Acetylenic Ketones. Part III (1). Reaction of Acetylenic Ketones with Nucleophilic Sulfur Compounds

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Received January 22, 1976

Aroylphenylacetylenes reacted with ammonium dithiocarbamate and ammonium hydrogen sulfide in 60% dioxane-water mixture at 15° to give mainly a mixture of the corresponding β-hydroxy-α-thiobenzoylstyrene derivatives (III) and (E,Z)-β,β′-di(α-aroylstyryl) sulfides (IV), whereas with sodium xanthate and sodium sulfide they gave only (III). However, when benzoyl-(Ia) or *p*-chlorobenzoyl-(Id)phenylacetylenes was refluxed with ammonium dithiocarbamate in ethyl alcohol, it gave a mixture of (IIIa or d) and the (E,E)-β,β′-di(α-aroylstyryl) sulfide (VIa or d).

β-Hydroxy-α-thiobenzoylstyrene derivatives (III), (E,Z)-(IV) and (E,E)-(VI)-β,β′-di(α-aroylstyryl) sulfides reacted with hydrazine hydrate and phenylhydrazine to give 3(5)-aryl-5(3)-phenyl-(IX)- and 5-aryl-1,3-diphenyl-(X)pyrazoles, respectively. The former compounds (III) reacted with guanidine and ethyl hydrazinecarboxylate to give the corresponding aminopyrimidines (XIII) and acetophenone-*N*-ethoxycarbonyl hydrazones (XI), respectively.

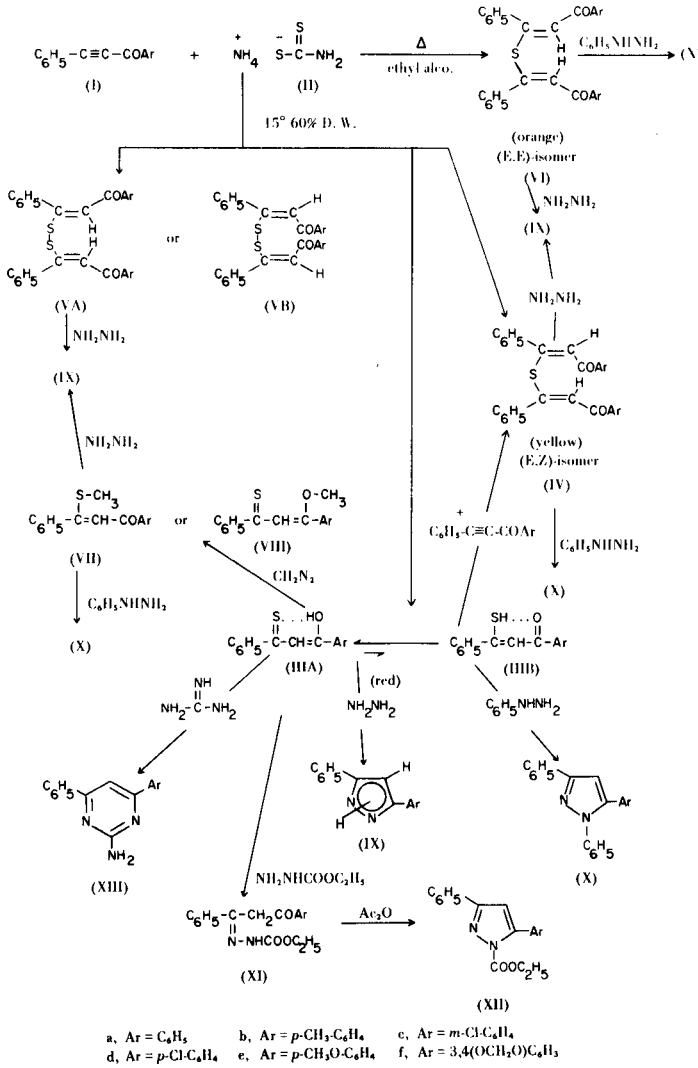
J. Heterocyclic Chem., 13, 691 (1976).

The present work deals with the exploitation of the reaction of aroylphenylacetylenes with nucleophilic sulfur compounds, such as ammonium dithiocarbamate, ammonium hydrogen sulfide, sodium sulfide and sodium xanthate in 60% dioxane-water mixture. Thus, the reaction of benzoyl-(Ia), *m*-chlorobenzoyl-(Ic), *p*-methoxybenzoyl-(Ie) and 3,4-methylenedioxybenzoyl-(If)-phenylacetylenes (1 mole) with ammonium dithiocarbamate (II) in 60% dioxane-water mixture at 15° gave a mixture of the corresponding β-hydroxy-α-thiobenzoylphenylstyrene derivatives (III) and (E,Z)-β,β′-di(α-aroylstyryl) sulfide (IV), in the ratio 1:2, respectively (*cf.* Scheme 1), whereas *p*-toluyl-(Ib)- and *p*-chlorobenzoyl-(Id)-phenylacetylenes gave in addition to the styrene derivatives (IIIb and d) and the styryl sulfides (IVb and d) a small amount of the corresponding (E,E)-β,β′-di(α-aroylstyryl) disulfides (Vb and d), respectively. However, when benzoyl-(Ia)- or *p*-chlorobenzoyl-(Id)-phenylacetylenes was refluxed with the above reagent in ethyl alcohol, the product was a mixture of the β-hydroxy-α-thiobenzoylstyrene derivative (IIIa or IIId) and the (E,E)-β,β′-di(α-aroylstyryl) sulfide (VIa or VId), respectively. The latter compounds were also obtained by refluxing (E,Z)-β,β′-di(α-benzoylstyryl) (IVa) or (E,Z)-β,β′-di[α-(*p*-chlorobenzoyl)styryl] (IVd) sulfide, respectively, with ethyl alcohol. The remaining (E,Z)-isomers (IVb,c,e and f) failed to isomerize to the (E,E)-isomers (VIb,c,e and f) even under more drastic conditions (heating with toluene or with aqueous hydrochloric acid for 13 hours) (4).

Establishment of the Structure and the Configuration of the Products.

