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Straightforward access to functionalized pentaarylbenzene derivatives through a quick lithiation

Tetsuo Iwasawa *, Toshinori Kamei, Kento Hama, Yoshiki Nishimoto, Masaki Nishiuchi, Yasuhiko Kawamura *

Department of Chemical Science and Technology, Faculty of Enginnering, The University of Tokushima, Minami-jyosanjima-cho, Tokushima 770-8506, Japan

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ABSTRACT

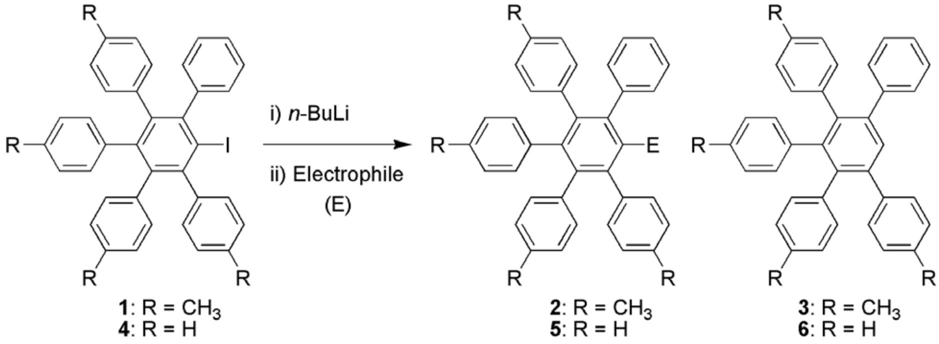
A straightforward route to functionalized pentaarylbenzene derivatives is described, involving the effective lithiation method of 1-iodo-2,3,4,5,6-pentaarylbenzene. The activated pentaarylbenzene is a potential synton for producing organic materials.

Polyarylbenzene derivatives reported by Müllen and co-wokers have drawn significant attention because of their potential application in organic materials science,[1] for example, electroluminescent materials,[2] optical devices,[3] supramolecular electronics,[4] and catalysts.[5] The essential core structure among the polyarylbenzene derivatives is based on a pentaarylbenzene moiety. Thus, the installation of functional groups into the core structure would amplify the potentiality. Hence, the fine tuning of chemical modification on the skeletal moiety is well worth developing.

Two procedures for permitting the chemical modification were mainly known: one is cobalt-catalyzed trimerization,[6,7] and the other is Diels–Alder cyclization.[8] Both install the functional groups along with construction of the core skeleton. The former allows symmetrically introducing the functionality, while it is laborious to obtain desymmetrically functionalized molecules.[9] The latter system, the reaction of tetraarylcyclopentadienone with terminal or internal ethynylarene, enables to desymmetrically functionalize, as well as to monofunctionalize.[1,2,5] The Diels–Alder reaction, for the present, is suitable for installation of diverse functionality into the core structure. However, the severe heat is required to limit the range of available functionalities.[4g,10,11]

Herein, we report a straightforward procedure for giving the fine tuning of chemical modification on the pentaarylbenzene core, which is outlined in Scheme 1. First, the Diels–Alder adduct **1** was synthesized to overcome the limited solubility of **4** in organic solvents. Then, the clean lithiation of sterically demanding **1** at −20 °C in toluene was found to quickly occur just in 5 min, thus providing a convenient access to functionalized pentaarylbenzene molecules.

At the outset of our study, the lithiation conditions of the novel iodide **1**[12] were surveyed through the reactions with dimethyl disulfide, which afforded the methyl sulfide adduct **2** (E = SMe). The results were summarized in Table 1. The iodide **1** was prepared



Scheme 1. Functionalizing a pentaary benzene through the lithiation.

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* Corresponding authors. Tel.: +81 88 656 7405; fax: +81 88 655 7025 (T.I.).
E-mail addresses: iwasawa@chem.tokushima-u.ac.jp (T. Iwasawa), kawamura@chem.tokushima-u.ac.jp (Y. Kawamura).

