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$Al_2O_3/MeSO_3H$ (AMA) as a new reagent with high selective ability for monoesterification of diols

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Abstract—A new facile method for monoesterification of diols has been developed. A variety of diols, in particular oligoethylene glycols, were selectively monoesterified in excellent yields by reaction with aromatic and aliphatic acids in the presence of $Al_2O_3/MeSO_3H$ as a new reagent without use of any solvents. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Selective protection of a hydroxyl group of polyols is very important in organic synthesis.[1–4] Furthermore, synthesis of glycol monoesters of diols has received considerable interest in view of their widespread applications as intermediates for sex pheromones of Lepidoptera,[5,6] and cross linking agents for polyesters or fungicides.[7] The major drawback in the preparation of these compounds from diols is the concurrent formation of diesters, necessitating a tedious separation procedure of monoesters from diprotected and unprotected diols.[8] It is well known that dibutyltin oxides are useful reagent for monobenzoylation of diols.[9–13] The method, however, possesses some drawbacks. Namely, heating a mixture of diol and dibutyltin oxide for extended periods of time prior to the benzoylation because of the slow dehydration reaction between diol and dibutyltin oxide.[9] This imposes the use of more than an equimolar amount of dibutyltin oxide, which complicates the purification process of the products and makes the large scale production of monobenzoylated products difficult.

A microwave irradiation method has been reported to reduce the amount of dibutyltin oxide. However, this method still possesses disadvantages in that a microwave apparatus is required and the irradiation conditions might be drastic.[14–16] Recently, organotin compounds and $YbCl_3$ catalyzed monobenzoylation of diols have been reported.[17–19] The report briefly described the characteristics of the method such as the high yields of monoesterified products, but these methods suffer from disadvantages such as use of solvents, long reaction times and the use of more reactive derivatives, acid chlorides or anhydrides instead of acids. The direct reaction of a carboxylic acid with alcohol is generally avoided because of the equilibrium that is established between reagents and products, which requires the use of excess reagents or the elimination of water from the reaction mixture in order to lead the process to its completion. These limitations make the use of more reactive derivatives, such as acid chloride or anhydride, preferable.

We have recently reported that a mixture of $Al_2O_3/MeSO_3H$ (AMA) was an effective reagent for Fries-rearrangement,[20] Beckmann rearrangement[21] and the dehydration of nitriles into amides.[22] This paper reports the esterification reaction of various acids with diols to form the monoester compounds (Fig. 1).

2. Results and discussion

Due to the identical or similar chemical environments for symmetrical 1,*n*-diols, monofunctionalisation of them is not a trivial process in organic chemistry. To exploit an efficient reagent for the monoesterification of diols, the reaction of benzoic acid (**1a**) with ethylene glycol (**2**) was chosen as a

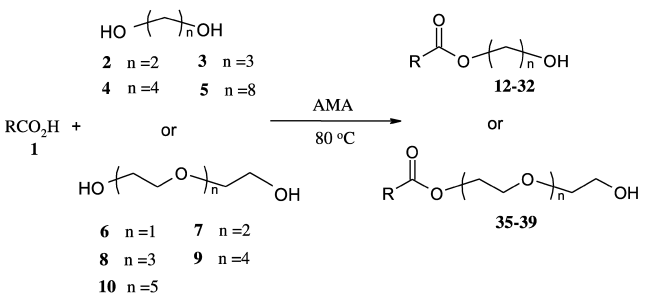

Figure 1.

Keywords: monoesterification; dibutyltin oxide; benzoic acid.

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model and its behavior was studied under a variety of conditions via TLC and ^{1}H NMR spectroscopy (Fig. 2, Table 1).

According to Table 1, the best results were obtained using a mixture of Al_2O_3 and $MeSO_3H$ in 1:5 molar ratio, when carried out at 80°C for 7 min. The results also show that the importance of using both Al_2O_3 and $MeSO_3H$. In the absence of $MeSO_3H$ (entry 4) or Al_2O_3 (entry 3), the attempted monobenzoylation did not afford product **12**.

A typical experimental procedure is as follows: to a mixture of $MeSO_3H$ (1 mL, 15 mmol) and Al_2O_3 (0.27 g, 3 mmol) was added benzoic acid (**1a**) (1 mmol) and ethylene glycol (**2**) (1 mmol). The mixture was stirred and heated in an oil bath at 80°C for 7 min. After a usual work-up 2-hydroxyethyl benzoate (**12**) was obtained in an excellent yield.

Under the best reaction conditions described above, diols (**2**–**11**) and aliphatic or aromatic carboxylic acids (**1a**–**o**) were converted into the corresponding monoesters (Table 2).

