

# One-pot aromatic bromination–rearrangement catalyzed by GaCl<sub>3</sub>

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](mailto: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<sub>3</sub> (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

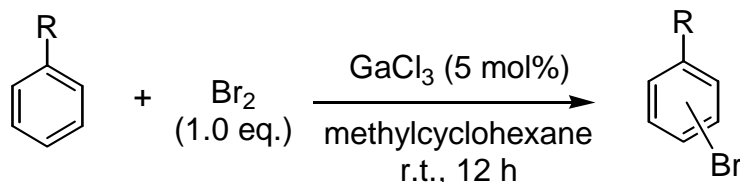
---

## Introduction

The bromination of aromatic compounds has been conducted using halogenating reagents such as Br<sub>2</sub> and HOBr in the presence or absence of catalysts.<sup>1</sup> 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.<sup>2</sup> A previous report that Al<sub>2</sub>Cl<sub>6</sub>–water catalyst promotes the isomerization of bromoarenes<sup>3</sup> 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.<sup>4</sup> We now show that GaCl<sub>3</sub><sup>5,6,7</sup> 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<sub>3</sub> (5 mol %) in methylcyclohexane 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<sub>3</sub> (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<sub>3</sub> (5 mol %), although the reaction was sometimes not reproducible, probably because of the insolubility of AlCl<sub>3</sub> in this solvent. The bromination using GaCl<sub>3</sub> 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<sub>3</sub> 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.



**Table 1.** Bromination of alkylbenzenes catalyzed by GaCl<sub>3</sub>

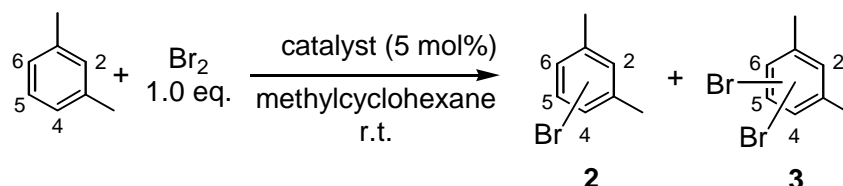
Entry	R	Yield <sup>a</sup> (%)		
		<i>o</i> -	<i>m</i> -	<i>p</i> -
1	CH <sub>3</sub>	32	32	11
2	CH <sub>3</sub> CH <sub>2</sub>	16	32	14
3	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> CH <sub>2</sub>	18	38	15
4 <sup>a</sup>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> CH <sub>2</sub>	23	3	42
5	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub> CH <sub>2</sub>	23	34	20
6	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	21	49	19
7	(CH <sub>3</sub> ) <sub>3</sub> CCH <sub>2</sub>	8	62	22

<sup>a</sup>Determined by <sup>1</sup>H-NMR. <sup>b</sup>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 *m*-xylene with AlCl<sub>3</sub> under the same conditions for 1 min gives 4-**2** predominantly, which is the usual orientation.

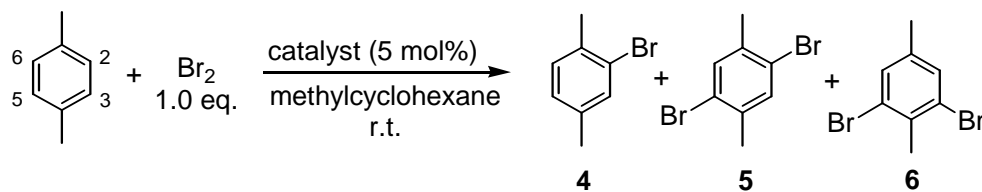
Similar tendencies are observed in the bromination of *p*-xylene with GaCl<sub>3</sub> (Table 3). The reaction for 5 min gives 2,5-dibrominated **5** predominantly, which is converted into 2-brominated **4** after 12 h. In this case, AlCl<sub>3</sub> also shows somewhat related isomerization behaviors,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



**Table 2.** Bromination of *m*-Xylene

Catalyst	Time	Position <sup>b</sup>	Yield <sup>a</sup> (%)						
			<b>2</b>	<b>3</b>	2-	4-	5-	2,4-	2,5-
GaCl <sub>3</sub>	1 min	5	15	trace	24	trace	40		
	12 h	11	30	19	2	11	18		
AlCl <sub>3</sub>	1 min	9	83	trace	nd <sup>c</sup>	nd <sup>c</sup>	trace		

<sup>a</sup>Based on bromine, as determined by <sup>1</sup>H-NMR. <sup>b</sup>Bromide positions. Numbering based on the starting *m*-xylene. <sup>c</sup>Not detected by GC-MS.