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Table 1

A survey on the lithiation conditions conducted via Scheme 1

$$\mathbf{1}\ (\text{or } \mathbf{4})\ \xrightarrow[\substack{\text{toluene}\\ T\,^\circ\text{C, time}}]{n\text{-BuLi}}\ \xrightarrow[T\,^\circ\text{C, 1 h}]{\text{MeSSMe}}\ \mathbf{2}\ (\text{or } \mathbf{5})\ +\ \mathbf{3}\ (\text{or } \mathbf{6})$$

Entry	**1** or **4**	*n*-BuLi (equiv)	*T* (°C)	Time (min)	**2** or **5**[a] (%)	**3** or **6**[a] (%)
1[b,c]	**4**	2.0	−20	30	32	54
2	**1**	2.0	−20	30	89	2
3	**1**	2.0	−45	30	83	1
4	**1**	2.0	−78	30	19	<2
5	**1**	2.0	−20	5	92	<1
6[d]	**1**	2.0	−78	5	62	27
7	**1**	1.5	−20	5	91	<1
8	**1**	1.2	−20	5	91	4

[a] Isolated yields with silica gel column chromatography.

[b] The reaction mixture was terribly suspended.

[c] Unreacted **4** was recovered in 9%.

[d] THF was used as a solvent.

to compensate for poor solubility of **4** in organic solvents.[13] Actually, the necessary amount of toluene to dissolve 1 g of iodides **1** and **4** was 15 mL and 138 mL, respectively. The iodide **1** bearing tetramethyl groups was dissolved in toluene ca. nine times higher as compared with **4**. The difference in the solubility affected the lithiation of **1** and **4** by *n*-BuLi, and the resultant yields of **2** and **5**, which were observed at entries 1 and 2. The lithiation of **4** in toluene with muddy state gave the desired **5** in only 32% yield (entry 1). Additionally, tremendous amounts of side-product **6** were found in 54% yield, along with 9% of the starting material **4**. On the other hand, the lithiation of **1** in a clear toluene solution yielded the desired **2** in 89% with suppressing the side-product **3** in only 2% yield, and the remaining **1** was not observed in TLC monitoring (entry 2). Thus, **1** endowed with four methyl groups was at a distinct advantage over **4**, and the efficient conditions for lithiation of **1** were further evaluated (entries 3–8). Low temperature conditions at −45 °C and −78 °C afforded **2** in 83% and 19% yields, respectively (entries 3 and 4). They did not exceed 89% yield given at −20 °C in entry 2. At the adequate temperature −20 °C, the aging time for the lithiation was shortened in from 30 min to 5 min (entry 5). Surprisingly, the starting material **1** was completely disappeared in TLC monitoring, providing **2** in 92% yield. The solvent of THF was also found to quickly lithiate all starting **1** just in 5 min; however, unfortunately a large number of side-product **3** were observed (entry 6).[14,15] Then, 2.0 equiv of *n*-BuLi in toluene was reduced to 1.5 equiv and 1.2 equiv (entries 7 and 8). Both reactions efficiently furnished methyl sulfide **2** in 91% yields, and any unreacted **1** was not observed in TLC. Thus, the clean lithiation of **1** in toluene solution was proved to quickly proceed at −20 °C in 5 min, in spite of the sterically demanding carbanion.[16,17]

After determining the condition for lithiation of **1** (at −20 °C for 5 min in toluene), we examined the scope of the reactivity, by preparing a series of 1-substituted-2,3,4,5-tetrakis(*p*-methylphenyl)-6-phenylbenzenes **7**–**17** (Fig. 1). The electrophile MeSSMe listed in Table 1 completed the reaction at −20 °C for 1 h; however, at −20 °C, other electrophiles were not so easy to react with the carbanion. Actually, none of the reaction reached completion even in overnight stirring. The electronic and steric discord between reaction partners would cause the addition step sluggish. Thus, the reaction temperature at the addition step raised to ambient temperature, and the results are summarized in Table 2.[20]

At entry 1, the hexaarylbenzene derivative **7** was obtained in 91% yield through the reaction with 1,2-dibromobenzene at ambient temperature for 2 h, although the reaction at −20 °C was slug-

Table 2

Evaluation of the reactivity of the lithiated **1** with electrophiles[a]

