A Practical Synthesis of *N*-Bromo Imides by Use of Sodium Bromite

Shoji KAJIGAESHI,* Takashi NAKAGAWA, Shizuo FUJISAKI, and Akiko NISHIDA
Department of Industrial Chemistry, Faculty of Engineering Yamaguchi University, Tokiwadai, Ube 755
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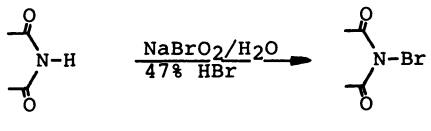
Synopsis. *N*-Bromo imides can be readily prepared under mild conditions by a reaction of imides with sodium bromite in the presence of hydrobromic acid in fairly good yields. The scope and limitation are also presented.

A new reagent, sodium bromite ($NaBrO_2$), has recently been noted in organic synthesis.[1-3] Durig the course of our investigation on the synthetic utilities of sodium bromite,[4] we found that the reaction of imides (**1**) with sodium bromite in the presence of hydrobromic acid under mild conditions gave *N*-bromo imides (**2**) in fairly good yields.

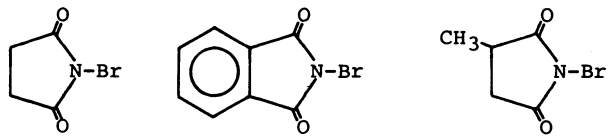
In general, *N*-bromo imides **2**, *e.g.*, familiar *N*-bromosuccinimide, have been prepared by the treatment of a corresponding **1** in an aqueous medium with bromine in the presence of a strong base, or with alkali hypobromite prepared separately by treatment of bromine with a strong base.[5] The derivatives **2** have been also prepared by the reaction of **1** with bromine in water by sodium bromate and sulfuric acid.[6] In our method, sodium bromite (which is available in stable crystals under an ordinary atmosphere and, hence, can be handle much more easily compared with the toxic liquid bromine) was used in place of bromine. *N*-bromo imides **2** such as *N*-bromosuccinimide[5] (**2a**), *N*-bromophthalimide[7] (**2b**), *N*-bromo-α-methylsuccinimide[6] (**2c**), *N*-bromoglutarimide[6] (**2d**), and 1,3-dibromohydantoin[6] (**2e**) were synthesized from the corresponding imides, succinimide (**1a**), phthalimide (**1b**), α-methylsuccnimide (**1c**), glutarimide (**1d**), and hydantoin (**1e**), respectively. *N*-bromo-ε-caprolactam (**3a**) was also prepared from ε-caprolactam.

When hydrobromic acid was added to an ice-cold aqueous solutuion of sodium bromite and imide under stirring, the desired **2** precipitated readily as white crystals. In the cases of syntheses of **2b**, **2c**, and **2d**, aqueous sodium hydroxide was used in order to dissolve the corresponding imides, **1b**, **1c**, and **1d**. These methods (using sodium bromite and hydrobromic acid) showed that one mole of sodium bromite was able to brominate 2 moles of **1** into **2**.

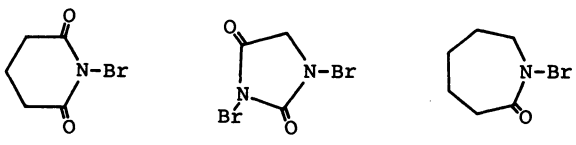


1 2

Scheme 1.



2a 2b 2c



2d 2e 3a

Scheme 2.

Our method could not be applied to imides which were insoluble in water or alkaline solution (*e.g.*, 1,8-naphthalimide). It was not applicable, furthermore, to imides having other active group in the molecule (*e.g.*, maleinimide) or chain imides (*e.g.*, diacetamide), because other reactions also proceeded under the conditions.

The reaction scheme for the synthesis of **2** may be presented in the following equations. That is, it can be

$$NaBrO_2 + HBr \rightleftharpoons HBrO_2 + NaBr, \quad (1)$$

$$HBrO_2 + HBr \rightleftharpoons 2HBrO, \quad (2)$$

$$2\text{>NH} + 2HBrO \rightleftharpoons 2\text{>N-Br} + 2H_2O, \quad (3)$$

overall:

$$2\text{>NH} + NaBrO_2 + 2HBr \longrightarrow 2\text{>N-Br} + NaBr + 2H_2O, \quad (4)$$

presumed that bromous acid ($HBrO_2$) produced by the reaction of sodium bromite with hydrobromic acid (Eq. 1) reacts with excess hydrobromic acid to give hypobromous acid (Eq. 2) and the subsequent reaction of **1** with the hypobromous acid give *N*-bromo imide (Eq. 3). We now postulate that a major active brominating species is the hypobromous acid derived from sodium bromite and hydrobromic acid as shown in equation 1 and 2. The overall reaction equation is shown is equation 4. Acutually, the experimental results described above concord stoichiometrically with equation 4.

