3-Halo-4-imino-2-azetidinones *via* Acylchloroformamidines

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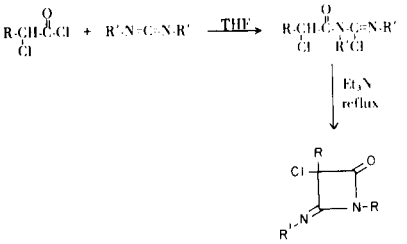
α-Haloacid halides react with carbodiimides to yield acylchloroformamidines which upon treatment with triethylamine undergo conversion to 3-halo-4-imino-2-azetidinones in good yield. Two pathways are possible for this conversion and these are discussed.

J. Heterocyclic Chem., **14**, 179 (1977).

Sir:

In some recent studies on the cycloaddition of trimethylsilylbromoketene and diisopropylcarbodiimide (1), we discovered an interesting method for the synthesis of 3-halo-4-imino-2-azetidinones. While it is known that acid halides react with carbodiimides to yield acylchloroformamidines (2), we have found that acylchloroformamidines prepared from α-haloacid halides undergo conversion upon treatment with triethylamine to form the azetidinones in good yield. Thus, to 0.05 mole of diisopropylcarbodiimide in 60 ml. of THF was added 0.025 mole of chloroacetyl chloride with stirring at room temperature. An infrared spectrum of the reaction solution reveals the loss of the acid chloride carbonyl at 1760 cm^{-1}, and the

Scheme I

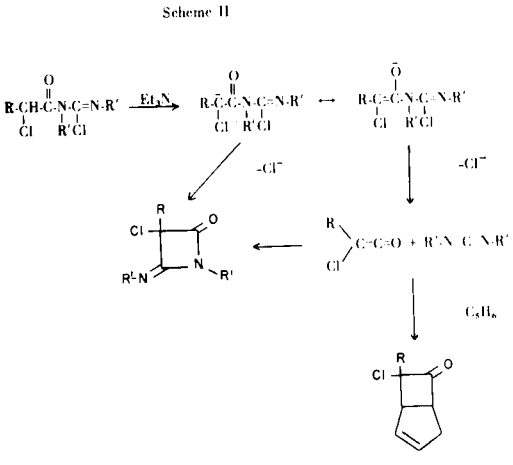


appearance of the 1-chloro-*N*-(chloroacetyl)-*N*,*N*′-di(isopropyl)formamidine carbonyl and carbon-nitrogen double bond at 1695 and 1670 cm^{-1}, respectively. To this refluxing solution was added 0.05 mole of triethylamine dropwise with stirring. After refluxing for 3 hours, the amine salt was removed by filtration and the solvent evaporated. The residue was dissolved in carbon tetrachloride and poured into dilute hydrochloric acid to hydrolyze the excess carbodiimide to the corresponding urea. The insoluble urea was filtered and the carbon tetrachloride solution evaporated and the residue distilled to give 3.3 g. (65%) of 3-chloro-1-isopropyl-4-isopropylimino-2-azetidinone at 65° at 0.1 Torr.; ir: 1830 and 1710 cm^{-1}; nmr, (carbon tetrachloride): δ, 1.16 (d of d, 6H), 1.38 (d, 6H), 3.7 (m, 2H), and 5.06 (s, 1H). Mass spectrum parent peak m/e 202 and 204. *Anal.* Calcd. for $C_9H_{15}ClN_2O$: C, 53.33; H, 7.46; N, 13.82. Found: C, 53.08; H, 7.20; N, 14.06.

3-Chloro-1-isopropyl-4-isopropylimino-3-methyl-2-azetidinone was prepared from α-chloropropionyl chloride and 3,3-dichloro-1-isopropyl-4-isopropylimino-2-azetidinone was prepared from dichloroacetyl chloride by the same procedure in 70% yield.

Previously 3-halo-4-imino-2-azetidinones had been reported by the *in situ* cycloaddition of halogenated ketenes with carbodiimides (3) but the yields were poor except for the *in situ* cycloaddition of dichloroketene reported by Hull (4) and we believe this occurred through the acylchloroformamidine although no mention was made of this intermediate (5).

Scheme II



There are two routes to the 3-halo-2-azetidinones from the acylchloroformamidines. Reaction with triethylamine will yield the enolate (6) which can undergo an intramolecular nucleophilic displacement to the azetidinone or elimination can occur from the enolate to yield the ketene which would subsequently undergo cycloaddition with the carbodiimide. Although the more likely pathway would be ring closure, we have evidence that the ketene is formed from the formamidine, *e.g.*, the ketene can be trapped with cyclopentadiene to yield the expected cyclopentadiene cycloadduct.

Acknowledgments.

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REFERENCES AND NOTES

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(2) K. Hartke and E. Palou, *Chem. Ber.*, **99**, 3155 (1966).

(3) W. T. Brady, E. D. Dorsey and F. H. Parry, III, *J. Org. Chem.*, **34**, 2846 (1969).

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(5) Hull's procedure involved the addition of triethylamine to a refluxing solution of dichloroacetyl chloride and dicyclohexylcarbodiimide in cyclohexane. We have repeated this procedure and observed the formamidine in solution as evidenced by infrared data.

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