



**HAL**  
open science

# N-Monochlorination and N-monobromomination of carbamates and carboxamides by sodium hypochlorite and hypobromite

C. Bachand, H. Driguez, J.M. Paton, D. Touchard, J. Lessard

► **To cite this version:**

C. Bachand, H. Driguez, J.M. Paton, D. Touchard, J. Lessard. N-Monochlorination and N-monobromomination of carbamates and carboxamides by sodium hypochlorite and hypobromite. *Journal of Organic Chemistry*, 1974, pp.3136-3138. hal-00307101

**HAL Id: hal-00307101**

**<https://hal.science/hal-00307101>**

Submitted on 28 Jul 2008

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

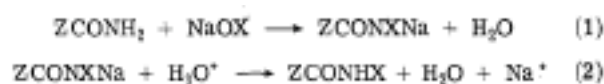
# N-Monochlorination and N-Monobromination of Carbamates and Carboxamides by Sodium Hypochlorite and Hypobromite<sup>1a</sup>

Carol Bachand, Hughes Driguez, John M. Paton, Daniel Touchard, and Jean Lessard

Centre de Recherche sur les Macromolécules Végétales, Grenoble, France  
Département de Chimie, Université de Sherbrooke, Sherbrooke, Québec, J1K 2R1, Canada

Our studies on the chromous chloride promoted addition of *N*-chlorocarbamates to olefins<sup>2</sup> led us to devise a convenient method for the preparation of *N*-monochlorocarbamates in high yield, free from the *N,N*-dichloro derivatives. This method was also applied to the preparation of *N*-monochlorocarboxamides and of *N*-monobromocarbamates and -carboxamides needed for the chromous chloride promoted addition studies<sup>2c</sup> and some photochemical work.<sup>3</sup> The recent publication of Swern and coworkers<sup>4</sup> on the preparation of ethyl and methyl *N*-chlorocarbamates prompted us to report our results.

The method consists of the formation of the sodium salt of the monohalo derivative followed by careful neutralization. The salt is prepared by treating a slight excess (0.5- 2%) of the amide with sodium hypochlorite or hypobromite<sup>5</sup> (5-6% solution) at ca. 0° (eq 1).



After the addition of methylene chloride, dilute (1-2 *N*) sulfuric acid is added slowly until the sodium salt (eq 2) and the excess sodium hydroxyde are neutralized (an excess of acid must be avoided). The solvent is removed at reduced pressure at 20-25°. The results are recorded in Table I.

***N*-Chlorocarbamates.** The yields of the *N*-monochloro- carbamates 1-6<sup>7</sup> are excellent (86-98%) with the purity of the crude reaction products being satisfactory for use in reactions without further purification. The method is thus very efficient.

***N*-Chlorocarboxamides.** The *N*-monochlorocarboxam- ides 8-16 were obtained in good yield, the purity of the crude reaction products being satisfactory for use in reactions. The method was not successful with the sterically hindered 2,2-dimethylpropionamide nor was it convenient for the preparation of the water-soluble *N*-chloroformamide (7). Beckwith and Goodrich<sup>8</sup> have prepared *N*-monochlorocarboxamides in good yield by the bromine-catalyzed reaction of primary carboxamides with *tert*-butyl hypo- chlorite.

***N*-Bromocarbamates.** We have studied the bromination of ethyl, 2,2,2-trichloroethyl, and benzyl carbamates (**17**, **18**, and **19**) and, to our knowledge, this is the first reported preparation of *N*-bromocarbamates. It appears that the disproportionation of the *N*- bromocarbamates **17** and **18** (eq 3) does occur to a significant extent ( $K^{\text{eq}} \approx 0.08$  and 0.1, respectively, at ca. 37°).