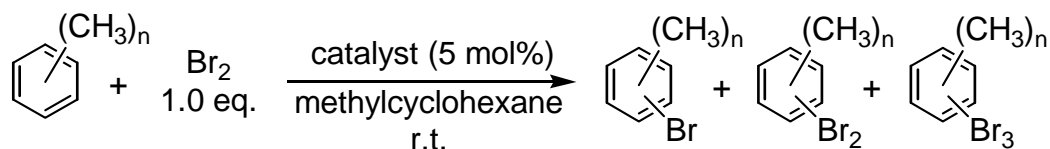


**Table 3.** Bromination of *p*-Xylene

Catalyst	Time	Yield <sup>a</sup> (%)		
		<b>4</b>	<b>5</b>	<b>6</b>
GaCl <sub>3</sub>	5 min	20	64	8
	12 h	64	28	6
AlCl <sub>3</sub>	5 min	47	46	6
	12 h	67	29	3

<sup>a</sup>Based on bromine, as determined by <sup>1</sup>H-NMR.

Bromination of 1,2,3- and 1,3,5-trimethylbenzene with GaCl<sub>3</sub> 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.<sup>8</sup> Reactions of both 1,2,3,4-tetramethyl- and 1,2,4,5-tetramethylbenzene with GaCl<sub>3</sub> 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 GaCl<sub>3</sub>. It seems that the bromide group behaves as an activating group in the electrophilic substitution. We propose that the interaction of GaCl<sub>3</sub> with Br, as well as the C-H bonds of neighboring methyl groups, promote such polybromination. Previously, we reported aromatic substitution reactions which involve interactions between GaCl<sub>3</sub> and C-H bonds.<sup>5</sup> 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.



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

Substrate	Catalyst	Time	Yield <sup>a</sup> (%)		
			Monobromide	Dibromide	Tribromide
1,2,3-Trimethylbenzene	GaCl <sub>3</sub>	1 min	18 (4), 15 (5)	25 (4,6)	42
		12 h	22 (4), 50 (5)	10 (4,6)	nd <sup>b</sup>
1,3,5-Trimethylbenzene	GaCl <sub>3</sub>	1 min	16	54	27
		12 h	40	34	22
	AlCl <sub>3</sub>	1 min	84	14	Trace
1,2,3,4-Tetramethylbenzene	GaCl <sub>3</sub>	1 min	52	41	-
		12 h	90	4	-
1,2,4,5-Tetramethylbenzene	GaCl <sub>3</sub>	1 min	50	41	-
		12 h	71	26	-
	AlCl <sub>3</sub>	1 min	76	22	-

<sup>a</sup>Based on bromine, as determined by <sup>1</sup>H-NMR. In parentheses is the brominated position. Numbering based on starting trialkylbenzene. <sup>b</sup>Not detected by GC-MS.

