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No-D NMR Study of the Pathway for *n*-BuLi “Oxidation” of 1,5-Cyclooctadiene to Dilithium Cyclooctatetraene Dianion [Li_2COT^{2-}]

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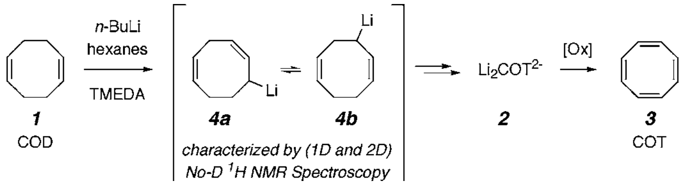
ABSTRACT



The transformation of 1,5-cyclooctadiene (1) into cyclooctatetraene (3) by way of dianion 2 is an interesting reaction of considerable preparative value. The mechanism was initially suggested to involve lithium hydride loss from 4a/4b, followed by two deprotonations to produce 2. This No-D ^{1}H NMR study indicates the long-term stability of 4a/4b (in the absence of additional *n*-BuLi) and suggests a different mechanistic sequence, in which 4a/4b is deprotonated a second time prior to LiH ejection.

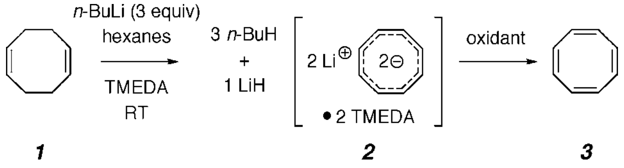
Gausing and Wilke first reported (Scheme 1) the reaction of 1,5-cyclodiene (COD, **1**) with 3 equiv of *n*-butyllithium (*n*-BuLi) and tetramethylethylenediamine (TMEDA) to produce dilithium cyclooctatetraene dianion (as its TMEDA complex: $Li_2COT{\cdot}TMEDA_2$, **2**).[1] The efficient subsequent oxidation of dianion **2** to cyclooctatetraene (COT, **3**) is of considerable preparative value (45−65%) and continuing interest[2] and has been effected by a variety of oxidants.

Formally, the remarkable transformation of **1** to **2** is the net result of loss from **1** of three protons and one lithium hydride. The order of these events is open to discussion.

Gausing and Wilke proposed that this reaction proceeded by way of triene **5** or **6** (Scheme 2), either of which could form by lithium hydride ejection from an initially generated allylic monolithiated species **4**. In principle, **5** or **6** could undergo two additional deprotonations to give, first, the heptatrienyllithium anion **8** and, in turn, **2**. In fact, they demonstrated that while **6** did not proceed on to **2** under the action of *n*-BuLi/TMEDA,[3] **5** did.

An alternative sequence for proceeding from **4** to **8** involves a second lithiation of **4** to generate one or both of the nonconjugated or conjugated dilithiohexadienyl dianions

Scheme 1



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(1) Gausing, W.; Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 371−372; *Angew. Chem.* **1978**, *90*, 380−381.

(2) In addition to oxygen (ref 1), oxidants used include: (a) $CdCl_2$, $ZnCl_2$, $CoCl_2$, $NiCl_2$, CuCl, $SnCl_4$: Antkowiak, T. A.; Shechter, H. *J. Am. Chem. Soc.* **1972**, *94*, 5361−5366. (b) $HgCl_2$: Burton, N. C.; Cloke, F. G. N.; Joseph, S. C. P.; Karamallakis, M.; Sameh, A. A. *J. Organomet. Chem.* **1993**, *462*, 39−43. Wetzel, T. G.; Dehnen, S.; Roesky, P. W. *Organometallics* **1999**, *18*, 3835−3842. (c) I_2: Simons, L. H.; Lagowski, J. J. *Tetrahedron Lett.* **2002**, *43*, 1771−1773. (d) $(t\text{-BuO})_2$: Gottfriedsen, J.; Miloslavinia, A.; Edelmann, F. T. *Tetrahedron Lett.* **2004**, *45*, 3583−3584.

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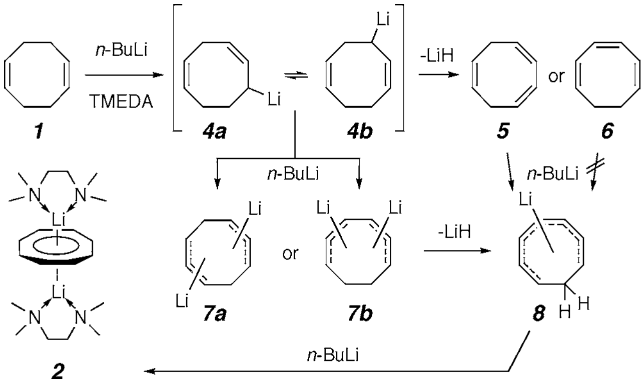
Scheme 2



7a or **7b** followed by the lithium hydride ejection event. This seemed to us a more likely course, considering that (i) there is no obvious driving force for monolithiated **4** to lose lithium hydride and (ii) the higher electron density in the dianion **7** might well serve as such an impetus.

