4029 Synthesis of dodecyl phenyl ether from bromododecane and phenol

\[
\begin{align*}
\text{C}_{12}\text{H}_{25}\text{Br} & \quad \text{(249.2)} \\
\text{Br} & \\
\text{NaOH} & \quad \text{(40.0)} \\
\text{Adogen 464} & \quad \text{C}_{25}\text{H}_{54}\text{ClN} & \quad \text{(404.2)} \\
\text{C}_{18}\text{H}_{30}\text{O} & \quad \text{(262.4)} \\
\text{C}_{6}\text{H}_{6}\text{O} & \quad \text{(94.1)} \\
\end{align*}
\]

\[
\begin{align*}
\text{C}_{18}\text{H}_{30}\text{O} & \quad \text{(262.4)} \\
\text{C}_{6}\text{H}_{6}\text{O} & \quad \text{(94.1)} \\
\end{align*}
\]

Classification

Reaction types and substance classes
Williamson's ether synthesis, nucleophilic substitution, phase transfer catalysis
bromoalkane, phenol, ether

Work methods
heating under reflux, stirring with magnetic stir bar, extracting, shaking out, filtering,
evaporating with rotary evaporator, distilling under reduced pressure, column distillation,
heating with oil bath

Instruction (batch scale 10 mmol)

Equipment
10 mL two-neck flask or 10 mL round bottom flask with Claisen adapter, reflux condenser,
separating funnel, Kugelrohr distillation apparatus or micro distillation apparatus, heatable
magnetic stirrer, magnetic stir bar, rotary evaporator, vacuum pump, oil bath

Substances
bromododecane (bp 139 °C/13 hPa; product from NOP 4028) 2.49 g (2.39 mL, 10.0 mmol)
sodium hydroxide 0.480 g (12.0 mmol)
phenol (mp 41 °C, bp 182 °C) 1.13 g (12.0 mmol)
methyltrioctylammonium chloride (Adogen 464 or Aliquat 336) 0.05 g (0.1 mmol)
water 2.5 mL (139 mmol)
tert-butyl methyl ether (bp 55 °C)  40 mL  
aqueous sodium hydroxide solution (2 M)  10 mL  
sodium sulfate for drying  about 1 g  

**Reaction**

0.480 g (12.0 mmol) sodium hydroxide, 1.13 g (2.39 mL, 12.0 mmol) phenol, 2.49 g (10 mmol) bromododecane and 0.05 g Adogen 464 in 2.5 mL water are filled in a 10 mL two-neck round bottom flask with magnetic stir bar and reflux condenser and are heated under strong stirring for 6 hours in an oil bath to 115°C, until the bromododecane has completely reacted. The course of the reaction is followed by means of thin layer or gas chromatography (see analytics).

**Work up**

After cooling down, the reaction mixture is shaken out with 10 mL tert-butyl methyl ether. The aqueous phase is again shaken out three times with 10 mL tert-butyl methyl ether each, then the combined organic phases are washed with 10 mL 2 M sodium hydroxide solution and then with 10 mL water. The organic phase is dried over Na₂SO₄. After the drying agent is filtered off, the solvent is evaporated at a rotary evaporator. Crude yield: 2.49 g

The crude product is distilled in a Kugelrohr distillation apparatus at 5.5·10⁻² hPa and 152 °C. Yield: 2.28 g (8.69 mmol, 87%); colourless liquid, which solidifies after standing for some time.

**Waste management**

**Recycling**
The evaporated tert-butyl methyl ether is collected and redistilled.

**Waste disposal**

<table>
<thead>
<tr>
<th>Waste</th>
<th>Disposal</th>
</tr>
</thead>
<tbody>
<tr>
<td>aqueous phase</td>
<td>solvent water mixtures, containing halogen</td>
</tr>
<tr>
<td>distillation residue</td>
<td>dissolve in a small amount of acetone, then:</td>
</tr>
<tr>
<td></td>
<td>organic solvents, containing halogen</td>
</tr>
<tr>
<td>sodium sulfate</td>
<td>solid waste, free from mercury</td>
</tr>
</tbody>
</table>

**Time**

Reaction 4.5 hours  
Distillation 2-3 hours

**Break**

After heating under reflux  
After shaking out  
Before distillation

**Degree of difficulty**

Medium
Instruction (batch scale 100 mmol)

Equipment
100 mL two- or three-neck flask, reflux condenser, separating funnel, distillation apparatus, 10 cm Vigreux column, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, vacuum pump, oil bath

