

Research Article

Synthesis of Novel Symmetrical and Unsymmetrical o-Phthalic Acid Diamides

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Phthalic anhydride was treated with secondary amines in acetic acid yielding 2-(diethyl (or) 4-alkylpiperazine or morpholine-1carbonyl) benzoic acids. The latter were reacted, again, with secondary amines and arylamines by using the coupling reagent HATU and Et_3N as a base in DMF giving the novel symmetrical o-phthalic acid diamides [o- $R_1R_1NCOC_6H_4CONR_1R_1$], unsymmetrical ophthalic acid diamides [o- $R_1R_1NCOC_6H_4CONR_1R_2$], and primary amidic-secondary amidic containing unsymmetrical o-phthalic acid diamides [o- $R_1R_1NCOC_6H_4CONR_1R_2$], respectively.

1. Introduction

Phthalic anhydride is used in the manufacture of dialkylphthalates [1, 2] which find application as plasticisers for polymers like polyvinyl chloride (PVC) and polyvinylacetate (PVA). It is used in the manufacture of phenolphthalein indicator [3, 4], anthraquinone [5] (a versatile, raw materials in the dye industry [6]), and metal phthalocyanines [7]. Phthalocyanine compounds are used in a variety of applications [7] in addition to their use as pigments, in paints [8] and in many types of dyestuffs [7]. Phthalic anhydride derivatives have been widely reported to possess beneficial pharmaceutical effects, like analgesic [9], anti-inflammatory [10] and antiviral effects [11].

Dunlap and Cummer reported [12] the preparation of symmetrical o-phthalic acid diamides [o- $ArNHCOC_6H_4CONHAr$] by the reaction of phthaloyl dichloride with two moles of aniline in ether at RT. Dann et al. reported [13] the preparation of symmetrical o-phthalic acid diamides by the reaction of phthaloyl dichloride with two moles of aniline in the presence of sodium fluoride in benzene under reflux for 1 h. de Toranzo and Brieux reported [14] the synthesis of unsymmetrical diamides $[ArNHCOC_6H_4CONHAr^1]$ by the reaction of phthalphenylisoimide with anilines in ether at RT. Reynolds reported [15] that unsymmetrical diamides $[ArNHCOC_6H_4CONHAr^1]$ can be made by the reaction of N-arylphthalamic acid with the sodium salt of o- or p-methylaniline in an atmosphere of nitrogen for 1 h at 75°C. However, these methods suffer from drawbacks such as long reaction times, excess use of organic solvents, harsh refluxing conditions, and preparation of difficult starting materials from phthalic anhydride by the reaction with primary amines in the presence of trifluoroacetic anhydride. Keeping these facts in mind, we wish to report our results on reactions of phthalic anhydride with primary and secondary amines using HATU as a coupling reagent. Probably, this appears to be the first ever case of facile preparation of symmetrical and unsymmetrical o-phthalic acid diamides. The use of HATU as a coupling agent has been reported in the literature for reactions such as amide bond formation in solid phase synthesis [16-18] and peptides synthesis [19]. However, its use in the preparation of diamides from phthalic anhydride with amines has probably not been reported so far.

Entry	Coupling reagent	Tertiary base	Temp./°C	Time/min	5a (%)
1	HATU	Et ₃ N	0-5	40-45	80
2	HATU	Et ₃ N	RT	40-45	78
3	HATU	DBU	0-5	55-65	70
4	HATU	DBU	RT	50-55	70
5	HATU	Et ₃ N	50-60	35-40	73
6	DCC	_	0-5	120-130	45
7	DCC	_	RT	100-110	48
8	DCC/HOBt	_	0-5	110-120	50
9	DCC/HOBt	_	RT	100-110	50
10	DCC/HOBt	_	50-60	55-60	72
11	EDC·HCl/HOBt	Et ₃ N	0-5	80-85	70
12	EDC·HCl/HOBt	Et ₃ N	RT	70-80	70
13	EDC·HCl/HOBt	DBU	0-5	70-80	60
14	EDC·HCl/HOBt	DBU	RT	70–75	65
15	EDC·HCl/HOBt	Et ₃ N	50-60	65-70	72
16	HBTU	Et ₃ N	0-5	70-75	70
17	HBTU	Et ₃ N	RT	65-70	70
18	HBTU	DBU	0-5	70-80	65
19	HBTU	DBU	RT	65-75	65
20	HBTU	Et ₃ N	50-60	50-55	70
21	PTSA	_	0-5	120-125	_
22	PTSA	_	RT	120-125	_
23	PPA	_	100	60–65	40

TABLE 1: Effect of coupling reagent, tertiary base, and temperature on condensation of 3a with 2b in DMF yielding 5a.

TABLE 2: Characterization data, reaction time, and yields of 3a-3e obtained 1 and 2a-2e.

Entry	Starting material used	Product obtained	Time (min)	Yield≠	M.P (°C)
1	2a	3a	10-12	85	145–148
2	2b	3b	12-15	85	>220
3	2c	3c	15-18	83	>220
4	2d	3d	15-18	80	>220
5	2e	3e	15-20	81	>220

^{*≠*} Refers to yields of crude products only.