Conflicting conclusions have been reported in the literature concerning the structure of monothio-β-dicarbonyl compounds. Some workers suggested that they exist in the chelated thione-enol form (5) (*cf.* IIIA), whereas others favored their existence as chelated enethiols (6) (*cf.* IIIB). However, the following chemical reactions indicated that the compounds obtained in the present investigation (IIIa-f) exist as an enethiol or as an equilibrium mixture of enol-enethiol tautomers: (i) Reaction of IIId or IIIe with diazomethane in ether gave a methyl derivative (VIId or e) (6a), which reacted with hydrazine hydrate and phenylhydrazine to give the corresponding 5(3)aryl-3(5)phenylpyrazole (IXd or e) and 5-aryl-1,3-diphenylpyrazole (Xd or e), respectively. This pointed out that these compounds are either the *S*-methyl (VII) or the *O*-methyl (VIII) derivatives. However, from the presence of a strong band in their ir spectra at 1633 cm^{-1} and 1628 cm^{-1} ($\nu_{C=O}$) (7a) and a medium band at 630 and 622 cm^{-1} (ν_{C-S}) (7b), respectively, it was concluded that they have structure (VII). This conclusion was sub-

Scheme I



a, Ar = C_6H_5 b, Ar = p-CH_3-C_6H_4 c, Ar = m-Cl-C_6H_4
d, Ar = p-Cl-C_6H_4 e, Ar = p-CH_3O-C_6H_4 f, Ar = 3,4(OCH_2O)C_6H_3

spectra of (VIId and e) show a singlet at δ 1.98 and δ 1.93 (SCH_3), respectively, whereas the mass spectrum of (VIIe) shows the following m/e peaks: 284 (14.7%) $[M]^+$; 237 (5.9%) $[M\text{-}SCH_3]^+$ and 47 (5.9%) $[SCH_3]^+$. The electronic spectra of compounds VIId and VIIe show two bands at 340 nm (ε = 20,170) and 267 (ε = 13,380); and at 339 nm (ε = 23,750) and 277 nm (ε = 7,790), respectively, which reflects their identity, (ii) (IIIa-f) reacted with the corresponding aroylphenylacetylene (Ia-f) to give (E,Z)-β,β′-di(α-aroylstyryl) sulfides (IVa-f) (see later), a reaction characteristic of thiols (8) and is not given by dibenzoyl methane, (iii) oxidation of IIIb and IIId with sodium nitrite and sodium hydrogen sulfate (9) gave the corresponding disulfides (Vd and d), respectively), (iv) ozonolysis of IIId and IIIe gave p-chlorobenzoic and p-methoxybenzoic acids, respectively, together with a small amount of benzoic acid. This reaction indicated that tautomer IIIA is present as the predominant component of the equilibrium mixture.

Spectral data also indicated the presence of these compounds as a mixture of the two tautomers IIIA and IIIB, in which the former is predominant. Thus, their nmr spectra (*cf.* Table I) show a sharp signal at δ 14.0-16.0, which disappeared when the solution is shaken with deuterium oxide; a phenomena characteristic of chelated OH protons (5a,10a). Chelated SH shows a signal at δ 7 (10b,c). Their ir spectra show bands characteristic of $\nu C{=}O$ and $\nu C\text{-}S$ (*cf.* Table I). The electronic spectra of these compounds are shown in Table I and reflect their identity. The bands are intence and blue shifted in a less polar solvent (*cf.* Table I) (π-π^* transition bands); Chaston and Livingstone (11) did not report the band at 263 nm for compound IIIa. The mass spectra of IIIb-e also reveal the presence of both enol and enethiol tautomers, since they show peaks corresponding to $[M]^+$, $[M\text{-}1]^+$, $[ArCO]^+$, $[M\text{-}OH]^+$, $[C_6H_5CS]^+$ and $[M\text{-}SH]^+$. Chaston *et al.* (6a), however, reported that the mass spectrum of IIIa reveal its existence as an enethiol IIIB only.

Structure and Configuration of (E,Z)-β,β′-Di(α-aroylstyryl)-Sulfides (IVa-g).

The structure of these compounds was inferred from the following reactions. (i) The same compounds were obtained by allowing the styrene derivatives (1 mole) (IIIa-f) to react with the corresponding acetylenic ketones (1 mole) (Ia-f, respectively) in 60% dioxane-water mixture containing ammonium hydroxide (1 mole). This reaction indicates that these compounds react as enethiol rather than as enol nucleophiles, which is expected since thiols are more nucleophilic than enols (12), (ii) ozonolysis of (IVd) and (IVe) gave p-chlorobenzoic and p-methoxybenzoic acids, respectively, together with benzoic and formic acids. The formation of benzoic and formic acids can be attributed either to the oxidation of the initially formed arylglyoxal by the liberated hydrogen peroxide or to a zwitterion rearrangement mechanism (13). These reactions do not throw light on the configuration of these compounds. However, spectroscopic studies substantiated the assigned structure and revealed the (E,Z)-configuration of these compounds. Thus, their ir spectra (*cf.* Table II) show two bands characteristic of $\nu C{=}O$, which indicates that they contain two CO groups in different environments. This condition is satisfied by the unsymmetrical (E,Z)-configuration (IV). The nmr spectra of IVa and IVb show two signals attributed to the olefinic protons, whereas that of the latter shows two signals for the methyl groups (*cf.* Table II). The fact that the two olefinic protons and the two methyl groups have different chemical shifts is a strong evidence for the (E,Z)-configuration (14). The mass spectrum of IVa also lends further

Table I

Physical Data for Compounds (IIIa-f)

