This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Selective I/Mg exchange reactions of 1,4-diiodo-1,3-dienes and o-iodo-2-(2-iodovinyl)benzenes were achieved via PrMgCl•LiCl. Various 1-iodo-4-MgCl-1,3-dienes and 1-iodovinyl phenylmagnesium chlorides were thus efficiently generated and synthetically applied to afford new C-C bonds via reactions of the alkenyl or aryl C-MgCl bonds with different electrophiles. Useful conjugated compounds including polysubstituted benzenes, naphthalenes and phosphine compounds could be synthesized readily via further applications of the remaining alkenyl C-I-bond and subsequent cyclization reactions.
Results and Discussion

Selective mono I/Mg exchange reactions of 1,4-diiodo-1,3-dienes (1a) and o-iodo-2-(2-iodovinyl)benzenes (1b): We first chose the tetraethyl 1,4-diiodo-1,3-diene 1a to react with PrMgCl·LiCl in THF at room temperature. Results are shown in Scheme 2. It was found that this mono I/Mg exchange reaction could selectively afford the desired 1-iodo-4-magnesia-1,3-diene IIa, which upon hydrolysis gave its corresponding mono iodide IIa. The undesired dimagnesia-1,3-diene IIa was not generated in most cases. With 1 or 2 equivalents of the Knochel reagent, compound 1a could be obtained in moderate to good yields, but remarkable amounts of diiodide 1a remained unreacted, even after 6 h (entry 4). This observation indicated that this I/Mg exchange reaction was slow. With 4 equivalents of PrMgCl·LiCl, the reaction completed after 6 h, affording the product 2a1 in 75% isolated yield after hydrolysis (entry 6).

For the I/Mg exchange reaction of o-iodo-2-(2-iodovinyl)benzenes 1b with the Knochel reagent, the reaction exchange rate was found to be faster than that of 1,4-diiodo-1,3-dienes 1a. As shown in Scheme 3, the I/Mg exchange reaction of 1b1 with the Knochel reagent would generate Ib1, Ib1’ and Ibb. However, no formation of the product 2b1’ was detected in all cases, which indicated that the alkenyl C-I bond did not undergo the I/Mg exchange reaction. The aryl C-I bond was selectively magnesiated. This high selectivity is probably because the aryl C-I bond is more reactive than the alkenyl C-I bond in the I/Mg exchange reaction and the possible transition state is considered resembling hypervalent halogen complex, for which aryl ring could provide more stabilization to the transition state than alkenyl via delocalization of the charge on halogen.[9] With 2 equivalents of PrMgCl·LiCl, the reaction of 1b1 completed after 3 h, affording the product 2b1 in 77% isolated yield after hydrolysis.

<table>
<thead>
<tr>
<th>entry</th>
<th>x</th>
<th>y</th>
<th>2b1</th>
<th>3b1</th>
<th>1b1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>1</td>
<td>26</td>
<td>0</td>
<td>69</td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>1</td>
<td>39</td>
<td>0</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>3</td>
<td>65</td>
<td>&lt;5</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>2.0</td>
<td>6</td>
<td>67</td>
<td>&lt;5</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>4.0</td>
<td>1</td>
<td>72</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>6</td>
<td>4.0</td>
<td>6</td>
<td>95(77)</td>
<td>&lt;5</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

* GC yields. Isolated yields are given in parentheses.

Scheme 2. I/Mg exchange reaction conditions of 1,4-diiodo-1,3-diene 1a.

Scheme 3. I/Mg exchange reaction conditions of o-iodo-2-(2-iodovinyl)benzene 1b1.
Scheme 4. In situ generation of 1-iodo-4-magnesia-1,3-dienes 1a and their reactions with electrophiles

Reactions of in situ generated 1-iodo-4-MgCl-1,3-dienes 1a and 1-iodovinyl phenylmagnesium chlorides Ib with electrophiles: New C-C bonds were highly efficiently generated when the in situ generated 1-iodo-4-MgCl-1,3-dienes 1a and 1-iodovinyl phenylmagnesium chlorides Ib were treated with electrophiles, such as allyl bromide and carbon dioxide (Schemes 4 and 5). In addition, the C-MgCl bond could be easily transformed to the C-B bond in high yields when treated with isopropoxyboronic acid pinacol ester.