2. Results and Discussion

Phthalic anhydride 1 was treated with the secondary amines 2a-2e in acetic acid at RT for 10-15 min resulting in the formation of 2-(diethyl (or) 4-alkylpiperazine (or) morpholine-1-carbonyl)benzoic acid 3a-3e. Reaction of 3a with the piperazine 2b in the presence of o-(7-azabenzotriazol-1-yl)-1,1,3,3tetramethyluroniumhexafluorophosphate (HATU) and Et₃N at 0-5°C for 40-45 min in DMF gave 5a. Alternatively, this compound was prepared by treating 2-(piperazine-1carbonyl)benzoic acid 3b withdiethylamine 2a by HATU and Et_3N at 0–5°C for 40–45 min in DMF to form N,Ndiethyl-2-(piperazine-1-carbonyl)benzamide 5a. This reaction was examined by carrying out the condensation of 2-(diethylcarbonyl)benzoic acid 3a (1 mmol) with piperazine 2b (1 mmol) in the presence different coupling reagents (HATU, EDC.HCl/HOBt (1-hydroxybenzotriazole), DCC (N,N'-dicyclohexylcarbodiimide), HBTU and PTSA (4methylbenzenesulfonic acid)) and tertiary bases (Et₃N and

DBU (2, 3, 4, 6, 7, 8, 9, 10-octahydropyrimido [1, 2-a] azepine) at different temperatures in DMF as a solvent (Table 1) with a view to study the generalisation of condensation between **3** and **2**. However, coupling of **3a** with **2b** in the presence of HATU and Et₃N at 0–5°C for 40–45 min in DMF was found to be the best method giving **5a** in quality and yield (\geq 80%) (Table 1, entry 1).

Using the above-stated optimised conditions, 3a-3e were condensed into 2a-2e using HATU and Et₃N at $0-5^{\circ}$ C for 40-65 min in DMF yielding 4a-4e and 5a-5j (Scheme 1) (Tables 2 and 3) in excellent yield. The structures of the products have been established on the basis of their spectral and analytical data. (Please see experimental section).

Condensation of 3a-3e with arylamines 6a-6e in the presence of HATU and Et_3N at $0-5^{\circ}C$ for 40-55 min in DMF gave primary amidic-secondary amidic containing unsymmetrical o-phthalic acid diamides [o- $R_1R_1NCOC_6H_4CONHAr$] 7a-7y (Scheme 2) (Table 4).



SCHEME 1: Synthetic routes to 4a-4e and 5a-5j.

The structures of the products have been established on the basis of their spectral and analytical data. An alternate protocol was attempted to synthesize 7a-7y by treatment of 1 with aniline **6a** in acetic acid at $0-5^{\circ}$ C for 10-15 min which gave 2-(phenylcarbamoyl)benzoic acid **8a**¹⁸ and subsequent reaction of **8a** with diethylamine **2a** in the presence of HATU and Et₃N at RT for 20-25 min in DMF which resulted in the formation of 2-phenylisoindoline-1, 3-dione **9a**¹⁸.

3. Conclusion

In conclusion, we have developed novel syntheses of symmetrical **4a–4e** and unsymmetrical **5a–5j** and **7a–7y** ophthalic acid diamides. This approach presents a simple and useful synthetic process which requires a few minutes of reaction time, easily available starting materials and straight forward and easy workup procedure. Probably, this appears to be the first ever case of facile preparation of symmetrical and unsymmetrical o-phthalic acid diamides. The use of HATU as a coupling agent has been reported in the literature for reactions such as amide bond formation in solid phase synthesis and peptides synthesis. However, its use in the preparation of diamides from phthalic anhydride with amines has probably not been reported so far. The overall yields of these compounds are very good.

4. Materials and Methods

Melting points are uncorrected and were determined in open capillary tubes in sulphuric acid bath, TLC was run on silica gel-G, visualization was done using iodine or UV light, and IR spectra were recorded using PerkinElmer 1000 instrument in KBr pellets. 1HNMR spectra were recorded in DMSO-d₆ using TMS as internal standard using 400 MHz spectrometer. Mass spectra were recorded on Agilent-LCMS instrument under CI conditions and given by Q + 1 values only. Starting 1, 2, and 6 were obtained from commercial sources and used as such.

4.1. Preparation of 3a-3e. A mixture of 1a (10 mM), 2a-2e (10 Mm) and CH₃COOH (20 mL) was stirred at RT for

10–20 min. A colourless solid separated out from reaction mixture which was filtered, washed with hexane (10 mL), and dried. The crude product was recrystallized from suitable solvent to obtain 3a-3e.

4.2. Preparation of 4a-4e & 5a-5j. A mixture of 3a-3e (10 mM), 2a-2e (10 mM) HATU (10 mM), Et₃N (10 mM), and DMF (15 mL) was stirred at 0–5°C for 40–65 min. Then, ice-cold water (50 mL) was added to the reaction mixture. The separated solid was filtered, washed with water (10 mL), and dried. The product was recrystallized from a suitable solvent to obtain 4a-4e and 5a-5j.

4.3. Preparation of 7a-7y. A mixture of 3a-3e (10 mM), 6a-6e (10 mM), HATU (10 mM), Et₃N (10 mM), and DMF (15 mL) was stirred at $0-5^{\circ}$ C for 40–55 min. Then, icecold water (50 mL) was added to the reaction mixture. The separated solid was filtered, washed with water (10 mL), and dried. The product was recrystallized from a suitable solvent to obtain 7a-7y.

5. Supporting Information

3a: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH and -OH groups put together), 1720 cm^{-1} (sharp, strong, -CO- of acid group), 1655 cm^{-1} (sharp, storng, -CO- of amide group); ¹H-NMR: δ 0.8 (t, 3H, -CH₃), δ 1.2 (t, 3H, -CH₃), δ 3.0 (q, 2H, -CH₂), δ 3.6 (q, 2H, -CH₂), 7.0-8.0 (m, 4H, Ar-H), 13.00 (s, 1H, -COOH, D2O exchangeable), 10.12 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.3, 41.4, 123.1, 128.5, 129.3, 129.5, 160.2, 165.5. Ms: m/z = 222 (M^{+.} + 1).

