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An expedient esterification of aromatic carboxylic acids using sodium bromate and sodium hydrogen sulfite

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Abstract—Treatment of aromatic carboxylic acids and substituted toluenes with a mixture of sodium bromate and sodium hydrogen sulfite in a two-phase system gave the corresponding esters in good yield. The intermediate α-brominated toluene was formed by the in situ generated hypobromous acid. The α-bromotoluene underwent an intermolecular nucleophilic substitution reaction with aromatic carboxylic acids present in the reaction mixture to afford the corresponding esters.

1. Introduction

Esterification of carboxylic acids by reaction with alkyl halides is a fundamental transformation in synthetic organic and medicinal chemistry.[1–3] Potassium and cesium salts are effectively used for this purpose.[4] Clark et al. in their extensive studies, revealed KF to be effective, but unfortunately the reaction usually requires high temperatures (110–130 °C).[4,5] Carboxylic esters have also been employed as key intermediates for the synthesis of a number of natural products.[6] Therefore, the synthesis of carboxylic esters is a very important transformation in organic chemistry. A number of reports[7–13] have been published to achieve this conversion, however, some of these require expensive reagents and tedious reaction work-up. More recently, the esterification of carboxylic acids with alkyl halides has been accomplished by employing CsF-Celite/CH_3CN.[14]

The present study describes a convenient and efficient one pot method for the esterification of substituted aromatic carboxylic acids with substituted toluenes by using the $NaBrO_3/NaHSO_3$ reagent at ambient temperature under a two-phase system.

The chemistry of the $NaBrO_3/NaHSO_3$ reagent has been widely studied. It can serve as an effective bromohydroxylation reagent and can react with olefins,[15] alkynes and allylic alcohols.[16] The oxidation of primary alcohols,[17] diols, ethers[18] and α-bromination of alkyl benzenes[19] was also reported. More recently, we have reported the conversion of *o*-alkylbenzoic acids into the corresponding γ-lactones by using this reagent.[20] In continuation of our study to extend the scope of the $NaBrO_3/NaHSO_3$ reagent in organic synthesis, we have found that the conversion of aromatic carboxylic acids with substituted toluenes into its corresponding esters can proceed using the $NaBrO_3/NaHSO_3$ reagent. To the best of our knowledge this is the first report of a one pot direct conversion of alkylbenzenes to the corresponding esters at room temperature.

2. Results and discussion

The $NaBrO_3/NaHSO_3$ reagent system appears to be most reactive, versatile, selective and useful for the conversion of aromatic carboxylic acids to their corresponding esters without affecting other susceptible functionalities.

In a typical experiment, to a two-phase system comprised of a solution of benzoic acid (**1a**) and toluene (**2a**) in ethyl acetate and aqueous $NaBrO_3$ (3 equiv.), aqueous $NaHSO_3$ (3 equiv.) was added over a period of about 15 min and stirred at room temperature for 40 h. The benzylbenzoate (**3a**) was obtained in 95% yield. However, the increase in reaction time from 40 to 60 h produced little increase in yield of product **3a** (from 95 to 99%). The yields using this two-phase system are generally higher than in a homogenous solution in acetonitrile, where **3a** is obtained only in a yield of 28%. Using the above procedure, the esters shown in Scheme 1 were prepared in very high yield.

The versatility of the reaction was demonstrated by its application to a wide range of structurally different aromatic carboxylic acids **1a**–**1j**. The reaction of **1b** with an alkyl

Keywords: aromatic carboxylic acids; substituted toluene; sodium bromate; sodium hydrogen sulfite; esters.

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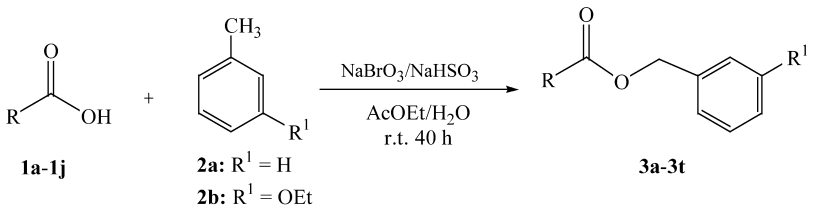
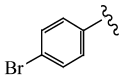
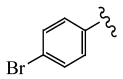
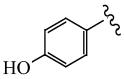
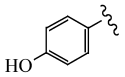
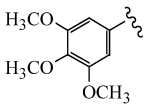
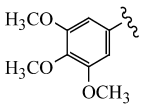
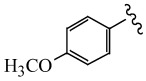
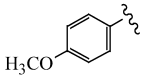
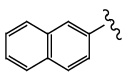
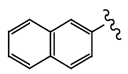


