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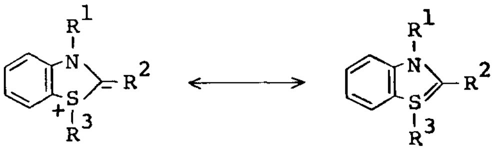
REACTION OF BENZOTHIAZOLINE WITH BENZYNE - GENERATION OF NOVEL HETEROCYCLIC SULFUR YLIDE, BENZOTHIAZOLINIUM S-YLIDE[1)]

Mikio Hori*, Tadashi Kataoka, Hiroshi Shimizu, and Norihiro Ueda
Gifu College of Pharmacy, 6-1, Mitahora-higashi 5-chome, Gifu 502, Japan

Summary: A novel heterocyclic sulfur ylide, 2-t-butyl-3-methyl-1-phenylbenzothiazolinium ylide (13) was generated as an intermediate in the reaction of 2-t-butyl-3-methylbenzothiazoline (2) with benzyne. The S-ylide 13 underwent a novel intermolecular [1,2] shift to give 2-t-butyl-3-methyl-2-phenylbenzothiazoline (4).

No study has been reported on the synthesis of a novel 6π-electronic nitrogen-containing sulfur ylide, benzothiazolinium S-ylide 1 which has an isoelectronic structure to benzothiazole, because of the difficulty of the selective S-alkylation and S-arylation of benzothiazolines.[2,3)] In the course of our studies on the selective S-alkylation of benzothiazoline derivatives with several alkylating agents, we found that 2-t-butyl-3-methylbenzothiazoline (2)[4)] having a sterically hindered substituent at C_2-position was exclusively methylated at sulfur atom with Meerwein reagent to give 2-t-butyl-1,3-dimethylbenzothiazolinium tetrafluoroborate, which was, however, very unstable and then decomposed into N-methyl-(o-methylthio)anilinium tetrafluoroborate.[5)] This finding prompted us to challenge the synthesis of the titled novel benzothiazolinium S-ylide. We carried out the reaction of 2 with benzyne, and recognized its generation as a reaction intermediate.



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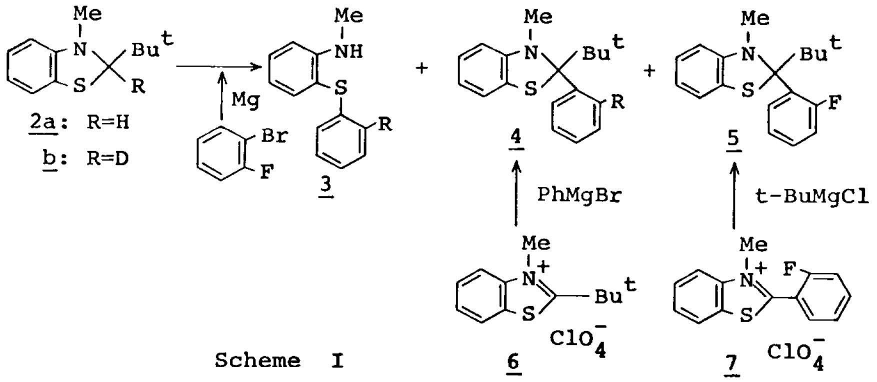
2-t-Butyl-3-methylbenzothiazoline (2a, R=H) was allowed to react with benzyne generated from the reaction[6)] of o-bromofluorobenzene with magnesium at room temperature for 4 hr in dry THF. The reaction products were separated by column chromatography on silica gel using $CHCl_3$-n-hexane (1:3) as an eluent. N-Methyl-(o-phenylthio)aniline (3a, R=H)[7)] in 18 % yield, 2-t-butyl-3-methyl-2-phenylbenzothiazoline (4a, R=H) as colorless prisms (EtOH), mp 113-114° in 34 % yield: NMR ($CDCl_3$) δ 1.38 (9H, s, t-Bu), 2.88 (3H, s, N-Me), 6.10-7.80 (9H, m, ArH); MS (m/e) 283 (M^+), 226 (base), and 2-t-butyl-2-(o-fluorophenyl)-3-methylbenzothiazoline (5) as colorless prisms (EtOH), mp 123-124° in 31 % yield: NMR ($CDCl_3$) δ 1.35 (9H, s, t-Bu), 2.80 (3H, d, J=1.5 Hz, N-Me), 6.10-7.90 (8H, m, ArH); MS (m/e) 301 (M^+), 244 (base). The structure of 4a or 5 was determined by comparison with the corresponding authentic sample, prepared from the reaction of benzothiazolium perchlorate (6 or 7)[8)] with Grignard reagent (phenylmagnesium bromide