3b: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH and –OH groups put together), 1725 cm⁻¹ (sharp, strong, –CO– of acid group), 1670 cm⁻¹ (sharp, storng, –CO– of amide group); ¹H-NMR: δ 2.2 (s, 1H, –NH), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 4H, Ar-H), 13.00 (s, 1H, –COOH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 49.4, 50.1, 51.4, 51.9, 124.1, 125.5, 127.3, 128.5, 161.2, 164.8. Ms: m/z = 235 (M⁺ + 1).



Plausible mechanism for 4, 5, and 7 from 3:



SCHEME 2: Synthetic routes to 7a–7y.

3c: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, –NH and –OH groups put together), 1730 cm^{-1} (sharp, strong, –CO– of acid group), 1655 cm^{-1} (sharp, storng, –CO– of amide group); ¹H-NMR: δ 1.2 (t, 3H, –CH₃), δ 2.6 (q, 2H, –CH₂), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 4H, Ar-H), 13.2 (s, 1H, –COOH, D2O

exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.5, 49.4, 50.1, 50.9, 51.9, 52.2, 123.1, 124.5, 125.3, 127.5, 163.2, 164.8. Ms: $m/z = 263 \text{ (M}^{+} + 1).$

3d: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, –NH and –OH groups put together), 1720 cm^{-1} (sharp, strong, –CO– of acid group), 1660 cm^{-1} (sharp, storng, –CO– of amide

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Entry	Starting m	naterial used	Product obtained	Time (min)	Yield≠	M.P (°C)
1	3a	2a	4a	40-45	85	>220
2	3b	2b	4b	40-45	85	>220
3	3c	2c	4c	50-55	80	>220
4	3d	2d	4 d	50-55	80	>220
5	3e	2e	4e	40-45	80	>220
6	3a	2b	5a	40-45	85	>220
7	3a	2c	5b	50-55	81	110–112
8	3a	2d	5c	50-55	84	115–118
9	3a	2e	5d	50-55	85	80-82
10	3b	2a	5a	40-45	83	>220
11	3b	2c	5e	50-55	84	>220
12	3b	2d	5f	50-55	85	>220
13	3b	2e	5g	60-65	85	85-87
14	3c	2a	5b	60-65	81	110–112
15	3c	2b	5e	50-55	83	>220
16	3c	2d	5h	50-55	85	>220
17	3c	2e	5i	50-55	85	90-92
18	3d	2a	5c	60-65	80	115–118
19	3d	2b	5f	50-55	80	>220
20	3d	2c	5h	40-45	85	>220
21	3d	2e	5j	40-45	83	>220
22	3e	2a	5d	40-45	80	80-82
23	3e	2b	5g	50-55	84	85-87
24	3e	2c	5i	50-55	84	90-92
25	3e	2d	5j	40-45	83	>220

TABLE 3: Characterization data, reaction time, and yields of 4a-4e and 5a-5j obtained from 3a-3e and 2a-2e.

[≠] Refers to yields of crude products only.

group); ¹H-NMR: δ 1.6 (t, 3H, -CH₃), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.8 (t, 2H, -CH₂), 7.0– 8.0 (m, 4H, Ar-H), 13.1 (s, 1H, -COOH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 39.4, 55.1, 55.9, 55.9, 55.2, 126.1, 127.5, 128.3, 129.5, 160.2, 165.8. Ms: m/z = 249 (M^{+.} + 1).

3e: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH and –OH groups put together), 1720 cm⁻¹ (sharp, strong, –CO– of acid group), 1655 cm⁻¹ (sharp, storng, –CO– of amide group); ¹H-NMR: δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 4H, Ar-H), 13.1 (s, 1H, –COOH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 50.2, 50.6, 71.9, 72.2, 125.1, 125.5, 126.3, 127.5, 162.2, 164.8. Ms: m/z = 236 (M⁺⁺ + 1).

4a: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of amide group), 1665 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.2 (t, 6H, –CH₃, –CH₃), δ 1.4 (t, 6H, –CH₃, –CH₃), δ 2.8 (q, 4H, –CH₂, –CH₂) δ 3.2 (q, 4H, –CH₂, –CH₂), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 12.9, 14.1, 31.6, 36.7, 39.1, 43.5, 125.3, 126.5, 127.1, 129.3, 163.6, 169.6. Ms: *m*/*z* = 277 (M^{+.} + 1).

4b: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1685 cm⁻¹ (sharp, strong, -CO- of amide group), 1665 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 2.2

(s, 2H, -NH, -NH), δ 3.0 (t, 8H, Four -CH₂ groups), δ 3.4 (t, 8H, Four -CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 47.4, 48.6, 49.7, 50.9, 51.5, 52.4, 125.3, 125.5, 127.1, 128.6, 164.3, 167.6. Ms: *m*/*z* = 303 (M⁺⁺ + 1).

4c: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1660 cm⁻¹ (sharp, strong, –CO– of amide group), 1665 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.3 (t, 6H, –CH₃, –CH₃), δ 2.8 (q, 4H, –CH₂, –CH₂), δ 3.2 (t, 8H, Four –CH₂ groups), δ 3.2 (t, 8H, Four –CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 12.3, 16.1, 46.4, 47.6, 48.7, 49.1, 50.5, 51.4, 123.3, 124.5, 128.1, 128.9, 164.6, 168.6. Ms: m/z = 359 (M⁺ + 1).

