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Preparation and Thermal Decomposition of 1,4,5- and 1,3,5-Trimethyltetrazolium Iodides

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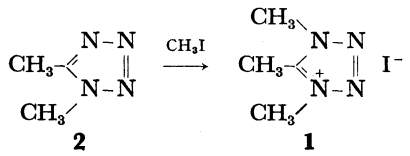
1,4,5- and 1,3,5-Trimethyltetrazolium iodides were prepared by the reaction of methyl iodide with 1,5- and 2,5-dimethyltetrazoles, and the reaction of methyl iodide with 5-methyltetrazole. The latter method is more facile for the preparation of these iodides. Upon thermal decomposition of the 1,3,5-trimethyl salt at 130°C, the 1-methyl group was eliminated predominantly to yield 2,5-dimethyltetrazole. When the 1,4,5-trimethyl salt was decomposed at 270°C, a mixture of 1,5- and 2,5-dimethyltetrazole was obtained in 74% and 21% yields, respectively. For the formation of 2,5-dimethyltetrazole from the 1,4,5-trimethyl salt, there has been shown an intermolecular methylation scheme that the 1,4,5-trimethyl salt methylated 1,5-dimethyltetrazole being formed *in situ* to give the 1,3,5-trimethyl salt.

In our previous paper,[1] quantitative isomerization of 1-alkyl-5-phenyltetrazole into the 2-alkyl isomer in the presence of alkyl iodide has been reported. The study of thermal decomposition of 1,3- and 1,4-dialkyl-5-phenyltetrazolium iodides revealed that 2-alkyl-5-phenyltetrazole was produced predominantly from the 1,3-dialkyl salt. The 1,4-dialkyl salt, more stable than the 1,3-dialkyl salt, was decomposed at 130°C to produce 1-alkyl-5-phenyltetrazole. As an extention of the preceding work, this paper presents a study of the preparation and thermal decomposition of 1,4,5- and 1,3,5-trimethyltetrazolium iodides.

As for the study of 5-methyltetrazolium iodides, there has been only one patent[2] in which was reported the preparation of 1,4,5-trimethyltetrazolium iodide (**1**) by the reaction of 1,5-dimethyltetrazole (**2**) with methyl iodide. In view of the formation of 1,3-dimethyl-5-phenyltetrazolium iodide as well as the 1,4-dimethyl salt from 1-methyl-5-phenyltetrazole,[1] formation of 1,3,5-trimethyltetrazolium iodide (**3**) from **2** was expected. However, in the reaction of **2** with methyl iodide carried out at 100°C for 2 hr or at room temperature for 10 days, the 1,4,5-trimethyl salt **1** was produced selectively without the formation of the other isomeric tetrazolium salts. The selective methylation at 4-nitrogen in 1,5-dimethyltetrazole might be

1) T. Isida, S. Kozima, K. Nabika, and K. Sisido, *J. Org. Chem.*, **36**, 3807 (1971).

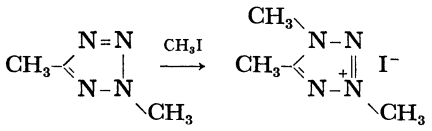
2) H. R. J. Waddington, G. F. Duffin, and J. S. Kendall, Brit. 785334 (1957); *Chem. Abstr.*, **52**, 6030i (1958).



2 **1**

attributed to more electron-donating property of the 5-methyl group than that of the 5-phenyl group. The structure of the colorless crystals **1**, (mp 266°[3] decomp) has been identified by the NMR spectrum which has two singlets at δ 4.27 ppm assigned to a couple of equivalent *N*-methyl protons and δ 2.95 ppm to 5-methyl protons.

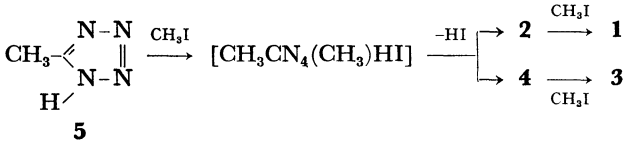
Preparation of 1,3,5-trimethyltetrazolium iodide (**3**) was carried out by the reaction of 2,5-dimethyltetrazole (**4**)[4] with methyl iodide at room temperature for a long time (90 days).