Compound	Nmr			Electronic Spectra (Ethanol)		Infrared Spectra (Potassium bromide)	
	δ	Assignments (No. of protons)	Solvent	λ max (nm)	ε	cm^{-1}	ν
IIIa	15.3 (s)	(1) -O-*H*...S	Deuterio-	506-490 (sh)	235	1590 (s)	C=O
	7.2-8.27 (m)	(11) Ar*H* + C:C*H*	chloroform	410	16,070	1565 (s)	C=C
				329	10,640	638 (w)	C-S (7a)
				263	7,660		
IIIb	15.43 (s)	(1) -O-*H*...S	Deuterio-	516-494 (sh)	230	1606 (s)	C=O
	7.20-8 07 (m)	(10) Ar*H* + C:C*H*	chloroform	414	17,500	1580 (s) }	C=C
	2.20 (s)	(3) Ar-CH_3		327	12,540	1550 (s) }	
				270	8,420	635 (w)	C-S
	16.0 (s)	(1) -O*H*...S	Carbon				
	7.07-8.0 (m)	(10) Ar*H* + C:C*H*	tetrachloride				
	2.33 (s)	(3) Ar-CH_3					
IIIc	14.83 (s)	(1) -O-*H*...S	Deuterio-	510-496 (sh)	215	1584 (s)	C=O
	7.33-8.22 (m)	(9) Ar*H*	chloroform	408	18,550	1560 (s)	C=C
	7.27 (s)	(1) C:C*H*		333	15,110	635 (w)	C-S
				261	10,780		
IIId	14.83 (s)	(1) -O-*H*...S	Deuterio-	508-490 (sh)	225	1595 (s)	C=O
	7.33-8.07 (m)	(9) Ar*H*	chloroform	412	20,420	1555 (s)	C=C
	7.3 (s)	(1) C:C*H*		332	14,100	637 (w)	C-S
				269	11,140		
IIIe (a)	16.3 (s)	(1) -O-*H*...S	Deuterio-	426	26,320	1605 (s)	C=O
	6.93-7.63 (m)	(10) Ar*H* + C:C*H*	chloroform	329	11,640	1582 (s) }	C=C
	4.07 (s)	(3) Ar-OCH_3		308-293 (sh)	9,290	1555 (w) }	
				255	6,500	633 (w)	C-S
	16.17 (s)	(1) -O-*H*...S	Carbon	421	22,220 }		
	6.8-8.13 (m)	(10) Ar*H* + C:C*H*	tetrachloride	326	10,100 }	in cyclohexane	
	3.8 (s)	(3) Ar-OCH_3		305-295 (sh)	7,300 }		
IIIf (a)	15.8 (s)	(1) -O-*H*...S	Carbon	434	23,210	1565 (s)	C=O
	6.67-7.87 (m)	(9) Ar*H* + C:C*H*	tetrachloride	356-342 (sh)	10,330	1555 (s)	C=C
	5.93 (s)	(2) O-CH_2-O		323	12,690	630 (w)	C-S
				258	9,430		

(a) The n- π^* band is submerged by the red-shifted π-π^* transition band.

support for the assigned configuration, since it shows peaks at m/e 446 (0.7%) $[M]^+$, 445 (2.8%) $[M-1]^+$. The latter fragment ion is expected to be easily formed if the compound has the (E,Z)-configuration (IV). Other fragment ions are at m/e 240 (5.7%) $[C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH=\overset{HS}{\overset{|}{C}}\text{-}C_6H_5]^+$ (cleavage at the C-S bond with rearrangement and elimination of a benzoylphenylacetylene), a peak at 121 (4.2%) $[C_6H_5CS]^+$ (fragmentation of the previous ion); and a peak at 105 (100%) $[C_6H_5CO]^+$, which supports the presence of a benzoyl group. The mass spectra of IVb and IVd show identical peaks. Their electronic spectra (*cf.* Table II) are identical, which reflects their identity in structure. The high intensity of the absorption bands indicates that they are due to π-π^* transition.

Structure and Configuration of (E,E)-β,β′-Di(α-aroylstyryl) Disulfides (Vb and d).

The strucutre of these two compounds was primarily based on analytical data, but received further support from the following experimental data. (i) (IVd) gave β-hydroxy-α-thiobenzoyl-*p*-chlorostyrene (IIId), when reduced with tin and hydrochloric acid, (ii) both compounds could be prepared from the corresponding thiobenzoylstyrene derivatives (IIIb and d) by oxidation with sodium nitrite and sodium hydrogen sulfate (9) or sodium nitrite in acetic acid.

The configuration of these compounds, however, was established spectroscopically. Thus, their infrared spectra show a strong band at 1632 and 1640 cm^{-1} (νC=O), respectively. The appearance of one band for (CO) indi-

Table II

Physical Data for Compounds (IVa-g)

Compound	Nmr (Deuteriochloroform)		Electronic Spectra (Ethanol)		Infrared Spectra (Potassium bromide)	
	δ	Assignments (No. of protons)	λ max (nm)	ε	cm^{-1}	ν
IVa	7.0-8.2 (m)	(20) Ar*H*	345	19,000	1650 (s)	C=O
	6.93 (s)	(1) C:C*H*	260	26,260	1600 (sh)	C=C
	6.90 (s)	(1) C:C*H*			1557 (s)	
					640 (w)	C-S
IVb	7.0-8.0 (m)	(18) Ar*H*	347	17,800	1666 (s)	C=O
	6.9 (s)	(1) C:C*H*	273	23,825	1640 (s)	
	6.85 (s)	(1) C:C*H*			1610 (s)	C=C
	2.45 (s)	(3) Ar-C*H*$_3$			1551 (s)	
	2.33 (s)	(3) Ar-C*H*$_3$			645 (w)	C-S
IVc	6.77-8.02 (m)	(18) Ar*H*	348	18.050	1680 (s)	C=O
	7.30 (s)	(1) C:C*H*	259	23,200	1640 (s)	
	7.25 (s)	(1) C:C*H*			1590 (s)	C=C
					1540 (m)	
					645 (w)	C-S
IVd	6.87-8.0 (m)	(18) Ar*H*	348	20,740	1660 (s)	C=O
	7.57 (s)	(1) C:C*H*	271	30,680	1640 (s)	
	7.53 (s)	(1) C:C*H*			1590 (s)	C=C
					1550 (m)	
IVe	6.67-8.1 (m)	(18) Ar*H*	347	25,460	1664 (s)	C=O
	6.87 (s)	(1) C:C*H*	298	24,780	1634 (s)	
	6.82 (s)	(1) C:C*H*	237	24,600	1603 (s)	C=C
	3.87 (s)	(3) Ar-OC*H*$_3$			1540 (m)	
	3.78 (s)	(3) Ar-OC*H*$_3$				
IVf	6.63-7.77 (m)	(16) Ar*H*	350	24,050	1650 (s)	C=O
	6.87 (s)	(1) C:C*H*	280	20,490	1638 (s)	
	6.83 (s)	(1) C:C*H*	237	32,760	1605 (s)	C=C
	6.08 (s)	(2) O-C*H*$_2$-O			1550 (m)	
	5.97 (s)	(2) O-C*H*$_2$-O			650 (w)	C-S
IVg			347	23,550	1664 (s)	C=O
			277	27,720	1640 (s)	
			226	26,500	1602 (s)	C=C
					1550 (s)	
					640 (w)	C-S