4d: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1670 cm⁻¹ (sharp, strong, -CO- of amide group), 1665 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.4 (t, 6H, $-\text{CH}_3$, $-\text{CH}_3$), δ 3.0 (t, 8H, Four $-\text{CH}_2$ groups), δ 3.2 (t, 8H, Four $-\text{CH}_2$ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 32.3, 33.4, 48.4, 48.9, 49.7, 50.5, 52.4, 55.3, 125.3, 125.6, 128.3, 129.9, 165.2, 169.3. Ms: m/z = 331(M⁺ + 1).

4e: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1675 cm⁻¹ (sharp, strong, -CO- of amide group), 1665 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 3.0 (t, 8H,

Entry	Starting n	naterial used	Product obtained	Time (min)	Yield≠	M.P (°C)
1	3a	6a	7a	40-45	85	115-118
2	3b	6a	7b	50-55	82	120-123
3	3c	6a	7c	40-45	84	123-125
4	3d	6a	7d	50-55	85	>220
5	3e	6a	7e	50-55	80	126-128
6	3a	6b	7f	40-45	83	128-130
7	3b	6b	7g	40-45	82	138–140
8	3c	6b	7h	50-55	82	120-123
9	3d	6b	7i	50-55	85	>220
10	3e	6b	7j	40-45	80	122-124
11	3a	6c	7k	50-55	82	120-124
12	3b	6c	71	40-45	85	130-132
13	3c	6c	7m	50-55	85	170–174
14	3d	6c	7 n	50-55	80	>220
15	3e	6c	70	40-45	80	140–143
16	3a	6d	7 p	40-45	80	125-128
17	3b	6d	7 q	50-55	82	135–137
18	3c	6d	7 r	50-55	82	180-183
19	3d	6d	7s	40-45	80	>220
20	3e	6d	7t	40-45	85	142-145
21	3a	6e	$7\mathbf{u}$	40-45	84	128-130
22	3b	6e	7v	40-45	85	133-135
23	3c	6e	7w	50-55	80	190–192
24	3d	6e	7x	50-55	82	>220
25	3e	6e	7y	40-45	84	145-148

TABLE 4: Characterization data reaction time and yield of 7a-7y obtained from 3a-3e and 6a-6e.

[≠] Refers to yields of crude products only.

Four $-CH_2$ groups), δ 3.2 (t, 8H, Four $-CH_2$ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 49.3, 49.9, 50.7, 52.8, 55.9, 56.8, 125.4, 126.3, 127.4, 128.9, 164.2, 167.3. Ms: m/z = 305 (M⁺⁻ + 1).

5a: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1690 cm⁻¹ (sharp, strong, –CO– of amide group), 1660 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0–1.2 (t, 6H, –CH₃, –CH₃), δ 2.2 (s, 1H, –NH), δ 3.0 (t, 4H, –CH₂, – CH₂), δ 3.2 (t, 4H, –CH₂, –CH₂), δ 3.4 (q, 2H, –CH₂), δ 3.6 (q, 2H, –CH₂, –CH₂), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSOd₆, 400 MHz): 12.9, 31.7, 43.5, 44.6, 51.1, 52.5, 123.1, 124.3, 128.3, 129.6, 161.7, 165.5. Ms: m/z = 290 (M⁺⁻ + 1).

5b: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of amide group), 1650 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0–1.2 (t, 6H, –CH₃, –CH₃), δ 1.4 (t, 3H, –CH₃), δ 2.2 (q, 2H, –CH₂), δ 3.0 (t, 4H, –CH₂, –CH₂), δ 3.2 (t, 4H, –CH₂, –CH₂), δ 3.4 (q, 2H, –CH₂), δ 3.6 (q, 2H, –CH₂, –CH₂), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 12.9, 13.6, 31.5, 44.5, 45.6, 48.6, 54.1, 55.5, 123.6, 125.3, 128.3, 129.6, 162.7, 165.4. Ms: m/z = 318 (M^{+.} + 1).

5c: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1695 cm⁻¹ (sharp, strong, -CO- of amide group), 1655 cm⁻¹

(sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.0–1.2 (t, 6H, $-CH_3$, $-CH_3$), δ 1.8 (t, 3H, $-CH_3$), δ 3.0 (t, 4H, $-CH_2$, $-CH_2$), δ 3.2 (t, 4H, $-CH_2$, $-CH_2$), δ 3.4 (q, 2H, $-CH_2$), δ 3.6 (q, 2H, $-CH_2$, $-CH_2$), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 13.9, 32.7, 41.5, 44.6, 45.5, 53.1, 54.5, 122.3, 125.3, 129.2, 129.9, 164.7, 166.4. Ms: m/z = 304 (M^{+.} + 1).

5d: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of amide group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0–1.2 (t, 6H, –CH₃, –CH₃), δ 3.0 (t, 4H, –CH₂, –CH₂), δ 3.2 (t, 4H, – CH₂, –CH₂), δ 3.4 (q, 2H, –CH₂), δ 3.6 (q, 2H, –CH₂, –CH₂), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 13.2, 33.4, 44.3, 45.2, 50.1, 52.4, 124.2, 123.5, 125.4, 125.7, 160.3, 165.6. Ms: *m*/*z* = 291 (M^{+.} + 1).

