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The Reaction of Cyclohexyl Isocyanide with Aromatic Diacyl Disulfides

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Synopsis. The reaction of cyclohexyl isocyanide with dibenzoyl disulfide in toluene at a reflux temperature gives cyclohexyl isothiocyanate, together with some unidentified compounds. Based on the substituent effects on the rate, a probable reaction path is proposed. The distinction between two reactions conducted in the absence and in the presence of soft metal salts is also described.

It has been reported previously that diacyl disulfides reacted smoothly with isocyanides in boiling chloroform (61 °C) to give only isothiocyanates in the presence of the salts of such soft metal ions as Tl^I and Pb^{II}, while without added metal salts there was only a low yield of the product.[1] It seemed that it would be of interest to investigate what kind of reaction occurs between isocyanide and dibenzoyl disulfide (DBDS) in the absence of metal salts, but at a higher temperature where a radical fission of the disulfide is still unexpected.[2] In relation to this, Shono *et al.* have reported that cyclohexyl isocyanide reacted with dibenzoyl peroxide at 80—90 °C to afford products derived from benzoyloxyl radical ($PhCO_2\cdot$).[3]

Results and Discussion

When cyclohexyl isocyanide (**1**) was heated with an equimolar amount of DBDS in toluene at a reflux temperature (111 °C) for 24 h, cyclohexyl isothiocyanate (**2**) was formed in a 49% yield; **1** was completely consumed, while 24% of DBDS was recovered (Scheme 1). At the same time we observed the formation of considerable amounts of brown solids which seemed to be a mixture of the reaction products between **1** and the initially formed dibenzoyl sulfide (DBS) (as determined by a study of the NMR, IR, and mass spectra) (Scheme 2); this was confirmed by a separate experiment (See Experimental). Several attempts to separate the solids into pure components have failed, and so each of them remains unidentified. It should be noted that the reaction (2) was accompanied by the formation of only a very low yield (3%) of **2**. The fact that the yield of **2** from DBDS does not exceed 50% in this case may suggest that the latter reaction is faster than the former one. In fact, when two equivalents of **1** were treated with DBDS, the yield of **2** increased to 94% (based on DBDS). Some typical results are shown in Table 1, together with those obtained by the use of *p,p′*-disubstituted DBDS. The addition of several radical scavengers, such as *p*-benzoquinone and *p-t*-butylcatechol, had no effect on the yield of the product, suggesting an ionic nature of the reaction. In accordance with this, the reaction rate increased with an increase in the solvent polarity; the treatment of DBDS with two equivalents of **1** in refluxing acetonitrile (bp 82 °C, $\varepsilon=37.5$) and in refluxing cyclohexane (bp 81 °C, $\varepsilon=2.02$) for 10 h gave **2** in 68% and 4% yields respectively.

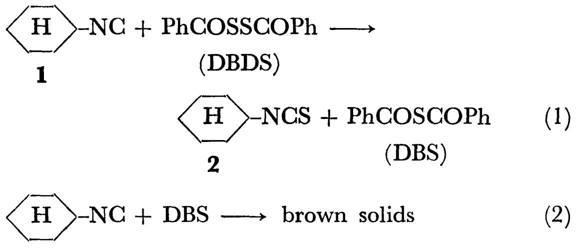

TABLE 1. THE REACTION OF **1** WITH AROMATIC DIACYL DISULFIDES[a)]

R′SSR′ (1 mmol)	**1** (mmol)	Time[b)] (h)	**2** (%)[c)]
R′=p-$NO_2C_6H_4CO$	1	10	47
p-$NO_2C_6H_4CO$	2	10	85
R′=C_6H_5CO	1	24	49
C_6H_5CO	2	24	94
C_6H_5CO[d)]	2	24	92
C_6H_5CO[e)]	2	24	84
R′=p-$MeOC_6H_4CO$	1	32	67
p-$MeOC_6H_4CO$	2	32	93

a) Toluene (10 ml) was used as the solvent; at reflux. b) **1** was completely consumed during this reaction time. c) By GLC (based on disulfide). d) *p*-Benzoquinone (0.5 mmol) was added. e) *p-t*-Butylcatechol (0.5 mmol) was added.

TABLE 2. THE EFFECT OF *p*- AND *p′*-SUBSTITUENTS IN DBDS ON THE RATE OF FORMATION OF **2** FROM **1**[a),b)]

R′SSR′ (1 mmol)	Time (h)	**2** (%)[c)]	Consumed **1** (%)[c)]
R′=p-$NO_2C_6H_4CO$	1	15	56
	3	25	88
	5	38	91
R′=C_6H_5CO	1	6	22
	5	12	39
	10	16	50
R′=p-$MeOC_6H_4CO$	5	9	9
	10	11	16

a) **1** (1 mmol). b) Toluene (10 ml) was used as the solvent; at reflux. c) By GLC (based on disulfide).

