Catalytic Friedel-Crafts Alkylation of Electron Rich Aromatic Derivatives with α-Aryl Diazoacetates Mediated by Brønsted Acids

Rafael D. C. Gallo, Patricia B. Momo, David P. Day and Antonio C. B. Burtoloso*

São Carlos Institute of Chemistry, University of São Paulo, 13560-970, São Carlos, SP, Brazil

SUPPORTING INFORMATION

Table of Contents

1. General Information............................................................................................................. S2
2. Experimental Procedures and Characterization Data .......................................................... S3
3. NMR Spectra.................................................................................................................. S18
4. References..................................................................................................................... S48
General Information

All commercially available reagents were used without further purification unless otherwise noted. All solvents used for reactions and chromatography were dried and purified by standard methods. All reactions were performed at the specified temperatures described in general procedures section. When necessary, a silicone oil bath with a heating probe was used to obtain the desired temperature. TLC analyses were performed using silica gel 60F 254 precoated plates, with detection by UV-absorption (254 nm) and by spraying with p-anisaldehyde, potassium permanganate and phosphomolybdic acid solutions followed by charring at ~150 °C for visualization. Flash column chromatography was performed using silica gel 200–400 Mesh. All NMR analyses were recorded using CDCl₃ as solvent and TMS as internal standard. Chemical shifts are reported in ppm downfield from TMS with reference to internal solvent. Infrared spectra were obtained using FT-IR (Bruker, model ALPHA) at 4.0 cm⁻¹ resolution and are reported in wavenumbers. The samples were dispersed in a ZnSe crystal (ATR mode), using DCM as solvent or when dealing with DCM insoluble samples, the solid was directly pressed in the crystal. Melting points were determined using a digital melting point apparatus (Fisatom, model 430D). High-resolution mass spectra (HRMS) were recorded using electron spray ionization in positive mode (ESI) in a Waters, model Xevo G2 or in a ThermoFischer, model Orbitrap LTQ Velos.
Experimental Procedures and Characterization Data

General Procedures

Preparation of diazo compounds

To a mixture of ester (0.5-20.0 mmol) and p-ABSA (1.2-1.5 equiv.) in anhydrous CH₃CN (2-60 mL) at 0 °C, DBU (1.4-1.5 equiv.) was added. The reaction mixture was stirred at room temperature overnight. Upon complete consumption of the starting materials, the reaction mixture was diluted with distilled water (2-20 mL), followed by extraction with diethyl ether (3 x 5-10 mL). After washing with 10% NH₄Cl solution (3 x 5-10 mL) and brine (3 x 5-10 mL), the combined organic extracts were dried over MgSO₄ and concentrated by rotary evaporation. The residue was purified by flash chromatography to afford the diazoesters.

Methyl 2-diazo-2-(4-methoxyphenyl)acetate 4

Following the general procedure for the preparation of diazo compounds, reaction of methyl 2-(4-methoxyphenyl)acetate (20.0 mmol), p-ABSA (24.0 mmol) and DBU (28.0 mmol) afforded the title compound 4 as an orange solid (2.39 g, 58%) m.p. 45-50 °C. Rf = 0.32 (10% EtOAc:Hexane). ¹H NMR (500 MHz, CDCl₃): δ 7.39 (d, J = 9.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H), 3.81 (s, 3H).

Ethyl 2-diazo-2-(4-methoxyphenyl)acetate S1

Following the general procedure for the preparation of diazo compounds, reaction of ethyl 2-(4-methoxyphenyl)acetate (4.10 mmol), p-ABSA (4.92 mmol) and DBU (6.15 mmol) afforded the title compound S1 as a red solid (755 mg, 84%) m.p. 49-51 °C. Rf = 0.42 (10% EtOAc:Hexane). ¹H NMR (500 MHz, CDCl₃): δ 7.38 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 9.0 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 3.81 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H).

Isopropyl 2-diazo-2-(4-methoxyphenyl)acetate S2

Following the general procedure for the preparation of diazo compounds, reaction of isopropyl 2-(4-methoxyphenyl)acetate (4.80 mmol), p-ABSA (5.76 mmol) and DBU (7.20 mmol) afforded the title compound S2 as an orange solid (822 mg, 73%) m.p. 48-50 °C. Rf = 0.32 (10% EtOAc:Hexane). ¹H NMR (500 MHz, CDCl₃): δ 7.39 (d, J = 9.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 5.20 (hept, J = 6.3 Hz, 1H), 3.82 (s, 3H), 1.33 (d, J = 6.3 Hz, 6H).
2,2,2-Trifluoroethyl 2-diazo-2-(4-methoxyphenyl)acetate S3

Following the general procedure for the preparation of diazo compounds, reaction of 2,2,2-trifluoroethyl 2-(4-methoxyphenyl)acetate (1.00 mmol), p-ABSA (1.20 mmol) and DBU (1.50 mmol) afforded the title compound S3 as an orange oil (199 mg, 73%). Rf = 0.35 (10% EtOAc:Hexane). \(^{1}H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.36 (d, \(J = 9.0\) Hz, 2H), 6.96 (d, \(J = 9.0\) Hz, 2H), 4.64 (q, \(J = 8.4\) Hz, 2H), 3.82 (s, 3H).

Methyl 2-diazo-2-(2-methoxyphenyl)acetate S4

Following the general procedure for the preparation of diazo compounds, reaction of methyl 2-(2-methoxyphenyl)acetate (4.80 mmol), p-ABSA (7.33 mmol) and DBU (7.20 mmol) afforded the title compound S4 as an orange solid (1.05 g, 95%). m.p. 39-40 °C. Rf = 0.35 (10% EtOAc:Hexane). \(^{1}H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.55 (dd, \(J = 7.8\), 1.6 Hz, 1H), 7.26 (ddd, \(J = 8.3\), 7.1, 1.7 Hz, 1H), 7.02 (td, \(J = 7.7\), 1.2 Hz, 1H), 6.90 (dd, \(J = 8.3\), 1.0 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H).

Methyl 2-diazo-2-phenylacetate S5

Following the general procedure for the preparation of diazo compounds, reaction of methyl 2-phenylacetate (6.70 mmol), p-ABSA (8.00 mmol) and DBU (10.0 mmol) afforded the title compound S5 as red oil (540 mg, 46%). Rf = 0.47 (10% EtOAc:Hexane). \(^{1}H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.49 – 7.47 (m, 2H), 7.39 – 7.36 (m, 2H), 7.19 – 7.18 (m, 1H), 3.86 (s, 3H).