According to Table 2, aromatic and aliphatic carboxylic acids (**1a**–**o**) gave the corresponding monoesters of ethylene glycol (**2**) with perfect selectivity in the presence of AMA in excellent yields. Benzoic acids having two and three substituents (**1e**–**g**) were also reacted with ethylene glycol with a high selectivity. In particular benzoic acid (**1e**), which contains two hydroxy groups underwent selective monobenzoylation of ethylene glycol to give the hydroxy monoester (**16**) in 95% yield. Special mention must be made of the monoesterification of 1 or 2-naphtoic acids (**1h**,**i**), 1-nicotinic acid (**1j**), levulinatic acid (**1l**), stearic acid (**1m**), 11-bromodecanoic acid (**1n**) and cyclohexanoic acid (**1o**). All of these compounds underwent the reaction to give the corresponding glycol monoesters (**19**–**21** and **23**–**26**), respectively (runs 8–10, 12–15). To the best of our knowledge, this constitutes the first satisfactory method for the direct conversion of these acids to glycol monoesters.

Our method is applicable to other 1,*n*-diols; such as 1,3 and 1,4-diols under similar reaction conditions. For example, 1,3-propanediol (**3**) was also monobenzoylated with a high selectivity, but the yield was less than that in cases of 1,2-diol (compare run 1 and 16). Furthermore, the yields of monoester (**12**, **27**, **29** and **31**) decreased as the number of *n* in 1,*n*-diols increased and diester compounds were obtained as a side product (runs 1, 16–18). Using AMA for monoesterification, indirectly provides a useful means of the selective monoprotection of some symmetrical diols. Unsymmetrical diols such as propylene glycol (**11**), however, yielded a mixture (approximately 1:1) of two esters corresponding to either the primary or secondary hydroxy groups being benzoylated (run 19).

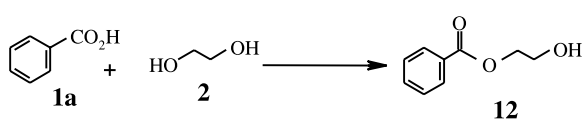


Figure 2.

Table 1. Monobenzoylation of ethylene glycol **2** with **1a** under various reaction conditions

Entry	Conditions	Time (min)	Yield[a] (%)
1	H_2SO_4, 80°C	180	No reaction
2	PPA, 80°C	90	41
3	$MeSO_3H$, 80°C	180	Trace
4	Al_2O_3, 80°C	180	No reaction
5	Al_2O_3 (1 mmol): $MeSO_3H$ (30 mmol), 80°C	10	74
6	Al_2O_3 (3 mmol): $MeSO_3H$ (30 mmol), 80°C	10	80
7	Al_2O_3 (3 mmol): $MeSO_3H$ (15 mmol), 100°C	10	83
8	Al_2O_3 (3 mmol): $MeSO_3H$ (15 mmol), 80°C	7	94

[a] Isolated yields.

Special mention must be made of the monobenzoylation of oligoethylene glycols (Fig. 1, Table 2). As can be seen from the data in Table 2, runs 20–24, the present method was also successful for monobenzoylation of representative di, tri, tetra, penta and hexa ethylene glycols (**6**–**10**) in high yields. This constitutes the first satisfactory method for the direct preparation of di, tri, tetra, penta and hexa ethyleneglycol monobenzoate (**35**–**39**). This sort of chemoselectivity was achieved with the AMA system, none of the other reagent systems reported earlier were that selective. The yields of these compounds are excellent and the reaction is very quick.

Furthermore, the high selectivity of the present method was observed by the use of amino alcohols and amino acids (runs 25–27). 2-Amino-1-ethanol (**12**) and /or amino acids such as tyrosine (**1p**) selectively gave the corresponding esters in excellent yields without the formation of any side products.

We know that esters are among the most important industrial products.[23] They are usually synthesized by one of three main methods[24]: (i) esterification of carboxylic acids, (ii) transesterification of methyl or ethyl esters, and (iii) alkylation of carboxylic anions. These reactions have been studied widely, but a great need still exists for versatile and simple processes whereby esters may be formed under very mild conditions.[25] This is specially so for the two first methods where equilibria are involved. The present method, which AMA use for monoesterification of diols, could be also applied to the preparation of esters (Fig. 3). Some of the results are shown in Table 3.

In conclusion, we have demonstrated that a readily available and inexpensive reagent $Al_2O_3/MeSO_3H$ (AMA) is very effective and highly selective for the monoesterification of diols. The extremely high 1,*n*-diol selectivity of this reaction may be very useful in organic synthesis. The low-cost and availability of the reagent, the easy procedure and work-up, the lack of solvent in the reaction step, and the high yields and short reaction time make this method a useful addition to the present methodologies. Hence, we believe that it will find wide application in organic synthesis as well as in industry.

