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Oxidative Cyclization of β-Stannyl Hydrazones

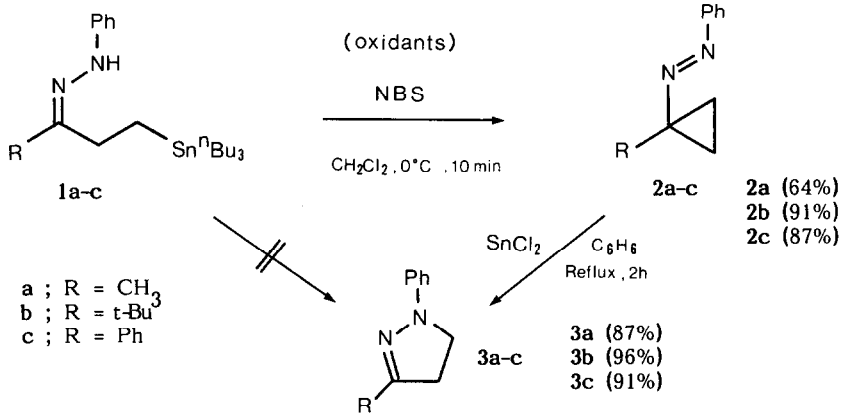
Hisao Nishiyama,* Hiroyuki Arai, Yuki Kanai, Hiroyuki Kawashima, and Kenji Itoh

School of Materials Science, Toyohashi University of Technology,
Tempaku-cho, Toyohashi 440, Japan

Abstract: Oxidation of β-stannyl hydrazones gave the corresponding azocyclopropanes in high yields. Homolytic cyclization involving hydrazonyl radicals (π-iminamino radicals) was postulated.

Oxidative cyclization of N-functionalized hydrazones has been considerably elaborated to show their synthetic versatility giving several heterocyclic compounds.[1] Feasibility of C-Sn bond cleavage in cationic[2] and radical cyclizations[3] lead us to examine a cyclization reaction of β-stannyl hydrazones by means of several oxidants.

We have found an oxidative cyclization of the stannyl hydrazones **1a-c** giving the azocyclopropanes **2a-c** in high yields. Formation of the corresponding pyrazolines was not observed via the direct five-membered ring closure. The pyrazolines **3a-c** can be obtained by treatment of **2a-c** with catalytic amounts of $SnCl_2$ in benzene at refluxing temperature.



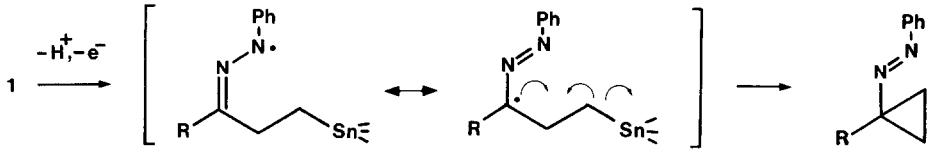
Starting β-stannyl phenylhydrazones **1a-c** were prepared by treatment of the corresponding stannyl ketones[4] with N-phenylhydrazine hydrochloride and sodium acetate in methanol at room temperature under argon atmosphere.

Addition of N-bromosuccinimide (1.2 equiv.) to a solution of the stannyl hydrazone **1a** (0.5 mmol) in dichloromethane (4 mL) at 0°C gave spontaneously the azocyclopropane **2a**. The reaction mixture was diluted with ether and was washed by aqueous sodium bicarbonate. After the organic layer was concentrated, the yellow residual oil was again diluted with ether (ca. 2 mL). The solution was treated with a large excess of KF overnight.[5] After filtration, the residual oil was purified by silica gel column chromatography to give the azocyclopropane **2a** (64%). Azocyclopropanes **2b** (91%) and **2c** (87%) were obtained similarly.[6]

Other oxidants were also examined for **1b**: yield of **2b**; 88% with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)(1.2 equiv.) in CH_2Cl_2at -20°C for 5 min.; 83% with lead tetraacetate (1.2 equiv.) in CH_2Cl_2 at -20°C for 10 min.; 45% with $(BrC_6H_4)_3NSbCl_6$ in CH_2Cl_2 at 0°C for 30 min.; low yields with NaClO or I_2-^{t}BuOK; no reaction with KOH-H_2O_2 in THF or MeOH; complicated products containing the starting ketone were obtained with HgO, SeO_2, $NaIO_4$, $CuCl_2$, $K_3Fe(CN)_6$, and MnO_2.

