One-pot aromatic bromination–rearrangement catalyzed by GaCl$_3$

Mieko Arisawa, Atsushi Suwa, Masanori Ashikawa, and Masahiko Yamaguchi*

Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba, Sendai 980-8578, Japan
E-mail: yama@mail.pharm.tohoku.ac.jp

This paper is dedicated to Prof. Keiichiro Fukumoto in recognition of his outstanding contributions to organic chemistry

(received 08 Mar 03; accepted 26 May 03; published on the web 29 May 03)

Abstract
Reaction of monoalkylbenzenes with bromine in the presence of a catalytic amount of GaCl$_3$ (5 mol \%) initially gives $o/p$-bromination products, which are converted into mixtures containing considerable amounts of the $m$-brominated products. Notably, the bromination of dimethyl-, trimethyl-, and tetramethylbenzenes gives dibromo- and/or tribromoarenes, which are converted into monobromoarenes.

Keywords: Gallium trichloride, aromatic bromination, isomerization

Introduction
The bromination of aromatic compounds has been conducted using halogenating reagents such as Br$_2$ and HOBr in the presence or absence of catalysts.\(^1\) These methods convert monoalkylbenzenes into $o/p$-brominated products. Since the $m$-derivatives are formed in small amounts, their preparations in general employ multistep processes.\(^2\) A previous report that Al$_2$Cl$_6$–water catalyst promotes the isomerization of bromoarenes\(^3\) led us to study one-pot catalytic procedures for the $o/p$- bromination of monoalkylbenzenes followed by isomerization to give mixtures containing the $m$- derivatives.\(^4\) We now show that GaCl$_3$\(^5,6,7\) catalyzes such bromination of alkylbenzenes. Also, it was found that the bromination of dimethyl-, trimethyl-, and tetramethylbenzenes initially gives dibromo- and/or tribromoarenes, which are converted into monobromoarenes.

Results and Discussion
To a solution of hexylbenzene and GaCl$_3$ (5 mol %) in methycyclohexane was added an equimolar amount of bromine, and the mixture was stirred at room temperature for 12 h giving the bromohexylbenzenes $o$-$1$, $m$-$1$, and $p$-$1$ in 18%, 38%, and 15% yields, respectively (Table 1, entry 3). The structures were determined by comparison with the authentic samples prepared separately (see Experimental Section). Benzyl bromination proceeded in the absence of the catalyst, and $1$ was not detected. The use of FeCl$_3$ (3.6 mol %) exhibited normal orientations, giving $o$-$1$ (20%) and $p$-$1$ (78%). Such aromatic bromination isomerization could also be carried out with AlCl$_3$ (5 mol %), although the reaction was sometimes not reproducible, probably because of the insolubility of AlCl$_3$ in this solvent. The bromination using GaCl$_3$ is rapid, and $o$-$1$ and $p$-$1$ are obtained in 5 min in 23% and 42% yields, respectively, with a very small amount of $m$-$1$ (entry 4). When the mixture is stirred for 12 h at room temperature, $p$-$1$ decreases and $m$-$1$ increases. Bromination of several alkylbenzenes catalyzed by GaCl$_3$ is shown in Table 1. In the case of neopentylbenzene and isobutylbenzene, larger amounts of the $m$-derivatives are obtained, which may be a result of steric reasons (entries 6 and 7). The different $o/p$ ratio of toluene and ethylbenzene may also be explained analogously (entries 1 and 2): a methyl group behaves as a considerably smaller group than an ethyl group in this reaction.

\[
\text{R} \quad \text{Br}_2 + \text{GaCl}_3 (5 \text{ mol%}) \quad \text{methylcyclohexane} \quad \text{r.t., 12 h} \quad \text{R} \quad \text{Br}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield$^a$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$o$-</td>
</tr>
<tr>
<td>1</td>
<td>CH$_3$</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>CH$_3$CH$_2$</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>CH$_3$(CH$_2$)$_2$CH$_2$</td>
<td>18</td>
</tr>
<tr>
<td>4$^a$</td>
<td>CH$_3$(CH$_2$)$_2$CH$_2$</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>CH$_3$(CH$_2$)$_3$CH$_2$</td>
<td>23</td>
</tr>
<tr>
<td>6</td>
<td>(CH$_3$)$_2$CHCH$_2$</td>
<td>21</td>
</tr>
<tr>
<td>7</td>
<td>(CH$_3$)$_3$CCH$_2$</td>
<td>8</td>
</tr>
</tbody>
</table>

$^a$Determined by $^1$H-NMR. $^b$The reaction was conducted for 5 min.