Scheme 5. In situ generation of 1-iodovinyl phenylmagnesium chlorides Ib and their reactions with electrophiles

Intramolecular Heck reaction of 1-iodo-1,3-diene analogues: As shown in Scheme 6, 1-iodo-1,3-butadiene analogues 4a and 5a were tested in the intramolecular Heck reaction. Pentasubstituted benzenes 8a were obtained in high yields via an intramolecular Heck reaction and a subsequent aromatization step. For 5a with an extra methyl group in the allyl unit, cycloheptatriene products 9a, other than the benzene-type products 8a, were generated in high yields. Cycloheptatrienes are useful and structurally interesting compounds. This synthetic method offered a new way to build such polysubstituted cycloheptatrienes.
As given in Scheme 7, compound 4b could also be converted into their corresponding polysubstituted naphthalenes 8b readily in high yields via a similar intramolecular Heck reaction and a subsequent aromatization step. It should be noted that these polysubstituted benzenes 8a and naphthalenes 8b are very difficult to synthesize by other methods.[12] However, when we chose the compound 5b1 with an extra methyl group to go through this Heck reaction under the same condition, a novel compound 9b1 containing a bicyclo[4.1.0] ring was obtained in a moderate yield (Scheme 7). Similarly, when the compound 5b2 was used, the product 9b2 was obtained in 70% isolated yield.

A proposed mechanism is shown in Scheme 7. After the oxidative addition of palladium and the subsequent intramolecular alkene insertion, the pivotal intermediate III was generated. When intermediate III had a β-hydrogen atom (R = H), the β-hydride elimination could happen to give naphthalene product 8b after aromatization. When there was no β-hydrogen atom (R = Me) in intermediate III, no β-hydride elimination could happen. In this situation, the intermediate III would go through the second intramolecular alkene insertion to offer the intermediate IV. Since the intermediate IV had syn-β hydrogens, thus the subsequent β-hydride elimination of IV would happen and lead to the final products 9b1.

Recently, reductive elimination of alkyl halides from alkylpalladium halide species without β-hydrogens has attracted much attention.[13,14] However, in our cases (R = Me), no corresponding C(sp³)-I reductive elimination product was observed, indicating that the intramolecular alkene insertion was more favored than C(sp³)-I reductive elimination.

Synthesis of functionalized phosphine compound starting from 1-iodo-1,3-diene analogues: As further demonstration of the synthetic utility of designed compounds containing one C-I bond and one C-M bond in the same molecule, we synthesized the phosphine compound 10 from 6b2 and Ph3P in 73% isolated yield (Scheme 8). The structure of 10 was confirmed by single crystal X-ray structural analysis (Figure 1).

Scheme 6. Intramolecular Heck reaction of allyl 1-iodo-1,3-diene derivatives.

Scheme 7. Intramolecular Heck reaction of allyl 2-iodovinylbenzene derivatives.

Scheme 8. Synthesis of phosphine ligands.
Conclusions

In summary, we have reported herein the I/Mg exchange reactions of 1,4-diiodo-1,3-dienes 1a and o-iodo-2-(2-iodovinyl)benzenes 1b and their synthetic applications. The reactions efficiently afforded diverse 1-iodo-4-magnesia-1,3-dienes and 1-iodovinyl phenylmagnesium chlorides in situ. After quenched with different electrophiles, various functionalized derivatives were obtained. Most of the reactions were under mild conditions. By taking advantage of the rich reactivity of the derivatives, useful conjugated compounds including polysubstituted benzenes, naphthalenes and phosphine compounds could be synthesized readily via the subsequent cross-coupling reactions.

Acknowledgements

This work was supported by the 973 Program (2012CB821600) and the National Natural Science Foundation of China (NSFC).

Notes and references


1 For a recent review of 1,4-diiodo-1,3-dienes, see: V. P. Ananikov, O. V. Hazipov and I. P. Beletskaya, Chem. Asian J., 2011, 6, 306.