	R		R	R^1	Yields % method A	Yields % method B
1a		**3a/3k**		H/OEt	95/88	-
1b		**3b/3l**		H/OEt	90/82	-
1c		**3c/3m**		H/OEt	85/84	-
1d		**3d/3n**		H/OEt	81/83	-
1e		**3e/3o**		H/OEt	86/83	-
1f		**3f/3p**		H/OEt	80/84	-
1g		**3g/3q**		H/OEt	-	61/63
1h		**3h/3r**		H/OEt	-	61/65
1i		**3i/3s**		H/OEt	-	63/68
1j		**3j/3t**		H/OEt	-	65/66

Scheme 1.

benzene such as toluene (**2a**) or 3-ethoxytoluene (**2b**) using $NaBrO_3/NaHSO_3$ in ethyl acetate/water at room temperature, led to the formation of the **3b** and **3l** in excellent yields (90 and 82%), respectively. Similarly, 4-hydroxybenzoic acid (**1c**) was converted with toluene (**2a**) and 3-ethoxytoluene (**2b**) into **3c** and **3m** in good yields (85 and 84%), respectively. Furthermore, 2-nitrobenzoic acid (**1d**), 3,4,5-trimethoxybenzoic acid (**1e**) and 4-methoxybenzoic acid (**1f**) were reacted with toluene (**2a**) using $NaBrO_3/NaHSO_3$ reagent under a two-phase system to form the corresponding **3d**,**3e** and **3f** products by this procedure in satisfactory yields. The compounds **1d**,**1e** and **1f** were also treated with

3-ethoxytoluene (**2b**) using this reagent under two-phase system (method A) in ethyl acetate/water for 40 h to obtain compounds **3n**, **3o** and **3p**, respectively.

The compounds **1g**–**1j**, which are not sufficiently soluble in ethyl acetate, gave under these conditions, the esters in lower yield 17–18%. However, when these reactions were carried out under homogeneous conditions (method B) using CH_3CN as a solvent the corresponding esters were obtained in 61–68% yields, which indicates the versatility of the reagent. On the basis of these results, nicotinic acid (**1g**) and isonicotinic acid (**1h**) were treated with toluene (**2a**) in the presence of $NaBrO_3/NaHSO_3$ reagent under homogeneous conditions using acetonitrile as the solvent to form compounds **3g** and **3h**, respectively. Similarly, the reaction of **1g** and **1h** with 3-ethoxytoluene (**2b**) gave **3q** and **3r** products in satisfactory yields. Moreover, benzyl 2-thiophenecarboxylate (**3i**) and benzyl 2-naphthoate (**3j**) were synthesized by treatment of toluene (**2a**) in acetonitrile with **1i** and **1j**, respectively in the presence of $NaBrO_3/NaHSO_3$ reagent. The synthesis of **3s** and **3t** were also accomplished by the treatment of 3-ethoxytoluene (**2b**) with **1i** and **1j** respectively using $NaBrO_3/NaHSO_3$ reagent under homogeneous conditions in satisfactory yield (68 and 66%). The results and spectroscopic data of the all esters were collected in Section 4. The reaction was found to be highly selective as only aromatic carboxylic acids are converted to esters in moderate to high yield, whereas aliphatic carboxylic acids did not yield esters even after four days stirring in CH_3CN at room temperature (Scheme 2). The chemoselectivity of this reagent system has been illustrated in the case of **1c**, where the carboxylic acid group alone has been converted to its ester form **3c** and **3m** without effecting OH group present in the molecule.

$NaBrO_3/NaHSO_3$ present in aqueous phase in situ generates HOBr which delivers a Br-radical in the aqueous solution[19] and the radical moves to the ethyl acetate phase, where **1** and **2** are dissolved, subsequently by intermolecular nucleophilic attack, the esters **3** form (Scheme 1).