Polymethylbenzenes exhibit interesting behaviors: polybrominated products are initially formed, which are converted into monobromides. Reaction of $m$-xylene for 1 min gives the 4,6-dibrominated 4,6-3 as the major product, and the monobromide 2 predominates after 12 h (Table
2). Such a phenomenon has not been reported before. Bromination of \textit{m}-xylene with AlCl$_3$ under the same conditions for 1 min gives 4-2 predominantly, which is the usual orientation.

Similar tendencies are observed in the bromination of \textit{p}-xylene with GaCl$_3$ (Table 3). The reaction for 5 min gives 2,5-dibrominated 5 predominantly, which is converted into 2-brominated 4 after 12 h. In this case, AlCl$_3$ also shows somewhat related isomerization behaviors, although less prominently than with GaCl$_3$.

\begin{align*}
\text{\textbf{Table 2.} Bromination of \textit{m}-Xylene} \\
\begin{tabular}{llcccccc}
\hline
Catalyst & Time & Position$^b$ & 2 & 4 & 5 & 2,4- & 2,5- & 4,6- \\
\hline
\text{GaCl}_3 & 1 \text{ min} & & 5 & 15 & trace & 24 & trace & 40 \\
 & 12 \text{ h} & & 11 & 30 & 19 & 2 & 11 & 18 \\
\text{AlCl}_3 & 1 \text{ min} & & 9 & 83 & trace & nd$^c$ & nd$^c$ & trace \\
\hline
\end{tabular}
\end{align*}

$^a$Based on bromine, as determined by $^1$H-NMR. $^b$Bromide positions. Numbering based on the starting \textit{m}-xylene. $^c$Not detected by GC–MS.

\begin{align*}
\text{\textbf{Table 3.} Bromination of \textit{p}-Xylene} \\
\begin{tabular}{llccc}
\hline
Catalyst & Time & \textbf{Yield}$^a$ (%) \\
\hline
\text{GaCl}_3 & 5 \text{ min} & 4 & 64 & 8 \\
 & 12 \text{ h} & & 64 & 28 & 6 \\
\text{AlCl}_3 & 5 \text{ min} & 4 & 47 & 46 & 6 \\
 & 12 \text{ h} & & 67 & 29 & 3 \\
\hline
\end{tabular}
\end{align*}

$^a$Based on bromine, as determined by $^1$H-NMR.
Bromination of 1,2,3- and 1,3,5-trimethylbenzene with GaCl₃ initially gives considerable amounts of dibromo- and tribromoarenes, which are converted into monobromoarenes (Table 4). It should be noted that 5-bromo-1,2,3-trimethylbenzene can be prepared in one step from the corresponding hydrocarbon. The previous preparation of this compound employed a multistep process.⁸ Reactions of both 1,2,3,4-tetramethyl- and 1,2,4,5-tetramethylbenzene with GaCl₃ give initially equal amounts of monobromides and dibromides, which are converted into the monobromides after 12 h (Table 4). Thus, the second and/or the third brominations are faster than the first bromination in the reactions catalyzed by GaCl₃. It seems that the bromide group behaves as an activating group in the electrophilic substitution. We propose that the interaction of GaCl₃ with Br₂ as well as the C-H bonds of neighboring methyl groups, promote such polybromination. Previously, we reported aromatic substitution reactions which involve interactions between GaCl₃ and C-H bonds.⁵ The monobrominated arenes obtained here are the thermodynamically controlled products, because of the lower numbers of o- interactions between the bromide and the methyl group.

![Chemical reaction diagram]

**Table 4. Bromination of tri- and tetramethylbenzenes**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Catalyst</th>
<th>Time</th>
<th>Yielda (%)</th>
<th>Monobromide</th>
<th>Dibromide</th>
<th>Tribromide</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2,3-Trimethylbenzene</td>
<td>GaCl₃</td>
<td>1 min</td>
<td>18 (4), 15 (5)</td>
<td>25 (4,6)</td>
<td>42</td>
<td>ndb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 h</td>
<td>22 (4), 50 (5)</td>
<td>10 (4,6)</td>
<td>ndb</td>
<td></td>
</tr>
<tr>
<td>1,3,5-Trimethylbenzene</td>
<td>GaCl₃</td>
<td>1 min</td>
<td>16</td>
<td>54</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 h</td>
<td>40</td>
<td>34</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AlCl₃</td>
<td>1 min</td>
<td>84</td>
<td>14</td>
<td>Trace</td>
<td></td>
</tr>
<tr>
<td>1,2,3,4-Tetramethylbenzene</td>
<td>GaCl₃</td>
<td>1 min</td>
<td>52</td>
<td>41</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 h</td>
<td>90</td>
<td>4</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>1,2,4,5-Tetramethylbenzene</td>
<td>GaCl₃</td>
<td>1 min</td>
<td>50</td>
<td>41</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 h</td>
<td>71</td>
<td>26</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AlCl₃</td>
<td>1 min</td>
<td>76</td>
<td>22</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

aBased on bromine, as determined by ¹H-NMR. In parentheses is the brominated position. Numbering based on starting trialkylbenzene. bNot detected by GC–MS.