Entry	Electrophiles	Products[b]	Yield[c] (%)	Time (h)
1	1,2-Dibromobenzene	**7**	91	2
2	Benzaldehyde	**8**	90	1
3	Pivalaldehyde	**9**	91	2
4	4-Methoxybenzoyl chloride	**10**	78	2
5	3,4,5-Trimethoxybenzoyl chloride	**11**	71	8
6[d]	Acetic anhydride	**12**	51	4
7	*N*,*N*-Dimethylformamide	**13**	82	5
8[e]	Carbon dioxide	**14**	72	2
9	Tributyltin chloride	**15**	88	2
10	Trimethylborate	**16**	26	2
11[f]	2,3-Dichloropyrazine	**17**	14	2

[a] All reactions were performed in accordance with the representative procedure in Ref. 20, unless otherwise stated.

[b] Elemental analysis data of all products showed good match.

[c] Isolated yields with silica gel column chromatography.

[d] Side-product **3** was yielded in 40%.

[e] The gaseous CO_2 was bubbled for 1 h.

[f] The solution of 2,3-dichloropyrazine in 0.5 mL THF was added.

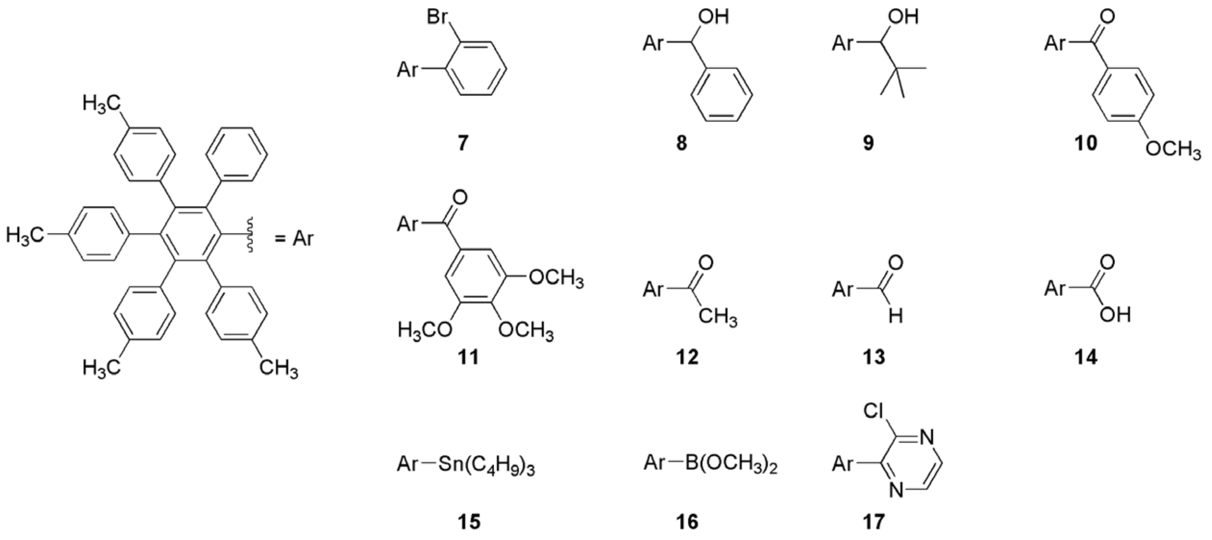

Figure 1. A series of 1-substituted-2,3,4,5-tetrakis(*p*-methylphenyl)-6-phenylbenzenes.

gish. With respect to the aldehyde, both aryl and alkyl aldehydes efficiently reacted with lithiated **1** to provide the corresponding alcohols **8** and **9** in excellent yields (entries 2 and 3). At entries 4 and 5, acid chlorides also gave target ketones **10** and **11** in good yields, while a longer reaction time was required for consuming 3,4,5-trimethoxybenzoyl chloride. This lithiation system worked in the reaction with acetic anhydride (entry 6), but the tremendous amount of **3** was produced in 40% yield.

The derivatives allowing for further functionalizations were obtained through the reactions with *N,N*-dimethylformamide and carbon dioxide (entries 7 and 8). Each electrophile furnished aldehyde **13** and carboxylic acid **14** in 82% and 72% yields, respectively. Then, the nucleophilic attack to a heteroatom, tributyltin chloride, afforded the desired tin molecule **15** in 88% yield (entry 9). On the other hand, the laborious bond-forming reactions were observed with trimethylborate, and 2,3-dichloropyrazine (entries 10 and 11).

