Preparation of Novel Monoesters of Succinic Acid from Succinic Anhydride using \( p \)-Toluensulphonic Acid as a Catalyst

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Abstract

The industrial and pharmaceutical applications of monoesters of succinic anhydride have always prompted the scientists for exploring new methods for the synthesis of the products without using toxic and expensive chemicals. However, up to now no significant approach has come forward. The available methods are not only ecologically unfriendly i.e. create heat, evolve toxic gases but also provide low yield. Therefore, a new technique has been proposed in which the opening of ring of succinic anhydride was performed by treating it with aryl alcohols, using \( p \)-toluene sulphonic acid as a catalyst and toluene as a solvent. In this way 1-27 monoesters of di-, and tri-substituted aryl alcohols have been synthesised with good yield; however, in case of 2,6-disubstituted alcohols the yield was considerably lower than others and was attributed to steric hindrance. The final products were purified using chromatographic techniques and their structure was confirmed by recording IR, UV, 1D, 2D, (\( ^1H \) and \( ^13C \)) NMR spectra, mass measurements and elemental analysis.

Keywords: Succinic Anhydride, Aryl Alcohols, Monoesters of Succinic Acid, 1D-NMR, 2D-NMR of Monoesters

1. Introduction

The mono-alkyl or mono-aryl esters of succinic are valuable synthons for several industrial, agrochemical and pharmaceutical targets (Kashima et al, 2001; Nardello et al, 2006; Marchal et al, 2008; Wang et al, 2009 and Zhang et al, 2010). These are also used as starting material in the synthesis of several bio-active compounds like alkaloids, flavonoids, glycosides, terpenoids, vitamins, \( \alpha \)-tocopherol, vitamin K1, polymers and other valuable and daily used products (Jiang et al, 2007 and Hekking et al, 2008). These compounds have also been used as resolving agents (Maeda et al, 1997). It has been reported that their derivatives with naturally occurring biologically active compounds showed enhancement of their activities used against HIV, bacteria and fungi (Cava et al, 1965; Chang et al, 1991; Fujimaki, 1998; Basak et al, 1999; Matsumura et al, 2000 and Vraka et al, 2006). Keeping in view all these facts, various synthetic techniques have been explored. However, they require huge amount of strong inorganic acids, carcinogenic transition metal hydrides and / or their complexes and hence face serious concerns from green chemistry. The huge disposal of waste product is a real threat to our ecological system and aquatic life (Matsumura et al, 1998 and Ostermeier et al, 2003). The production of heat and gases during the reactions results global warming and hence create pollution (Luman et al, 2004 and Maeda et al, 2005). Use of expensive materials, multi-step preparation, use of protecting groups to mask the active sites and their recovery make the techniques uneconomical i.e. formation of side products results low yield of final product (Matsumura et al, 1998; Ostermeier et al, 2003; Luman et al, 2004 and Maeda et al, 2005). Recently, we reported the synthesis and structural characterization of novel monoesters of succinic anhydride with aryl alcohols using two-step synthesis from low-cost substrates and
solvents (Iqbal et al., 2012). Following the same technique, we have synthesized twenty seven (1-27) new monoesters of succinic acid by reacting succinic anhydride with di-, and tri-substituted aryl alcohols using toluene as a solvent and p-toluenesulphonic acid as a catalyst (Scheme 1) and established their structure with the help of modern (2D-NMR) spectroscopic techniques (Table 1).

\[
\text{Scheme 1. Preparation of Monoesters 1-27}
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<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Time (Hrs)</th>
<th>Compound</th>
<th>Ar</th>
<th>Time (Hrs)</th>
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<td>14</td>
<td>14</td>
<td>3,5(NO₂)₂C₂H₅</td>
<td>17</td>
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<td>14</td>
<td>15</td>
<td>2,6(EtO)₂C₂H₅</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
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<td>16</td>
<td>3,4(EtO)₂C₂H₅</td>
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<td>17</td>
<td>3,5(HO)₂C₂H₅</td>
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<td>18</td>
<td>2,3,4(MeO)₃C₆H₃</td>
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<tr>
<td>6</td>
<td>2,3(F)C₂H₅</td>
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<td>19</td>
<td>2,4,5(MeO)₃C₆H₃</td>
<td>14</td>
</tr>
<tr>
<td>7</td>
<td>2,4(F)C₂H₅</td>
<td>16</td>
<td>20</td>
<td>3,4,5(MeO)₃C₆H₃</td>
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<td>9</td>
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<td>4-MeO-3-NO₂-C₆H₃</td>
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<tr>
<td>14</td>
<td>3,5(NO₂)₂C₂H₅</td>
<td>17</td>
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2. Experimental

