Supplementary Information

Reductive dehalogenation and dehalogenative sulfonation of phenols and heteroaromatics with sodium sulfite in an aqueous medium

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1. General information

1.1 Chemicals

Starting materials and reagents were purchased from various commercial sources (VWR, Sigma-Aldrich, Fluorochem, Acros Organics) and used as received. Starting compounds 25 and 26 were prepared according literature procedures.\textsuperscript{1,2} Concentrated hydrochloric acid was purchased from VWR (37\%, Ana\textsuperscript{R} NORMAPUR®). Ethyl acetate, CHCl\textsubscript{3} and hexane for a reaction workup and for a column chromatography were purchased from VWR (HiPerSolv CHROMANORM\textsuperscript{®} for HPLC) and used as received. Deuterated solvents for NMR spectroscopy were purchased from VWR (> 99.8\%, without TMS) and stored in a desiccator at ambient temperature. Dimethyl sulfone used as a standard for quantitative NMR was purchased from Sigma-Aldrich (TraceCERT®) and stored in a fridge. Anhydrous sodium sulfite was purchased from Lach-Ner (98.8\%), stored at ambient temperature and used without further purification. Local tap water was purified by reverse osmosis and purged with a stream of nitrogen before use.

1.2 Reaction monitoring

The reactions were monitored with LC/MS (ACQUITY UPLC, Waters) consisting of auto-sampler, quaternary solvent manager system, PDA detector and quadrupole mass spectrometer. The separations were performed using C18 column (tempered to 30 °C) and a mobile phase consisted of: (A) 0.01 mol/L ammonium acetate in water and (B) acetonitrile. A linearly programmed gradient elution was used at a flow rate of 0.6 mL/min.

The quantitative \textsuperscript{1}H NMR NMR was performed on JEOL 400 MHz spectrometer. A stock solution of the NMR standard (dimethyl sulfone) was added to a crude reaction mixture, which was then diluted with DMSO-d\textsubscript{6} and filtered to remove precipitated salts. An aliquot (0.6 mL) of a filtrate was then withdrawn for the NMR analysis.

1.3 Compound characterization

Compounds were characterized by their \textsuperscript{1}H and \textsuperscript{13}C NMR spectra, high resolution mass spectra (HRMS), and melting point.

NMR spectra were recorded at room temperature on JEOL 400 MHz spectrometer (400 MHz for \textsuperscript{1}H and 100 MHz for \textsuperscript{13}C) using CDCl\textsubscript{3}, DMSO-d\textsubscript{6} or D\textsubscript{2}O as a solvent. Chemical shifts (δ) for proton and carbon signals were referenced to the residual solvent peak and are reported in parts per million (ppm). Coupling constants (J) are reported in Hertz (Hz) and multiplicity reported according to the
following convention: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, brs = broad singlet.

HRMS analyses were performed on Thermo Exactive Plus high resolution mass spectrometer with electrospray ionization (ESI) and Orbitrap analyzer operating at positive or negative full scan mode in the range of 60-800 m/z.

1.4 Microwave reactor

All reactions carried out under microwave irradiation were performed with the CEM Discover® SP microwave synthesizer, using the Dynamic mode in the following settings: maximum amount of microwave power (150 W), premixing time (1 minute), stirring speed (high), hold time (depending on the reaction), temperature control point (depending on the reaction), simultaneous cooling (PowerMax ON/OFF). In the Dynamic mode a specified amount of power (150 W) is applied in order to reach the reaction temperature (temperature control point); then the power is modulated automatically, based on the temperature sensor feedback data, to hold the set temperature for a specific reaction time (hold time). A simultaneous cooling of the reaction vessel provided by a compressed air (24 psi) was applied during entire experiment (PowerMax option “ON”).

All 0.5 mmol scale reactions were performed in a 10 mL borosilicate glass reaction vessel closed with a disposable silicon cap and equipped with Teflon coated egg-shaped magnetic stir bar. The temperature was monitored by an external infrared sensor.

The 5 mmol scale reaction was performed in an 80 mL borosilicate glass reaction vessel equipped with Teflon coated egg-shaped magnetic stir bar. The reaction vessel was equipped with a cover assembly allowing introduction of a fiber optic temperature sensor, used for monitoring a reaction temperature.
2. Dehalogenation of 4-bromophenol at various temperatures

The mixture of substrate 1 (0.5 mmol), Na$_2$SO$_3$ (6.0 mmol) and water (2.5 mL) was stirred at given temperature for 3h. The reaction was performed either under microwave irradiation (150 W) or in a glass pressure tube inserted into preheated oil bath. Yield of 2 was determined by a quantitative HPLC. No significant difference between convective and microwave heating was observed at 100 °C.

![Chemical structure of 1 and 2](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Heating</th>
<th>T (°C)</th>
<th>2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>microwave</td>
<td>130</td>
<td>&gt;98</td>
</tr>
<tr>
<td>2</td>
<td>microwave</td>
<td>120</td>
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</tr>
<tr>
<td>5</td>
<td>convective</td>
<td>100</td>
<td>11</td>
</tr>
</tbody>
</table>
3. Kinetic study

A 10 mL Shlenk flask was charged with sodium sulfite (7.5 – 15.0 mmol, 15.0 – 30.0 equivalents, 1.5 – 3.0 M) and water (5 mL). The mixture was heated in oil bath to 40 °C (internal temperature) under nitrogen atmosphere. When the internal temperature reached 40 °C, 4-bromoresorcinol 20 (94 mg, 0.5 mmol) was added in a single portion to start the reaction, which was monitored by HPLC.

The reaction was carried out under pseudo first order conditions using at least 15 equivalents of sodium sulfite. The slope of a graph (-ln[SM] vs. time) corresponded to k´ (for the pseudo first order reaction). Rate constant k´ was determined at six different concentrations of sodium sulfite: 1.50, 2.00, 2.25, 2.50, 2.75 and 3.00 mol/L.

<table>
<thead>
<tr>
<th>[Na₂SO₃] (mol/L)</th>
<th>k’ (s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.50</td>
<td>5.81 x 10⁻⁴</td>
</tr>
<tr>
<td>2.00</td>
<td>8.05 x 10⁻⁴</td>
</tr>
<tr>
<td>2.25</td>
<td>10.05 x 10⁻⁴</td>
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<td>2.50</td>
<td>11.68 x 10⁻⁴</td>
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<td>2.75</td>
<td>12.75 x 10⁻⁴</td>
</tr>
<tr>
<td>3.00</td>
<td>14.02 x 10⁻⁴</td>
</tr>
</tbody>
</table>

The slope of a graph (k’ vs. [Na₂SO₃]) corresponded to k₁ (second order): k₁ = 5.65 x 10⁻⁴ M⁻¹s⁻¹).

