

SmI₂-Mediated Cyclization of Vinyl radicals

Laura Capella and Pier Carlo Montecocchi

Dipartimento di Chimica Organica 'A. Mangini', Viale Risorgimento 4, I-40136 Bologna, Italy

Abstract: SmI₂-Mediated formation of vinyl radicals give stereoselective 5- or 6-exo cyclization on the intramolecular carbon-carbon triple bond in addition to 1,5-hydrogen shift; further reduction of the resulting alkyl radical would lead to a transient carbanion which can undergo [2,3] sigmatropic Wittig rearrangement.

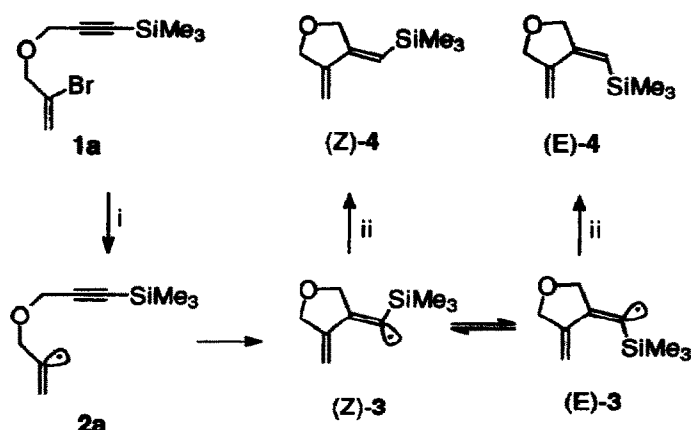
In the last decade the samarium Barbier reaction has been developed into a powerful synthetic method.¹ This reaction was discovered by Kagan in 1980, but its mechanism is not fully understood yet. It is certain that radicals are involved in key steps and SmI₂-promoted reactions of organic halides have usefully been employed to perform radical cyclizations.² However, primary and secondary alkyl radicals can be further reduced by SmI₂;³ Kagan⁴ cited evidence in favour of the possible intermediacy of transient anions and against the intermediacy of alkylsamarium reagents. In contrast, Curran and co-workers⁵ brought clear evidences in favour of samarium reagents.

We have undertaken a study on the SmI₂-mediated cyclization of vinyl radicals and now we report preliminary accounts obtained from the reaction of the ethers **1a,b** showing that: (i) vinyl radicals can undergo both 5- and 6-exo cyclizations on an adjacent triple bond in a stereoselective mode and (ii) transient carbanions can actually be intermediates in the reduction of secondary alkyl radicals.

The SmI₂-promoted reactions were carried out by stirring at room temperature for ca. 3 h, under a nitrogen atmosphere, a 0.1 M solution of the appropriate ether **1a,b** containing a three-fold excess of samarium iodide in a 95:5 tetrahydrofuran (THF) [or acetonitrile]/hexamethylphosphoric triamide (HMPA) mixture. After standard workup with saturated aqueous solutions of NH₄Cl and NaCl the reaction mixture was chromatographed on silica gel column. Reaction products were identified by ¹H NMR and MS spectral analysis.

The 2-bromopropenyl ether **1a** reacted in acetonitrile to give a 60:40 (Z)/(E) isomeric mixture of the 5-exo-dig ring closure product **4⁶** as the only identifiable product. (Scheme 1) The actual stereochemistry was determined by n.o.e. effect measurements. No traces of any 6-endo-dig cyclization product were detected, according to the Baldwin-Beckwith rule.⁷ The occurrence of comparable amounts of both (E)- and (Z)-isomers indicates that intermediate radical **3** can abstract rather freely a hydrogen atom in both the (E) and (Z) interconverting forms. On the other hand, no structural features appear to exist in radical **3** that can favour the approach of the radical scavenger to one rather than the other isomeric form.⁸ In contrast, the reaction of

1a carried out in THF under similar conditions gave the (Z)-isomer (Z)-**4** almost exclusively (Z/E ratio > 9:1). The high stereoselectivity observed in this good hydrogen donor solvent might be explained assuming that radical (Z)-**3** can abstract a hydrogen atom before equilibrating. This would imply that the cyclization of vinyl radical **2a** on the adjacent triple bond occurs in a *cis*-stereoselective mode to give the "cisoid" alkadienyl radical (Z)-**3**.

