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Unique reactivity of a 1,4-dilithiobutadiene with methyl iodide

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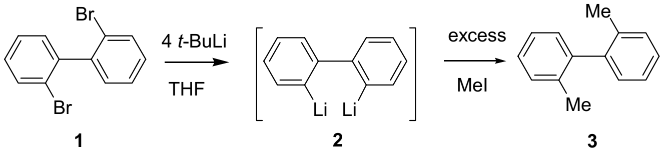
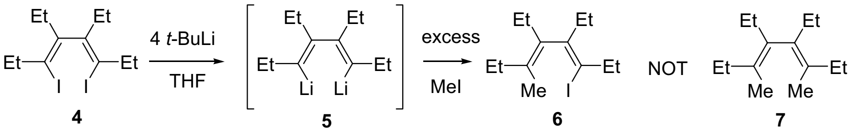
Abstract—Reactions of 1,4-dilithiobutadiene **5** with MeI in THF gave predominantly methyl iododiene **6**. Monolithio monoiodo intermediate **8** was shown not to be involved in the formation of **6**, but the results were consistent with the involvement of monolithio monomethyl intermediate **11**, which could lead to **6** by metal–halogen exchange. Several other lithioalkenes also reacted with MeI to give alkenyl iodides.

1,4-Dilithiobutadienes are of considerable theoretical interest,[1] and their unique reactivity has recently been studied for synthetic applications.[2] 1,4-Dimetallobutadienes have also been widely used for preparing siloles and other metalloles.[3] In the course of using 1,4-dilithiobutadienes for the preparation of siloles, we attempted to characterize these intermediates by trapping reactions. When dibromide **1**[4a] and diiodide **4**[4b,c] were each treated with *t*-BuLi in THF (to generate the corresponding dilithio compounds, **2** and **5**), followed by Me_3SiCl/Et_3N,[5] siloles were formed instead of the expected disilylated compounds.[6] We therefore investigated the reactions with MeI. In the case of dibromide **1**, the expected dimethylated compound **3**[7] was obtained in 87% yield (Eq. 1). However, in the case of diiodide **4**, there was no evidence for the analogous dimethylated diene (**7**). Instead, the methyl iododiene **6**[7] was obtained in 81–87% yields (Eq. 2).

The reaction of **5** with MeI (in THF, ca. −60 °C→rt) was carried out a number of times. In some cases, especially when only ca. 2 equiv of MeI was used, significant amounts of compounds **9** (below) and **10**[8] were formed in addition to **6**.[9] A series of reactions in which excess MeI was added at various temperatures showed little reaction after 10 min at −70 °C (major product after



(1)



(2)

Keywords: Alkenyllithium; Dilithiobutadiene; Methyl iodide; Metal–halogen exchange.

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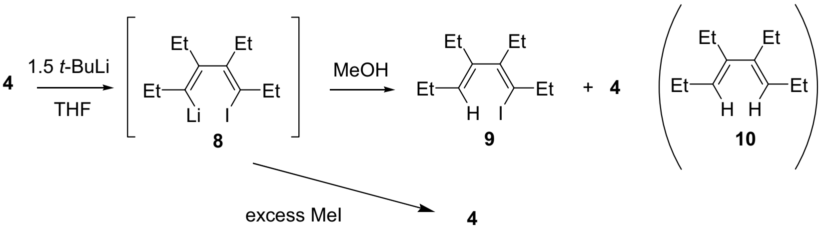
workup was diene **10**), and significant reaction at −30 °C (1:1 ratio of **6**:**10**).[10] Monomethyldiene **12** (see below) was not observed.

