3. The formation of the cyanohydrin cation-radical and its isomerization with 1,5- and 1,6-migration of the hydrogen atom are the most probable initial stages of the reaction of peroxydisulfates with alkanal cyanohydrins.

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CONDENSATION OF THIOAMIDES AND THIOUREAS IN THE PRESENCE OF RADICAL-FORMING COMPOUNDS

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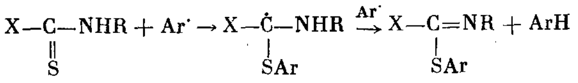
547.496.3

We have previously shown that in many instances compounds which are able to generate aryl radicals [phenylazotriphenylmethane (PAT), N-nitrosoacetanilide (NAA), and aryldiazonium salts in the presence of $CuCl_2$] arylate thioamides and thioureas at the sulfur atom to give the corresponding S-arylisothioamides and S-arylisothiuronium compounds [1].



$$X-\underset{S}{\underset{\|}{C}}-NHR + Ar^{\cdot} \rightarrow X-\underset{SAr}{\underset{|}{\dot{C}}}-NHR \xrightarrow{Ar^{\cdot}} X-\underset{SAr}{\underset{|}{C}}=NR + ArH \tag{1}$$

X = Ar, alkyl, , NH_2, NHR.

We here describe the reaction of thioamides and thioureas with radical-forming compounds to give imidosulfides (I), S-cyanoisopropylisothiobenzanilides (II), and heterocyclic products of the thiourea condensation (Hector bases).

Reactions of Thioamides with Azobisisobutyronitrile (AIBN). There are literature reports of the reaction of α-cyanoisopropyl radicals, formed by the thermolysis of AIBN, with organosulfur compounds. Thus, it has been shown [2] that these radicals add to the sulfur atom in diaryl disulfides

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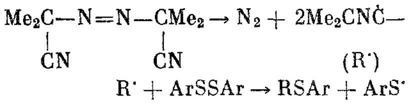
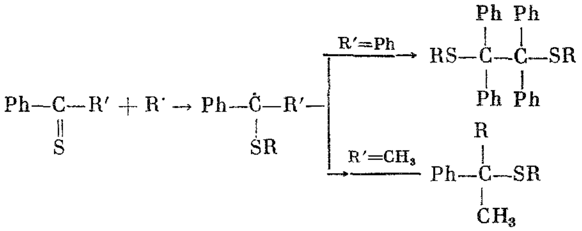


$$\underset{\mathrm{CN}}{\mathrm{Me_2C}}\mathrm{{-}N{=}N{-}}\underset{\mathrm{CN}}{\mathrm{CMe_2}} \rightarrow \mathrm{N_2} + \underset{(\mathrm{R^\cdot})}{\mathrm{2Me_2CN\dot{C}{-}}}$$

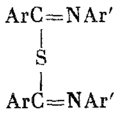
$$\mathrm{R^\cdot + ArSSAr \rightarrow RSAr + ArS^\cdot}$$

Here and subsequently, $R = CMe_2CN$.

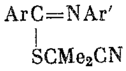
Is is also known [3] that in the reaction of AIBN with thioketones, the cyanoisopropyl radicals add to sulfur, the adduct radicals formed then dimerizing or recombining with a second cyanoisopropyl radical



Cyanoisopropyl radicals react similarly with thiobenzanilides $\mathrm{Ar}\underset{\overset{\|}{\mathrm{S}}}{\mathrm{C}}\mathrm{{-}NHAr'}$, but less readily than with phenyl radicals, the extent of reaction of thioamides being no greater than 5-15%. Furthermore, depending on the nature of Ar and Ar' in the original thioamide, the reaction products are the bisimidosulfides (I) or the S-2-cyanopropyl esters of the corresponding N-arylimidothiobenzoic acids (II):



(I)



(II)

$$\mathrm{ArC{=}NAr'}{-}\mathrm{S}{-}\mathrm{ArC{=}NAr'}\ \text{(I)} \qquad \mathrm{ArC(SCMe_2CN){=}NAr'}\ \text{(II)}$$

As will be seen from Table 1 (Nos. 1 and 2), in the case of thiobenzanilide and its p-methoxy derivative the reaction products are the bisimidosulfides (I), which do not contain the cyanoisopropyl group. The structures of these compounds were confirmed by comparing their melting points with the literature values [4] and by mass spectrometry (in addition to the molecular ion peaks, the mass spectra contained strong peaks corresponding to the fragments $M^+ - ArCNAr'$ and $M^+ - ArCSNAr'$).