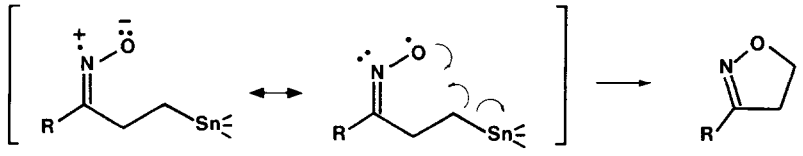
Oxidation of hydrazones has been well investigated spectroscopically to show specific formation of hydrazonyl radicals (A) having the characteristic π-electron structure.[7] Therefore, we propose the following homolytic cyclopropanation in relation to the homolytic isoxazoline-formation[3] via iminoxyl radicals (B) derived from the corresponding oximes, having σ-electron structure.

π - radical



(A)

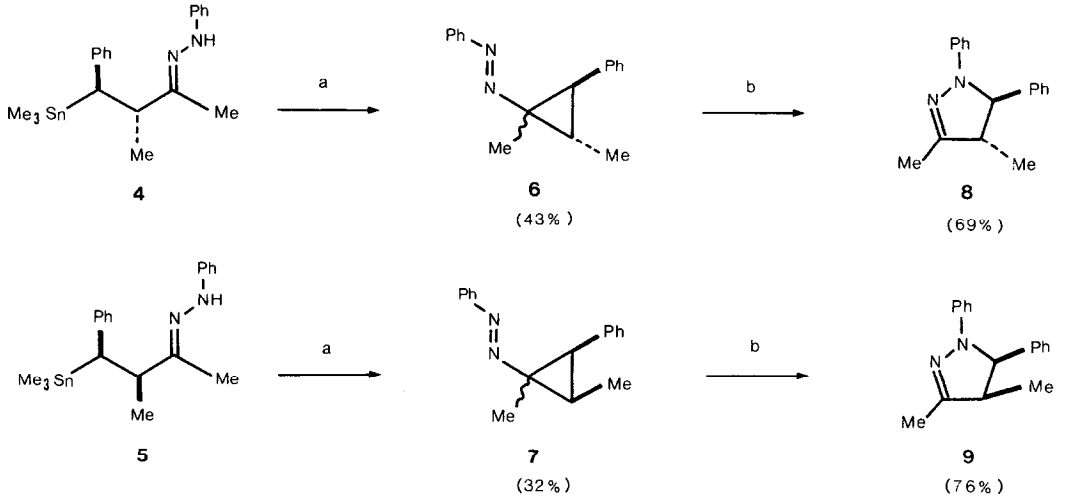
σ - radical



(B)

Interestingly, thermal rearrangement of the azocyclopropanes **2a-c** can be realised in the presence of catalytic amounts of stannous chloride in refluxing benzene for 2 h to give the Δ^2-pyrazolines **3a-c** in high yields.[8]

We have intrigued the stereochemical course of the cyclopropanation involving the cleavage of the C-Sn bond. Treatment of the stannyl hydrazones **4** and **5**[2a] with NBS at -20°C gave stereospecifically the corresponding azocyclopropanes **6** and **7**[9], respectively. It is proved that the cyclopropanation proceeds by inversion of the C-Sn bond. Although an inversion process of the C-Sn bond was already investigated in cationic reactions,[10] the inversion in our case is also interesting in terms of homolytic path on the hydrazonyl radicals. Further transformation of **6** and **7** by thermal rearrangement with stannous chloride gave regio- and stereospecifically the pyrazolines **8** and **9**[11] in good yields, respectively.



[a] NBS (1.2 equiv.), CH_2Cl_2, -20°C, 10 min. [b] cat. $SnCl_2$, toluene, 100°C, 5-6 h.

References and Notes.

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(2) For cyclopropanation see (a) I. Fleming, C. J. Urch, Tetrahedron Lett. **1983**, 24, 4591. (b) Y. Ueno, M. Ohta, M. Okawara, Ibid. **1982**, 23, 2577. (c) H. G. Kuivila, N. M. Scarpa, J. Am. Chem. Soc. **1970**, 92, 6990. (d) D. D. Davis, R. L. Cham ers, H. T. Johnson, J. Organomet. Chem. **1970**, 25, C13. (e) S. Teratake, Chemistry Lett. **1974**, 1123. (f) E. Murayama, M. Uematsu, H. Nishio, T. Sato, Tetrahedron Lett. **1984**, 25, 313. For other cationic cyclization see (g) T. L. Macdonald, S. Mahalingam, D. E. O'Dell, J. Am. Chem. Soc. **1981**, 103 6767 and references cited therein.