Indeed, although both the io- dometric and neutralization analyses of the crude *N*-bromocarbamates **17** and **18** indicated a purity of 100%, their ir and nmr spectra showed the presence of nonbrominated carbamate. A careful examination of the integration for the various protons of the nmr spectra indicated clearly the presence of a third product, most probably the *N,N*- dibromocarbamate, the aliphatic protons of which had the same chemical shift as those of the *N*- monobromocarbamate, the molar ratio being approximately equal to that of the non- brominated carbamate (see Experimental Section for details).

The crude benzyl *N*-bromocarbamate (**19**) was found to decompose rapidly under reduced pressure, as evidenced by continuous evolution of gas within the oily product, the loss of active bromine, and reduction in weight of material (the yield and active bromine content reported in **Table I** refer to a crude product kept under reduced pressure for 10 min after evaporation to dryness). The crude *N*-bromocarbamates **17**, **18**, and **19** could be stored in the refrigerator for several days without any loss of active bromine.

Table I  
Preparation of *N*-Haloamides

<i>N</i> -Halo amide	(No.)	Yield, %	Purity, % of theory		% starting amide <sup>b</sup>	Mp, °C			Registry no.
			Iodometric	Neutralization		Crude	Purified <sup>c</sup>	Lit.	
CH <sub>3</sub> CH <sub>2</sub> OCONHCl	(1)	98	99	100		17-19		9 <sup>d</sup>	51-79-6
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OCONHCl	(2)	86	98			Oil			
CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub> OCONHCl	(3)	93	96			Oil			
ClCH <sub>2</sub> CH <sub>2</sub> OCONHCl	(4)	91	96	98		53-55	56.5-57.5	42 <sup>e</sup>	
Cl <sub>2</sub> CCH <sub>2</sub> OCONHCl	(5)	92	98	99		61-63	63-63.5		
C <sub>2</sub> H <sub>5</sub> CH <sub>2</sub> OCONHCl	(6)	98	98	99		27-29			621-84-1
HCONHCl	(7)	50	86			Oil			75-12-7
CH <sub>3</sub> CONHCl	(8)	70 <sup>f</sup>	100				109-110	110 <sup>f</sup>	60-35-5
CH <sub>3</sub> CH <sub>2</sub> CONHCl	(9)	78	94	95		Oil			79-05-0
ClCH <sub>2</sub> CH <sub>2</sub> CONHCl	(10)	88	96			69-74	74-74.5		5875-24-1
BrCH <sub>2</sub> CONHCl	(11)	80	101			67-68	68.5-69		683-57-8
ClCH <sub>2</sub> CONHCl	(12)	83	98	100		66-68	68-69.5		79-07-2
FCH <sub>2</sub> CONHCl	(13)	79	101			98.5-100	100.5-101		640-19-7
Cl <sub>2</sub> CHCONHCl	(14)	81	101			70-71	70-71		683-72-7
Cl <sub>3</sub> CCONHCl	(15)	85	99			120-122	122-123		594-85-0
F <sub>3</sub> CCONHCl	(16)	63	99			Oil <sup>h</sup>			354-38-1
CH <sub>3</sub> CH <sub>2</sub> OCONHBr	(17)	85	100	101	~10	Oil			
Cl <sub>2</sub> CCH <sub>2</sub> OCONHBr	(18)	92	100	101	~13	Oil			
C <sub>2</sub> H <sub>5</sub> CH <sub>2</sub> OCONHBr	(19)	79	83		~15	Oil			
CH <sub>3</sub> CH <sub>2</sub> CONHBr	(20)	87	100	100		74-75	76-77		
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CONHBr	(21)	80	94	96		Oil			626-97-1
ClCH <sub>2</sub> CH <sub>2</sub> CONHBr	(22)	89	97			87-88	89-90		
BrCH <sub>2</sub> CONHBr	(23)	78	99	100		103-104.5			
ClCH <sub>2</sub> CONHBr	(24)	79	98	98	~4	74-76	77-78	75 <sup>i</sup>	
FCH <sub>2</sub> CONHBr	(25)	65	99		~6	82-83	83.5-84		
Cl <sub>2</sub> CHCONHBr	(26)	57	83		~18	73-77	94.5-95.5	96 <sup>i</sup>	
Cl <sub>3</sub> CCONHBr	(27)	45	77			95-97 <sup>j</sup>		125 <sup>i</sup>	
F <sub>3</sub> CCONHBr	(28)	19	52					82 <sup>i</sup>	