It may be assumed that in these cases an adduct radical of type A is formed as an intermediate, and this then reacts with a second molecule of the thioamide. The resulting radical B is stabilized by fragmentation and disproportionation to give the end products. (See Scheme 1.)

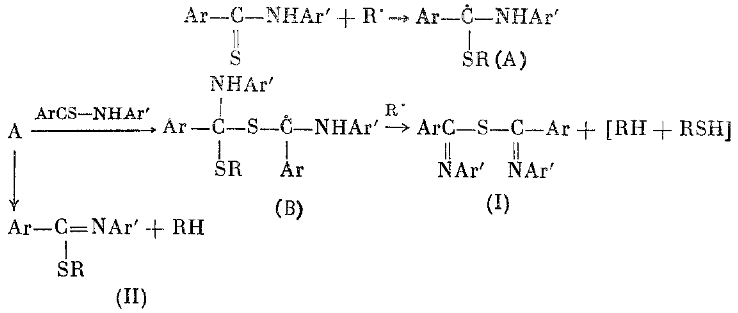
This reaction pathway differs from radical arylation [reaction (1)], apparently in that the cyanoisopropyl radicals, being much less effective hydrogen abstractors than phenyl radicals [5], are not capable of converting radical A into the isothioamide (II) to any significant extent. This obviously favors the competing step, namely, growth of the radical A.

In the case of the dimethylamino-substituted thiobenzanilide (Table 1, No. 3), the reaction affords an even lower yield of the imidosulfide (I), and the latter could not be ob-

TABLE 1. Reaction of Thiobenzanilides $\mathrm{Ar}\underset{\overset{\|}{\mathrm{S}}}{\mathrm{C}}\mathrm{{-}NHAr'}$ with AIBN (toluene, 110°C), 3 h)

No.	Ar	Ar'	Product	Yield, %
1	Ph	Ph	(I)	13
2	$MeOC_6H_4$	Ph	(I) (II)	7 <2
3	Ph	$C_6H_4NMe_2$-*p*	(I)	<2
4	*p*-$NO_2C_6H_4$	Ph	(II)	<2

Scheme 1

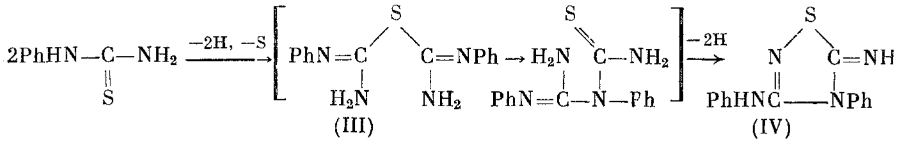


tained in the pure state, but its formation was shown by the molecular ion peaks and its fragments in the mass spectrum.

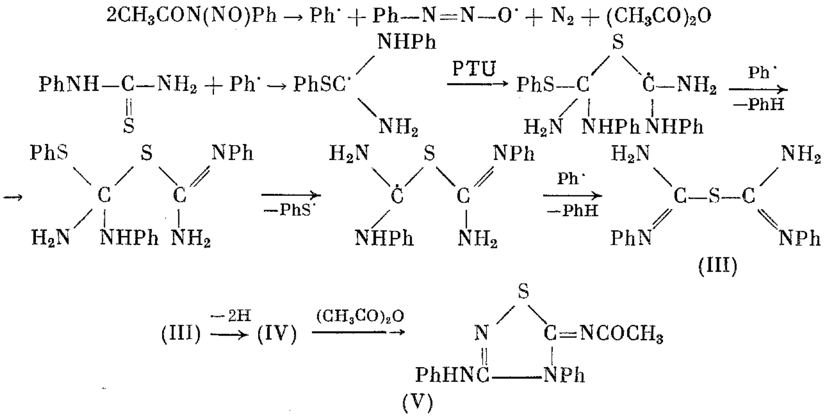
The participation of cyanoisopropyl radicals in this reaction was confirmed by the fact that in the absence of AIBN, or when it was replaced by other nitriles incapable of forming radicals, such as acetonitrile, the thioamides totally failed to react. Yet another argument in favor of the intermediate formation of adduct-radicals of type A as the fact that on reaction of p-methoxy- and p-nitrothiobenzanilides with AIBN (Nos. 2 and 4), mass spectrometry of the reaction mixtures showed the presence of the isothioamides (II), although the yields were, as would be expected, extremely small.