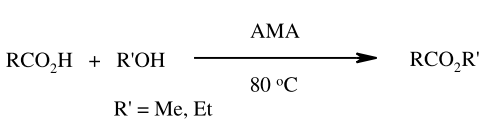
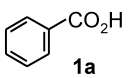
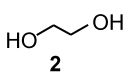
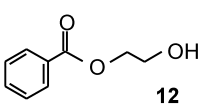
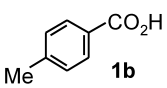
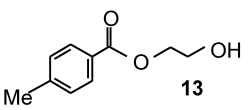
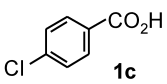
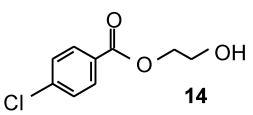
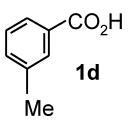
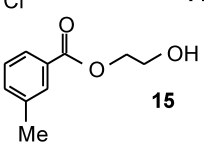
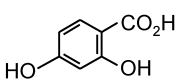
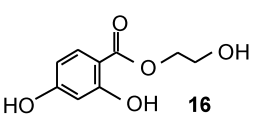
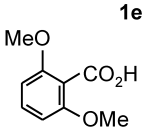
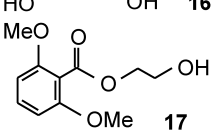
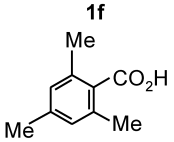
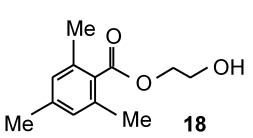
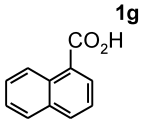
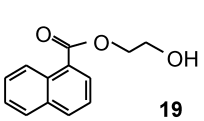
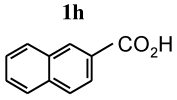
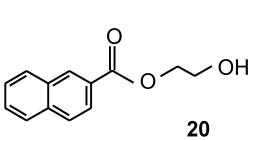
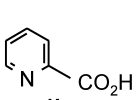
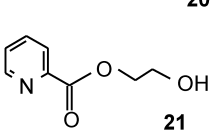
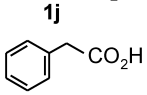
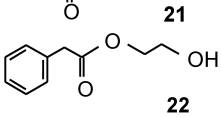
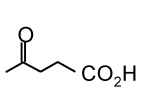
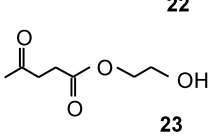
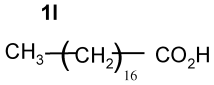
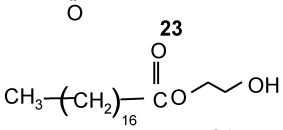
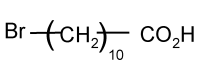
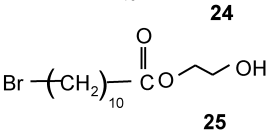


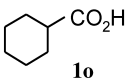
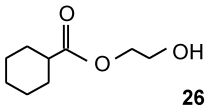
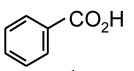
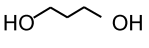
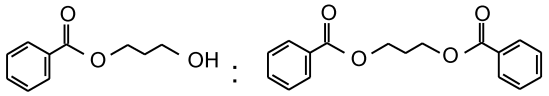
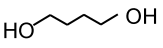
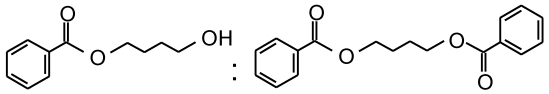
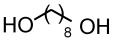
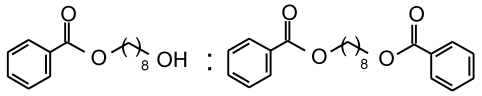
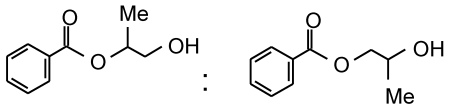
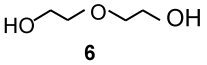
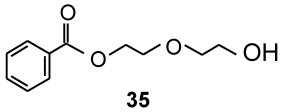
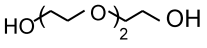
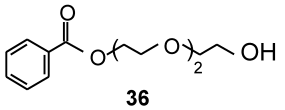
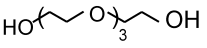
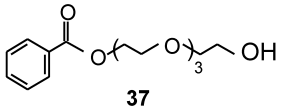
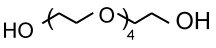
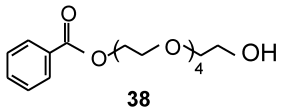
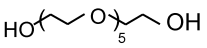
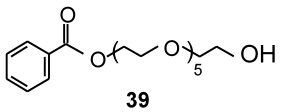
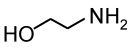
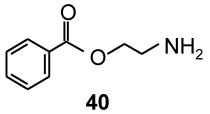
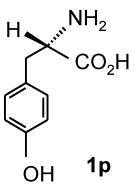
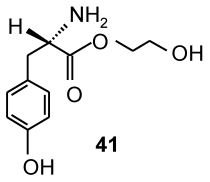
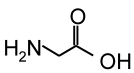
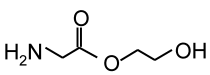
Figure 3.