## Experimental Section

**Typical procedures for bromination.** Under an argon atmosphere, a 1.0 M solution of GaCl<sub>3</sub> in methylcyclohexane (0.25 mL, 5 mol %) was added to a methylcyclohexane (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 Na<sub>2</sub>SO<sub>3</sub> was added, and the organic materials were extracted three times with hexane, the extracts dried over MgSO<sub>4</sub>, 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. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 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, *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*). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 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<sup>-1</sup>. MS (EI) *m/z* 242 (M<sup>+</sup>+2, 37), 240 (M<sup>+</sup>, 38), 172 (M<sup>+</sup>-68, 54), 171 (M<sup>+</sup>-69, 71), 169 (M<sup>+</sup>-71, 68), 91 (M<sup>+</sup>-149, 100), 43 (M<sup>+</sup>-197, 63). HRMS. Calcd for C<sub>12</sub>H<sub>17</sub>Br: 240.0513. Found: 240.0523. Anal. Calcd for C<sub>12</sub>H<sub>17</sub>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-pentyltriphenylphosphonium 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 2 h at room temperature, then saturated aq. NH<sub>4</sub>Cl was added. The organic materials were extracted three times with *n*-hexane, dried over MgSO<sub>4</sub> 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 PtO<sub>2</sub> (158.5 mg, 1.8 mol %) was stirred for 5 h at room temperature. Then PtO<sub>2</sub> was removed by filtration, and the solution concentrated. Flash chromatography over silica gel (*n*-hexane) gave 1-bromo-3-hexylbenzene (6.25 g, 95%). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) 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). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) 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<sup>-1</sup>. MS (EI) *m/z* 242 (M<sup>+</sup>+2, 27), 240 (M<sup>+</sup>, 27), 172 (M<sup>+</sup>-68, 68), 171 (M<sup>+</sup>-69, 41), 170 (M<sup>+</sup>-70, 69), 169 (M<sup>+</sup>-71, 37), 91 (M<sup>+</sup>-149, 100), 43 (M<sup>+</sup>-197, 54). HRMS. Calcd for C<sub>12</sub>H<sub>17</sub>Br: 240.0513. Found: 240.0541.

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

**1-Bromo-2-hexylbenzene.**  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $658\text{ cm}^{-1}$ . MS (EI)  $m/z$  242 ( $\text{M}^+ + 2$ , 22), 240 ( $\text{M}^+$ , 23), 172 ( $\text{M}^+ - 68$ , 24), 171 ( $\text{M}^+ - 69$ , 38), 170 ( $\text{M}^+ - 70$ , 25), 169 ( $\text{M}^+ - 71$ , 36), 91 ( $\text{M}^+ - 149$ , 100), 43 ( $\text{M}^+ - 197$ , 57). HRMS. Calcd for  $\text{C}_{12}\text{H}_{17}\text{Br}$ : 240.0513. Found: 240.0512.

**1-Bromo-4-hexylbenzene.**<sup>9</sup>  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $801\text{ cm}^{-1}$ . MS (EI)  $m/z$  242 ( $\text{M}^+ + 2$ , 46), 240 ( $\text{M}^+$ , 47), 171 ( $\text{M}^+ - 69$ , 98), 169 ( $\text{M}^+ - 71$ , 100), 91 ( $\text{M}^+ - 149$ , 46), 43 ( $\text{M}^+ - 197$ , 27). HRMS. Calcd for  $\text{C}_{12}\text{H}_{17}\text{Br}$ : 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  $-78\text{ }^\circ\text{C}$ . After stirring for 1 h at room temperature, *m*-bromobenzaldehyde (1.94 mL, 16.6 mmol) was added at  $-78\text{ }^\circ\text{C}$ , and the mixture was stirred for 1 h at room temperature. Then saturated  $\text{NH}_4\text{Cl}$  aq. was added. The organic materials were extracted three times with *n*-hexane, dried over  $\text{MgSO}_4$  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  $\text{PtO}_2$  (92 mg, 1.8 mol %), and the mixture was stirred for 5 h under a hydrogen atmosphere at room temperature. Pt/ $\text{PtO}_2$  were removed by filtration, and the solution concentrated. Flash chromatography over silica gel (*n*-hexane) gave 1-bromo-3-isobutylbenzene (72.6 mg, 34%).  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.4, 30.2, 45.0, 122.0, 127.6, 128.6, 129.4, 131.9, 143.8. IR (neat) 2955, 2924, 2868, 1591, 1566, 1471, 1425, 1073, 770, 693,  $669\text{ cm}^{-1}$ . MS (EI)  $m/z$  214 ( $\text{M}^+ + 2$ , 50), 212 ( $\text{M}^+$ , 51), 172 ( $\text{M}^+ - 40$ , 86), 171 ( $\text{M}^+ - 41$ , 62), 170 ( $\text{M}^+ - 42$ , 87), 169 ( $\text{M}^+ - 43$ , 58), 91 ( $\text{M}^+ - 121$ , 58), 43 ( $\text{M}^+ - 169$ , 100). HRMS. Calcd for  $\text{C}_{10}\text{H}_{13}\text{Br}$ : 212.0200 Found: 212.0241.

