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The Reaction of Isocyanates with Carboxylic Acids and Thiocarboxylic Acids

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Synopsis. Thiocarboxylic acids reacted with isocyanates or acyl isocyanates to give the stable addition products. However, similar products obtained from benzoic acid and acyl isocyanates dissociated into their components in solution.

Isocyanates are known to react with carboxylic acids to give mixed carbamic carboxylic anhydrides (I).[1-3] These anhydrides are relatively unstable and decompose to give a mixture of amide, *sym*-substituted urea and carboxylic anhydride with evolution of carbon dioxide on heating.[2,3] Some of them dissociate into isocyanates and carboxylic acids in solution.[2,4] It appeared of interest to study the reactions of isocyanates and acyl isocyanates with carboxylic acids and thiocarboxylic acids.

Thiobenzoic acid was allowed to react with phenyl isocyanate in *n*-hexane at room temperature. The reaction proceeded immediately and benzoyl phenylcarbamoyl sulfide (IIa) was obtained as white precipitates. Though I* was readily decomposed on heating and difficult to be recrystallized, IIa was relatively stable and could be purified by recrystallization. Thus analogous sulfides (IIa)—(IIf) were prepared by a similar procedure. The results are summarized in Table 1. The IR spectra of II showed a N–H band at 3220—3250 cm^{-1}, two C=O bands at 1700—1730 cm^{-1} and 1675—1680 cm^{-1} and no absorption due to S–H in the region 2500—2600 cm^{-1}.** The reaction of phenyl isocyanate with thioacetic acid gave acetyl phenylcarbamoyl sulfide (IIg), mp 37—39 °C. IIg decomposed on standing for a few days. Elementary analyses were not in good agreement with the calculated values, but the structure was confirmed by IR spectra (3250 cm^{-1} (N–H), 1720, and 1680 cm^{-1} (C=O)) and NMR spectra (2.67 τ (5H, C_6H_5) and 7.66 τ (3H, CH_3)). The reaction of methyl isocyanate with thioacetic acid or thiobenzoic acid resulted in the corresponding decomposition products, *N*-methylacetamide and *N*-methylbenzamide.

Table 1. RNH–COSCO–R′ (II)

Compd	R	R′	Yield (%)	Mp (°C)
IIa	C_6H_5	C_6H_5	86	95—97
IIb	*m*-$O_2NC_6H_4$	C_6H_5	95	124
IIc	*m*-$O_2NC_6H_4$	CH_3	83	98
IId	C_6H_5	*p*-$O_2NC_6H_4$	76	125—126
IIe	C_6H_5	*p*-ClC_6H_4	81	118—120
IIf	C_6H_5	*p*-$CH_3C_6H_4$	93	109

* For the preparation of I, it is necessary to carry out the reaction in a very concentrated solution.[2]

** Wheeler, who examined the reaction of phenyl isocyanate and thiobenzoic acid, erroneously gave the structure *N*-benzoyl phenyl thiocarbamic acid to the product. (H. L. Wheeler, *J. Amer. Chem. Soc.*, **23**, 444 (1901)).

Table 2. RCONH–COSCO–R′ (III)

Compd	R	R′	Yield (%)	Mp (°C)
IIIa	C_6H_5	C_6H_5	93	75—76
IIIb	C_6H_5	*p*-ClC_6H_4	69	85—86
IIIc	C_6H_5	*p*-$O_2NC_6H_4$	74	82—83
IIId	C_6H_5	CH_3	85	59—61
IIIe	*p*-ClC_6H_4	C_6H_5	91	83—84
IIIf	*p*-$O_2NC_6H_4$	C_6H_5	89	105—106
IIIg	CH_2Cl	C_6H_5	81	107—109
IIIh	$CHCl_2$	C_6H_5	84	105—108
IIIi	CCl_3	C_6H_5	89	112—114

Acyl isocyanates reacted with thiocarboxylic acids also to give acyl acylcarbamoyl sulfides (IIIa)—(IIIi). The results are shown in Table 2. The IR spectra of III showed a broad N–H band at 3100—3400 cm^{-1} and three C=O bands at 1750—1790 cm^{-1}, 1660—1720 cm^{-1} and 1640—1660 cm^{-1}.

Table 3. RCONH–COOCO–R′ (IV)

Compd	R	R′	Yield (%)	Mp (°C)	Dissociation percent (25 °C) (0.5 mol/l)	
					$CHCl_3$	C_6H_6
IVa	C_6H_5	C_6H_5	82	62—65	100	100
IVb	CH_2Cl	C_6H_5	54	101—103	55	100
IVc	$CHCl_2$	C_6H_5	48	102—105	70	100
IVd	CCl_3	C_6H_5	80	70—73	80	100

Satisfactory analytical data (±0.3% for C, H, N, S) were obtained for all new compounds listed in Tables 1, 2, and 3.