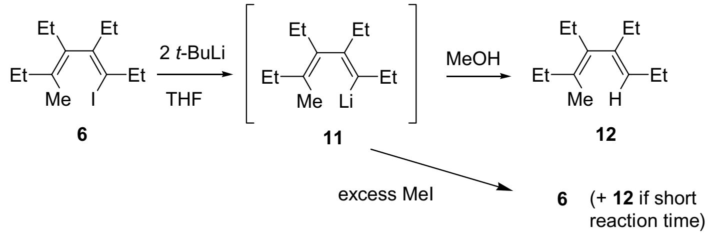
In order to learn more about this reaction, we generated the monolithio intermediates **8** and **11**, and treated them with MeI. Intermediate **8** was generated by treating diiodide **4** with 1.5 equiv of *t*-BuLi; quenching with MeOH gave the monoiododiene **9** as the major product, along with some of the starting diiodide, and a small amount of diene **10** (Eq. 3) (GC areas: **9**:**4**:**10** = 48:34:6; molar ratio by ^{1}H NMR **9**:**4**:**10** = 63:32:5). Column chromatography gave monoiododiene **9**[7] in 49% yield, and some recovered diiodide **4** (16%). When intermediate **8** was generated as above, and then treated with excess MeI, the major product was diiodide **4** (Eq. 4) (90% crude yield, 87% pure by GC).[11] This result shows that **8** is not an important precursor to methyl iododiene **6**.



(3)

(4)

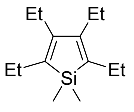
Monolithio intermediate **11** was generated by treating compound **6** with *t*-BuLi (2 equiv). Quenching with MeOH gave monomethyldiene **12**[7] (Eq. 5) (63% after chromatography). When intermediate **11** was treated with excess MeI, the major product was methyl iododiene **6** (Eq. 6). (GC areas of the crude product were 87% **6** and 5% **12**; column chromatography gave **6** in 71% yield.) These results demonstrate that lithio methyldiene **11** could be a precursor to methyl iododiene **6** in Eq. 2.



(5)

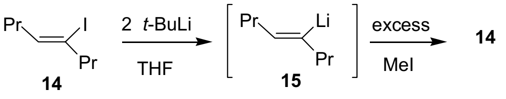
(6)

The relative reactivity of MeI and Me_3SiCl to the dilithiodiene **5** (generated from diiodide **4**) was determined. When **4** was treated with *t*-BuLi (in THF) followed by (1) excess Me_3SiCl/Et_3N (ca. −64 °C, 10 min) and (2) excess MeI (at −63 °C, and then warmed to rt), methyl iododiene **6** was the major product, with none of the silole **13** (see Ref. 6) (or a bis(trimethylsilyl) diene) observed. These results show that MeI is more reactive to the dilithiodiene intermediate **5** than is Me_3SiCl.



13

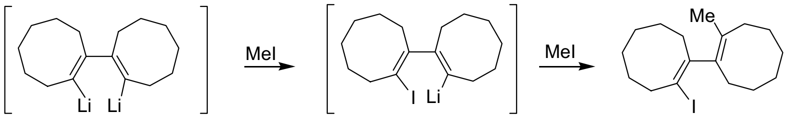
The reactions of vinyllithium reagents with MeI to give methyl-substituted alkenes are well known,[12,13] and there are also reports of such reactants giving alkenyl iodides.[13b,14] Neumann and Seebach found that the product ratio can depend on solvent and on the number of equivalents of MeI, and interpreted the results in terms of a fast reversible metal–halogen exchange between the alkenyllithium and the MeI.[13b] We decided to study the reaction of a simple monolithioalkene with MeI using our conditions. Iodoalkene **14**[15] (*Z*:*E* 93:7, by ^{1}H NMR) was treated with *t*-BuLi in THF (Eq. 7). GC analysis of an aliquot (aqueous workup) showed the absence of **14**, and the major component (98%), having a GC retention time very similar to the original starting material 4-octyne, presumably *trans*-4-octene. Excess MeI was added to the reaction mixture, and after workup, GC analysis of the crude sample showed **14** to be the major product (89% of GC area). Iodide **14** was isolated by Kugelrohr distillation in 80% yield with a GC purity of 93%. ^{1}H and ^{13}C NMR, and GC/MS analyses also showed the presence of the *E* isomer (*Z*:*E* = 93:7 by ^{1}H NMR). As expected, the *Z*:*E* ratio was essentially identical to that of the starting iodide.