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

**1-Bromo-2-isobutylbenzene.**  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $659\text{ cm}^{-1}$ . MS (EI)  $m/z$  214 ( $\text{M}^+ + 2$ , 46), 212 ( $\text{M}^+$ , 47), 172 ( $\text{M}^+ - 40$ , 90), 171 ( $\text{M}^+ - 41$ , 100), 170 ( $\text{M}^+ - 42$ , 91), 169 ( $\text{M}^+ - 43$ , 97), 133 ( $\text{M}^+ - 79$ , 32), 91 ( $\text{M}^+ - 121$ ,

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.**  $^1H$  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.

**Bromooctylbenzenes (mixture of isomers).** The structures were determined by analogy with bromohexylbenzenes. For 1-bromo-4-octylbenzene, see ref. 11.  $^1H$  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).**  $^1H$  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  $C_{10}H_{13}Br$ : 212.0200. Found: 212.0187. Anal. Calcd for  $C_{10}H_{13}Br$ : 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-neopentylbenzene, see ref. 12.  $^1H$ -NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.89 (9H, s, *p*), 0.90 (9H, s, *m*), 0.97 (9H, s, *o*), 2.44 (2H, s, *p*), 2.45 (2H, s, *m*), 2.74 (2H, s, *o*), 6.99 (2H, d,  $J = 8.8$  Hz, *p*), 7.00–7.03 (1H, m, *o*) 7.04 (1H, d,  $J = 7.6$  Hz, *m*), 7.13 (1H, t,  $J = 7.2$  Hz, *m*), 7.20–7.21 (2H, m, *o*), 7.27 (1H, s, *m*), 7.33 (1H, d,  $J = 8.0$  Hz, *m*), 7.38 (2H, d,  $J = 8.0$  Hz, *p*), 7.54 (1H, d,  $J = 8.0$  Hz, *o*).  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ )  $\delta$  29.4, 29.4, 29.7, 31.8, 31.9, 33.3, 48.0, 49.6, 49.9, 119.6, 121.6, 125.9, 126.4, 127.3, 128.7, 128.9, 129.0, 130.5, 132.0, 132.2, 132.8, 133.1, 138.5, 139.2, 141.9  $cm^{-1}$ . IR (neat) 2953, 2865, 1592, 1567, 1488, 1474, 1423, 1393, 1364, 1236, 1205, 1073, 997, 890, 841, 804, 785, 741, 696. MS (EI)  $m/z$  228 ( $M^+$ +2, 10), 226 ( $M^+$ , 11), 172 ( $M^+$ -54, 19), 170 ( $M^+$ -56, 20), 57 ( $M^+$ -169, 100). HRMS. Calcd for  $C_{11}H_{15}Br$ : 226.0357. Found: 226.0346. Anal. Calcd for  $C_{11}H_{15}Br$ : C; 58.17, H; 6.66, Br; 35.18%. Found: C; 57.93, H; 6.71, Br; 35.01%.

**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,  $CDCl_3$ )  $\delta$  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).  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ )  $\delta$  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  $C_8H_8Br_2$ : 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.**<sup>14</sup>  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  2.65 (9H, s).  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ )  $\delta$  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  $C_9H_9Br_3$ : 353.8255. Found: 353.8283.

**1-Bromo-2,3,4-trimethylbenzene.**<sup>14,15</sup>  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  2.23 (6H, s), 2.39 (3H, s), 6.84 (1H, d,  $J = 8.0$  Hz), 7.28 (1H, d,  $J = 8.0$  Hz).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  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  $C_9H_{11}Br$ : 198.0044 Found: 198.0028.



