%. Found: C, 71.73; H, 5.93; N, 4.08%.

N-[(4-Methyl-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide (Table 3, Entry 18)

^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 1.96$ (s, 3H), 2.21 (s, 3H), 7.03–7.08 (m, 5H), 7.19 (d, $J = 8.8$ Hz, 1H), 7.24 (t, $J = 7.1$ Hz, 1H), 7.34 (m, 1H), 7.74 (d, $J = 8.8$, 1H), 7.78 (d, $J = 7.9$ Hz, 1H), 7.82 (br, 1H), 8.36 (d, $J = 8.1$, 1H), 9.91 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 20.4, 22.6, 47.6, 118.4, 118.9, 122.2, 123.1, 125.9, 126.1, 128.3, 128.4, 128.9, 132.2, 134.9, 139.4, 143.2, 152.9, 168.9 ppm; IR (KBr, cm^{-1}): 3396, 3055, 2923, 1625, 1515, 1437, 1276, 1181, 813, 744, 482.; MS: $m/z = 305$ (M^+, 21%), 246 (29.158%), 245 (50.55%), 231 (100%), 232

(31.20%), 202 (16.12%), 115 (10.04%). Anal. calcd. for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59%. Found: C, 78.72; H, 6.21; N, 4.63%.

N-[(4-Nitro-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide (Table 3, Entry 19)

^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 2.02$ (s, 3H), 7.19 (d, $J = 8.0$ Hz, 1H), 7.22 (d, $J = 8.8$ Hz, 1H), 7.28 (t, $J = 7.5$ Hz, 1H), 7.41 (t, $J = 7.3$ Hz, 1H), 7.52–7.58 (m, 2H), 7.81 (t, $J = 9.4$ Hz, 2H), 7.87 (d, $J = 7.0$ Hz, Hz, 1H), 8.03 (m, 2H), 8.60 (d, $J = 8.0$ Hz, 1H), 10.11 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 22.5, 47.6, 117.7, 118.4, 120.3, 121.1, 122.5, 126.6, 128.3, 129.4, 129.8, 132.1, 132.7, 145.3, 147.7, 153.2, 169.5 ppm; IR (KBr, cm^{-1}): 3391, 3267, 2593, 1648, 1603, 1522, 1438, 1063, 825, 739, 447.; MS: m/z = 336 (M^+, 26.66%), 319 (75.99%), 276 (52.02%), 260 (54.15%), 231 (63.80%), 202 (45.11%), 230 (100%), 115 (18.05%). Anal. calcd. for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33%. Found: C, 67.91; H, 4.81; N, 8.24%.

N-[(3-Fluoro-phenyl)-(2-hydroxy-napthalen-1-yl)-methyl]-acetamide (Table 3, Entry 20)

^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 1.98$ (s, 3H), 6.92–6.98 (m, 3H), 7.12 (d, $J = 8.3$ Hz, 1H), 7.19–7.27 (m, 3H), 7.37 (t, $J = 7.3$ Hz, 1H), 7.76 (d, $J = 8.6$ Hz, 1H), 7.80 (d, $J = 8.0$ Hz, 1H), 7.84 (br, 1H), 8.44 (d, $J = 8.2$ Hz, 1H), 10.01 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): 22.5, 47.5, 112.5 (d, $^2J_{C\text{-}F} = 22.1$ Hz), 112.7 (d, $^2J_{C\text{-}F} = 20.9$ Hz), 118.3, 118.4, 122.1, 122.4, 122.9, 126.4, 128.3, 128.5, 129.4, 129.8 (d, $^3J_{C\text{-}F} = 8.1$ Hz), 132.1, 145.9 (d, $^3J_{C\text{-}F} = 6.6$ Hz), 153.1, 162.0 (d, $^1J_{C\text{-}F} = 241.2$ Hz), 169.3 ppm; IR (KBr, cm^{-1}): 3410, 3160, 1640, 1589, 1545, 1484, 1439, 1335, 1280, 1064, 989, 814, 497.; MS: m/z = 310 (4.79%), 309 (M^+, 21.45%), 251 (9.00%), 250 (51.75%), 249 (100.00%), 231 (14.44%), 220 (16.11%), 122 (7.31%), 115 (9.01%). Anal. calcd. for $C_{19}H_{16}FNO_2$: C, 73.77; H, 5.21; N, 4.53%. Found: C, 73.74; H, 5.25; N, 4.48%.

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