The reaction of 4-bromoresorcinol 20 (0.5 mmol) with sodium sulfite (15 equivalents) at 40 °C was repeated in D₂O (5 mL). The pseudo first order rate constant was determined: k’ = 1.14 x 10⁻⁴ s⁻¹, providing k’_{H/D} = 5.81/1.14 = 5.09.
4. General procedure

A 10 mL reaction vessel equipped with a magnetic stir bar was charged with aryl halide (0.5 mmol), anhydrous sodium sulfite (amount specified for every compound), and demineralized water (2.5 mL). Without microwave irradiation: the mixture was stirred at ambient temperature or in preheated oil bath in closed vessel for specified time. Under microwave irradiation: the vessel was sealed and premixed for one minute at high stirring speed in the CEM Discover SP microwave synthesizer. Then, the reaction mixture was irradiated at maximum power of 150 W with simultaneous cooling by a compressed air (24 psi). When the desired temperature was reached (ramping time ~ 1 min), the power was automatically adjusted in order to maintain the set reaction temperature for specified time. Finally, the vessel was cooled to approximately 40 °C by a compressed air (cooling time ~ 1 min). The workup procedure is described for individual compounds. Generally, hydrodehalogenated products were obtained after liquid-liquid extraction in a sufficient purity, no chromatographic purification was required. Sulfonated products were obtained after acidification with hydrochloric acid.

5. Procedures and analytical data for individual compounds

Phenol 2 (Table 2, entry 1)

Compound 2 was prepared according to the general procedure from 4-bromophenol 1 (87 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 3 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄ and evaporation under reduced pressure yielded compound 2 as a pale brown crystalline solid (42 mg, 88 %).

Melting point 38-39 °C; ¹H NMR (400 MHz, DMSO-d₆): δ = 9.32 (brs, 1 H), 7.15 (t, J = 7.8 Hz, 2 H), 6.82 – 6.65 (m, 4 H) ppm; ¹³C NMR (100 MHz, DMSO-d₆): δ = 157.3, 129.4, 118.8, 115.2 ppm; HRMS: m/z calculated for C₆H₆O [M – H] 93.0335, found 93.0337.

Phenol 2 (Table 2, entry 2)
Compound 2 was prepared according to the general procedure from 4-iodophenol 3 (87 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 3 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 2 as a pale brown crystalline solid (43 mg, 91 %).

Analytical data were in accordance with compound 2 obtained from 4-bromophenol 1.

Phenol 2 (Table 2, entry 3)

Compound 2 was prepared according to the general procedure from 2-bromophenol 4 (87 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 3 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 2 as a pale brown crystalline solid (42 mg, 88 %).

Analytical data were in accordance with compound 2 obtained from 4-bromophenol 1.

Phenol 2 (Table 2, entry 4)

Compound 2 was prepared according to the general procedure from 2,4,6-tribromophenol 5 (166 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 5 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 2 as a pale brown crystalline solid (37 mg, 78 %).
Analytical data were in accordance with the compound 2 obtained from 4-bromophenol 1.

**3-Methylphenol 27 (Table 2, entry 5)**

![Chemical Structure 27]

Compound 27 was prepared according to the general procedure from 4-bromo-3-methylphenol 6 (94 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 2 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 27 as a pale yellow oil (43 mg, 80 %).

$^1$H NMR (400 MHz, CDCl₃): δ = 7.13 (t, $J = 7.7$ Hz, 1 H), 6.76 (d, $J = 7.4$ Hz, 1 H), 6.68 – 6.63 (m, 2 H), 4.49 (brs, 1 H), 2.32 (s, 3 H) ppm; $^{13}$C NMR (100 MHz, CDCl₃): δ = 155.5, 139.9, 129.5, 121.7, 116.1, 112.4, 21.4 ppm; HRMS: m/z calculated for C₇H₈O [M – H] - 107.0491, found 107.0494.

**3,5-Dimethylphenol 28 (Table 2, entry 6)**

![Chemical Structure 28]

Compound 28 was prepared according to the general procedure from 4-bromo-3,5-dimethylphenol 7 (101 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100°C for 4 hour. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 28 as a white crystalline solid (51 mg, 84 %).

Melting point 60-61 °C; $^1$H NMR (400 MHz, CDCl₃): δ = 6.59 (s, 1 H), 6.48 (s, 2 H), 5.00 (brs, 1 H), 2.27 (s, 6 H). $^{13}$C NMR (100 MHz, CDCl₃): δ = 155.5, 139.9, 122.63, 113.13, 21.4 ppm; HRMS: m/z calculated for C₈H₁₀O [M – H] - 121.0648, found 121.0643.
2,6-Dimethylphenol 29 (Table 2, entry 7)

\[
\begin{align*}
\text{Br} & \quad \text{Me} \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

Compound 29 was prepared according to the general procedure from 4-bromo-2,6-dimethylphenol 8 (101 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 10 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 29 as a pale brown solid (53 mg, 87%).

Melting point 40-42 °C; \textsuperscript{1}H NMR (400 MHz, CDCl₃): \( \delta = 6.98 \) (d, \( J = 7.4 \) Hz, 2H), \( 6.76 \) (t, \( J = 7.5 \) Hz, 1H), \( 4.58 \) (s, 1H), \( 2.25 \) (s, 6H) ppm; \textsuperscript{13}C NMR (100 MHz, CDCl₃): \( \delta = 152.27, 128.72, 123.08, 120.33, 15.98 \) ppm; HRMS: m/z calculated for C₈H₁₀O \([\text{M – H}]\) 121.0648, found 121.0641.

3-Hydroxybenzoic acid 31 (Table 2, entry 9)

\[
\begin{align*}
\text{OH} & \quad \text{COOH} \\
\text{Br} & \quad \text{COOH}
\end{align*}
\]

Compound 31 was prepared according to the general procedure from 2-bromo-3-hydroxybenzoic acid 10 (109 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 3 hours. Then, a clear colorless solution was acidified with concentrated hydrochloric acid to pH \( \approx 1 \). The precipitate was collected via filtration and washed with water (1 mL), yielding 3-hydroxybenzoic acid 31 as a pale yellow crystalline solid (58 mg, 85%).

Melting point 199-200°C; \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d₆}): \( \delta = 7.38 – 7.32 \) (m, 2 H) \( 7.28 \) (t, \( J = 7.8 \) Hz, 1 H), \( 6.99 \) (ddd, \( J = 8.2, 2.6, 1.1 \) Hz, 1 H) ppm; \textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d₆}): \( \delta = 167.8, 157.9, 132.6, 130.1, 120.5, 120.4, 116.3 \) ppm; HRMS: m/z calculated for C₇H₆O₃ \([\text{M – H}]\) 137.0233, found 137.0233.
4,4’-(Propane-2,2-diyl)diphenol 32 (Table 2, entry 10)

![Chemical structure](image)

Compound 32 was prepared according to the general procedure from Tetrabromobisphenol A 11 (272 mg, 0.5 mmol) and sodium sulfite (1.01 g, 8.0 mmol, 16.0 equivalents) in a two-fold amount of water (5 mL). The reaction mixture was irradiated with the microwave reactor at 130 °C for 12 hours. Extraction to EtOAc (3x5 mL), washing with 10% aqueous solution of Na$_2$CO$_3$, drying over anhydrous MgSO$_4$, and evaporation under reduced pressure yielded compound 32 as a white amorphous solid (91 mg, 80%).

