Cyclization of samarium diiodide-generated vinyl radicals in 6-(π-*exo*)-*exo-dig* mode

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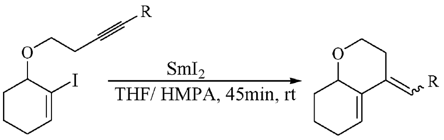
Radical cyclization of vinyl iodides in 6-(π-*exo*)-*exo-dig* mode were effected by SmI$_2$ to give *exo*-cyclic dienes fused to six- membered rings.

The use of radical cyclizations for the syntheses of five and six-membered rings has become widespread in organic chemistry.[1] Those radical cyclizations involving vinyl radicals seem particularly attractive.[2] Vinyl radicals can be generated in three ways: (i) by addition to the alkyne triple bond of silicon-, tin-, carbon-, sulfur- or selenium-centered radicals;[3] (ii) from vinyl halides through halogen abstraction by stannyl or silyl radicals;[4] (iii) by chemical reduction of vinyl bromides, the latter can be achieved by SmI$_2$,[5] where electron transfer between samarium(II) and the organic halide leads to the corresponding free radical through loss of the halide ion.

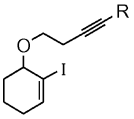
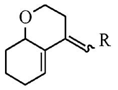
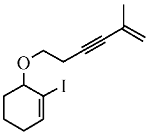
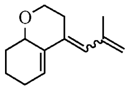
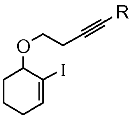
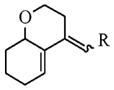
Exo-cyclic dienes are versatile and useful diene components in Diels–Alder reactions.[6] Among the various methodologies for the synthesis of *exo*-cyclic dienes, vinyl radical cyclization would be straightforward.[7–9] However, according to the previous study, this approach proved efficient only in the 5-(π-*exo*)-*exo-dig* radical cyclization and for the corresponding 6-(π-*exo*)-*exo-dig* radical cyclization it was reported to be unfavorable.[8] To the best of our knowledge, there are only two cases of 6-(π-*exo*)-*exo-dig* radical cyclizations with poor yields reported in the literature;[9] Montevecchi reported that when vinyl bromide was treated with SmI$_2$, the yield of the 6-(π-*exo*)-*exo-dig* radical cyclization was only 8%. Recently, we have successfully effected 6-(π-*exo*)-*exo-dig* radical cyclization of vinyl iodides by Bu$_3$SnH–AIBN to give *exo*-cyclic dienes in moderate to good yields.[10] Encouraged by this result, we attempted radical cyclization of vinyl iodides in 6-(π-*exo*)-*exo-dig* modes by SmI$_2$. We report herein the results of our exploratory work (Scheme 1).



Scheme 1

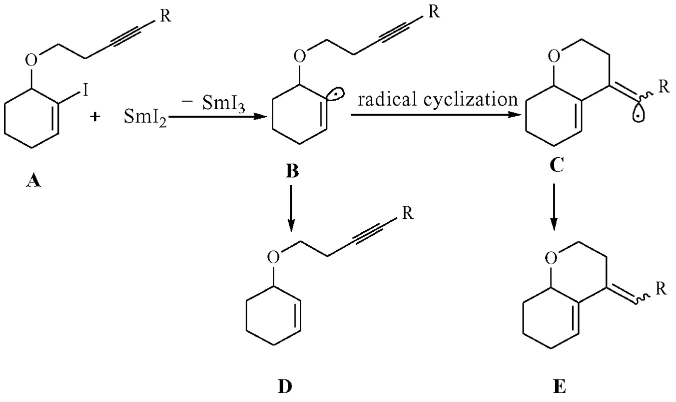
All the vinyl iodides in Table 1 were treated with SmI$_2$ to mediate 6-(π-*exo*)-*exo-dig* radical cyclization.[11] We found that when the triple bond was substituted with an isopropenyl group or aromatic rings (entries **1–6**), vinyl iodides underwent cyclization smoothly to give *exo*-cyclic dienes in good yield. When the triple bond was substituted with such groups as ethyl, TMS, and H (entries **7–9**), the yields of the *exo*-cyclic dienes apparently decreased. In entry **8**, compound **8** which has a TMS group on adjacent triple bond was converted to corresponding *exo*-cyclic diene in only 30% yield. Yet in comparasion with the method of achieving 6-(π-*exo*)-*exo-dig* radical cyclization of vinyl bromide whose triple bond was also substituted with a TMS group, where the yield of *exo*-cyclic diene was only 8%,[9a] our approach to the *exo*-cyclic diene through radical cyclization of vinyl iodide was more efficient. Thus, we propose that in terms of the reactivity of radical cyclization, vinyl iodides are better than vinyl bromides.

