CHEMISTRY LETTERS, pp. 713 - 714, 1984. © The Chemical Society of Japan 1984

SODIUM BROMITE: A NEW REAGENT FOR THE HOFMANN DEGRADATION OF AMIDES

Shoji KAJIGAESHI,* Takashi NAKAGAWA, Shizuo FUJISAKI,
Akiko NISHIDA, and Michihiko NOGUCHI
Department of Industrial Chemistry, Faculty of Engineering,
Yamaguchi University, Tokiwadai, Ube 755

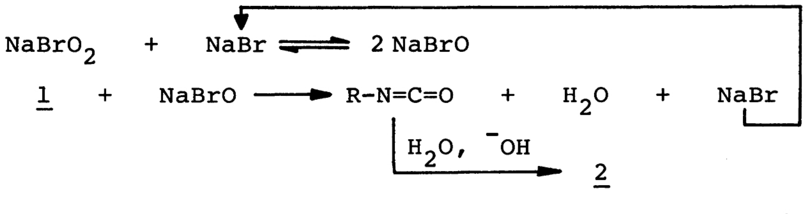
Amines are prepared in fairly good yields by the reaction of amides with sodium bromite in the presence of catalytic amount of sodium bromide in aqueous sodium hydroxide. The scope and limitations are also presented.

Recently, sodium bromite ($NaBrO_2$) has been noted as a new reagent in organic synthesis.[1-3] We have now found that amides (1) react with sodium bromite in the presence of a catalytic amount of sodium bromide in aqueous sodium hydroxide to give amines (2) in fairly good yields.

$$\underset{1}{RCONH_2} \xrightarrow[NaBr,\ aq.\ NaOH]{NaBrO_2} \underset{2}{R\text{-}NH_2}$$

Although 2 are obtained from 1 and alkaline solution of bromine or chlorine through a reaction known as the Hofmann Degradation,[4] it is not always easy to treat a liquid bromine or gaseous chlorine in laboratories. However, the reagent, sodium bromite, is a stable crystal under the atmosphere and hence can handle much more easily compared with bromine or chlorine.

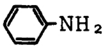
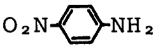
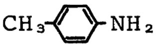
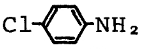
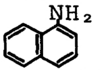
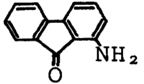
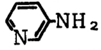
The treatments of 1 with commercial sodium bromite[5] in aqueous sodium hydroxide were carried out at 20-100 °C for 0.5-1.5 h under stirring. The results are summarized in the Table 1. It is postulated that the reaction of 1 with sodium bromite should be catalyzed by sodium bromide as follows.



Our methods may be applied to 1 of various types: aliphatic amides, aromatic amides, and heterocyclic amides. However, in the case of reactions of aliphatic amides ($CH_3(CH_2)_nCONH_2$) with sodium bromite, the yields of 2 were gradually decreased, and the yields of corresponding ureas ($CH_3(CH_2)_nNHCONH(CH_2)_nCH_3$), by-product, increased with increasing CH_2 unit of the 1. It is not applicable, furthermore, to diamides (*e.g.*, phthalamide, isophthalamide, and terephthalamide *etc.*) because of formation of complex mixtures, probably N-bromo derivatives formations and subsequent reactions.

A general procedure is as follows: To a suspension of *p*-toluamide (1j) (1 g, 7.4 mmol) in water (10 ml) is added all at once an aqueous solution of the commercial sodium bromite (94.7% purity, 0.7 g, 4.9 mmol) and sodium hydroxide (1 g, 25 mmol) in water (5 ml) at 80 °C. The mixture is stirred for 30 min at 100 °C, and distilled together with water. The distillate is extracted with ether (10 ml x 3). The ether layer is dried with magnesium sulfate, and concentrated to give *p*-toluidine (2j) as colorless needles; yield 0.58 g (73%); mp 42-44 °C (Lit., mp 44-45 °C).

Table 1. Reaction of Amides (1) with Sodium Bromite

	Product (2)	Reaction conditions time /h	temp /°C	Yielda)/%	Mp /°C or Bp /°C(mmHg)
a	CH_3NH_2	0.5	70	91b)	226-228c)
b	$CH_3CH_2NH_2$	0.5	70	90b)	108-109c)
c	$CH_3(CH_2)_2NH_2$	0.5	70	73b)	155-157c)
d	$CH_3(CH_2)_4NH_2$	0.5	75	60	100-102(760)
e	$CH_3(CH_2)_6NH_2$	0.5	80	31	153-155(755)
f	$CH_3(CH_2)_8NH_2$	1	80	16	198-200(755)
g	$CH_3(CH_2)_{10}NH_2$	1.5	80	-d)	-
h		3	20	90	181-183(760)
i		0.5	100	54	145-147
j		0.5	100	73	42-44
k		0.5	100	67	70-72
l		0.5	100	51	48-50
m		0.5	100	85	117-118
n		1	80	52	59-62

a) Isolated yield. b) Yield of HCl-salt. c) Mp of HCl-salt.
d) Urea, $CH_3(CH_2)_{10}NHCONH(CH_2)_{10}CH_3$, was only obtained.

References

1) T. Kageyama, S. Kawahara, K. Kitamura, Y. Ueno, and M. Okawara, *Chem. Lett.*, 1983, 1097.

2) T. Kageyama, Y. Tobito, A. Katoh, Y. Ueno, and M. Okawara, *Chem. Lett.*, 1983, 1481.

3) T. Kageyama, Y. Ueno, and M. Okawara, *Synthesis*, 1983, 815.

4) E. S. Wallis and J. F. Lane, "The Hofmann Reaction", in "Organic Reactions," ed by R. Adams, John Wiley & Sons, Inc., New York (1967), Vol. 3, Chap. 7.

5) Commercial sodium bromite (analytical data: $NaBrO_2$; 94.7%, NaBr; 3.8%, $NaBrO_3$; 0.6%, H_2O; 0.4%) was gifted from Nippon Silica Co. Ltd.

(Received February 15, 1984)