Novel Intramolecular Cyclization Reaction Involving a Thionitroso Group: Formation of a 3,3a-Dihydro-2,1-benzisothiazole from an *o*-Alkylthionitrosoarene

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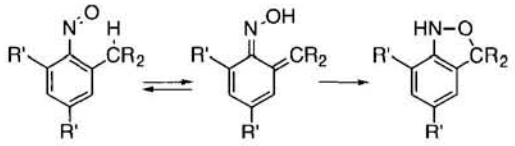
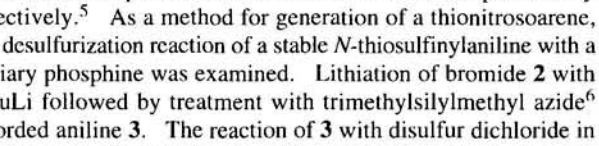
A thionitrosoarene generated by the desulfurization reaction of a stable *N*-thiosulfinylaniline bearing a bowl-type substituent underwent the intramolecular cyclization reaction involving the *ortho*-alkyl group to afford the corresponding 3,3a-dihydro-2,1-benzisothiazole. The intermediacy of the thionitrosoarene was corroborated by a trapping experiment with aniline.

Thionitroso compounds (R-N=S) have been attracting much attention as sulfur analogs of nitroso compounds.[1] However, the study of their chemistry has been hampered by their extreme instability, especially high liability to dimerization, and their reactivities except those for cycloaddition reactions[2] have been almost unexplored although we previously reported the oxidation and sulfurization of a thionitrosoarene.[3] Nitrosoarenes bearing an *ortho*-alkyl group are known to undergo ready intramolecular cyclization via [1,5] hydrogen shift (Scheme 1),[4] but it has never been described if thionitrosoarenes show such reactivity. In this communication, we report a novel intramolecular cyclization reaction of an *o*-alkylthionitrosoarene to afford a 3,3a-dihydro-2,1-benzisothiazole.

Scheme 1.

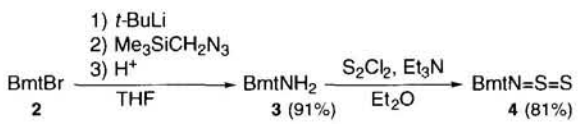


We have recently developed a bowl-type substituent **1** (denoted as Bmt hereafter) and found that its bowl-shaped framework can prevent dimerization of a reactive species very effectively.[5] As a method for generation of a thionitrosoarene, the desulfurization reaction of a stable *N*-thiosulfinylaniline with a tertiary phosphine was examined. Lithiation of bromide **2** with *t*-BuLi followed by treatment with trimethylsilylmethyl azide[6] afforded aniline **3**. The reaction of **3** with disulfur dichloride in the presence of triethylamine afforded *N*-thiosulfinylaniline **4**, which was isolated as purple crystals by silica gel chromatography in 81% yield (Scheme 2).[7] Compound **4** showed high stability both in the solid state and in solution, but prolonged heating in solution (80 °C, 4 d, in toluene-d_8) converted **4** to 2,1-benzisothiazole **5**[8] and **3** (Scheme 3). Similar cyclization reactions were also reported for *N*-thiosulfinylanilines **6**[9] and **7**.[10]

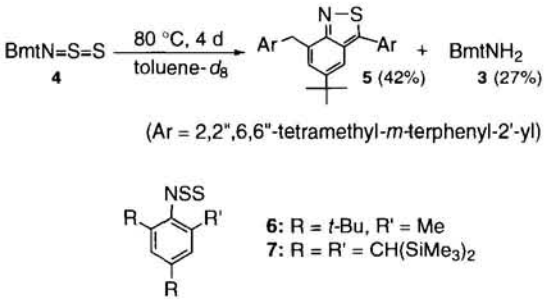


1 = **Bmt**

Scheme 2.

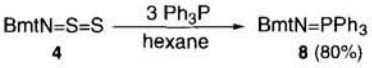


Scheme 3.

