The Preparation and Spectral Properties of Some Thioncarbamate Esters

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Aromatic isothiocyanates react with equimolar quantities of primary and secondary alcohols or diols by warming in methyl sulfoxide to give good yields of O-alkyl thiocarbanilates. Since aliphatic isothiocyanates react very slowly under these conditions, the alcohols are first converted to the highly reactive alkoxides by exchange with potassium *tert*-butoxide. The infrared and N.M.R. spectra of the products are compared among themselves and with some newly synthesized carbanilate esters.

THE simple *O*-alkyl esters of thiocarbanilic acids are usually prepared by heating an aryl isothiocyanate with a large excess of an alcohol (*2, 3, 7*), a reaction which is subject to catalysis by a tertiary amine (*17*). This procedure is satisfactory in the case of the lower alcohols, but for preparing thioncarbanilates of higher molecular weight alcohols and glycols, it is of limited use (*2*). It is then necessary to react the isothiocyanate with the sodium derivative of the alcohol, but again for higher molecular weight alcohols these are not conveniently prepared. Other methods of preparation—from thioureas and alcohols (*15*) and from amines and *O*-alkyl chlorothioformates (*13*)—are likewise limited in usefulness.

EXPERIMENTAL

All melting points are uncorrected. The infrared spectra were recorded for KBr pellets containing 1% of compound on a Perkin-Elmer Model 21 spectrometer calibrated with polystyrene. The N.M.R. spectra were recorded on a Varian DP-60 spectrometer operating at 56.4 Mc. for 0.45 molar solutions in $CDCl_3$ with TMS internal standard.

Starting Materials. The methyl sulfoxide was a Fisher reagent distilled from and stored over Linde Molecular Sieve 13×. Potassium *tert*-butoxide was from MSA Research Corp. *p*-Chlorophenyl and *p*-bromophenyl isothiocyanates were prepared from the amines (*6*) and freed from the thioureas by solution in Skellysolve B. 1,10-Decanediol was from Aldrich Chemical Co. Inc., 1-tridecanol from Lachat Chemicals Inc., and the rest of the reagents were Eastman Organic Chemicals.

Thioncarbanilate Preparation from Primary and Secondary Alcohols. The isothiocyanate and the alcohol were mixed in 10-mmole quantities in 5 ml. of methyl sulfoxide. The solution was covered and heated on the steam bath for 3 hours. After it had cooled to room temperature, the reaction mixture was poured with stirring into 100 ml. of cold water. The precipitate was removed, washed with water, and air-dried. The monofunctional esters were extracted into hydrocarbon solvent (Skellysolve B) and allowed to crystallize. The difunctional esters were washed free of impurities with ether and recrystallized from alcohols or aqueous alcohol.

O-(*tert*-Butyl)*p*-Chlorothiocarbanilate. A methyl sulfoxide solution (5 ml.) of 1.45 grams (13 mmoles) of potassium *tert*-butoxide was prepared and centrifuged free of a small amount of insoluble material. On admixture with 2.0 grams (12 mmoles) of *p*-chlorophenyl isothiocyanate, heat was liberated and a deep amber-colored solution resulted. The solution was cooled under tap water and allowed to stand a few minutes at room temperature. The product was precipitated by stirring into cold water. The 2.2 grams of yellow solid was completely soluble in 100 ml. of hexane from which it crystallized in long needles.

O-Tridecyl *N*-Ethylthiocarbamate. To a solution of 1.68 grams (15 mmoles) of potassium *tert*-butoxide in 10 ml. of methyl sulfoxide was added 3.0 grams (15 mmoles) of 1-tridecanol. The resultant slurry was stirred 35 minutes, and then 1.3 grams (15 mmoles) of ethyl isothiocyanate was stirred in. The reaction mixture turned to a yellow solution and after 1 hour was poured into 200 ml. of water and neutralized with hydrochloric acid. The product separated as an oil which, after washing, crystallized spontaneously. The 3.4 grams of product was recrystallized from aqueous alcohol to 2.9 grams of tiny needles (68% of theory).

