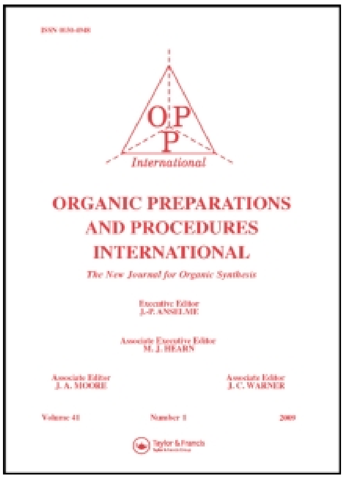

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A FACILE SYNTHESIS OF N-CHLORO FATTY AMIDES

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OPPI BRIEFS

A FACILE SYNTHESIS OF N-CHLORO FATTY AMIDES

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(10/07/85)

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N-Chloro fatty acid amides are highly reactive compounds useful as synthetic intermediates. A new and very convenient method has been found for their synthesis in 85-95% purity by the reaction of chlorine with an emulsion of the amide in boiling water.

$$RCONH_2 + Cl_2 \xrightarrow[100^\circ]{H_2O} RCONHCl + HCl$$

Low molecular weight, hence often water soluble, amides have been N-halogenated in the past using chlorine, bromine, sodium hypochlorite or hypobromite in water or organic solvents.[1] In many cases, it is recommended that the reaction be carried out at low temperature and under mild conditions to avoid decomposition of the product. N-chlorination of higher molecular weight amides such as fatty amides is made difficult by their low solubility in organic solvents at ambient temperatures. Zengel _et al_.[2] were able to chlorinate cyclohexane-1,4-dicarboxylic acid diamide by adding chlorine to a suspension of the amide in aqueous HCl at 10°, but were limited to working with a very dilute (7% solids) system. Orthner[3] chlorinated finely ground (ball milled) stearamide in water at 30°C to give what was believed to be N-chlorostearamide. The reaction takes several hours, and Orthner states that the product is unstable, losing chlorine on standing. It has been found, however, that control of the reaction is difficult, and the difficultly filterable product is a variable mixture of non-chlorinated, mono- and dichlorinated amide.

Surprisingly, it has now been found that an emulsion of up to 20% of molten stearamide can be chlorinated quickly and cleanly in boiling water. On cooling to about 60°, the product crystallizes as prills which can be separated from the by-product (HCl) by simple decantation and washing, mp. 69-73°, lit.[3] mp. 67-68°. The product unlike Orthner's material, was stable for weeks at room temperature after drying. Recrystallization from methanol raised the mp. to 77-78°. Iodimetric analysis of crude material showed, for different preparations, 90-96% positive chlorine as N-chlorostearamide. Derivatization of the N-chloroamide from several preparations by Hofmann rearrangement to the corresponding methyl carbamate, following by GC analysis, showed the presence of 90-96% of the carbamate plus 1-5% stearic acid and 1-9% of unreacted amide. Similar results were obtained by TLC. Minor (<2%) amounts of acyl urea and dialkyl urea were also detected by TLC.

A number of other N-chloro fatty acid amides were synthesized by the same method. Their properties are described in the Table. The reaction has been used to synthesize other types of N-chloroamides, and is applicable to any amide insoluble in water but melting at or below about 105°.

TABLE I. Properties and Analysis of N-Chloro Fatty Amides

		GC Analysis (mole %)		
Starting Amide	mp. (°C)	N-Chloroamide	Amide	Acid
Docosanamide	83-87	81	7	0
Eicosanamide	83-86	94	3	1
Octadecanamide	69-73	90	5	4
Hexadecanamide	67-74	83	10	3
Tetradecanamide	63-66	89	3	5

EXPERIMENTAL SECTION

Synthesis of N-Chlorooctadecanamide. Typical Procedure.- The reaction was carried out in a 500 ml, three-necked, creased (Morton) flask equipped with a paddle stirrer powered by a synchronous motor, an 8 mm ID glass gas inlet tube for introduction of Cl_2 below the surface of the reaction mixture, and a water-cooled condenser. The flask was charged with 28.4 g (0.10 mole) of stearamide (Aldrich Chemical Co.) and 180 ml of water (higher concentrations of amide lead to poorer results), and then heated with an oil bath maintained at 120-145°. After the amide had melted and the water was boiling, stirring was begun and maintained at 1000 rpm or greater (lower stirring rates lead to poorer yields). Chlorine (0.15 mole) was then added using a calibrated rising bead flowmeter over 10-15 min. (0.125-0.20 mole of Cl_2 gave similar results). After the first 1-2 minutes, the initially very fluid emulsion of the amide thickened to a creamy consistency, but reverted to its former state after ca. one equivalent of Cl_2 had been added. The mixture was stirred for an additional 15 min., after which it was cooled in an ice-water bath with continued stirring. Prills of product began to precipitate at 60-70°, and these were decanted or filtered from the by-product (HCl) after the temperature had reached 25°. The product, washed with water and dried either at room temperature or at 55° and 1 mm pressure, was obtained in quantitative yield. It showed bands (Nujol^R and halocarbon mulls) at 3210 (NH cis to C=O), 1654 and 1660 (C=O doublet) and 1460 cm^{-1} (NH cis to C=O). NMR ($CDCl_3$): δ 0.82 (t, 3H), R 1.22 (broad s, 30H), 2.28 (t, 2H).

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SYNTHESIS OF 1,3,4-THIADIAZOLYL UREAS

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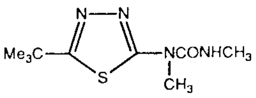
In connection with studies directed toward the synthesis of tebuthiuron, N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N,N'dimethylurea, (1), known as Graslan^{R}, Spike^{R}, or Perflan^{R}, a broad-spectrum herbicide,[1] it became of interest to synthesize compounds 4 and 5 for structure-activity relationship. This brief note describes a facile method for the preparation of these two compounds as shown below.



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