cates that they are stereochemically identical, *i.e.*, the compounds Vb and d should have either the (E,E)-(VA) or the (Z,Z)-configuration (VB). The $\nu_{C\text{-}S}$ for both compounds appears as a weak band at 645 and 635 cm^{-1}, respectively (7b). The nmr spectrum of Vd also supports the symmetrical configuration of these compounds. Thus, the signal for the two olefinic protons appears as a singlet at δ 7.0 which indicates that they are magnetically equivalent. However, the mass spectrum of Vd favours the (E,E)-configuration (VA) rather than the (Z,Z)-configuration (VB), since it shows a triplet at m/e 512 (40.3%), 514 (29%) and 516 (6%) corresponding to $[M\text{-}H_2S]^+$. The loss of H_2S to give this fragment ion supports the (E,E)-configuration (VA). This fragmentation is known to be characteristic of disulfides (6c). The mass spectrum also shows a base peak as a doublet at m/e 139 (100%) and 141 (41.4%), which corresponds to $[p\text{-Cl-}C_6H_4CO]^+$, and an abundant peak as a doublet at m/e 273 (98.5%) and 275 (53.5%), corresponding to the fragment ion resulting from the cleavage of the S-S bond. The electronic spectra of Vb and Vd are identical and show two maxima at 346 nm (ε = 16,870), 267 nm (ε = 22,190), and 335 nm (ε = 21,900), 274 nm (ε = 22,450), respectively.

Structure and Configuration of (E,E)-β,β′-Di(α-aroylstyryl) Sulfides (VIa and d) (orange).

Basyouni *et al.*, (4) obtained the orange sulfides (VIa,d and e) together with the yellow sulfides (IVa,d and e) when benzoyl-(Ia), *p*-chlorobenzoyl-(Id) and *p*-methoxybenzoyl-(Ie)-phenylacetylenes were allowed to react at room temperature with a variety of thiocarbonyl compounds in methyl alcohol, but they assigned to the former compounds the (Z,Z)-configuration. In the present investigation the orange sulfides (VIa and d) were obtained together with

the thio-compounds (IIIa and d), when the corresponding acetylenic ketones were refluxed with ammonium dithiocarbamate (II) in ethyl alcohol (30 minutes). They were also obtained from the yellow sulfides (IVa and d) by refluxing with ethyl alcohol (10 hours). The yellow sulfides (IVb and e) failed to undergo this transformation even under more drastic conditions (reflux with ethyl alcohol, toluene or dilute hydrochloric acid for 13 hours [*cf.* Basyouni, *et al.*, (4)].

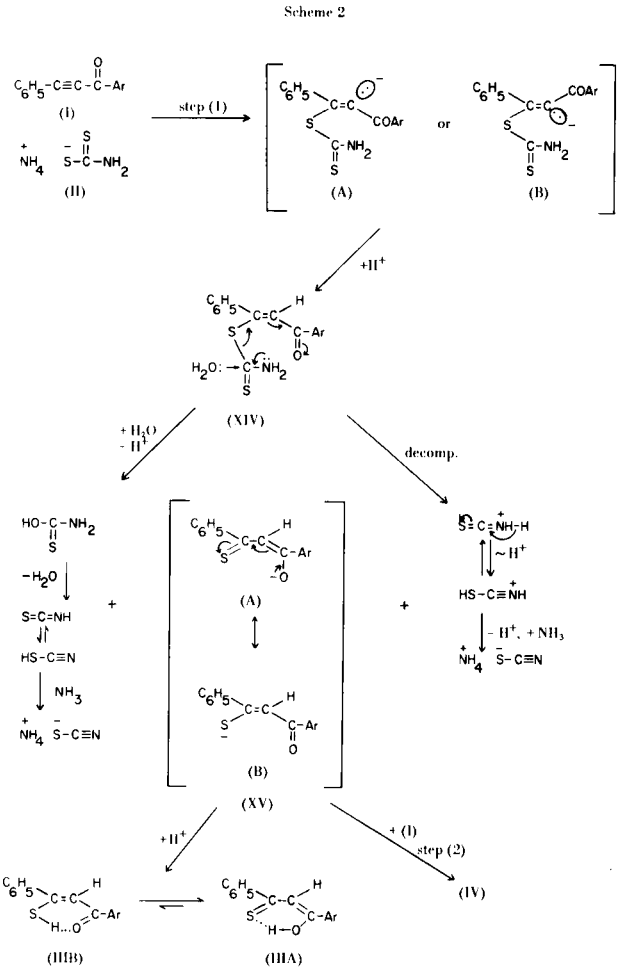
The mass spectra of the sulfides (VIa and d) using 70 eV electron beam showed the molecular ions as a singlet at m/e 444 and as a triplet at 512/514/516, respectively. This led to the false conclusion that their molecular weights are 444 and 513, respectively, and that these compounds are probably dehydrogenation products of the yellow sulfides (IVa and d). However, when the mass spectrum of (IVd) was run using 14.5 eV electron beam the molecular ion appeared as a triplet at m/e 514/516/518 indicating that it has the same molecular weight as the yellow sulfide (IVd), *i.e.*, they are geometrical isomers. Accordingly, the sulfides (VIa and d) may have either (E,E)- or the (Z,Z)-configuration. Their exact configuration was established by a study of their ir, nmr and mass spectra. Their ir spectra show only one $\nu_{C=O}$ at 1645 and 1633 cm^{-1}, respectively, which indicates that the two carbonyl groups are present in identical environments. The nmr spectra of the orange isomers of β,β′-di(α-benzoylstyryl) and β,β′-di[α-(*p*-chlorobenzoyl)styryl] sulfides (VIa and d) show only a complex pattern at δ 7.0-8.2 and δ 7.0-8.1, respectively, attributable to the aromatic and the two olefinic protons. Dallas, *et al.*, (15) concluded from the nmr spectra of *trans*-, *trans*- and *cis*-, *cis*-3,3′-thiodiacrylates that the signal for the α-olefinic protons of the *trans*-, *trans*-isomer appears at lower field (δ 7.63) than that of the *cis*-, *cis*-isomer (δ 7.08). By comparison, it appears that the orange isomers have the (E,E)- (VIa and d) rather than the (Z,Z)-configuration. The mass spectra of the orange isomers resemble those of the corresponding yellow isomers (IVa and d) with the exception of an extra peak which appears at m/e $[M-2]^+$. This peak is attributed to the formation of a thiophen molecular ion under the effect of the electron impact. The formation of such molecular ion is more likely for compounds having the (E,E)-configuration rather than the (Z,Z)-configuration. This is supported by the fact that by the use of the new courtauld atomic models it was possible only to build up the molecule which has the (E,E)-configuration.