Table 1 6-(π-*exo*)-*exo-dig* Radical cyclization of vinyl iodides

Entry	Vinyl iodides	*exo*-Cyclic diene	Yield (%)[a]
			
1	**1** R = Ph	**10** R = Ph	71 (*E* : *Z* = 1.7 : 1)[b]
2	**2** R = *p*-MeO–Ph	**11** R = *p*-MeO–Ph	70 (*E* : *Z* = 1.9 : 1)[b]
3	**3** R = *o*-Me–Ph	**12** R = *o*-Me–Ph	68 (*E* : *Z* = 1.9 : 1)[b]
4	**4** R = thien-2-yl	**13** R = thien-2-yl	58 (*E* : *Z* = 1 : 1.5)[b]
5	**5** R = furan-3-yl	**14** R = furan-3-yl	63 (*E* : *Z* = 1 : 1.1)[b]
			
6	**6**	**15**	70 (*E* : *Z* = 1 : 1.2)[b]
			
7	**7** R = Et	**16** R = Et	29 (*E* : *Z* = 1.3 : 1)[b]
8	**8** R = TMS	**17** R = TMS	30 (*E* : *Z* = 1.1 : 1)[b]
9	**9** R = H	**18** R = H	14

[a] Isolated yield. [b] The structures of the *exo*-cyclic dienes were confirmed by NOE experiments, and the ratios of *E* and *Z* isomers were determined by ^{1}H NMR integration.

Considering the cyclization process described in Scheme 2, we propose that vinyl iodide firstly obtained an electron from SmI$_2$ to form radical **B**, which can either carry on intramolacular radical cyclization leading to radical **C**, or directly abstract a



Scheme 2

hydrogen from the solvent to give acyclic product **D**. Here the stability of radical **C** is the key to whether radical cyclization would be favorable. When R was a saturated group such as ethyl, TMS, and H, radical **C** was unstable, so *exo*-cyclic dienes **E** were formed in low yields, however when R was an unsaturated group such as an isopropenyl group or an aromatic ring, a large conjugated system with two double bonds was composed in radical **C**, hence radical **C** was stable. Radical **B** could undergo radical cyclization smoothly to form radical **C**. As a result, *exo*-cyclic diene **E** was obtained in good yield.

In conclusion, radical cyclization of vinyl iodides in 6-(π-*exo*)-*exo-dig* mode were effected by SmI$_2$. When the triple bond of vinyl iodides was substituted with a vinyl group or aromatic rings, the *exo*-cyclic dienes fused to six-membered ring were formed in good yields. The notable advantages of this method are the mild reaction conditions and the simple and rapid procedure. In terms of the reactivity of radical cyclization, vinyl iodides are better than vinyl bromides.

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11 Satisfactory spectral and analytical data were obtained for all new compounds. A typical experimental procedure for the radical cyclization of **2** is as follows: To SmI$_2$ (0.1 M SmI$_2$ in THF 30 ml, 3 mmol) was added the solution of **2** (382 mg, 1 mmol in 1 ml THF) followed by HMPA 1.5 ml. The mixture was stirred for 45 min, followed by saturated NH$_4$Cl quenching. Subsequently, this was extracted with ether and the extract was washed with water, 5% Na$_2$S$_2$O$_3$, and brine, and dried with Na$_2$SO$_4$. Silica gel flash column chromatography (hexane–CH$_2$Cl$_2$, 1 : 1) gave compound **11** as a mixture of *E* and *Z* isomers. (179 mg, 70%). *E* and *Z* isomers were separated by silica gel preparative TLC (hexane–CH$_2$Cl$_2$, 1 : 1). Data for the *E* isomer: colorless crystals from hexane; mp 105–106 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.18 (d, J = 8.7 Hz, 2 H), 6.85 (d, J = 8.7 Hz, 2 H), 6.48 (d, J = 2.1 Hz, 1 H), 5.85 (dd, appears as t, J = 3.6 Hz, 3.6 Hz, 1 H), 4.03 −3.97 (m, 2 H), 3.78 (s, 3 H), 3.53–3.43 (m, 1 H), 2.75–2.69 (m, 1 H), 2.62–2.50 (m, 1 H), 2.28–2.13 (m, 1 H), 2.11–1.99 (m, 2 H), 1.84–1.71 (m, 1 H), 1.63–1.49 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 20.3, 26.2, 29.9, 30.9, 55.3, 66.8, 75.6, 113.6,123.0, 123.1, 130.2, 130.5, 136.5, 139.3, 158.3; IR (CHCl$_3$) 2939, 1606, 1509, 1249, 1101 cm^{-1}; MS (EI) *m*/*z* 256 (M$^+$, 100); HRMS calcd for C$_{17}$H$_{20}$O$_2$ 256.1463, found 256.1453. Data for the *Z* isomer: pale yellow oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.20 (d, J = 8.7 Hz, 2 H), 6.75 (d, J = 8.7 Hz, 2 H), 6.12 (d, J = 2.0 Hz, 1 H), 5.59 (dd, appears as t, J = 3.6 Hz, 3.6 Hz, 1 H), 4.15–3.97 (m, 2 H), 3.77 (s, 3 H), 3.68–3.58 (m, 1 H), 2.61–2.49 (m, 1 H), 2.25–2.17 (m, 1 H), 2.12–1.50 (m, 6 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 20.0, 25.6, 30.0, 38.7, 55.2, 68.4, 75.3, 113.4, 123.5, 127.4, 130.0, 130.3, 134.8, 137.0, 157.8; IR (CHCl$_3$) 2938, 1607, 1509, 1247, 1094 cm^{-1}; MS (EI) *m*/*z* 256 (M$^+$, 100); HRMS calcd for C$_{17}$H$_{20}$O$_2$ 256.1463, found 256.1464.