The advantages of $NaBrO_3/NaHSO_3$ method over other existing procedures for this transformation are: (1) It is a direct one pot method of esterification of aromatic carboxylic acids by reaction with substituted toluenes. (2) The reaction takes place at room temperature. (3) In situ generation of arylhalides takes place, so it may be a useful method for preparation of those aryl halides which may unstable.[2,10,14]

3. Conclusion

The convenient, efficient, simple, highly selective and high yielding esterification of aromatic carboxylic acids with toluene using $NaBrO_3/NaHSO_3$ reagent under two-phase system at ambient temperature, described in this paper, serves as a useful synthetic tool to obtain valuable esters. Products obtained were pure in most cases with no C-, S- or N-alkylation or quaternary salt formation being detected. The reaction protocol described is promising in the sense that it offers an easy access to ester structures which frequently occur in natural products.

4. Experimental

4.1. General

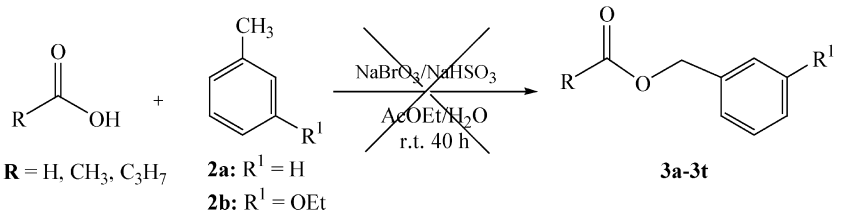
Ultraviolet spectra were recorded in methanol on a Hitachi U-3200 spectrophotometer. Infrared (IR) spectra were measured on a Shimadzu IR 460 spectrophotometer in $CHCl_3$. Electron impact mass spectra were determined with a Finnigan MAT-312 or Varian MAT-112 double focusing mass spectrophotometer connected to a PDP 11/34 (DEC) computer system. Elemental analyses were carried out on a Perkin–Elmer 2400 CHN Elemental Analyzer. The ^1H NMR spectra were recorded in $CDCl_3$ or CD_3OD with Bruker AM 400 spectrophotometers operating at 400 MHz. ^1H NMR chemical shifts are reported in δ (ppm) and coupling constants in Hz. Reactions were monitored by TLC using silica gel type $60F_{254}$ of E. Merck for preparing TLC plates and visualized with ultra violet light at 254 and 366 nm and spraying with iodine vapors.

4.2. Materials

All substituted benzoic acids, toluene (**2a**) and 3-ethoxytoluene (**2b**) are commercially available (Fluka, Aldrich). All reagents $NaBrO_3$, $NaHSO_3$, $Na_2S_2O_3$ and $MgSO_4$ are also available from Aldrich. The acetonitrile, ethyl acetate and diethyl ether were purchased from Merck and used without purification.

4.3. General procedure for the preparation of 3a-3t

Method A. To a solution of **1** (1 mmol) and substituted toluene **2** (1 mmol) in ethyl acetate (5 mL) was added a solution of $NaBrO_3$ (3 mmol) in H_2O (3 mL). To this mixture $NaHSO_3$ (3 mmol) in H_2O (6 mL) during a period of 15 min was added and the mixture was stirred at room temperature for 40 h. The mixture was extracted with



Scheme 2.

diethyl ether (25×3 mL). Then the combined organic layer was washed with aqueous $Na_2S_2O_3$ and dried over $MgSO_4$. After filtration, the solvent was evaporated (under vacuum) to leave the crude material. The crude product was purified by column chromatography over silica gel using *n*-hexane/ethyl acetate (9:1) as an eluent to afford pure esters **3**.

Method B. To a solution of **1** (1 mmol) and substituted toluene **2** (1 mmol) in acetonitrile (10 mL) was added a solution of $NaBrO_3$ (3 mmol) in H_2O (6 mL). To this mixture $NaHSO_3$ (3 mmol) in H_2O (12 mL) during a period of 15 min was added and the mixture was stirred at ambient temperature for 40 h. The product was worked up as described above.

4.3.1. Benzyl benzoate (3a).[21,23,25] Yield: 0.20 g (95%); oily compound; [Found: C, 79.29; H, 5.66. $C_{14}H_{12}O_2$ requires C, 79.22; H, 5.70%] R_f=0.69 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 256 (ε=3.92) nm; ν_{max} ($CHCl_3$) 2913, 1721, 1135, 1083, 761, 663 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.92–7.49 (5H, m, Ar-*H*), 7.45–7.19 (5H, m, Ar-*H*), 5.31 (2H, s, ArCH_2); *m*/*z* 212 ($28M^+$), 121 (100), 105 (32), 91 (52), 77 (19), 56 (11%).