2.1. Physical Measurements

All the required chemicals (aryl alcohols, anhydride, p-toluenesulphonic anhydride, toluene, hexane, benzene, methanol, ethanol, ethyl acetate, diethyl ether, chloroform, sodium sulphate and sodium bicarbonate) were purchased from Sigma-Aldrich, St. Louis, New York, USA. All the reagents were of analytical grade and used as such, except toluene. The toluene was dried and then stored over sodium metal before use. The purity of alcohols and succinic anhydride was checked by taking IR and NMR spectra. The melting points were determined using Gallenkamp digital melting point apparatus and are uncorrected. The UV spectra were recorded in absolute MeOH employing IRMECO UV/VIS Model U-2020 spectrophotometer. IR spectra were obtained on a TENSOR 27 FT-IR spectrophotometer supplied by Bruker, Ettlingen, Germany. ¹H-NMR and ¹³C-NMR (1D, 2D-NMR) spectra were procured in CDCl₃ at (¹H) 300 MHz, (¹³C) 75 MHz using Bruker Biospin, AMX 300 MHz FT NMR spectrometer; trimethylsilane (TMS) was used as an internal reference. Column chromatography was carried out using silica gel (PF₂₅₄, mesh size 60-70), E. Merck, Darmstadt, Germany; analytical and preparative thin layer chromatography was performed on pre-coated silica gel plate (20 x 20 cm, 0.2 mm thickness) with UV fluorescence indicator (PF₂₅₄), E. Merck, Darmstadt, Germany, using n-hexane-ethylacetate mixture.

2.2. General Procedure for the Preparation of Monoesters 1-27

Twenty (1-27) aryl succinic acids were synthesized by
adding 20 mmol of corresponding alcohol into a single-necked round-bottom flask (100 mL), already containing succinic anhydride (20 mmol), anhydrous p-toluenesulfonic acid (0.08 mmol) and toluene (20 mL) under nitrogen atmosphere. The apparatus was equipped with magnetic stirrer, Dean–Stark trap and a reflux condenser. The mixture was refluxed for variable times (Table 1) and allowed to cool to 25 °C. After cooling, it was poured into saturated aqueous NaHCO₃ solution (12.5 mL) and the organic layer was extracted with hexane (3 × 25 mL). The organic phase was then washed with brine (10 mL), dried over anhydrous Na₂SO₄ and the excess of the solvent was removed under vacuum to give a resins product. The obtained mixture was subjected to separation on column chromatography using mixture of n-hexane-ethyl acetate (1:0→0:1) to get thirty fractions (1-30). The fractions (17-22) were combined and re-chromatographed on preparative thin layer chromatography using n-hexane-ethyl acetate mixture (4:6) as an eluant which yielded colourless amorphous solid pure compounds (1-27). Recording UV, IR, ¹H- and ¹³C-NMR, analysis and mass measurement, characterized the target substrates. Physical properties and spectroscopic data are listed below.

### 2.2.1. Spectral Data of 1-27 Compounds

#### 2,4-dichlorobenzyl hydrogen succinate (1): Yield 60%, 3.33 g (12.0 mmol). Colourless, amorphous solid, m.p 71-73 °C; UV (EtOH) λₘₐₓ nm (log ε): 259 (3.4). ¹H-NMR (300 MHz, CDCl₃): δ (ppm): 2.93 (t, J = 6.9 Hz, 2H, CH₂CO), 2.82 (t, J= 6.9 Hz, 2H, CH₂CO), 5.24 (s, 2H, OCH₂), 7.36-7.87 (m, 3H, Ar-H), 11.82 (brs, 1H, exchangeable with D₂O, OH). ¹³C-NMR (75 MHz, CDCl₃ multiplicity in DEPT): δC (ppm): 33.2 (t, CH₂CO), 32.2 (t, CH₂CO), 171.3 (s, CO), 176.9 (s, CO), 65.8 (s, CH₂O), 137.6 (s, C-1), 135.8 (s, C-2), 131.4 (d, C-3), 134.1 (s, C-4), 128.9 (d, C-5), 129.7 (d, C-6). FT-IR (Neat) νₘₐₓ (cm⁻¹): 3386 (OH), 3063 (Ar-H), 1722 (CO), 1773 (CO), 1510, 1473 (C=O), 1247, 1123, 1022 (C-O), 723 (C-Cl). Analysis calculated for C₁₃H₁₀Cl₂O₄ (277.10): C, 47.68%; H, 3.64 %, Cl 25.59%; Found: C, 47.44%; H, 3.32%, Cl, 25.64%.