5e: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1690 cm⁻¹ (sharp, strong, –CO– of amide group), 1665 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.4 (t, 3H, –CH₃), δ 2.2 (q, 2H, –CH₂), δ 2.2 (s, 1H, –NH), δ 2.8–3.6 (t, 16H, eight –CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 12.4, 29.4, 30.2, 31.7, 33.4, 34.3, 42.5, 43.6, 50.2, 51.2, 124.1, 125.2, 127.3, 129.3, 160.3, 164.2. Ms: *m*/*z* = 331 (M⁺⁺ + 1).

5f: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1690 cm⁻¹ (sharp, strong, -CO- of amide group), 1650 cm⁻¹

(sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.6 (t, 3H, -CH₃), δ 2.2 (s, 1H, -NH), δ 2.8–3.6 (t, 16H, eight – CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 28.4, 31.4, 32.5, 33.3, 35.4, 41.4, 42.4, 51.4, 52.3, 125.2, 126.1, 128.3, 129.2, 161.6, 165.1. Ms: *m*/*z* = 317 (M⁺⁺ + 1).

5g: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of amide group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 2.2 (s, 1H, –NH), δ 2.8–3.6 (t, 16H, eight –CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 30.1, 31.3, 33.5, 34.2, 42.6, 43.8, 50.1, 51.4, 123.2, 125.1, 128.2, 129.3, 160.3, 165.3. Ms: m/z = 304 (M⁺⁻ + 1).

5h: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1690 cm⁻¹ (sharp, strong, –CO– of amide group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.4 (t, 3H, –CH₃), δ 1.8 (t, 3H, –CH₃), δ 2.2 (q, 2H, –CH₂), δ 2.8–3.6 (t, 16H, eight –CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 13.2, 28.6, 29.5, 32.2, 33.7, 34.5, 35.4, 43.5, 44.5, 53.5, 54.6, 125.5, 126.4, 126.9, 129.5, 161.3, 165.9. Ms: m/z = 345 (M⁺⁺ + 1).

5i: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of amide group), 1650 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.4 (t, 3H, –CH₃), δ 2.2 (q, 2H, –CH₂), δ 2.8–3.6 (t, 16H, eight – CH₂ groups), 7.0–8.0 (m, 4H, Ar-H). ¹³C NMR (DMSO-d₆, 400 MHz): 13.2, 29.4, 31.2, 32.2, 33.2, 34.5, 42.7, 44.8, 50.9, 51.9, 124.3, 125.9, 127.8, 129.0, 160.7, 168.9. Ms: *m*/*z* = 332 (M⁺⁺ + 1).

5j: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1670 cm⁻¹ (sharp, strong, -CO- of amide group), 1655 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.6 (t, 3H, -CH₃), δ 2.8–3.6 (t, 16H, Eight -CH₂ groups), 7.0–8.0 (m, 4H, Ar-H).¹³C NMR (DMSO-d₆, 400 MHz): 28.4, 33.2, 34.7, 35.4, 39.3, 44.5, 47.6, 53.2, 55.2, 127.1, 128.2, 129.3, 129.9, 163.3, 169.4. Ms: m/z = 318 (M⁺⁺ + 1).

7a: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of acid group), 1645 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0 (t, 6H, –CH₃, –CH₃), δ 3.2 (q, 2H, –CH₂), δ 3.4 (q, 2H, –CH₂), 7.0–8.0 (m, 9H, Ar-H), 10.6 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.2, 13.4, 37.9, 42.5, 123.4, 126.2, 127.8, 128.1, 128.5, 130.3, 134.1, 137.4, 139.1, 165.8, 169.2. Ms: m/z = 297 (M^{+.} + 1).

7b: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of acid group), 1645 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 2.2 (s, 1H, –NH), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 9H, Ar-H), 10.4 (s, 1H, –NH, D2O exchangeable).¹³C NMR (DMSO-d₆, 400 MHz): 49.3, 50.3, 51.5, 51.3, 124.3, 124.5, 125.5, 126.4, 127.3, 128.5, 129.5, 129.9, 131.5, 163.2, 164.5. Ms: m/z = 310 (M⁺⁻ + 1).

7c: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1690 cm⁻¹ (sharp, strong, -CO- of acid group), 1645 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.2 (t, 3H, -CH₃), δ 2.6 (q, 2H, -CH₂), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.8 (t, 2H, -CH₂), 7.0-8.0 (m, 9H, Ar-H), 10.4 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.6, 44.5, 47.3, 48.5, 50.5, 51.3, 120.3, 122.7, 125.4, 126.3, 127.7, 128.3, 129.2, 130.9, 131.4, 160.6, 164.9. Ms: $m/z = 338 \; (\mathrm{M^{+}} + 1).$

7d: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1690 cm⁻¹ (sharp, strong, -CO- of acid group), 1655 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.6 (t, 3H, $-CH_3$), δ 3.0 (t, 2H, $-CH_2$), δ 3.2 (t, 2H, $-CH_2$), δ 3.4 (t, 2H, $-CH_2$), δ 3.8 (t, 2H, $-CH_2$), 7.0–8.0 (m, 9H, Ar-H), 13.00 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 34.5, 46.4, 47.2, 48.6, 50.2, 121.2, 123.4, 123.9, 124.6, 125.6, 126.3, 128.2, 131.9, 132.4, 164.2, 169.2. Ms: m/z = 324 (M⁺⁺ + 1).

7e: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of acid group), 1660 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 13.00 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 50.3, 51.3, 71.5, 72.3, 120.3, 121.2, 124.2, 125.6, 128.1, 128.9, 129.1, 129.9, 131.4, 165.1, 166.3. Ms: m/z = 311 (M⁺⁺ + 1).