We have used No-D NMR spectroscopy[4] to probe the conversion of **1** to **2**. In a typical experiment, 3 equiv each of TMEDA and *n*-BuLi in hexanes (~2.4 M) was added at room temperature to a solution of COD (**1**) in hexanes so that the final concentration of **1** was ~0.5 M. In most runs (including those for all of the spectra shown below), the reaction vessel was a 5 mm NMR tube. A series of No-D NMR spectra were recorded to monitor and thereby define certain aspects of the course of the reaction. For example, the half-life for consumption of COD ([**1**] = 0.5 M in the presence of 3.3 equiv of *n*-BuLi and TMEDA) is ~60 min. Most of **2** that is produced in the reaction precipitates from the reaction solution. This does not preclude spectral acquisition; samples were shimmed using the “shimming using the spectrum” protocol described earlier.[4a]

Shown in Figure 1 is a set of spectra recorded for an experiment in which 1 equiv (rather than 3 equiv) each of *n*-BuLi and TMEDA was used. Under these conditions of incomplete formation of Li_2COT^{2-}, better quality spectra were obtainable. The intermediacy of the monolithiated 1,5-COD (**4**) is clear from interpretation of the resonances for the unsymmetrical species produced. The spectral assignments indicated in the expansions [Figure 1, panels b and c] were made on the basis of analysis of the coupling patterns [including even allylic couplings with J = 1.6 Hz (cf.