Methyl 2-(4-chlorophenyl)-2-diazoacetate S6

Following the general procedure for the preparation of diazo compounds, reaction of methyl 2-(4-chlorophenyl)-2-diazoacetate (5.2 mmol), p-ABSA (6.2 mmol) and DBU (7.8 mmol) afforded the title compound S6 as an orange solid (924 mg, 85%). m.p. 77-78 °C. Rf = 0.40 (10% EtOAc:Hexane). \(^{1}H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.42 (d, \(J = 8.8\) Hz, 2H), 7.35 (d, \(J = 8.8\) Hz, 2H), 3.87 (s, 3H).
Methyl 2-(4-bromophenyl)-2-diazoacetate S7

Following the general procedure for the preparation of diazo compounds, reaction of methyl 2-(4-bromophenyl) acetate (1.32 mmol), p-ABSA (1.58 mmol) and DBU (1.98 mmol) afforded the title compound S7 as an orange solid (142 mg, 43%). m.p. 39-40 °C. Rf = 0.48 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 7.51 (d, J = 8.9 Hz, 2H), 7.36 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H).

Preparation of sulfuric acid adsorbed on silica gel (H₂SO₄−SiO₂)

The preparation of H₂SO₄−SiO₂ was carried out following some modifications of the originally reported procedure. To a suspension of silica gel (10 g, 230–400 mesh) in EtOAc (20 mL) was added H₂SO₄ (0.5 g, 5.2 mmol, 0.27 mL of a 98% aq. solution of H₂SO₄) and the mixture was stirred magnetically for 30 min at rt. Remaining EtOAc was removed under reduced pressure (rotary evaporator) and the residue was heated at 100 °C for 4 h under vacuum to afford H₂SO₄−SiO₂ (0.5 mmol H₂SO₄ in 1g of silica).

General procedure for Friedel-Crafts synthesis

To a 4 mL vial equipped with a magnetic stir-bar was added 0.1 mmol of diazoester (1 equiv), aryl species (1.5 equiv) and dissolved in DCE (0.3 mL) at 25 °C. After 1 min of pre-stirring, H₂SO₄−SiO₂ (5 mol%) was added in one portion. After 5 minutes, the reaction was judged to be complete (TLC), the solid filtered off, and washed with ethyl acetate (2 x 10 mL) and organic solvents were removed under reduced pressure. The resulting residue was purified by flash column chromatography using silica gel (230-400 mesh) and a hexane: ethyl acetate (9:1) mobile phase, affording the desired products.

*N.B. A noticeable colour change was observed in all Friedel-Crafts reactions conducted, with the bright orange / yellow colour of the reaction mixture disappearing with time. Upon reaction completion, all colour in the mixture had gone (see below).

Before H₂SO₄−SiO₂ Addition

During Reaction N₂ evolution

Completion
(+)-Methyl 2,2-bis(4-methoxyphenyl)acetate 5

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and anisole (0.15 mmol, 16.3 µL) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 5 as colorless oil (23.7 mg, 83%). For the specific case of anisole as substrate, different yields were obtained later when other batches of the catalyst were employed (35-83%). R$_f = 0.25$ (10% EtOAc:Hexane; pink color in CAM stain). ¹H NMR (500 MHz, CDCl$_3$): δ 7.22 – 7.20 (m, 4H), 6.86 – 6.83 (m, 4H), 4.93 (s, 1H), 3.77 (s, 6H), 3.72 (s, 3H).

13C NMR (125 MHz, CDCl$_3$): δ 173.6, 158.8, 131.2, 129.6, 114.0, 55.4, 55.3, 52.3. IR $\nu$ max (cm$^{-1}$): 3000, 2952, 2918, 2848, 2837, 1734, 1609, 1583, 1509, 1462, 1437, 1302, 1289, 1246, 1176, 1152, 1032, 818, 757. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{17}$H$_{18}$O$_4$Na 309.1103, found 309.1095.

1 mmol scale reaction: To a 10 mL round bottom flask equipped with a magnetic stir-bar was added diazoester 4 (1.31 mmol, 269.8 mg), anisol (2.0 mmol, 217 µL) and dissolved in DCE (4 mL) at 25 °C. After 1 min of pre-stirring, H$_2$SO$_4$-SiO$_2$ (5 mol%, 130 mg) was added in one portion. After 10 minutes, the reaction was judged to be complete (TLC), the solid filtered off, and washed with ethyl acetate (2 x 25 mL) and organic solvents were removed under reduced pressure. The resulting residue was purified by flash column chromatography using silica gel (230-400 mesh) and a hexane: ethyl acetate (9:1) mobile phase, affording compound 5 as a colorless oil (start to solidify after some hours in the refrigerator) (149 mg, 40%).

(+)-Methyl 2-(4-hydroxyphenyl)-2-(4-methoxyphenyl)acetate 6

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and phenol (0.15 mmol, 14.1 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 6 as white solid (22.6 mg, 83%). m.p. 108-109 °C (lit. 112.6 °C)$^{11}$ R$_f = 0.10$ (10% EtOAc:Hexane). ¹H NMR (500 MHz, CDCl$_3$): δ 7.20 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 8.7 Hz, 2H), 5.67 (s, 1H), 4.92 (s, 1H), 3.77 (s, 3H), 3.72 (s, 3H). ¹³C NMR (125 MHz, CDCl$_3$): δ 173.7, 158.7, 154.8, 131.0, 130.9, 129.7, 129.5, 115.4, 114.0, 55.3, 55.2, 52.3. IR $\nu$ max (cm$^{-1}$): 3403, 3003, 2952, 2937, 1734, 1609, 1583, 1509, 1462, 1437, 1302, 1289, 1174, 1112, 1032, 830, 759. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{16}$H$_{16}$O$_4$Na 295.0946, found 295.0933.