Table 2. Monoesterification of diols and acids using a mixture of Al_2O_3 and $MeSO_3H$ (AMA) in 1:5 molar ratio at 80°C

Entry	Acids **1a–o**	*T* (min)	Diols **2–11**	Product[a]	Yield[b] (%)
1	 **1a**	7	 **2**	 **12**	94
2	 **1b**	10	**2**	 **13**	97
3	 **1c**	15	**2**	 **14**	96
4	 **1d**	15	**2**	 **15**	95
5	 **1e**	15	**2**	 **16**	95
6	 **1f**	15	**2**	 **17**	90
7	 **1g**	15	**2**	 **18**	90
8	 **1h**	30	**2**	 **19**	84
9	 **1i**	10	**2**	 **20**	87
10	 **1j**	30	**2**	 **21**	88
11	 **1k**	120	**2**	 **22**	82
12	 **1l**	15	**2**	 **23**	80
13	 **1m**	20	**2**	 **24**	80
14	 **1n**	20	**2**	 **25**	80

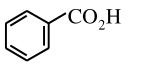
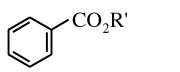
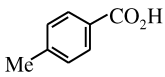
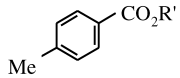
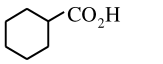
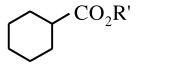
(*continued on next page*)

Table 2 (*continued*)

Entry	Acids **1a–o**	*T* (min)	Diols **2–11**	Product[a]	Yield[b] (%)
15	 **1o**	90	**2**	 **26**	80
16	 **1a**	30	 **3**	 **27** : **28**	87 (9:1)[c]
17	**1a**	30	 **4**	 **29** : **30**	86 (4:1)[c]
18	**1a**	30	 **5**	 **31** : **32**	94 (1:1)[c]
19	**1a**	35	 **11**	 **33** : **34**	82 (1:1)[c]
20	**1a**	60	 **6**	 **35**	92
21	**1a**	60	 **7**	 **36**	87
22	**1a**	60	 **8**	 **37**	84
23	**1a**	60	 **9**	 **38**	80
24	**1a**	60	 **10**	 **39**	80
25	**1a**	30	 **12**	 **40**	92
26	 **1p**	30	**2**	 **41**	91
27	 **1q**	60	**2**	 **42**	80

[a] Products were characterized by their IR, and NMR spectra.
[b] Yields refer to pure isolated products.
[c] The ratio of the products were estimated by ^{1}H NMR integration.

Table 3. Esterification of carboxylic acids

Entry	Acids	Product[a]	R′	T (min)	Yield[b] (%)
1			Me	5	90
			Et	4	96
2			Me	5	92
			Et	6	90
4	CH_3CO_2H	CH_3CO_2R'	Me	7	87
			Et	5	80
5			Me	7	98
			Et	10	95

[a] Products were characterized by their IR, and NMR spectroscopic data and compare with the authentic sample in the literature.
[b] Yields refer to pure isolated products.

3. Experimental

^1H NMR and ^{13}C NMR spectra were measured on Bruker Advance DPX FT 250 and 62.9 MHz spectrometry with TMS as an internal standard. IR spectra were obtained on a Perkin–Elmer or FTIR-800 instruments. Mass spectra were obtained on a Shimadzu GCMS0QP 1000EX at 20 and/or 70 eV. Elemental analyses were performed at the National Oil Co. of Iran, Tehran Research Center.

3.1. Materials

All starting materials, acids and diols, were used as purchased from Fluka or Merck. Acidic alumina (Al_2O_3) type 540 C and methanesulfonic acid 98% were purchased from Fluka.

3.2. General procedure for synthesis of monoesters

To a mixture of $MeSO_3H$ (1.0 mL, 1.5×10 mmol) and Al_2O_3 (0.27 g, 3.0 mmol) were added the appropriate acid (1.0 mmol) and diol (1.0 mmol), successively. The mixture was stirred and heated in an oil bath at 80°C for 7–120 min (see Table 2). Then the mixture was poured into water and extracted two times with ethyl acetate or chloroform (20 mL). Then organic layer was washed with a saturated solution of sodium bicarbonate (20 mL). Then the organic layer dried over $CaCl_2$ and evaporated in vacuo to give a residue, which was almost a pure monoester product. Further purification of the products was carried out by silica-gel short column chromatography.

Compounds **12**–**14**, **22**, **27**–**30**, **33** and **34** were known and the data for these compounds have been published previously in Refs. 17,26. Specific detailed data for each of the new compounds are given below.

3.2.1. 2-Hydroxyethyl 3-methylbenzoate (15). [Found: C, 66.52; H, 6.50. $C_{10}H_{12}O_3$ requires C, 66.65; H, 6.71%]; δ_H ($CDCl_3$) 2.37 (s, 3H, $-CH_3$), 3.94 (t, 2H, J=3.78 Hz, $-CH_2OH$), 4.43 (t, 2H, J=3.48 Hz, $-OCH_2CH_2OH$), 7.19–7.37 (m, 2H, Ar-H), 7.83–8.18 (m, 2H, Ar-H); δ_C (TMS): 21.49, 61.16, 67.79, 127.14, 128.59, 130.16, 130.49, 134.20, 138.46, 167.46; ν_{max} (neat) 3440, 1715, 1610, 1580, 1450, 1370, 1280, 1200, 1115, 1080, 925, 740, 680 cm^{-1}; m/z 180 (3.5, M^+), 163 (51.6), 119 (100), 91 (31.7%).

