Synthesis and Structure Elucidation of some Acyl Thiocarbamates from 8-Hydroxyquinoline

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(Received 25th November 1979)

Summary: Reaction of acyl isothiocyanate (1 to 4) with 8-hydroxyquinoline gave thiocarbamate derivatives (6 to 9). Structure of these compounds is discussed in the light of IR and NMR spectral evidence.

Introduction

Friesen in 1929 noticed that some carbamates have phytotoxic properties[1]. Sixteen years later Templemann-Sexton reported using carbamates as herbecides[2]. In the present work we have described synthesis of new carbamates derived from the reaction of some acyl isothiocyanates with 8-hydroxyquinoline. However, biological activity of these compounds have been tested showing positive results which will be presented in a separate paper.

The rapid increase of the world population urges governments to increase food production. This situation created the need for food protection by many means. Synthetic chemicals have the advantage of being effective tools for weed control and can be used as herbecides, fungicides and insecticides. The importance of these kinds of chemicals arise from their rapid cost increase in the last few years. For example, the United States of America spent $500 millions in 1965. This figure is expected to exceed $2000 million by 1985[3].

Isocyanate was first obtained in 1849 by the double decomposition of a dialkyl sulphate with potassium cyanide[4]. Significant progress was made in later years and many isocyanates have been investigated. Now, there are more than 25 methods for the preparation of isocyanates[5]. Neverthless, the reactions of acylisocyanates still have not received considerable attention and newer synthetic methods are constantly appearing in literature. On the other hand there are only few reports on isothiocyanates and their derivatives synthesis.

Many reactions of different isocyanates with 8-hydroxyquinoline and their carbamate derivatives had been investigated[6]. Biological activity of carbamates and correlation with structure has been also studied[7-11]. However, recent literature survey showed that the reaction of 8-hydroxyquinoline with haloacyl isothiocyanates has not been attempted.

Experimental

All solvents used were dried, distilled, then treated with sodium metal[12]. IR spectra were recorded on Perkin-Elmer 727 or Beckman Model 4240 spectrophotometers. NMR spectra were run on a Varian T60 operating at 60 MHz.

Preparation of $Pb(SCN)_2$

Lead nitrate (1 mole) was dissolved in boiling water, sodium thiocyanate (2 moles) in 100 ml boiling water was added with stirring for ca. 1 hr. The mixture was cooled to room temperature. Lead thiocyanate precipitate was separated by filtration then dried over P_2O_5. Yield was 99%[13,14].

Acetyl chloride

Anhydrous sample Riedel-De Haen were used without further purification.

Preparation of monochloroacetyl chloride

Monochloroacetic acid (1 mole), thionyl chloride (1.5 mole) and 10 drops of dimethyl formamide (DMF) were heated to 90-100° until HCl evolution ceased (ca. 25 hr.)[15]. The excess thionyl chloride was distilled off and the pure product was collected at 101-102° (Lit,[16] 107°), yield 98%. IR for >C = O (neat) at 1810 cm^{-1}. NMR in $CDCl_3$ for $-CH_2$ at 4.6 δ.

Preparation of dichloroacetyl chloride

Dichloroacetyl chloride was obtained from the corresponding acid (1 mole) by treatment with thionyl chloride (1.5 mole) and DMF (10 drops). Yield was 84% collected at 100-103° (lit[16] 108-110°). IR for >C = O (neat) at 1805 cm^{-1}. NMR in $CDCl_3$ for >CH- at 6.2δ.

Preparation of trichloroacetyl chloride

Similarly, trichloroacetic acid (1 mole), thionyl

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Table 1.

Compound	Observed B.P.	Lit. B.P	Yield	Ref:
1	130-132°	132-133°	80%	17 , 18
2	78- 79°/15 mmHg	–	74%	–
3	74- 76°/12 mmHg	–	70%	–
4	71- 72 / 8 mmHg	58-59/mmHg	90%	19

chloride (1.5 moles) and DMF (10 drops) gave trichloroacetyl chloride. Yield 70%, B.P. at 113-115° (lit.[16] 118°). IR for $\rangle C = O$ (neat) at 1800 cm^{-1}.

Preparation of acyl isothiocyanates

Lead thiocyanate (0.1 mole) and sodium dried benzene (100 ml) were mixed in 2-necked round bottom flask fitted with reflux condenser and dropping funnel (both were guarded with $CaCl_2$ tubes). The mixture was heated at 60-75° and the solution of the required acyl chloride (0.2 mole) in dry benzene (20 ml) was added in portions with stirring over a period of 2 hr. The stirring was continued for another 2 hr. The reaction mixture was then left overnight at room temperature. The ppt was removed by filtration, excess benzene was removed and the remaining liquid was fractionated under reduced pressure 8-16 mm Hg using oil pump to give the required isothiocynates. Data are listed in Table 1.