<sup>a</sup> Of active halogen compound before purification, based on the amide. <sup>b</sup> Starting amide present in the crude product as determined by nmr. <sup>c</sup> By recrystallization from methylene chloride or methylene chloride-hexane mixtures (iodometric purity >99%). <sup>d</sup> D. Saika and D. Swern, *J. Org. Chem.*, **33**, 4548 (1968). <sup>e</sup> P. Chabrier, *C. R. Acad. Sci.*, **214**, 353 (1942). <sup>f</sup> Of recrystallized product. <sup>g</sup> K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.*, 986 (1927). <sup>h</sup> Crystalline in the refrigerator. <sup>i</sup> Reference 10. <sup>j</sup> The active bromine content was not significantly increased by recrystallization: 82%, mp 96-96°.

***N*-Bromocarboxamides.** Kergomard<sup>6</sup> has prepared *N*- bromoacetamide by adding a sodium hypobromite solution<sup>5</sup> to a solution of acetamide in acetic acid. *N*-Bromo- benzamides have been prepared by using bromine in aqueous alkaline solution with subsequent rapid acidification using acetic acid<sup>9</sup> Our procedure gave better yields for the preparation of *N*-bromopropionamide (**20**) and *N*-bromopentanamide (**21**) and we have used it successfully also to prepare the *N*- bromocarboxamides 22-25. The method is not convenient for the *N*-bromination of the dichloro-, trichloro-, and trifluoroacetamides (26, 27, and 28), the yield and the purity of the crude product decreasing in the order 26 > 27 > 28. Park, et al<sup>10</sup> has used bromine and silver oxide in anhydrous trifluoroacetic acid to prepare *N*- bromo- $\alpha$ -haloacetamides in good yield and Beebe and Wolfe<sup>11</sup> have obtained *N*- bromotrifluoroacetamide (**26**) in high yield using acetyl hypobromite.

In comparison to the *N*-bromocarbamates, the *N*-bromo- carboxamides have much less tendency to undergo dispro- portionation into the carboxamide and the *N,N*-dibromo derivative. In the ir and nmr spectra of the pure (>99%) samples of the *N*-bromo- $\alpha$ -haloacetamides **23-26**, there is a small but detectable amount (2-4%) of nonbrominated carboxamide.<sup>12</sup>

### Experimental Section<sup>14</sup>

Melting points were determined on a Buchi apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer spectro- photometer, Model 257. Nmr spectra were determined on a Varian A-60 spectrometer using TMS as internal standard. The sodium hypochlorite solution was obtained from Anachemia Chemicals Ltd.<sup>15</sup> and contained between 5.0 and 5.7% active chlorine (0.67- 0.77 mmol/ml) and excess sodium hydroxide (-0.15 mmol/ml). The carbamates and carboxamides, unless specified otherwise, were obtained from Aldrich Chemical Co.

**Iodometric Analyses.** The samples (about 1 mmol accurately weighed) were dissolved in 50 ml of a 50350 mixture of methanol and water. An excess of potassium iodide dissolved in water (5 ml) was added followed by sulfuric acid (1 ml of a 4 N solution). The solution was then titrated with 0.1 N sodium thiosulfate.

**Neutralization Analyses.** The samples (about 1 mmol accurately weighed) were dissolved in a 10:40 mixture of methanol and water. The solution was cooled in an ice bath and titrated with 0.1 N NaOH using a pH meter.