Substances
bromododecane (bp 139 °C/13 hPa; product from NOP 4028) 24.9 g (23.9 mL, 100 mmol)
sodium hydroxide 4.80 g (120 mmol)
phenol (mp 41 °C, bp 182 °C) 11.3 g (120 mmol)
methyltrioctylammonium chloride (Adogen 464 or Aliquat 336) 0.5 g (1.2 mmol)
water 25 mL (1.4 mol)
tert-butyl methyl ether (bp 55 °C) 100 mL
aqueous sodium hydroxide solution (2 M) 25 mL
sodium sulfate for drying about 5 g

Reaction
4.80 g (120 mmol) sodium hydroxide, 11.3 g (120 mmol) phenol, 24.9 g (23.9 mL, 100 mmol) bromododecane and 0.5 g Adogen 464 in 25 mL water are filled in a 100 mL two- or three-neck flask with magnetic stir bar and reflux condenser and are heated under strong stirring for 6 hours in an oil bath to 115°C, until the bromododecane has completely reacted. The course of the reaction is followed by means of a thin layer or gas chromatography (see analytics).

Work up
After cooling down, the reaction mixture is shaken out with 25 mL tert-butyl methyl ether. The aqueous phase is again shaken out three times with 25 mL tert-butyl methyl ether each, then the combined organic phases are washed with 25 mL 2 M aqueous sodium hydroxide solution and then with 25 mL water. The organic phase is dried over Na₂SO₄. After the drying agent is filtered off, the solvent is evaporated at a rotary evaporator. Crude yield: 24.2 g

The crude product is fractional distilled over a 10 cm Vigreux column. To avoid a solidifying of the distillate in the distillation bridge it is cooled with air instead of water.
Yield: 21.8 g (83.1 mmol, 83%); head temperature 131 °C, colourless liquid, which solidifies after standing for some time.

Waste management

Recycling
The evaporated tert-butyl methyl ether is collected and redistilled.
Waste disposal

<table>
<thead>
<tr>
<th>Waste</th>
<th>Disposal</th>
</tr>
</thead>
<tbody>
<tr>
<td>aqueous phase</td>
<td>solvent water mixtures, containing halogen</td>
</tr>
<tr>
<td>distillation residue</td>
<td>dilute in a small amount of acetone, then: organic solvents, containing halogen</td>
</tr>
<tr>
<td>sodium sulfate</td>
<td>solid waste, free from mercury</td>
</tr>
</tbody>
</table>

Time

Reaction 5 hours
Distillation 2-3 hours

Break

After heating under reflux
After shaking out
Before distillation

Degree of difficulty

Medium

Instruction (batch scale 1 mol)

Equipment

1 L two- or three-neck flask, reflux condenser, separating funnel, distillation bridge, 30 cm Vigreux column with vacuum jacket and reflective coating, "pig type" receiving adapter, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, vacuum pump, oil bath

Substances

bromododecane (bp 139 °C/13 hPa; product from NOP 4028) 249 g (239 mL, 1.00 mol)
sodium hydroxide 48.0 g (1.20 mol)
phenol (mp 41 °C, bp 182 °C) 113 g (1.20 mol)
methyltrioctylammonium chloride (Adogen 464 or Aliquat 336) 5 g (0.012 mol)
water 200 mL (11.1 mol)
tert-butyl methyl ether (bp 55 °C) 1.00 L
aqueous sodium hydroxide solution (2 M) 200 mL
sodium sulfate for drying

Reaction

48.0 g (1.20 mol) sodium hydroxide, 113 g (1.20 mol) phenol, 249 g (239 mL, 1.00 mol) bromododecane and 5 g Adogen 464 in 2.5 mL water are filled in a 1 L two- or three-neck flask with magnetic stir bar and reflux condenser and are heated under strong stirring for 6 hours in an oil bath to 115°C, until the bromododecane has completely reacted. The course of the reaction is followed by means of thin layer or gas chromatography (see analytics).
Work up
After cooling down, the reaction mixture is shaken out with 250 mL tert-butyl methyl ether. The aqueous phase is again shaken out three times with 250 mL tert-butyl methyl ether each, then the combined organic phases are washed with 200 mL 2 N NaOH and then with 200 mL water. The organic phase is dried over Na₂SO₄. After the drying agent is filtered off, the solvent is evaporated. Crude yield: 246 g

The crude product is fractional distilled over a 30 cm Vigreux column. To avoid a solidifying of the distillate, the distillation bridge is cooled with air instead of water.
Yield: 221 g (0.842 mol, 84%); head temperature 145 °C, colourless liquid, which solidifies after standing for some time.

Waste management
Recycling
The evaporated tert-butyl methyl ether is collected and redistilled.