Melting point 155-157 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 9.13$ (s, 2 H), 6.99 – 6.95 (m, 4 H), 6.65 – 6.62 (m, 4 H), 1.52 (s, 6 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 154.9$, 141.1, 127.3, 114.5, 40.9, 30.9 ppm; HRMS: m/z calculated for C$_{15}$H$_{16}$O$_2$ [M – H] 227.1067, found 227.1065.

Naphtalen-1-ol 37 (Table 2, entry 15)

![Chemical structure](image)

Compound 37 was prepared according to the general procedure from 4-bromonaphthalen-1-ol 16 (112 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 30 minutes. Extraction to EtOAc (2x5 mL), drying over anhydrous MgSO$_4$, and evaporation under reduced pressure provided a crude product. The purification by a column chromatography (silica gel, hexane - ethyl acetate 20:1) yielded compound 37 as a white crystalline solid (43 mg, 60%).

Melting point 92-93°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.20 – 8.16$ (m, 1 H), 7.84 – 7.80 (m, 1 H), 7.53 – 7.47 (m, 2 H), 7.45 (d, $J = 8.2$ Hz, 1 H), 7.32 (dd, $J = 8.2$, 7.5 Hz, 1 H), 6.82 (d, $J = 7.5$, 1 H), 5.21 (brs, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 151.4$, 134.9, 127.8, 126.58, 126.0, 125.4, 124.4, 121.6, 120.9, 108.8 ppm; HRMS: m/z calculated for C$_{15}$H$_{16}$O$_2$ [M – H] 227.1067, found 227.1065.
2-Amino-3-(4-(4-hydroxyphenoxy)-3,5-diiodophenyl)propanoic acid 38 (Table 2, entry 16)

![Chemical structure of compound 38]

Compound 38 was prepared according to the general procedure from L-thyroxine 17 (78 mg, 0.1 mmol) and sodium sulfite (126 mg, 10.0 mmol, 10.0 equivalents) in water (2 mL). The reaction mixture was irradiated with the microwave reactor at 130°C for 2 hours. Then, the white precipitate was collected and washed with water (3x 2 mL). After drying under high vacuum, compound 38 was obtained as a white solid (48 mg, 92%).

Melting point 248-250 °C; $^1$H NMR (400 MHz, D$_2$O, NaOH): 7.60 (s, 2 H), 6.45 – 6.41 (m, 2 H), 6.38 – 6.34 (m, 2 H), 3.28 (dd, $J$ = 7.5, 5.5 Hz, 1 H), 2.74 (dd, $J$ = 13.6, 5.5 Hz, 1 H), 2.55 (dd, $J$ = 13.6, 7.5 Hz, 1 H) ppm; $^{13}$C NMR (100 MHz, D$_2$O-H$_2$O 1:6, NaOH): $\delta$ = 181.6, 161.1, 152.5, 146.0, 140.9, 139.4, 118.8, 116.5, 91.0, 57.4, 39.4 ppm; HRMS: m/z calculated for C$_{15}$H$_{13}$I$_2$NO$_4$ [M + H]$^+$ 525.9007, found 525.9008.

3-Aminophenol 39 (Table 2, entry 17)

![Chemical structure of compound 39]

Compound 39 was prepared according to the general procedure from 3-amino-4-bromophenol 18 (96 mg, 0.5 mmol) and sodium sulfite (630 mg, 5.0 mmol, 10.0 equivalents). The reaction mixture was heated on an oil bath at 60 °C for 18 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO$_4$, and evaporation under reduced pressure yielded compound 39 as a white crystalline solid (52 mg, 96 %).

Melting point 118-120°C; $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ = 8.80 (s, 1 H), 6.77 (t, $J$ = 8.2 Hz, 1 H), 6.04 – 5.95 (m, 2 H), 5.95 – 5.84 (m, 1 H), 4.85 (s, 2 H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$): $\delta$ = 158.1, 149.9, 129.5, 105.4, 103.3, 101.0 ppm; HRMS: m/z calculated for C$_6$H$_7$NO [M – H]$^-$ 108.0444, found 108.0441.
3-Aminophenol 39 (Table 2, entry 18)

\[
\begin{align*}
\text{OH} & \quad \text{Br} & \quad \text{Na}_2\text{SO}_3 & \quad \text{H}_2\text{O} & \quad 60 \, ^\circ\text{C} & \quad 18\text{h} & \quad \text{OH} & \quad \text{NH}_2
\end{align*}
\]

Compound 39 was prepared according to the general procedure from 3-amino-2-bromophenol 19 (96 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was heated on an oil bath at 60 °C for 18 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO\(_4\), and evaporation under reduced pressure yielded compound 39 as a white crystalline solid (50 mg, 91 %).

Analytical data were in accordance with compound 39 obtained from 3-amino-4-bromophenol 18.

Resorcinol 40 (Table 2, entry 19)

\[
\begin{align*}
\text{OH} & \quad \text{Br} & \quad \text{Na}_2\text{SO}_3 & \quad \text{H}_2\text{O} & \quad \text{rt} & \quad 18\text{h} & \quad \text{OH} & \quad \text{OH}
\end{align*}
\]

Compound 40 was prepared according to the general procedure from 4-bromoresorcinol 20 (95 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was mixed for 18 hours at ambient temperature. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO\(_4\), and evaporation under reduced pressure yielded compound 40 as a pale brown crystalline solid (53 mg, 96%).

Melting point 101-103 °C; \(^1\text{H}\) NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 9.14\) (s, 2 H), 6.93 – 6.89 (m, 1 H), 6.21 – 6.17 (m, 3 H) ppm; \(^{13}\text{C}\) NMR (100 MHz, DMSO-\(d_6\)): \(\delta = 159.0, 130.2, 106.7, 103.0\) ppm; HRMS: m/z calculated for C\(_6\)H\(_6\)O\(_2\) [M – H] 109.0284, found 109.0282.

Mixture of sulfonic acids 41 and 42 (Table 2, entry 20)

\[
\begin{align*}
\text{OH} & \quad \text{Cl} & \quad \text{Na}_2\text{SO}_3 & \quad \text{H}_2\text{O} & \quad 150\text{W, }130\, ^\circ\text{C} & \quad 1\text{h} & \quad \text{OH} & \quad \text{SO}_3\text{H} & \quad \text{HO}_3\text{S} & \quad \text{HO}_3\text{S} & \quad \text{OH}
\end{align*}
\]

89 : 11
The mixture of sulfonic acids 41 and 42 was prepared according to the general procedure from 4-chlororesorcinol 21 (72 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 1 hour. Then, the solution was acidified with concentrated hydrochloric acid to pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compounds 41/42 (89:11) as a pale pink amorphous solid (76 mg, 73%).

The ratio of 41/42 was determined by \(^1\)H NMR (the copy of the \(^1\)H spectrum is provided in section 5).