Reaction of N-Phenylthiourea (PTU) with NAA. In reactions of thiocarbonyl compounds with NAA, the latter is known to function simultaneously as an arylating agent and oxidant, oxidizing, for example, 2-thiopyridone to di-2-pyridyl disulfide [6]. We have now found that reaction of NAA with PTU in acetone affords the N-acyl derivative (V) of the Hector base (IV). This was confirmed by the direct synthesis of (V) by oxidizing PTU with hydrogen peroxide, followed by acylation with acetic anhydride as described in [7].

It has been assumed on several occasions [8-10] that the oxidative conversion of PTU into Hector's base proceeds via the intermediate formation of bis-(N-phenylformamidine) sulfide (III)

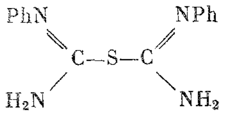


The possibility cannot be excluded, however, that the same sulfide (III) could be formed by radical arylation of PTU followed by growth of the intermediate adduct-radical, as follows:



Oxidation of the sulfide (III) gives the Hector base (IV). This mechanism is analogous to that described previously for the formation of bisimidosulfides (I) in the reaction of thioamides with AIBN, and with that put forward by us to explain the formation of bisformamidine sulfide in the reaction of thiourea with PTU [1]. Further support for this mechanism is the fact that in this reaction the Hector base is formed as the acyl derivative (V). It appears that the acylation is effected by acetic anhydride formed in the radical decomposition of NAA [11].

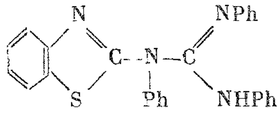
The course of the reaction of N,N'-diphenylthiourea (DPTU) with NAA is solvent-dependent. In a neutral medium (acetone), S,N,N'-triphenylisothiuronium is formed, isolated as the picrate [1], whereas in glacial acetic acid another product is formed to which we have previously [12] assigned the structure (VI), by analogy with the reaction of thiourea with PAT:



(VI)

We have now found that this compound is identical with the product obtained by the oxidation of DPTU with hydrogen peroxide [13], as shown by the absence of a depression in the melting point of the mixed samples, and the identity of their IR spectra.

It is noteworthy that the structures of heterocyclic Hector bases and related compounds have been the subject of research over several decades, which still continue (see, for example, [14] and review [8]). Specifically, according to the latest findings [14], the oxidation product of PTU is assigned the structure (IV), whereas the product of the oxidation of DPTU in acid solution is regarded as being not the corresponding Hector base, but rather its isomer, the Hugershoff base:



(VII)

For the purpose of the present studies, however, it is important to note that in its reactions with thioureas (and with thioamides), NAA functions simultaneously as a source of aryl radicals, and an oxidant.

To summarize the findings obtained here and in [1], it can be concluded that in all these reactions of thiocarbonyl compounds with radicals, the latter add to sulfur to form adduct-radicals. The variety of end products obtained is due to the differing routes of stabilization and subsequent reactions of the adduct-radicals.

EXPERIMENTAL

All the reactions were carried out under argon. Mass spectra were obtained on an MS-30 mass spectrometer, and IR spectra on a UR-20 spectrometer, in KBr disks.

Reaction of Thiobenzanilide with AIBN. A solution of 3.9 g (18 mmole) of thiobenzanilide and 3 g (18 mmole) of AIBN in 100 ml of toluene was boiled for 3 h, and the solvent removed in vacuo, and the residue dissolved in 75 ml of alcohol and kept overnight at 0°C. The yellow crystals which separated were filtered off and recrystallized from benzene to give 0.4 g (13%) of bis-(α-phenyliminobenzyl) sulfide, mp 210-212°C (cf. [4]). Found, %: C 79.11; H 5.14; N 7.18; S 8.20. $C_{26}H_{20}N_2S$. Calculated, %: C 79.56; H 5.14; N 7.14; S 8.17. Mass spectrum, m/z (rel. intensity, %): 392 (2) M^+, 212 (5) $[Ph-Cs = NPh]^+$, 180 (100) $[PhC\equiv N-Ph]^+$, 121 (29) $[Ph-CS]^+$, 103 (35) $[PhCN]^+$. From the mother liquors there was obtained 3.1 g (80%) of the thiobenzanilide starting material.

The reactions of thioanilides with AIBN were carried out similarly, using the same molar ratios of reactants.