Preparation of thiocarbamates:

Pre-sublimed 8-hydroxyquinoline (0.03 mole) in dry diethyl ether (30 ml) were mixed in 100 ml 2-necked round bottom flask fitted with reflux condenser and dropping funnel. The acetyl isothiocyanates (0.03 mole) was then slowly added under reflux over a period of 3.0 hr. with stirring. The reaction mixture was left overnight at room temperature, the precipitate was collected by filtration and dried over P_2O_5. The product was pale yellow solid recrystallized from anhydrous acetone m.p. 107-108°. Yield 80%. Found: C, 58.52; H, 4.09; N, 11.38; S, 13.02, $C_{12}H_{10}N_2O_2S$ requires C, 58.4; H, 4.0; N, 11.7; S, 13.7%.

The other thiocarbamate derivatives were obtained similarly from treatment of 8-hydroxyquinoline (0.03 mole) with the corresponding isothiocyanate (0.03 mole). Data are listed below.

Results and Discussion:

The present work deals with synthesis of some thiocarbamate derived from 8-hydroxyquinoline. We introduced sulphur and electron withdrawing substituted acyl groups in order to achieve an increase of their toxic properties against macro and micro organisms. The acyl isothiocyanate (1 to 4) were obtained from freshly prepared anhydrous acyl chloride samples when reacted

$$R - \overset{O}{\overset{\|}{C}} - N = C = S$$

1) $R = CH_3-$
2) $R = Cl - CH_2-$
3) $R = Cl_2CH-$
4) $R = Cl_3C-$

with lead thiocyanate in presence of sodium dried benzene as a solvent and under dry conditions. Lead thiocyanate was also obtained fresh from the reaction of lead nitrate with sodium thiocyanate[13,14,20]. The isothiocyanate requires delicate experimental conditions which includes highly dried atmosphere, solvent and glassware since presence of moisture (or any other nucleophile) to the isothiocyanate double bond will destroy the sample. The isothiocyanates must be carefully protected from moisture throughout the course of preparation and purification, as they react vigorously with water to give the corresponding thioacetamide. This addition will be similar to the addition of various nucleophiles to carbonyl groups[21] and to the polarized carbon-nitrogen double bonds in imines which has received considerable attention[22-25]. Recently nucleophilic addition to azomethine double bonds of some isocyanates has been reported[5]. Normal distillation of the above described isothiocyanate needs high temperature which caused partial decomposition of the monochloro and dichloro isothiocyanate. Yield losses were also observed due to sample decomposition. Accordingly, the successful alternative was distillation under reduced pressure ranging from 8 to 16 mmHg using oil pump. It was found that the isothiocyanate neat liquid decomposes partially in few days when standing at ambient or normal refrigerator temperature. However, addition of

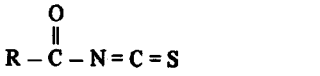
Compound	m.p.	Yield
7	112	90%
8	127	90%
9	147	80%

anhydrous solvent (e.g. diethyl ether) to the pure compounds prevented deterioration for several weeks at normal refrigerator temperature. The ether has the advantage of being volatile when recovery of the sample is immediately needed and can be easily obtained in anhydrous condition. Deterioration might also occur on exposure to light and can be minimized by using dark containers. The stability of the foregoing isothiocyanates was found to be proportional directly to the number of the chlorine atoms in the molecule. Thus trichloroacetyl isothiocyanate was the most stable compound while monochloroacetyl isothiocyanate has the lowest stability. The stability of the former compound relative to the last can be rationalized due to the inductive effect of the three chlorine atoms in the molecule. The acetyl isothiocyanate was the most stable compound in this study. Normal distillation was possible with negligible decomposition. However, leaving the neat solution at room temperature lead to considerable decomposition which was minimized by adding dry diethyl ether and keeping in a refrigerator.

Structure of the acyl isothiocyanates (1 to 4) was confirmed by infrared and proton nuclear magnetic resonance methods. Infrared spectra showed intensive peaks ranging from 1950 to 1975 cm^{-1} concerning stretching the N = C = S group. The carbonyl stretching absorption appeared in the region 1715 to 1735 cm^{-1}. Proton NMR spectra showed the expected signals (see table 2).