Mechanism of the Reaction.

The reaction of aroylphenylacetylenes (Ia-f) with ammonium dithiocarbamate (II) is believed to proceed according to the mechanism outlined in Scheme 2. The dithiocarbamate anion attacks the positively charged acetylenic carbon leading to the formation of either the carbanion (A) or its isomer (B). The formation of the former anion (A) is more favored since it is the one which can lead finally to the formation of III. This picks up a proton to give the adduct (XIV), which is either hydrolyzed or decomposed, to give III and ammonium thiocyanate. The presence of ammonium thiocyanate in the reaction product was established qualitatively and quantitatively.

The formation of the (E,Z)-β,β′-di(α-aroylstyryl) sulfide (IV) may take place either by the interaction between one molecule of the acetylenic ketone with (i) the intermediate (XIV), or (ii) the anion of the enethiol (XVB). However, the following evidence indicate that the latter mechanism is more probable. (a) Ammonium hydrogen sulfide, which is a weak nucleophile, reacted with the acetylenic ketone (I) to give a mixture of the styryl derivatives (III) and the sulfide (IV) in the ratio 1:2, (b) when sodium xanthate (XVI) or sodium sulfide, which are strong nucleophiles, were used, the only product was the styrene derivative (III), (*cf.* Scheme 3), (c) the styryl derivatives (III) reacted readily with the acetylenic ketones in the presence of ammonium hydroxide to give the corresponding sulfides

Scheme 2



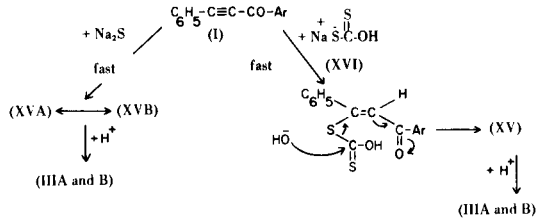
(IV). In addition to these experimental facts, the interaction between the intermediate (XIV) and the acetylenic ketone is less probable, since it proceeds through a highly crowded transition state. These facts also indicate that the initial attack of the reagent more probably takes place by the dithiocarbamate anion and not by the dithiocarbonyl group as claimed by Kishida and Terada (16). The above mechanism explains the experimental results. Thus, in the presence of weak nucleophiles such as ammonium hydrogen sulfide and ammonium dithiocarbamate, step (1) is much slower than step (2) (*cf.* Scheme 2) and therefore the product is a mixture of III and IV in the ratio 1:2, respectively. However, in the presence of strong nucleophiles such as sodium xanthate (XVI) and sodium sulfide, step (1) is very fast compared with step (2), and accordingly no sulfide (IV) is formed when the substrate and the reagent are used in stoichiometric amounts (*cf.* Scheme 3).

Conversion of β-Hydroxy-α-thioaroylstyrene (III), (E,Z)-β,β′-Di(α-aroylstyryl) sulfides (IV) and (E,E)-β,β′-Di(α-aroylstyryl) Disulfides (IV) to Heterocyclic Compounds [*cf.* Scheme (1)].

The styrene derivatives (III) react readily with hydrazine hydrate, phenylhydrazine, guanidine and ethyl hydrazinecarboxylate in boiling ethyl alcohol to give the corresponding 5(3)-aryl-3(5)-phenylpyrazole (IX), 5-aryl-1,3-diphenylpyrazoles (X), 2-amino-4-aryl-6-phenylpyrimidines (XIII) and ω-aroylacetophenone-*N*-ethoxycarbonyl hydrazones (XI), respectively, identical with authentic samples obtained by the reaction of these reagents with aroylphenylacetylenes (I). The latter compounds (XI) on heating with acetic anhydride were converted into *N*-ethoxycarbonylpyrazole derivative (XII). The phenylpyrazoles appear to be the 5-aryl-1,3-diphenyl derivatives (X) rather than the 3-aryl-1,5-diphenyl derivatives as claimed by Baddar, *et al.*, (17), since the product obtained from the reaction of *p*-chlorobenzoylphenylacetylene with phenylhydrazine was shown to be 5-*p*-chlorophenyl-1,3-diphenylpyrazole (Xd) and not 3-*p*-chlorophenyl-1,5-diphenylpyrazole. This was established by comparing the product with authentic samples of the two compounds, prepared by reacting the dibromides of *p*-chlorobenzalacetophenone and benzal-*p*-chloroacetophenone, respectively, with phenylhydrazine in methanolic potassium hydroxide (18).

