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Organic Synthesis Using Sodium Bromate. II.[1)]
A Facile Synthesis of *N*-Bromo Imides and Amides Using Sodium Bromate and Hydrobromic Acid (or Sodium Bromide) in the Presence of Sulfuric Acid

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Synopsis. The reaction of imides and amides in water (or aqueous acetic acid) with sodium bromate and hydrobromic acid (or sodium bromide) in the presence of sulfuric acid under mild conditions gave the corresponding *N*-bromides in high yields.

During our studies concerning the regioselective bromination of aromatic compounds using *N*-bromo compounds,[2)] useful methods for the synthesis of these reagents were earnestly desired. *N*-Bromo imides **3** and *N*-bromo amides **4** are usually prepared by treating the corresponding imides **1** and amides **2** in an aqueous medium with bromine in the presence of a strong base, or with alkali hypobromite prepared separately by treating bromine with a strong base.[3)] In these processes it is difficult to efficiently isolate lower aliphatic *N*-bromoamides from an aqueous alkali solution. We recently reported on the preparation of **3** and **4** using sodium bromite in acetic acid, or in the presence of hydrobromic acid, in fairly good yields.[4,5)] Furthermore, Waugh and Waugh already suggested that the derivatives **3** and **4** could be prepared by the reaction of **1** and **2** in water with bromine, sodium bromate, and sulfuric acid.[6)] In their method, one of merit is that the bromine used is completely spent on the *N*-bromination of **1** and **2**.

In this paper we report on the facile synthesis of **3** and **4** by the use of handy hydrobromic acid (or sodium bromide), instead of free bromine at room temperature, for only 20—30 min.

Results and Discussion

There are two procedure in the experiment. One of them is that hydrobromic acid is added to a mixture of the substrates, sodium bromate, and sulfuric acid in water (or aqueous acetic acid) (Method A). Another is that sodium bromide is added to the same mixture (Method B). The starting imides and amides, which are slightly soluble in water, are dissolved in aqueous acetic acid. Each reaction scheme may be presented according to the following equations:

$$\text{Method A}: \quad 6\rangle\text{NH} + 2\text{NaBrO}_3 + 4\text{HBr} + \text{H}_2\text{SO}_4 \longrightarrow 6\rangle\text{NBr} + \text{Na}_2\text{SO}_4 + 6\text{H}_2\text{O}$$

and

$$\text{Method B}: \quad 6\rangle\text{NH} + 2\text{NaBrO}_3 + 4\text{NaBr} + 3\text{H}_2\text{SO}_4 \longrightarrow 6\rangle\text{NBr} + 3\text{Na}_2\text{SO}_4 + 6\text{H}_2\text{O}.$$

The results are summarized in Table 1. Our method is simple to use in the laboratory, and is applicable to the synthesis of various aliphatic, aromatic, and heterocyclic *N*-bromo imides and amides, even lower aliphatic *N*-bromo amides, such as *N*-bromoformamide (**4a**) and *N*-bromo-*N*-methylformamide (**4b**). Compounds **4a** and **4b** were obtained in 40—60% because of their solubility in water and their instability at room temperature. Since a further excess of hydrobromic acid or sodium bromide reacts with the products to reduce to the starting materials, it is required to avoid the use of excess amounts of the above-mentioned reagents.

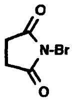
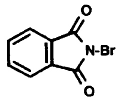
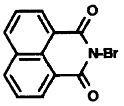
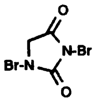
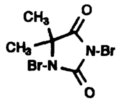
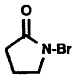
Experimental

***N*-Bromosuccinimide (NBS) (3a). Method A. General Procedure:** To a solution of succinimide (**1a**) (990 mg, 10 mmol), sodium bromate (760 mg, 5 mmol), and concentrated sulfuric acid (280 mg, 2.5 mmol) in water (3 ml) was added (dropwise, slowly) hydrobromic acid (47%, 0.78 ml, 6.7 mmol) under stirring. The reaction mixture was further stirred for 10 min. The obtained precipitation was filtered, washed with cold water and dried to give **3a** as white crystals. Weight 1.69 g (95% of theoretical amount). The material was assayed by iodometric titration. The analysis showed 44.4% active bromine, as compared with the theoretical value for $C_4H_4BrNO_2$ of 44.9%: mp 185—190 °C (lit,[7)] mp 180 °C).

