Reaction of 3-trimethylsilyloxy-2-aza-1,3-dienes with zirconocene: a transition metal promoted retro-Brook rearrangement

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Abstract

2-Aza-1,3-dienes bearing trimethylsilyloxy group at C3 undergo an unusual zirconium-mediated retro-Brook rearrangement to produce, after hydrolysis, silylated amides. Both [1,3]- and [1,4]-oxygen to carbon silyl migrations are observed depending on the substrate structure. © 2000 Elsevier Science Ltd. All rights reserved.

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Although 2-aza-1,3-dienes appear now as valuable heterodiene components for Diels–Alder and some other cycloaddition and heterocyclization reactions,[1] their use in organometallic reactions is rather limited.[2] For instance, to the best of our knowledge, there is no report on the early transition metal (Ti, Zr) chemistry involving 2-azadienes, and only a few studies deal with the formation and properties of titanium and zirconium 1-azadiene complexes.[3] Yet, hetero-unsaturated molecules bound to group IV metallocenes often reveal unique and synthetically useful reactivity. Among them, titanocene- and zirconocene-imine complexes (metalla-aziridines, N,C-dianion equivalents) undergo coupling reactions with various polar and non-polar unsaturated organic groups.[4] It appeared worthwhile to activate by a transition metal the 2-azadiene (*N*-alkenylimine) synthon, in order to confer on it a reactivity different from that displayed in the free state.

In the course of our research directed toward the reactivity of metal-coordinated heterodienes, we recently described the direct conversion of α,β-unsaturated ketones into vinylcyclopropanes by Cp$_2$Zr-ethylene.[5] We report herein the preliminary results on the complexation of some electron-rich 2-azadienes having a trimethylsilyloxy group at C3 to zirconocene, 'Cp$_2$Zr'. This reaction involves an unusual transition metal mediated retro-Brook rearrangement, leading after hydrolysis to silylated amides.

Our investigation began with 1-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene (**1**).[6] In the first experiment, Cp$_2$ZrBu$_2$ was prepared in situ from Cp$_2$ZrCl$_2$ and 2 equiv. of *n*-BuLi in THF at −78°C, and

zirconocene–butene (Negishi reagent) generated by warming the reaction mixture to room temperature in the presence of 1 equiv. of azadiene **1**.[7] After stirring at this temperature for 1 h the reaction mixture was quenched with 3 M HCl. Extraction with ether followed by flash chromatography purification afforded *N*-benzylacetamide **2** in 72% yield (Scheme 1). This reaction appears as synthetically equivalent to the selective reduction of the carbon–nitrogen bond in **1**. Using an aqueous solution of $NaHCO_3$ instead of 3 M HCl for hydrolysis, a quite different product, i.e. the α-silylated amide **3** was isolated in 72% yield.[8]
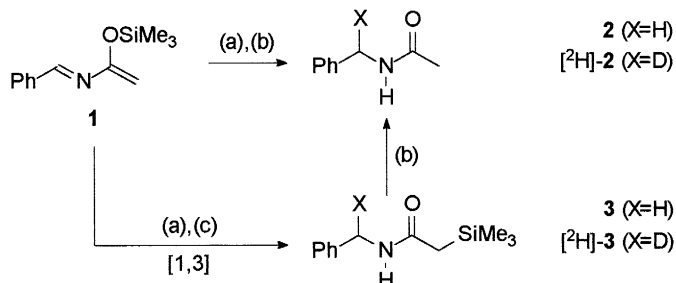
Scheme 1. (a) Cp_2ZrCl_2, 2 equiv. *n*-BuLi, THF, $-78°C$ to rt or Cp_2ZrCl_2, Mg, THF, rt; (b) 3 M HCl or DCl; (c) $NaHCO_3$ aq. or D_2O then $NaHCO_3$ aq.

This unexpected result, revealing a migration of the silyl fragment from oxygen to carbon, prompted us to study further the reaction.

