

Reaction of Isocyanides with 1-Halogeno-acetylenes: *N*-Substituted 3-Halogeno-acrylamides

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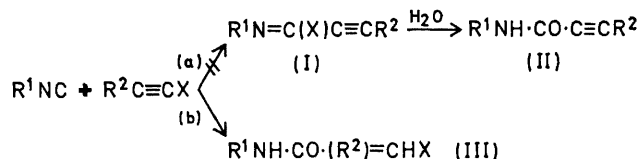
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Summary Isocyanides react with 1-halogeno-acetylenes to give *N*-substituted 3-halogeno-acrylamides.

ISOCYANIDES, R^1NC , usually react with positive halogen compounds such as R^2OCl ¹ and R^2SCl ² to give the products of α -addition, $R^1N=C(Cl)OR^2$ and $R^1N=C(Cl)SR^2$ respectively. With the objective of developing a new synthetic method for $\alpha\beta$ -acetylenic carboxamides (II) we have examined the interaction of isocyanides with 1-halogeno-1-alkynes in the hope that an analogous reaction [pathway (a)] would occur.

Initial attempts to effect the reaction of 1,3-dichloropropyne³ with cyclohexyl isocyanide in anhydrous non-protonic solvents such as ether or tetrahydrofuran afforded

only traces of crystalline material and much tar. Nevertheless, since the crystalline fraction showed amide absorption in the i.r. spectrum, indicating the incorporation of



water, the reaction was repeated in boiling 10% aqueous MeOH. Under these conditions there was produced, after 4 hours, a 51% yield of a material whose physical properties

indicated it to be (III; $R^1=C_6H_{11}$, $R^2=CH_2Cl$; R^2 *trans* to the vinylic Cl). Raney-nickel reduction of this material to *N*-cyclohexylisobutyramide completed proof that the initial reaction had taken an alternate course, [pathway (b)].

Here, besides the expected compound, a small amount of its dehydration product, the cyclohexene, was obtained.

We believe that the mechanism of the reaction is probably similar to that postulated⁴ for the production of (IV) and

TABLE

R^1	R^2	X	Yield of (III)* (%)	Position of vinyl CHX in n.m.r. (p.p.m.)	Time of reflux (hr)
C_6H_{11}	$ClCH_2$	Cl	51	6.58	4
C_6H_{11}	$Pr^iCH(OH)$	Cl	20	6.40	72
C_6H_{11}	$EtMeC(OH)$	Cl	39	6.39	24
C_6H_{11}	1-Hydroxycyclohexyl	Cl	39	6.38	24
C_6H_{11}	Cyclohexenyl	Cl			
C_6H_{11}	Bu^i	I	14	6.42	72
C_6H_{11}	$Pr^iCH(OH)$	I	15	6.14	72
Bu^t	$ClCH_2$	Cl	43	6.67	72
Bu^t	$EtMeC(OH)$	Cl	26	6.51	72
Bu^t	Ph	I	6.3	6.32	48
Ph†	$ClCH_2$	Cl	13	6.77	720
				6.98	

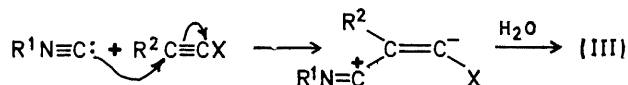
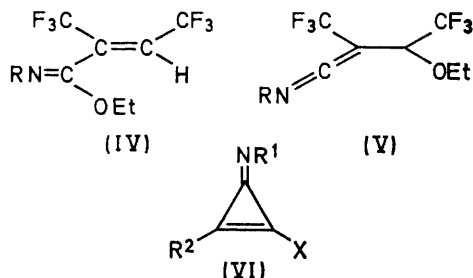
* Satisfactory elemental analyses have been obtained for all compounds.

† In 10% aqueous $Me_2N \cdot CHO$, six d., room temp.

The reaction appears to be quite general (Table). Despite the rather poor yields the method would appear to have value because of the multifunctionality that can be achieved in the products, in one step. Only with 1-(chloroethynyl)-cyclohexanol was any further transformation observed.

(V) from cyclohexyl isocyanide, perfluorobut-2-yne, and EtOH.

Based on this surprising behaviour of an isocyanide as a nucleophile, in our case the reaction would take the form shown below.



So far no positive information for this pathway has been obtained and a three-membered ring intermediate such as (VI) cannot be ruled out. However all attempts to isolate any intermediate of this type have to date been unsuccessful.

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