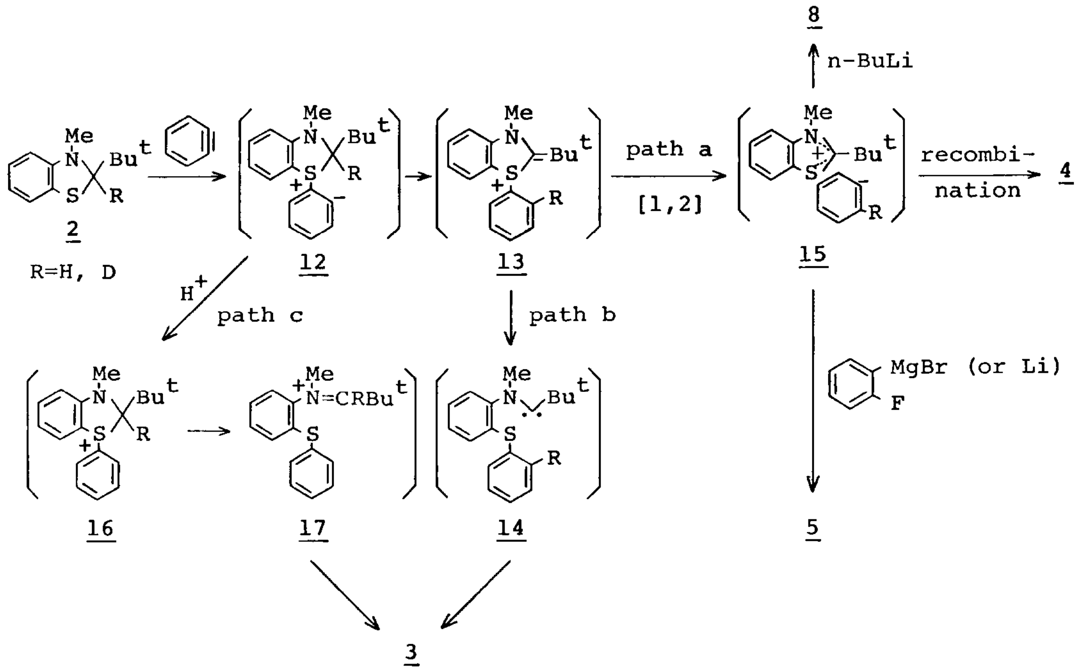


Scheme I

or t-butylmagnesium chloride), respectively, as shown in Scheme I.

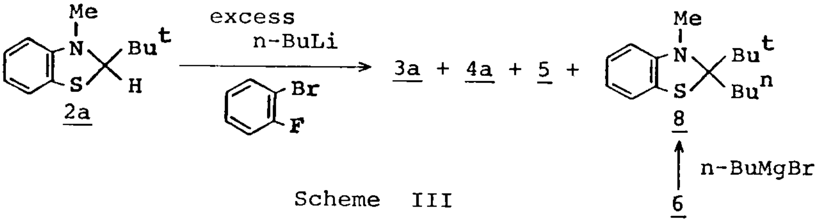
In order to elucidate the above reaction mechanism, the following experiments were carried out. The reaction of 2-t-butyl-2-deuterio-3-methylbenzothiazoline (2b, R=D)[9] with benzyne under the same conditions gave 5 and other two products, having a deuterium in the phenyl group derived from benzyne, respectively. One of them was o-(o-deuteriophenylthio)-N-methylaniline (3b,R=D) as an oil: IR (neat) ν max cm^{-1} 3390 (NH), 2200 (C-D); NMR ($CDCl_3$) δ 2.78 (3H, s, N-Me), 4.9 (1H, broad s, NH), 6.50-7.50 (8H, m, ArH); high-resolution MS (m/e) 216.0833 (Calcd for $C_{13}H_{12}NDS$, 216.0833), and the other was 2-t-butyl-2-(o-deuteriophenyl)-3-methylbenzothiazoline (4b, R=D) as colorless prisms (EtOH), mp 113-114°: NMR ($CDCl_3$) δ 1.35 (9H, s, t-Bu), 2.85 (3H, s, N-Me), 6.10-7.10 (8H, m, ArH); high-resolution MS (m/e) 284.1432 (Calcd for $C_{18}H_{20}NDS$, 284.1434). And the sulfone derivative of 2a, whose sulfur atom has no nucleophilicity, did not react with benzyne, and was recovered completely, which exclude the possibility of the direct insertion of benzyne to the C_2-position of benzothiazoline to give the product 4. Thus, it was suggested that the expected benzothiazolinium S-ylide 13 was formed by the intramolecular abstraction of C_2-proton by the anion site of the betaine 12 formed by the initial attack of benzyne at the sulfur atom of 2, and then the cleavage of C_2-S bond of the S-ylide 13 afforded the product 3a via the postulated carbene intermediate 14 as shown in the path b of Scheme II.