1 mmol scale reaction: To a 10 mL round bottom flask equipped with a magnetic stir-bar was added diazoester 4 (1.02 mmol, 210.8 mg), phenol (1.53 mmol, 144 mg) and dissolved in DCE (3.1 mL) at 25 °C. After 1 min of pre-stirring, H$_2$SO$_4$-SiO$_2$ (5 mol%, 102 mg) was added in
one portion. After 10 minutes, the reaction was judged to be complete (TLC), the solid filtered off, and washed with ethyl acetate (2 x 25 mL) and organic solvents were removed under reduced pressure. The resulting residue was purified by flash column chromatography using silica gel (230-400 mesh) and a hexane: ethyl acetate (7:3) mobile phase, affording compound 6 as a colorless oil (177.3 mg, 64%).

\[(+)\text{-Methyl 2-(4-methoxyphenyl)-2-(phenylthio)acetate 7}^{8}\]

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and thiophenol (0.15 mmol, 15.3 µL) catalyzed by H₂SO₄-SiO₂ (5 mol%, 10.0 mg) afforded the title compound 7 as colorless oil (26.5 mg, 92%). Rₚ = 0.15 (5% EtOAc:Hexane). The spectroscopy data were in good agreement with the literature.\(^8\) ¹H NMR (500 MHz, CDCl₃): δ 7.36-7.34 (m, 4H), 7.25-7.24 (m, 3H), 6.85 (d, J = 8.8 Hz, 2H), 4.87 (s, 1H), 3.77 (s, 3H), 3.65 (s, 3H).

\[\text{IR } \nu_{\text{max}} (\text{cm}^{-1}): 3003, 2951, 2838, 1737, 1607, 1509, 1443, 1251, 1154, 1027.\]

\[\text{HRMS (ESI-TOF) } m/z: [M+K]^{+} \text{Calcd for C}_{18}\text{H}_{19}\text{NO}_{4}\text{K 352.0951, found 352.0905.}\]

\[(+)\text{-Methyl 2-(4-acetamidophenyl)-2-(4-methoxyphenyl)acetate 11}^{11}\]

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and N-phenylacetamide (0.15 mmol, 20.3 mg) catalyzed by H₂SO₄-SiO₂ (5 mol%, 10.0 mg) afforded the title compound 11 as colorless oil (12.8 mg, 41%). Rₚ = 0.15 (10% EtOAc:Hexane). ¹H NMR (500 MHz, CDCl₃): δ 7.43 (d, J = 8.5 Hz, 3H), 7.21 (dd, J = 11.1, 8.6 Hz, 4H), 6.84 (d, J = 8.7 Hz, 2H), 4.94 (s, 1H), 3.78 (s, 3H), 3.73 (s, 3H), 2.13 (s, 3H).

\[\text{IR } \nu_{\text{max}} (\text{cm}^{-1}): 3304, 3191, 403122, 3002, 2952, 2928, 2838, 2349, 1734, 1666, 1603, 1510, 1461, 1436, 1410, 1370, 1301, 1250, 1199, 1153, 1032, 1005, 966, 915, 811, 758, 658.\]
(+)-Methyl 2-(4-hydroxy-3-methoxyphenyl)-2-(4-methoxyphenyl)acetate 12

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 2-methoxyphenol (0.15 mmol, 18.6 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 12 as colorless oil (25.4 mg, 84%). R$_f$ = 0.25 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.22 – 7.20 (m, 2H), 6.87 – 6.84 (m, 3H), 6.82 – 6.78 (m, 2H), 5.57 (s, 1H), 4.91 (s, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 173.4, 158.7, 146.5, 144.8, 131.0, 130.7, 129.4, 121.4, 114.2, 113.9, 111.0, 55.8, 55.7, 55.3, 52.3. IR $\nu_{max}$ (cm$^{-1}$): 3400, 3002, 2952, 2838, 1735, 1712, 1612, 1510, 1465, 1336, 1296, 1247, 1176, 1113, 1034, 1008, 957, 833, 802, 762, 635, 608. HRMS (ESI-TOF) m/z: [M]$^+$ Calcd for C$_{17}$H$_{18}$O$_5$ 302.1154, found 302.1142.

(+)-Methyl 2-(4-hydroxy-2-methoxyphenyl)-2-(4-methoxyphenyl)acetate 13

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 3-methoxyphenol (0.15 mmol, 18.6 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 13 as colorless oil (14.5 mg, 48%). R$_f$ = 0.1 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.24 – 7.18 (m, 2H), 6.89 – 6.85 (m, 2H), 6.82 (d, $J$ = 8.3 Hz, 1H), 6.39 – 6.38 (m, 1H), 6.29 (dd, $J$ = 8.3, 2.4 Hz, 1H), 5.15 (s, 1H), 5.10 (s, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.71 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 176.3, 160.8, 158.9, 156.0, 131.8, 129.2, 129.0, 128.9, 116.4, 114.2, 106.7, 103.6, 55.45, 55.41, 53.5, 53.1. IR $\nu_{max}$ (cm$^{-1}$): 3400, 3001, 2952, 2837, 1735, 1712, 1612, 1509, 1465, 1336, 1295, 1247, 1175, 1112, 1033, 1008, 957, 832, 801, 762, 635, 607. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{17}$H$_{18}$NaO$_5$ 325.1052, found 325.1038.

(+)-Methyl 2-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)acetate 14

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 3-methoxyphenol (0.15 mmol, 18.6 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg)
afforded the title compound 14 as colorless oil (7.0 mg, 23%). R<sub>f</sub> = 0.2 (10% EtOAc:Hexane).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.56 (s, 1H), 7.14 (dd, J = 8.9, 0.6 Hz, 2H), 6.99 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 6.48 (d, J = 2.6 Hz, 1H), 6.45 (dd, J = 8.4, 2.6 Hz, 1H), 5.00 (s, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 176.3, 160.8, 158.9, 156.0, 131.8, 129.2, 128.9, 116.4, 114.2, 106.7, 103.6, 55.5, 55.4, 53.5, 53.1.

IR <sup>ν</sup> <sub>max</sub> (cm<sup>-1</sup>): 3390, 3001, 2953, 2911, 2837, 1736, 1711, 1613, 1511, 1462, 1440, 1331, 1290, 1249, 1203, 1176, 1164, 1109, 1091, 1034, 959, 829, 798, 767. HRMS (ESI-TOF) m/z: [M+Na]<sup>+</sup>
Calcd for C<sub>17</sub>H<sub>18</sub>NaO<sub>5</sub> 325.1052, found 325.1034.

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 2,6-dimethylphenol (0.15 mmol, 18.3 mg) catalyzed by H<sub>2</sub>SO<sub>4</sub>-SiO<sub>2</sub> (5 mol%, 10.0 mg) afforded the title compound 15 as colorless oil (26.4 mg, 88%). R<sub>f</sub> = 0.10 (10% EtOAc:Hexane).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.22 (dd, J = 8.9, 0.6 Hz, 2H), 6.90 (d, J = 0.6 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 4.86 (s, 1H), 4.62 (s, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 2.21 (s, 6H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 173.8, 158.8, 145.3, 143.5, 130.1, 129.9, 127.7, 114.5, 113.9, 113.0, 55.9, 55.2, 52.5, 52.2, 19.3. IR <sup>ν</sup> <sub>max</sub> (cm<sup>-1</sup>): 3487, 2923, 2859, 1727, 1605, 1505, 1458, 1260, 1149, 1078, 1025, 800, 744. HRMS (ESI-TOF) m/z: [M+Na]<sup>+</sup>
Calcd for C<sub>18</sub>H<sub>20</sub>NaO<sub>4</sub> 339.1209, found 339.1206.