The migration of a silyl group from oxygen to a formally anionic carbon, referred to as a retro-Brook rearrangement, is not frequently encountered.[9] Particularly, to the best of our knowledge, this reaction has never been observed using transition metal complexes. The retro-Brook rearrangement proceeds especially when lithiated compounds are used as substrates. We thought that a lithium-promoted rearrangement could not be completely ruled out at this stage, since we employed *n*-BuLi to generate the zirconium reagent. In order to clarify the role of the metal, we envisaged lithium-free conditions to preform the zirconocene equivalent and used magnesium as the reductant, similarly to the procedure developed for 1-azadiene zirconocene complexes.[3a] Thus, addition of magnesium turnings to an equimolar mixture of Cp_2ZrCl_2 and the azadiene **1** in THF at room temperature resulted in the progressive formation of a dark red solution. After stirring for 6 h, basic workup ($NaHCO_3$ aq.) and column chromatography on alumina, silylated amide **3** was invariably obtained in 90% yield.

Owing to this encouraging result, further experiments were performed. We first tried to isolate the intermediate organometallic complex but without success. Quenching the reaction mixture with DCl in D_2O instead of 3 M HCl afforded monodeuterated amide [²H]-**2** with >98% D incorporation. Also, when the reaction mixture was treated with D_2O followed by $NaHCO_3$ aq., monodeuterated α-silylated amide [²H]-**3** was obtained as the only product (Scheme 1). These results suggests that a Zr–C1 (but not a Zr–C4) bond was present in the intermediate organometallic complex. Monitoring the reaction by ¹H NMR spectroscopy in THF-d_8 at room temperature indicated the formation of a $ZrCp_2$ complex, exhibiting sharp singlets at δ 6.49 and 0.11 for the Cp and Me_3Si groups, respectively.[10] The latter is upfield-shifted compared to that of the free azadiene **1** (δ 0.46). This high-field resonance of the Me_3Si group, quite similar to that in **3** (δ 0.15 in THF-d_8), is indicative of the O- to C-silyl migration.

To estimate the effect of the steric bulk on the rearrangement process, we next used azadiene **4**, having the additional phenyl group at C4 (i.e. at the carbon on which the migration occurred for **2**) (Scheme 2). The reaction of azadiene **4** with the Negishi reagent was performed in the same manner and conditions as above. After basic ($NaHCO_3$ aq.) treatment and chromatographic purification, silylated amide **5** was isolated in 60% yield.[8b] No trace of amide silylated on C4 was detected. Deuterolysis of the reaction mixture afforded [²H]-**5**, in accordance with an intermediate containing a Zr–C4 (and not a Zr–C1) bond

(Scheme 2). The migration of the Me$_3$Si group from oxygen to the C1 atom in **4** (retro-[1,4]-Brook rearrangement) contrasts strikingly with the O to C4 migration in **1** (retro-[1,3]-Brook rearrangement). Additionally, we have noticed that both migrations (to C1 and C4) took place starting from a moderately crowded 1-phenyl-3-trimethylsilyloxy-2-aza-1,3-pentadiene (**6**). Thus, the direction of the silyl group migration is markedly influenced by the substitution pattern of the reaction center.
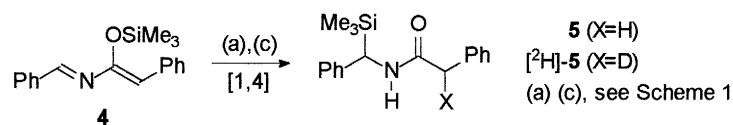
Scheme 2.