In summary, we have developed a new procedure for leading functionalized pentaarylbenzene derivatives. The synthetic approach, which employs simple reagents **1** in toluene and *n*-BuLi, accomplished to quickly react with several electrophiles in good yields, providing novel functionalized molecules. Because of the necessity of a functionalized pentaarylbenzene moiety, we anticipate that this approach is likely to find widespread use in the field of organic materials science.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.06.111.

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12. *Synthetic procedure for the iodide* **1**: To the 100 mL flask charged with 2,3,4,5-tetrakis(*p*-methylphenyl)cyclopenta-2,4-dienone[18] (1.19 g, 2.7 mmol) under an argon atmosphere was added (iodoethynyl)benzene[19] (800 mg, 3.5 mmol) in distilled *ortho*-xylene (4.5 mL), and the mixture was refluxed for 11 h. After evaporation of the solvent, the residue was reprecipitated from $CHCl_3$/MeOH system. Purification by silica gel column chromatography with hexane/CH_2Cl_2 (2:1) as an eluent gave the desired compound **1** in 71% (1.22 g) as white solid materials. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.11 (m, 5H), 7.05–6.97 (m, 4H), 6.75–6.62 (m, 12H), 2.27 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 145.7, 145.6, 142.9, 141.5, 141.1, 141.0, 137.5, 137.4, 136.7, 135.9, 134.6, 134.5, 134.3, 130.7, 130.5, 130.3, 130.1, 127.9, 127.1, 126.4, 107.4, 21.3, 21.0 (three peaks were overlapped). MS (EI) *m/z*: 640 (M^+). Anal. Calcd for $C_{40}H_{33}I$: C, 75.00; H, 5.19. Found: C, 75.13; H, 5.16.
13. To dissolve 1 g of iodide **1** at room temperature, each solvent of $CHCl_3$, and $CHCl_2$, and THF required 11 mL, and 6.6 mL, and 17 mL, respectively. On the other hand, in the case of iodide **4**, each solvent of $CHCl_3$, and $CHCl_2$, and THF required 105 mL, and 88 mL, and 99 mL, respectively.
14. We attributed this annoying side-product **3** to a partial protonation of the lithio intermediate by THF; see Ref. 15.
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20. *Representative experimental procedure for Table 2, entry 9, compound* **15**: To a solution of **1** (256 mg, 0.4 mmol) in anhydrous toluene (6 mL) at −20 °C was added *n*-BuLi (0.48 mmol, 1.6 M in hexane) dropwise over 5 min, and the solution was stirred for 5 min. The electrophile of tributyltin chloride (0.16 mL, 0.6 mmol) was slowly added over 5 min, and the mixture was allowed to warm to ambient temperature, and stirred for 2 h. After the reaction was quenched with methanol (3 mL), the solvent was evaporated. The resultant residue was purified by silica gel column chromatography with hexane/CH_2Cl_2 (4:1) as an eluent to give the desired compound **15** in 88% yield (284 mg) as white powders. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.08 (m, 5H), 7.04 (d, $J = 8.2$ Hz, 2H), 6.92 (d, $J = 8.2$ Hz, 2H), 6.75–6.70 (m, 6H), 6.65–6.60 (m, 6H), 2.26 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 1.18–1.06 (m, 12H), 0.80 (t, $J = 7.1$ Hz, 9H), 0.13–0.08 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 144.7, 143.1, 141.8, 141.7, 140.1, 139.9, 138.3, 138.2, 138.0, 135.6, 134.13, 134.11, 134.07, 131.5, 131.3, 131.23, 131.20, 131.0, 128.0, 127.3, 127.15, 127.13, 126.2, 29.3, 27.4, 21.3, 21.2, 13.7, 11.9. MS (ESI) *m/z*: 827 ($[M+Na]^+$). Anal. Calcd for $C_{52}H_{60}Sn$: C, 77.71; H, 7.52. Found: C, 77.76; H, 7.43.