(+) -Methyl 2 - (4-hydroxy - 3,5 - dimethylphenyl) - 2 - (4 - methoxyphenyl) acetate 16

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 2-methoxy-4-methylphenol (0.15 mmol, 20.7 mg) catalyzed by H<sub>2</sub>SO<sub>4</sub>-SiO<sub>2</sub> (5 mol%, 10.0 mg) afforded the title compound 16 as colorless oil (25.3 mg, 80%). R<sub>f</sub> = 0.20 (10% EtOAc:Hexane).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.15 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 6.81 (s, 1H), 6.66 (s, 1H), 5.45 (s, 1H), 5.05 (s, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.72 (s, 3H), 2.20 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 173.4, 158.6, 145.3, 143.5, 130.1, 129.9, 127.7, 114.5, 113.9, 113.0, 55.9, 55.2, 52.5, 52.2, 19.3. IR <sup>ν</sup> <sub>max</sub> (cm<sup>-1</sup>): 3390, 3001, 2953, 2911, 2837, 1736, 1711, 1613, 1511, 1462, 1440, 1331, 1290, 1249, 1203, 1176, 1164, 1109, 1091, 1034, 959, 829, 798, 767. HRMS (ESI-TOF) m/z: [M+H]<sup>+</sup>
Calcd for C<sub>18</sub>H<sub>20</sub>NaO<sub>4</sub> 339.1208, found 339.1206.
(+)-Methyl 2-(4-hydroxy-3,5-dimethoxyphenyl)-2-(4-methoxyphenyl)acetate 17

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 2,6-dimethoxyphenol (0.15 mmol, 23.1 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 17 as colorless oil (27.9 mg, 84%). R$_f$ = 0.15 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.21 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.54 (s, 2H), 5.46 (s, 1H), 4.89 (s, 1H), 3.85 (s, 6H), 3.79 (s, 3H), 3.74 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 173.5, 158.9, 147.1, 134.1, 130.9, 129.9, 129.5, 114.1, 105.5, 56.5, 56.1, 55.4, 52.4. IR $\nu$_{max} (cm$^{-1}$): 3443, 3000, 2952, 2938, 2839, 1732, 1611, 1510, 1460, 1429, 1364, 1325, 1304, 1247, 1215, 1179, 1158, 1112, 1032, 835, 748. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{18}$H$_{20}$NaO$_6$ 355.1158, found 355.1151.

(+)-Methyl 2-(2-hydroxy-2,6-dimethylphenyl)-2-(4-methoxyphenyl)acetate 18

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 3,5-dimethylphenol (0.15 mmol, 18.3 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 18 as colorless oil (20.1 mg, 67%). R$_f$ = 0.12 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.04 – 6.99 (m, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.55 (s, 2H), 5.26 (s, 1H), 5.15 (s, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 2.14 (s, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 174.4, 158.4, 154.4, 139.3, 129.9, 128.9, 128.1, 115.9, 113.7, 55.4, 52.5, 49.8, 21.1. IR $\nu$_{max} (cm$^{-1}$): 3493, 3061, 3028, 2951, 2921, 2839, 1732, 1611, 1510, 1460, 1429, 1364, 1325, 1304, 1247, 1215, 1179, 1158, 1112, 1032, 835, 748. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{18}$H$_{20}$NaO$_4$ 323.1259, found 323.1244.

(+)-Methyl 2-(5-butyl-2-hydroxyphenyl)-2-(4-methoxyphenyl)acetate 19

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 4-butylphenol (0.15 mmol, 22.5 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 19 as colorless oil (24.6 mg, 75%). R$_f$ = 0.10 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.16 (d, J = 8.4 Hz, 2H), 7.01 (dd, J = 8.1,
2.2 Hz, 2H), 6.91 (d, $J = 2.1$ Hz, 1H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 8.2$ Hz, 1H), 5.05 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 2.49 (d, $J = 7.5$ Hz, 1H), 2.47 (d, $J = 7.5$ Hz, 1H), 1.58 (td, $J = 15.1$, 7.4 Hz, 4H), 0.91 (t, $J = 7.3$ Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 175.8, 158.9, 152.6, 135.1, 130.9, 129.3, 129.21, 129.16, 123.8, 117.7, 114.2, 55.4, 53.8, 53.0, 37.3, 29.8, 24.8, 13.9. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3399, 2955, 2926, 2870, 2852, 1803, 1736, 1716, 1610, 1510, 1462, 1435, 1249, 1203, 1178, 1033, 822.

HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{20}$H$_{24}$O$_4$Na = 351.1567, found 351.1543.

(+)-Methyl 2-(2,4-dimethoxyphenyl)-2-(4-methoxyphenyl)acetate 20

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 1,3-dimethoxybenzene (0.15 mmol, 20.7 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 20 as colorless oil (26.5 mg, 84%). R$_f$ = 0.30 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.21 (d, $J = 8.4$ Hz, 2H), 6.93 (dd, $J = 8.4$, 0.4 Hz, 1H), 6.86 (d, $J = 8.8$ Hz, 2H), 6.46 (d, $J = 2.4$ Hz, 1H), 6.40 (dd, $J = 8.5$, 2.5 Hz, 1H), 5.16 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.70 (s, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 174.0, 160.1, 158.8, 157.8, 130.2, 130.1, 129.6, 120.7, 114.0, 104.1, 98.7, 55.6, 55.4, 55.3, 52.2, 49.6. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3000, 2950, 2836, 1736, 1611, 1586, 1509, 1462, 1438, 1333, 1296, 1249, 1208, 1177, 1157, 1103, 936, 925, 831, 798, 762, 635. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{18}$H$_{20}$O$_5$Na 339.1208, found 339.1191.