**Mixture of sulfonic acids 41 and 42 (Table 2, entry 21)**

![Mixture of sulfonic acids 41 and 42](image)

The mixture of sulfonic acids 41 and 42 was prepared according to the general procedure from 4-chlororesorcinol 21 (72 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was stirred at ambient temperature for 90 days. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compounds 41/42 (59:41) as a pale pink amorphous solid (85 mg, 82%).

The ratio of 41/42 was determined by \(^1\)H NMR (the copy of the \(^1\)H spectrum is provided in section 5).

**2,4-Dihydroxybenzenesulfonic acid 41 (Table 2, entry 22)**

![2,4-Dihydroxybenzenesulfonic acid 41](image)

Compound 41 was prepared according to the general procedure from 4-fluororesorcinol 22 (64 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was mixed at ambient temperature for 14 days. Then, the solution was acidified with concentrated hydrochloric acid pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by a filtration and washed with acetone (2 mL). The
filtrate was concentrated under reduced pressure to yield compound 41 as a white crystalline solid (86 mg, 83%).

Melting point 308-310°C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 7.17$ (d, $J = 8.4$ Hz, 1 H), 6.15 (dd, $J = 8.4$, 2.3 Hz, 1 H), 6.06 (d, $J = 2.3$ Hz, 1 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 159.6, 154.7, 128.2, 122.4, 106.3, 102.2$ ppm; HRMS: m/z calculated for C$_6$H$_6$O$_5$S [M – H] 188.9852, found 188.9855.

Mixture of sulfonic acids 41 and 42 (Table 2, entry 23)

The mixture of sulfonic acids 41 and 42 was prepared according to the general procedure from 4-fluoresorcinol 22 (64 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 6 hours. Then, the solution was acidified with concentrated hydrochloric acid pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compounds 41/42 (11:89) as a pale yellow amorphous solid (95 mg, 91%).

The ratio of 41/42 was determined by $^1$H NMR (the copy of the $^1$H spectrum is provided in section 5).

3,5-Dihydroxybenzenesulfonic acid 42 (Table 2, entry 24)

Compound 42 was prepared according to the general procedure from 5-bromoresorcinol 23 (64 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 6 hours. Then, the solution was acidified with concentrated hydrochloric acid pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compound 42 as a pale yellow crystalline solid (69 mg, 66%).
Melting point 286-288°C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 9.26$ (s, 2 H), 6.52 (d, $J = 2.2$ Hz, 2 H), 6.15 (t, $J = 2.2$ Hz, 1 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 157.6, 149.6, 104.1, 102.7$ ppm; HRMS: m/z calculated for C$_6$H$_6$O$_5$S [M-H] - 268.9431, found 268.9429.

2,5-Dihydroxybenzene-1,4-disulfonic acid 43 (Table 2, entry 25)

Compound 43 was prepared according to the general procedure from 2,5-dibromobenzene-1,4-diol 24 (134 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 30 minutes. Then, the mixture was acidified with concentrated hydrochloric acid to pH ≈ 1 and stirred at room temperature overnight. The precipitate was filtered off and washed with water (1 mL) to yield compound 43 as a white crystalline solid (118 mg, 77%).

Melting point >360 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 9.77$ (s, 2 H), 6.81 (s, 2 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 145.15, 132.88, 114.01$ ppm; HRMS: m/z calculated for C$_6$H$_6$O$_8$S$_2$ [M – H]- 268.9431, found 268.9429.

Quercetin 44 (Table 2, entry 26)

Compound 44 was prepared according to the general procedure from brominated Quercetin 25(ref. 1) (114 mg, 0.25 mmol) and sodium sulfite (315 mg, 2.5 mmol, 10.0 equivalents) in water (5 mL). The reaction mixture was vigorously stirred on an oil bath at 60 °C for 18 hours. Then the mixture was cooled in ice water bath and acidified with concentrated hydrochloric acid to pH = 1. The precipitated solid was collected by filtration, washed with water (2x2 mL), and dried under reduced pressure to yield Quercetin 44 as a yellow crystalline solid (66 mg, 87%).

Melting point 314-316 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.49$ (s, 1 H), 10.77 (brs, 1 H), 9.51 (brs, 1 H), 7.68 (d, $J = 2.3$ Hz, 1 H), 7.54 (dd, $J = 8.5, 2.3$ Hz, 1 H), 6.88 (d, $J = 8.5$ Hz, 1
H), 6.40 (d, J = 2.0 Hz, 1 H), 6.18 (d, J = 2.0 Hz, 1 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 175.9$, 163.9, 160.7, 156.2, 147.7, 146.8, 145.1, 135.8, 122.0, 120.0, 115.6, 115.1, 103.0, 98.2, 93.4 ppm; HRMS: m/z calculated for C$_{15}$H$_{10}$O$_7$ [M – H] $^-$ 301.0354, found 301.0356.

**Resveratrol 45 (Table 2, entry 27)**

![Resveratrol 45](image)

Compound 45 was prepared according to the general procedure from brominated Resveratrol 26$^{[ref. 2]}$ (116 mg, 0.25 mmol) and sodium sulfite (473 mg, 3.75 mmol, 15.0 equivalents) in water (5 mL). The reaction mixture was vigorously stirred on an oil bath at 60 °C for 6 hours. Then the mixture was cooled on an ice water bath and acidified with concentrated hydrochloric acid to pH $\approx$ 1. The precipitated solid was collected by filtration, washed with water (2x2 mL), and dried under reduced pressure to yield Resveratrol 45 as a white crystalline solid (51 mg, 90%).

Melting point 255-256 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 9.54$ (s, 1 H), 9.19 (s, 1 H), 7.39 (d, J = 8.4 Hz, 2 H), 6.93 (d, J = 16.1 Hz, 1 H), 6.81 (d, J = 16.1 Hz, 1 H), 6.75 (d, J = 8.4 Hz, 2 H), 6.38 (d, J = 2.0 Hz, 2 H), 6.11 (t, J = 2.0 Hz, 1 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 158.5$, 157.2, 139.3, 128.1, 127.9, 125.7, 115.5, 104.3, 101.8 ppm; HRMS: m/z calculated for C$_{14}$H$_{12}$O$_3$ [M – H] $^-$ 227.0703, found 227.0706.

**1H-Pyrazole 60 (Table 3, entry 1)**

![1H-Pyrazole 60](image)

Compound 60 was prepared according to the general procedure from 4-bromo-$^1$H-pyrazole 46 (73 mg, 0.5 mmol) and sodium sulfite (504 mg, 4.0 mmol, 8.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 5 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO$_4$, and evaporation under reduced pressure yielded compound 60 as a white crystalline solid (31 mg, 91%).

Melting point 67-69 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.02$ (s, 1 H), 7.64 (d, J = 2.1 Hz, 2 H), 6.36 (t, J = 2.1 Hz, 1 H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 133.7$, 104.9 ppm; HRMS: m/z calculated for C$_3$H$_4$N$_2$ [M + H]$^+$ 69.0453, found 69.0452.
1H-Pyrazole 60 (Table 3, entry 2)

\[
\text{N} \text{H} \quad \text{I} \quad \text{Na}_2\text{SO}_3 \\ \text{H}_2\text{O} \\ 150 \text{ W, 130 °C} \\ 1\text{h} \\
\text{N} \text{H}
\]

Compound 60 was prepared according to the general procedure from 4-iodo-1H-pyrazole 47 (97 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 60 as a white crystalline solid (32 mg, 94%).