#### 2,6-dichlorobenzyl hydrogen succinate (3): Yield 58%, 3.21 g (11.6 mmol). Colourless, amorphous solid, m.p 77-79 °C; UV (EtOH) λₘₐₓ nm (log ε): 258 (3.7). ¹H-NMR (300 MHz, CDCl₃): δH (ppm): 2.95 (t, J= 6.9 Hz, 2H, CH₂CO), 2.85 (t, J= 6.9 Hz, 2H, CH₂CO), 5.26 (s, 2H, OCH₂), 7.69-7.71 (m, 3H, Ar-H), 11.75 (brs, 1H, exchangeable with D₂O, OH). ¹³C-NMR (75 MHz, CDCl₃ multiplicity in DEPT): δC (ppm): 32.5 (t, CH₂CO), 32.1 (t, CH₂CO), 171.7 (s, CO), 176.8 (s, CO), 59.8 (t, CH₂O), 142.3 (s, C-1), 132.7 (s, C-2,6), 128.4 (d, C-3,5)130.5 (d, C-4). FT-IR (Neat) νₘₐₓ (cm⁻¹): 3385 (OH), 3023 (Ar-H), 1771 (CO), 1726 (CO), 1512, 1441 (C=C), 1249, 1111, 1014 (C-O), 724 (C-Cl). Analysis calculated for C₁₃H₁₀Cl₂O₄ (277.10): C, 47.68%; H, 3.64 %, Cl 25.59; Found: C, 47.35%; H, 3.46%, Cl, 25.75%.

#### 3,4-dichlorobenzyl hydrogen succinate (4): Yield 66%, 3.66 g (13.2 mmol). Colourless, amorphous solid, m.p 72-74 °C; UV (EtOH) λₘₐₓ nm (log ε): 259 (3.6). ¹H-NMR (300 MHz, CDCl₃): δH (ppm): 2.93 (t, J= 6.9 Hz, 2H, CH₂CO), 2.84 (t, J= 6.9 Hz, 2H, CH₂CO), 5.22 (s, 2H, OCH₂), 7.30-7.79 (m, 3H, Ar-H), 11.68(brs, 1H, exchangeable with D₂O, OH). ¹³C-NMR (75 MHz, CDCl₃ multiplicity in DEPT): δC (ppm): 33.1 (t, CH₂CO), 32.6 (t, CH₂CO), 171.4 (s, CO), 177.9 (s, CO), 66.8 (s, CH₂O), 138.3 (s, C-1), 129.6 (d, C-2), 133.3 (s, C-3), 133.6 (s, C-4), 131.5 (d, C-5), 128.7 (d, C-6). FT-IR (Neat) νₘₐₓ (cm⁻¹): 3375 (OH), 3058 (Ar-H), 1778 (CO), 1725 (CO), 1594, 1415 (C=C), 1247, 1123, 1022 (C-O), 721 (C-Cl). Analysis calculated for C₁₃H₁₀Cl₂O₄ (277.10): C, 47.68%; H, 3.64 %, Cl 25.59; Found: C, 47.49%; H, 3.71%, Cl, 25.45%.

#### 3,5-dichlorobenzyl hydrogen succinate (5): Yield 65%, 3.60 g (13.0 mmol). Colourless, amorphous solid, m.p 74-76 °C; UV (EtOH) λₘₐₓ nm (log ε): 259 (3.8). ¹H-NMR (300 MHz, CDCl₃): δH (ppm): 2.93 (t, J= 6.9 Hz, 2H, CH₂CO), 2.84 (t, J= 6.9 Hz, 2H, CH₂CO), 5.22 (s, 2H, OCH₂), 7.56-7.74 (m, 3H, Ar-H), 11.89 (brs, 1H, exchangeable with D₂O, OH). ¹³C-NMR (75 MHz, CDCl₃ multiplicity in DEPT): δC (ppm): 33.1 (t, CH₂CO), 32.6 (t, CH₂CO), 171.4 (s, CO), 177.9 (s, CO), 66.8 (s, CH₂O), 146.2 (s, C-1), 126.3 (d, C-2,6), 136.5 (s, C-3,5), 129.8 (d, C-4). FT-IR (Neat) νₘₐₓ (cm⁻¹): 3379 (OH), 3055 (Ar-H), 1764 (CO), 1721 (CO), 1529, 1432 (C=C), 1247, 1123, 1022 (C-O), 723 (C-Cl). Analysis calculated for C₁₃H₁₀Cl₂O₄ (277.10): C, 47.68%; H, 3.64 %, Cl 25.59; Found: C, 47.53%; H, 3.36%, Cl, 25.61%.