**5-Bromo-1,2,3-trimethylbenzene.**<sup>16</sup> <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 2.10 (3H, s), 2.24 (6H, s), 7.14 (2H, s). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 15.1, 20.5, 20.7, 118.1, 129.9, 133.8, 138.3. IR (neat) 2920, 1579, 1470, 1455, 1377, 1185, 1000, 851, 801 cm<sup>-1</sup>. MS (EI) *m/z* 200 (M<sup>+</sup>+2, 59), 198 (M<sup>+</sup>, 60), 119 (M<sup>+</sup>-79, 100). HRMS. Calcd for C<sub>9</sub>H<sub>11</sub>Br: 198.0044 Found: 198.0046.

**1,5-Dibromo-2,3,4-trimethylbenzene.**<sup>17</sup> <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 2.30 (3H, s), 2.35 (6H, s), 7.64 (1H, s). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) 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<sup>-1</sup>. MS (EI) *m/z* 280 (M<sup>+</sup>+4, 50), 278 (M<sup>+</sup>+2, 100), 276 (M<sup>+</sup>, 53), 199 (M<sup>+</sup>-77, 57), 197 (M<sup>+</sup>-79, 58). HRMS. Calcd for C<sub>9</sub>H<sub>10</sub>Br<sub>2</sub>: 275.9149. Found: 375.9164.

**1,2,3-Tribromo-4,5,6-trimethylbenzene.**<sup>14</sup> <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 2.30 (3H, s), 2.49 (9H, s). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ 19.0, 23.0, 125.5, 125.7, 136.2, 137.2. IR (KBr) 2919, 1430, 1371, 1354, 1232, 1004, 930, 657 cm<sup>-1</sup>. MS (EI) *m/z* 358 (M<sup>+</sup>+4, 96), 356 (M<sup>+</sup>+2, 100), 354 (M<sup>+</sup>, 36), 277 (M<sup>+</sup>-77, 62), 115 (M<sup>+</sup>-239, 40). HRMS. Calcd for C<sub>9</sub>H<sub>9</sub>Br<sub>3</sub>: 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.**<sup>14</sup> <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 2.48 (12H, s). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ 22.4, 127.9, 134.8. IR (KBr) 2922, 1414, 1381, 1173, 987, 690 cm<sup>-1</sup>. MS (EI) *m/z* 294 (M<sup>+</sup>+4, 50), 292 (M<sup>+</sup>+2, 100), 290 (M<sup>+</sup>, 53), 213 (M<sup>+</sup>-77, 69), 211 (M<sup>+</sup>-79, 74). HRMS. Calcd for C<sub>10</sub>H<sub>12</sub>Br<sub>2</sub>: 289.9305. Found: 289.9333.

**1-Bromo-2,3,4,5-tetramethylbenzene.**<sup>14,15</sup> <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 2.14 (3H, s), 2.22 (3H, s), 2.24 (3H, s), 2.37 (3H, s), 7.23 (1H, s). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) 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<sup>-1</sup>. MS (EI) *m/z* 214 (M<sup>+</sup>+2, 60), 212 (M<sup>+</sup>, 62), 133 (M<sup>+</sup>-79, 100). HRMS. Calcd for C<sub>10</sub>H<sub>13</sub>Br: 212.0200. Found: 212.0191.