Analytical data are in accordance with the compound 60 obtained from 4-bromo-1H-pyrazole 46.

3,5-Dimethyl-1H-pyrazole 61 (Table 3, entry 3)

\[
\text{N} \text{H} \quad \text{Br} \quad \text{Na}_2\text{SO}_3 \\ \text{H}_2\text{O} \\ 150 \text{ W, 130 °C} \\ 1\text{h} \\
\text{N} \text{H}
\]

Compound 61 was prepared according to the general procedure from 4-bromo-3,5-Dimethyl-1H-pyrazole 48 (88 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 61 as a white crystalline solid (43 mg, 90%).

Melting point 102-103 °C; 1H NMR (400 MHz, CDCl₃): δ = 11.20 (s, 1 H), 5.82 (s, 1 H), 2.28 (s, 6 H) ppm; 13C NMR (100 MHz, CDCl₃): δ = 144.3, 104.0, 12.2 ppm; HRMS: m/z calculated for C₅H₈N₂ [M + H]+ 97.0760, found 97.0760.

3,5-Dimethyl-1H-pyrazole 61 (Table 3, entry 4)

\[
\text{N} \text{H} \quad \text{I} \quad \text{Na}_2\text{SO}_3 \\ \text{H}_2\text{O} \\ 150 \text{ W, 100 °C} \\ 4\text{h} \\
\text{N} \text{H}
\]

Compound 61 was prepared according to the general procedure from 4-iodo-3,5-dimethyl-1H-pyrazole 49 (111 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction
mixture was irradiated with the microwave reactor at 100 °C for 4 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound 61 as a white crystalline solid (44 mg, 92%).

Analytical data are in accordance with compound 61 obtained from 4-bromo-3,5-dimethyl-1H-pyrazole 48.

1H-Imidazole 63 (Table 3, entry 6)

\[
\begin{align*}
\text{Br} & \quad \text{Na}_2\text{SO}_3 \\
\text{N} & \quad \text{H}_2\text{O} \\
150 \text{ W, 130 °C} & \quad 5 \text{h} \\
\text{H} & \quad \text{N}
\end{align*}
\]

Compound 63 was prepared according to the general procedure from 4-bromo-1H-imidazole 51 (73 mg, 0.5 mmol) and sodium sulfite (504 mg, 4.0 mmol, 8.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 5 hours. The product was not extracted due to its high water solubility. The yield was determined by a quantitative ¹H NMR using dimethyl sulfone as an internal standard. Compound 63 was obtained in the 84% NMR yield together with the two minor impurities.

1H-Imidazole 63 (Table 3, entry 7)

\[
\begin{align*}
\text{Br} & \quad \text{Na}_2\text{SO}_3 \\
\text{N} & \quad \text{H}_2\text{O} \\
150 \text{ W, 100 °C} & \quad 1 \text{h} \\
\text{H} & \quad \text{N}
\end{align*}
\]

Compound 63 was prepared according to the general procedure from 2-bromo-1H-imidazole 52 (73 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 1 hour. The product was not extracted due to its high water solubility. The yield was determined by a quantitative ¹H NMR using dimethyl sulfone as an internal standard. Compound 63 was obtained in the 97% NMR yield.

4-Bromo-1H-imidazole 51 (Table 3, entry 8)

\[
\begin{align*}
\text{Br} & \quad \text{Na}_2\text{SO}_3 \\
\text{N} & \quad \text{H}_2\text{O} \\
150 \text{ W, 100 °C} & \quad 1 \text{h} \\
\text{Br} & \quad \text{H}
\end{align*}
\]

Compound 51 was prepared from 2,4-dibromo-1H-imidazole 53 (113 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave
reactor at 100 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound **51** as a white amorphous solid (52 mg, 71%).

Melting point 130 – 132 °C; ¹H NMR (400 MHz, DMSO-d₆): δ = 12.42 (brs, 1 H), 7.63 (d, J = 1.2 Hz, 1 H), 7.25 (d, J = 1.2 Hz, 1 H) ppm; ¹³C NMR (100 MHz, DMSO-d₆): δ = 135.9, 115.7, 113.5 ppm; HRMS: m/z calculated for C₃H₃BrN₂ [M – H] - 144.9396 and 146.9375, found 144.9392 and 146.9370.

1H-Benzimidazole 64 (Table 3, entry 9)

![Chemical structure of 1H-Benzimidazole 64](image)

Compound **64** was prepared according to the general procedure from 2-bromo-1H-benzimidazole **54** (99 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 3 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO₄, and evaporation under reduced pressure yielded compound **64** as a white crystalline solid (54 mg, 92%).

Melting point 169-170 °C; ¹H NMR (400 MHz, DMSO-d₆): δ = 12.42 (s, 1 H), 8.20 (s, 1 H), 7.56 – 7.57 (m, 2 H), 7.20 – 7.16 (m, 2 H) ppm; ¹³C NMR (100 MHz, DMSO-d₆): δ = 142.0, 138.1, 121.7, 115.3 ppm; HRMS: m/z calculated for C₇H₆N₂ [M – H] - 117.0447, found 117.0445.

1H-Benzimidazole-2-sulfonic acid 65 (Table 3, entry 10)

![Chemical structure of 1H-Benzimidazole-2-sulfonic acid 65](image)

Compound **65** was prepared according to the general procedure from 2-chloro-1H-benzimidazole **55** (76 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Then, the solution was acidified with concentrated hydrochloric acid to pH ≈ 1. The resulting white suspension was stirred at ambient temperature for 4h. After that, the white precipitate was collected by filtration, washed with water (1 mL), and dried under stream of nitrogen for 4h to yield compound **65** as a white crystalline solid (93 mg, 94%).
Melting point > 360 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.75 – 7.70 (m, 2 H), 7.60 – 7.56 (m, 2 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 152.8, 130.6, 126.6, 114.7 ppm; HRMS: m/z calculated for C$_7$H$_6$N$_2$O$_3$S [M – H]: 197.0015, found 197.0012.

1-Methyl-1H-benzo[d]imidazole 66 (Table 3, entry 11)

Compound 66 was prepared according to the general procedure from 2-bromo-1-methyl-1H-benzo[d]imidazole 56 (105 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 3 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO$_4$, and evaporation under reduced pressure yielded compound 64 as a colorless amorphous solid (45 mg, 68%).

Melting point 60-62 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.94 (s, 1 H), 7.83 – 7.80 (m, 1 H), 7.43 – 7.39 (m, 1 H), 7.36 – 7.28 (m, 2 H), 3.86 (s, 3 H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 143.7, 143.6, 134.6, 123.0, 122.2, 120.3, 109.4, 31.1 ppm; HRMS: m/z calculated for C$_8$H$_8$N$_2$ 133.0760, found 133.0761.

