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Abnormal Four-Membered Ring Formation in Intramolecular Radicalic Cyclization. High Stability of the Alkyl Radical Substituted with Methylthio and *p*-Tolylsulfonyl Groups†

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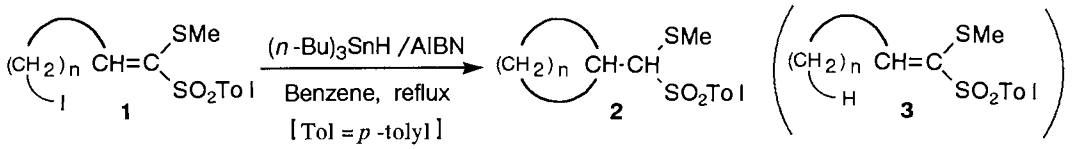
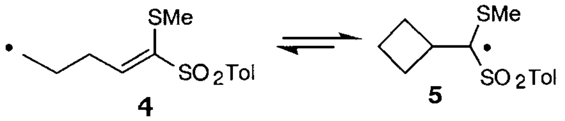
Treatment of 5-iodo-1-(methylthio)-1-(*p*-tolylsulfonyl)-1-pentene with (n-Bu)$_3$SnH and AIBN gave [(methylthio)(*p*-tolylsulfonyl)methyl]cyclobutane. This is due to the stability of an intermediary radical attached to methylthio and *p*-tolylsulfonyl groups.

Hitherto the combined action of an electron-withdrawing (captive) substituent and an electron-donating (dative) substituent on a radical has been discussed by many investigators.[1] Here we report the extraordinary stability of the alkyl radical substituted with methylthio and *p*-tolylsulfonyl groups.



When a 0.025 M benzene solution of ω-iodo-1-methylthio-1-(*p*-tolylsulfonyl)-1-alkene (**1**, n = 4 or 5) was heated under reflux in the copresence of (n-Bu)$_3$SnH (1.2 mol-equiv.) and AIBN (ca. 0.07 mol-equiv.), a cyclization product (**2**) was obtained in 74% (n = 4) [2] or 89% (n = 5) yield, respectively. To our surprise, the similar treatment of **1** (n = 3) gave a four-membered product (**2**, n = 3) though its yield was low (4% yield). A higher yield was attained by a "high-dilution" method: After a benzene solution of **1** (n = 3) and (n-Bu)$_3$SnH (1.0 mol-equiv.) was dropwise added over a period of 1 h to a refluxing benzene solution of AIBN (0.17 mol-equiv.) [the final concentration of **1** (n = 3) = 0.001 M], the resulting solution was further refluxed for 1 h. By the usual workup, **2** (n = 3) was isolated in 48% yield along with a reduction product (**3**, n = 3; 34% yield).

Formation of four-membered rings by 4-exo radical cyclizations has rarely been reported.[3] Generally cyclobutylmethyl radical cleaves the ring with high rate to form the more stable acyclic radical.[4] Since the present cyclization of an intermediary radical (**4**) to form a cyclic radical (**5**) is reversible,[5] the favorable exo-cyclization of **4** is attributable to the stability of **5**. The synergistic effect of methylthio and *p*-tolylsulfonyl groups on the stabilization of a radical was also implied by exclusive formation of 1-(*p*-tolylsulfonyl)-1-pentene in the reaction of 5-iodo-1-(*p*-tolylsulfonyl)-1-pentene with (n-Bu)$_3$SnH and AIBN.



By MNDO/PM3 method,[6] we estimated the radical stabilization energy (RSE) of the most stable conformer for the methyl radical substituted by methylthio group and/or *p*-tolylsulfonyl group. As the RSE of a

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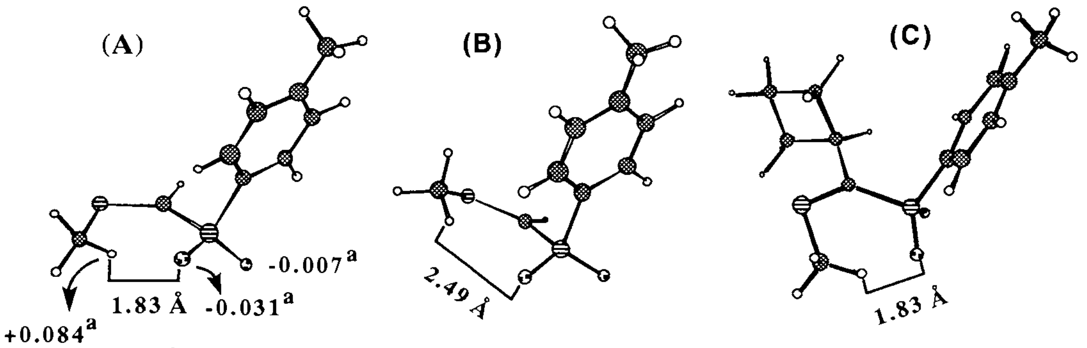
†Dedicated to celebrate 80th birthday of Professor Emeritus Osamu Simamura of The University of Tokyo.

radical (•R), we calculated the relative difference in "heat of formation" (ΔH) between R-H and •R based on the difference between CH_4 and •CH_3:7) RSE = (ΔH of R• - ΔH of RH) - (ΔH of •CH_3 - ΔH of CH_4).

RSE (kcal mol^{-1}) : •CH_2-SO_2Tol -4.2 ; •CH_2-SMe -14.7 ; •CH(SMe)(SO_2Tol) -25.5

From the above results, the substitution of both methylthio and *p*-tolylsulfonyl groups brings about a combined action that stabilizes a radical. This is in accordance with many facts that the presence of strong donor and acceptor groups attached to a radical center introduces synergistic effect on the stabilization of radicals.1) It should be noted that (methylthio)(*p*-tolylsulfonyl)methyl radical undergoes additional stabilization by electrostatic) interaction between methyl hydrogen and sulfonyl oxygen. This radical has more positive thiomethyl hydrogens and more negative oxygens than the parent (methylthio)methyl *p*-tolyl sulfone. In the most stable conformer (**A**) of this radical, these atoms are enough close to each other to interact. The second most stable conformer (**B**) and other energy-minimized conformers are less stable by 0.66 kcal mol^{-1} and more than 1.0 kcal mol^{-1}, respectively, than **A**. The most stable conformer of **5** was calculated to be **C**, closely related to **A**.

Stable alkyl radicals substituted with methylthio and *p*-tolylsulfonyl groups are thought to provide a new method for C-C bond formation, which is one of our on-going subjects.



a charge difference from CH_2(SMe)(SO_2Tol)

References

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2) Irradiation with a high-pressure Hg lamp improved the yield of **2** (n = 4) to 96%.

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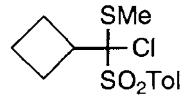
5) The radical (**5**; n = 3) is an intermediate for reduction of a chloro derivative (**6**) of **2** (n = 3) with (*n*-Bu)$_3$SnH. Treatment of **6** with (*n*-Bu)$_3$SnH and AIBN in refluxing benzene gave **2** (n = 3) and **3** (n = 3) in 53% and 21% yields, respectively.



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6) With MOPAC ver. 5.0; QCPE#455 programmed by J. J. P. Stewart.

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