#### 2,3-difluorobenzyl hydrogen succinate (6): Yield 64%, 3.12 g (12.8 mmol). Colourless, amorphous solid, m.p 88-90 °C; UV (EtOH) λₘₐₓ nm (log ε): 255 (4.1). ¹H-NMR (300 MHz, CDCl₃): δH (ppm): 2.91 (t, J= 6.9 Hz, 2H,
CH₃CO), 2.77 (t, J = 6.9 Hz, 2H, CH₃CO), 5.15 (s, 2H, OCH₃), 7.21-7.26 (m, 3H, Ar-H), 11.98 (brs, 1H, exchangeable with D₂O, OH). ¹³C-NMR (75 MHz, CDCl₃): δc (ppm): 32.4 (t, CH₃CO), 33.2 (t, CH₂CO), 172.9 (s, CO), 178.7 (s, CO), 62.6 (t, CH₂O), 130.7 (s, C-1), 138.6 (s, C-2), 150.6 (s, C-3), 117.5 (d, C-4), 127.5 (d, C-5), 125.4 (d, C-6). FT-IR (Neat) δmax (cm⁻¹): 3410 (OH), 3074 (Ar-H), 1770 (CO), 1729 (CO), 1601, 1408 (C=C), 1246, 1123, 1014 (C-O), 1155 (C-F). Analysis calculated for C₁₇H₁₆F₂O₄ (244.19): C, 54.10%; H, 4.13; F, 15.56%; Found: C, 54.18%; H, 4.18; F, 15.54%.

2.4-dimethylbenzyl hydrogen succinate (10): Yield 68%, 3.21 g (13.6 mmol). Colourless, amorphous solid, m.p 77-79 °C; UV (EtOH) δmax nm (log ε): 253 (3.4). ¹³C-NMR (300 MHz, CDCl₃): δc (ppm): 2.42 (s, 6H, 2CH₃), 2.87 (t, J = 6.9 Hz, 2H, CH₂CO), 2.76 (t, J = 6.9 Hz, 2H, CH₂O), 5.10 (s, 2H, OCH₃), 7.04-7.20 (m, 3H, Ar-H), 11.99 (brs, 1H, exchangeable with D₂O, OH). ¹¹B-NMR (75 MHz, CDCl₃): δb (ppm) in DEPT): δc (ppm): 19.1 (t, CH₃), 21.7 (t, CH₂), 171.7 (s, CO), 171.2 (s, CO), 62.1 (t, CH₂O), 124.6 (s, C-1), 163.2 (s, C-2), 105.4 (d, C-3), 102.2 (d, C-4), 112.2 (d, C-5), 133.6 (d, C-6). FT-IR (Neat) δmax (cm⁻¹): 3366 (OH), 3037 (Ar-H), 1764 (CO), 1727 (CO), 1499, 1402 (C-C), 1248, 1125, 1008 (C-O), 1155 (C-F). Analysis calculated for C₁₇H₁₆B₂O₄ (370.32): C, 56.10%; B, 9.53%; H, 3.73%; Found: C, 56.28%; B, 9.51%; H, 3.75%.

2.5-dimethylbenzyl hydrogen succinate (11): Yield 67%, 3.17 g (13.4 mmol). Colourless, amorphous solid, m.p 84-86 °C; UV (EtOH) δmax nm (log ε): 253 (3.6). ¹³C-NMR (300 MHz, CDCl₃): δc (ppm): 2.39 (s, 6H, 2CH₃), 2.87 (t, J = 6.9 Hz, 2H, CH₂CO), 2.74 (t, J = 6.9 Hz, 2H, CH₂O), 5.20 (s, 2H, OCH₃), 7.10-7.24 (m, 3H, Ar-H), 11.91 (br, 1H, exchangeable with D₂O, OH). ¹¹B-NMR (75 MHz, CDCl₃): δb (ppm): 19.7 (t, CH₃), 22.8 (t, CH₂), 33.1 (t, CH₂CO), 32.6 (t, CH₂CO), 171.9 (s, CO), 177.2 (s, CO), 66.3 (t, CH₂O), 143.6 (s, C-1), 132.6 (s, C-2), 131.5 (d, C-3), 129.9 (d, C-4), 129.6 (d, C-5), 136.3 (s, C-5), 129.6 (d, C-6). FT-IR (Neat) δmax (cm⁻¹): 3360 (OH), 3040 (Ar-H), 1758 (CO), 1721 (CO), 1502, 1485 (C=C), 1245, 1135, 1014 (C-O). Analysis calculated for C₁₇H₁₆B₂O₄ (370.32): C, 56.10%; B, 9.53%; H, 3.73%; Found: C, 56.28%; B, 9.51%; H, 3.75%.