Table 2

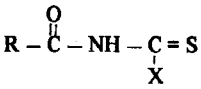
Spectroscopic characters of acyl isothiocyanates



R	Infrared cm^{-1} C = O	-N = C = S	^1H nmr δ in $CDCl_3$
CH_3-	1730	1975	2.32
$Cl-CH_2-$	1725	1960	4.50
Cl_2CH-	1715	1955	6.10
Cl_3C-	1735	1950	–

Treatment of purified 8-hydroxyquinoline with the foregoing acyl isothiocyanates gave thiocarbamate derivatives in solid form. Addition of electron donating substance activates the reaction. Thus few drops of triethylamine were added to enhance the reaction velocity[26]. However, the 8-hydroxyquinoline can itself play as an activator since it contains lone pair electrons on the nitrogen atom. The reaction must be performed in anhydrous solvent to increase activation. Accordingly sodium dried benzene was used for this purpose. We also observed that the isothiocyanate differs in their reaction rate with 8-hydroxyquinoline. The trichloroacetyl isothiocyanate formed yellow precipitate immediately after mixing the reactants while the monochloroacetyl isothiocyanate gave similar results after stirring for few minutes.

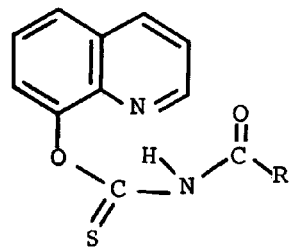
Mechanism of the reaction is believed to proceed by nucleophilic addition to the isothiocyanate carbon atom. Since the reaction occurs in basic medium (presence of triethylamine), we suggest that the mechanism proceeds by adding the 8-hydroxyquinoline anion (x in 5) across the azomethine double bond. At the same time the hydroxyl proton of the 8-hydroxyquinoline will migrate to isothiocyanate nitrogen atom.



$X = C_9H_6NO$ 5

This mechanism is similar to what have been found for addition of nucleophiles to C = N bond in imines[27,28].

Structures elucidation of these thiocarbamates have been achieved by IR and NMR Spectroscopy. The spectral data indicated that the adduct is in the type (6 to 9) rather than any other alternative structure. IR spectra in the solid state (KBr disc) showed peaks at ca. 1630 cm^{-1} and ca. 3380 cm^{-1} (see table 3) which are



6) $R = CH_3-$ 7) $R = Cl\text{-}CH_2-$

8) $R = Cl_2-CH-$ 9) $R = Cl_3C-$

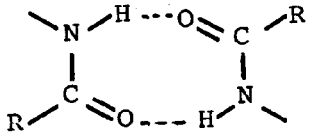
Table 3

IR and NMR data for compounds 6 to 9

R	Infrared cm^{-1} >C = O stretching	N – H stretching	NMR δ in DMSO -d_6
CH_3	1638	3100	CH_3 = 2.1 (s); aromatics 7.7 (dd), 7.2-7.93
$ClCH_2$–	1635	3360	$ClCH_2$ = 4.97 (s); aromatics 7.5-8.15 (m)
Cl_2CH–	1625	3380	Cl_2CH– deuterated; aromatics 9.12 (d), 7.4-82
Cl_3C–	1630	3385	Aromatics 7.4-9.12 (m)

s = singlet, d = doublet, dd = doublet of doublet, m= multiplet

quite consistant with carbonyl and N-H stretching respectively. The carbonyl stretching frequency tends to give slightly low values which would normally be expected for the carbonyl absorption in the solid state of the CONH group due to the presence of the nitrogen lone pair electrons[29]. The low stretching frequency values found for the N-H bonds probably imply that these spectra related to the associated states of type 10 which is more favourable as long as the carbonyl absorption is at low frequency too. It was found that the sharp peak at around 1600 cm^{-1} is quite consistent with the C = C



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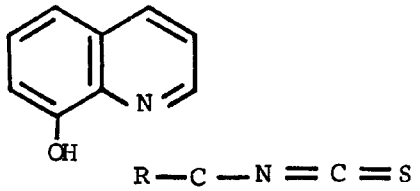
stretching vibrations of the aromatic system. Another confirmation of the above suggested structures (6 to 9) was disappearance of the O-H and N = C = S peaks which excludes formation of compounds in the type 11. NMR spectra of compound 6 to 9 in DMSO-d_6 showed clearly the expected protons resonances and unambiguous



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structural confirmation was achieved (see table 3).

Acknowledgement

The authors are grateful to Prof. M. Afzal, Dept. of of Chemistry, Faculty of Science, Riyad University, Saudi Arabia for correcting the manuscript.

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