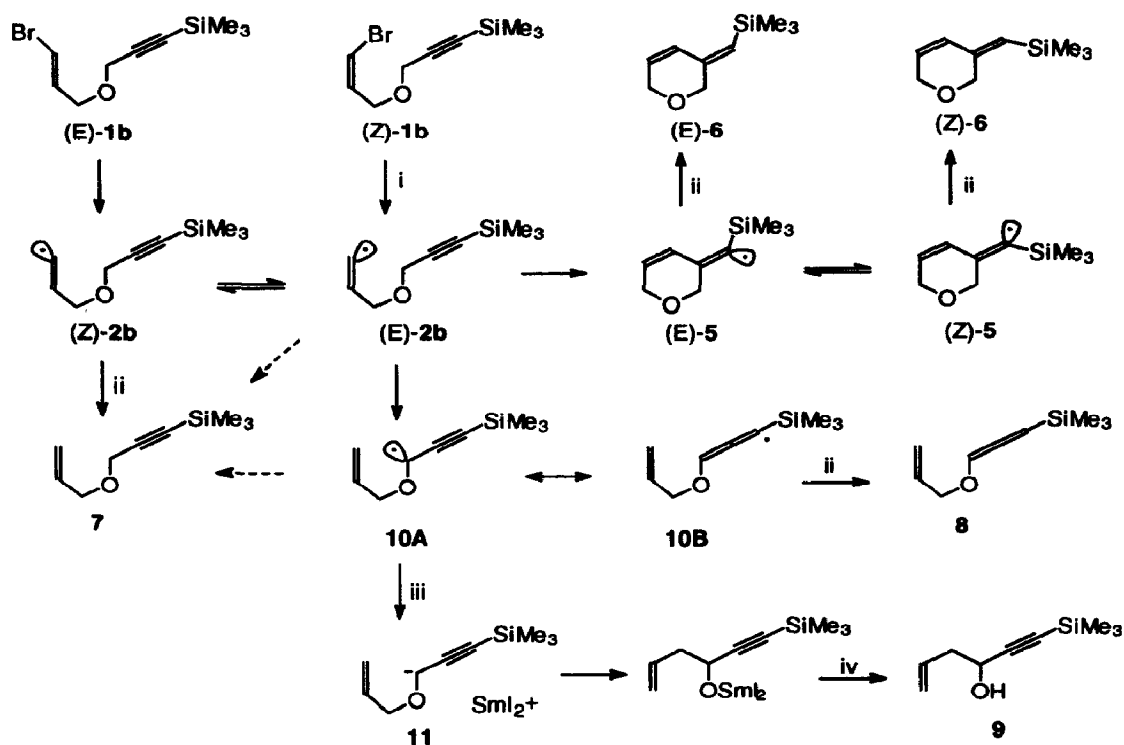


Scheme 1. Reagents: i, +Sml₂, -Sml₂Br; ii, +H-

A 1:1 mixture of (E)- and (Z)-bromopropenyl ether (E)- and (Z)-**1b** reacted with Sml₂ in THF/HMPA to give the 6-*exo* ring closure product **6**⁹ in a 2:1 (E)/(Z) isomer ratio and in 23% overall yield. In addition, the reduction product **7**¹⁰ (22%), the allene **8**¹¹ (12%) and the rearranged compound **9**¹² (5%) were also isolated. The reaction carried out in acetonitrile gave major amounts of the compound **9** (35%), which was formed at the expense of **7** and **8**, besides the cyclization product **6**. This was isolated in roughly unchanged yields, but as a ca. 50:50 (E)/(Z) mixture. The actual structure of (E)- and (Z)-**6** was unambiguously assigned by n.O.e. effect measurements. It can be observed that the 6-*exo-dig* cyclization product **6** preferentially occurred in the (E)-configuration when the reaction was carried out in THF. Thus, in contrast with that claimed above for radical **2a**, it might be suggested that radical (E)-**2b** adds to the adjacent triple bond in a *trans*-stereoselective mode to give the "transoid" alkadienyl radical (E)-**5**.

The 6-ring closure is a somewhat rare process for vinyl radicals, although it has been previously reported, at least in one case.¹³ In addition to the 6-*exo* cyclization reaction, radical (E)-**2b** can undergo intramolecular 1,5-hydrogen shift. This reaction was expected, since the Barton-type rearrangement easily occurs in vinyl radicals;¹⁴ the resulting radical **10** can be responsible for the formation of the products **8** and **9** through two competing kinds of reaction: (i) hydrogen abstraction reaction from THF by the mesomeric form **10B** leading to the allene **8**¹⁵; (ii) reduction by Sml₂ leading to the intermediate **11**, which could be responsible for the product **9** through a [2,3] sigmatropic Wittig rearrangement (Scheme 2). For radical **10**, this is the exclusive reaction occurring in acetonitrile, a good solvent for promoting ET reactions.