Reaction of p-Methoxybenzanilide with AIBN. The residue obtained following removal of the solvent was chromatographed on a silica column, eluent benzene:alcohol (10:1). Yield 0.3 g (7%) of bis-(α-phenylimino-p-methoxybenzyl) sulfide, yellow crystals, mp 157°C (from alcohol). Found, %: C 73.72; H 5.96; N 5.88; S 7.06. $C_{28}H_{24}N_2O_2S$. Calculated, %: C 74.32; H 5.34; N 6.19; S 7.07. Mass spectrum, m/z (rel. intensities, %): 452 (12) M^+, 242 (13) $[CH_3OC_6H_4CS = NPh]^+$, 210 (100) $[CH_3OC_6H_4-C = NPh]^+$. In addition, 4 g (87%) of the original thioamide and 0.2 g of a mixture of tetramethylsuccinic dinitrile (TSD), a breakdown product of AIBN, and S-(2-cyanopropyl) N-phenylimino-p-methoxybenzoate, identified in the mass spectrum by peaks with m/z 310 M^+ and 210 $[M-S(CN)Me_2]^+$.

Reaction of p-Nitrobenzanilide with AIBN. Conversion of thioamide, 8% S-2-cyanopropyl N-phenylimino-p-nitrobenzoate was isolated (in admixture with TSD), identified in the mass spectrum by the peaks with m/z 325 M^+, and 225 $[M-S(CN)Me_2]^+$.

Reaction of Thiobenz-p-dimethylaminoanilide with AIBN. Conversion of thioamide ∼10%. Bis(α-p-dimethylaminophenylaminobenzyl) sulfide (in admixture with TSD), was isolated and identified in the mass spectrum with the peaks m/z 478 M^+, 255 $[M-PhCNC_6H_4-NMe_2]^+$, and 223 $[M-Ph-CS-C_6H_4NMe_2]^+$.

Reaction of N-Phenylthiourea (PTU) with NAA in Acetone. A solution of 1.52 g (10 mmole) of PTU and 1.7 g (10 mmole) of NAA in 50 ml of acetone was stirred for 4 h at 20°C, and kept overnight. Chromatography on a silica column (eluent hexane:acetone, 1:1) gave 0.3 g (20%) of 5-N-acetylimino-4-phenyl-3-phenylamino-4H-1,2,4-thiadiazoline (V), mp 237°C (cf. [7]). The melting point of a mixed sample with material obtained by direct synthesis [7] showed no depression. The IR spectra of the two samples were identical. Found, %: C 61.47; H 4.45; N 18.33; S 10.73. $C_{16}H_{14}N_4OS$. Calculated, %: C 61.93; H 4.51; N 18.06; S 10.32. Mass spectrum, m/z: 310 (80) M^+, 43 (100) $[MeCO]^+$. Picrate, mp 213-214°C. Found, %: C 48.97; H 3.39; N 17.34; S 5.25. $C_{22}H_{17}N_7O_8S$. Calculated, %: C 48.97; H 3.15; N 18.10; S 5.93. There was also isolated 0.75 g (50%) of the original PTU.

Reaction of N,N'-Diphenylthiourea (DPTU) with NAA in Glacial Acetic Acid. The reaction was carried out as in the preceding example with a mixture of 5.28 g (30 mmole) of NAA and 7 g (30 mmole) of DPTU in 70 ml of glacial acetic acid. The reaction was accompanied by the evolution of brownish gases. A precipitate of sulfur first separated, then redissolved. Chromatography on a silica column (eluent chloroform:alcohol, 1:1) afforded 2.2 g (70%) of 2-(triphenylguanidino)benzthiazole (VII), mp 137-138°C [8]. The melting point of a sample mixed with material obtained by direct synthesis [13] showed no depression. The IR spectra were identical. Found, %: C 73.07; H 4.36; N 13.19; S 8.04. $C_{26}H_{22}N_4S$. Calculated, %: C 73.84; H 4.76; N 13.33; S 7.80. Addition of alcoholic picric acid to (V) gave the picrate, mp 158-160°C. Found, %: C 58.82; H 3.27; N 15.82; S 4.93. $C_{32}H_{25}N_7O_7$. Calculated, %: C 59.12; H 3.69; N 15.04; S 4.92.

CONCLUSIONS

1. Reaction of azobisisobutyronitrile with thiobenzanilides results in addition of 2-cyanoisopropyl radicals to the sulfur atom, and subsequent reactions of the adduct-radical result in the formation of the corresponding imidosulfides and/or S-cyanoisopropylisothiobenzanilides.

2. In the reactions of N-phenyl- and N,N'-diphenylthiourea with N-nitrosoacetanilide, the latter functions simultaneously as a phenylating agent and oxidant, to give heterocyclic condensation products of thiourea (Hector bases).

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