7f: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of acid group), 1644 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0 (t, 6H, –CH₃, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 3.2 (q, 2H, –CH₂), δ 3.4 (q, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 10.6 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.6, 13.8, 19.4, 39.9, 43.6, 123.6, 124.6, 125.2, 126.6, 127.6, 129.8, 131.2, 133.5, 136.5, 166.7, 168.3. Ms: m/z = 311 (M⁺⁻ + 1).

7g: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1685 cm⁻¹ (sharp, strong, –CO– of acid group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 2.2 (s, 1H, –NH), δ 2.4 (s, 3H, –CH₃), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 10.6 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 20.5, 44.5, 49.3, 50.5, 51.5, 120.2, 122.4, 123.4, 124.5, 125.3, 126.6, 128.5, 130.1, 133.5, 163.7, 166.6. Ms: m/z = 324 (M⁺⁺ + 1).

7h: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1695 cm⁻¹ (sharp, strong, -CO- of acid group), 1655 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.2 (t, 3H, $-CH_3$), δ 2.4 (s, 3H, $-CH_3$), δ 2.6 (q, 2H, $-CH_2$), δ 3.0 (t, 2H, $-CH_2$), δ 3.2 (t, 2H, $-CH_2$), δ 3.4 (t, 2H, $-CH_2$), δ 3.8 (t, 2H, $-CH_2$), 70–8.0 (m, 8H, Ar-H), 10.6 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.2, 19.3, 44.2, 47.6, 48.3, 51.2, 52.2, 119.3, 121.3, 124.2, 124.9, 126.2, 127.1, 130.4, 131.3, 132.3, 161.1, 165.1. Ms: m/z = 352 (M⁺⁺ + 1).

7i: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1680 cm⁻¹ (sharp, strong, -CO- of acid group), 1650 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 1.6 (t, 3H, -CH₃), δ 2.4 (s, 3H, -CH₃), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.8 (t, 2H, -CH₂), 7.0-8.0 (m, 8H, Ar-H), 13.00 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 18.4, 35.4, 45.4, 46.3, 47.3, 51.3, 120.1, 122.2, 122.6, 124.5, 124.7, 127.4, 128.6, 131.0, 132.8, 164.6, 169.9. Ms: $m/z = 338 (M^{+} + 1)$.

7j: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1685 cm⁻¹ (sharp, strong, -CO- of acid group), 1650 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 2.4 (s, 3H, -CH₃), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.8 (t, 2H, -CH₂), 7.0-8.0 (m, 8H, Ar-H), 13.00 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 17.9, 51.2, 52.0, 70.2, 72.4, 121.2, 122.4, 125.3, 126.0, 126.9, 127.0, 129.6, 130.1, 131.5, 160.4, 166.7. Ms: *m*/*z* = 325 (M^{+.} + 1).

7k: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1685 cm⁻¹ (sharp, strong, –CO– of acid group), 1645 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.1 (t, 6H, –CH₃, –CH₃), δ 2.6 (s, 3H, –CH₃), δ 3.2 (q, 2H, –CH₂), δ 3.4 (q, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 10.6 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.4, 13.5, 19.6, 40.9, 43.5, 124.6, 125.6, 126.7, 128.6, 129.4, 130.6, 131.2, 136.5, 135.5, 166.9, 168.7. Ms: m/z = 311 (M⁺⁺ + 1).

7l: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1685 cm⁻¹ (sharp, strong, -CO- of acid group), 1655 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 2.4 (s, 1H, -NH), δ 2.4 (s, 3H, -CH₃), δ 3.0 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.6 (m, 8H, Ar-H), 10.6 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 19.5, 43.4, 45.5, 52.5, 53.4, 119.3, 123.4, 123.9, 124.9, 125.5, 127.6, 128.7, 130.2, 132.5, 161.3, 166.5. Ms: m/z = 324 (M⁺ + 1).

7m: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1695 cm⁻¹ (sharp, strong, –CO– of acid group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.4 (t, 3H, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 2.6 (q, 2H, –CH₂), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 10.4 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 11.23, 18.2, 42.1, 43.4, 45.2, 50.8, 51.3, 119.5, 120.4, 124.5, 126.9, 127.4, 126.1, 130.6, 131.3, 132.6, 160.1, 165.6. Ms: m/z = 352 (M⁺⁺ + 1).

7n: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1683 cm⁻¹ (sharp, strong, –CO– of acid group), 1650 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.6 (t, 3H, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), δ 3.2 (t, 2H, 8H, Ar-H), 13.00 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 18.3, 36.3, 43.5, 45.2, 46.2, 50.2, 121.2, 121.1, 122.4, 124.4, 125.6, 126.3, 127.2, 130.0, 131.4, 162.6, 166.8. Ms: m/z = 338 (M^{+.} + 1).

70: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1685 cm⁻¹ (sharp, strong, -CO- of acid group), 1650 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 2.4 (s, 3H, -CH₃), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.8 (t, 2H, -CH₂), 7.0-8.0 (m, 8H, Ar-H), 13.00 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 18.5, 50.1, 51.6, 73.5, 74.3, 119.2, 120.2, 121.2, 122.1, 123.4, 124.1, 125.3, 127.3, 128.3, 163.5, 167.4. Ms: m/z = 325 (M⁺⁺ + 1).