4.3.2. Benzyl 4-bromobenzoate (3b).[22,24] Yield: 0.26 g (90%); oily compound; [Found: C, 57.81; H, 3.77; Br, 27.53. $C_{14}H_{11}BrO_2$ requires C, 57.76; H, 3.81; Br, 27.45%]; R_f=0.65 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 257 (ε=3.97) nm; ν_{max} ($CHCl_3$) 2898, 1723, 1248, 1145, 836, 745, 663 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.96 (2H, d, *J*=8.1 Hz, *H*-2/*H*-6), 7.49 (2H, d, *J*=8.1 Hz, *H*-3/*H*-5), 7.41–7.13 (5H, m, Ar-*H*), 5.34 (2H, s, ArCH_2); *m*/*z* 293 ($19M^+$+2), 291 ($21M^+$), 211 (11), 200 (100), 184 (31), 156 (13), 91 (25), 76 (21), 55 (12%).

4.3.3. Benzyl 4-hydroxybenzoate (3c).[21,23] Yield: 0.19 g (85%); oily compound; [Found: C, 73.72; H, 5.36. $C_{14}H_{12}O_3$ requires C, 73.67; H, 5.30%]; R_f=0.59 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 261 (ε=4.32) nm; ν_{max} ($CHCl_3$) 3311, 2906, 1721, 1156, 1047, 834, 732 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, *J*=8.3 Hz, *H*-2/*H*-6), 6.83 (2H, d, *J*=8.3 Hz, *H*-3/*H*-5), 7.39–7.16 (5H, m, Ar-*H*), 5.29 (2H, s, ArCH_2); *m*/*z* 228 ($18M^+$), 211 (8), 137 (100), 121 (41), 93 (12), 91 (31), 75 (17), 55 (9%).

4.3.4. Benzyl 2-nitrobenzoate (3d).[23] Yield: 0.21 g (81%); oily compound; [Found: C, 65.31; H, 4.36; N, 5.49. $C_{14}H_{11}NO_4$ requires C, 65.37; H, 4.31; N, 5.44%]; R_f=0.67 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 263 (ε=4.35) nm; ν_{max} ($CHCl_3$) 2905, 1719, 1585, 1210, 1055, 735, 665 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.12–7.56 (4H, m, Ar-*H*), 7.45–7.18 (5H, m, Ar-*H*), 5.32 (2H, s, ArCH_2); *m*/*z* 257 ($31M^+$), 211 (11), 166 (100), 150 (17), 122 (31), 91 (15), 76 (22), 54 (9), 46 (8%).

4.3.5. Benzyl 3,4,5-trimethoxybenzoate (3e).[24] Yield: 0.26 g (86%); oily compound; [Found: C, 67.59; H, 5.95. $C_{17}H_{18}O_5$ requires C, 67.54; H, 6.00%]; R_f=0.68 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 263 (ε=4.58) nm; ν_{max} ($CHCl_3$) 2892, 1723, 1411, 1144, 1026, 818, 742 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.56–7.21 (5H, m, Ar-*H*), 7.09 (2H, s, Ar-*H*), 3.85 (6H, s, 2OCH_3), 3.81 (3H, s, OCH_3), 5.28 (2H, s, ArCH_2); *m*/*z* 302 ($25M^+$), 211 (100), 195 (43), 167 (32), 287 (9), 27 (7), 91 (15), 74 (19), 54 (8%).

4.3.6. Benzyl 4-methoxybenzoate (3f).[23,25] Yield: 0.19 g (80%); oily compound; [Found: C, 74.41; H, 5.78. $C_{15}H_{14}O_3$ requires C, 74.36; H, 5.82%]; R_f=0.61 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 267 (ε=4.56) nm; ν_{max} ($CHCl_3$) 3028, 2916, 2824, 1721, 1493, 1128, 764, 684 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.79 (2H, d, *J*=8.1 Hz, *H*-2/*H*-6), 7.27–7.05 (5H, m, Ar-*H*), 6.81 (2H, d, *J*=8.1 Hz, *H*-3/*H*-5), 5.31 (2H, s, ArCH_2), 3.83 (3H, s, OCH_3); *m*/*z* 242 ($41M^+$), 151 (100), 135 (56), 107 (31), 91 (23), 76 (9), 54 (8%).