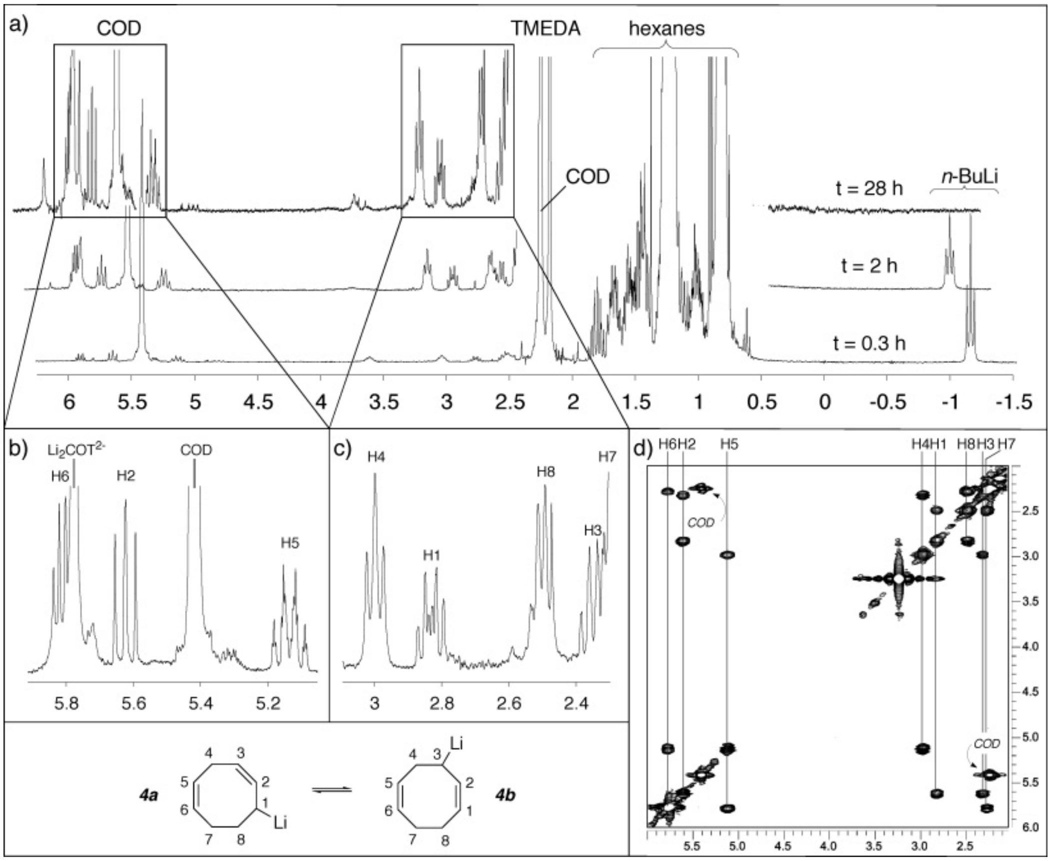


Figure 1. No-D ^{1}H NMR spectra (one-dimensional and gCOSY) of the reaction mixture during lithiation of 1,5-cyclooctadiene (**1**) by *n*-BuLi in TMEDA and hexanes. For all spectra shown, starting [COD] = 0.5 M + 1.0 equiv each of *n*-BuLi and TMEDA in hexanes at 20 °C. Panel a: Spectra showing the time course of reaction progress during the formation of monolithiated 1,5-cyclooctadiene (**4**). Panel b: Expansion of the 28 h spectrum showing resonances for H2, H5, and H6 in **4** (as well as **2** plus unconverted **1**). Panel c: Expansion of the 28 h spectrum showing resonances for H1, H3, H4, H7, and H8 in **4**. Panel d: No-D/gCOSY spectrum of **4**.

resonance for H5 at δ 5.14 ppm)] and relative chemical shifts. These assignments were then confirmed by a gCOSY experiment [Figure 1, panel d], which also demonstrates the feasibility of collecting quality two-dimensional (2D) NMR data sets for spectra recorded in unlocked mode (2D/No-D), in this case over the course of ~5 min.[5] The resonance for the H7 methylene protons (δ 2.31) is largely buried by the COD allylic methylene protons but is clearly discernible in the gCOSY spectrum. Finally, the Li_2COT^{2-} (**2**) remaining in solution is evident from the singlet at δ 5.75 ppm. That this resonance arises from **2** and not neutral COT (**3**) itself[6] was confirmed by the fact that protonation (dilute HCl) of the reaction slurry under nitrogen gave rise to a mixture of the trienes **5** and **6** (~1:2) containing only a trace of COT (**3**) (NMR and GC-MS).

The persistence of intermediate **4** argues against the originally suggested pathway (cf. Scheme 2), wherein its conversion to **5** would need to have been both fast and highly regioselective (because, as Gausing and Wilke showed, **6** enters into anionic oligomerization when independently treated with *n*-BuLi). We propose, therefore, that the most likely mechanistic pathway is via one of the dilithio species **7a** or **7b**, in which increased electron density is at least partially responsible for an enhanced rate of lithium hydride loss. Finally, this study demonstrates that No-D ^{1}H NMR spectroscopy is an effective and easily applied tool that can provide otherwise difficult to obtain mechanistic insight.

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Supporting Information Available: Experimental protocol for preparing and monitoring the reaction on either a small (NMR tube) or large (conventional flask) scale and full page version of the spectra in Figure 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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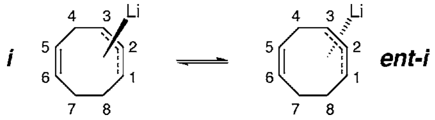
(3) Higher molecular weight hydrocarbons were formed, presumably initiated by addition of *n*-BuLi to the conjugated triene in **6** and further carried by oligomerization. In a related experiment, we treated 1,3-cyclooctadiene (COD) with 1 equiv each of *n*-BuLi/hexanes and TMEDA at ambient temperature. TMS−Cl was added to the resulting slurry. GC-MS analysis provided evidence for COD−TMS, *n*-Bu−COE*−TMS, COD−COE−TMS (*COE = cyclooctene). This suggests that *n*-BuLi undergoes competitive allylic deprotonation of and addition to 1,3-COD under these conditions.

(4) (a) Hoye, T. R.; Eklov, B. M.; Ryba, T. D.; Voloshin, M.; Yao, L. J. *Org. Lett.* **2004**, *6*, 953−956. (b) Hoye, T. R.; Eklov, B. M.; Voloshin, M. *Org. Lett.* **2004**, *6*, 2567−2570.

(5) It is interesting that the resonances assigned to the allylic methylene protons H4, H7, and H8 show no evidence of diastereotopicity. Each of anions **4a** and **4b** is chiral (as is the related π-allyl like representation **i**). The spectral data suggest that racemization is rapid on the NMR time-scale, which could be indicative of facile facial exchange of lithium cations within aggregate structures of **4**. Cf.: Fraenkel, G.; Halasa, A. F.; Mochel, V.; Stumpe, R.; Tate, D. *J. Org. Chem.* **1985**, *50*, 4563−4565.



(6) Katz, T. J. *J. Am. Chem. Soc.* **1960**, *82*, 3784−3785. Katz, T. J. *J. Am. Chem. Soc.* **1960**, *82*, 3785−3786.