4 **3**

In the NMR spectrum of **3** prepared herewith, there were three singlets at δ 2.82, 4.34 and 4.62 ppm which could be assigned to the 5-, 1-, and 3-methyl protons, respectively. The similar assignment was reported with 1,3-dimethyltetrazolium iodide[5] and 1,3-dimethyl-5-phenyltetrazolium iodide.[1]

The above preparation of the 1,4,5-trimethyl salt **1** or the 1,3,5-trimethyl salt **3** from 1,5-dimethyltetrazole **2** or 2,5-dimethyltetrazole **4**, respectively, however, is not a convenient method, compared with the following facile one using readily prepared 5-methyltetrazole (**5**) as the starting material. When **5** was heated in an excess of methyl iodide at 40°C for 10 days, a mixture of **1** and **3** (68:32) was obtained in 77% yield together with hydrogen iodide, methane and iodine. Separation of **1** and **3** was carried out by the selective extraction of **3** from the mixture with acetone. The remaining crystals undissolved in acetone were identified as pure **1**. The crystalline **3** was precipitated by the addition of diethyl ether to the acetone extract. In the first step of this reaction there might be formed 1,5- and 2,5-dimethyltetrazole hydrogen iodides, CH_3-$CN_4(CH_3)HI$, as intermediates. These compounds not isolated yet are considered to be unstable under the reaction condition and eliminated readily hydrogen iodide to produce **2** and **4** which reacted with methyl iodide to give **1** and **3**, respectively. A part of the liberated hydrogen iodide reduced methyl iodide to give iodine and methane.[6]



5

Thermal decomposition of tetrazolium salts has never been studied in detail until our recent investigation[1] of 1,3-dimethyl-5-phenyltetrazolium iodide (**6**) and the 1,4-dimethyl-5-phenyl salt (**7**). In the case of the 5-phenyltetrazolium salts, the 1,3-dimethyl salt **6** decomposed at a lower temperature (dp below 70°C) than the 1,4-dimethyl salt **7** (dp 130°C). The analogous relation has been found between the 1,3,5-trimethyl salt **3** (dp 130°C) and 1,4,5-trimethyl salt **1** (dp 266°C).

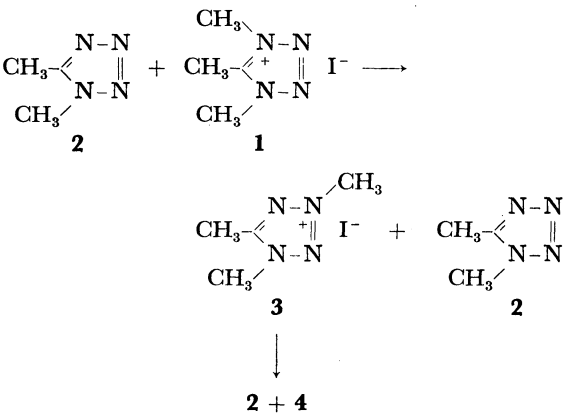
Thermal treatment of 1,3,5-trimethyltetrazolium iodide at 135°C for 30 min gave a mixture of 1,5-dimethyltetrazole **2** and 2,5-dimethyltetrazole **4** in a ratio of 15:85. 1-Methyl group was liberated predominantly to yield **4**. This is consistent with the selective elimination of the 1-methyl group in the thermal decomposition of **6**.[1] When decomposition of **3** was carried out at 180°C and 270°C, there were obtained mixtures of **2** and **4** in ratios of 42:58 and 60:40, respectively. The selectivity in the elimination of methyl iodide decreased with the elevation of the decomposition temperature.

$$\mathbf{3} \xrightarrow{-CH_3I} \mathbf{2} + \mathbf{4}$$

Thermal decomposition of 1,4,5-trimethyltetrazolium iodide **1** was carried out at 270°C, a slightly higher temperature than the decomposition point 266°C, for 3 min to afford 2,5-dimethyltetrazole **4** in 21% yield as well as 1,5-dimethyltetrazole **2** (74%) together with methyl iodide. The product **4** should be formed in the course of the thermal decomposition

$$\mathbf{1} \xrightarrow[-CH_3I]{270^\circ} \mathbf{2} + \mathbf{4}$$

of **1**, since there was no formation of **4** when pure **2** was heated at 270°C. For the formation of **4**, the following experiment showed an intermolecular methylation scheme: 1,5-dimethyltetrazole **2** formed *in situ* from 1,4,5-trimethyl salt **1** was methylated by the remaining **1** to give intermediate **3**, whose decomposition products were **2** and **4** as described above.



