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A NOVEL ETHER FORMATION REACTION VIA CHLOROACETYLHYDRAZONES

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Chloroacetylhydrazones were allowed to react with sodium alkoxide in alcohol to give acetic ester of the alcohol and unsymmetrical ethers derived from the alkoxide and the alkylidene moiety of the hydrazones. Secondary and tertiary alkoxides failed to afford any amount of ethers. High yields of ethers were realized especially in the reaction of cyclohexanone chloroacetylhydrazone.

In our previous paper, we reported a convenient method of preparing chloroacetylhydrazones which had been unavailable without complication.1) In the present paper, we should like to report an interesting reaction between chloroacetylhydrazones and sodium alkoxides.

A mixture of a chloroacetylhydrazone and a primary alcohol containing equimolar quantities of the corresponding sodium alkoxide was refluxed for 1 hr in a slow stream of nitrogen. An evolution of gas was observed, and acetic ester of the alcohol and an unsymmetrical ether derived from the alkoxide and the alkylidene moiety of the hydrazone were obtained.

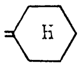
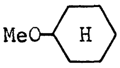
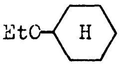
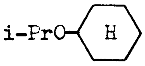
The formation of the ethers was not observed from secondary and tertiary alcohols. The acetic esters and the ethers were detected directly from the reaction mixtures by means of GLC. No olefinic product could be found in each case. The results obtained are summarized in Table 1.

In the reactions of the hydrazone of benzaldehyde and of acetophenone, the main products were 1,4-bis(benzylideneamino)- and 1,4-bis(α-methylbenzylideneamino)-2,5-piperazinedione respectively. In general, the yields of ethers increased with increasing quantity of solvent, as shown in Table 1.

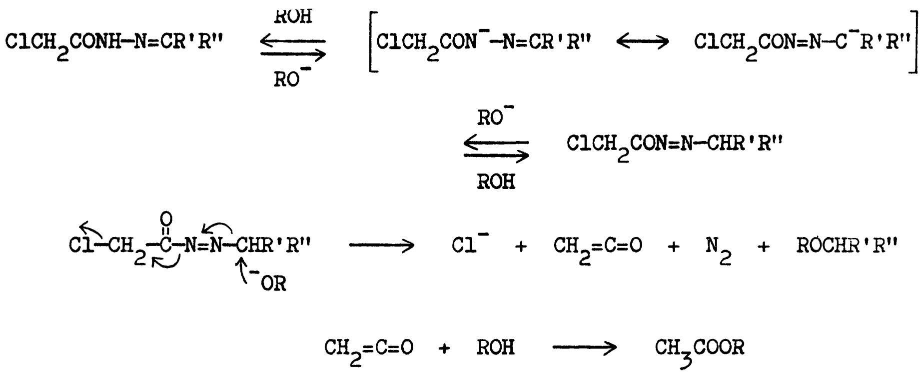
Ioffe and Stopskii2) obtained benzeneazomethane in 35 % yield by distilling formaldehyde phenylhydrazone from alkali, and also3) confirmed the formation of tautomeric azo compounds, though in low yields, from alkylhydrazones by the action of alkali.

Thus, the formation of ethers from chloroacetylhydrazones was presumed to proceed through isomerization of hydrazone to azo-tautomer followed by nucleophilic attack by alkoxide anion.

Table 1. **The Reaction of Chloroacetylhydrazones with Sodium Alkoxides***

Alkylidene Moiety of Chloroacetylhydrazone	Alkoxide	Corresponding Alcohol, ml	Ether (Yield, %)		Acetate (Yield, %)	
=CHPh	Methoxide	10	$MeOCH_2Ph$	(17)	AcOMe	(27)
		30		(20)		(36)
		50		(20)		(31)
	Ethoxide	10	$EtOCH_2Ph$	(2.8)	AcOEt	(2.0)
		30		(5.6)		(5.8)
		50		(7.9)		(9.3)
	Isopropoxide	50	$i\text{-}PrOCH_2Ph$	(0)	i-PrOAc	(trace)
	tert-Butoxide	50	$t\text{-}BuOCH_2Ph$	(0)	t-BuOAc	(trace)
=C(Me)Ph	Methoxide	30	MeOCH(Me)Ph	(3.7)	AcOMe	(5.2)
		50		(4.6)		(5.9)
	Ethoxide	30	EtOCH(Me)Ph	(0.43)	AcOEt	(1.3)
		50		(0.53)		(1.9)
	Isopropoxide	50	i-PrOCH(Me)Ph	(0)	i-PrOAc	(trace)
	Methoxide	30		(100)	AcOMe	(89)
		50		(100)		(98)
	Ethoxide	30		(59)	AcOEt	(52)
		50		(74)		(69)
	Isopropoxide	50		(0)	i-PrOAc	(trace)
$=CHCH_2CH_2CH_3$	Methoxide	30	n-BuOMe	(51)	AcOMe	(71)
		50		(52)		(77)
	Ethoxide	30	n-BuOEt	(52)	AcOEt	(62)
		50		(54)		(63)
	Isopropoxide	50	i-Pr–O–n-Bu	(0)	i-PrOAc	(trace)

* A portion of 10 mmol of hydrazone and equimolar amount of alkoxide were used, and the yields of the products are shown in mole percentage.



$$ClCH_2CONH{-}N{=}CR'R'' \underset{RO^-}{\overset{ROH}{\rightleftharpoons}} \left[ClCH_2CON^-{-}N{=}CR'R'' \longleftrightarrow ClCH_2CON{=}N{-}C^-R'R''\right] \underset{ROH}{\overset{RO^-}{\rightleftharpoons}} ClCH_2CON{=}N{-}CHR'R''$$

$$Cl{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}N{=}N{-}\underset{\uparrow\,^-OR}{C}HR'R'' \longrightarrow Cl^- + CH_2{=}C{=}O + N_2 + ROCHR'R''$$

$$CH_2{=}C{=}O + ROH \longrightarrow CH_3COOR$$

In these reactions, steric effects are operative both in nucleophiles and in hydrazones; the less reactivity of secondary and tertiary alcohols is probably due to their steric hindrance. The reason for the high yields of ethers realized in the reaction of cyclohexanone hydrazone may be that the hydrazone should prefer the azo form on account of the fact that the strain of the carbon ring in the hydrazone form disappears in the azo form. The low yields of ethers from the hydrazone of benzaldehyde and of acetophenone can be accounted for by the increased stability of the hydrazone form of these compounds based on conjugation in the benzylideneamino group.

References

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