(E,Z)-β,β′-Di[α-(*p*-chlorobenzoylstyryl)] sulfide (IVd) and (E,E)-β,β′-di[α-(*p*-chlorobenzoyl)styryl] disulfide (Vd) reacted with hydrazine hydrate and phenylhydrazine in boiling ethyl alcohol or acetic acid to give 5(3)-*p*-chlorophenyl-3(5)-phenylpyrazole (IXd) and 5-*p*-chlorophenyl-1,3-diphenylpyrazole (Xd), respectively. Similarly, β-[α-(*p*-chlorobenzoyl)styryl] β′-[α′-(*p*-methoxybenzoyl)styryl sulfide (IVg; Ar = *p*-Cl.C_6H_4 and *p*-$CH_3O.C_6H_4$) reacted with hydrazine hydrate to give a mixture of 5(3)-*p*-chlorophenyl-(IXd)- and 5(3)-*p*-methoxyphenyl-(IXe)-3(5)-phenylpyrazoles.

Scheme 3



EXPERIMENTAL

Melting points are uncorrected. Ir spectra were recorded using a Pye-Unicam SP 1000 and Beckman IR12 spectrophotometers (potassium bromide). Nmr were recorded on a Varian T-60A spectrometer using TMS as external standard. Electronic spectra were recorded on a Pye-Unicam SP 8000 spectrometer (ethyl alcohol). The purity of the analytical samples was checked by tlc (silica gel). Microanalyses were determined by Alfred Bernhardt, West Germany.

(A) Reaction of Aroylphenylacetylenes with Ammonium Dithiocarbamate, Ammonium Hydrogen Sulfide, Sodium Sulfide and Sodium Xanthate.

(i) Reaction with Ammonium Dithiocarbamate (II) and Ammonium Hydrogen Sulfide.

A solution of ammonium dithiocarbamate (II) (19) or ammonium hydrogen sulfide (0.01 mole) (saturated solution of hydrogen sulfide in 60% dioxane-water mixture) in 60:40 dioxane-water mixture (20 ml.) was added to a stirred solution of aroylphenylacetylene (I) (0.01 mole) in dioxane-water mixture (25 ml.) cooled at 15°. The reaction mixture which acquired an orange color was allowed to stand for 90 minutes (20), then poured into cold water and extracted with ether. The ethereal layer was washed with 10% sodium hydroxide solution, with water and dried (sodium sulfate). Evaporation of the ether left a yellow solid which was crystallized from a suitable solvent to give (E,Z)-β,β′-di(α-aroylstyryl) sulfides (IV). In the reaction of Ib and Id with ammonium dithiocarbamate the product contained, in addition to the sulfides IVb and IVd, β,β′-di(α-*p*-toluylstyryl) (Vb) and β,β′-di[α-(*p*-chlorobenzoyl)styryl] (Vd) disulfides, respectively. These were separated from the corresponding sulfide (IV) by fractional crystallization from cyclohexane (*cf.* Table III).

and the precipitated solid was extracted with ether. The residue left on evaporation of the solvent was crystallized from a suitable solvent to give β-hydroxy-α-thiobenzoylstyrene derivatives (III) as red crystals. The separation of (III) from (IV) can also be easily accomplished by fractional crystallization from cyclohexane. The ratio of (IV) and (V) to (III) was 2:1, and the results are reported in Table III.

(ii) Reaction with Sodium Sulfide and Sodium Xanthate.

General Procedure.

A solution of sodium sulfide (0.024 mole) in 60:40 dioxane-water mixture (100 ml.) or sodium xanthate (0.024 mole) [prepared from carbon disulfide (1.8 ml.) and sodium hydroxide (1.0 g.) in dioxane-water mixture (100 ml.)] was added to a stirred cold solution (15°) of aroylphenylacetylene (I) (0.024 mole) in

Table III

β-Hydroxy-α-thiobenzoylstyrene Derivatives (III), (E,Z)-β,β′-Di(α-aroylstyryl) Sulfides (IV) and β,β′-Di(α-aroylstyryl) Disulfides (V)

Compound	Yield (%)	M.p., °C	Formula	Calcd. %					Found %				
				C	H	S	Cl	M.W.	C	H	S	Cl	M.W. (ms)
IIIa (6a)	30	84-85 (a)											
IVa (4)	65	135-136 (b)	$C_{30}H_{22}O_2S$	80.70	4.95	7.18	---	446	80.22	4.87	7.18	---	446
IIIb	15	130-131 (b)	$C_{16}H_{14}OS$	75.55	5.55	12.61	---	254	75.72	5.45	12.54	---	254
IVb	29.5	136-137 (a)	$C_{32}H_{26}O_2S$	80.98	5.57	6.76	---	474	80.91	5.44	6.71	---	474
Vb	9	174-175 (c)	$C_{32}H_{26}O_2S_2$	75.86	5.17	12.66	---	---	75.77	5.08	12.79	---	---
IIIc	26	98-99 (a)	$C_{15}H_{11}ClOS$	65.58	4.05	11.67	12.90	274	65.59	4.07	11.72	12.84	274
VIc	65	105-106 (b)	$C_{30}H_{20}Cl_2O_2S$	69.90	3.91	6.22	13.76	---	69.82	4.01	6.21	13.99	---
IIId	26	122-123 (b)	$C_{15}H_{11}ClOS$	65.58	4.05	11.67	12.90	274	65.71	4.08	11.83	13.09	274
IVd (4)	56	168-169 (b)	$C_{30}H_{20}Cl_2O_2S$	69.90	3.91	6.22	13.76	515	69.60	4.07	5.84	13.97	515
Vd	9	170-171 (c)	$C_{30}H_{20}Cl_2O_2S_2$	65.81	3.68	11.71	12.95	547	65.92	3.71	11.28	12.49	547
IIIe (6a)	29	133-134 (b)	$C_{16}H_{14}O_2S$	71.08	5.22	11.86	---	270	71.28	5.20	11.92	---	270
IVe (4)	66	169-170 (c)	$C_{32}H_{26}O_4S$	75.86	5.17	6.33	---	---	75.99	4.92	6.20	---	---
IIIf	27	103-104 (b)	$C_{16}H_{12}O_3S$	67.80	4.36	11.20	---	---	67.59	4.25	11.72	---	---
IVf	53	69-70 (b)	$C_{32}H_{22}O_6S$	71.90	4.15	6.00	---	---	72.11	4.35	6.44	---	---

(a) Crystallized from light-petroleum (60-80°). (b) Crystallized from cyclohexane. (c) Crystallized from benzene-cyclohexane; OCH_3% of (IIIe): Found = 11.52; Calcd. for = 11.48. OCH_3% of (IVe): Found = 12.07; Calcd. for = 12.25.

the same solvent (100 ml.), and allowed to stand with stirring for 90 or 180 minutes, respectively. The reaction mixture was filtered to remove any precipitate (in the case of sodium sulfide), and the filtrate acidified with concentrated hydrochloric acid. The precipitated product was extracted with ether, dried, and the solvent evaporated. The red semi-solid residue, which solidified on trituration with light-petroleum (b.p. 60-80°) was crystallized from cyclohexane to give the corresponding β-hydroxy-α-thiobenzoylstyrene (III) (quantitative yield).