1-Methyl-1H-benzo[d]imidazole-2-sulfonic acid 67 (Table 3, entry 12)

Compound 67 was prepared according to the general procedure from 2-chloro-1-methyl-1H-benzo[d]imidazole 57 (83 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Then the mixture was diluted with 10% aqueous Na$_2$CO$_3$ (10 mL) and washed with EtOAc (3x5 mL). The aqueous layer was acidified with concentrated hydrochloric acid to pH ≈ 1. The precipitated solid was collected by filtration, washed with water (3x2 mL), and dried under stream of nitrogen to yield compound 67 as a white amorphous solid (65 mg, 61%).

Melting point 328 – 330 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.99 – 7.96 (m, 1 H), 7.75 – 7.72 (m, 1 H), 7.68 – 7.60 (m, 2 H), 4.18 (s, 3 H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 151.6, 132.7, 129.0, 127.1, 126.7, 114.9, 113.6, 32.2 ppm; HRMS: m/z calculated for C$_8$H$_8$N$_2$O$_3$S [M – H]: 213.0328, found 213.0329.
2-Methyl-1H-indole 68 (Table 3, entry 13)

\[
\begin{array}{c}
\text{Br} \\
\text{Me} \\
\text{H}
\end{array}
\xrightarrow{\text{Na}_2\text{SO}_3, \text{H}_2\text{O}}
\begin{array}{c}
\text{Me} \\
\text{H}
\end{array}
\]

150 W, 130 °C 1h

Compound 68 was prepared according to the general procedure from 3-bromo-2-methyl-1H-indole 58 (104 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous MgSO\(_4\), and evaporation under reduced pressure yielded compound 68 as a colorless amorphous solid (60 mg, 92%).

Melting point 56-58 °C; \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 10.86 \text{ (s, 1 H)}, 7.37 \text{ (d, } J = 7.7 \text{ Hz, 1 H)}, 7.25 \text{ (dd, } J = 7.7, 1.1 \text{ Hz, 1 H}), 6.96 \text{ (ddd, } J = 7.7, 7.3, 1.1 \text{ Hz, 1 H}), 6.90 \text{ (ddd, } J = 7.7, 7.3, 1.1 \text{ Hz, 1 H}), 6.10 - 6.08 \text{ (m, 1 H)}, 2.37 \text{ (d, } J = 0.9 \text{ Hz, 3 H) ppm; } \text{^{13}C NMR (100 MHz, DMSO-\(d_6\))}: \delta = 136.1, 135.5, 128.7, 119.9, 118.9, 118.6, 110.5, 99.0, 13.4 \text{ ppm; } \text{HRMS: m/z calculated for C}_{9}H_{9}N [M + H]^+ 132.0808, found 132.0809.

6-Methylpyrimidine-2,4(1H,3H)-dione 69 (Table 3, entry 14)

\[
\begin{array}{c}
\text{Br} \\
\text{Me} \\
\text{H}
\end{array}
\xrightarrow{\text{Na}_2\text{SO}_3, \text{H}_2\text{O}}
\begin{array}{c}
\text{Me} \\
\text{H}
\end{array}
\]

150W, 100°C 30 min

Compound 69 was prepared according to the general procedure from 5-bromo-6-methylpyrimidine-2,4(1H,3H)-dione 59 (102 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100°C for 30 minutes. After cooling on an ice bath, the white solid was collected by filtration and washed with water (1 mL) to yield compound 69 as a white crystalline solid (50 mg, 80%).

Melting point 272-274 °C (decomp.); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 10.82 \text{ (s, 2 H)}, 5.31 \text{ (s, 1 H)}, 2.00 \text{ (s, 3 H) ppm; } \text{^{13}C NMR (101 MHz, DMSO-\(d_6\))}: \delta = 164.11, 152.88, 151.57, 98.72, 18.22 \text{ ppm; } \text{HRMS: m/z calculated for C}_{5}H_{6}N_{2}O_{2} [M – H]^- 125.0346, found 125.0343.
6. One-pot chlorination/debromination:

2,6-Dichlorophenol 71

A 10 mL microwave reaction vessel equipped with a magnetic stir bar was charged with 4-bromophenol (87 mg, 0.5 mmol), sodium carbonate (106 mg, 1.0 mmol, 2.0 eq.), and water (2.5 mL). The mixture was vigorously stirred until both reagents dissolved, forming a pale red (or pink) solution. The reaction mixture was cooled to 0 °C using an ice-water bath and freshly crystalized N-chlorosuccinimide (168 mg, 1.25 mmol, 2.5 equiv.) was added in several portions. The reaction mixture was vigorously stirred at 0 °C for 90 minutes. After that time, anhydrous sodium sulfite (630 mg, 5.0 mmol, 10.0 equivalents) was added and the vessel was removed from the ice-water bath, flushed with argon, sealed with disposable silicon cap, and inserted into the CEM Discover SP microwave synthesizer. The content of the flask was premixed at high stirring speed for one minute, and then irradiated at the maximum power of 150 W with simultaneous cooling (compressed air, 24 psi). The power input was automatically adjusted in order to hold the reaction temperature at 130 °C for 4h. After that time, the HPLC showed complete consumption of intermediate 4-bromo-2,6-dichlorophenol 70. Finally, the reaction mixture was extracted with EtOAC (3x5 mL), dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to yield 2,6-dichlorophenol 71 as a colorless oil, which formed colorless needles upon standing (63 mg, 77% over two steps).

Melting point 63-65 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.26 (d, J = 8.2 Hz, 2 H), 6.82 (t, J = 8.2 Hz, 1 H), 5.85 (s, 1 H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ = 148.0, 128.4, 121.3, 121.2 ppm; HRMS: m/z calculated for C₆H₄Cl₂O [M – H]⁻ 160.9555 and 162.9526, found 160.9555 and 162.9527.
Compound 2

\[ \text{Na}_2\text{SO}_3 \rightarrow \text{H}_2\text{O} \]

\[ \text{153W, 130°C, 3 h} \]

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S23
Compound 2

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Compound 27

\[
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\text{OH} \\
\downarrow \\
\text{Br} \quad \text{Me} \\
\text{Na}_2\text{SO}_3 \quad \text{H}_2\text{O} \\
150\text{W, } 130^\circ\text{C} \\
2 \text{ h}
\end{array}
\]

\[
\begin{array}{c}
\text{OH} \\
\downarrow \\
\text{H} \quad \text{Me}
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**Chemical Reaction:**

\[
\text{H}_2\text{O} \quad 150\text{W}, 130\text{°C} \quad 2\text{ h}
\]