Since further excess hydrobromic acid reacts with hypobromous acid to form free bromine, we can recognize the end point of *N*-bromination by a red coloration due to bromine formed in the reaction mixture. This is one of the merits of our method.

$$HBrO + HBr \rightleftharpoons Br_2 + H_2O \quad (5)$$

Experimental

N-Bromosuccinimide (NBS) (2a). A solution of 94.7% sodium bromite[9] (0.95 g, 6.7 mmol) in water (2 ml) was added to a solution of **1a** (1 g, 10.1 mmol) in water (5 ml). To the cold (0—5 °C) solution was added (dropwise, slowly) 47% hydrobromic acid (1.3 ml, 11.2 mmol) under stirring,[10] and then the reaction mixture was further stirred for 10 min at

0 °C. The precipitate obtained was filtered, washed with cold water and dried at room temperature to give **2a** as white crystals. Weight 1.54 g (86% of theoretical amount). Analysis by iodometric titration[11] showed 44.8% active bromine, as compared with the theoretical value for $C_4H_4BrNO_2$ of 44.9%. Mp 175—178 °C (from water) (lit,[5] mp 173—175 °C). MS: *m/z* 177, 179 (M^+).

N-Bromophthalimide (2b). A solution of 94.7% sodium bromite (0.63 g, 4.4 mmol) in water (5 ml) was added to an aqueous solution of **1b** (1 g, 6.8 mmol) and sodium hydroxide (0.3 g, 7.5 mmol) in water (15 ml). To the ice-cold solution was added (dropwise, slowly) 47% hydrobromic acid (1.8 ml, 15.5 mmol) under stirring,[10] and then the reaction mixture was further stirred for 10 min at 0 °C. The obtained precipitate was filtered, washed with cold water and dried to give **2b** as white crystals. Weight 1.25 g (81% of theoretical amount). Analysis showed 33.6% active bromine, as compared with the theoretical value for $C_8H_4BrNO_2$ of 35.4%. Mp 227—229 °C (from water). MS: *m/z* 225, 227 (M^+).

N-Bromo-α-methylsuccinimide (2c). Compound **2c** could be obtained from **1c** (0.5 g, 4.4 mmol) in the same manner as that of **2b**. Weight 0.38 g (45% of theoretical amount). Analysis showed 38.4% active bromine, as compared with the theoretical value for $C_5H_6BrNO_2$ of 41.4%. Mp 154—157 °C. MS: *m/z* 191, 193 (M^+).

N-Bromoglutarimide (2d). Compound **2d** could be obtained from **1d** (0.6 g, 5.3 mmol) in the same manner as that of **2b**. Weight 0.31 g (30% of theoretical amount). Analysis showed 37.9% active bromine, as compared with the theoretical value for $C_5H_6BrNO_2$ of 41.6%. Mp 149—151 °C. MS: *m/z* 191, 193 (M^+).

1,3-Dibromohydantoin (2e). A 47% hydrobromic acid (1.5 ml, 12.9 mmol) was added to a solution of **1e** (0.5 g, 5.0 mmol) in water (5 ml). To the ice-cold solution was added (dropwise, slowly) a solution of 94.7% sodium bromite (1 g, 7.0 mmol) in water (2 ml) under stirring,[10] and then the reaction mixture was further stirred for 1 h at 0 °C. The precipitate obtained was filtered, washed with cold water and dried to give **2e** as white crystals. Weight 0.9 g (70% of theoretical amount). Analysis showed 59.4% active bromine, as compared with the theoretical value for $C_3H_2Br_2N_2O_2$ of 62.0%. Mp 135—136 °C. MS: *m/z* 256, 258, 260 (M^+).

N-Bromo-ε-caprolactam (3a). Compound **3a** could be obtained from ε-caprolactam (2 g, 17.7 mmol) in the same manner as that of **2a**. Weight 2.7 g (80% of theoretical amount). Analysis showed 39.5% active bromine, as compared with the theoretical value for $C_6H_{10}BrNO$ of 41.6%. Mp 60—63 °C (lit,[8] mp 64—66 °C). MS: *m/z* 191, 193 (M^+).

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9) Commercial sodium bromite is now available from Kanto Kagaku Co. Ltd.
10) During the treatment, the mixture was instantaneously colored red owing to bromine formed (see Eq. 5) and soon decolorized. Whereupon a white precipitate was gradually deposited. The hydrobromic acid addition was done until the red color did not disappear. Thus, the amount of hydrobromic acid was employed as noted in the text.
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