When two moles of the acetylenic ketone were used, and the stirred reaction mixture left for 90 minutes, then diluted with water, and worked up as usual, the corresponding (E,Z)-β,β′-di(α-aroylstyryl) sulfides (IV) were obtained, identified by m.p. and mixed m.p. (yield = 85%). The alkaline aqueous layer was acidified with dilute sulfuric acid, but no β-hydroxy-α-thiobenzoylstyrene derivative (III) was precipitated.

(B) Reaction of β-Hydroxy-α-thiobenzoylstyrene Derivatives (IIId and e) with Diazomethane.

An ethereal solution of diazomethane [from nitrosomethylurea (1.0 g.)] was added to a cold solution (0-5°) of the styrene derivative (IIId and e) (0.003 mole) in ether (25 ml.), left for 12 hours, and worked up as usual (6a). The solid left on evaporation of the ether was crystallized from a suitable solvent to give the corresponding α-aroyl-β-methylmercaptostyrene (VIId and e) as pale yellow needles.

α-*p*-Chlorobenzoyl-β-methylmercaptostyrene (VIId).

This compound was crystallized from light-petroleum (b.p. 60-80°), m.p. 106-107°, yield = 94%.

Anal. Calcd. for $C_{16}H_{13}ClOS$ (21): C, 66.54; H, 4.51; S, 11.10; Cl, 12.28. Found: C, 66.58; H, 4.48; S, 11.13; Cl, 12.41.

α-*p*-Methoxybenzoyl-β-methylmercaptostyrene (VIIe).

This compound was crystallized from cyclohexane-light petroleum (b.p. 40-60°), m.p. 74-75°, yield = 91%.

Anal. Calcd. for $C_{17}H_{16}O_2S$ (21): C, 71.80; H, 5.67; S, 11.28; OCH_3, 10.92; M.W. 284. Found: C, 71.52; H, 5.90; S, 11.24; OCH_3, 10.89; M.W. 284 (ms).

(C) Oxidation of β-Hydroxy-α-thiobenzoyl-*p*-chlorostyrene (IIId) to the Disulfide (Vd).

A solution of sodium nitrite (0.004 mole) and sodium hydrogen sulfate (0.004 mole) in water (3 ml.) was added to a solution of β-hydroxy-α-thiobenzoyl-*p*-chlorostyrene (IIId) (1.0 g.) in ethyl alcohol (15 ml.), heated for 5 minutes, worked up as usual (9) and extracted with ether. Evaporation of the solvent gave the disulfide (Vd), identified by m.p. and mixed m.p. 170-171°.

(D) Reaction of β-Hydroxy-α-thiobenzoylstyrene Derivatives (IIId and e) with Aroylphenylacetylenes (I).

General Procedure.

(i) A solution of β-hydroxy-α-thiobenzoyl-*p*-chlorostyrene (IIId and e) (0.003 mole) in dioxane-water mixture (60:40) (20 ml.), containing ammonium hydroxide (28%; 5 ml.), was treated with the corresponding aroylphenylacetylenes (Id and e, respectively) and the mixture stirred at 15° for 30 minutes. The reaction mixture was diluted with water (100 ml.) and kept at room temperature overnight. The precipitated yellow solid was filtered off and crystallized from a suitable solvent to give (E,Z)-β,β′-di(α-aroylstyryl) sulfide (IVd and e) as yellow needles, identified by m.p. and mixed m.p., yield = 96-98%.

(ii) *p*-Chlorobenzoylphenylacetylene (Id) (0.5 g.) reacted with the above conditions to give (E,Z)-β-[α-(*p*-chlorobenzoyl)styryl] β′-[α′-(*p*-methoxybenzoyl)styryl] sulfide (IVg) as yellow crystals, m.p. 139-140°, yield = 96%.

Anal. Calcd. for $C_{31}H_{23}ClO_3S$: C, 72.85; H, 4.54; Cl, 6.94; S, 6.27; OCH_3, 6.07. Found: C, 72.51; H, 4.22; Cl, 7.27; S, 6.14; OCH_3, 6.33.

Action of Ozone on β-Hydroxy-α-thiobenzoylstyrene (IIId and e) and (E,Z)-β,β′-Di(α-aroylstyryl) sulfides (VId and e).

The solution of the sulfur compound (IIId and e) and (IVd and e) (0.008 mole) in chloroform (30 ml.) was treated with ozone (2 hours) at (-10°), and worked up as usual. The product soluble in sodium hydrogen carbonate was found to be *p*-chlorobenzoic acid (m.p. 236°) [in the case of IIId and IVd (0.6 g.)] and *p*-methoxybenzoic acid (185-186°) [in the case of IIIe (0.6 g.) and IVe (0.55 g.)]. The mother liquor of the acidified solution was extracted with ether. Evaporation of the solvent gave in each case benzoic acid (0.05 g.).

Distillation of the chloroform solution under reduced pressure left an oil (0.5 g.) which failed to solidify, and was not identified.

The aqueous solution remaining after extraction of benzoic acid [only in the case of (IVd and e)] proved to contain formic acid (22).