**NMR Spectrum:**

- **f1 (ppm):**
  - 80
  - 70
  - 60
  - 50
  - 40
  - 30
  - 20
  - 10
  - 0
Compound 28

\[
\text{OH} \quad \text{Me} \quad \text{Br} \quad \text{Me} \quad \text{OH} \\
\begin{array}{c}
\text{Me} \\
\text{Me}
\end{array} \\
\begin{array}{c}
\text{Na}_2\text{SO}_3 \\
\text{H}_2\text{O}
\end{array} \\
\text{150W, 100°C} \\
\text{4 h}
\]

\[
f_1 \text{(ppm)}
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|          | 0.97     |
|          | 2.00     |
|          | 6.48     |
|          | 6.59     |
|          | 7.26     |
Compound 29

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{Br} & \quad \text{H}_2\text{O} \\
\text{Na}_2\text{SO}_3
\end{align*}
\]

150W, 130°C
10 h

\[\begin{array}{c}
\text{f1 (ppm)} \\
2.00 & 1.02 & 0.88 & 6.03
\end{array}\]

\[\begin{array}{c}
\end{array}\]
Compound 29

\[
\begin{align*}
\text{Me} & \quad \text{OH} \\
\text{Me} & \quad \text{Me} \\
\text{Br} & \quad \rightarrow \quad \text{Me} \\
\text{Me} & \quad \text{CH} \\
\text{H} & \quad \\
\end{align*}
\]

\[
\text{Na}_{2}\text{SO}_{3} \quad \text{H}_{2}\text{O} \\
\text{150°C, 130°C} \quad 10 \text{ h}
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</tbody>
</table>

1H NMR spectrum of Compound 29.
Compound 31

\[ \text{Na}_2\text{SO}_3 \rightarrow \text{H}_2\text{O} \]

150W, 130°C

OH

Br

COCH

OH

COOH

\( f_1 \) (ppm)

1.00

1.07

1.90

2.50

6.98

6.98

6.98

6.98

7.00

7.00

7.00

7.00

7.26

7.28

7.30

7.33

7.34

7.36

7.36

7.37

7.38

7.38

7.38
Compound 32
Compound 37

\[
\begin{align*}
\text{Br} & \quad \text{CH} \\
\text{N}_2\text{S}_2\text{O}_3 & \quad \text{H}_2\text{O} \\
150^\circ\text{C}, 130^\circ\text{C} & \quad 0.5\text{ h}
\end{align*}
\]
Compound 37

\[
\begin{align*}
\text{CH} & \quad \xrightarrow{\text{Na}_2\text{SO}_3, \text{H}_2\text{O}} \quad \text{CH} \\
\text{Br} & \quad 150 \text{Y, } 130^\circ \text{C, } 0.5 \text{ h}
\end{align*}
\]
Compound 38

[Chemical structure and spectra diagram]
Compound 38
Compound 39

\[
\begin{align*}
\text{OH} & \quad \text{N}_2\text{CO}_3 \\
\text{Br} & \quad \text{H}_2\text{O}
\end{align*}
\]

150W, 100°C
30 min

\[
\begin{align*}
\text{OH} & \quad \text{NH}_2 \\
\text{H} & \quad \text{NH}_2
\end{align*}
\]
Compound 39

- 158.09
- 149.85
- 129.46
- 105.44
- 103.31
- 100.97

- 40.15
- 39.94
- 39.73
- 39.52
- 39.31
- 38.89

f1 (ppm)
Compound 40

\[
\begin{align*}
\text{Br} & \quad \text{HO} \\
\text{OH} & \quad \text{Na}_2\text{SO}_3 \\
\text{H}_2\text{O} & \quad \text{rt} \\
\text{HO} & \quad 24\text{h} \\
\text{H} & \quad \text{HO}
\end{align*}
\]
Compound 41

\[ \text{OH} \rightarrow \begin{array}{c} \text{Na}_2\text{SO}_3 \\ \text{H}_2\text{O} \\ \text{160 W, 120°C, 1 h} \end{array} \rightarrow \text{OH} + \begin{array}{c} \text{SO}_3\text{H} \\ \text{HO}_2\text{S} \end{array} \]

<table>
<thead>
<tr>
<th>f1 (ppm)</th>
<th>1</th>
<th>1</th>
<th>1</th>
<th>1</th>
<th>1</th>
<th>1</th>
<th>1</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>128.19</td>
<td>122.42</td>
<td>106.30</td>
<td>104.07</td>
<td>102.61</td>
<td>102.16</td>
<td>38.89</td>
<td>39.10</td>
</tr>
</tbody>
</table>

[Diagram of chemical structures and NMR spectrum]
Compound 41 + 42

\[
\begin{align*}
\text{CH} & \quad \text{Na}_2\text{SO}_3 \\
\text{HO} & \quad \text{H}_2\text{O} \\
\text{Cl} & \quad \text{90 days} \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_1 & \quad 7.24 \\
\text{H}_2 & \quad 7.22 \\
\text{H}_3 & \quad 6.53 \\
\text{H}_4 & \quad 6.20 \\
\text{H}_5 & \quad 6.13 \\
\end{align*}
\]
Compound 41

$\text{Na}_2\text{SO}_3$

$\text{H}_2\text{O}$

$t$

14 days

\[
\begin{align*}
\text{OH} & \quad \text{OH} \\
\text{SO}_3\text{H} & \quad \text{SO}_3\text{H}
\end{align*}
\]

$\text{f1 (ppm)}$

$\text{0.97}$

$\text{1.02}$

$\text{1.00}$

$\text{0.95}$

$\text{0.99}$

$\text{2.49}$

$\text{2.50}$

$\text{2.50}$

$\text{2.50}$

$\text{2.51}$

$\text{6.10}$

$\text{6.11}$

$\text{6.18}$

$\text{6.19}$

$\text{6.20}$

$\text{6.21}$

$\text{7.20}$

$\text{7.22}$

$\text{9.50}$

$\text{10.51}$
<table>
<thead>
<tr>
<th>Compound 41 +42</th>
</tr>
</thead>
</table>

![Diagram of Compound 41 +42 with NMR spectrum]
Compound 41 + 42

![Chemical structure diagram]

Na$_2$SO$_4$  
H$_2$O

130°C, 130°C  
6h

<table>
<thead>
<tr>
<th>f1 (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>38.89</td>
</tr>
<tr>
<td>39.10</td>
</tr>
<tr>
<td>39.31</td>
</tr>
<tr>
<td>39.73</td>
</tr>
<tr>
<td>39.94</td>
</tr>
<tr>
<td>40.15</td>
</tr>
<tr>
<td>102.66</td>
</tr>
<tr>
<td>104.08</td>
</tr>
<tr>
<td>149.81</td>
</tr>
<tr>
<td>157.70</td>
</tr>
<tr>
<td>149.81</td>
</tr>
</tbody>
</table>

S50
Compound 42

![Chemical structure](image)

1.01, 2.00, 2.11, 6.10, 6.50, 6.51, 6.51

**Reaction Conditions:**
- $\text{Na}_2\text{SO}_3$
- $\text{H}_2\text{O}$
- 150 W, 130°C
- 5 h

**NMR Spectrum:**
- f1 (ppm)
Compound 43

\[ \text{OH} \quad \text{Na}_2\text{SO}_3 \quad \text{H}_2\text{O} \quad 150^\circ\text{C}, 30\text{ min} \]

\[ \text{OH} \quad \text{SO}_3\text{H} \quad \text{OH} \quad \text{HO}_2\text{S} \quad \text{OH} \]