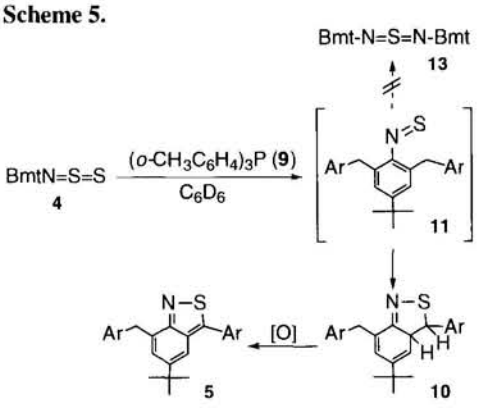


Treatment of **4** with an equimolar amount of triphenylphosphine afforded the fully desulfurized product, iminophosphorane **8**, along with recovered **4**. When three equimolar amount of phosphine was employed, **8** was formed almost quantitatively (isolated yield 80%, Scheme 4). For the prevention of the second desulfurization process, a more hindered phosphine, tri-*o*-tolylphosphine (**9**), was employed. The ^{1}H NMR monitoring of the reaction of **4** with an equimolar amount of **9** in C_6D_6 at room temperature indicated that the reaction was almost completed within 12 h to afford one diastereomer of 3,3a-dihydro-2,1-benzisothiazole **10**[11] as a main product although its stereochemistry has not been determined (Scheme 5). The signals assignable to the other diastereomer of **10** were observed

Scheme 4.

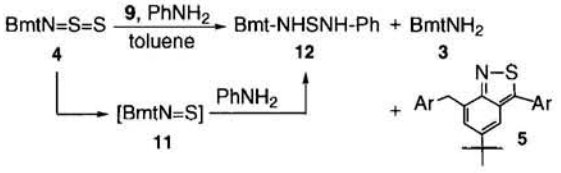


Scheme 5.



but only very slightly. During the purification, **10** was partially oxidized to **5** and their combined yield was 77%. The formation of **10** can be most reasonably explained in terms of the intramolecular cyclization reaction of the intermediary thionitrosoarene **11**, which is analogous to that of nitrosoarenes. The intermediacy of **11** was corroborated by a trapping experiment with aniline. The desulfurization reaction of **4** with **9** in the presence of an equimolar amount of aniline afforded thiodiamide **12**, an adduct of **11** with aniline, along with **3** and **5** (ratio 1:5:3, Scheme 6). The structure of **12** was confirmed by X-ray crystallographic analysis as shown in Figure 1.[12] Compound **3** is considered to be formed by the reaction of **12** with a second molecule of aniline. The independent experiment indicated that **12** reacts with aniline to give **3**. It is of note that thiodiimide **13**, which could be formed via dimerization of thionitrosoarene **11** followed by spontaneous desulfurization, was not detected in these desulfurization reactions of **4** with phosphines (see Scheme 5). We previously reported that the reaction of *N*-thiosulfinylaniline **6** with triphenylphosphine afforded the corresponding thiodiimide along with the iminophosphorane bearing the same substituent.[13] Even in a similar reaction of **7** with a very bulky substituent, the corresponding thiodiimide was found to be the main product.[1] In these cases, the dimerization of the intermediary thionitrosoarenes is considered to be faster than the cyclization to the *ortho*-alkyl group. It is likely that the effective prevention of the dimerization process of thionitrosoarene **11** by the bowl-shaped framework of **1** enabled its intramolecular cyclization reaction to be observed.

Scheme 6.



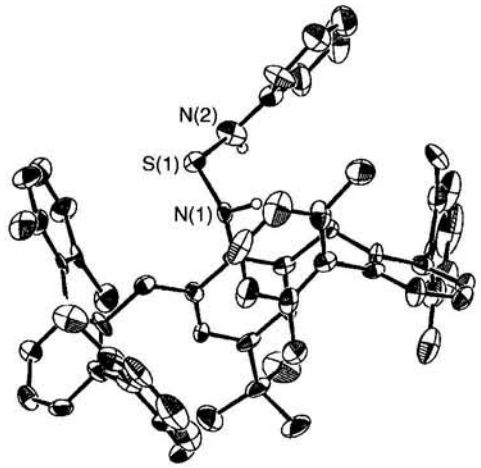


Figure 1. ORTEP drawing of **12** (30% probability).

