Communications to the Editor

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A New Aspect on Alkylation of Benzothiazolines

A striking difference between the reactions of 3-methylbenzothiazoline derivatives with trimethyloxonium tetrafluoroborate and with methyl iodide has been found. Especially, by the treatment of 2,2,3-trimethylbenzothiazoline with methyl iodide, N-methyl-N-(*o*-methylthiophenyl)-N-isopropylideneiminium iodide has been obtained. Mechanism for the reaction was also proposed.

Keywords——benzothiazoline; benzothiazolinium tetrafluoroborate; benzothiazolium iodide; S-alkylation; alkylidene iminium iodide

In the preceding paper,[1] we published a facile synthesis of benzothiazoline derivatives by the reactions between 3-alkylbenzothiazolium halides with Grignard reagent or metal hydrides such as lithium aluminum hydride and sodium borohydride. At the same time, a similar method as mentioned above has also been reported by Akiba, *et al.*[2] However, investigation on the reactivity of benzothiazolines has not been done. In connection with our studies on thiabenzenes,[3] we found a striking difference between the reaction of benzothiazolines with trimethyloxonium tetrafluoroborate (Meerwein reagent) and with methyl iodide. In this communication, description will be made on a novel aspect on the alkylation of 3-methylbenzothiazoline derivatives.

Stirring 5-chloro-3-methyl-2-phenylbenzothiazoline (**1a**)[1] with an equimolar amount of Meerwein reagent in dichloroethane for 24 hr at room temperature gave 5-chloro-3,3-dimethyl-2-phenylbenzothiazolinium tetrafluoroborate (**2a**, 84%, colorless prisms (ethanol), mp 202—203° (decomp.)). Similarly, the same type of reaction products, 2,2,3,3-tetramethyl- (**2b**, 59%, colorless plates, mp 177—180° (decomp.)), 3,3-dimethyl-2-(*p*-nitrophenyl)- (**2c**, 96%, colorless needles, 209—210° (decomp.)), and 2-benzoyl-3,3-dimethylbenzothiazolinium tetrafluoroborate (**2d**, 83%, colorless prisms, mp 199—200° (decomp.)) were respectively obtained from 2,2,3-trimethyl- (**1b**),[4b] 3-methyl-2-(*p*-nitrophenyl)- (**1c**),[4a] 2-benzoyl-3-methylbenzothiazoline (**1d**)[4b] with Meerwein reagent under the above conditions as shown in Chart 1. These structures (**2a**—**d**) were assigned on the basis of the physical data summarized in Table I. Furthermore, **2a** was chemically also confirmed by desulfurization reaction using Raney-Ni (W-7) to give *m*-chloro-N,N-dimethylaniline (46%, picrate, yellow plates, mp 145°).[5] **2d** was also stirring with sodium hydride in THF under N_2 stream at room temperature to give Stevens rearrangement product, 2-benzoyl-2,3-dimethylbenzothiazoline (32%, colorless oil, bp_1 196—198°, *Anal.* Calcd. for $C_{16}H_{15}ONS$; C, 71.34; H, 5.61; N, 5.20. Found: C, 71.21; H, 5.78; N, 5.14, NMR ($CDCl_3$) δ: 1.90 (3H, s, C_2–CH_3), 2.67 (3H, s, N–CH_3), 6.20—7.60 (7H, m, aromatic H), 8.00—8.25 (2H, m, aromatic H), IR ν_{max}^{Film} cm^{-1}: 1680 (C=O)).

On the other hand, the reactions of 3-methyl- (**1e**),[4a] 2,3-dimethyl- (**1f**),[4b] 3-methyl-2-phenyl- (**1h**),[1] and 2,2,3-trimethylbenzothiazoline (**1b**) with excess methyl iodide in refluxed ether for 8 hr were quite different from the cases of **1a**—**d** with Meerwein reagent as shown in Chart 2. Namely, the treatment of **1e** with methyl iodide gave 3,3-dimethylbenzothiazolinium

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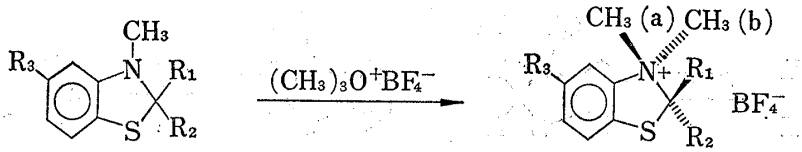