**Preparation of *n*-Propyl, 2-Methoxyethyl, 2-Chloroethyl, and 2,2,2-Trichloroethyl Carbamate (29,30, 31, and 32).** These compounds were prepared from the corresponding alcohols according to the procedure described by Loev and Korrnendy:<sup>16</sup> 29, 65% yield (crude), mp 49-52° (lit.<sup>17</sup> mp 52.5°); 30, 55% yield (crude), mp 44-46° (lit. mp 46.8°); 31, 33% yield (crude), mp 71-73° (lit.<sup>18</sup> mp 77°); 32, 40% yield (recrystallized), mp 63-64°, ir (CHCl<sub>3</sub>) 3540, 3430, 2940, 1750, 1585, 1385, 1325, 1115, and 1050 cm<sup>-1</sup>, nmr (CDCl<sub>3</sub>) δ 4.70 (s, 2 H), 5.62 (broad s, 2 H).

*Anal.* Calcd for C<sub>3</sub>H<sub>4</sub>Cl<sub>3</sub>N<sub>2</sub>O: Cl, 56.25. Found C, 54.88.

**2,2,2-Trichloroacetamide (31)** was prepared by treating the acid chloride with concentrated NH<sub>4</sub>OH: 76% yield; mp 141-142.5° (lit.<sup>20</sup> mp 137°).

**Typical Procedure for the Monochlorination of Carbamates and Carboxamides. Preparation of Ethyl *N*-Chlorocarbamate (1).** To 35.6 g (400 mmol) of ethyl carbamate in a 2-l. conical flask cooled in an ice bath was added 545 ml of yellow NaOCl solution (0.73 mmol/ml, 398 mmol). The mixture was stirred until it became colorless (15 min). Methylene chloride (300 ml) was added. Then 241 ml (482 mequiv) of 2 N Na<sub>2</sub>SO<sub>4</sub> was added dropwise with vigorous stirring. The addition took 2 hr. The organic phase was decanted and the aqueous layer was extracted with methylene chloride (4 X 100 ml). The combined extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed on the rotatory evaporator at ca. 25° to yield 49.0 g of 1 as a pale yellow oil which crystallized upon cooling (see Table I): ir (CCl<sub>4</sub>) 3400, 3300 (broad), 1770, 1730, 1700, 1380, 1330, 1310, 1200, and 1060 cm<sup>-1</sup>; nmr (CDCl<sub>3</sub>) δ 1.30 (t, *J* = 7 Hz, 3 H), 4.28 (q, *J* = 7 Hz, 2 H), and 6.63 (broad s, 1 H).

The other *N*-chloroamides listed in Table I were prepared in the same way but on a smaller scale (from 10 to 100 mmol), the excess of amide varying from 1 to 2%. With amides very insoluble in water, a larger reaction time was needed (up to 30 min) with a few milliliters of methylene chloride being added to speed up the reaction. When working on a 10-40-mmol scale, acidifications were carried out with 1 N H<sub>2</sub>SO<sub>4</sub>. Because of the higher solubility of *N*-chlorocarboxamides in water, four to ten extractions with methylene chloride were performed. The ir spectra (CCl<sub>4</sub>) of the *N*-chlorocarbamates 2-6 are quite similar to that of ethyl *N*-chlorocarbamate (1) and they all show a band in the following regions: 3400 (free NH), 3200-3180 (broad, associated NH), 1770 (C=O), 1740-1730 (C-O), 1710-1700 (C-O), 1410-1380, 1350-1330, 1200 (ester), and 1080-1000 cm<sup>-1</sup> (ester).