7p: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1670 cm⁻¹ (sharp, strong, –CO– of acid group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0 (t, 6H, –CH₃, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 3.2 (q, 2H, –CH₂), δ 3.4 (q, 2H, –CH₂), 70–8.0 (m, 8H, Ar-H), 10.6 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.4, 14.4, 32.9, 40.5, 121.4, 125.8, 126.8, 129.1, 130.3, 131.4, 134.6, 138.4, 139.9, 163.6, 169.9. Ms: m/z = 331 (M^{+.} + 1).

7q: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1684 cm⁻¹ (sharp, strong, -CO- of acid group), 1650 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 2.2 (s, 1H, -NH), δ 2.4 (s, 3H, -CH₃), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, $-CH_2$), δ 3.4 (t, 2H, $-CH_2$), δ 3.8 (t, 2H, $-CH_2$), 7.0–8.0 (m, 8H, Ar-H), 10.4 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 44.5, 44.9, 53.2, 54.2, 119.6, 120.5, 121.9, 122.9, 127.5, 128.5, 129.6, 130.2, 131.3, 162.4, 164.2. Ms: m/z = 344 (M⁺⁻ + 1).

7r: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1650 cm⁻¹ (sharp, strong, –CO– of acid group), 1640 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.2 (t, 3H, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 2.6 (q, 2H, –CH₂), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 10.4 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.8, 44.2, 45.4, 46.2, 51.8, 52.4, 119.6, 121.5, 124.5, 125.6, 127.3, 125.6, 130.2, 132.4, 135.7, 160.7, 165.9. Ms: m/z = 372 (M⁺⁺ + 1).

7s: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1640 cm⁻¹ (sharp, strong, –CO– of acid group), 1635 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.6 (t, 3H, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 8H, Ar-H), 13.00 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 38.3, 45.6, 46.2, 47.5, 50.6, 123.2, 126.6, 127.3, 128.3, 129.1, 129.9, 130.2, 131.4, 132.4, 160.3, 166.4. Ms: m/z = 358 (M⁺⁺ + 1).

7t: IR (KBr): $3100-3400 \text{ cm}^{-1}$ (broad medium, -NH-), 1690 cm⁻¹ (sharp, strong, -CO- of acid group), 1650 cm⁻¹ (sharp, strong, -CO- of amide group); ¹H-NMR: δ 2.4 (s, 3H, $-CH_3$), δ 3.0 (t, 2H, $-CH_2$), δ 3.2 (t, 2H, $-CH_2$), δ 3.4 (t, 2H, $-CH_2$), δ 3.8 (t, 2H, $-CH_2$), 7.0–8.0 (m, 8H, Ar-H), 13.00 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 48.1, 50.6, 72.5, 73.1, 119.5, 120.6, 122.3, 122.9, 123.5, 124.3, 125.7, 126.3, 129.3, 165.7, 169.4. Ms: m/z = 345 (M⁺⁻ + 1).

7u: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1680 cm⁻¹ (sharp, strong, –CO– of acid group), 1650 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.0 (t, 6H, –CH₃, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 3.2 (q, 2H, –CH₂), δ 3.4 (q, 2H, –CH₂), 7.0–8.0 (m, 9H, Ar-H), 10.6 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.5, 15.4, 37.9, 43.5, 125.4, 126.5, 126.8, 129.6, 131.2, 131.3, 135.6, 138.6, 139.3, 164.6, 169.8. Ms: m/z = 375 (M^{+.} + 1).

7v: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1687 cm⁻¹ (sharp, strong, –CO– of acid group), 1655 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 2.2 (s, 1H, –NH), δ 2.4 (s, 3H, –CH₃), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), δ 3.2 (t, 2H, 9H, Ar-H), 13.00 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 41.5, 45.9, 52.3, 54.5, 118.4, 121.3, 125.9, 126.9, 127.7, 128.4, 129.7, 131.4, 133.5, 165.4, 167.7. Ms: *m*/*z* = 388 (M^{+.} + 1).

7w: IR (KBr): 3100–3400 cm⁻¹ (broad medium, -NH–), 1681 cm⁻¹ (sharp, strong, -CO– of acid group), 1655 cm⁻¹ (sharp, strong, -CO– of amide group); ¹H-NMR: δ 1.2 (t, 3H, -CH₃), δ 2.4 (s, 3H, -CH₃), δ 2.6 (q, 2H, -CH₂), δ 3.0 (t, 2H, -CH₂), δ 3.2 (t, 2H, -CH₂), δ 3.4 (t, 2H, -CH₂), δ 3.8 (t, 2H, -CH₂), δ 3.2 (m, 9H, Ar-H), 10.4 (s, 1H, -NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 12.4, 43.5, 45.7, 47.3, 52.9, 53.4, 118.4, 121.6, 124.7, 125.5, 128.3, 129.5, 130.5, 131.3, 135.4, 164.5, 165.9. Ms: m/z = 416 (M⁺⁺ + 1).

7x: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1690 cm⁻¹ (sharp, strong, –CO– of acid group), 1658 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 1.6 (t, 3H, –CH₃), δ 2.4 (s, 3H, –CH₃), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, –CH₂), δ 3.8 (t, 2H, –CH₂), 7.0– 8.0 (m, 9H, Ar-H), 13.00 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 39.2, 46.4, 47.3, 48.4, 49.5, 121.2, 124.3, 124.9, 125.7, 126.4, 128.3, 130.6, 131.1, 131.3, 166.1, 169.3. Ms: m/z = 402 (M⁺ + 1).