Sigmatropic rearrangements in allyl (trimethylsilyl)propenyl ethers have already been reported;¹⁶ these well-known reactions are generally believed to occur through anion intermediacy¹⁷. On this basis it can be inferred that the intermediate 11 could have carbanion character. Our findings strongly support the suggestion that samarium reagents would generally result from coupling of ion pairs formed by outer-sphere ET reaction between alkyl radicals and SmI_2 .^{4, 5b}



Scheme 2. Reagents: i, SmI_2 , $-\text{SmI}_2\text{Br}$; ii, $+\text{H}\cdot$; iii, SmI_2 ; iv, hydrolysis.

The alkene 7 could derive, in principle, through hydrogen abstraction reaction from both radicals (E)- and (Z)-2b and 10A as well (Scheme 2). Actually, we showed that the radical (Z)-2b is the main one responsible for 7. In fact, pure (Z)-1b reacted in THF with SmI_2 to give essentially compounds 8, 9 and 10. The almost complete absence of product 7 indicates that for radical (E)-2b both the cyclization reaction on the adjacent triple bond and the 1,5-hydrogen shift prevale over the (E) \rightarrow (Z) isomerization.

Despite the fact that vinyl radicals are generally claimed to undergo rapid interconversion^{8,18}, our findings clearly show that, for the vinyl radicals 2b, 3 and 5, hydrogen abstraction reaction from THF, 1,5-hydrogen shift or 6-*exo* cyclization can favourably compete with the (E) \rightleftharpoons (Z) isomerization.

Acknowledgment. We thank the Ministero della Ricerca Scientifica e Tecnologica (MURST) for financial support.

References and Notes

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6. **4**: ^1H NMR (200 MHz) δ (Z-isomer) 0.1 (9H, s), 4.43 (2H, t, $J = 2.5$ Hz), 4.46 (2H, d, $J = 2.5$ Hz) 4.92 (1H, br t), 5.4 (1H, t, $J = 2.5$ Hz), 6.0 (1H, t, $J = 2.5$ Hz); δ (E-isomer) 0.15 (9H, s), 4.40 (2H, d, $J = 2.5$ Hz), 4.46 (2H, t, $J = 2.5$ Hz), 5.08 (1H, br t), 5.40 (1H, br t), 5.52 (1H, br t).
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9. **6**: ^1H NMR (200 MHz) δ (E-isomer) 0.1 (9H, s), 4.2 (4H, m), 5.25 (1H, br s), 5.93 (1H, ddt, $J_{d1} = 10$ Hz, $J_{d2} = 1.2$ Hz, $J_t = 2.7$ Hz), 6.46 (1H, ddt, $J_{d1} = 10$ Hz, $J_{d2} = 0.8$ Hz, $J_t = 1.9$ Hz); δ (Z-isomer) 0.1 (9H, s), 4.15 (2H, m), 4.35 (2H, d, $J = 1.4$ Hz), 5.33 (1H, br s), 5.85 (1H, br dt, $J_d = 10$ Hz, $J_t = 2.5$ Hz), 6.18 (1H, ddt, $J_{d1} = 10$ Hz, $J_{d2} = 0.8$ Hz, $J_t = 2$ Hz).
10. **7**: ^1H NMR (200 MHz) δ 0.15 (9H, s), 4.03 (2H, dt, $J_d = 5.7$ Hz, $J_t = 1.5$ Hz), 4.12 (2H, s), 5.20 (1H, br d, $J = 10.5$ Hz), 5.28 (1H, ddt, $J_{d1} = 16.5$ Hz, $J_{d2} = J_t = 1.5$ Hz), 5.90 (1H, ddt, $J_{d1} = 16.5$ Hz, $J_{d2} = 10.5$ Hz, $J_t = 5.7$ Hz).
11. **8**: ^1H NMR (200 MHz) δ 0.1 (9H, s), 4.0 (2H, m), 5.18 (1H, ddt, $J_{d1} = 10.5$ Hz, $J_{d2} = J_t = 1.5$ Hz), 5.28 (1H, ddt, $J_{d1} = 17.5$ Hz, $J_{d2} = J_t = 1.5$ Hz), 5.94 (1H, ddt, $J_{d1} = 17.5$ Hz, $J_{d2} = 10.5$ Hz, $J_t = 5.5$ Hz), 5.94 (1H, d, $J = 6.3$ Hz), 6.67 (1H, d, $J = 6.3$ Hz).
12. **9**: ^1H NMR (200 MHz) δ 0.15 (9H, s), 1.9 (1H, br s, OH), 2.45 (2H, dd, $J_1 = J_2 = 7$ Hz), 4.4 (1H, br dt, $J_d = J_t = 5.5$ Hz), 5.10-5.22 (2H, m), 5.86 (1H, ddt, $J_{d1} = 17.3$ Hz, $J_{d2} = 9.5$ Hz, $J_t = 7$ Hz).
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(Received in UK 13 July 1994; revised 1 September 1994; accepted 9 September 1994)