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Preliminary communication

Reversibility of the lithiation of η^6-naphthalenetricarbonylchromium

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Abstract

The lithiation of naphthalenetricarbonylchromium with n-BuLi or tetramethylpiperidyllithium is under kinetic control, and with the latter reagent is highly regioselective in the 2-position. Addition of isopropylamine renders the process reversible, and an approximately 1/1 equilibrium mixture of 1- and 2-substitution product is formed.

Electrophilic aromatic substitution via lithiation of arenes complexed to the $Cr(CO)_3$ fragment offers a mild and selective method for the introduction of functional groups into the arene and is increasingly used in synthesis [1–7]. We recently demonstrated that the regioselectivity of the lithiation of naphthalene-$Cr(CO)_3$ (**1**) is subject to pronounced steric effects. While the sequential reaction of n-BuLi and electrophiles yielded 1- and 2-substituted naphthalene complexes in the ratio of 3/7, the latter were formed exclusively and in high yields when the sterically more demanding base tetramethylpiperidyllithium (TMPLi) was used [8]. Here we report on the initial results of an investigation of kinetic versus thermodynamic control in the deprotonation step and of equilibration of a kinetically formed lithiation product. The results presented refer only to complex **1**, and are presented now in reference to a recent article concerned with the same problem [9].

Lithiation of **1** by n-BuLi in THF is under kinetic control. Addition of solid **1** to a −78°C THF solution of n-BuLi (1 molar equivalent) resulted in fast and quantitative deprotonation. Samples were removed periodically via a cooled (−78°C) transfer tube and added to a THF solution of an excess of $ClSiMe_3$ at the

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* Reference numbers with asterisks indicate notes in the list of references.

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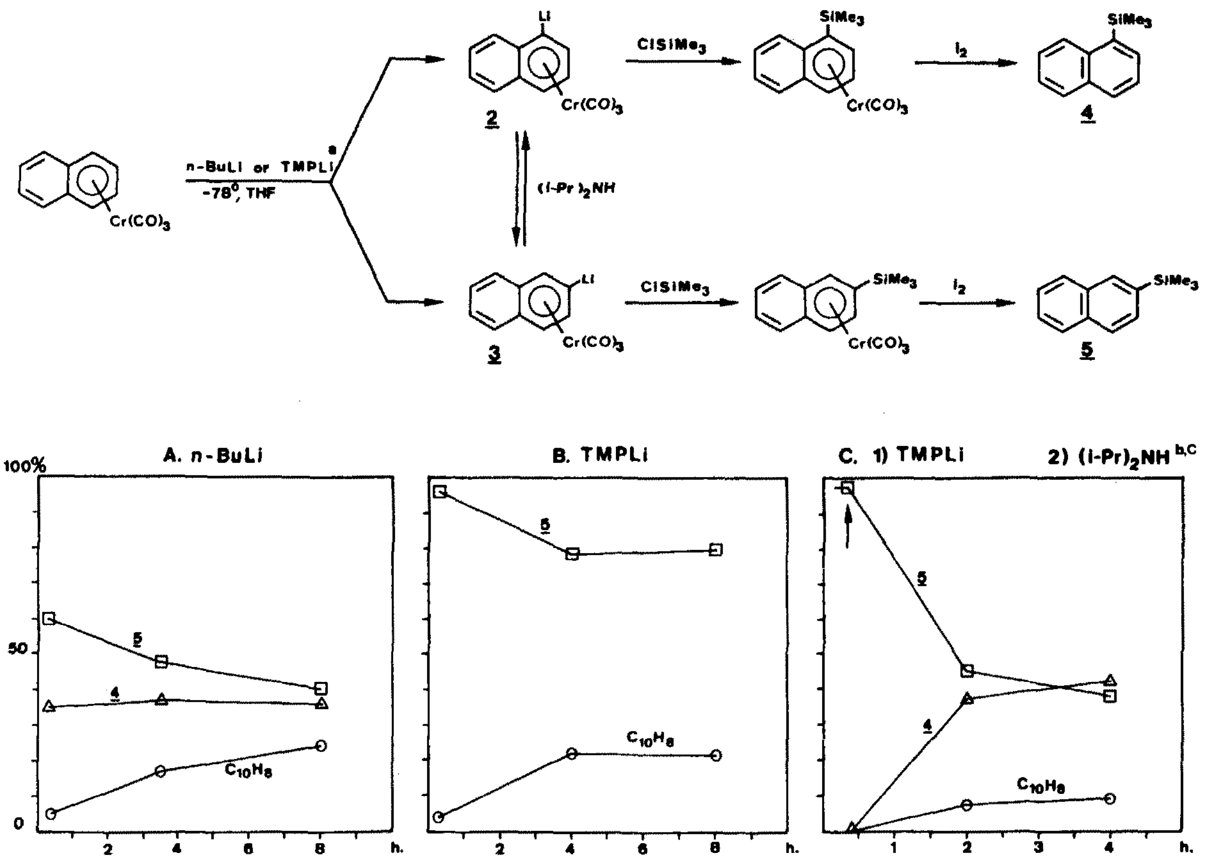