Further investigations are currently in progress on the stabilization of a thionitroso compound by taking advantage of a steric protection group without an *ortho*-alkyl group which is responsible for the intramolecular cyclization.

We are grateful to Associate Prof. N. Tokitoh of the University of Tokyo for the determination of the X-ray structure of **12**. We also thank Shin-etsu Chemical Co., Ltd. and Tosoh Akzo Co., Ltd. for the generous gifts of chlorosilanes and alkyllithiums, respectively.

References and Notes

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7 Spectral and analytical data for **4**: dark purple crystals; mp 166 °C (dec); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (s, 9H, $C(CH_3)_3$), 1.88 (s, 24H, CH_3), 2.94 (s, 4H, CH_2), 6.52 (s, 2H), 6.81 (d, J = 7.5 Hz, 8H), 6.97 (t, J = 7.5 Hz, 4H), 7.00 (d, J =7.5 Hz, 4H), 7.32 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8 (q), 31.1 (q), 32.6 (t), 34.5 (s), 124.1 (d), 126.7 (d), 127.1 (d), 127.4 (d), 127.5 (s), 129.1 (d), 135.9 (s), 136.9 (s), 140.4 (s), 142.0 (s), 145.2 (s), 147.5 (s). UV/Vis (hexane) λ_{max} 207(ε 140000), 273 (3500, sh), 348 (3900), 477 (1900), 559 (940, sh) nm. Found: C, 83.18; H, 7.40; N, 1.84; S, 8.05%. Calcd for $C_{56}H_{57}NS_2$: C, 83.22; H, 7.11; N, 1.73; S, 7.94%. HRMS (FAB): Found m/z 808.4036. Calcd for $C_{56}H_{58}NS_2$: $[M+H]^+$ 808.4011.

8 Selected spectral and analytical data for **5**: colorless crystals; mp 293-295 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.84 (s, 12H), 2.06 (s, 6H), 2.07 (s, 6H), 3.83 (s, 2H), 6.60 (s, 1H), 6.63 (d, J = 7.5 Hz, 4H), 6.76 (t, J = 7.5 Hz, 2H), 6.81 (s, 1H), 6.82 (d, J = 7.2 Hz, 2H), 6.92 (d, J = 7.5 Hz, 2H), 6.91-6.96 (m, 4H), 6.99 (t, J = 7.5Hz, 1H), 7.21 (d, J = 7.5Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H). Found: C, 86.68; H, 7.38; N, 1.91; S, 3.86%. Calcd for $C_{56}H_{55}NS$: C, 86.89; H, 7.16; N, 1.81; S, 4.14%.

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11 Selected spectral data for **10**: ^{1}H NMR (270 MHz, $CDCl_3$) δ = 1.03 (s, 9H), 1.90 (s, 12H), 2.06 (s, 3H), 2.12 (s, 6H), 2.31 (s, 3H), 2.94 (d, J = 16.2 Hz, 1H, -CHH'-), 3.33 (d, J = 16.2 Hz, 1H, -CHH'-), 5.25 (dd, J = 7.3 and 2.7 Hz, 1H, H^{3a}), 5.47 (d, J = 2.7 Hz, 1H, H^3), 6.32 (d, J = 1.6 Hz, 1H, H^6), 6.79 (dd, J = 7.3 and 1.6 Hz, 1H, H^4), 6.96-7.37 (m, 18H).

12 Crystal data for **12**: $C_{62}H_{64}N_2S$, FW = 869.26, *monoclinic*, space group $P2_1/c$, a = 11.758(4) Å, b = 15.599(3) Å, c = 28.144(4) Å, β = 92.57(2)°, V = 5156(1) Å^3, Z = 4, D_{calcd} = 1.120 g/cm^3, μ = 1.03 cm^{-1}, R (R_w) = 0.083 (0.086).

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