4.3.7. Benzyl nicotinate (3g).[26] Yield: 0.12 g (61%); oily compound; [Found: C, 73.27; H, 5.16; N, 6.61. $C_{13}H_{11}NO_2$ requires C, 73.22; H, 5.20; N, 6.57%]; R_f=0.51 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 265 (ε=4.73) nm; ν_{max} ($CHCl_3$) 3011, 2925, 1719, 1487, 1311, 1135, 829 cm^{-1}; δ_H (400 MHz, CD_3OD) 9.19–7.83 (4H, m, pyridine-*H*), 7.48–7.16 (5H, m, Ar-*H*), 5.36 (2H, s, ArCH_2); *m*/*z*: 213 ($43M^+$), 122 (100), 106 (21), 91 (17), 78 (19), 55 (9%).

4.3.8. Benzyl isonicotinate (3h).[26,27] Yield: 0.13 g (61%); oily compound; [Found: C, 73.29; H, 5.17; N, 6.55. $C_{13}H_{11}NO_2$ requires C, 73.22; H, 5.20; N, 6.57%]; R_f=0.53 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 258 (ε=4.16) nm; ν_{max} ($CHCl_3$) 3013, 2926, 1724, 1496, 1315, 1136, 832 cm^{-1}; δ_H (400 MHz, CD_3OD) 8.91 (2H, d, *J*=8.4 Hz, *H*-2/*H*-6), 7.92 (2H, d, *J*=8.4 Hz, *H*-3/*H*-5), 7.47–7.15 (5H, m, Ar-*H*), 5.35 (2H, s, ArCH_2); *m*/*z* 213 ($39M^+$), 122 (100), 106 (23), 91 (19), 77 (18), 56 (11%).

4.3.9. Benzyl 2-thiophenecarboxylate (3i). Yield: 0.14 g (63%); oily compound; [Found: C, 66.07; H, 4.67; S, 14.62. $C_{12}H_{10}O_2S$ requires C, 66.03; H, 4.62; S, 14.69%]; R_f=0.55 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 244 (ε=3.87) nm; ν_{max} ($CHCl_3$) 3015, 2861, 1721, 1256, 1035, 811, 648 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.08–6.79 (3H, m, thiophene-*H*), 7.46–7.16 (5H, m, Ar-*H*), 5.27 (2H, s, ArCH_2); *m*/*z* 218 ($33M^+$), 127 (100), 111 (21), 91 (19), 83 (25), 46 (9%).

4.3.10. Benzyl 2-naphthoate (3j).[25,28] Yield: 0.17 g (65%); oily compound; [Found: C, 82.46; H 5.33. $C_{18}H_{14}O_2$ requires C, 82.42; H, 5.38%]; R_f=0.56 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 272 (ε=4.69) nm; ν_{max} ($CHCl_3$) 2895, 1719, 1408, 1263, 1134, 732, 678 cm^{-1}; δ_H (400 MHz, CD_3OD) 8.51–7.76 (7H, m, naphthol-*H*), 7.45–7.18 (5H, m, Ar-*H*), 5.33 (2H, s, ArCH_2); *m*/*z* 262 ($34M^+$), 171 (100), 155 (21), 127 (24), 91 (18), 76 (9), 75 (14), 52 (13%).

4.3.11. 3-Ethoxy benzylbenzoate (3k). Yield: 0.22 g (88%); oily compound; [Found: C, 74.93; H, 6.33. $C_{16}H_{16}O_3$ requires C, 74.98; H, 6.29%]; R_f=0.75 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 254 (ε=3.91) nm; ν_{max} ($CHCl_3$) 2913, 1722, 1138, 1083, 763, 662 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.92–7.45 (5H, m, Ar-*H*), 7.34–6.76 (4H, m, Ar-*H*), 5.33 (2H, s, ArCH_2), 3.82 (2H, q, *J*=7.4 Hz, CH_2), 1.31 (3H, t, *J*=7.4 Hz, CH_3); *m*/*z* 256 ($23M^+$), 227 (14), 211 (21), 122 (100), 105 (31), 91 (43), 77 (17), 56 (9%).