2.6-dimethylbenzyl hydrogen succinate (12): Yield 67%, 3.21 g (13.6 mmol). Colourless, amorphous solid, m.p 92-94 °C; UV (EtOH) δmax nm (log ε): 256 (3.5). ¹³C-NMR (300 MHz, CDCl₃): δc (ppm): 2.96 (t, J = 6.9 Hz, 2H, CH₂CO), 2.82 (t, J = 6.9 Hz, 2H, CH₂CO), 5.10 (s, 2H, OCH₃), 7.41-7.84 (m, 3H, Ar-H), 11.90 (br, 1H, exchangeable with D₂O, OH). ¹¹B-NMR (75 MHz, CDCl₃): δb (ppm) in DEPT): δc (ppm): 33.1 (t, CH₂CO), 32.6 (t, CH₂CO), 171.4 (s, CO), 177.9 (s, CO), 56.5 (t, CH₂O), 115.4 (s, C-1), 162.6 (s, C-2), 113.6 (d, C-3,5), 129.9 (d, C-4). FT-IR (Neat) δmax (cm⁻¹): 3425 (OH), 3066 (Ar-H), 2.5-dimethylbenzyl hydrogen succinate (13): Yield 69%,
3.26 g (13.8 mmol). Colourless, amorphous solid, m.p 87-
86 °C; UV (EtOH) λmax nm (log e): 253 (3.6). 1H-NMR
(300 MHz, CDCl3): δH (ppm): 2.40 (s, 6H, 2 × CH3), 2.86
(t, J = 6.9 Hz, 2H, CH2CO), 2.75 (t, J = 6.9 Hz, 2H,
CH2CO), 5.24 (s, 2H, OCH2), 7.10-7.38 (m, 3H, Ar-H),
11.72 (brs, 1H, exchangeable with D2O, OH). 13C-NMR
(75 MHz, CDCl3) multiplicity in DEPT): δc (ppm): 15.7 (q,
2CH3), 65.7 (t, 2CH3), 32.6 (t, CH2CO), 31.4 (t, CH3CO),
172.1 (s, CO), 175.9 (s, CO), 56.6 (t, CH2O), 119.7 (s, C-1),
155.5 (s, C-2), 105.7 (d, C-3,5), 130.1 (d, C-4). FT-IR (Neat) λmax
(cm⁻¹): 3455 (OH), 3086 (Ar-H), 1776 (CO), 1732 (CO),
1505, 1496 (C=C), 1250, 1124, 1022 (C-O). Analysis calculated
calculated for C14H20O6 (296.32): C, 60.80%; H, 6.80%;
Found: C, 60.74%; H, 6.65%.

3.4-dithioxybenzyl hydrogen succinate (17): Yield 67%,
3.97 g (13.4 mmol). Colourless, amorphous solid, m.p
114-116 °C; UV (EtOH) λmax nm (log e): 270 (4.2). 1H-
NMR (300 MHz, CDCl3): δH (ppm): 1.37 (t, J=7.6 Hz, 6H,
2CH3), 4.16 (q, J=7.6 Hz, 4H, 2CH2), 2.88 (t, J=6.9 Hz,
2H, CH2CO), 2.70 (t, J=6.9 Hz, 2H, CH2CO), 5.21 (s, 2H,
OCH2), 6.66-7.21 (m, 3H, Ar-H), 11.57 (br, s, 1H, exchangeable
with D2O, OH). 13C-NMR (75 MHz, CDCl3) multiplicity in DEPT):
δc (ppm): 15.5 (q, 2CH3), 65.8 (t, 2CH3), 32.9 (t, CH3CO),
31.3 (t, CH2CO), 172.4 (s, CO), 175.8 (s, CO), 67.8 (t, CH2O),
124.6 (s, C-1), 115.5 (d, C-2), 150.3 (s, C-3), 151.2 (s, C-4),
113.7 (d, C-5), 122.3 (d, C-6). FT-
IR (Neat) λmax cm⁻¹: 3454 (OH), 3085 (Ar-H), 1775
(CO), 1731 (CO), 1506, 1495 (C=C), 1252, 1120, 1021 (C-
O). Analysis calculated for C14H20O6 (296.32): C, 60.80%;
H, 6.80%; Found: C, 60.77%; H, 6.68%.

