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EPR Support for the Ketyl Radical-Anion "Triggered" [3,3]-Sigmatropic Rearrangement

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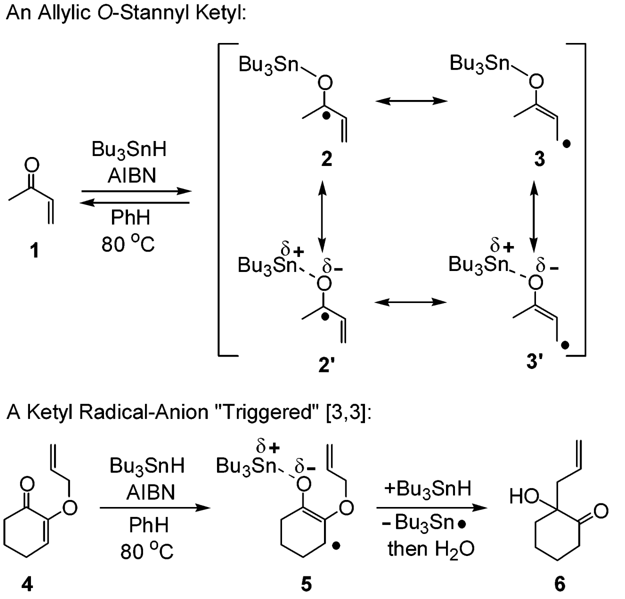
Abstract: New physical evidence to support a ketyl radical-anion mechanism for the [3,3]-sigmatropic rearrangement is presented. With use of EPR spectroscopy, spectra are observed that can be attributed to **8**, an acyl radical-anion species resulting from a [3,3]-rearrangement; this also functions as a key intermediate in the process. The spectrum of an additional paramagnetic species resulting from further addition of tin-centered radicals to the reaction product was also observed.

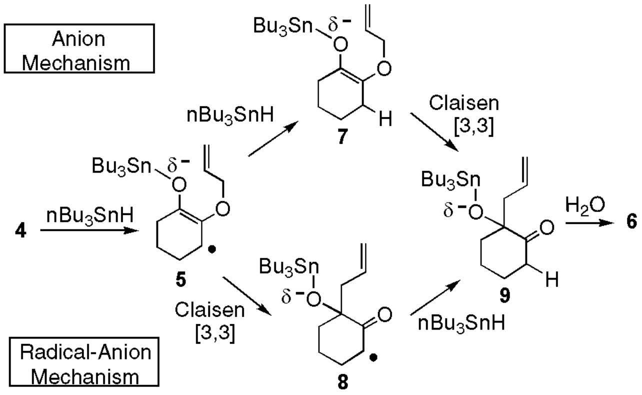
The [3,3]-sigmatropic shift is a versatile rearrangement used extensively in organic synthesis.[1] It is also well-established that an anionic or cationic charge can accelerate the rate of this reaction.[2] Acceleration due to a radical-anion, however, has only recently been proposed via a metal-associated ketyl species.[3] In the presence of a radical initiator, enone **1** and tributyltin hydride form the intermediate radical **2** ↔ **3** that, because of the polarization of the O−Sn bond, can also be viewed as the radical ion pair **2′** ↔ **3′**, where formal negative and positive charges are localized on the oxygen and the Group 14 metal, respectively (see Scheme 1). The allylic *O*-stannyl ketyl is a resonance-stabilized radical that can independently undergo both radical and anionic reactions.[3]

In particular, these intermediates can be used to "trigger" a Claisen-type [3,3]-sigmatropic shift. When **4** is treated with tin hydride under standard thermal radical conditions, radical-anion **5** is initially formed, which subsequently rearranges to alcohol **6**, the driving force of the latter process being the formation of the strong sp^2 ketone bond in **6** (see Scheme 1). As outlined in Scheme 2, two mechanistic scenarios, differing mostly for the timing of events, can be envisioned for this reaction. Both mechanisms involve the initial formation of the allylic *O*-stannyl ketyl intermediate **5**. Once this species has been formed, the two paths bifurcate following either an anionic mechanism going through species **5** → **7** → **9** → **6**[4] or a radical-anion mechanism going through species **5** → **8** → **9** → **6**.[3] In the former mechanism, a hydrogen atom transfer occurs first in **5** → **7**, followed by the [3,3]-rearrangement of **7** → **9**. On the other hand, in the radical-anion mechanism, the [3,3]-rearrangement **5** → **8** occurs first, being subsequently followed by the hydrogen atom transfer. We now favor the latter pathway, which represents an entirely new mechanistic path for the [3,3] rearrangement, based on new EPR evidence (vide infra).