3.2.2. 2-Hydroxyethyl 2,4-dihydroxybenzoate (16). [Found: C, 54.31; H, 4.97. $C_9H_{10}O_5$ requires C, 54.55; H, 5.09%]; δ_H (DMSO) 3.70 (t, 2H, J=2.50 Hz, $-CH_2OH$), 4.28 (t, 2H, J=3.47 Hz, $-OCH_2CH_2OH$), 6.30 (s, 1H, Ar-H), 6.38 (d, 1H, J=1.77 Hz, Ar-H) 7.72 (d, 1H, J=4.83 Hz, Ar-H); δ_C (DMSO): 59.28, 66.79, 102.75, 104.37, 108.59, 132.18, 163.10, 164.56, 169.62; ν_{max} (neat) 3312, 1700, 1625, 1515, 1425, 1390, 1315, 1266, 1210, 1150, 1100, 1066, 999, 900, 834 cm^{-1}; m/z 198 (28.6, M^+), 180 (32.9), 137 (74), 136 (100), 108 (43.9%).

3.2.3. 2-Hydroxyethyl 2,6-dimethoxybenzoate (17). [Found: C, 58.24; H, 5.98. $C_{11}H_{14}O_5$ requires C, 58.40; H, 6.24%]; δ_H ($CDCl_3$) 3.82 (s, 6H, –OMe), 3.88 (t, 2H, J=4.60 Hz, $-CH_2OH$), 4.47 (t, 2H, J=3.53 Hz, $-OCH_2CH_2OH$), 6.47–6.60 (d, 2H, J=4.33 Hz, Ar-H), 7.33 (t, 1H, J=3.75 Hz, Ar-H); δ_C ($CDCl_3$): 55.60, 61.21, 66.90, 104.45, 113.02, 131.79, 157.70, 166.66; ν_{max} (neat) 3440, 1720, 1600, 1590, 1455, 1430, 1280, 1230, 1180, 1110, 1080, 1045, 755, 665 cm^{-1}; m/z 226 (19.8, M^+), 209 (24.6), 165 (100), 138 (15.8%).

3.2.4. 2-Hydroxyethyl 2,4,6-trimethylbenzoate (18). [Found: C, 68.99; H, 7.53. $C_{12}H_{16}O_3$ requires C, 69.21; H, 7.74%]; δ_H ($CDCl_3$) 2.20 (s, 9H, Me), 3.78 (t, 2H, J=3.75 Hz, $-CH_2OH$), 4.31 (t, 2H, J=4.58 Hz, $-OCH_2CH_2OH$), 6.76 (s, 2H, Ar-H); δ_C ($CDCl_3$): 20.12, 21.39, 60.85, 66.56, 128.86, 131, 09, 135.64, 139.90, 170.53; ν_{max} (neat) 3440, 1733, 1610, 1440, 1266, 1260, 1199, 1060, 870, 840 cm^{-1}; m/z 208 (11.5, $M^{+)}$, 147 (100), 146 (67.1), 119 (31), 91 (30.4%).

3.2.5. 2-Hydroxyethyl 1-naphthoate (19). [Found: C, 71.98; H, 5.31. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%]; δ_H ($CDCl_3$): 3.81 (t, 2H, J=4.65 Hz, $-CH_2OH$), 4.35 (t, 2H, J=4.53 Hz, $-OCH_2CH_2OH$), 7.28–7.48 (m, 3H, Ar-H), 7.70 (d, 1H, J=8.13 Hz, Ar-H), 7.82 (d, 1H, J=8.20 Hz, Ar-H), 8.04 (d, 1H, J=7.28 Hz, Ar-H), 8.75 (d, 1H, J=8.60 Hz, Ar-H); δ_C ($CDCl_3$): 61.40, 66.86, 124.87–134.18, 168.08; ν_{max} (neat) 3500, 1715, 1600, 1520, 1360, 1285, 1250, 1205, 1180, 1140, 1050, 960, 790 cm^{-1}; m/z 216 (25.1, M^+), 199 (18.2), 172 (30.2), 155 (100), 127 (48.9%).

3.2.6. 2-Hydroxyethyl 2-naphthoate (20). δ_H ($CDCl_3$) 4.02 (t, 2H, J=2.93 Hz, $-CH_2OH$), 4.55 (t, 2H, J=4.50 Hz, $-OCH_2CH_2OH$), 7.54–7.63 (m, 2H, Ar-H), 7.86–8.09 (m, 4H, Ar-H), 8.63 (s, 1H, Ar-H); δ_C ($CDCl_3$): 61.10, 67.02, 125.28–135.86, 167.39; ν_{max} (neat) 3460, 1710, 1630, 1460, 1390, 1370, 1350, 1285, 1230, 1197, 1130, 1105, 1087, 1015, 955, 915, 875, 847, 780, 755 cm^{-1}; m/z 216 (0.9, M^+), 199 (57.7), 172 (12.4), 155 (100), 127 (45.5%).