The reaction of mono- or dichloroacetyl isocyanate with benzoic acid proceeded similarly to give carbamic benzoic anhydride (IVb) or (IVc). Treatment of benzoyl isocyanate or trichloroacetyl isocyanate with benzoic acid in ether at room temperature gave no precipitate of the product. However, the corresponding anhydride (IVa) or (IVd) was obtained in good yield by evaporation of the solvent. The results are shown in Table 3. The IR spectra of solid IVa—IVd were those of true anhydride (3200—3300 cm^{-1} (N–H), 1800—1820, 1740—1760, 1690—1720 cm^{-1} (C=O)). In $CHCl_3$, however, the spectra apparently consist of both of the absorption of the anhydride and its dissociated components, acyl isocyanate (2250 cm^{-1}

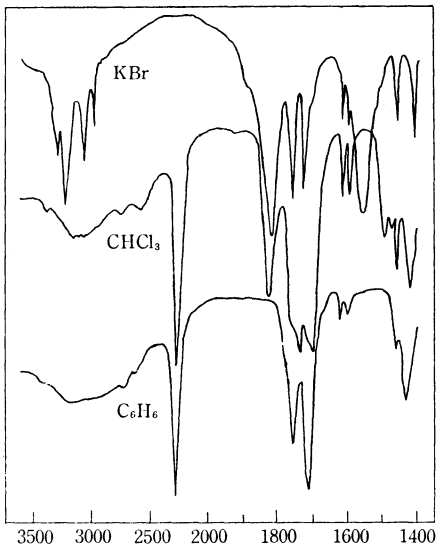

Fig. 1 IR spectra of IVb

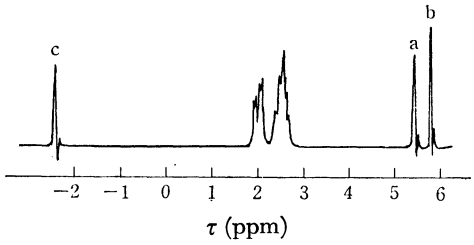

Fig. 2 NMR spectra of IVb ($CDCl_3$)

$ClCH_2CONHCOOCOC_6H_5 \rightleftharpoons ClCH_2CONCO + C_6H_5COOH$

a 5.42 τ b 5.79 τ c −2.24 τ

(NCO), and 1705—1760 cm^{-1} (C=O)) and benzoic acid (1700 cm^{-1} (C=O)). In C_6H_6, the spectra showed only those of dissociation components. The dissociation percentage of IVa—IVd were estimated by means of their NMR absorption. For illustration the spectra of IVb are given in Figs. 1 and 2. From the results shown in Table 3, it is concluded that the compounds IVa—IVd are partly dissociated into their components in solution, the degree of dissociation depending on the structure of the anhydrides and nature of the solvents. In the IR spectra of II and III, a very weak absorption of NCO appeared in $CHCl_3$ or C_6H_6 solution. The amount of dissociated species seemes to be negligible.

$$R\text{-}N{=}C{=}O + R'COOH \longrightarrow R\text{-}\underset{H}{N}\text{-}\underset{O}{C}\text{-}O\text{-}\underset{O}{C}\text{-}R' \quad (I)$$

$$I \longrightarrow RNHCONHR + (R'CO)_2O + CO_2$$

$$I \longrightarrow RNHCOR' + CO_2$$

$$R\text{-}N{=}C{=}O + R'COSH \longrightarrow R\text{-}\underset{H}{N}\text{-}\underset{O}{C}\text{-}S\text{-}\underset{O}{C}\text{-}R' \quad (II)$$

$$R\text{-}CO\text{-}N{=}C{=}O + R'COX \longrightarrow R\text{-}\underset{O}{C}\text{-}\underset{H}{N}\text{-}\underset{O}{C}\text{-}X\text{-}\underset{O}{C}\text{-}R'$$

X=S III
X=O IV

Experimental

Materials. Commercial phenyl isocyanate, methyl isocyanate, thioacetic acid and thiobenzoic acid employed were used. *p*-Nitrothiobenzoic, *p*-chlorothiobenzoic and *p*-thiotoluic acids were prepared according to the method given in literature.[5] *m*-Nitrophenyl isocyanate was prepared from *m*-nitroaniline and phosgene.[6] Acyl isocyanates were prepared from the corresponding amides and oxalyl chloride.[7,8]

Acylcarbamoyl Sulfides (IIa)—(IIf). To a solution of 4.76 g (0.04 mol) of phenyl isocyanate in 50 ml of *n*-hexane was added a solution of 5.52 g (0.04 mol) of thiobenzoic acid in 10 ml *n*-hexane at room temperature with vigorous stirring. The yellow color of thiobenzoic acid disappeared and white precipitates formed. Recrystallization of the product from *n*-hexane yielded 8.2 g (86%) of IIa melting at 95—97 °C with decomposition. The other compounds (IIb)—(IIf) were prepared in a similar way. The results are shown in Table 1.

Acyl Acylcarbamoyl Sulfides (IIIa)—(IIIi), Chloroacetylcarbamoyl Benzoic Anhydride (IVb) and Dichloroacetylcarbamoyl Benzoic Anhydride (IVc). To a solution of 7.36 g (0.05 mol) of benzoyl isocyanate in 80 ml of ether was added a solution of 6.91 g (0.05 mol) of thiobenzoic acid in 50 ml of ether at 0 to −5 °C with stirring. The yellow color of thiobenzoic acid soon disappeared. Colorless needles were formed immediately. Recrystallization of the product from ligroin yielded 13.3 g (93%) of IIIa melting at 75—76 °C with decomposition. The other compounds (IIIb)—(IIIi), (IVb) and (IVc) were prepared in a similar way. The results are shown in Tables 2 and 3.

Benzoylcarbamoyl Benzoic Anhydride (IVa) and Trichloroacetylcarbamoyl Benzoic Anhydride (IVd). To a solution of 7.36 g (0.05 mol) of benzoyl isocyanate in 50 ml of ether was added a solution of 6.10 g (0.05 mol) of benzoic acid in 50 ml of ether at room temperature with stirring. After the addition of benzoic acid, the solvent was immediately evaporated under reduced pressure. White solid thus obtained was washed with ether and dried to yield 11.2 g (82%) of VIa melting at 62—65 °C with decomposition. As the compound was difficult to be recrystallized, it was analyzed without further purification. IVd was prepared in a similar way. The results are shown in Table 3.

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