***N*-Bromo-*N*-methylformamide (4b).** White crystals, mp 81—83 °C. IR (KBr) 1660 (CON) cm^{-1}. ^1H NMR ($CDCl_3$) $\delta=3.39$ (3H, br. s, CH_3), 7.50 and 8.19 (0.64H and 0.36H, two br. s, N=CH (OBr) and N(Br)–CHO). Ms *m/z* 137 (M^+), 139 (M^++2).

***N*-Bromobenzamide (4i). Method B. General Procedure:** Solid sodium bromide (690 mg, 6.7 mmol) was added slowly to a solution of benzamide (**2i**) (1.21 g, 10 mmol), sodium bromate (760 mg, 5 mmol), and concentrated sulfuric acid (740 mg, 7.5 mmol) in aqueous acetic acid (70%, 7 ml) under stirring. The reaction mixture was worked up as described in Method A to afford **4i** as white crystals. Weight 1.55 g, (84% of theoretical amount). The material was assayed by iodometric titration. The analysis showed 38.9% active bromine, as compared with the theoretical value for C_7H_6BrNO of 40.0%: mp 124—126 °C (lit,[14)] mp 124—127 °C).

Table 1. *N*-Bromination of Imides **1** and Amides **2**

Product		Method	Reaction condition		Solvent	Yield[a]	Mp/°C		Active Br/%	
			Time/min	Temp/°C		%	Found	Reported	Found	Calcd
3a		A B	10	rt	H_2O	95 92	185—190	180[7]	44.4	44.9
3b		A B	20	rt	AcOH-H_2O	99 99	203—207	201—203[8]	34.9	35.3
3c		A B	120	rt	AcOH-H_2O	96 98	250—252	245—249[8]	28.5	28.9
3d		A B	30	40	H_2O	90 99	133—134	135—136[5]	61.2	62.0
3e		A B	30	rt	H_2O	93 90	205—208	198—199[9]	55.1	55.9
3f		A	60	rt	H_2O	78	113—115	95[10]	48.6	48.8
4a	$HCONHBr$	A B	30	rt	H_2O	48 38	91—92	87—88[11]	62.7	64.5
4b	$HCONCH_3Br$	A B	30	rt	H_2O	62 49	81—83	—[12]	57.2	57.9
4c	$CH_3CONHBr$	A B	30	rt	H_2O	84 90	105—108	104—105[7]	57.8	57.9
4d	$CH_3CH_2CONHBr$	A B	30	rt	H_2O	82 78	80—81	76—77[13]	50.8	52.6
4e	$CH_3(CH_2)_6CONHBr$	A B	20	rt	AcOH-H_2O	97 96	62—63	63—65[4]	34.9	36.0
4f	$CH_3(CH_2)_8CONHBr$	A B	20	rt	AcOH-H_2O	98 99	75—77	72—74[4]	30.2	31.9
4g	$CH_3(CH_2)_{10}CONHBr$	A B	5	rt	AcOH-H_2O	97 96	80—82	85—87[4]	27.3	28.7
4h	$C_6H_5CH_2CONHBr$	A B	25	rt	AcOH-H_2O	80 78	126—128	128—130[14]	36.4	37.3
4i	$C_6H_5CONHBr$	A B	20	rt	AcOH-H_2O	94 84	124—126	124—127[14]	38.9	40.0
4j	*p*-$CH_3C_6H_4CONHBr$	A B	20	rt	AcOH-H_2O	83 99	126—129	127—130[15]	35.5	37.3
4k	*p*-$NO_2C_6H_4CONHBr$	A B	20	rt	AcOH-H_2O	96 99	196—200	196—199[13]	31.5	32.6
4l	*o*-$NO_2C_6H_4CONHBr$	A B	20	rt	AcOH-H_2O	93 96	175—181	170—176[14]	32.3	32.6

a) Isolated yield.

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