SCHEME 1



SCHEME 2



With the aim to ascertain the actual pathway followed by the reaction, we decided to try and observe **8** by spectroscopic means. Since this radical intermediate is not a possibility in the anionic mechanism, its detection would strongly support the radical-anion pathway. We therefore repeated the reaction between **4** and tin hydrides inside the cavity of an EPR spectrometer[5] to intercept and identify any intervening radical species. In this manner, an argon-purged *tert*-butylbenzene solution of compound **4** was heated inside the cavity of an EPR spectrometer in the presence of either Ph_3SnH or *n*-Bu$_3$-

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[1] Wipf, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Chapter 8.3, p 999.

[2] Chubert, P. S.; Srebnik, M. *Aldrichimica Acta* **1993**, *26*, 17.

[3] Enholm, E. J.; Moran, K. M.; Whitley, P. E.; Battiste, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3807.

[4] Curran, D. P.; Nishii, Y. *J. Am. Chem. Soc.* **1999**, *121*, 8955.

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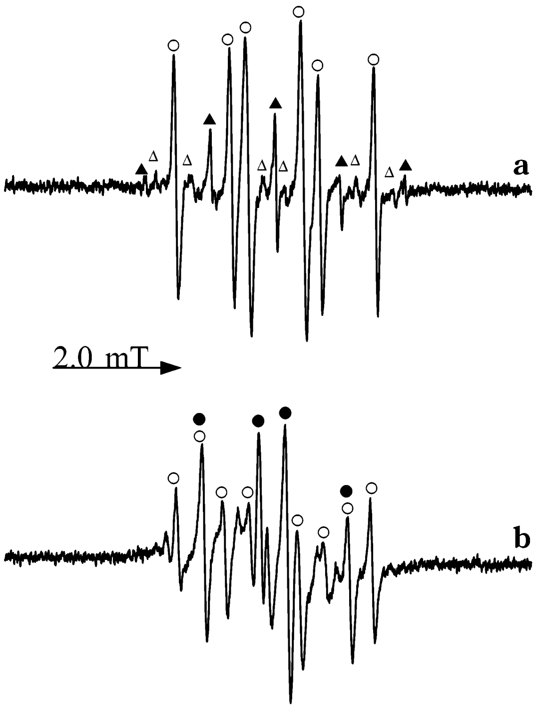

FIGURE 1. EPR spectra observed after thermal reaction of **4** with Ph_3SnH in the presence of AIBN at (a) 353 K and (b) after cooling to 273 K: ○, radical **8**; △, tin satellites of radical **8**; ▲, 1,2-cyclohexanedione radical anion; and ●, radical **10**.

SnH and a small amount of AIBN. In both cases the observed spectra were very similar and exhibited a marked temperature dependence. At high temperature ($T \geq 353$ K) the spectrum (see Figure 1a) was dominated by a triplet of doublets [$a(1H_{\alpha}) = 1.059$ mT, $a(2H_{\beta}) = 1.367$ mT, $a(^{217/219}Sn) = 0.76$ mT, $g = 2.0040_5$], the central lines of the triplets being somewhat broader and less intense than expected. A weak additional quintet [$a(4H) = 1.228$ mT, $g = 2.0042_6$] could also be observed, which we tentatively attribute to the radical anion of 1,2-cyclohexanedione[6] as its corresponding *O*-stannyl ketyl radical-anion.

On the basis of the spectral parameters,[7] we assign this spectrum to radical **8**, where the conformational interchange of the six-member ring is “nearly” fast enough to render equivalent the two hydrogen atoms adjacent to the allylic carbon in position 4. Consistent with this assignment, as the temperature is lowered, the triplet approximates a doublet of doublets [$a(1H_{\alpha}) = 0.901$ mT, $a(1H_{\beta}) = 0.472$ mT, and $a(1H_{\beta}) = 2.332$ mT] indicating that, although the conformational interchange of the six-membered ring is not completely frozen out, the two hydrogen atoms in position 4 are magnetically non-equivalent. The presence of paramagnetic impurities combined with the rather low intensity of the spectra did not allow an accurate kinetic study of the conformational motion of the six-member ring.

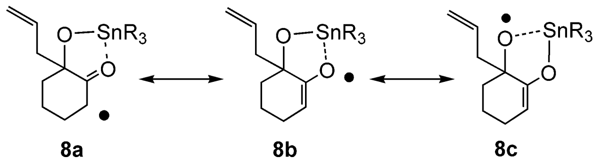

FIGURE 2. Resonance forms of **8**: experiment, R = *n*-butyl; DFT calculations, R = H.