When thermal decomposition of **1** was carried out in the presence of 1-methyl-5-phenyltetrazole (**8**) at 270°C, there were obtained 2-methyl-5-phenyltetrazole (**9**) (23% yield based on **8**) together with **2** and **4**. It has already been established[1] that **9** was obtained from 1,3-dimethyl-5-phenyltetrazolium iodide (**6**) which was formed by the reaction of **8** with methyl iodide, and that in the absence of methyl iodide there was no

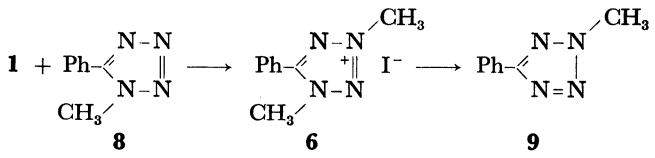
3) The reported decomposition point was 216°C.[2]

4) J. H. Markgraf, W. T. Bachman, and D. P. Hollis, *J. Org. Chem.*, **30**, 3472 (1965).

5) W. P. Norris and R. A. Henry, *Tetrahedron Lett.*, **1965**, 1213.

6) A. Butlerow, *Ann. Chem.*, **144**, 36 (1867); R. A. Ogg, Jr., *J. Amer. Chem. Soc.*, **56**, 526 (1934).

formation of **9** from **8**. Thus **8** was apparently methylated by **1** to produce **6** which liberated the 1-methyl group predominantly to yield **9** under the reaction condition. This result presented a sufficient support for the intermolecular methylation by the quaternary salt **1**.



8 **6** **9**

Experimental

Reaction of 1,5-Dimethyltetrazole (2) with Methyl Iodide. A solution of 0.125 g (1.30 mmol) of **2**[4] in 10 m*l* of methyl iodide was heated in a sealed glass bottle at 100°C for 5 hr. Upon cooling to room temperature, colorless needles were precipitated. The crystals isolated by filtration were identified as 1,4,5-trimethyltetrazolium iodide (**1**), by the elemental analysis and the NMR spectrum, 0.239 g (77.2%), dp (decomposition point) 266°, (lit,[2] dp 216°). NMR [D_2O, sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal standard] δ 2.95 (s, 3H, 5-methyl protons), δ 4.27 ppm (s, 6H, 1,4-dimethyl protons), IR (Nujol) 1590 (vs), 1540 (m), 1355 (w), 1330 (w), 1240 (w), 1213 (w), 1043 (sh), 1030 (vs), 766 (vs), 618 cm^{-1}(m).

Found: C, 20.00; H, 3.78; N, 23.34%. Calcd for $C_4H_9N_4I$: C, 20.01; H, 3.78; N, 23.34%. Evaporation of methyl iodide of the filtrate gave 0.011 g (8.8%) of **2** recovered unchanged.

Reaction of **2** with methyl iodide was also carried out at room temperature in an NMR tube. After 10 days, a singlet at δ 4.05 ppm assigned to the 1-methyl protons of **2** disappeared completely. Colorless needles precipitated were identified as pure **1** by the mixed decomposition point determination and by the IR and NMR spectra.

Reaction of 5-Methyltetrazole (5) with Methyl Iodide. To a methanol solution of 1.378 g (16.4 mmol) of **5**[4,7] was added a large excess of methyl iodide. After 10 days heating at 40°C, the reaction mixture was cooled to precipitate yellowish crystals which were filtered and washed with acetone twice to give 1.795 g of pure **1**. The collected filtrate was evaporated off to dryness *in vacuo* without heating. To the residual crystals was added 10 m*l* of acetone to give additional 0.225 g of **1** insoluble in acetone (in total, 2.020 g (51.2%) of **1**), and to the acetone solution was added 100 m*l* of dry ether to precipitate 1.04 g (26.4%) of crystals. By the additional reprecipitation procedure there were obtained colorless crystals, dp 130°C, whose structure was determined as 1,3,5-trimethyltetrazolium iodide (**3**) by the NMR spectrum (D_2O, DSS): δ 2.82 (s, 3H, 5-methyl protons), δ 4.34 (s, 3H, 1-methyl), δ 4.62 ppm (s, 3H, 3-methyl), IR (Nujol) 1554 (vs), 1336 (m), 1293 (m), 1077 (m), 1038 (s), 1026 (m), 808 cm^{-1} (vs). Elemental analysis was given up because of its highly deliquescent property.