3.2.7. 2-Hydroxyethyl nicotinate (21). [Found: C, 57.11; H, 5.24. $C_8H_9NO_3$ requires C, 57.48; H, 5.43%]; δ_H (250 MHz) 3.95 (t, 2H, J=2.50 Hz, $-CH_2OH$), 4.47 (t, 2H, J=2.50 Hz, $-OCH_2CH_2OH$), 7.46 (m, 1H, Ar-H), 7.82 (m, 1H, Ar-H), 8.11 (m, 1H, Ar-H), 8.69 (m, 1H, Ar-H); δ_C (CCl_4, TMS): 61.69, 66.32, 122.61, 128.10, 136.01, 147.3, 147.6, 165.01; ν_{max} 3400, 1725, 1590, 1495, 1452, 1310, 1293, 1250, 1124,

1075, 800, 750, 701, 665 cm^{-1}; *m/z* 167 (19.9, M^+), 150 (12.4), 124 (13.5), 106 (40.7),78 (100), 51 (65.6%).

3.2.8. 2-Hydroxyethyl levulinate (23). [Found: C, 52.3; H, 7.31 $C_7H_{12}O_4$ requires C, 52.49; H, 7.55%]; δ_H ($CDCl_3$) δ 2.19 (s, 3H, CH_3CO-), 2.61 (t, 2H, J=5.00 Hz, $-CH_3COCH_2CH_2CO_2-$), 2.77 (t, 2H, J=5.50 Hz, $CH_3COCH_2CH_2CO_2-$), 3.77 (t, 2H, J=1.50 Hz, $-CH_2OH$), 4.25 (t, 2H, J=8.00 Hz, $-CO_2CH_2CH_2OH$); δ_C ($CDCl_3$): 28.10, 30.170, 38.04, 62.31, 67.58, 172.73, 206.92; ν_{max} (neat) 3450, 1740, 1415, 1410, 1350, 1175, 1075, 1015, 975, 920, 804 cm^{-1}; *m/z* 160 (1.6, M^+), 143 (64.4), 123 (15.1), 99 (100), 43 (63.3%).

3.2.9. 2-Hydroxyethyl stearate (24). δ_H (CCl_4) 0.88 (t, 3H, J=6.20 Hz, CH_3-), 1.26–1.58 (m, 30H, $CH_3(CH_2)_{15}CH_2CO_2-$), 2.30 (t, 2H, J=6.25 Hz, $CH_3(CH_2)_{15}CH_2CO_2-$), 3.70 (t, 2H, J=4.86 Hz, $-CH_2OH$), 4.12 (t, 2H, $-CO_2CH_2CH_2OH$); δ_C (CCl_4): 16.64, 25.12, 27.225, 31.58–34.35, 36.31, 63.19, 67.99, 175.27; ν_{max} (KBr) 3400, 2920, 2860, 1740, 1518, 1185, 720 cm^{-1}; *m/z* 328 (0.7, M^+), 104 (14.6), 69 (17.8), 43 (100), 41 (72.9%).

3.2.10. 2-Hydroxyethyl 11-bromoundecanoate (25). [Found: C, 50.21; H, 7.95. $C_{13}H_{25}BrO_3$ requires C, 50.49; H, 8.15%]; δ_H ($CDCl_3$) 1.29–1.63 (m, 16H, $BrCH_2(CH_2)_8CH_2CO_2-$), 2.33 (t, 2H, J=7.25 Hz, $BrCH_2(CH_2)_8CH_2CO_2-$), 3.40 (t, 2H, J=6.72 Hz, $BrCH_2(CH_2)_8CH_2CO_2-$), 3.83 (t, 2H, J=4.47 Hz, $-CH_2OH$), 4.22 (t, 2H, J=4.37 Hz, $-OCH_2CH_2OH$); δ_C ($CDCl_3$): 25.02, 25.13–29.61, 33.09, 34.23, 61.09, 66.03, 173.65; ν_{max} (KBr) 3416, 2916, 2840, 1750, 1460, 1200 cm^{-1}; *m/z* 309 (4.7, M^+), 291 (27.8), 79 (12.1), 45 (100), 43 (21.1%).

3.2.11. 2-Hydroxyethyl cyclohexanoate (26). δ_H ($CDCl_3$) 1.23–1.89 (m, 10H, C_6H_{10}), 3.79 (t, 2H, J=3.00 Hz, $-CH_2OH$), 4.18 (t, 2H, J=2.92 Hz, $-OCH_2CH_2OH$); δ_C ($CDCl_3$): 25.59, 25.93, 29.17, 43.19, 60.84, 65.85, 176.34; ν_{max} (neat) 3440, 2940, 2870, 1740, 1455, 1320, 1255, 1200, 1180, 1140, 1050 cm^{-1}; *m/z* 172 (3.0, M^+), 155 (100), 129 (10.0), 11 (40.8), 83 (39.9), 55 (30.9%).