1a: $R_1=C_6H_5$, $R_2=H$, $R_3=Cl$ **2a**: $R_1=C_6H_5$, $R_2=H$, $R_3=Cl$
1b: $R_1=R_2=CH_3$, $R_3=H$ **2b**: $R_1=R_2=CH_3$, $R_3=H$
1c: $R_1=C_6H_4NO_2(p)$, $R_2=R_3=H$ **2c**: $R_1=C_6H_4NO_2(p)$, $R_2=R_3=H$
1d: $R_1=COC_6H_5$, $R_2=R_3=H$ **2d**: $R_1=COC_6H_5$, $R_2=R_3=H$

Chart 1

TABLE I. ^1H NMR Spectral Data for the Structural Assignment of the Compounds

Compound[a]	(CF_3CO_2H) δ (ppm)
2a	3.22 (3H, s, N-CH_3 (a)), 3.71 (3H, s, N-CH_3 (b)), 6.57 (1H, s, C_2-H), 7.45—8.10 (8H, m, aromatic H)
2b	2.02 (3H, broad s, C_2-CH_3), 2.04 (3H, broad s, C_2-CH_3), 3.52 (6H, s, N-CH_3), 7.34—7.64 (4H, m, aromatic H)
2c	3.33 (3H, s, N-CH_3 (a)), 3.85 (3H, s, N-CH_3 (b)), 6.68 (1H, s, C_2-H), 7.56—7.86 (4H, broad s, aromatic H), 8.36 (4H, q (A_2B_2 type), $J_{AB}=9$ Hz, $\Delta\nu=31.7$ Hz, C_2 and aromatic H)
2d	4.00 (3H, s, N-CH_3 (b)), 4.10 (3H, s, N-CH_3 (a)), 6.95 (1H, s, C_2-H), 7.35—7.55 (7H, m, aromatic H), 7.55—8.25 (2H, m, aromatic H)
2e	3.76 (6H, s, N-CH_3), 5.23 (2H, s, C_2-H), 7.30—7.70 (4H, m, aromatic H)
2f	1.99 (3H, d, $J=6.75$ Hz, C_2-CH_3), 3.40 (3H, s, N-CH_3 (a)), 3.75 (3H, s, N-CH_3 (b)), 5.53 (1H, q, $J=6.75$ Hz, C_2-H), 7.15—7.70 (4H, m, aromatic H)
2j[b]	2.45 (3H, broad s, =C-CH_3 (b)), 2.57 (3H, s, S-CH_3), 3.05 (3H, broad s, =C-CH_3 (a)), 3.93 (3H, broad s, N-CH_3), 7.10—7.53 (3H, m, aromatic H), 8.10—8.35 (1H, m, aromatic H)

a) All new compounds gave satisfactory elemental analysis.
b) **2j** was measured in $CDCl_3$.

iodide (**2e**, 87%, colorless needles (methanol), mp 168—169° (decomp.)). However, under the same reaction condition with **1e**, **1f** gave 2,3,3-trimethylbenzothiazolinium iodide (**2f**, 54%, colorless prisms (ethanol), mp 143—146° (decomp.)) besides 2,3-dimethylbenzothiazolium iodide (**2g**, 18%, mp 229—230° (decomp.))[4c] and in addition, **1h** gave only 3-methyl-2-phenylbenzothiazolium iodide (**2h**, 90%, mp 218° (decomp.)).[1]

Thus, carrying out the reaction of methyl iodide and more crowded **1b** in boiling benzene[6] for 8 hr or in a sealed tube (100°) without benzene for 3 hr, a ring-opening product, N-methyl-N-(*o*-methylthiophenyl)-N-isopropylideneiminium iodide (**2j**, 65%, colorless needles (dichloroethane–ether), mp 175—178° (decomp.), *Anal.* Calcd. for: $C_{11}H_{16}INS$; C, 41.13; H, 5.02; N, 4.36. Found: C, 41.07; H, 4.93; N, 4.39) has been obtained. The structural assignment of **2e—j** is based on NMR data (see Table I). Especially, **2j** was strongly supported by the IR ν_{max}^{KBr} cm^{-1}: 1650 ($>\overset{+}{N}=C<$) and also chemically confirmed by the hydrolysis using K_2CO_3 aq. solution to afford *o*-methylthio-N-methylaniline (91%, colorless oil, $bp_{0.18}$ 62—64°, NMR ($CDCl_3$) δ: 2.33 (3H, s, S-CH_3), 2.90 (3H, s, N-CH_3), 6.55—6.90 (2H, m, aromatic H), 7.10—7.60 (2H, m, aromatic H), IR ν_{max}^{Film} cm^{-1}: 3380 (NH)), which was synthesized by the methylation of sodium methylaminobenzenethiolate.