**Typical Procedure for the Monobromination of Carbamates and Carboxamides. Preparation of Ethyl *N*-Bromocarbamate (17).** To 4.43 g (43 mmol) of NaBr was added 53.4 ml of NaOCl solution (0.75 mmol/ml, 40 mmol). The mixture was stirred for 15 min at room temperature. The deep yellow hypobromite solution was cooled in an ice bath and 3.60 g (40.4 mmol) of ethyl carbamate was added. The reaction mixture was stirred until it became pale yellow (almost colorless). Methylene chloride (50 ml) was added followed by the dropwise addition of 41 ml (47 mequiv) of 1.15 N H<sub>2</sub>SO<sub>4</sub> with vigorous stirring. The addition took 1.5 hr. The reddish organic phase was decanted and the aqueous layer was extracted with methylene chloride (3 X 15 ml). The combined extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed on the rotatory evaporator to yield 5.71 g of 17 as a yellow oil (see Table I): ir (CCl<sub>4</sub>) 3400, 3200 (broad), 1720 (broad, strong), 1415, 1375, 1330, 1220, 1190 (shoulder), and 1065 cm<sup>-1</sup>, and weak bands at 3500 and 1590 cm<sup>-1</sup> due to the presence of ethyl carbamate; nmr (CCl<sub>4</sub>) δ 1.28 (t, *J* = 7 Hz, carbamate CH<sub>3</sub>) and 1.33 (t, *J* = 7 Hz, N-bromo- and N,N-dibromocarbamate CH<sub>2</sub>), 4.17 (q, *J* = 7 Hz, carbamate CH<sub>2</sub>) and 4.28 (q, *J* = 7 Hz, N-bromo- and N,N-dibromocarbamate CH<sub>2</sub>), 5.41 (broad s, carbamate NH), and 6.55 (broad s, N-bromocarbamate NH) with the following relative integrations-7.7 (the two overlapping triplets), 5.0 (the two overlapping quadruplets), 1.0, and 1.6.

The other *N*-bromoamides listed in Table I were prepared in exactly the same way except that for water-insoluble amides, longer reaction time was needed (up to 30 min) for the reaction with NaOBr. The ir and nmr absorptions of the crude *N*-bromocarbamates 18 and 19 are given below.

Crude 18: ir (CHCl<sub>3</sub>) 3400, 3200 (broad), 1745 (broad, strong), 1390, 1325, 1230, 1185, 1110, and 1045, and weak bands at 3530 and 1585 cm<sup>-1</sup> (nonbrominated carbamate); nmr (CCl<sub>4</sub>) δ 4.75 (s,

carbamate CH<sub>2</sub>), 4.81 (s, N-bromo- and *N,N*-dibromocarbamate CH<sub>2</sub>), 5.60 (broad s, carbamate NH<sub>2</sub>), 6.40 (broad s, *N*-bromocarbamate NH) with a relative integration of 1.9:8.7:1.0:4.6.

Crude **19**: ir (cc14) 3400, 3240 (broad), 1720 (broad, strong), 1395, 1325, 1210, 1180 (shoulder), and 1050, and weaker bands at 3500 and 1590 cm<sup>-1</sup> (nonbrominated Carbamate); nmr (CCl<sub>4</sub>) 6 5.05 (8, carbamate CH<sub>2</sub>), 5.85 (s, N-bromocarbamate CH<sub>2</sub>), 5.35 (broad s, carbamate NH<sub>2</sub>), 6.48 (broad s, *N*-bromocarbamate NH), 7.30 and 7.33 (s, aromatic H of the carbamate and the *N*-bromo derivative) with a relative integration of 1.0:2.3:1.1:1.2:7.7.

Registry No.-1, 16844-21-6; 2, 52175-97-0; 3, 52175-98-1; 4, 30830-84-3; 5, 30830-85-4; 6, 30830-47-8; 7, 52175-99-2; 8, 598-49-2; 9, 36448-95-0; 10, 52176-00-8; 11, 35070-76-9; 12, 35070-77-0; 13, 35077-08-8; 14, 35077-09-9; 15, 35077-10-2; 16, 52176-01-9; 17, 52176-02-0; 18, 52176-03-1; 19, 52176-04-2; 20, 3699-17-0; 21, 3699-20-5; 22, 52176-05-3; 23, 52176-06-4; 24, 35077-11-3; 25, 36015-63-1; 26, 52259-82-2; 27, 35077-12-4; 28, 359-45-5; 29, 627-12-3; 30, 1616-88-2; 31, 2114-18-3; 32, 107-69-7; sodium hypochlorite, 7681-52-9; sodium hypobromite, 13824-96-9.