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

1. Taylor, R. *Electrophilic Aromatic Substitution*; John Wiley & Sons: New York, 1990.
2. For example, (a) Acree, S. F. *Chem. Ber.* **1904**, *37*, 994. (b) Bigelow, L. A.; Jonson, J. R.; Sandboan, L. T. *Org. Syn.* **1941** *Coll. Vol. I*, 133. (c) Compennolle, F.; Toppet, S. *J. Heterocycl. Chem.* **1986**, *23*, 541.
3. (a) Olah, G. A.; Tolgyesi, W. S.; Dear, R. E. A. *J. Org. Chem.* **1962**, *27*, 3464. (b) Crump, J. W.; Gornowicz, G. A. *J. Org. Chem.* **1963**, *28*, 949. (c) De Valois, P. J.; Van Albada, M. P.; Veenland, J. U. *Tetrahedron* **1968**, *24*, 1835. (d) Olah, G. A.; Lapierre, J. C.; Carlson, C. G. *J. Org. Chem.* **1965**, *30*, 541. (e) Olah, G. A.; Tolgyesi, W. S.; Dear, R. E. A. *J. Org. Chem.* **1962**, *27*, 3441. (f) Olah, G. A.; Tolgyesi, W. S.; Dear, R. E. A. *J. Org. Chem.* **1962**, *27*, 3449. (g) Olah, G. A.; Tolgyesi, W. S.; Dear, R. E. A. *J. Org. Chem.* **1962**, *27*, 3455.
4. One-pot *m*-bromination reaction of toluene using a stoichiometric amount of AlBr<sub>3</sub> has been reported. Brown, H. C.; McGary, C. W. *J. Am. Chem. Soc.* **1955**, *77*, 2306.
5. (a) Yonehara, F.; Kido, Y.; Morita, S.; Yamaguchi, M. *J. Am. Chem. Soc.* **2001**, *123*, 11310. (b) Yonehara, F.; Kido, Y.; Yamaguchi, M. *Chem. Commun.* **2000**, 1189.
6. (a) Kido, Y.; Yonehara, F.; Yamaguchi, M. *Tetrahedron* **2001**, *57*, 827. (b) Kido, Y.; Arisawa, M.; Yamaguchi, M. *J. Synth. Org. Chem. Jpn.* **2000**, *58*, 1030. (c) Kido, Y.; Yoshimura, S.; Yamaguchi, M.; Uchimar, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1445. (d) Kido, Y.; Yamaguchi, M. *J. Org. Chem.* **1998**, *63*, 8086. (e) Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hiram, M. *Angew., Chem. Int. Ed. Engl.* **1997**, *36*, 1313.
7. (a) Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2002**, *124*, 8528. (b) Arisawa, M.; Amemiya, R.; Yamaguchi, M. *Org. Lett.* **2002**, *4*, 2209. (c) Arisawa, M.; Miyagawa, C.; Yamaguchi, M. *Synthesis* **2002**, 138. (d) Arisawa, M.; Miyagawa, C.; Yoshimura, S.; Kido, Y.; Yamaguchi, M. *Chem. Lett.* **2001**, 1080. (e) Arisawa, M.; Akamatsu, K.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 789. (f) Yamaguchi, M.; Tsukagoshi, T.; Arisawa, M. *J. Am. Chem. Soc.* **1999**, *121*, 4074. (g) Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *Inorg. Chim. Acta* **1999**, *296*, 67. (h) Yamaguchi, M.; Sotokawa, T.; Hiram, M. *Chem. Commun.* **1997**, 743.
8. Gruber, R.; Kirsch, G.; Cagniant, D. *Bull. Soc. Chim. Fr.* **1987**, 498.
9. Franks, S.; Hartley, F. R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2233.
10. Lunazzi, L.; Mazzanti, A.; Alvarez, M. *J. Org. Chem.* **2000**, *65*, 3200.
11. Peng, Z.; Gharavi, A. R.; Yu, L. *J. Am. Chem. Soc.* **1997**, *119*, 4622.
12. Hellwinkel, D.; Knabe, B. *Chem. Ber.* **1971**, *104*, 1761. Archer, W. J.; Hossaini, M. A.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1982**, 181.
13. Itoh, T.; Matsuda, K.; Iwamura, H.; Hori, K. *J. Am. Chem. Soc.* **2000**, *122*, 2567. Allinson, G.; Bushby, R. J.; Jesudason, M. V.; Paillaud, J.; Taylor, N. *J. Chem. Soc., Perkin Trans. 2* **1997**, 147.
14. Kajigaeshi, S.; Kakinami, T.; Moriwaki, M.; Tanaka, T.; Fujisaki, S.; Okamoto, T. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 439.
15. Mitchell, R. H.; Lai, Y.; Williams, R. V. *J. Org. Chem.* **1979**, *44*, 4733.

16. Baciocchi, E.; Dalla, C. A.; Ebersson, L.; Mandolini, L.; Roi, C. *J. Org. Chem.* **1986**, *51*, 4544.
17. Suzuki, H.; Mishina, T.; Hanafusa, T. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3099.