<table>
<thead>
<tr>
<th>Compound</th>
<th>2.00</th>
<th>2.20</th>
<th>6.81</th>
<th>9.77</th>
<th>3.33</th>
<th>2.50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Graph showing peaks at 11.5, 10.5, 9.5, 9.0, 8.5, 8.0, 7.5, 7.0, 6.5, 6.0, 5.5, 5.0, 4.5, 4.0, 3.5, 3.0, 2.5, 2.0, 1.5, 1.0, 0.5, 0.0, -0.5, -1.0, -1.5.
Compound 43

\[
\begin{align*}
\text{Br} & \\
\text{Br} & \\
\text{H} & \\
\text{H} & \\
\text{Br} & \\
\text{OH} & \\
\end{align*}
\]

\[\text{Na}_2\text{SO}_3 \quad \text{H}_2\text{O} \quad \text{150}^\circ\text{C} \quad \text{30 min}\]

\[
\begin{align*}
\text{CH} & \\
\text{CH} & \\
\text{SO}_3\text{H} & \\
\end{align*}
\]

\[
\begin{align*}
\text{f1 (ppm)} & \\
220 & 210 & 200 & 190 & 180 & 170 & 160 & 150 & 140 & 130 & 120 & 110 & 100 & 90 & 80 & 70 & 60 & 50 & 40 & 30 & 20 & 10 & 0 & -10 & -20
\end{align*}
\]
<table>
<thead>
<tr>
<th>Compound 44</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.03</td>
</tr>
<tr>
<td>0.99</td>
</tr>
<tr>
<td>1.00</td>
</tr>
<tr>
<td>1.00</td>
</tr>
<tr>
<td>1.00</td>
</tr>
<tr>
<td>2.92</td>
</tr>
<tr>
<td>0.89</td>
</tr>
<tr>
<td>1.04</td>
</tr>
</tbody>
</table>

**Reaction:**

\[
\text{Na}_2\text{SO}_3 + \text{H}_2\text{O} \rightarrow 60 \degree \text{C, 23h}
\]

**NMR Spectrum:***

- f1 (ppm): 1.04, 0.89, 2.92, 1.00, 1.00, 1.00, 0.99, 1.03
Compound 44

- 175.85
- 163.91
- 160.74
- 156.15
- 151.67
- 147.72
- 146.81
- 145.07
- 135.75
- 121.96
- 119.98
- 115.62
- 115.07
- 103.02
- 98.19
- 93.36
Compound 45

\[\text{Na}_2\text{SO}_3 \quad \text{H}_2\text{O} \quad 80 ^\circ \text{C}, 6\text{h}\]

1.01 × 2.02 × 1.01 × 1.00 × 1.00 × 1.99 × 0.99 × 7.40 × 7.38 × 6.95 × 6.691 × 6.679 × 6.764 × 6.38 × 6.12 × 6.11 × 3.36 × 2.50 × 2.50

11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Compound 45
Compound 61

- 144.31
- 104.00
- 77.48
- 77.16
- 76.84
- 12.24

C4
C3(C5)
Me
Comp. 63 (crude NMR)

\[
\begin{align*}
\text{Imd} & \xrightarrow{\text{N}_2\text{SO}_3, \text{H}_2\text{O}, 150 \, \text{W}, 130 \, ^\circ\text{C}, 5h} \text{Imd} \\
\text{dimethyl sulfone}
\end{align*}
\]
Comp. 63 (crude NMR)

\( \text{Na}_2\text{SO}_3 \xrightarrow{150 \text{ W}, 100 \text{ °C}} \text{H}_2\text{O} \)

H2 \( \approx 0.84 \) ppm
H4 and H5 \( \approx 1.95 \) ppm
H2 \( \approx 7.66 \) ppm
DMSO \( \approx 2.50 \) ppm

water

dimethyl sulfone

H4 and H5
Compound 51

\[
\begin{align*}
\text{Br} & \quad \text{N} & \quad \text{N} & \quad \text{Br} \\
\text{Br} & \quad \text{H} & \quad \text{N} & \quad \text{H} \\
\end{align*}
\]

\[\begin{array}{c}
\text{Na}_2\text{SO}_3 \\
\text{H}_2\text{O} \\
150 \text{ W, 100 °C} \\
1 \text{h}
\end{array}\]

- 39.10
- 39.31
- 39.52
- 39.73
- 39.94
- 113.52
- 115.68
- 135.92
Compound 64

\[ \text{Compound 64} \]

\[ \text{Na}_2\text{SO}_3 \text{H}_2\text{O} \quad 150 \text{ W}, 100 \text{ °C} \quad 0.5 \text{h} \]

DMSO

water

H2

H4, H7

7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7

H2

0.91

12.42

0.50

1.00

2.00

2.11

3.33
Compound 64

C2 141.97
C3a(7a) 138.10
C4(7) 115.33

DMSO 39.10 39.31 39.52 39.73 39.94

S68
Compound 65

\[ \text{Compound 65} \]

\[ \begin{array}{c}
\text{Cl} & \xrightarrow{\text{Na}_2\text{SO}_3, \text{H}_2\text{O}} & \text{SO}_\text{H}
\end{array} \]

160 W, 130 °C
1 h

$\text{H}_4, \text{H}_7$

$\text{H}_5, \text{H}_6$

DSMO
Compound 66

- 143.69
- 143.58
- 122.99
- 122.15
- 109.42
- 77.48
- 77.16
- 76.84
- 31.06
Compound 67

\[
\text{Cl} \quad \xrightarrow{\text{Na}_2\text{SO}_3, \text{H}_2\text{O}} \quad \text{SO}_3\text{H} \\
160 \, \text{W}, 130 \, ^\circ \text{C} \quad 1 \, \text{h}
\]
Compound 67

- 151.56
- 132.65
- 128.95
- 127.07
- 114.85
- 113.64
- 32.19
Compound 68

\[
\text{Experimental Procedure:}\ 
\text{\textit{Na}_2\text{SO}_3, H_2O, 150 W, 130 °C, 1h}}
\]
Compound 69

$$\text{Br} \quad \text{NH} \quad \text{Me}$$

$$\text{Na}_{2}\text{SO}_{3}$$

$$\text{H}_{2}\text{O}$$

150$^\circ$C, 30 min

$$\text{Me} \quad \text{NH}$$
Compound 69

\[
\begin{array}{c}
\text{Br} \quad \text{O} \\
\text{Me} \quad \text{N} \\
\text{H} \quad \text{O} \\
\end{array}
\]

150V, 100°C, 30 min

\[
\begin{array}{c}
\text{H} \quad \text{O} \\
\text{Me} \quad \text{N} \\
\end{array}
\]

f1 (ppm)

98.72
152.88
153.57
164.11
40.15
39.94
39.73
39.52
39.31
39.10
38.89
38.22
8. References