(+)-Methyl 2-(2-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 21

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 2,4-dimethylphenol (0.15 mmol, 18.3 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 21 as colorless oil (24.6 mg, 82%). R$_f$ = 0.25 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.19 – 7.14 (m, 2H), 6.93 – 6.88 (m, 2H), 6.87 – 6.82 (m, 2H), 6.76 (d, $J = 1.6$ Hz, 1H), 5.03 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 2.22 (s, 3H), 2.21 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 175.8, 158.8, 150.6, 151.3, 129.3, 129.01, 129.00, 128.9, 125.9, 123.4, 114.0, 55.2, 53.8, 52.8, 20.4, 16.1. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3468, 3002, 2952, 2922, 2838, 1810, 1790, 1736, 1710, 1609, 1510, 1482, 1462, 1439, 1302, 1249, 1218, 1177, 1163, 1094, 1031, 899, 833, 757, 728. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{18}$H$_{26}$NaO$_4$ 323.1259, found 323.1246.
(+)-Methyl 2-(2-hydroxynaphthalen-1-yl)-2-(4-methoxyphenyl)acetate 22

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and naphthalen-2-ol (0.15 mmol, 21.6 mg) catalyzed by H2SO4-SiO2 (5 mol%, 10.0 mg) afforded the title compound 22 as colorless oil (19.3 mg, 60%). Rf = 0.15 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 8.09 (s, 1H), 8.00 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.50 (ddd, J = 8.5, 6.8, 1.4 Hz, 1H), 7.36 (ddd, J = 7.9, 6.8, 1.0 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 7.12 (dd, J = 8.9, 0.7 Hz, 2H), 6.81 (d, J = 8.9 Hz, 2H), 5.95 (s, 1H), 3.83 (s, 3H), 3.75 (s, 3H). 13C NMR (125 MHz, CDCl3): δ 176.8, 158.9, 154.0, 133.3, 130.4, 129.6, 129.1, 128.8, 128.4, 127.3, 121.8, 120.5, 114.9, 114.1, 55.3, 53.3, 47.7. IR νmax (cm⁻¹): 3445, 3001, 2952, 2839, 1732, 1609, 1587, 1509, 1462, 1444, 1282, 1246, 1195, 1175, 1156, 1088, 1028, 1005, 883, 829, 761, 733, 701. HRMS (ESI-TOF) m/z: [M+H]+ Calcd for C20H19O3 323.1283, found 323.1262.

(+)-Methyl 2-(5-bromo-1H-indol-3-yl)-2-(4-methoxyphenyl)acetate 23

Following the general procedure for Friedel-Crafts, reaction of diazoester 4 (0.10 mmol, 20.6 mg) and 5-bromo-1H-indole (0.15 mmol, 29.1 mg) catalyzed by H2SO4-SiO2 (5 mol%, 10.0 mg) afforded the title compound 23 as colorless oil (22.7 mg, 77%). Rf = 0.25 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 8.24 (s, 1H), 7.54 (d, J = 1.8 Hz, 1H), 7.29 (d, J = 8.7 Hz, 2H), 7.23 (dd, J = 8.6, 1.9 Hz, 1H), 7.16 (d, J = 8.6 Hz, 1H), 7.13 (d, J = 2.2 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 5.13 (s, 1H), 3.77 (s, 3H), 3.74 (s, 3H). 13C NMR (125 MHz, CDCl3): δ 173.5, 159.0, 153.0, 130.3, 129.4, 128.4, 128.3, 124.5, 121.6, 114.2, 113.8, 113.1, 112.8, 55.4, 52.5, 47.9. IR νmax (cm⁻¹): 3415, 3371, 3003, 2944, 2839, 1732, 1609, 1587, 1509, 1462, 1444, 1282, 1246, 1195, 1175, 1156, 1088, 1028, 1005, 883, 829, 761, 733, 701. HRMS (ESI-TOF) m/z: [M-H]⁻ Calcd for C18H14BrO3N 372.0241, found 372.0226.

1 mmol scale reaction: To a 25 mL round bottom flask equipped with a magnetic stir-bar was added diazoester 4 (1 mmol, 206 mg), 5-bromoindole (1.5 mmol, 290 mg) and dissolved in DCE (3 mL) at 25 °C. After 1 min of pre-stirring, H2SO4-SiO2 (5 mol%, 100 mg) was added in one portion. After 10 minutes, the reaction was judged to be complete (TLC), the solid filtered off, and washed with ethyl acetate (2 x 25 mL) and organic solvents were removed under reduced pressure. The resulting residue was purified by flash column chromatography using silica gel (230-400 mesh) and a hexane: ethyl acetate (9:1) mobile phase, affording compound 23 as a colorless oil (227 mg, 61%).
(+)-Ethyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 25

Following the general procedure for Friedel-Crafts, reaction of diazoester S1 (0.10 mmol, 22.0 mg) and 2,6-dimethylphenol (0.15 mmol, 18.3 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 25 as colorless oil (27.6 mg, 88%). R$_f$ = 0.23 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.22 (d, $J$ = 8.5 Hz, 2H), 6.90 (s, 2H), 6.84 (d, $J$ = 8.8 Hz, 2H), 4.83 (s, 1H), 4.63 (s, 1H), 4.22 – 4.15 (m, 2H), 3.78 (s, 3H), 2.20 (s, 6H), 1.25 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 173.2, 158.6, 151.4, 131.4, 130.6, 129.5, 128.6, 123.1, 113.9, 61.0, 55.5, 55.2, 16.0, 14.2. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3485, 2965, 2920, 2844, 1721, 1607, 1500, 1480, 1453, 1375, 1294, 1247, 1151, 1098, 1023, 875, 800, 746, 646. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{19}$H$_{22}$NaO$_4$ 337.1416, found 337.1391.

(+)-Isopropyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 26

Following the general procedure for Friedel-Crafts, reaction of diazoester S2 (0.10 mmol, 21.8 mg) and 2,6-dimethylphenol (0.15 mmol, 18.3 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 26 as colorless oil (28.2 mg, 86%). R$_f$ = 0.18 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.22 (d, $J$ = 8.5 Hz, 2H), 6.90 (s, 2H), 6.85 (d, $J$ = 8.8 Hz, 2H), 5.06 (hept, $J$ = 6.3 Hz, 1H), 4.79 (s, 1H), 4.59 (s, 1H), 3.79 (s, 3H), 2.20 (s, 6H), 1.22 (d, $J$ = 6.3 Hz, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 172.8, 158.7, 151.4, 131.7, 130.9, 129.6, 128.7, 123.1, 114.0, 68.5, 55.8, 55.4, 21.8, 16.1. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3485, 2977, 2928, 2845, 1718, 1608, 1502, 1480, 1455, 1371, 1294, 1246, 1177, 1104, 1030, 977, 946, 903, 830, 793, 733, 644. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{20}$H$_{24}$NaO$_4$ 351.1572, found 351.1544.