RESULTS AND DISCUSSION

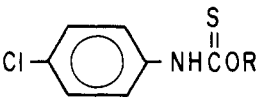
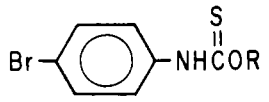
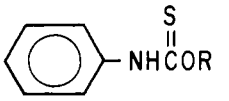
The reaction of equimolar quantities of an aryl isothiocyanate and an alcohol proceeds smoothly and in good yield by warming the reactants in methyl sulfoxide solution. Even allyl esters, reported to be unobtainable by reaction of an isothiocyanate and allyl alcohol (*2*), did form in methyl sulfoxide. Since experiments with ethanol showed that 2 to 3 hours of heating on the steam bath was sufficient to use up all the isothiocyanate, a 3-hour reaction period was used for the other alcohols and diols as well. Even without determining the optimum time for each specific case, the yields of purified compounds ranged from 50 to 75% of theory. In one experiment (using *n*-butyl alcohol), dimethylformamide was also found to be a suitable medium for the reaction. The compounds prepared by the new method are described in Table I.

The reaction mixture was easily worked up by pouring it into water which precipitated the thioncarbanilate as a solid. All the compounds prepared from monohydric alcohols were soluble in petroleum ether, which permitted their ready separation from an insoluble by-product—the symmetrical thiourea derived from the isothiocyanate. The esters of diols were purified by washing with ethyl ether, which dissolved the thiourea but not the thioncarbanilate.

To minimize the formation of the thiourea, it is important to use dry methyl sulfoxide. Indeed, a measure of how dry a given batch of solvent is can be had by warming a quantity of it with an isothiocyanate, pouring the mixture into water, and isolating and weighing the petroleum ether–insoluble material.

In the presence of an alcohol, however, all the thiourea formed does not arise from the side reaction with moisture in the solvent. This alcohol dehydration has been noted

Table I. Melting Points and Analytical Data for Thioncarbamate Esters

R	M.P., °C.	Formula	C Calcd.	C Found	H Calcd.	H Found.	N Calcd.	N Found	S	
										
C_2H_5	101–103[a]									
$C_3H_7(n)$	53.5–58[b]									
$CH_2CH=CH_2$	87–88	$C_{10}H_{10}ClNOS$	52.74	52.60	4.43	4.47	6.15	6.36	14.08	14.88
$C_4H_9(n)$	73.2–74.7[c]									
$C_4H_9(iso)$	68–69	$C_{11}H_{14}ClNOS$	54.20	54.22	5.79	5.88	5.75	5.66	13.15	13.07
$C_4H_9(sec)$	87.5–89	$C_{11}H_{14}ClNOS$	54.20	54.91	5.79	5.94	5.75	5.75	13.15	13.11
$C_4H_9(tert)$	105.0–105.1	$C_{11}H_{14}ClNOS$	54.20	53.76	5.79	5.76	5.75	5.83	13.15	13.21
$C_{10}H_{21}(n)$	46–47.5	$C_{17}H_{26}ClNOS$	62.26	62.09	7.99	7.89	4.27	4.89	9.78	9.94
$C_{16}H_{33}(n)$	67–68	$C_{23}H_{38}ClNOS$	67.04	67.66	9.29	9.27	3.40	3.47	7.78	7.69
$CH_2CH_2OC_2H_5$	101–103.5	$C_{11}H_{14}ClNO_2S$	50.86	51.20	5.43	5.51	5.39	5.48	12.34	12.27
$CH_2CH_2N(CH_3)_2$	73.5–75	$C_{11}H_{15}ClN_2OS$	51.05	51.28	5.84	5.88	10.83	10.34	12.39	12.86
$(CH_2)_6$	126.5–129.5	$C_{20}H_{22}Cl_2N_2O_2S_2$	52.51	52.43	4.85	4.35	6.13	5.92	14.02	13.45
$(CH_2)_{10}$	151–152	$C_{24}H_{30}Cl_2N_2O_2S_2$	56.13	56.78	5.89	5.99	5.46	5.55	12.49	12.58
$(CH_2)_2O(CH_2)_2$	130.3–132	$C_{18}H_{18}Cl_2N_2O_3S_2$	48.54	48.04	4.07	3.82	6.29	6.19	14.40	13.83
										
CH_3	103–104[d]									
C_2H_5	105–106.5[e]									
$(CH_2)_{10}$	140–142	$C_{24}H_{30}Br_2N_2O_2S_2$	47.84	47.84	5.02	4.52	4.65	4.68	10 64	10.56
										