The formation of **2j** is considered to proceed *via* the unstable intermediate (**2i**) formed by the initial S-alkylation, followed by the ring opening reaction as shown in Chart 2.

Further related studies directed toward the applications to synthetic and theoretical organic chemistry are also in progress.

6) In the case of ether, the reaction was slow.

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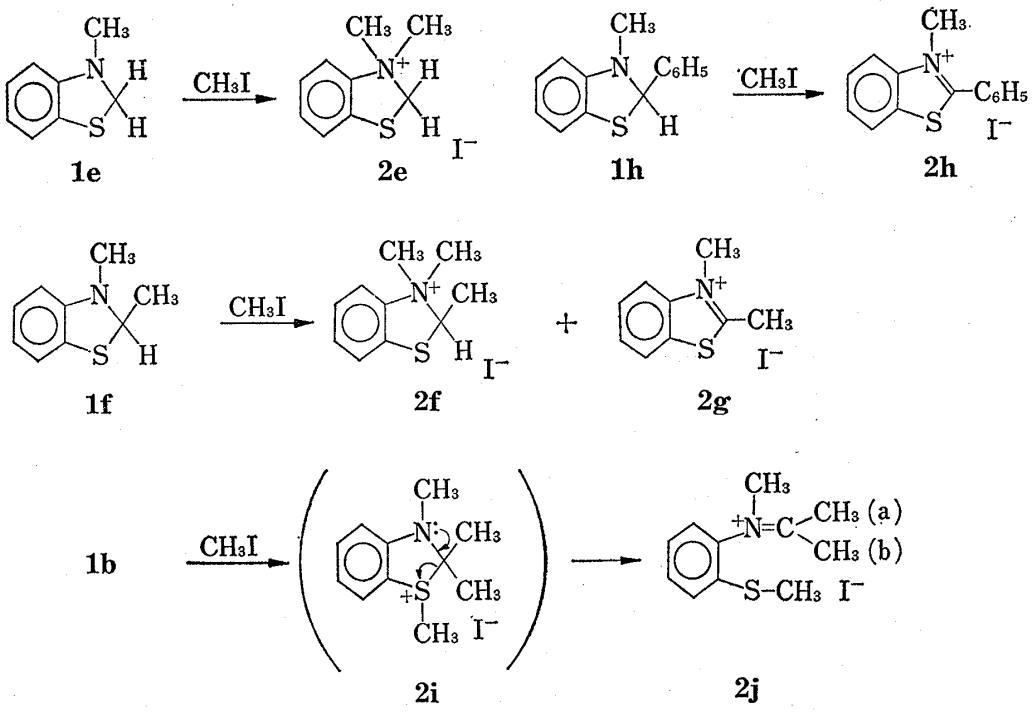

Chart 2

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Chemical Structure and Sweet Taste of Isocoumarins and Related Compounds[1] Synthesis of 5-Hydroxyflavanones and Related Dihydrochalcones

On the basis of the information obtained from our previous studies on relationship between structure and sweet taste of 3,4-dihydroisocoumarins, 5-hydroxyflavanones and related dihydrochalcones were synthesized. Compounds (**2**, **3**, **4**, and **7**) had a sweet taste while the others were tasteless. The relationship of structure-sweet taste of 5-hydroxyflavanones was similar to that of 3,4-dihydroisocoumarins.

Keywords——structure-sweet relationship; 3,4-dihydroisocoumarin; flavanone; dihydrochalcone; phyllodulcin

The taste of flavanones, chalcones, and dihydrochalcones were reported by Horowitz, *et al.*[2] Subsequently, Krbechek, *et al.* clarified the relationship between sweet taste and the substituent in B ring of the dihydrochalcone-4′-glycosides.[3] According to their reports,

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