N-Chlorination of Amides and Carbamates by Oxone® and Sodium Chloride

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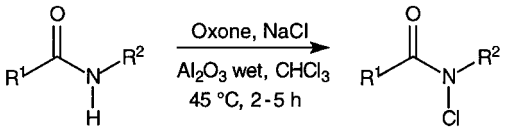
Abstract: A new method for the preparation of *N*-chloroamides, lactams and carbamates using Oxone® and sodium chloride supported on wet alumina is described.

Key words: amides, amino acids, *N*-chlorination, oxidations, Oxone®

N-Halo compounds are versatile reagents in organic synthesis, mainly used in rearrangement[1] and oxidation reactions.[2] However, other transformations have been studied. *N*-Chloroamides and carbamates are sources of amidyl and carbamyl radicals[3] and *N*-chloro-*N*-acyl and *N*-chloro-*N*-carbamoyl aminoacids are precursors of α,β-dehydro aminoacids.[4] These compounds are usually prepared by chlorination with chlorine,[5] sodium hypochlorite (commercial bleach),[6] or t-butyl hypochlorite.[4,7] Unfortunately some of these procedures have limitations. t-Butyl hypochlorite is an unstable and hazardous reagent and the concentration of "active" chlorine in commercial bleach decreases over time so that high yields of *N*-chloro derivatives are obtained only by using freshly prepared solutions.

Recently, we reported that potassium hydrogen monopersulfate, commercially available as Oxone®, supported on wet basic alumina,[8,9] in the presence of metal halides,[10] can be effectively used for the conversion of oximes into *gem*-halo-nitro compounds in good yields.[11,12] In continuation of our studies to develop new methods using Oxone® as oxidant, we decided to investigate its use in the conversion of amides and carbamates into their corresponding *N*-chloro derivatives (Scheme 1).

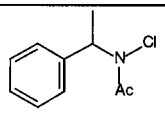
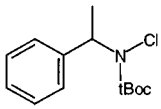
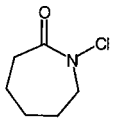
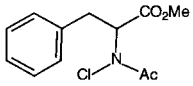
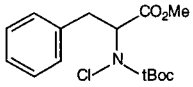
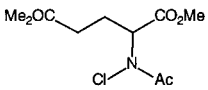
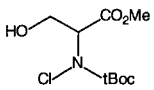
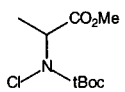


Scheme

When the substrate is treated with Oxone® and NaCl supported on wet alumina in chloroform at 45 °C, *N*-chloroamides, lactams and carbamates are obtained in very good yields (Table). The reaction is carried out by the species produced as a result of the monopersulfate-oxidation of the chloride anion.[13,14] It is important to note that under our reaction conditions the hydroxyl group of the serine side chain remains unreactive (entry 7).

The method described in this communication is equally effective or better than any procedure yet reported and it is applicable without any significant differences to amides, lactams and carbamates derived from simple amines or aminoacids. Therefore the present method should be useful in synthetic organic chemistry.

Table Chlorination of Amides, Lactams and Carbamates with Oxone® and NaCl on Wet Alumina.

Entry	Product	Time (h)	Yield (%)[a]
1	 **1**	4	93
2	 **2**	3	91
3	 **3**	2	97
4	 **4**	4	94
5	 **5**	3	89
6	 **6**	5	86
7	 **7**	2	96
8	 **8**	3	86

[a] Yields in pure isolated products.

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(14) **Typical Procedure**: Oxone® (5 mmol) was added to a well stirred suspension of NaCl (5 mmol) and wet alumina (5 g) in chloroform (20 mL) and the mixture heated at 45 °C for 5 min. A solution of the starting material (1 mmol) in chloroform (5 mL) was then added and the reaction mixture stirred for the appropriate time (2-5 h). The mixture was filtered under vacuum and the solution evaporated under reduced pressure. The crude material was purified by chromatography on Al_2O_3 (activity III, eluent dichloromethane) affording the desired *N*-chloro derivative.

Analytical data

1: Colorless liquid; IR (neat) 1240; ^{1}H NMR δ ($CDCl_3$) 1.51 (d, J = 6.77 Hz, 3H), 2.18 (s, 3H), 5.94 (q, J = 6.77 Hz, 1H), 7.12 - 7.28 (m, 5H); ^{13}C NMR δ ($CDCl_3$) 16.32, 22.12, 55.41, 127.07, 127.64, 128.14, 138.99, 171.55.
2: Colorless liquid; IR (neat) 1238; ^{1}H NMR δ ($CDCl_3$) 1.40 (s, 9H), 1.52 (d, J = 6.83 Hz, 3H), 5.52 (q, J = 6.83 Hz, 1H), 7.15 - 7.30 (m, 5H); ^{13}C NMR δ ($CDCl_3$) 16.97, 28.03, 58.38, 82.74, 127.09, 127.65, 128.22, 139.80, 154.57.
3: Colorless liquid; IR (neat) 1247; ^{1}H NMR δ ($CDCl_3$) 1.60 − 1.85 (m, 6H), 2.58 − 2.71 (m, 2H), 3.75 − 3.85 (m, 2H); ^{13}C NMR δ ($CDCl_3$) 22.04, 26.21, 28.26, 35.07, 57.36, 172.58.
4: Colorless liquid; IR (neat) 1240; ^{1}H NMR δ ($CDCl_3$) 2.05 (s, 3H), 3.05 − 3.47 (m, 2H), 3.70 (s, 3H), 5.45 − 5.62 (m, 1H), 7.01 - 7.25 (m, 5H); ^{13}C NMR δ ($CDCl_3$) 21.21, 34.15, 52.39, 59.64, 126.68, 128.23, 128.59, 135.92, 171.39, 172.54.
5: Colorless liquid; IR (neat) 1235; ^{1}H NMR δ ($CDCl_3$) 1.25 (s, 9H), 2.95 − 3.28 (m, 2H), 3.68 (s, 3H), 4.98 − 5.10 (dd, J = 4.52 Hz, J = 10.56 Hz, 1H), 7.05 - 7.28 (m, 5H); ^{13}C NMR δ ($CDCl_3$) 27.71, 34.68, 52.46, 64.22, 83.33, 126.72, 128.41, 129.03, 136.65, 154.66, 169.57.
6: Colorless liquid; IR (neat) 1242; ^{1}H NMR δ ($CDCl_3$) 2.25 (s, 3H), 1.95 − 2.42 (m, 4H), 3.62, 3.70 (2s, 6H), 5.20 − 5.34 (m, 1H); ^{13}C NMR δ ($CDCl_3$) 21.52, 23.69, 29.81, 51.63, 52.51, 59.29, 169.01, 172.66, 176.22.
7: Colorless liquid; IR (neat) 1236; ^{1}H NMR δ ($CDCl_3$) 1.45 (s, 9H), 3.72 (s, 3H), 3.82 − 4.12 (m, 2H), 4.81 − 4.93 (dd, J = 5.39 Hz, J = 7.87, 1H); ^{13}C NMR δ ($CDCl_3$) 27.73, 52.41, 60.02, 65.38, 83.95, 154.76, 168.58.
8: Colorless liquid; IR (neat) 1240; ^{1}H NMR δ ($CDCl_3$) 1.35 − 1.45 (m, 12H), 3.72 (s, 3H), 4.85 − 4.98 (q, J = 6.91 Hz, 1H); ^{13}C NMR δ ($CDCl_3$) 14.66, 27.56, 52.04, 58.68, 83.14, 154.43, 170.24.

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