3.2.12. 8-Hydroxyoctyl benzoate (31). [Found: C, 71.74; H, 8.64. $C_{15}H_{22}O_3$ requires C, 71.97; H, 8.86%]; δ_H ($CDCl_3$): 1.26–1.79 (m, 12H, $PhCO_2CH_2(CH_2)_6CH_2OH$), 3.63 (t, 2H, J=6.40 Hz, $-CH_2OH$), 4.29 (t, 2H, J=6.50 Hz, $PhCO_2CH_2(CH_2)_6CH_2OH$), 7.29–7.55 (m, 3H, Ar-H), 8.05 (d, 2H, J=7.25 Hz, Ar-H); δ_C ($CDCl_3$): 26.06, 26.49, 29.06, 29.68, 33.03, 63.19, 65.49, 128.7, 129.59, 130.30, 133.22, 167.14; ν_{max} (neat) 3425, 2941, 2904, 1724, 1604, 1450, 1284, 1120, 715 cm^{-1}; *m/z* 250 (1.2, M^+), 123 (58.8), 105 (100), 77 (40.8), 41 (43.8%).

3.2.13. 8-(Benzoyloxy)octyl benzoate (32). δ_H ($CDCl_3$) 1.18–2.08 (m, 12H, $PhCO_2CH_2(CH_2)_6CH_2-$), 4.24 (t, 4H, J=5.00 Hz, $PhCO_2CH_2(CH_2)_6CH_2-$), 7.18–7.49 (m, 6H, Ar-H), 7.97 (d, 4H, J=7.70 Hz, Ar-H); δ_C ($CDCl_3$): 26.38, 29.09, 29.57, 65.44, 128.71, 129.92, 130.90, 133.20, 167.08; ν_{max} (KBr) 2933, 2891, 1718, 1600, 1475, 1315, 1280, 1114, 717 cm^{-1}; *m/z* 354 (6.7, M^+), 329 (3.8), 123 (58.8), 105 (100).

3.2.14. Diethyleneglycol monobenzoate (35). [Found: C, 62.69; H, 6.58. $C_{11}H_{14}O_4$ requires C, 62.85; H, 6.71%]; δ_H ($CDCl_3$) 3.72 (m, 4H, $-OCH_2CH_2OH$), 3.85 (t, 2H, J=2.50 Hz, $PhCO_2CH_2CH_2O-$), 4.50 (t, 2H, J=2.75 Hz, $PhCO_2CH_2CH_2O-$), 7.41–7.59 (m, 3H, Ar-H), 8.06 (d, 2H, J=5.00 Hz, Ar-H); δ_C ($CDCl_3$): 63.20, 64.91, 66.18, 68.65, 130.53, 131.82, 132.07, 135.29, 169.14; ν_{max} (neat): 3416, 2916, 1717, 1600, 1449, 1320, 1274, 1200, 1165, 1130, 1066, 1033, 890 cm^{-1}; *m/z* 210 (1.1, M^+), 149 (19.7), 105 (100), 77 (31.6), 45 (32.5%).

3.2.15. Triethyleneglycol monobenzoate (36). δ_H ($CDCl_3$) 3.62–3.97 (m, 10H, $PhCO_2CH_2(CH_2OCH_2)_2CH_2OH$), 4.46 (t, 2H, J=2.90 Hz, $PhCO_2CH_2(CH_2OCH_2)_2CH_2OH$), 7.39–7.75 (m, 3H, Ar-H), 8.05 (d, 2H, J=7.25 Hz, Ar-H); δ_C ($CDCl_3$): 61.38, 64.49, 69.58, 70.38, 72.75, 128.74, 130.05, 130.37, 133.48, 166.98; ν_{max} (neat) 3416, 2916, 1717, 1600, 1592, 1440, 1260, 1200, 1115, 1043, 860 cm^{-1}; *m/z* 254 (0.8, M^+), 149 (20), 105 (100), 77 (29.5), 45 (32%).

3.2.16. Tetraethyleneglycol monobenzoate (37). δ_H ($CDCl_3$) 3.54–4.70 (m, 16H, $-O(CH_2CH_2O)_3CH_2CH_2OH$), 7.31–7.47 (m, 3H, Ar-H), 7.95 (d, 2H, J=7.00 Hz, Ar-H); δ_C ($CDCl_3$): 61.44, 63.17, 63.99, 66.91, 128.77, 130.07, 130.41, 133.54, 166.89; ν_{max} (neat) 3416, 2916, 1717, 1600, 1592, 1440, 1315, 1260, 1200, 1115, 1043, 860 cm^{-1}; *m/z* 298 (0.2, M^+), 149 (56.2), 105 (100), 77 (24.6), 45 (23.9%).

3.2.17. Pentaethyleneglycol monobenzoate (38). [Found: C, 59.46; H, 7.50. $C_{17}H_{26}O_7$ requires C, 59.64; H, 7.65%]; δ_H ($CDCl_3$) 3.91–4.83 (m, 20H, $-O(CH_2CH_2O)_4CH_2CH_2OH$), 7.70–7.89 (m, 3H, Ar-H), 8.39 (d, 2H, J=7.15 Hz, Ar-H); δ_C ($CDCl_3$): 61.58, 67.56, 128.78, 128.91, 130.14, 133.69, 167.37; ν_{max} (neat) 3445, 2970, 1726, 1610, 1593, 1500, 1460, 1380, 1325, 1285, 1185, 1130, 1078, 1035, 720 cm^{-1}; *m/z* 342 (M^+), 149 (95), 105 (100), 77 (18.8), 45 (11.1%).

