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A CONVENIENT SYNTHESIS OF N-BROMOAMIDES BY USE OF SODIUM BROMITE

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Reaction of aliphatic and aromatic amides in acetic acid with aqueous sodium bromite ($NaBrO_2$) under mild conditions gave N-bromoamides in fairly good yields.

In recent years, sodium bromite has been proved to be a useful reagent in organic synthesis.[1-3] During our studies on the synthetic utilities of sodium bromite, we found that sodium bromite is used very effectively as a reagent for the Hofmann degradation of amides,[4] and the haloform reaction of methyl ketones.[5]

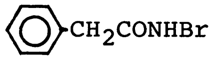
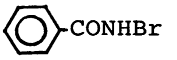
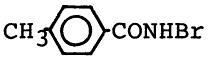
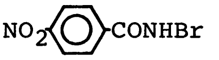
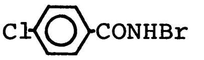
We have now found that amides (1) react with sodium bromite in acetic acid under mild conditions to give N-bromoamides (2) in fairly good yields. The treatments of 1 in acetic acid with aqueous sodium bromite were carried out at room temperature for 3-4 h under stirring. The results are summarized in Table 1.

$$\underset{\underline{1}}{R\text{-}CONH_2} \xrightarrow[\text{rt, 3-4 h}]{\text{AcOH, aq NaBrO}_2} \underset{\underline{2}}{R\text{-}CONH\text{-}Br}$$

Although N-brominations of 1 with bromine and alkali have been widely investigated as the first step of Hofmann degradation,[6] it is not so easy to isolate 2 because the subsequent reactions of 2 should proceed more readily under the alkaline conditions. There are some examples for the preparation of 2 which are reported by use of special techniques.[7-9]

Our method is straightforward and simple to use, and applicable to synthesis of various aliphatic and aromatic N-bromoamides except lower aliphatic N-bromoamides which are unstable under the operating acidic conditions. Nevertheless, we were still unable to indicate clearly any active brominating species for the N-bromination of amides with sodium bromite in the presence of acetic acid.

Table 1. N-Bromoamides (2) prepared

Entry	Product (2)	Yield[a]/%	Mp/°C[b]	Active bromine/% Calcd	Active bromine/% Found
1	$CH_3(CH_2)_6CONHBr$ (2a)	81	63-65	36.0	34.5
2	$CH_3(CH_2)_8CONHBr$ (2b)	88	74-76	31.9	28.7
3	$CH_3(CH_2)_{10}CONHBr$ (2c)	90	85-87	28.7	28.7
4	$CH_3(CH_2)_{12}CONHBr$ (2d)	98	86-88	26.1	25.4
5	$CH_3(CH_2)_{14}CONHBr$ (2e)	97	85-87	23.9	23.0
6	 (2f)	60	126-129	37.3	36.6
7	 (2g)	70	128-131 (129-131)[8]	40.0	38.7
8	 (2h)	75	130-133 (131-133)[8]	37.3	36.7
9	 (2i)	96	207-209 (198-202)[8]	32.6	31.9
10	 (2j)	96	175-177 (170-174)[8]	34.1	33.0

a) Yield of isolated product. b) Uncorrected.

A general and typical procedure is as follows: To a solution of benzamide (1g) (1 g, 8.3 mmol) in acetic acid (7 ml) is added dropwise slowly s solution of 94.7% sodium bromite[10] (2 g, 14 mmol) in water (3 ml) at room temperature under stirring, and then the reaction mixture is further stirred for 3 h. The precipitate obtained is filtered, washed with water (30 ml) and dried. The white product, identified as N-bromobenzamide (2g), weighed 1.16 g (70% of the theoretical amount); mp 128-131 °C.

References

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10) Commercial sodium bromite is now available from Kanto Kagaku Co. Ltd.

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