4.3.12. 3-Ethoxybenzyl 4-bromobenzoate (3l). Yield: 0.27 g (82%); oily compound; [Found: C, 57.37; H, 4.56; Br, 23.79. $C_{16}H_{15}BrO_3$ requires C, 57.33; H, 4.51; Br, 23.84%]; R_f=0.72 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 259 (ε=3.99) nm; ν_{max} ($CHCl_3$) 2889, 1721, 1241, 1146, 837, 746, 661 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.93 (2H, d, *J*=8.4 Hz, *H*-2/*H*-6), 7.41 (2H, d, *J*=8.4 Hz, H-3/H-5), 7.31–6.67 (4H, m, Ar-*H*), 5.31 (2H, s, ArCH_2), 3.79 (2H, q, *J*=7.5 Hz, CH_2), 1.29 (3H, t, *J*=7.5 Hz, CH_3); *m/z* 337 ($18M^+ + 2$), 335 ($19M^+$), 306 (21), 290 (16), 201 (100), 184 (32), 156 (15), 91 (43), 76 (13), 55 (9%).

4.3.13. 3-Ethoxybenzyl 4-hydroxybenzoate (3m). Yield: 0.23 g (84%); oily compound; [Found: C, 70.61; H, 5.88. $C_{16}H_{16}O_4$ requires C, 70.57; H, 5.92%]; R_f=0.66 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 261 (ε=4.42) nm; ν_{max} ($CHCl_3$) 3315, 2909, 1719, 1151, 1048, 835, 731 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.85 (2H, d, *J*=7.9 Hz, *H*-2/*H*-6), 6.83 (2H, d, *J*=7.9 Hz, *H*-3/*H*-5), 7.39–6.72 (4H, m, Ar-*H*), 5.28 (2H, s, ArCH_2), 3.83 (2H, q, *J*=7.6 Hz, CH_2), 1.31 (3H, t, *J*=7.6 Hz, CH_3); *m/z* 272 ($24M^+$), 243 (35), 227 (21), 138 (100), 121 (43), 93 (15), 91 (27), 75 (11), 55 (8%).

4.3.14. 3-Ethoxybenzyl 2-nitrobenzoate (3n). Yield: 0.25 g (83%); oily compound; [Found: C, 63.76; H, 5.07; N, 4.61. $C_{16}H_{15}NO_4$ requires C, 63.78; H, 5.02; N, 4.65%]; R_f=0.73 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 266 (ε=4.35) nm; ν_{max} ($CHCl_3$) 2909, 1721, 1588, 1211, 1056, 741, 665 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.15–7.52 (4H, m, Ar-*H*), 7.35–6.73 (4H, m, Ar-*H*), 5.31 (2H, s, ArCH_2), 3.84 (2H, q, *J*=7.3 Hz, CH_2), 1.33 (3H, t, *J*=7.3 Hz, CH_3); *m/z* 301 ($23M^+$), 272 (16), 256 (13), 167 (100), 150 (21), 122 (33), 91 (14), 76 (9), 54 (8), 46 (11%).

4.3.15. 3-Ethoxybenzyl 3,4,5-trimethoxybenzoate (3o). Yield: 0.29 g (83%); oily compound; [Found: C, 65.92; H, 6.35. $C_{19}H_{22}O_6$ requires C, 65.88; H, 6.40%]; R_f=0.74 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 269 (ε=4.64) nm; ν_{max} ($CHCl_3$) 2899, 1725, 1416, 1145, 1036, 816, 739 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.41–6.76 (4H, m, Ar-*H*), 7.11 (2H, s, Ar-*H*), 5.29 (2H, s, Ar-CH_2), 3.84 (6H, s, 2OCH_3), 3.82 (3H, s, OCH_3), 3.79 (2H, q, *J*=7.5 Hz, CH_2), 1.31 (3H, t, *J*=7.5 Hz, CH_3); *m/z* 346 ($34M^+$), 317 (11), 301 (19), 212 (100), 195 (45), 167 (33), 287 (9), 271 (6), 91 (14), 74 (21), 54 (11%).

4.3.16. 3-Ethoxybenzyl 4-methoxybenzoate (3p). Yield: 0.24 g (84%); oily compound; [Found: C, 71.38; H, 6.29. $C_{17}H_{18}O_4$ requires C, 71.31; H, 6.34%]; R_f=0.71 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 273 (ε=5.04) nm; ν_{max} ($CHCl_3$) 3031, 2917, 2825, 1722, 1492, 1131, 765, 683 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.68 (2H, d, *J*=7.7 Hz, *H*-2/*H*-6), 7.27–6.84 (4H, m, Ar-*H*), 6.79 (2H, d, *J*=7.7 Hz, *H*-3/*H*-5), 5.33 (2H, s, ArCH_2), 3.85 (3H, s, OCH_3), 3.82 (2H, q, *J*=7.5 Hz, CH_2), 1.34 (3H, t, *J*=7.5 Hz, CH_3); *m/z* 286 ($41M^+$), 257 (19), 241 (31), 151 (100), 135 (51), 107 (27), 91 (21), 76 (9), 54 (14%).

