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**ANALYSIS ON MICROWAVE BASED N-
CHLORINATION OF AMIDES**

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Analysis on Microwave Based N-Chlorination of Amides

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Abstract – Chlorination of amides is of utmost importance in biochemistry and environmental chemistry. Despite the huge body of data, the mechanism of reaction between amides and hypochlorous acid in aqueous environment remains unclear. In this article, Synthesis of microwave based n-chlorination cyclic amides has been considered.

Keywords: Chlorination, Amides, N-Haloamidcs

INTRODUCTION

N-Haloamides are used as photoinitiators for radical polymerization and in room temperature vulcanization for the preparation of adhesives, caulks and sealants. They are also versatile reagents in organic synthesis as oxidizing agents in aqueous and non-aqueous media; Photolysis of N-haloamidcs gives amidy radicals and halogen atom intermediates. The amidy radicals so produced undergo efficient intramolecular addition to olefinic bonds. Olefinic amidyl radicals can ring-close to lactams or N-heterocyclic amides. N-chloroamides undergo the Hofmann reaction and Orton rearrangements. [1]

Many literature methods are reported for the synthesis of primary N-chloroamides. Routes to synthesize secondary N-chloroamides include chlorination of secondary amides with NaCl in the presence of oxone, t-butyl hypochlorite, sodium hypochlorite, and N-chlorosuccinimide these methods for the synthesis of secondary N-chloroamides have their own limitations. t-Butyl hypochlorite is unstable and hazardous, reaction with NaCl in presence of oxone can require 2-5 hours Microwave heating has emerged as an environmental friendly technique to accelerate a variety of chemical reactions Automated and focused microwave flash heating has recently been demonstrated to improve the preparative efficacy and to dramatically reduce reaction times for many different types of organic transformations. We now report that by applying microwave heating, the N-chlorination of cyclic and acyclic secondary amides can be done in 15-20 minutes using N-chlorobenzotriazole as the chlorinating agent.

REVIEW OF LITERATURE –

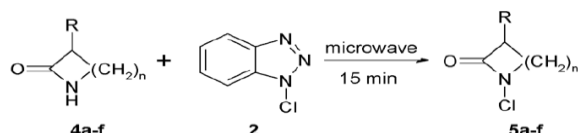
Optimization of the reaction conditions was carried out for the chlorination of secondary amides and different combinations of temperature, time and irradiation power were studied for N-methylbenzamide (1a) in order to achieve the maximum chemical yield at the lowest reaction temperature. Microwave irradiation of 1a for more than 20 minutes caused decomposition. The power and the temperature of reaction for the different compounds were set according to the melting points of the starting materials. Maximum yields were observed when the power is 80-90 W. On increasing the power above 90 W, decomposition took place. The completion of reaction was checked by disappearance of the secondary amide in TLC. Scheme shows the time and temperature used for the preparation of secondary N-chloroamidcs.

The reaction of N-methylbenzamide (1a) with N-chlorobenzotriazole was attempted in the absence of microwave irradiation. After refluxing N-methylbenzamide (1a) with N-chlorobenzotriazole in acetonitrile for 16 h. a yield of 60 % of the product was obtained. In contrast, the reaction was completed (as monitored by TLC) in 20 minutes in the case of microwave heating.

Literature reports have characterized secondary N-chloroamides by IR. UV and NMR spectroscopy, chlorine estimation, iodometric assay and CHN analysis." The NMR data showed the absence of N-H protons. In ¹H and ¹³C NMR, the N(Cl)-CH₂ protons showed a downfield shift as compared to the -NH-CH₂ protons. In our experiments, the completion of the reaction was confirmed by the disappearance of the amide on TLC followed by the disappearance of NH proton in NMR, which was further confirmed by CHN analysis. The NMR data of chloro-2-azobenzonitrile was in close agreement with the literature data. The

synthesis of N-chloro-N-methylbenzamide was reported with t-butylhypochlorite in high yields but requires 12 hour reaction conditions are mild and the reaction can be finished in 15 minutes time. The same methodology converted cyclic secondary amides into the corresponding

N-chloro amides in good to excellent yields in 15 minutes. The benzotriazole formed in the reactions was removed by washing with a saturated solution of sodium carbonate to give pure products.



Scheme: Synthesis of N-chloro cyclic secondary amides [1]

	n	R	Time (min)	Temp (°C)	Power (Watts)	Yield (%)	Lit. yield
5a	1	H	15	60	80	80	
5b	2	Me	15	60	80	56	
5c	3	H	15	60	80	55	64 ⁹
5d	4	H	15	60	80	65	73, 5 ³¹ 43 ³⁵
5e	6	H	15	60	80	81	*
5f	10	H	15	60	80	85	*

Table: Microwave conditions and yields for the preparation of N-chloro cyclic secondary amides [1]

It has been observed that the $\text{TiCl}_4\text{-NR}_3$ system reacts with 1-alkynes to give the corresponding diynes, through the intermediacy of the alkynyltitanium species. [2] Also, the alkynyltitanium species can be readily functionalised using certain electrophiles (Scheme 23). [2] Such direct metalation is an interesting observation, as previously alkynyl titanium reagents were prepared via metalation of 1-alkynes with alkyllithium reagents followed by exchange reaction with titanium complexes. [3] Interesting oxidative coupling reactions have been observed using N, N-dialkylaniline derivatives. [4] The corresponding benzidine derivatives are the products. Again, this transformation can be rationalized considering the intermediacy of the corresponding aryltitanium species. [4] The aryltitanium species prepared in this way can be readily functionalized using certain electrophiles (Scheme 24). [4]

In 1955, it was reported that the TiCl_4 oxidises tertiary amines. Presumably, the corresponding iminium ions would be the organic product and the reaction can be rationalized by the intermediates shown in Scheme 25 [5].

N-chlorination of poly (m-phenylene isophthalamide)

The N-chlorination of N-methyl benzamide by hypochlorite was studied in depth by Hardy et al. in 1967 [7], who found the reaction to be reversible. Figure 1 shows an adapted version of Hardy's

mechanism for poly (m-phenylene isophthalamide). Hardy et al. observed that the reaction of amide with hypochlorite was reversible in alkaline media and proposed a transition state based on a six-membered ring. Values of 2.5 ± 0 and $13.7 \pm 1.1 \text{ L mol}^{-1} \text{ min}^{-1}$ for the second order rate constant were calculated in his study at 293 K for the N-chlorination and the basic hydrolysis for the N-chloro N-methyl benzamide, respectively. Furthermore, a raise in the temperature to 303 K increases the rate constant for the hydrolysis to a value of $47.5 \pm 4.8 \text{ L mol}^{-1} \text{ min}^{-1}$.

CONCLUSION:

In this analysis we found that synthesis of 5d and 5e comprises exposing a solution of lactam in an organic solvent to chlorine gas in the presence of UV light which also promotes polymerization to some extent. However, in our reactions we didn't observe any polymerization and the reagents used are non-hazardous with minimal solvent and short reaction time. The preparation of N-chloro secondary amides: microwave irradiation leads to reaction rate enhancement, improved yields and safe conditions.

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