**Experimental Section**
Typical procedures for bromination. Under an argon atmosphere, a 1.0 M solution of GaCl₃ in methylecyclohexane (0.25 mL, 5 mol %) was added to a methylecyclohexane (7.5 mL) solution of hexylbenzene (0.90 mL, 5.0 mmol) at room temperature. After 5 min, bromine (0.25 mL, 5.0 mmol) was added, and the mixture was stirred for 12 h. Then saturated aqueous Na₂SO₄ was added, and the organic materials were extracted three times with hexane, the extracts dried over MgSO₄, and concentrated. The residue was purified by silica gel chromatography (n-hexane) to give a mixture (852 mg) of o-1, m-1, and p-1 in 18%, 38%, and 15% yield, respectively. ¹H-NMR (400 MHz, CDCl₃): δ 0.88–0.91 (9H, m, o, m, p), 1.29–1.39 (18H, m, o, m, p), 1.55–1.62 (6H, m, o, m, p), 2.52–2.58 (4H, m, p), 2.71 (2H, t, J = 8.0 Hz, o), 7.00–7.05 (m, 1H, o, 2H, p), 7.06 (1H, d, J = 8.8 Hz, m), 7.13 (1H, t, J = 8.0 Hz, m), 7.19–7.21 (2H, m, o), 7.29 (1H, d, J = 7.2 Hz, m), 7.34 (1H, s, m), 7.37 (2H, d, J = 8.8 Hz, p), 7.51 (1H, d, J = 8.0 Hz, o). ¹³C-NMR (100 MHz, CDCl₃): δ 14.2 (o, m, p), 22.7 (m, p), 22.7 (o), 29.0 (p), 29.0 (m), 29.2 (o), 30.0 (o), 31.3 (m), 31.4 (p), 31.8 (o, m, p), 35.4 (p), 35.7 (m), 36.3 (o), 119.1 (p), 122.2 (m), 124.3 (o), 126.9 (m), 127.1 (o), 127.2 (o), 128.5 (m), 129.6 (m), 130.0 (o), 130.1 (o), 131.1 (p), 131.3 (m), 132.6 (o), 141.7 (p), 142.0 (o), 145.1 (m). IR (neat) 2955, 2927, 2856, 1595, 1568, 1488, 1469, 1378, 1072, 1024, 1011, 774, 749, 692 cm⁻¹. MS (EI) m/z 242 (M⁺+2, 37), 240 (M⁺, 38), 172 (M⁺-68, 54), 171 (M⁺-69, 71), 169 (M⁺-71, 68), 91 (M⁺-149, 100), 43 (M⁺-197, 63). HRMS. Calcd for C₁₂H₁₇: Br: C; 59.76, H; 7.10, Br; 33.13%. Found: C; 59.60, H; 7.09, Br; 33.28%.