Fig. 1. Reversibility in the lithiation of naphthalene-Cr(CO)$_3$ (1). Trapping with ClSiMe$_3$. Ordinates represent GC yields (int. standard: decalin; calibration with independently synthesized products) of naphthalene and trimethylsilylnaphthalenes 4 and 5. The abscissa indicates the time (in h) during which the solutions containing 2 and/or 3 were stirred at −78°C prior to reaction with ClSiMe$_3$. (a) TMPLi deprotonated selectively in the 2-position. (b) The arrow indicates the addition of isopropylamine. (c) The difference between the sum of the plotted yields and 100% is due to a fourth product (1,3-(SiMe$_3$)$_2$C$_{10}$H$_6$ (3–10%)), which arises from sequential lithiation/electrophile trapping [8]. Its formation here can be traced back to a small excess (10%) of TMPLi used in this particular experiment.

same temperature [10 *]. Subsequent treatment of the solution with an excess of iodine yielded the decomplexed naphthalenes and quantitative GC analysis furnished the data shown graphically in the Fig. 1 [11 *]. The initially observed ratio (37/63) of the lithiated naphthalene complexes **2** and **3** in the mixture clearly changes with time, but the data show this to be due to the decay of the 2-Li intermediate **3** and not to a rearrangement. Naphthalene [14 *] is thus formed at the expense of the 2-substituted product. Presumably this occurs by proton abstraction from the solvent. It is important to note that no significant change in the concentration of the 1-substituted isomer is observed under these conditions.

When TMPLi was used in the deprotonation (1 equiv.), the 2-substituted product was formed in 96% yield (GC) at −78° C [15 *]. Slow decay was noticed in some reactions at this temperature with, as in the reactions with n-BuLi, naphthalene being the only product. Thus, again, no deprotonation of H-C(1) was observed with time. One set of data is shown in Fig. 1. The data, at this point, did not allow for a differentiation between an irreversible or a reversible deprotonation step in the TMPLi reaction. An additional qualitative experiment removed this ambiguity. $(\eta^6\text{-}C_{10}D_8)Cr(CO)_3$ [8] was treated with 0.5 mol equivalents of TMPLi and to the solution was added TMPH (4 equiv.), followed, after 2 h at −78° C, by $ClSiMe_3$. ^1H NMR analysis of the mixture of complexes showed that no significant incorporation [16 *] of H into the 1 position of the deuterio-naphthalene or the deuterio-trimethylsilylnaphthalene complex had occurred. This would have been expected, even assuming the operation of a primary isotope effect, if the lithiation had been reversible. We take this result to be a strong indication that lithiation of **1** by TMPLI at −78° C is under kinetic control. This finding is supported by recently published quantitative data on acidities of several arenetricarbonylchromium complexes [17] that show the pK_a for benzene-$Cr(CO)_3$ to be 34.8. The value for TMPH is 37.3 [18]. The high regioselectivity is therefore due to the higher accessibility of H-C(2). When H-C(2) is not available, TMPLi does react readily with H-C(1); this was shown by the formation of $1\text{-}4a,8a\text{-}\eta\text{-}[1,3\text{-}(SiMe_3)_2C_{10}H_6]Cr(CO)_3$ when a twofold excess of TMPLi was used, and the mixture then treated with $ClSiMe_3$ [8].