(+)-2,2,2-Trifluoroethyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 27

Following the general procedure for Friedel-Crafts, reaction of diazoester S3 (0.10 mmol, 27.4 mg) and 2,6-dimethylphenol (0.15 mmol, 18.3 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 27 as colorless oil (26.9 mg, 73%). R$_f$ = 0.30 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.21 (d, $J$ = 8.4 Hz, 2H), 6.89 (d, $J$ = 0.5 Hz, 2H), 6.86 (d, $J$ = 8.8 Hz, 2H), 4.94 (s, 1H), 4.62 (s, 1H), 4.55 – 4.47 (m, 2H), 3.78 (s, 3H), 2.20 (s, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 171.8, 159.0, 151.8, 130.4, 129.62, 129.60, 128.6, 123.4, 123.0 (q, $J$ = 277 Hz), 114.9, 60.7 (q, $J$ = 36.6 Hz), 55.4, 55.0, 16.0. IR $\nu_{\text{max}}$ (cm$^{-1}$):
Following the general procedure for Friedel-Crafts, reaction of diazoester S4 (0.10 mmol, 20.6 mg) and 2,6-dimethoxyphenol (0.15 mmol, 23.1 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 28 as colorless oil (21.9 mg, 66%). R$_f$ = 0.12 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.28-7.23 (m, 1H), 7.00 (ddd, $J$ = 7.8, 1.8, 0.7 Hz, 1H), 6.89 (ddd, $J$ = 6.6, 3.5, 2.4 Hz, 2H), 6.56 (s, 2H), 5.47 (s, 1H), 5.16 (s, 1H), 3.85 (s, 6H), 3.84 (s, 3H), 3.73 (s, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 173.7, 156.9, 147.2, 134.2, 129.1, 128.6, 128.4, 128.1, 120.7, 110.5, 106.0, 56.4, 55.7, 52.4, 51.2. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3443, 3000, 2952, 2938, 2839, 1732, 1612, 1510, 1460, 1247, 1112, 835, 748. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{19}$H$_{20}$F$_3$O$_4$ 369.1308, found 369.1333.

Following the general procedure for Friedel-Crafts, reaction of diazoester S4 (0.10 mmol, 20.6 mg) and 2,6-dimethoxyphenol (0.15 mmol, 18.3 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 29 as colorless oil (18.3 mg, 61%). R$_f$ = 0.20 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.25-7.21 (m, 1H), 7.02 (ddd, $J$ = 8.0, 1.8, 0.7 Hz, 1H), 6.92 (d, $J$ = 0.5 Hz, 2H), 6.90-6.86 (m, 2H), 5.16 (s, 1H), 4.70 (s, 1H), 3.82 (s, 3H), 3.71 (s, 3H), 2.20 (s, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 174.1, 156.9, 151.6, 123.4, 120.6, 110.5, 55.7, 52.3, 50.3, 16.1. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3485, 3004, 2952, 2923, 2842, 1735, 1600, 1493, 1462, 1437, 1332, 1286, 1245, 1189, 1166, 1115, 1073, 1048, 1024, 979, 941, 911, 868, 802, 788, 755. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{18}$H$_{20}$NaO$_4$ = 355.1158, found 355.1161.

Following the general procedure for Friedel-Crafts, reaction of diazoester S4 (0.10 mmol, 20.6 mg) and 1,3-dimethoxybenzene (0.15 mmol, 20.7 mg) catalyzed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10.0 mg) afforded the title compound 30 as colorless oil (21.9 mg, 66%). R$_f$ = 0.12 (10% EtOAc:Hexane). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.28-7.23 (m, 1H), 7.00 (ddd, $J$ = 7.8, 1.8, 0.7 Hz, 1H), 6.89 (ddd, $J$ = 6.6, 3.5, 2.4 Hz, 2H), 6.56 (s, 2H), 5.47 (s, 1H), 5.16 (s, 1H), 3.85 (s, 6H), 3.84 (s, 3H), 3.73 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 173.7, 156.9, 147.2, 134.2, 129.1, 128.6, 128.4, 128.1, 120.7, 110.5, 106.0, 56.4, 55.7, 52.4, 51.2. IR $\nu_{\text{max}}$ (cm$^{-1}$): 3443, 3000, 2952, 2938, 2839, 1732, 1612, 1510, 1460, 1247, 1112, 835, 748. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{18}$H$_{20}$NaO$_4$ = 355.1158, found 355.1161.
mg) afforded the title compound 30 as colorless oil (22.1 mg, 70%). Rf = 0.30 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 7.27 – 7.23 (m, 1H), 7.02 (dd, J = 7.7, 1.7, 0.5 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H). 6.89 (ddd, J = 6.2, 5.7, 1.0 Hz, 2H), 6.48 (d, J = 2.4 Hz, 1H), 6.43 (dd, J = 8.4, 2.5 Hz, 1H), 5.54 (s, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.70 (s, 3H). 13C NMR (125 MHz, CDCl3): δ 174.2, 160.2, 158.2, 157.3, 129.9, 129.3, 128.4, 127.2, 120.6, 119.2, 110.7, 104.2, 98.8, 55.7 (2C), 55.4, 52.2, 44.2. IR νmax (cm⁻¹): 3000, 2949, 2837, 1734, 1611, 1586, 1492, 1460, 436, 1334, 1292, 1242, 1206, 1171, 1153, 1106, 1010, 936, 925, 833, 785, 754, 638. HRMS (ESI-TOF) m/z: [M+Na]+ Calcd for C18H20NaO5 339.1208, found 339.1198.

(+)-Methyl 2-(benzo[d][1,3]dioxol-4-yl)-2-(2-methoxyphenyl)acetate 31

Following the general procedure for Friedel-Crafts, reaction of diazoester S4 (0.10 mmol, 20.6 mg) and benzo[d][1,3]dioxole (0.15 mmol, 18.3 mg) catalyzed by H2SO4·SiO2 (5 mol%, 10.0 mg) afforded the title compound 31 as colorless oil (17.4 mg, 58%). Rf = 0.35 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 7.25 – 7.23 (m, 1H), 7.08 (dd, J = 7.6, 1.5 Hz, 1H), 6.89 (ddd, J = 15.3, 7.7, 0.9 Hz, 2H), 6.83 – 6.82 (m, 1H), 6.77 (d, J = 1.1 Hz, 2H), 5.94 (s, 2H), 5.21 (s, 1H), 3.82 (s, 3H), 3.72 (s, 3H). 13C NMR (125 MHz, CDCl3): δ 174.1, 157.0, 153.3, 131.8, 129.6, 129.2, 128.5, 128.3, 127.8, 124.1, 120.7, 115.2, 110.6, 55.7, 52.3, 50.3, 16.0. IR νmax (cm⁻¹): 2952, 2923, 2841, 1736, 1599, 1489, 1461, 1440, 1290, 1232, 1194, 1157, 1035, 930, 810, 755, 654. HRMS (ESI-TOF) m/z: [M+Na]+ Calcd for C17H16NaO5 323.0895, found 323.0889.