In order to ascertain some characteristics of the reaction, the following experiments were also carried out. First, the rates of the formation of **2** from **1** and aromatic diacyl disulfides were roughly examined in refluxing toluene. The results in Table 2 show that rates decrease in the following order; p-NO_2>H>p-

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MeO. Second, the competitive reaction between **1** and phenyl isocyanide with DBDS (1 mmol of each reactant) in refluxing toluene (10 ml) for 6 h afforded **2** (20%) and phenyl isothiocyanate (14%), in addition to unreacted **1** (33%) and phenyl isocyanide (84%), showing that the more nucleophilic **1** reacted faster.

Based on all our results, we propose Scheme 3 for this reaction. It involves the initial nucleophilic attack of isocyanide on the sulfur atom of DBDS. The subsequent removal of benzoyl cation from the transient imidoyl cation affords isothiocyanate. The combination of the benzoyl cation with thiobenzoate anion gives DBS, which then reacts with **1** to give brown solids.

$$\begin{aligned}
&\mathrm{RNC} + \mathrm{ArCOSSCOAr} \xrightarrow{\text{(A)}} \mathrm{R{-}N{=}\overset{+}{C}{-}SCOAr} + \mathrm{ArCOS}^- \\
&\qquad\qquad\qquad\qquad\qquad\qquad \downarrow \\
&\qquad\qquad\qquad\qquad\qquad \mathrm{R{-}NCS} + \mathrm{ArCO}^+ \qquad\qquad (3) \\
&\mathrm{ArCO}^+ + \mathrm{ArCOS}^- \longrightarrow \mathrm{ArCOSCOAr} \xrightarrow[\text{(B)}]{\mathrm{RNC}} \text{brown solids}
\end{aligned}$$

Now we can compare the reactions with or without added soft metal salts. In the absence of metal salts, the rates of (A) and (B) are comparable, or Step (B) may be faster than (A). On the other hand, the presence of soft metal salts considerably accelerates Step (A) by coordination with the sulfur atom, as was clarified in the previous report,[1] and therefore Step (B) becomes comparatively very slow if such acceleration is not significant in it. In fact, when **1** was treated with DBS in the presence of TlSCOPh in chloroform at reflux for 3 h (1 mmol of each reactant), the consumption of **1** was only 25%, much lower than that in the case of DBDS (79%).

Experimental

The IR and NMR spectra analyses and GLC analyses were carried out as has been described in a previous paper.[1] The mass spectra were recorded on a JEOL-01SG spectrometer.

Materials. The isocyanides (RNC: R=c-C_6H_{11}, Ph) and disulfides (R′SSR′: R′=PhCO, p-$MeOC_6H_4CO$, p-$NO_2C_6H_4CO$) were prepared by a method reported previously.[1] Dibenzoyl sulfide was prepared by a modification of the method of Kodomari *et al.*[4] Cyclohexyl isothiocyanate (**2**) prepared previously in our laboratory and commercial phenyl isothiocyanate were used as authentic samples for the GLC analyses. TlSCOPh was prepared by the reported method.[5]

Reaction of 1 with DBDS. A mixture of **1** (0.545 g, 5 mmol) and DBDS (1.37 g, 5 mmol) in toluene (10 ml) was stirred at reflux for 24 h. After it had been cooled, the GLC analysis of toluene solution revealed the presence of 2.45 mmol of **2** (49% yield: based on DBDS). The evaporation of the solvent, followed by the addition of ether to the residue, gave 0.33 g (24%) of DBDS as an insoluble precipitate. By removing the ether from the above ether washing and by adding hexane to the residue, brown solids (1.12 g, mp 186—192 °C) were separated out as precipitates. The hexane washing contained **2**. The NMR spectrum of this solid revealed the presence of cyclohexyl and phenyl groups, and the IR spectrum had strong absorptions at 1660 and 1630 cm^{-1}, these spectra being the same as those of the solids obtained from **1** and DBS (in toluene, 111 °C, 14 h). The mass spectrum showed peaks at m/e 351, 460, and 569 which may correspond to the three adducts of DBS-**1**, 1 : 1, 1 : 2, and 1 : 3 respectively. None of the compounds could be separated by column chromatography or preparative TLC on activated alumina.

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