Reaction of 2,5-Dimethyltetrazole (4) with Methyl Iodide. A solution of **4**[4] in methyl iodide was kept at room temperature in an NMR tube. After 90 days, two singlets at δ 2.53 and δ 4.30 ppm assigned to the 5- and the 2-methyl protons of **4** disappeared. A pale yellowish oily substance insoluble in methyl iodide was separated by decantation, dissolved in 1 m*l* of acetone followed by the addition of dry ether to precipitate colorless needles which were identified as **3** by the NMR and the IR spectra.

Thermal Decomposition of 1,4,5-Trimethyltetrazolium Iodide (1). Thermal decomposition of 1.2354 g (5.14 mmol) of crystalline **1** was carried out at 270°C for 5 min in a small Claisen flask heated in a molten metal bath. Methyl iodide, **4** and a part of **2** were distilled out to be trapped through a cold condenser. After pyrolysis the condenser was rinsed with additional amount of methyl iodide to collect the whole distillate. It was calculated from the total weight and the integral ratio of the NMR spectrum that the distillate contained 0.024 g of **2** and 0.102 g (21.3%) of **4**. Pure **4** was isolated by preparative gas chromatography, bp 97—98°C /760 mmHg (lit.,[4] bp 57—57.2°C/13 mmHg). The chemical shifts of **4** in the NMR spectrum were coincided with the reported ones.[4] To the residue (0.5025 g) in the flask was added 20 m*l* of acetone to separate the starting ingredient **1** unchanged. The insoluble **1** (0.090 g) was removed by filtration, and the acetone of the filtrate was evaporated *in vacuo* to give 0.3466 g of pure **2**. In total, 0.370 g (73.5%) of **2** was obtained by the pyrolysis.

Thermal decomposition of **1** was also carried out in an NMR tube. To the top of the tube was attached an effective condenser made of a long (30 cm) needle of a syringe. The needle was cooled outside by dry-ice, and the syringe was packed with granulated calcium chloride. Crystalline **1** (0.0718 g) was heated in the tube at 270°C for 3 min. After cooling the tube in an ice bath, 0.4 m*l* of deuterochloroform was added through the needle, and NMR spectrum was measured. The starting iodide **1** was completely decomposed. The distribution of **2** and **4** produced was found to be 72: 28. This is in good agreement with the former isolation results indicating little loss of vaporizable **4** in this micro-procedure. Analogous equipments were used in the following experiments.

Thermal Decomposition of 1 in the Presence of 1-Methyl-5-phenyltetrazole (8). A mixture of 0.067 g (0.279 mmol) of **1** and 0.011 g (0.069 mmol) of **8** was heated at 270°C for 3 min in an NMR tube with the cooled needles as described above. After the mixture was cooled to room temperature, methyl iodide and 2,5-dimethyltetrazole **4** were evaporated off *in vacuo*, since the chemical shifts of **4** in the NMR spectrum was close to those of 2-methyl-5-phenyltetrazole (**9**). After evaporation of **4**, the residue was dissolved in deuterochloroform and the NMR spectrum was measured. The ratio of **8** and **9** was determined as 23: 77 by the integral ratio of the peaks at δ 4.18 and 4.38 ppm,[1] respectively.

Thermal Treatment of 2 at 270°C. In an NMR tube was heated 0.0464 g of **2** at 270°C for 30 min. After the tube was cooled in an ice bath, 0.4 m*l* of deuterochloroform was added through the needle, and NMR spectrum was measured. There was not detected even a trace of **4** in the NMR spectrum indicating no formation of **4** from **2** on heating at the decomposition condition at 270°C.

Thermal Decomposition of 1,3,5-Trimethyltetrazolium Iodide (3). On heating **3** at 135°C for 30 min in an NMR tube as described above, a mixture of **2** and **4** was obtained in a ratio of 14: 86 which was determined by NMR analysis. Analogous decompositions of **3** at 180°C for 15 min and at 270°C for 3 min gave mixtures of **2** and **4** in ratios of 42: 58 and 60: 40, respectively.

7) R. M. Herbst and K. R. Wilson, *J. Org. Chem.*, **22**, 1142 (1957).