7y: IR (KBr): 3100–3400 cm⁻¹ (broad medium, –NH–), 1675 cm⁻¹ (sharp, strong, –CO– of acid group), 1635 cm⁻¹ (sharp, strong, –CO– of amide group); ¹H-NMR: δ 2.4 (s, 3H, –CH₃), δ 3.0 (t, 2H, –CH₂), δ 3.2 (t, 2H, –CH₂), δ 3.4 (t, 2H, – CH₂), δ 3.8 (t, 2H, –CH₂), 7.0–8.0 (m, 9H, Ar-H), 13.00 (s, 1H, –NH, D2O exchangeable). ¹³C NMR (DMSO-d₆, 400 MHz): 48.9, 51.4, 73.5, 74.5, 119.6, 121.4, 122.5, 123.8, 124.7, 125.7, 126.4, 127.3, 129.3, 165.8, 169.3. Ms: m/z = 389 (M⁺⁺ + 1).

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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References

- O. R. Louis and R. G. Harry, "Alcoholysis of alkyl benzyl esters of phthalic acid," *The Journal of Organic Chemistry*, vol. 24, no. 12, pp. 1997–2000, 1959.
- [2] P. K. Dubey, S. M. G. Mohiuddin, and D. Ramesh, "Reactions of phthalic anhydride with alcohols," *Asian Journal of Chemistry*, vol. 9, no. 3, pp. 379–387, 1997.
- [3] P. A. Kober, J. T. Marshall, and E. N. Rosenfeld, "Phenolphthalein and its colorless salts. [Third paper.]. Preparation of monobasic phenolphthalates," *Journal of the American Chemical Society*, vol. 34, no. 10, pp. 1424–1433, 1912.
- [4] D. Williamm, "Salts of phenolphthalein," *Journal of the American Chemical Society*, vol. 54, no. 7, pp. 2947–2951, 1932.
- [5] S. A. Carlson and D. M. Hercules, "Delayed thermal fluorescence of anthraquinone in solutions," *Journal of the American Chemical Society*, vol. 93, no. 22, pp. 5611–5616, 1971.
- [6] L. Lunazzi, M. Mancinelli, and A. Mazzani, "Stereodynamics and conformational chirality of the atropisomers of ditolyl anthrones and anthraquinone," *The Journal of Organic Chemistry*, vol. 73, no. 14, pp. 5354–5359, 2008.
- [7] D. Guay, G. Tourillon, L. Gastonguay et al., "Highly photoactive chemically modified thin films of chloroaluminum (and bromoaluminum) phthalocyanines probed by NEXAFS and UPS: determination of the electronic structure and the molecular orientation," *Journal of Physical Chemistry*, vol. 95, no. 1, pp. 251– 257, 1991.
- [8] P. K. Dubey, S. M. G. Mohiuddin, and D. Ramesh, "Assay of phthalic anhydride and some related compounds by volumetric

methods," Asian Journal of Chemistry, vol. 7, no. 3, pp. 597–603, 1995.

- [9] L. O. Okunrobo, C. O. Usifoh, and S. O. Okpo, "Reactions of phthalimides with 1-methylethylamine: analgesic and antiinflammatory properties of resulting carboxamides," *Pakistan Journal of Pharmaceutical Sciences*, vol. 19, no. 1, pp. 34–38, 2006.
- [10] V. K. Pandey and N. Raj, "Synthesis of α-methylarylamido-βnaphthyl-(1-methylamino-2-methyl-benzimi-dazolyl)-ethers," *Current Science*, vol. 53, no. 5, pp. 256–258, 1984.
- [11] A. M. Alaa and A. Abdel, "Novel and versatile methodology for synthesis of cyclic imides and evaluation of their cytotoxic, DNA binding, apoptotic inducing activities and molecular modeling study," *European Journal of Medicinal Chemistry*, vol. 42, no. 5, pp. 614–626, 2007.
- [12] F. L. Dunlap and F. W. Cummer, "The action of the sodium salts of dibasic acids on aniline hydrochloride, and of aniline on phthalyl chloride and succinyl chloride," *Journal of the American Chemical Society*, vol. 25, no. 6, pp. 612–621, 1903.
- [13] A. T. Dann, W. Davies, A. N. Hambly, R. E. Paul, and G. S. C. Semmens, "Phthalyl fluoride," *Journal of the Chemical Society*, pp. 15–21, 1933.
- [14] E. G. D. de Toranzo and J. A. Brieux, "Syntheses of unsymmetric o-phthalic acid diamides," *Journal of Medicinal Chemistry*, vol. 10, no. 5, pp. 982–983, 1967.
- [15] A. Reynolds, "Synthesis and characterization of some toluides of o-phthalic acid," *The Journal of Organic Chemistry*, vol. 28, no. 11, pp. 3223–3225, 1963.
- [16] A. El-Faham and F. Albericio, "Peptide couplingreagents, more than a letter soup," *Chemical Reviews*, vol. 111, no. 11, pp. 6557– 6602, 2011.
- [17] L. A. Carpino and A. El-Faham, "Tetramethylfluoroformamidinium hexafluorophosphate: a rapid-acting peptide coupling reagent for solution and solid phase peptide synthesis," *Journal of the American Chemical Society*, vol. 117, no. 19, pp. 5401–5402, 1995.
- [18] R. Subiros-Funosas, G. A. Acosta, A. El-Faham, and F. Albericio, "Microwave irradiation and COMU: a potent combination for solid-phase peptide synthesis," *Tetrahedron Letters*, vol. 50, no. 45, pp. 6200–6202, 2009.
- [19] S.-Y. Han and Y.-A. Kim, "Recent development of peptide coupling reagents in organic synthesis," *Tetrahedron*, vol. 60, no. 11, pp. 2447–2467, 2004.



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