C_2H_5	68–69.5[f]									
$CH_2CH=CH_2$	66.5–66.7[g]	$C_{10}H_{11}NOS$	62.14	61.97	5.74	5.76	7.25	7.23	16.59	16.10
$(CH_2)_{10}$	113–115	$C_{24}H_{32}N_2O_2S_2$	64.83	64.97	7.26	6.96	6.30	6.50	14.42	14.26
$C_4H_9(tert)$	88–89[h]									
		$C_2H_5NHCSOR$								
$C_{13}H_{27}(n)$	36.6–37.9	$C_{16}H_{33}NOS$	66.84	67.35	11.57	11.55	4.87	5.11	11.15	11.28
$(CH_2)_{10}$	58–60	$C_{16}H_{32}N_2O_2S_2$	55.13	55.61	9.26	8.53	8.04	7.92	18.40	18.47

[a] M.p., 103–104° C., (7). [b] M.p., 51–52° C., (7). [c] M.p., 72–74° C., (7). [d] M.p., 101–102° C., (7). [e] M.p., 104–105° C., (7). [f] M.p., 67–68° C., (7). [g] M.p. 75–77° C., (2). [h] M.p., 86.5° C., (2).

previously (2) when no solvent was used other than excess of the reacting alcohol, so it is not a result of the use of methyl sulfoxide. The extent to which this dehydration occurs and its effect on the yield of thioncarbanilate is dependent on the structure of the alcohol as shown in Table II where the results of the reactions of the butyl alcohols with *p*-chlorophenyl isothiocyanate are given.

Since alkyl isothiocyanates require much longer reaction times with alcohols than do the aromatic compounds (*19*), *N*-alkylthiocarbamates have usually been made from a potassium alkyl xanthate and an amine (*9, 14*). In methyl sulfoxide, also, an alkyl isothiocyanate reacts too slowly for this to be a practicable synthesis. Even after 60 hours of heating ethyl isothiocyanate and 1-decanol in methyl sulfoxide, there were still substantial amounts of both reactants present. Therefore, an alternate procedure for aliphatic compounds was developed based on the above-noted unreactivity of *tert*-butyl alcohol. This consists in adding a primary alcohol to a methyl sulfoxide solution of potassium *tert*-butoxide, followed by addition of the alkyl isothiocyanate. This variation was also successful with *p*-chlorophenyl isothiocyanate and 2-dimethylaminoethanol, an alcohol which gave some unidentified by-products in the absence of the alkoxide.

Since an isothiocyanate reacts very rapidly with alkoxide ion, but only very slowly with an alcohol, it is possible that the beneficial effect of methyl sulfoxide is due to strong hydrogen bonding of the alcohol (*4*) which weakens the hydrogen-oxygen bond of the latter and, hence, increases its nucleophilicity. From what is known of the mechanism of the reaction of isocyanates with alcohols (*8*), however, and of catalysis by methyl sulfoxide in other reactions (*11*), it seems more likely that the sulfoxide acts through enhanced polarization of the isothiocyanate.

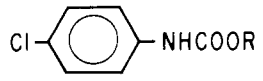
Table II. Reaction of the Butyl Alcohols with *p*-Chlorophenyl Isothiocyanate

Alcohol	Thioncarbanilate Yield[a], %	Thiourea Yield[a], %	Isothiocyanate Recovered[a], %
Blank	..	4	90
n-Butyl	83	8	..
Isobutyl	79	14	..
sec-Butyl	70	20	..
tert-Butyl	0	41	52

[a] Before recrystallization.

Infrared Spectra. The most prominent bands which appear in the infrared spectra of all the compounds studied are found at 1540 ± 9 (Amide II), 1337 ± 6, 1300 ± 10 (Amide III), 1282 ± 4, 1218 ± 8 (ester), and 1198 ± 8 cm.$^{-1}$. These spectra have been compared with those of a few oxygen analogs of the *p*-chlorothioncarbanilates (described in Table III), for which the pertinent absorption bands were 1700 ± 3 (Amide I), 1536 ± 8 (Amide II), 1302 ± 3 (Amide III), 1284 ± 2, and 1243 ± 7 cm.$^{-1}$. The 1337 and 1198 cm.$^{-1}$ bands are entirely missing in the spectra of the carbanilates, and the ester band appears about 25 cm.$^{-1}$ higher in frequency.