(+)-Methyl 2-(4-hydroxy-3-methylphenyl)-2-(2-methoxyphenyl)acetate 32

Following the general procedure for Friedel-Crafts, reaction of diazoester S4 (0.10 mmol, 20.6 mg) and o-cresol (0.15 mmol, 16.2 mg) catalyzed by H2SO4·SiO2 (5 mol%, 10.0 mg) afforded the title compound 32 as colorless oil (21.2 mg, 74%). Rf = 0.25 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 7.23 (td, J = 7.9, 1.7 Hz, 1H), 7.05 (d, J = 2.1 Hz, 1H), 7.03 – 7.01 (m, 1H), 6.99 (dd, J = 8.2, 2.3 Hz, 1H), 6.88 (dd, J = 11.8, 4.4 Hz, 2H), 6.70 (d, J = 8.2 Hz, 1H), 5.19 (s, 1H), 4.95 (s, 1H), 3.82 (s, 3H), 3.71 (s, 3H), 2.21 (s, 3H). 13C NMR (125 MHz, CDCl3): δ 174.0, 156.9, 153.2, 131.7, 129.6, 129.2, 128.4, 128.2, 127.8, 124.1, 120.6, 115.1, 110.5, 55.6, 52.3, 50.3, 15.9. IR νmax (cm⁻¹): 3420, 3004, 2952, 2925, 2839, 1717, 1600, 1588, 1507, 1490, 1461, 1436, 1326, 1265, 1241, 1195, 1172, 1161, 1118, 1106, 1027, 908, 814, 728, 635. HRMS (ESI-TOF) m/z: [M+Na]+ Calcd for C17H17NaO5 308.1103, found 308.1090.
(±)-Methyl 2-(2-hydroxy-5-methylphenyl)-2-(2-methoxyphenyl)acetate 33

Following the general procedure for Friedel-Crafts, reaction of diazoester S4 (0.10 mmol, 20.6 mg) and p-cresol (0.15 mmol, 16.2 mg) catalyzed by H2SO4-SiO2 (5 mol%, 10.0 mg) afforded the title compound 33 as colorless oil (20.9 mg, 73%). Rf = 0.25 (10% EtOAc:Hexane). 1H NMR (500 MHz, CDCl3): δ 7.29-7.25 (m, 1H), 7.04-7.02 (m, 2H), 6.96 (d, J = 2.0 Hz, 1H), 6.92-6.89 (m, 3H), 6.84 (d, J = 8.2 Hz, 1H), 6.19 (s, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 2.26 (s, 3H). 13C NMR (125 MHz, CDCl3): δ 175.7, 156.7, 153.0, 131.7, 130.2, 130.1, 129.2, 128.9, 125.2, 121.9, 121.0, 117.7, 110.7, 55.8, 52.9, 49.2, 20.7. IR νmax (cm⁻¹): 3413, 2951, 2923, 2839, 1713, 1611, 1509, 1491, 1460, 1435, 1325, 1264, 1243, 1200, 1175, 1161, 1102, 1026, 815, 753. HRMS (ESI-TOF) m/z: [M+Na]+ Calcd for C17H18NaO4 309.1103, found 309.1095.
Synthesis of Methyl 2-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(4-hydroxy-3,5-dimethylphenyl)acetate S9

To a round bottom flask was added methyl 2-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(4-hydroxy-3,5-dimethylphenyl)acetate S8 (20 mg, 0.07 mmol) and dissolved in dichloromethane (0.3 mL) under argon. To the stirring solution was added 2,6-dimethylphenol (13 mg, 0.11 mmol), followed by H$_2$SO$_4$-SiO$_2$ (10 mol%, 14.0 mg). The reaction was left to stir for 24 h. Upon completion (as detected by consumption of the starting materials by TLC), the reaction was filtered to remove the catalyst, and remaining organic solvents removed under reduced pressure. The residue was purified by silica gel chromatography using hexane-acetone (8:1). methyl 2-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(4-hydroxy-3,5-dimethylphenyl)acetate (20 mg, 72%) was isolated as a pale yellow oil. $^1$H NMR (CDCl$_3$, 500 MHz) δ 7.12 (2H, s), 6.95 (2H, s), 5.13 (1H, s), 4.79 (1H, s), 4.55 (1H, s), 3.71 (3H, s), 2.21 (6H, s), 1.41 (18H, s). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 174.1, 153.0, 151.4, 135.8, 130.9, 129.6, 128.8, 125.3, 123.1, 56.3, 52.3, 34.5, 30.4, 16.2. IR $\nu$ max (cm$^{-1}$): 3637, 3494, 2954, 2917, 2873, 1724, 1605, 1489, 1434, 1320, 1235, 1195, 1152, 1024, 732. HRMS (ESI-TOF) m/z: [M-H]$^-$ Calcd for C$_{25}$H$_{33}$O$_4$ 397.2379, found 397.2364.

Attempted synthesis of Methyl (+)-2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 15 from methyl 2-hydroxy-2-(4-methoxyphenyl)acetate S10

To a round bottom flask was added methyl 2-hydroxy-2-(4-methoxyphenyl)acetate S10 (20 mg, 0.1 mmol) and dissolved in dichloromethane (0.3 mL) under argon. To the stirring solution was added 2,6-dimethylphenol (18 mg, 0.15 mmol), followed by H$_2$SO$_4$-SiO$_2$ (5 mol%, 10 mg). The reaction was left to stir for 24 h. During this time, TLC analysis confirmed no desired product 15 was formed, with both starting materials remaining in the reaction mixture.
$^1$H NMR (500 MHz, CDCl$_3$) methyl 2-diazo-2-(4-methoxyphenyl)acetate 4

![Chemical structure of methyl 2-diazo-2-(4-methoxyphenyl)acetate]