3.5-dithioxybenzyl hydrogen succinate (18): Yield 70%,
3.36 g (14.0 mmol). Colourless, amorphous solid, m.p
122-123 °C; UV (EtOH) λmax nm (log e): 272 (4.1). 1H-
NMR (300 MHz, CDCl3): δH (ppm): 2.88 (t, J=6.9 Hz,
2H, CH2CO), 2.70 (t, J=6.9 Hz, 2H, CH2CO), 5.21 (s, 2H,
OCH2), 6.36-6.75 (m, 3H, Ar-H), 11.75 (br, s, 1H, exchangeable
with D2O, OH). 13C-NMR (75 MHz, CDCl3 multiplicity in DEPT):
δc (ppm): 33.3(t, CH2O), 31.5 (t, CH2CO), 172.2 (s, CO),
175.9 (s, CO), 67.7 (t, CH2O), 139.2 (s, C-1), 103.1 (d, C-2,6),
157.9 (s, C-3,5), 101.7 (d, C-4). FT-IR (Neat) λmax cm⁻¹:
3450 (OH), 3082 (Ar-H), 1774
(CO), 1731 (CO), 1507, 1494 (C=C), 1265, 1132,
1025 (C-O). Analysis calculated for C14H20O6 (296.32): C, 55.00%;
H, 5.04%; Found: C, 55.16%; H, 4.97%.

2.3,6-trimethoxybenzyl hydrogen succinate (19): Yield
71%, 4.24 g (14.2 mmol). Colourless, amorphous solid, m.p
67-68 °C; UV (EtOH) λmax nm (log e): 272 (3.97). 1H-
NMR (300 MHz, CDCl3): δH (ppm): 3.87 (s, 9H, 3 × CH3),
2.89 (t, J= 6.9 Hz, 2H, CH2CO), 2.71 (t, J= 6.9 Hz, 2H,
CH2CO), 5.27 (s, 2H, OCH2), 6.30-6.75 (m, 2H, Ar-H),
11.74 (brs, 1H, exchangeable with D2O, OH). 13C-NMR
(75 MHz, CDCl3 multiplicity in DEPT): δc (ppm): 57.5 (s,
9H, 3 × CH3), 33.3(t, CH2O), 31.1 (t, CH3CO), 172.6 (s, CO),
175.9 (s, CO), 63.7 (t, CH2O), 121.2 (s, C-1), 150.5 (s,
C-2), 141.5 (s, C-3), 154.2 (s, C-4), 105.7 (d, C-5),
122.3 (d, C-6). FT-IR (Neat) λmax cm⁻¹: 3450 (OH), 3082
(Ar-H), 1774 (CO), 1730 (CO), 1508, 1498 (C=C), 1262,
1135, 1015 (C-O). Analysis calculated for C14H20O7
(298.29): C, 56.37%; H, 6.08%; Found: C, 56.25%; H,
2,4,5-trimethoxybenzyl hydrogen succinate (20): Yield 71%, 4.24 g (14.2 mmol). Colourless, amorphous solid, m.p. 94-96 °C; UV (EtOH) λmax nm (log ε): 272 (4.15). 1H-NMR (300 MHz, CDCl3): δH (ppm): 3.86 (s, 9H, 3 × CH3). 2.88 (t, J = 6.9 Hz, 2H, CH2CO), 2.71 (t, J = 6.9 Hz, 2H, CH2CO), 5.22 (s, 2H, OCH2), 7.22-8.18 (m, 3H, Ar-H), 11.96 (br, s, 1H, exchangeable with D2O, OH). 13C-NMR (75 MHz, CDCl3) multiplicity in DEPT): δC (ppm): 55.6 (s, 3H, CH3), 33.8 (t, CH2CO), 31.1 (t, CH2CO), 171.6 (s, CO), 177.7 (s, CO), 66.7 (t, CH2O), 135.4 (s, C-1), 125.6 (d, C-2), 142.1 (s, C-3), 151.4 (s, C-4), 113.7 (d, C-5), 136.5 (d, C-6). FT-IR (Neat) νmax cm⁻¹: 3396 (OH), 3067 (Ar-H), 1777 (CO), 1728 (CO), 1607, 1585, 1388 (C=C), 1373 (NO2), 1253, 1133, 1018 (C-O). Analysis calculated for C12H18O3 (283.07): C, 50.89%; H, 4.63%; N, 4.95%; Found: C, 50.77%; H, 4.73%; N, 4.84%.

