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REACTION OF N-HALO-AMIDES AND -IMIDES WITH DIAZOMETHANE

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A number of N-halo-amides and -imides have found important applications through a variety of interesting reactions. On the other hand, diazoalkanes participate in many reactions which are also very important from theoretical and practical viewpoints.

Following our studies on the chemistry of positive-halogen compounds[1], we should like to report here a new organic reaction with the coparticipation of both classes of compounds: by interaction of equimolecular amounts of a N-halo-amide or -imide (I) and diazomethane the corresponding N-halomethyl-derivative (II) is formed by insertion of a carbon atom between the N-X linkage.

It is considered that the reaction takes place through a polar mechanism since N-iodosuccinimide, which does not show homolytic reactivity[2], reacts at least as easily as the analogous

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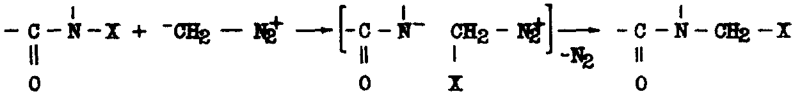
[1] R.A.Corral and O.O.Orazi, J.Org.Chem., 28, 1100 (1963) and references therein cited.

[2] C.Djerassi and C.T.Lenk, J.Am.Chem.Soc., 75, 3493 (1953).

N-chloro or N-bromocompounds.

(a)


$$-\underset{\underset{O}{\|}}{C}-\overset{|}{N}-X + {}^{-}CH_2-N_2^{+} \longrightarrow \left[-\underset{\underset{O}{\|}}{C}-\overset{|}{N}^{-}\quad \underset{\underset{X}{|}}{CH_2}-N_2^{+}\right] \xrightarrow[-N_2]{} -\underset{\underset{O}{\|}}{C}-\overset{|}{N}-CH_2-X$$

(I) (II)

Departing from other substances which also undergo polar methylenation reactions[3], the atom supporting the halogen in compound (I) lacks of orbitals for coördination with diazomethane.

The heterolytic fission of the N-X bond might occur by displacement of halide anion or, as depicted in (a), by abstraction of halogen cation. Although no experimental evidence is available at this time, the authors prefer the latter process considering it more consistent with the general chemical behaviour[4] of compounds (I); $S_{N}1$ or $S_{N}2$ displacements are less likely due to the positive character of the halogen[4] and the molecular geometry[5] of the substances so far examined (table I).

The reaction is noticeably exothermic and proceeds very rapidly; the occurrence and the end of the reaction are easily visualized taking into account the disappearance of the yellow color of the diazomethane, the nitrogen gas evolution or the positive-halogen consumption (iodometric analysis).

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[3] D.Seyferth, Chem.Rev., 55, 1155 (1955); A.G.Davies, D.G.Hare, O.R.Khan and J.Sikora, J.Chem.Soc., 4461 (1963); H.Böhme and E.Boll, Chem.Ber., 90, 2013 (1957).

[4] For a recent review, see S.S.Novikov, V.V.Sevost'yanova and A.A.Fainzil'berg, Russian Chem.Rev., 31, 671 (1962).

[5] L.Horner and E.H.Winkelmann, in Neuere Meth.Präpar.Organ.Chemie (Ed. W.Foerst, Verlag Chemie) 3, 98 (1961).

Table I

N-halocompound	N-morpholinomethylderiv.		Morpholine.HX	
	% yield	m.p.	% yield	m.p.
1-Chloro-3,5,5-tri methyl-hydantoin	75	76-78°	77	175-176°
3-Chloro-1,5,5-tri methyl-hydantoin	76	75-76,5°	48	173-176°
N-Chlorosuccinimide	84	184-185° (dec.)[a]	70	168-173°
N-Bromosuccinimide	55	183-184° (")[a]	71	208-209°
N-Iodosuccinimide[b]	52	185-186° (")[a]		

a) isolated as picrate; b) reactions at 0-5°.

In order to avoid difficulties encountered[6] in the isolation of the N-halomethylderivatives (II), the reaction solution was treated directly with two moles of morpholine giving in high yields the corresponding N-morpholinomethyl-derivative and the morpholine hydrohalide (table I).

These results, all together with the known chemical behaviour of N-halomethyl-amides and -imides[7], provide a secure proof about the nature of the compounds (II) resulting in the reaction here described. Besides, this is a new method for converting amides or imides in their N-aminomethylderivatives through the readily accesible N-halocompounds.

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[6] See also H.Böhme, A.Dick and G.Driesen, Chem.Ber., 94, 1879 (1961).

[7] H.Böhme, R.Broese, A.Dick, F.Eiden and D.Schünemann, Chem.Ber., 92, 1599 (1959); E.Cherbuliez and G.Sulzer, Helv.Chim.Acta, 8, 567 (1925).

These reactions can be illustrated with the following example:

	R
III)	Cl
IV)	CH_2-Cl
V)	CH_2-N O

To a magnetically stirred solution of 0.001 mole of 1-chloro-3,5,5-trimethylhydantoin[1] (III) in anhydrous dioxane (or dichloromethane) maintained at 15-20° and protected from humidity, a dried solution (ethyl ether or benzene) of 0.001 mole of diazomethane was added dropwise. Subsequent addition of 0.002 mole of morpholine gave immediately a crystalline precipitate of morpholine hydrochloride (yield 77%), identified by m.p. and mixed m.p..

The filtered solution was evaporated to dryness and the residue was repeatedly extracted with hot hexane; removal of the solvent, disolution of the extract in benzene followed by rapid filtration through neutral alumina (Woelm, activity II) afforded 75% yield of 1-morpholinomethyl-3,5,5-trimethylhydantoin (V), which after crystallizations from hexane melted at 76-78°; it was identified by infrared spectra comparison and mixture m.p. with an authentic sample[8].

These data and those obtained in other examples carried out in similar way are summarized in table I; the yields of the reaction products clearly indicate that the non-isolated N-halomethylcompounds (v.gr. IV) are formed in very high yields.

This last point and the simplicity of the procedure associated with the remarkable reactivity[7,9] of the resulting N-halomethyl-amides (and -imides) allows to presume that reaction (a) will find several other applications.

Examination of other examples of both classes of reactants and extension of the reaction to other compounds (as N-haloamines and organic hypohalites) in which the atom supporting the positive halogen cannot coördinate with diazomethane, are in progress.

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[8] O.O.Orazi and R.A.Corral, Tetrahedron, **15**, 93 (1961).

[9] N.Kreutzkamp, H.Meerwein and R.Stroh in Methoden d.organ.Chemie (Houben-Weyl) **5/4**, 694 (1960).