Preparation of 1-bromo-3-hexylbenzene. Under an argon atmosphere, a 1.6 M hexane solution of n-BuLi (44 mL, 70 mmol) was added to a THF solution (100 mL) of 1-pentyldiphenylphosphonium bromide (24.8 g, 60 mmol) at –78 °C. After stirring for 1 h at room temperature, m-bromobenzaldehyde (5.83 mL, 50 mmol) was added at –78 °C, and the mixture was stirred for 5 h at room temperature, then saturated aq. NH₄Cl was added. The organic materials were extracted three times with n-hexane, dried over MgSO₄ and concentrated. Flash chromatography over silica gel (n-hexane) gave 1-bromo-3-(2-hexenyl)benzene (9.24 g, 78%, E:Z = 2:5). Under a hydrogen atmosphere, a mixture of methanol (35 mL), 1-bromo-3-(2-hexenyl)benzene (9.24 g, 38.8 mmol) and PtO₂ (158.5 mg, 1.8 mol %) was stirred for 5 h at room temperature. Then PtO₂ was removed by filtration, and the solution concentrated. Flash chromatography over silica gel (n-hexane) gave 1-bromo-3-hexylbenzene (6.25 g, 95%). ¹H-NMR (400 MHz, CDCl₃) δ 0.88 (3H, t, J = 7.2 Hz), 1.25–1.35 (6H, m), 1.58 (2H, quintet, J = 7.2 Hz), 2.56 (2H, t, J = 8.0 Hz), 7.08 (1H, d, J = 7.2 Hz), 7.12 (1H, t, J = 8.0 Hz), 7.29 (1H, d, J = 7.6 Hz), 7.32 (1H, s). ¹³C-NMR (100 MHz, CDCl₃) δ 14.2, 22.7, 29.0, 31.3, 31.7, 35.7, 122.1, 126.9, 128.5, 129.6, 131.2, 145.1. IR (neat) 2955, 2928, 2856, 1594, 1567, 1470, 1424, 1071, 776, 691 cm⁻¹. MS (EI) m/z 242 (M⁺+2, 27), 240 (M⁺, 27), 172 (M⁺-68, 68), 171 (M⁺-69, 41), 170 (M⁺-70, 69), 169 (M⁺-71, 37), 91 (M⁺-149, 100), 43 (M⁺-197, 54). HRMS. Calcd for C₁₂H₁₇Br: 240.0513. Found: 240.0541.
1-Bromo-2-hexylbenzene and 1-bromo-4-hexylbenzene were also synthesized by this method.

**1-Bromo-2-hexylbenzene.** $^1$H-NMR (400 MHz, CDCl$_3$) δ 0.89 (3H, t, $J = 7.2$ Hz), 1.29–1.41 (6H, m), 1.60 (2H, quintet, $J = 7.6$ Hz), 2.71 (2H, t, $J = 8.0$ Hz), 7.00–7.04 (1H, m), 7.18–7.23 (2H, m), 7.51 (1H, d, $J = 8.0$ Hz). $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 14.2, 22.7, 29.1, 30.0, 31.7, 36.3, 124.3, 127.1, 127.1, 130.1, 132.5, 141.9. IR ( neat) 2955, 2927, 2857, 1566, 1469, 1438, 1377, 1024, 748, 658 cm$^{-1}$. MS (El) $m/z$ 242 (M$^+$+2, 22), 240 (M$^+$, 23), 172 (M$^+$-68, 24), 171 (M$^-$-69, 38), 170 (M$^-$-70, 25), 169 (M$^-$-71, 36), 91 (M$^-$-149, 100), 43 (M$^-$-197, 57). HRMS. Calcd for C$_{12}$H$_{17}$Br: 240.0513. Found: 240.0512.

**1-Bromo-4-hexylbenzene.** $^1$H-NMR (400 MHz, CDCl$_3$) δ 0.87 (3H, t, $J = 6.4$ Hz), 1.24–1.32 (6H, m), 1.57 (2H, quintet, $J = 7.2$ Hz), 2.54 (2H, t, $J = 10.8$ Hz), 7.40 (2H, d, $J = 8.0$ Hz), 7.37 (2H, d, $J = 8.0$ Hz). $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 14.2, 22.7, 28.9, 31.3, 31.7, 35.4, 119.1, 130.0, 131.0, 141.6. IR (neat) 2955, 2927, 2856, 1487, 1465, 1072, 1011, 801 cm$^{-1}$. MS (El) $m/z$ 242 (M$^+$+2, 46), 240 (M$^+$, 47), 171 (M$^-$-69, 98), 169 (M$^-$-71, 100), 91 (M$^-$-149, 46), 43 (M$^-$-197, 27). HRMS. Calcd for C$_{12}$H$_{17}$Br: 240.0513. Found: 240.0525.