4.3.17. 3-Ethoxybenzyl nicotinate (3q). Yield: 0.16 g (63%); oily compound; [Found: C, 70.06; H, 5.84; N, 5.48. $C_{15}H_{15}NO_3$ requires C, 70.02; H, 5.88; N, 5.44%]; R_f=0.67 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 253 (ε=4.73) nm; ν_{max} ($CHCl_3$) 3015, 2924, 1721, 1491, 1311, 1135, 829 cm^{-1}; δ_H (400 MHz, CD_3OD) 9.19–7.91 (4H, m, pyridine-*H*), 7.35–6.78 (4H, m, Ar-*H*), 5.35 (2H, s, ArCH_2), 3.81 (2H, q, *J*=7.4 Hz, CH_2), 1.31 (3H, t, *J*=7.4 Hz, CH_3); *m/z* 257 ($38M^+$), 228 (23), 212 (34), 123 (100), 106 (25), 91 (19), 78 (11), 55 (9%).

4.3.18. 3-Ethoxybenzyl isonicotinate (3r). Yield: 0.17 g (65%); oily compound; [Found: C, 70.07; H, 5.83; N, 5.41. $C_{15}H_{15}NO_3$ requires C, 70.02; H, 5.88; N, 5.44%]; R_f=0.63 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 254 (ε=4.09) nm; ν_{max} ($CHCl_3$) 3011, 2921, 1716, 1479, 1311, 1138, 827 cm^{-1}; δ_H (400 MHz, CD_3OD) 8.89 (2H, d, *J*=8.5 Hz, *H*-2/*H*-6), 7.93 (2H, d, *J*=8.5 Hz, *H*-3/*H*-5), 7.36–6.79 (4H, m, Ar-*H*), 5.37 (2H, s, ArCH_2), 3.84 (2H, q, *J*=7.6 Hz, CH_2), 1.34 (3H, t, *J*=7.6 Hz, CH_3); *m/z* 257 ($41M^+$), 228 (19), 212 (31), 123 (100), 106 (25), 91 (16), 77 (17), 56 (9%).

4.3.19. 3-Ethoxybenzyl 2-thiophenecarboxylate (3s). Yield: 0.18 g (68%); oily compound; [Found: C, 64.15; H, 5.32; S, 12.25. $C_{14}H_{14}O_3S$ requires C, 64.10; H, 5.38; S, 12.22%]; R_f=0.61 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 239 (ε=3.91) nm; ν_{max} ($CHCl_3$) 3021, 2893, 1721, 1251, 1037, 811, 649 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.06–6.84 (3H, m, thiophene-*H*), 7.35–6.78 (4H, m, Ar-*H*), 5.29 (2H, s, ArCH_2), 3.79 (2H, q, *J*=7.1 Hz, CH_2), 1.29 (3H, t, *J*=7.1 Hz, CH_3); *m/z* 262 ($35M^+$), 233 (21), 217 (19), 128 (100), 111 (22), 91 (9), 83 (21), 46 (11%).

4.3.20. 3-Ethoxybenzyl 2-naphthoate (3t). Yield: 0.20 g (66%); oily compound; [Found: C, 74.45; H, 5.88. $C_{20}H_{18}O_3$ requires C, 74.41; H, 5.92%]; R_f=0.63 (hexane/ethyl acetate, 5:2); λ_{max} (MeOH) 281 (ε=5.11) nm; ν_{max} ($CHCl_3$) 2896, 1724, 1411, 1261, 1134, 737, 672 cm^{-1}; δ_H (400 MHz, CD_3OD) 8.79–7.76 (7H, m, naphthol-*H*), 7.38–6.76 (4H, m, Ar-*H*), 5.34 (2H, s, ArCH_2), 3.81 (2H, q, *J*=7.3 Hz, CH_2), 1.32 (3H, t, *J*=7.3 Hz, CH_3); *m/z* 306 ($41M^+$), 277 (17), 261 (11), 172 (100), 159 (19), 127 (23), 91 (14), 76 (11), 75 (9), 52 (14%).

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