**Supplementary Material Available.** Characteristic ir absorptions (position of the NH and C=O bands) of the *N*-chlorocarboxamides 9-16 and of the *N*-bromocarboxamides 20-26, and the nmr absorptions of these N-haloamides and of the *N*-chlorocarbamates 2-6 will appear in Table II (ir) and Table III (nmr) following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 X 148 mm, 24X reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-74-3136.

## References and Notes

- (1) (a) Supported by a grant from the National Research Council of Canada; (b) Arts Council of Canada Predoctoral Fellow, 1969-1971; (c) NRCC Postdoctoral Fellow, 1968-1970; (d) France-Quebec Predoctoral Fellow, 1970-1972.
- (2) (a) J. Lessard and J. M. Paton, *Tetrahedron Lett.*, 4883 (1970); (b) J. Lessard and H. Driguez, *ibid.*, 4887 (1970); (c) H. Driguez and J. Lessard, unpublished work.
- (3) D. Touchard and J. Lessard, *Tetrahedron Lett.*, 4425 (1971); 3827 11R7RI
- (4) S. C. Czupf, H. Gottleb, O. F. Whitfield, and D. Swern, *J. Org. Chem.*, 38, 2555 (1973)
- (5) Sodium hypobromite was prepared from sodium hypochlorite and sodium
- (6) A. Kergomard, *Bull. Soc. Chim. Fr.*, 2360 (1961).
- (7) As shown by Swern and coworker<sup>^</sup>,<sup>^</sup> the equilibrium of the disproportionation reaction of the *N*-chlorocarbamates seems to lie completely toward the monochloro derivative at ambient temperature. Indeed, we could not detect the presence of any nonchlorinated carbamate in the ir (no bands at 3530 and 1565 cm<sup>-1</sup>) and nmr spectra of *N*-chlorocarbamates of purity 299% (iodometric analysis and acid value determination).
- (8) A. L. J. Beckwith and J. E. Goodrich, *Aust. J. Chem.*, 18, 747 (1965).
- (9) T. Imamoto, Y. Tsuno, and Y. Yukawa, *Bull. Chem. Soc. Jap.*, 44, 1632 (1971), and references cited therein.
- (10) J. D. Park, H. J. Gerjovich, W. R. Lycan, and J. R. Lacker, *J. Amer. Chem. Soc.*, 74, 2189 (1952).
- (11) T. R. Beebe and J. W. Woife, *J. Org. Chem.*, 35, 2056 (1970).
- (12) Wolfe and Awang<sup>13</sup> have reported that *N*-bromoacetamide, when irradiated (photoflood lamp) in refluxing carbon tetrachloride and in the presence of an olefin, undergoes disproportionation. The *N,N*-dibromoacetamide formed reacts rapidly with the olefin to give a *o*-bromo-*N*-bromoacetamide.
- (13) S. Woife and D. V. C. Awang. *Can. J. Chem.*, 49, 1384 (1971).
- (14) See paragraph at end of paper regarding supplementary material.
- (15) Commercial hypochlorite solutions from other sources were also used
- (16) G. Loev and M. F. Kormendy, *J. Org. Chem.*, 28, 3421 (1963). (17) W. M. Kraft and R. M. Herbst, *J. Org. Chem.*, 10, 483 (1945).
- (18) H. G. Ashburn, A. R. Collett, and C. L. Lazzell, *J. Amer. Chem. Soc.*, 60, but were found to give less satisfactory results. 2934 (1936).
- (19) J. I. Jones, *J. Chem. Soc.*, 2735 (1957).
- (20) L. McMaster and F. 6. Langreck, *J. Amer. Chem. Soc.*, 39, 108 (1917).