An important driving force for the above retro-Brook rearrangements may be the strongly oxophilic character of zirconium. A plausible mechanistic rationale implies two zirconium-assisted competing rearrangement processes (i) and/or (ii), starting from the initial zirconaaziridine complexes **A′** and **A″** (Fig. 1).[11] The cleavage of a Zr–C bond (path (ii)) must generally be favored over the cleavage of a stronger Zr–N bond (path (i)). However, starting from azadiene **1**, the cleavage of the Zr–N rather than the Zr–C bond takes place for steric reasons. In fact, the Zr–N bond-breaking process in path (i) is favorably accompanied by the formation of the C4-Si rather than the much more crowded C1–Si bond. In contrast, a similar structural environment at C1 and C4 in azadiene **4** induced selectively the easier Zr–C bond-breaking process in path (ii).
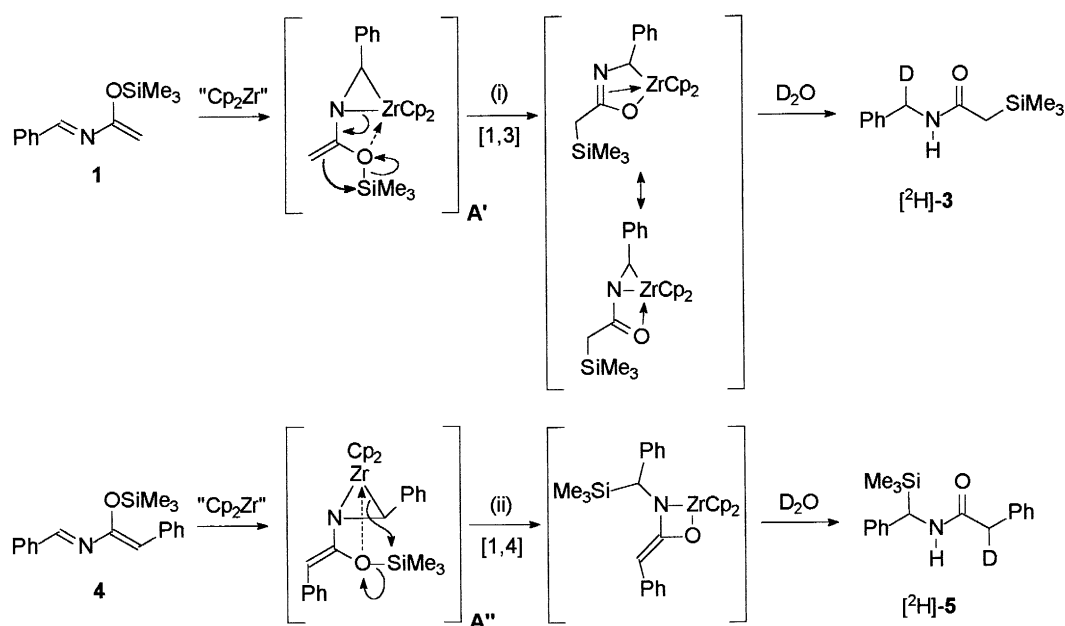
Fig. 1. Proposed formation of silylated amides **3** and **5**

In conclusion, we have described a zirconium mediated retro-Brook rearrangement reaction which provides silylated amides directly from 3-trimethylsilyloxy-2-azadienes. We are currently exploring the new synthetic utility of silyloxy 2-azadienes through their complexation to zirconocene.

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6. (a) The electronically neutral 1-phenyl-2-aza-1,3-pentadiene does not react with zirconocene. This lack of reactivity may be related to a generally low HOMO activity of the neutral 2-azadienes, see Ref. 1; (b) for the preparation of silyloxy azadienes **1**, **4** and **6**, see Ref. 1c.

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8. (a) Compound **3** was converted to **2** by treatment with 3 M HCl; (b) selected data for silylated amides **3** and **5** follow: **3**: ^{1}H NMR (CDCl$_3$) δ 0.10 (s, 9H), 1.79 (s, 2H), 4.40 (d, J=5.3 Hz, 2H), 5.61 (m, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (CDCl$_3$) δ −1.4, 29.0, 43.6, 127.3, 127.8, 128.3, 138.7, 171.9; IR (neat) 3287, 2961, 1630, 1254 cm^{-1}; HRMS *m/z* (M$^+$): 221.1236; calcd for C$_{12}$H$_{19}$NOSi: 221.1236; **5**: ^{1}H NMR (CDCl$_3$) δ −0.14 (s, 9H), 3.62 (d, J=16.2 Hz, 1H), 3.67 (d, J=16.2 Hz, 1H), 4.59 (d, J=9.0 Hz, 1H), 5.72 (d, J=8.2 Hz, 1H), 6.82–6.90 (m, 2H), 7.10–7.40 (m, 8H); ^{13}C NMR (CDCl$_3$) δ −3.8, 44.0, 46.0, 125.5, 125.6, 127.6, 128.3, 129.2, 129.5, 129.6, 135.2, 141.2, 170.4; IR (KBr) 3312, 2961, 1643, 1253 cm^{-1}; HRMS *m/z* (M$^+$): 297.1549; calcd for C$_{18}$H$_{23}$NOSi: 297.1549.

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10. At a lower temperature (−80°C) the singlet of the Cp ligands broadened, suggesting the presence of two diastereotopic Cp units. The fluxionality of the complex may be related to the dynamic behavior of zirconocene complexes with 1-aza- and 1,4-diazadienes, see Ref. 3.

11. The zirconaaziridines are readily formed, starting from aldimines as well as 1-azadienes and 'Cp$_2$Zr', see Refs. 3 and 4.