In the presence of the more acidic isopropylamine (pK_a 35.7) [19], the behaviour of the intermediates is different. This is readily seen from the data in Fig. 1. Addition of 1 mol equivalent of isopropylamine to a solution of the 2-lithio complex **3**, prepared from **1** and TMPLi (98% yield (GC)), resulted in the rearrangement **3** → **2** (Fig. 1). After ca. 2 h the mixture, as indicated by the proportions of 1- and 2-$SiMe_3$-naphthalene after usual work-up, contained roughly equal amounts of **2** and **3**. No further increase in the amount of **2** was observed after this time, and the ca. 1/1 (52/48) mixture thus probably represents the equilibrium situation [20*] between **2**, **3** and diisopropylamine [21*]. The proportions of **2** and **3** did continue to change, slowly at −78° C and much faster at higher temperatures, but GC analysis showed this to be the result of the faster rate of decay of **3** than of **2**.

We conclude that, as we previously indicated [8], the regioselective electrophilic substitution at C(2) of naphthalene is readily achieved in high yield via kinetic deprotonation of complex **1** with TMPLi. The results presented here demonstrate that reversibility of the lithiation can be induced by the addition of diisopropylamine and that an equilibrium is reached. Attempts to change the equilibrium ratio significantly in favor of the 1-isomer **2** [22*] by changing reaction conditions while maintaining high yields have had only marginal success to date.

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10 See ref. 8 for isolation and characterization of the resulting complexes.

11 The $Cr(CO)_3$ group was removed by oxidation with I_2. Concentration of the THF solution was followed by addition of ether and washing with a saturated aq. $NaHSO_3$ solution and water. Control experiments with independently synthesized 1- and 2-$SiMe_3$-naphthalenes [12] showed the products to be inert under these conditions. Decalin was used as internal standard in the GC analysis and concentrations were calculated from calibration curves obtained from pure materials.

12 1- and 2-$SiMe_3$-naphthalenes [13] (**4** and **5**) were synthesized in 78 and 98% yields via lithiation (n-BuLi/THF/−78 °C) of the corresponding bromides, followed by reaction with $ClSiMe_3$.

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14 No attempt was made to detect the intermediates in the overall sequence from complex **3** to free naphthalene.

15 GC analysis of a sample, taken after 0.3 h at −78 °C and treated as described above [11], showed a 96% yield of 2-$SiMe_3$-naphthalene.

16 The deuterionaphthalene used was 98% D. The ^{1}H NMR spectrum showed no detectable increase in H(Ar) after the reaction. The products therefore consist entirely of 2-trimethylsilylnaphthalene-d_7 (42% by GC) and naphthalene-d_8 (58% by GC).

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20 The reaction was carried out several times. The rate of naphthalene formation varied somewhat from run to run (always at the expense of the thermally less stable product **3**). Equilibrium was always reached after ca. 2 h and ratios of **3** to **2** were in the range 45/55 (±5) (combined yields (GC) of **4** and **5**: > 80%. A 2/3 ratio of (2-methylnaphthalene)- and (1-methylnaphthalene)-tricarbonylchromium (34% yield) was also obtained by Treichel and Kirss [9] on treating **1** with 4 equivalents of LDA at −95 °C for 10 h followed by trapping with CH_3I.

21 No attempts were made to determine the equilibrium between **2**, **3** and diisopropylamine but the high yield of trapped **2** and **3** indicate the equilibrium to be far on the side of the lithiated complexes. It is noteworthy that diethylamine protonated **3** quantitatively in < 10 min at −78 °C.

22 The conclusion to this effect in a recent publication [9] was based on arguments which failed to take account of the mass balance of the reaction, and must thus be reevaluated in the light of the results described here.