(7)

We have found one example of the reaction of a 1,4-dilithiobutadiene with MeI (Eq. 8).[16] The dilithio intermediate **16** (in Et_2O), generated from cyclooctyne and

Li, was treated with excess MeI to give the iodo- and methyl-substituted product **18** in 28% yield, while the dimethyl-substituted product was not observed. Formation of MeLi was postulated based on detection of Me_4Si when Me_3SiCl was added to the reaction mixture, and the reaction was suggested to involve lithio iododiene intermediate **17**.[16] Based on our results, the involvement of **17** is unlikely.



16 **17** **18** (8)

The simplest explanation of our results[17] is that the dilithio intermediate **5** reacts with MeI by initial C-alkylation to give monolithio intermediate **11**, and that this undergoes metal–halogen exchange with MeI to give methyl iododiene **6**. The reverse process (metal–halogen exchange followed by alkylation) is ruled out, since monolithium intermediate **8** was shown to not be a precursor to **6**. The reactions in which conversion to **6** is incomplete suggest that **11** reacts faster with MeI than does **5**. Dilithio intermediates such as **5** are believed to have a bridged structure, and to be somewhat stabilized,[1] but we are unaware of reactivity comparisons between them and simple monolithio intermediates. It is noteworthy that all of the monolithio alkenes we studied (**8**, **11**, and **13**) react with MeI under these conditions to give iodides, and only the dilithio compound **5** undergoes alkylation. This is further evidence for the unique reactivity of the 1,4-dilithiobutadienes.

Acknowledgements

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Supplementary data

The experimental procedure for methyl iododiene **6**, and ^{1}H and ^{13}C NMR spectra for **6** and **12** are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.03.067.

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5. We often use mixtures of Me_3SiCl with Et_3N for quenching reactions. Et_3N reacts with (and precipitates) traces of HCl in the chlorosilane, and minimizes hydrolysis during aqueous workup.
6. Hudrlik, P. F.; Dai, D.; Hudrlik, A. M. *J. Organomet. Chem.* **2006**, *691*, 1257–1264.
7. Compound **3**, methyl iododiene **6**, monoiododiene **9**, and monomethyldiene **12** were identified by their IR, ^{1}H NMR, ^{13}C NMR (with DEPT), and mass spectra. The ^{1}H and ^{13}C NMR spectra of **3**[18] and **9**[19] were consistent with those reported.
8. A sample of diene **10**[20] was prepared by treatment of diiodide **4** in THF with *t*-BuLi (4 mol per mol of **4**) followed by hydrolysis.
9. GC areas: **6**:**10**:**9** = 65.5:16:7; assignments confirmed by GC and GC/MS comparisons with the previously prepared samples; molar ratio by ^{1}H NMR: **6**:**10**:**9** = 76:15:9. No evidence for the monomethyldiene **12** was obtained.
10. By GC and ^{1}H NMR; a small peak at the retention time of monoiododiene **9** (3%) was also observed by GC, but negligible amount (<0.2%) at that of the monomethyldiene **12**.
11. Small GC peaks corresponding to monoiododiene **9** (3%) and methyl iododiene **6** (5%) were also visible, with no significant peaks (>0.2%) for **10** or **12**. In a separate experiment, GC analysis of an aliquot (before addition of MeI) worked up with water showed considerable amounts of monoiododiene **9** as well as diiodide **4**, with a smaller amount of diene **10** (GC ratio **9**:**4**:**10** = 21:48:15). Excess MeI was added to the reaction mixture, and after workup, GC analysis showed diiodide **4** to be the major product (72% of GC area). Small peaks corresponding in retention time to **9** (4%), methyl iododiene **6** (7.5%) and monomethyldiene **12** (1%) were also visible.
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17. The difference between the reactions of the dilithio biphenyl intermediate **2** and diene intermediate **5** is consistent with the pK_a's of ethylene and methane (which are similar) compared to the lower pK_a of benzene.
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