**Preparation of 1-bromo-3-isobutylbenzene.** Under an argon atmosphere, a 1.6 M hexane solution of n-BuLi (14.5 mL, 23.3 mmol) was added to a THF solution (40 mL) of 2-propyltriphenylphosphonium bromide (5.70 g, 20 mmol) at –78 ºC. After stirring for 1 h at room temperature, m-bromobenzaldehyde (1.94 mL, 16.6 mmol) was added at –78 ºC, and the mixture was stirred for 1 h at room temperature. Then saturated NH$_4$Cl aq. was added. The organic materials were extracted three times with n-hexane, dried over MgSO$_4$ and concentrated. Flash chromatography over silica gel (n-hexane) gave 1-bromo-3-(2-methyl-1-propenyl)benzene (1.80 g, 51%). To a methanol solution (5.0 mL) of 1-bromo-3-(2-methyl-1-propenyl)benzene (210.0 mg, 1.0 mmol) was added PtO$_2$ (92 mg, 1.8 mol %), and the mixture was stirred for 5 h under a hydrogen atmosphere at room temperature. Pt/PtO$_2$ were removed by filtration, and the solution concentrated. Flash chromatography over silica gel (n-hexane) gave 1-bromo-3-isobutylbenzene (72.6 mg, 34%). $^1$H NMR (400 MHz, CDCl$_3$) δ 0.89 (6H, d, $J = 6.8$ Hz), 1.84 (1H, septet, $J = 6.8$ Hz), 2.43 (2H, d, $J = 6.4$ Hz), 7.05 (1H, d, $J = 7.2$ Hz), 7.13 (1H, t, $J = 8.0$ Hz), 7.29 (1H, s), 7.30 (1H, d, $J = 8.4$ Hz). $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 122.4, 130.2, 145.0, 130.0, 131.9, 143.8. IR (neat) 2955, 2924, 2868, 1591, 1566, 1471, 1425, 1073, 770, 693, 669 cm$^{-1}$. MS (El) $m/z$ 214 (M$^+$+2, 50), 212 (M$^+$, 51), 172 (M$^-$-40, 86), 171 (M$^-$-41, 62), 170 (M$^-$-42, 87), 169 (M$^-$-43, 58), 91 (M$^-$-121, 58), 43 (M$^-$-169, 100). HRMS. Calcd for C$_{10}$H$_{13}$Br: 212.0200 Found: 212.0241.

1-Bromo-2-isobutylbenzene and 1-bromo-4-isobutylbenzene were also synthesized by this method.

**1-Bromo-2-isobutylbenzene.** $^1$H NMR (400 MHz, CDCl$_3$) δ 0.93 (6H, d, $J = 6.4$ Hz), 0.98 (1H, septet, $J = 7.2$ Hz), 2.60 (2H, d, $J = 7.2$ Hz), 7.04 (1H, t, $J = 7.2$ Hz), 7.16 (1H, d, $J = 7.2$ Hz), 7.21 (1H, t, $J = 7.2$ Hz), 7.52 (1H, d, $J = 8.0$ Hz). $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 22.4, 28.8, 45.2, 124.7, 126.8, 127.2, 131.1, 132.6, 140.8. IR (neat) 2956, 2927, 2867, 1566, 1468, 1438, 1383, 1366, 1166, 1076, 1021, 746, 659 cm$^{-1}$. MS (El) $m/z$ 214 (M$^+$+2, 46), 212 (M$^+$, 47), 172 (M$^-$-40, 90), 171 (M$^-$-41, 100), 170 (M$^-$-42, 91), 169 (M$^-$-43, 97), 133 (M$^-$-79, 32), 91 (M$^-$-121,
95), 90 (M$^+$-122, 48), 89 (M$^+$-123, 38), 43 (M$^+$-169, 85). HRMS. Calcd for C$_{10}$H$_{13}$Br: 212.0200 Found: 212.0211.

**1-Bromo-4-isobutylbenzene.** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.88 (6H, d, $J = 6.8$ Hz), 1.82 (1H, septet, $J = 6.8$ Hz), 2.42 (2H, d, $J = 7.2$ Hz), 7.01 (2H, d, $J = 8.0$ Hz), 7.37 (2H, d, $J = 8.0$ Hz). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 22.3, 30.2, 44.8, 119.2, 130.6, 130.9, 140.4. IR (neat) 2955, 2923, 2868, 1591, 1488, 1466, 1073, 1012, 839, 785 cm$^{-1}$. MS (EI) m/z 214 (M$^+$+2, 32), 212 (M$^+$, 32), 172 (M$^+$-40, 34), 171 (M$^+$-41, 98), 170 (M$^+$-42, 35), 169 (M$^+$-43, 100), 91 (M$^+$-121, 27), 90 (M$^+$-122, 28), 43 (M$^+$-169, 38). HRMS. Calcd for C$_{10}$H$_{13}$Br: 212.0200 Found: 212.0200.

**Bromotoluene (mixture of isomers).** The structures of the products were determined by comparison with authentic commercial samples.

**Bromoethylbenzenes (mixture of isomers).** The structures of 1-bromo-2-ethylbenzene and 1-bromo-4-ethylbenzene were determined by comparison with authentic commercial samples. For 1-bromo-3-ethylbenzene, see ref. 10.