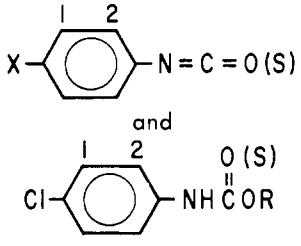
Table III. Melting Points and Analytical Data for O-Alkyl *p*-Chlorocarbanilates



R	M.P., °C.	Formula	C		H		N	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
C_2H_5[a]	68–68.5[b]							
$C_4H_9(n)$[a]	52.6–53.9[c]	$C_{11}H_{14}ClNO_2$	58.02	57.84	6.20	6.41	6.15	6.04
$C_{12}H_{25}$[a]	72.0–73.8	$C_{19}H_{30}ClNO_2$	67.13	67.18	8.90	8.98	4.12	4.31
$(CH_2)_6$[d]	176.5–178.5	$C_{20}H_{22}Cl_2N_2O_4$	56.48	56.76	5.22	5.32	6.59	6.57
$(CH_2)_{10}$[d]	149.5–151[e]	$C_{22}H_{30}Cl_2N_2O_4$	59.87	60.36	6.28	6.28	5.82	5.89

[a] Prepared by mixing *p*-chlorophenyl isocyanate and the alcohol and recrystallizing from Skellysolve B. [b] M.p. 66–67° C. (*12*). [c] M.p. 72° C. (*5*). [d] Prepared in ether and recrystallized from chloroform. [e] Solidified and remelted at 164–166° C.

Table IV. Proton Chemical Shifts[a] for



Compound	Ring 1	Ring 2	NH	OCH_2	J_{12}, C.P.S.
ClC_6H_4NCO	7.27	7.00			9.0
ClC_6H_4NCS	7.30	7.12			8.5
BrC_6H_4NCS	7.46	7.09			8.5
$ClC_6H_4NHCOOC_2H_5$	7.32	7.24	6.84	4.24	9.6
$ClC_6H_4NHCSOC_2H_5$	7.28	7.28	9.07	4.64	
$ClC_6H_4NHCSOC_{10}H_{21}$	7.33	7.33	8.93	4.62	

[a] P.p.m. downfield from tetramethylsilane. Measured on equimolar solutions in $CDCl_3$.

Rao has picked three bands as typical of compounds containing a thiocarbonyl group linked to one or two nitrogen atoms (*16*). These bands located at 1395 to 1570, 1260 to 1420, and 940 to 1140 cm.$^{-1}$ he has designated the N—C=S I, II, and III bands, respectively. In a subsequent publication (*18*), he has narrowed these bands for thiourethanes to 1492 to 1507, 1304 to 1341, and 1130 to 1134 cm.$^{-1}$, respectively. This assignment was based on a study of the spectra of five compounds not specifically identified, but it is implied that they were ring-substituted derivatives of *O*-ethyl thiocarbanilate.

In the spectra of the author's larger sampling of thioncarbanilates and thioncarbamates, only the 1304 to 1341 cm.$^{-1}$ band could be confirmed as typical; the actual band present in the sulfur compounds, but not in the oxygen analogs is a 1337 ± 6 cm.$^{-1}$.

In the 1492 to 1507 cm.$^{-1}$ region there is absorption only in the aromatic compounds, which was consequently attributed to the 1500-cm.$^{-1}$ phenyl nucleus absorption (*1*); the aliphatic compounds have no more than weak absorption in this region. The aromatic compounds do have either a shoulder on the 1500-cm.$^{-1}$ band or a distinct band in the region of 1470 to 1484 cm.$^{-1}$, and the aliphatic compounds have a band at 1470 cm.$^{-1}$, but the carbanilates also all show this band at 1474 to 1478 cm.$^{-1}$, which makes any association with the thiocarbonyl group doubtful.

In the 1130 to 1134 cm.$^{-1}$ region, only a minority of these compounds absorb. Indeed, in the entire 1000 to 1200 cm.$^{-1}$ region, the multiplicity and variability of bands in the spectra make any assignment hazardous.

A recent article (*10*) by Jensen in which he reports finding the spectra of corresponding thioamides and selenoamides identical between 1000 and 3000 cm.$^{-1}$ has led him to assert that there are no C=S vibrations in this region and no complex bands containing a contribution from C=S. This work does not contradict the possibility that the same may hold true for thioncarbanilates.

N.M.R. Spectra. The chemical shifts for some of the compounds used in this work are given in Table IV.

The greater deshielding effect of sulfur as compared with oxygen is most apparent in the shift of the proton on the adjacent nitrogen, but it extends in diminished form to the alkyl group and the ring protons as well.

ACKNOWLEDGMENT

The author wishes to thank M. Camara for assistance in the preparative work and K. Kellenbach and G. Suarez for assistance in obtaining the infrared and N.M.R. spectra.

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RECEIVED for review August 27, 1965. Accepted December 26, 1965.