3.2.18. Hexaethyleneglycol monobenzoate (39). δ_H ($CDCl_3$) 3.49–4.63 (m, 20H, $-O(CH_2CH_2O)_5CH_2CH_2OH$), 7.36–7.69 (m, 3H, Ar-H), 8.03 (d, 2H, J=6.87 Hz, Ar-H); δ_C ($CDCl_3$): 61.24, 66.92, 128.74, 128.89, 130.02, 133.66, 167.34; ν_{max} (neat) 3440, 2950, 1720, 1605, 1585, 1452, 1275, 1178, 1125, 1070, 1029, 928, 710 cm^{-1}; *m/z* 386 (M^+), 167 (20), 149 (84.4), 123 (17), 105 (100), 77 (20.8), 45 (22.4%).

3.2.19. 2-Aminoethyl benzoate (40). To a mixture of $MeSO_3H$ (1.0 mL, 1.5×10 mmol) and Al_2O_3 (0.27 g, 3.0 mmol) were added benzoic acid (**1a**) (0.12 g, 1.0 mmol) and 2-amino-1-ethanol (**12**) (0.06 mL, 1.0 mmol), respectively. The mixture was stirred and heated in an oil bath at 80°C for an appropriate time. Then the mixture was poured into a saturated solution of sodium bicarbonate and extracted two times with ethyl acetate (20 mL). The organic layer was dried over $CaCl_2$ and evaporated in vacuo to give the products.

[Found: C, 65.27; H, 6.52. $C_9H_{11}NO_2$ requires C, 65.44; H, 6.71%]; δ_H ($CDCl_3$) 3.53 (t, 2H, J=2.50 Hz, $-OCH_2CH_2NH_2$), 3.73 (t, 2H, J=3.00 Hz, $-OCH_2CH_2NH_2$), 4.67 (s, 2H, $-NH_2$), 7.31 (m, 3H, Ar-H), 7.74 (d, 2H, J=7.35 Hz, Ar-H); δ_C ($CDCl_3$): 43.19, 61.98, 127.44, 128.87, 130.09, 133.69, 169.19; ν_{max} (neat) 3357, 3074, 2948, 1724, 1652,

1556, 1519, 1388, 1313, 1974, 806, 717 cm^{-1}; MS (*m*/*z*) 165 (10.3, M^+), 149 (48.9), 105 (100), 77 (31.6%).

3.2.20. 2-Hydroxyethyl(2*S*)-2-amino-3-(4-hydroxyphenyl) propanoate (41). To a mixture of $MeSO_3H$ (1.0 mL, 1.5×10 mmol) and Al_2O_3 (0.27 g, 3.0 mmol) were added tyrosine (**1p**) (0.18 g, 1.0 mmol) and ethylene glycol (**2**) (0.06 mL, 1.0 mmol), successively. The mixture was stirred and heated in an oil bath at 80°C for an appropriate time. Then the mixture was poured into a saturated solution of sodium bicarbonate and extracted twice with ethyl acetate (20 mL). The organic layer was dried over $CaCl_2$ and evaporated in vacuo to give the products.

[Found: C, 58.47; H, 6.56. $C_{11}H_{15}NO_4$ requires C, 58.66; H, 6.71%]; δ_H ($CDCl_3$) 2.84 (m, 2H, Ar-CH_2–), 3.17 (d, 1H, *J*=10.37 Hz, –$CH_2CH(NH_2)$–, 4.19 (t, 2H, *J*=4.15 Hz, –$CO_2CH_2CH_2OH$), 4.38 (t, 2H, *J*=2.50 Hz, –$CO_2CH_2CH_2OH$), 6.69 (d, 2H, *J*=7.50 Hz, Ar-H), 7.02 (d, 2H, *J*=7.50 Hz, Ar-H); δ_C ($CDCl_3$): 41.93, 60.35, 65.30, 77.64, 120.58, 136.24, 156.54, 174.01; ν_{max} (neat) 3369, 3311, 2935, 1741, 1612, 1517, 1456, 1353, 1174, 927, 811 cm^{-1}; MS (*m*/*z*) 225 (M^+).

3.2.21. 2-Hydroxyethyl 2-aminoacetate (42). [Found: C, 40.24; H, 7.39. $C_4H_9NO_3$ requires C, 40.33; H, 7.62%]; δ_H ($CDCl_3$) 2.18 (s, 2H, –NH_2), 3.14 (s, 2H, NH_2CH_2CO–), 3.93 (t, 2H, *J*=5.00 Hz, –$CO_2CH_2CH_2OH$), 4.38 (t, 2H, *J*=2.50 Hz, –$CO_2CH_2CH_2OH$); δ_C ($CDCl_3$): 33.67, 57.02, 67.37, 168.19; ν_{max} (neat) 3562, 342945, 1760, 1650, 1352, 1174, 921, 811 cm^{-1}; MS (*m*/*z*) 119 (M^+).

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