**Bromoocytylbenzenes (mixture of isomers).** The structures were determined by analogy with bromohexylybenzenes. For 1-bromo-4-octylbenzene, see ref. 11. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.88 (9H, t, $J = 7.2$ Hz, o, m, p), 1.26–1.29 (30H, m, o, m, p), 1.53–1.62 (6H, m, o, m, p), 2.52–2.58 (4H, m, m, p), 2.71 (2H, t, $J = 8.0$ Hz, o), 7.00–7.05 (m, 1H, o, 2H, p), 7.08 (1H, d, $J = 7.4$ Hz, m), 7.13 (1H, t, $J = 7.2$ Hz, m), 7.19–7.21 (2H, m, o), 7.30 (1H, d, $J = 8.0$ Hz, m), 7.32 (1H, s, m), 7.37 (2H, d, $J = 8.0$ Hz, p), 7.51 (1H, d, $J = 8.0$ Hz, o). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 14.3 (o, m, p), 22.8 (m, p), 22.8 (o). 29.3 (o, m, p), 29.3 (o, m, p), 29.4 (m, p), 29.5 (o), 30.1 (o), 31.4 (m), 31.4 (p), 32.0 (m, p), 32.0 (o), 35.5 (p), 35.7 (m), 36.3 (o), 119.1 (p), 122.2 (m), 124.3 (o), 126.9 (m), 127.1 (o), 127.2 (o), 128.5 (m), 129.6 (m), 130.0 (o), 130.1 (o), 131.1 (p), 131.3 (m), 132.6 (o), 141.7 (p), 142.0 (o), 145.1 (m). IR (neat) 2954, 2925, 2855, 1595, 1568, 1488, 1469, 1072, 1023, 1011, 777, 748, 692 cm$^{-1}$. MS (EI) m/z 270 (M$^+$+2, 17), 268 (M$^+$, 17), 172 (M$^+$-96, 28), 171 (M$^+$-97, 37), 170 (M$^+$-98, 29), 169 (M$^+$-99, 37), 91 (M$^+$-177, 100), 57 (M$^+$-211, 78), 43 (M$^+$-225, 60). HRMS. Calcd for C$_{14}$H$_{21}$Br: 268.0826. Found: 268.0799. Anal. Calcd for C$_{14}$H$_{21}$Br: C; 62.46, H; 7.86, Br: 29.68%. Found: C; 61.98, H; 8.03, Br; 29.76%.

**Bromoisobutylbenzenes (mixture of isomers).** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.89 (6H, d, $J = 6.8$ Hz, p), 0.89 (6H, d, $J = 6.8$ Hz, m), 0.93 (6H, d, $J = 6.4$ Hz, o), 1.79–1.90 (2H, m, m, p), 1.99 (1H, septet, $J = 7.2$ Hz, o), 2.41–2.44 (4H, m, m, p), 2.60 (2H, d, $J = 7.2$ Hz, o), 7.00 (2H, d, $J = 8.0$ Hz, p), 7.01–7.06 (2H, m, o, m), 7.13 (1H, t, $J = 8.0$ Hz, m), 7.16 (1H, d, $J = 8.0$ Hz, o), 7.21 (1H, t, $J = 7.6$ Hz, o), 7.29 (1H, s, m), 7.30 (1H, d, $J = 8.4$ Hz, m), 7.37 (2H, d, $J = 8.0$ Hz, p), 7.52 (1H, d, $J = 8.4$ Hz, o). $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 22.4 (o), 22.4 (m), 22.4 (p), 28.9 (o), 30.2 (m, p), 44.8 (p), 45.1 (m), 45.2 (o), 119.2 (p), 122.1 (m), 124.7 (o), 126.8 (o), 127.2 (o), 127.6 (m), 128.6 (m), 129.5 (m), 130.7 (p), 131.0 (p), 131.2 (o), 131.9 (m), 132.6 (o), 140.4 (p), 140.8 (o), 143.9 (m). IR (neat) 2955, 2925, 2868, 1592, 1567, 1488, 1469, 1384, 1366, 1167, 1074, 1021, 841, 771, 747, 693, 669 cm$^{-1}$. MS (EI) m/z 214 (M$^+$+2, 62), 212 (M$^+$, 63), 172 (M$^+$-40, 90), 171 (M$^+$-41, 100), 170 (M$^+$-42, 93), 169 (M$^+$-43, 95), 91 (M$^+$-121, 48), 43
(M⁺-169, 90). HRMS. Calcd for C₁₀H₁₃Br: 212.0200. Found: 212.0187. Anal. Calcd for C₁₀H₁₃Br: C; 56.36, H; 6.15, Br; 37.49%. Found: C; 56.12, H; 6.08, Br; 37.52%.