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(4) K. Nakatani, S. Isoe, Tetrahedron Lett. **1984**, 25, 5335. As a typical procedure for preparation of t-butyl 2-(tri-n-butylstannyl)ethyl ketone. The imine (2.0 g, 10.0 mmol) prepared from pinacolone and n-hexylamine was treated with LDA (11.0 mmol) in THF (7 mL) and HMPA (3 mL) at 0°C for 1 h. Tri-n-butyl(iodomethyl)stannane (3.7 g, 8.5 mmol) was added to the mixture, which was then stirred for 30 min. at 0°C. After usual workup, the crude product was purified by silica gel column chromatography to give the desired ketone (3.0 g, 7.5 mmol, 88% yield).

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(6) ^{1}H NMR (60 MHz, $CDCl_3$); **2a**, 1.12 (m, 2 H, CHCH), 1.54 (s, 3 H, CH_3), 1.60 (m, 2 H, CHCH), 7.18-7.30 (m, 5 H); **2b**, 1.08 (m, 2 H, CHCH), 1.90 (s, 9 H, t-Bu), 1.92 (m, 2 H, CHCH), 7.20-7.80 (m, 5 H); **2c**, 1.53 (m, 2 H, CHCH), 1.90 (m, 2 H, CHCH), 7.15-7.80 (m, 10 H). MS m/e; **2a**, 160 (M^+), 91 (100);**2b**, 202 (M^+, 44), 187 (63), 91 (100), 77 (43);**2c**, 222 (M^+, 51), 117 (41), 77 (79).

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(8) ^{1}H NMR (60 MHz, $CDCl_3$); **3a**, 2.04 (s, 3 H, CH_3), 2.76 (m, 2 H, J = 10.0, 9.5, and 2.0 Hz, $CH_2C{=}N$), 3.67 (m, 2 H, J = 10.0, 9.5, and 2.0 Hz, CH_2N), 6.70-7.80 (m, 5 H); **3b**, 1.26 (s, 9 H, t-Bu), 2.84 (m,2 H, J = 10.0, 9.5, and 2.0 Hz, $CH_2C{=}N$), 3.64 (m, J = 10.0, 9.5, and 2.0 Hz, CH_2N), 6.6-7.7 (m, 5 H); **3c**, 3.13 (m, 2 H, J = 10.0, 9.8, and 2.3 Hz, $CH_2C{=}N$), 3.80 (m, 2 H, J = 10.0, 9.8, and 2.3 Hz, CH_2N), 6.70-8.00 (m, 10 H). MS m/e; **3a**, 160 (M^+, 100), 91 (35), 77 (31); **3b**, 202 (M^+, 100), 187 (97), 180 (60), 77 (28); **3c**, 222 (M^+, 100), 91 (22), 77 (27). **3a**, mp 74.0-75.5; **3c**, mp 149.5-151.5 °C.

(9) ^{1}H NMR (60 MHz, $CDCl_3$); **6**, 1.13 (s, 3 H, CH_3), 1.40 (d, 3 H, J = 7.0 Hz, CH_3), 1.87 (m, 1 H, CH), 3.14 (d, 1 H, J = 7.3 Hz, CHPh), 7.10-7.80 (m, 10 H); **7**, 1.22 (d, 3 H, J = 6.9 Hz, CH_3), 1.43 (s, 3 H, CH_3), 2.30 (m, 1 H, CH), 3.22 (d, 1 H, J = 10.0 Hz, CHPh), 7.10-7.80 (m, 10 H).

(10) (a) H. A. Olszowy, W. Kitching, Organometallics, **1984**, 3, 1676 (b) J. M. Fukuto, F. R. Jensen, Acc. Chem. Res. **198**, 16, 177. Also see ref (2a).

(11) ^{1}H NMR (60 MHz, $CDCl_3$); **8**, 1.25 (d, 3 H, J = 7.5 Hz, CH_3), 2.00 (s, 3 H, CH_3), 2.98 (m, 1 H, CH), 4.36 (d, 1 H, J = 8.6 Hz, CHPh), 6.80-7.60 (m, 10 H); **9**, 0.72 (d, 3 H, J = 7.6 Hz, CH_3), 2.01 (s, 3 H, CH_3), 3.45 (m, 1 H, CH), 5.02 (d, 1 H, J = 11.2 Hz, CHPh), 6.70-7.50 (m, 10 H).

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