Waste disposal

<table>
<thead>
<tr>
<th>Waste</th>
<th>Disposal</th>
</tr>
</thead>
<tbody>
<tr>
<td>aqueous phase</td>
<td>solvent water mixtures, containing halogen</td>
</tr>
<tr>
<td>distillation residue</td>
<td>dilute in a small amount of acetone, then:</td>
</tr>
<tr>
<td></td>
<td>organic solvents, containing halogen</td>
</tr>
<tr>
<td>sodium sulfate</td>
<td>solid waste, free from mercury</td>
</tr>
</tbody>
</table>

Time
Reaction 12 hours
Distillation 6 hours

Break
After heating under reflux
After shaking out
Before distillation

Degree of difficulty
Medium
Analytics

Reaction monitoring with TLC
Sample preparation:
Using a Pasteur pipette, one drop from the reaction mixture is taken and diluted with 0.5 mL diethyl ether.

TLC-conditions:
adsorbant: TLC-aluminium foil (silica gel 60)
eluent: petroleum ether (60-80 °C)
visualizing agent: The TLC-aluminium foil is dipped in 2 M H₂SO₄ and then dried with a hot-air dryer.

\[ R_f (\text{dodecylphenyl ether}) \ 0.22 \]
\[ R_f (\text{bromododecane}) \ 0.53 \]

Reaction monitoring with GC
Sample preparation:
Using a Pasteur pipette, one drop of the crude or pure product is taken and diluted with 10 mL dichloromethane. 0.2 µL from this solution are injected.

GC-conditions:
column: DB-1, 28 m, internal diameter 0.32 mm, film 0.25 µm
inlet: on-column-injection
carriergas: hydrogen(40 cm/sec)
oven: 90 °C (5 min), 10 °C/min on 240 °C (30 min)
detector: FID, 270 °C

Percent concentration was calculated from peak areas.

<table>
<thead>
<tr>
<th>Retention time (min)</th>
<th>Substance</th>
<th>Peak area %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>crude product</td>
</tr>
<tr>
<td>18.85</td>
<td>product (dodecyl phenyl ether)</td>
<td>94.4</td>
</tr>
<tr>
<td>13.54</td>
<td>educt (bromododecane)</td>
<td>4.4</td>
</tr>
<tr>
<td>Others</td>
<td>unknown impurities</td>
<td>&lt; 0.5 per peak</td>
</tr>
</tbody>
</table>

GC of the crude product (1 mol batch scale)
GC of the pure product (1 mol batch scale)
$^1$H NMR spectrum of the crude product (300 MHz, CDCl$_3$)

![1H NMR spectrum of the crude product](image1)

$^1$H NMR spectrum of the pure product (300 MHz, CDCl$_3$)

![1H NMR spectrum of the pure product](image2)

<table>
<thead>
<tr>
<th>$\delta$ (ppm)</th>
<th>Multiplicity</th>
<th>Number of H</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.88</td>
<td>t</td>
<td>3</td>
<td>12-H</td>
</tr>
<tr>
<td>1.27</td>
<td>m</td>
<td>16</td>
<td>remaining CH$_2$</td>
</tr>
<tr>
<td>1.44</td>
<td>m</td>
<td>2</td>
<td>3-H</td>
</tr>
<tr>
<td>1.75</td>
<td>m</td>
<td>2</td>
<td>2-H</td>
</tr>
<tr>
<td>3.91</td>
<td>t</td>
<td>2</td>
<td>1-H</td>
</tr>
<tr>
<td>6.88</td>
<td>m</td>
<td>3</td>
<td>14-H, 16-H, 18-H</td>
</tr>
<tr>
<td>7.25</td>
<td>dd</td>
<td>2</td>
<td>15-H, 17-H</td>
</tr>
</tbody>
</table>
\[ \delta \text{ (ppm)} \quad \text{Assignment} \]

<table>
<thead>
<tr>
<th>( \delta \text{ (ppm)} )</th>
<th>\text{Assignment}</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.0</td>
<td>C-12</td>
</tr>
<tr>
<td>22.7</td>
<td>C-11</td>
</tr>
<tr>
<td>67.9</td>
<td>C-1</td>
</tr>
<tr>
<td>114.5</td>
<td>C-14, C-18</td>
</tr>
<tr>
<td>120.4</td>
<td>C-16</td>
</tr>
<tr>
<td>129.4</td>
<td>C-15, C-17</td>
</tr>
<tr>
<td>159.2</td>
<td>C-13</td>
</tr>
<tr>
<td>76.5-77.5</td>
<td>solvent</td>
</tr>
</tbody>
</table>
IR spectrum of the pure product (film)

<table>
<thead>
<tr>
<th>cm⁻¹</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>3070, 3041</td>
<td>C-H-valence, arene</td>
</tr>
<tr>
<td>2995</td>
<td>C-H-valence, alkane</td>
</tr>
<tr>
<td>2854</td>
<td>C-H-valence, alkane, ether</td>
</tr>
<tr>
<td>1601, 1587, 1497</td>
<td>C=C-valence, arene</td>
</tr>
</tbody>
</table>