**Bromoneopentylbenzenes (mixture of isomers).** The structures of all the isomers were determined by analogy with bromo-isobutylbenzenes. For 1-bromo-2-neopentylbenzene and 1-bromo-4-neopentyl-benzene, see ref. 12.

**Dibromo-1,3-dimethylbenzene (mixture of isomers).** The structures of all the isomers were determined by analogy with bromo-isobutylbenzenes. For 1-bromo-2-neopentylbenzene and 1-bromo-4-neopentyl-benzene, see ref. 12.

**2-Bromo-1,3-dimethylbenzene, 1-bromo-2,4-dimethylbenzene and 1-bromo-3,5 dimethylbenzene.**

Structures determined by comparison with commercial authentic samples.

**1-Bromo-2,5-dimethylbenzene and 1,4-dibromo-2,5-dimethylbenzene.**

Structures determined by comparison with commercial authentic samples.

**Dibromo-1,3-dimethylbenzene (mixture of isomers).** For 2,5-dibromo-1,3-dimethylbenzene and 4,6-dibromo-1,3-dimethylbenzene, see ref. 13. ¹H NMR (400 MHz, CDCl₃) δ 2.30 (6H, s, 4, 6), 2.37 (3H, s, 2, 4), 2.38 (6H, s, 2, 5), 2.60 (6H, s, 2, 4), 6.93 (1H, d, J = 8.0 Hz, 2, 4), 7.09 (1H, s, 4, 6), 7.21 (1H, s, 2, 5), 7.38 (1H, d, J = 8.0 Hz, 2, 4), 7.67 (1H, s, 4, 6). ¹³C-NMR (100 MHz, CDCl₃) δ 22.3, 23.7, 24.2, 24.4, 120.1, 121.8, 126.1, 127.9, 128.7, 130.6, 130.7, 132.4, 134.7, 136.6, 137.1, 137.6, 140.0. FT-IR (neat) 2978, 2952, 2920, 1560, 1456, 1378, 1261, 1122, 1051, 1029, 997, 854. MS (EI) m/z 266 (M⁺+4, 51), 264 (M⁺+2, 100), 262 (M⁺, 55), 185 (M⁺-77, 68), 183 (M⁺-79, 72), 104 (M⁺-158, 53), 103 (M⁺-159, 59), 51 (M⁺-211, 48). HRMS. Calcd for C₈H₈Br₂: 261.8992. Found: 261.8980.

**1-Bromo-2,4,6-trimethylbenzene and 1,3-dibromo-2,4,6-trimethylbenzene.** The structures of the products were determined by comparison with commercial authentic samples.

**1,3,5-Tribromo-2,4,6-trimethylbenzene.**

¹H NMR (400 MHz, CDCl₃) δ 2.65 (9H, s). ¹³C-NMR (100 MHz, CDCl₃) δ 26.4, 124.8, 136.8. IR (KBr) 2919, 1538, 1434, 1375, 1349, 1017, 954, 647 cm⁻¹. MS (EI) m/z 358 (M⁺+4, 97), 356 (M⁺+2, 100), 354 (M⁺, 279 (M⁺-75, 50), 277 (M⁺-77, 95), 275 (M⁺-79, 50), 117 (M⁺-237, 56), 116 (M⁺-238, 66), 115 (M⁺-239, 72). HRMS. Calcd for C₉H₉Br₃: 353.8255. Found: 353.8283.

**1-Bromo-2,3,4-trimethylbenzene.**

¹H NMR (400 MHz, CDCl₃) δ 2.23 (6H, s), 2.39 (3H, s), 6.84 (1H, d, J = 8.0 Hz), 7.28 (1H, d, J = 8.0 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 16.9, 20.1, 20.7, 122.7, 128.4, 129.2, 135.4, 135.4, 136.8. IR (neat) 2942, 1582, 1455, 1405, 1378, 1250, 1181, 1134, 1077, 1000, 893, 851, 826, 801 cm⁻¹. MS (EI) m/z 200 (M⁺+2, 69), 198 (M⁺, 72), 119 (M⁺-79, 100). HRMS. Calcd for C₉H₁₁Br: 198.0044 Found: 198.0028.
5-Bromo-1,2,3-trimethylbenzene.\textsuperscript{16} \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ 2.10 (3H, s), 2.24 (6H, s), 7.14 (2H, s). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 15.1, 20.5, 20.7, 118.1, 129.9, 133.8, 138.3. IR (neat) 2920, 1579, 1455, 1377, 1185, 1000, 851, 801 cm\textsuperscript{-1}. MS (EI) m/z 200 (M\textsuperscript{+}+2, 59), 198 (M\textsuperscript{+}, 60), 119 (M\textsuperscript{+}-79, 100). HRMS. Calcd for C\textsubscript{9}H\textsubscript{11}Br: 198.0044 Found: 198.0046.