2-methoxy-5-nitrobenzyl hydrogen succinate (24): Yield 64%, 3.63 g (12.8 mmol). Light yellow, amorphous solid, m.p. 115-117 °C; UV (EtOH) λmax nm (log ε): 267 (3.99). 1H-NMR (300 MHz, CDCl3): δH (ppm): 3.84 (s, 3H, CH3), 2.87 (t, J = 6.9 Hz, 2H, CH2CO), 2.74 (t, J = 6.9 Hz, 2H, CH2CO), 5.26 (s, 2H, OCH2), 7.20-8.21 (m, 3H, Ar-H), 11.97 (br, s, 1H, exchangeable with D2O, OH). 13C-NMR (75 MHz, CDCl3) multiplicity in DEPT): δC (ppm): 56.9 (s, 3H, CH3), 33.4 (t, CH2CO), 31.7 (t, CH2CO), 171.3 (s, CO), 177.6 (s, CO), 66.7 (t, CH2O), 129.3 (s, C-1), 163.2 (s, C-2), 113.4 (d, C-3), 125.1 (d, C-4), 141.1 (s, C-5), 125.6 (d, C-6). FT-IR (Neat) νmax cm⁻¹: 3393 (OH), 3064 (Ar-H), 1774 (CO), 1725 (CO), 1503, 1484 (C=C), 1372 (NO2), 1249, 1128, 1014 (C-O). Analysis calculated for C12H18NO3 (283.07): C, 50.89%; H, 4.63%; N, 4.95%; Found: C, 50.97%; H, 4.80%; N, 4.81%.

2,4,6-trichlorobenzyl hydrogen succinate (25): Yield 58%, 3.61 g (11.6 mmol). Colourless, amorphous solid, m.p. 98-100 °C; UV (EtOH) λmax nm (log ε): 267 (3.98). 1H-NMR (300 MHz, CDCl3): δH (ppm): 2.89 (t, J = 6.9 Hz, 2H, CH2CO), 2.75 (t, J = 6.9 Hz, 2H, CH2CO), 5.12 (s, 2H, OCH2), 7.71 (s, 2H, Ar-H), 11.96 (br, s, 1H, exchangeable with D2O, OH). 13C-NMR (75 MHz, CDCl3) multiplicity in DEPT): δC (ppm): 33.2 (t, CH2CO), 172.1 (s, CO), 178.7 (s, CO), 59.3 (t, CH2O), 140.2 (s, C-1), 136.3 (s, C-2), 129.1 (d, C-3), 135.9 (s, C-4). FT-IR (Neat) νmax cm⁻¹: 3390 (OH), 3061 (Ar-H), 1779 (CO), 1728 (CO), 1612-1390 (C=C), 1248, 1125, 1010 (C-O), 729 (C=Cl). Analysis calculated for C12H11Cl3O4 (311.55): C, 42.41%; H, 2.91%; Cl, 34.14%; Found: C, 42.49%; H, 2.86%; Cl, 34.22%.

2,4,5-trichlorobenzyl hydrogen succinate (26): Yield 58%, 5.07 g (11.4 mmol). Colourless, amorphous solid, m.p. 106-108 °C; UV (EtOH) λmax nm (log ε): 266 (4.2). 1H-NMR (300 MHz, CDCl3): δH (ppm): 2.85 (t, J = 6.9 Hz, 2H, CH2CO), 2.70 (t, J = 6.9 Hz, 2H, CH2CO), 5.12 (s, 2H, OCH2), 7.25 (s, 1H, Ar-H), 7.90 (s, H, Ar-H), 11.99 (brs, 1H, exchangeable with D2O, OH). 13C-NMR (75 MHz, CDCl3) multiplicity in DEPT): δC (ppm): 33.7 (t, CH2CO), 31.2 (t, CH2CO), 173.2 (s, CO), 178.7 (s, CO), 64.3 (t, CH2O), 140.7 (s, C-1), 124.6 (s, C-2), 136.8 (d, C-3), 143.9 (s, C-4), 124.6 (s, C-2), 136.8 (d, C-3), 143.9 (s, C-4).
127.9 (s, C-4), 123.9 (s, C-5), 136.8 (d, C-6), FT-IR (Neat) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3386 (OH), 3078 (Ar-H), 1778 (CO), 1729 (CO), 1514, 1491 (C=C), 1257, 1132, 1015 (C-O), 527 (C-Br). Analysis calculated for C\(_{11}\)H\(_8\)Br\(_2\)O\(_4\) (444.90): C, 29.70%; H, 2.04%; Br, 53.88%; Found: C, 29.62%; H, 2.22%; Br, 53.76%.