$^1$H NMR (500 MHz, CDCl$_3$) ethyl 2-diazo-2-(4-methoxyphenyl)acetate S1

![Chemical structure of ethyl 2-diazo-2-(4-methoxyphenyl)acetate]
$^1$H NMR (500 MHz, CDCl$_3$) isopropyl 2-diazo-2-(4-methoxyphenyl)acetate S2

$^1$H NMR (500 MHz, CDCl$_3$) 2,2,2-trifluoroethyl 2-diazo-2-(4-methoxyphenyl)acetate S3
$^1$H NMR (500 MHz, CDCl$_3$) methyl 2-diazo-2-(2-methoxyphenyl)acetate S4

$^1$H NMR (500 MHz, CDCl$_3$) methyl 2-diazo-2-phenylacetate S5
$^1$H NMR (500 MHz, CDCl$_3$) methyl 2-(4-chlorophenyl)-2-diazoacetate S6

$^1$H NMR (500 MHz, CDCl$_3$) methyl 2-(4-bromophenyl)-2-diazoacetate S7
\(^1\)H NMR (500 MHz, CDCl\(_3\)) \((\pm)\)-methyl 2,2-bis(4-methoxyphenyl)acetate 5

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \((\pm)\)-methyl 2,2-bis(4-methoxyphenyl)acetate 5
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxyphenyl)-2-(4-methoxyphenyl)acetate 6

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxyphenyl)-2-(4-methoxyphenyl)acetate 6
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-methoxyphenyl)-2-(phenylthio)acetate 7

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-methoxyphenyl)-2-(phenylthio)acetate 7
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(4-acetamidophenyl)-2-(4-methoxyphenyl)acetate

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(4-acetamidophenyl)-2-(4-methoxyphenyl)acetate
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3-methoxyphenyl)-2-(4-methoxyphenyl)acetate 12

13C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3-methoxyphenyl)-2-(4-methoxyphenyl)acetate 12
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(4-hydroxy-2-methoxyphenyl)-2-(4-methoxyphenyl)acetate 13

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(4-hydroxy-2-methoxyphenyl)-2-(4-methoxyphenyl)acetate 13
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)acetate 14

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)acetate 14
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 15

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 15
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(4-hydroxy-3-methoxy-5-methylphenyl)-2-(4-methoxyphenyl)acetate 16

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(4-hydroxy-3-methoxy-5-methylphenyl)-2-(4-methoxyphenyl)acetate 16
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3,5-dimethoxyphenyl)-2-(4-methoxyphenyl)acetate 17

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3,5-dimethoxyphenyl)-2-(4-methoxyphenyl)acetate 17
\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3) \ (\pm) \text{-methyl} \ 2-(4\text{-hydroxy}-2,6\text{-dimethylphenyl})-2-(4\text{-methoxyphenyl})\text{acetate 18} \]

\[ ^13C \text{ NMR} \ (125 \text{ MHz, CDCl}_3) \ (\pm) \text{-methyl} \ 2-(4\text{-hydroxy}-2,6\text{-dimethylphenyl})-2-(4\text{-methoxyphenyl})\text{acetate 18} \]
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(5-butyl-2-hydroxyphenyl)-2-(4-methoxyphenyl)acetate 19

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(5-butyl-2-hydroxyphenyl)-2-(4-methoxyphenyl)acetate 19
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(2,4-dimethoxyphenyl)-2-(4-methoxyphenyl)acetate 20

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(2,4-dimethoxyphenyl)-2-(4-methoxyphenyl)acetate 20
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(2-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 21

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(2-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 21
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(2-hydroxynaphthalen-1-yl)-2-(4-methoxyphenyl)acetate 22

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(2-hydroxynaphthalen-1-yl)-2-(4-methoxyphenyl)acetate 22
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(5-bromo-1H-indol-3-yl)-2-(4-methoxyphenyl)acetate 23

![H NMR spectrum](image)

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(5-bromo-1H-indol-3-yl)-2-(4-methoxyphenyl)acetate 23

![C NMR spectrum](image)
$^1$H NMR (500 MHz, CDCl$_3$) (+)-ethyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 25

![H NMR spectrum](image)

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-ethyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 25

![C NMR spectrum](image)
$^1$H NMR (500 MHz, CDCl$_3$) (+)-isopropyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 26

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-isopropyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 26
$^1$H NMR (500 MHz, CDCl$_3$) $(\pm)$-2,2,2-trifluoroethyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 27

\[
\begin{array}{c}
\text{Me}_3CN \\
\text{MeO} \\
\end{array}
\]

$^{13}$C NMR (125 MHz, CDCl$_3$) $(\pm)$-2,2,2-trifluoroethyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(4-methoxyphenyl)acetate 27

\[
\begin{array}{c}
\text{Me}_3CN \\
\text{MeO} \\
\end{array}
\]
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3,5-dimethoxyphenyl)-2-(2-methoxyphenyl)acetate 28

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3,5-dimethoxyphenyl)-2-(2-methoxyphenyl)acetate 28
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(2-methoxyphenyl)acetate 29

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3,5-dimethylphenyl)-2-(2-methoxyphenyl)acetate 29
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(2,4-dimethoxyphenyl)-2-(2-methoxyphenyl)acetate 30

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(2,4-dimethoxyphenyl)-2-(2-methoxyphenyl)acetate 30
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(benzo[d][1,3]dioxol-4-yl)-2-(2-methoxyphenyl)acetate 31

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(benzo[d][1,3]dioxol-4-yl)-2-(2-methoxyphenyl)acetate 31
$^1$H NMR (500 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3-methylphenyl)-2-(2-methoxyphenyl)acetate 32

$^{13}$C NMR (125 MHz, CDCl$_3$) (+)-methyl 2-(4-hydroxy-3-methylphenyl)-2-(2-methoxyphenyl)acetate 32
$^1$H NMR (500 MHz, CDCl$_3$) (±)-methyl 2-(2-hydroxy-5-methylphenyl)-2-(2-methoxyphenyl)acetate 33

$^{13}$C NMR (125 MHz, CDCl$_3$) (±)-methyl 2-(2-hydroxy-5-methylphenyl)-2-(2-methoxyphenyl)acetate 33
^1^H NMR (500 MHz, CDCl\textsubscript{3}) (+)-2-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(4-hydroxy-3,5-dimethylphenyl)acetate S9

\[ \text{S9} \]

\( ^{13} \text{C} \) NMR (125 MHz, CDCl\textsubscript{3}) (+)-2-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(4-hydroxy-3,5-dimethylphenyl)acetate S9

\[ \text{S9} \]
References