1,5-Dibromo-2,3,4-trimethylbenzene.\textsuperscript{17} \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ 2.30 (3H, s), 2.35 (6H, s), 7.64 (1H, s). \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) δ 18.4, 20.2, 122.5, 132.6, 134.8, 138.1. IR (KBr) 2920, 1557, 1440, 1415, 1378, 1160, 1008, 904, 856, 655 cm\textsuperscript{-1}. MS (EI) m/z 280 (M\textsuperscript{+}+4, 50), 278 (M\textsuperscript{+}+2, 100), 276 (M\textsuperscript{+}, 53), 199 (M\textsuperscript{+}-77, 57), 197 (M\textsuperscript{+}-79, 58). HRMS. Calcd for C\textsubscript{9}H\textsubscript{10}Br\textsubscript{2}: 275.9149. Found: 275.9164.

1,2,3-Tribromo-4,5,6-trimethylbenzene.\textsuperscript{14} \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ 2.30 (3H, s), 2.49 (9H, s). \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) δ 19.0, 23.0, 125.5, 125.7, 136.2, 137.2. IR (KBr) 2919, 1430, 1371, 1354, 1232, 1004, 930, 657 cm\textsuperscript{-1}. MS (EI) m/z 358 (M\textsuperscript{+}+4, 96), 356 (M\textsuperscript{+}+2, 100), 354 (M\textsuperscript{+}, 36), 277 (M\textsuperscript{+}-77, 62), 115 (M\textsuperscript{+}-239, 40). HRMS. Calcd for C\textsubscript{9}H\textsubscript{9}Br\textsubscript{3}: 353.8254. Found: 353.8244.

3-Bromo-1,2,4,5-tetramethylbenzene. The structure of the product was determined by comparison with commercial authentic sample.

1,4-Dibromo-2,3,5,6-tetramethylbenzene.\textsuperscript{14} \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ 2.48 (12H, s). \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) δ 22.4, 127.9, 134.8. IR (KBr) 2922, 1414, 1381, 1173, 987, 690 cm\textsuperscript{-1}. MS (EI) m/z 294 (M\textsuperscript{+}+4, 50), 292 (M\textsuperscript{+}+2, 100), 290 (M\textsuperscript{+}, 53), 213 (M\textsuperscript{+}-77, 69), 211 (M\textsuperscript{+}-79, 74). HRMS. Calcd for C\textsubscript{10}H\textsubscript{12}Br\textsubscript{2}: 289.9305. Found: 289.9333.

1-Bromo-2,3,4,5-tetramethylbenzene.\textsuperscript{14,15} \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ 2.14 (3H, s), 2.22 (3H, s), 2.24 (3H, s), 2.37 (3H, s), 7.23 (1H, s). \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) δ 16.1, 17.4, 20.1, 20.5, 122.0, 130.6, 132.8, 134.0, 135.2, 136.6. IR (neat) 2922, 1460, 1379, 1199, 941, 859, 752 cm\textsuperscript{-1}. MS (EI) m/z 214 (M\textsuperscript{+}+2, 60), 212 (M\textsuperscript{+}, 62), 133 (M\textsuperscript{+}-79, 100). HRMS. Calcd for C\textsubscript{10}H\textsubscript{13}Br: 212.0200. Found: 212.0191.

1,2-Dibromo-3,4,5,6-tetramethylbenzene.\textsuperscript{14} \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ 2.24 (6H, s), 2.49 (6H, s). \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) δ 17.9, 22.8, 125.3, 135.2, 135.4. IR (KBr) 2918, 1374, 1255, 1193, 992, 951, 889, 770 cm\textsuperscript{-1}. MS (EI) m/z 294 (M\textsuperscript{+}+4, 51), 292 (M\textsuperscript{+}+2, 100), 290 (M\textsuperscript{+}, 53), 213 (M\textsuperscript{+}-77, 55), 211 (M\textsuperscript{+}-79, 56). HRMS. Calcd for C\textsubscript{10}H\textsubscript{12}Br\textsubscript{2}: 289.9305. Found: 289.9316.

Acknowledgments

M. A. expresses her thanks to JSPS for a Grant-in-Aid for Encouragement of Young Scientists (No. 13771323), and the Hayashi Memorial Foundation for Female Natural Scientists.

References