2.4.6-trimethylbenzyl hydrogen succinate (27): Yield 60%, 3.0 g (12.0 mmol). Colourless, amorphous solid, m.p 101-102 °C; UV (EtOH) \( \lambda_{\text{max}} \) (log \( e \)): 264 (3.4). \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta \) (ppm): 2.46 (s, 9H, 3 \times CH\(_3\)), 2.85 (t, \( J = 6.9 \) Hz, 2H, CH\(_2\)), 2.69 (t, \( J = 6.9 \) Hz, 2H, CH\(_2\)), 5.12 (s, 2H, OCH\(_2\)), 6.97 (s, 2H, Ar-H), 12.02 (brs, 1H, exchangeable with D\(_2\)O, OH). \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) multiplicity in DEPT; \( \delta \) (ppm): 19.9 (q, 2CH\(_3\)), 33.9 (t, CH\(_2\)), 171.2 (s, CO), 176.5 (s, CO), 63.9 (t, CH\(_2\)), 133.7 (s, C-1), 135.2 (s, C-2), 130.1 (d, C-3,5), 136.8 (s, C-4), FT-IR (Neat) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3376 (OH), 3078 (Ar-H), 1778 (CO), 1729 (CO), 1612-1392 (C=C), 1254, 1133, 1016 (C-O). Analysis calculated for C\(_{27}\)H\(_{33}\)O\(_4\): C, 67.18%; H, 7.25%; O, 15.57%; Br, 9.84%; Found; C, 67.24%; H, 7.21%; Br, 9.81%.

3. Results and Discussion

The esterification of the di- and tri-substituted aryl alcohols with succinic anhydride afforded novel aryl-succinic acids (1-27) in good yield (Scheme 1). The TLC and \(^1\)H-NMR of the crude reaction mixture proved that the esterification reaction gave single product with reasonable high selectivity. The structure of all (1-27) compounds was established by different spectroscopic (UV, IR, NMR, and MS) techniques. The UV spectrum of 1 displayed a peak at 254 nm due to presence of an aryl chromophore in the product.

![Scheme 2](https://via.placeholder.com/150)

**Scheme 2.** Presentation of 2D NMR in 1

The IR spectrum of 1 displayed a broad band for O-H at 3386 cm\(^{-1}\), C=O at 1722 and 1777 cm\(^{-1}\), and C-O at 1247 cm\(^{-1}\). Presence of an aromatic moiety was evident in IR spectrum of 1 from the peaks observed for Ar-H and C=C at 3063 cm\(^{-1}\) and 1600-1423 cm\(^{-1}\), respectively. In \(^1\)H-NMR spectrum, 1 displayed multiplet in the low-field region, peaks at \( \delta \) 7.36-7.87 due to aromatic protons and two resonances at \( \delta \) 2.93 (\( J = 6.9 \) Hz, 2H) and \( \delta \) 2.82 (\( J = 6.9 \) Hz, 2H) assigned to methylene groups between acid and ester functions. A singlet at \( \delta \) 5.24 was due to protons of oxymethylene (OCH\(_2\)) attached to oxygen on one side and aromatic ring on the other side. Presence of the carboxylic acid functionality was also verified by proton resonating at \( \delta \) 11.82 which disappear on addition of D\(_2\)O.

In the DEPT (\(^{13}\)C-NMR) spectrum, spectra of compound 1 displayed eleven peaks for eleven carbon atoms corresponding to molecular formula C\(_{11}\)H\(_8\)Cl\(_2\)O\(_4\). DEPT \(^{13}\)C-NMR displayed three CH\(_2\) two C (carbons), three CH (aromatic) and three C (aromatic) atoms. Further, the chemical shift of two carbons showed that these are attached to two oxygen atoms. The 2D-NMR (\(^1\)H-\(^1\)H) spectra of 1 (COSY-45° and HOHAHA) disclosed two fragments i) CH-CH and ii) CH=CH=CH and were verify-ied by the HMBC technique (Scheme 2). Esterification was further confirmed by HMBC in which the CH\(_3\) resonating at \( \delta \) 5.24 and the CH\(_2\) at \( \delta \) 2.82 displayed interactions with aryl C-1.2 and the carbonyl group of ester functio-n (\( \delta \) C 171.3), respectively. In the same spectrum, there was another interaction between the methylene proton (\( \delta \) 2.85) and the acidic carbon (\( \delta \) C 176.9) (Scheme 2). In the ROESY 2D-NMR (\(^1\)H-\(^1\)H) spectrum, interactions were observed between two CH\(_2\) protons resonating at \( \delta \) 2.82 adjacent to the C=O group. Interaction between CH\(_2\) (\( \delta \) 2.82) and C=O (\( \delta \) C 171.3) was also observed. In the light of all the spectral evidence, the formation 1 was confirm- ed. Thus, the structure of synthesized (2-27) compounds was established in this way.

4. Conclusion

In summary, by the ring opening technique the succinic anhydride has been successfully converted to aryl succinic acids using various di and tri substituted aryl alcohols with good yield. The products were purified and characterized using chromatographic and spectroscopic techniques, respectively.
References


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