In addition, the reaction of 2a with benzyne generated from the reaction[10] of o-bromofluorobenzene with excess n-butyllithium[11] at -40°C in dry ether gave 2-n-butyl-2-t-butyl-3-methylbenzothiazoline (8) as colorless prisms (EtOH), mp 42-43° in 3 % yield, besides 3a, 4a, and 5: NMR ($CDCl_3$) δ 0.65-2.60 (9H, m, n-Bu), 1.05 (9H, s, t-Bu), 2.85 (3H, s, N-Me), 5.95-7.25 (4H, m, ArH); MS (m/e) 263 (M^+). The compound 8 was identified with the authentic sample synthesized by the Grignard reaction of 6 with n-butylmagnesium bromide (Scheme III). This result indicates that 4 was given by the intermolecular [1,2] shift of the phenyl group of the ylide 13. As shown in the path a of Scheme II, the ylide 13 was decomposed to the phenyl anion and the benzothiazolium cation 15, and then recombined to give 4. The cation 15 was trapped with an excess of n-butyllithium to form 8, and besides, with o-fluorophenylmagnesium bromide



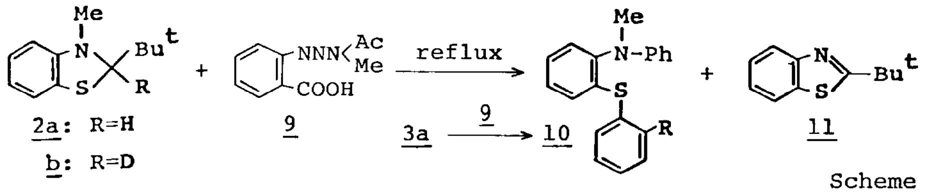
Scheme II

or o-fluorophenyllithium, the precursor of benzyne, to produce 5.



Scheme III

On the other hand, the reaction of 2a with the benzyne generated by the thermolysis of 3-acetyl-3-methyl-1-(2-carboxyphenyl)triazene (9)[12] in chlorobenzene did not give 4a, but N-methyl-N-phenyl-(o-phenylthio)aniline (10a, R=H) as an oil in 45 % yield: NMR ($CDCl_3$) δ 3.22 (3H, s, N-Me), 6.48-7.60 (14H, m, ArH); MS (m/e) 291 (M^+), and 2-t-butylbenzothiazole (11)[13] in 46 % yield as shown in Scheme IV. Compound 10a was formed from the further reaction of the intermediate 3a with an excess of benzyne. This was confirmed by the fact that 3a was treated with benzyne under the same conditions to give 10a. Moreover, on treating with benzyne generated thermally as above, benzothiazoline 2b gave a mixture[14] of 10a and 10b (R=D), different from the case with benzyne generated by the Grignard and the n-butyllithium method. From these results, it is reasonable to consider that a part of 3, a precursor of 10, was formed by the mechanism depicted in the path c of Scheme II; the intermediate 16 was derived from the betaine 12 by the protonation with the acid 9, and decomposed to give 3 via 17.



Scheme IV

Attempts to isolate the titled novel heterocyclic sulfur ylide are intensively being continued in our laboratory.

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5) Physico-chemical data of the product are: colorless prisms (AcOH), mp 147-148°; IR (KBr) ν max cm^{-1} 1070 (BF_4^-); NMR (CF_3COOH) δ 2.61 (3H, s, S-Me), 3.36 (3H, t, J=4 Hz, N-Me), 7.53-7.90 (4H, m, ArH), 8.5 (2H, broad s, NH_2).
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7) M. Hisaoka, K. Akiba, and N. Inamoto, Bull. Chem. Soc. Jpn., 48, 3274 (1975).
8) Satisfactory physico-chemical data were obtained for 6 and 7.
9) Compound 2b was prepared in high yield by the reaction of 6 with lithium aluminum deuteride at 0° in ether, and satisfactory physico-chemical data were obtained for it: colorless oil, bp 85°/ 1 mm Hg; IR (neat) ν max cm^{-1} 2150 (C-D); NMR ($CDCl_3$) δ 0.93 (9H, s, t-Bu), 2.96 (3H, s, N-Me), 6.33-7.17 (4H, m, ArH); high-resolution MS (m/e) 208.1153 (Calcd for $C_{12}H_{16}NDS$, 208.1152).
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11) Compound 2a did not react with only n-butyllithium in ether, and was recovered completely.
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14) Two peaks of 291 (M^+ of 10a) and 292 (M^+ of 10b) were observed intensively in the MS spectra of the reaction mixture.

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