The values of the splittings measured for **8** were compared to those reported for structurally related radicals[8] and our somewhat narrower hfs constants can be supported by two lines of reasoning. First, a consideration of the three resonance forms **8a**, **8b**, and **8c** unique to radical **8** can be envisioned, as shown in Figure 2. Thus, the resonance contribution of structure **8c**, with little spin density on the ring carbons, leads to splittings readily in line with our observations. Second, the splittings for model compound **8c** (R = H) were briefly checked by means of calculation studies by using the DFT method at the B3LYP/6-311G*/UHF/6-31G* level, using the Gausssion 98 system of programs.[9] For the Sn atom the LANL2DZ pseudopotential was used along with a d polarization function. The corresponding hfs constants for radical **8c** were computed to be very small, i.e., 0.13, 0.11, and 0.24 mT, respectively, since in this species the unpaired electron is mostly localized on the oxygen atom. Though this resonance contributor was evaluated separately here, collectively, the three species as resonance contributors should indeed lead to hfs constant values in agreement with the present experiments. The contribution of resonance structure **8b** to the system would also nicely account for the ca. 0.76 mT hyperfine splitting measured for the tin atom, a small value when considering that the A_0 for tin exceeds 1.5 T.[10] It should be

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(5) EPR spectra were recorded on an upgraded Bruker ER200D/ESP 300 spectrometer equipped with a NMR gaussmeter for the calibration of the field, a frequency counter for the determination of *g*-factors that were corrected with respect to that of perylene radical cation in concentrated sulfuric acid, and with standard variable temperature accessories. In a typical experiment an argon-purged *tert*-butylbenzene solution of ketone **4** and either triphenyl or tributyl tin hydride was added with a small amount of AIBN and heated to 323 K. Once the radicals had been formed, spectra could be recorded in the temperature range 373−273K. Almost identical spectra were observed by photolysis of solutions where AIBN had been replaced with di-*tert*-butylperoxide. Similar but less resolved spectra were also detected by photolysis of solutions of **4** and hexabutylditin.

(6) (a) Russell, G. A.; Osuch, C. E. *J. Am. Chem. Soc.* **1978**, *100*, 5979. (b) We attribute the formation of this radical-anion species at higher temperatures to an interesting thermal elimination of tributylallylstannane from compound **9** (vide supra, Scheme 3) to form 1,2-cyclohexanedione. This dione next reacts a second time with tributyltin radical. Importantly, this semidione radical is not observed at lower temperatures, thus rendering its formation by a competing radical or anionic process unlikely.

(7) Hudson, A.; Waterman, D.; Della Bona, M. A.; Alberti, A.; Altieri, A.; Benaglia, M.; Macciantelli, D. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2255.

(8) Landolt-Börnstein, New Series. *Magnetic Properties of Free Radicals*; Fischer, H., Hellwege, K.-H., Eds.; Springer-Verlag: Heidelberg, Germany, 1977; Group II, Vol. 9, Part b. Landolt-Börnstein, New Series. *Magnetic Properties of Free Radicals*; Fischer, H., Ed.; Springer-Verlag: Heidelberg, Germany, 1987; Group II, Vol. 17, Part c.

(9) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A7; Gaussian Inc.: Pittsburgh, PA, 1998.

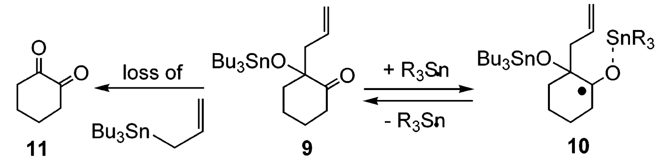
(10) Morton, R. J.; Preston, K. F. *J. Magn. Reson.* **1978**, *30*, 577.

mentioned that DFT calculations predict radical **8a** to be more stable than **8c** by ca. 15 kcal mol^{-1}, although the actual energy difference might be somewhat smaller because DFT methods favor π-delocalized vs σ-delocalized radicals.[11]

Besides these interesting features of this spectral pattern, as the temperature was lowered, an additional doublet of doublets originating from a different species could also be clearly identified [a(1H) = 1.212 mT, a(1H) = 1.555 mT, g = 2.0040$_0$]. We assign these signals to radical **10**,[7] most likely resulting from addition of tin-centered radicals to the reaction product **9** (see Scheme 3).[9] This radical species is not observed at higher temperatures presumably due to the reversibility depicted (Scheme 3) or to decomposition.[6]

In conclusion, the observation and identification of radical **8**, along with the previously mentioned pieces of chemical evidence,[3] lends convincing support to the radical anion mechanism, proceeding through species **5** → **8** → **9** → **6**. The ketyl radical anion mechanism proposed above for a new type of [3,3]-sigmatropic rearrangement is supported by EPR spectroscopy with the spectra observed clearly attributed to radical-anion species **8**, a key intermediate in the process.

SCHEME 3



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(11) Guerra, M. *Theor. Chem. Acc.* **2000**, *104*, 455.