Conversion of (E,Z)-β,β′-di(α-aroylstyryl) Sulfides (IVa and d) (Yellow) to (E,E)-Isomers (VIa and d) (Orange):

A solution of (E,Z)-β,β′-di(α-benzoylstyryl) sulfide (IVa) (0.5 g.) in ethyl alcohol (20 ml.) was refluxed on a boiling water-bath for 10 hours. The solid precipitated on concentration and cooling was filtered off. It was crystallized from cyclohexane to give (E,E)-β,β′-di(α-benzoylstyryl) sulfide (VIa) as orange needles, m.p. 183-184° [reported m.p. 179° (4)], yield = 71%.

Anal. Calcd. for $C_{30}H_{22}O_2S$: C, 80.69; H, 4.97; S, 7.18; M.W. 446. Found: C, 80.64; H, 5.05; S, 7.13; M.W., 446 (ms).

Similarly, (E,Z)-β,β′-[α-(*p*-chlorobenzoyl)styryl) sulfide (IVd) gave the corresponding (E,E)-isomer (VId), as orange needles (from acetic acid), m.p. 197-198° (4), yield = 81%.

Anal. Calcd. for $C_{30}H_{20}Cl_2O_2S$: C, 69.90; H, 3.91; S, 6.22; Cl, 13.76; M.W., 515. Found: C, 70.28; H, 3.61; S, 6.20; Cl, 13.41; M.W., 513 (ms).

Compounds IVb and IVe were recovered unchanged when refluxed in ethyl alcohol, toluene or dilute hydrochloric acid (10%) for 13 hours.

A mixture of (E,E)-β,β′-di(α-aroylstyryl) sulfides (VIa and d) and the corresponding β-hydroxy-α-thiobenzoylstyrene derivatives (IIIa and d) was also obtained when the alcoholic solution of the corresponding acetylenic ketone (0.004 mole of ketone/20 ml. of ethyl alcohol) was refluxed with ammonium dithiocarbamate (II) (0.004 mole) for 30 minutes. The product precipitated on addition of water was dissolved in ether and extracted with alkali to separate (E,E)-β,β′-di(α-aroylstyryl) sulfide (VI) from III, which were identified by m.p. and mixed m.p.

Reduction of β,β′-Di[α-(*p*-chlorobenzoyl)styryl] disulfide (Vd).

A mixture of the disulfide (Vd) (0.2 g.), tin (0.1 g.) and concentrated hydrochloric acid (2 ml.) was refluxed for 5 minutes. The cold reaction mixture was diluted with water (15 ml.), and then extracted with ether. Evaporation of the solvent left an oil, which solidified on trituration with light-petroleum (b.p. 60-80°). It was crystallized from cyclohexane to give (IIId) identified by m.p. and mixed m.p. (122-123°).

Conversion of β-Hydroxy-α-thiobenzoylstyrene Derivatives (III), α-Aroyl-β-methylmercaptostyrene (VII), (E,Z)-β,β′-Di(α-aroylstyryl)

styryl) Disulfides (V) to Heterocyclic Compounds.

a) By Reaction with Hydrazine Hydrate.

General Procedure.

Hydrazine hydrate (99% w/w; 5 ml.) was added to the above sulfur compounds [(III)-(VII)] (0.003 mole) and the mixture was refluxed for 30 minutes. The reaction product was diluted with water and the solid was filtered off and crystallized from ethyl alcohol to give the corresponding 5(3)-aryl-3(5)-phenylpyrazole (IX) as colorless needles, identified by m.p. and mixed m.p. (1), and ir spectra, yield = 80-90%.

Similarly, β-[α-(*p*-chlorobenzoyl)styryl] β'-[α'-(*p*-methoxybenzoyl)styryl] sulfide (IVg) reacted with hydrazine hydrate to give a mixture of 5(3)-*p*-chlorophenyl-3(5)-phenylpyrazole (IXd) (m.p. 214-215°) and 5(3)-*p*-methoxyphenyl-3(5)-phenylpyrazole (IXe) (m.p. 168-169°), separated by fractional crystallization form ethyl alcohol, and identified by m.p. and mixed m.p.

b) By Reaction with Phenylhydrazine.

General Procedure.

Phenylhydrazine (2.0 ml.) was refluxed for 3 hours with a solution of the sulfur compound (IIId, IVd, Vd, VId and VIId) (0.003 mole) in ethyl alcohol (20 ml.). The product precipitated on concentration was crystallized from methyl alcohol to give in each case 5-*p*-chlorophenyl-1,3-diphenylpyrazole (X) as colorless needles identified by m.p. and mixed m.p. (115-116°) with an authentic sample, prepared by the method outlined by Barnes and Dodson (18).

When (E,Z)-β,β'-[α-(*p*-chlorobenzoyl)styryl] sulfide (IVd) (1.0 g.) was refluxed for 20 minutes with phenylhydrazine (0.5 ml.) in acetic acid (10 ml.), the solid precipitated on cooling was found to be (E,E)-β,β'-di[α-(*p*-chlorobenzoyl)styryl] sulfide (VId), (orange needles from acetic acid m.p. and mixed m.p. 197-198°, yield = 30%). The original acetic acid mother liquor was poured into water and extracted with ether. Evaporation of the solvent left an oil, which solidified on trituration with light-petroleum (b.p. 40-60°). It was crystallized form methyl alcohol to give 5-(*p*-chlorophenyl)-1,3-diphenylpyrazole (Xd), identified by m.p. and mixed m.p. 115-116°. This was the sole product when the reaction mixture was refluxed for 2 hours.

c) By Reaction with Guanidine Hydrochloride.

A solution of guanidine hydrochloride (0.5 g.) and β-hydroxy-α-thiobenzoyl-*p*-chlorostyrene (IIId) (1.0 g.) in ethyl alcohol (10 ml.) was refluxed, while a solution of sodium carbonate (0.27 g.) in water (2 ml.) was added portion-wise during 12 hours. The reaction mixture was concentrated, and extracted with benzene. Evaporation of the solvent gave 2-amino-6-*p*-chlorophenyl-4-phenylpyrimidine (XIIId) as colorless needles, identified by m.p. and mixed m.p. (157-158°) (1), yield = 78%.

d) By Reaction with Ethyl Hydrazinecarboxylate.

A mixture of the styrene derivative (IIIa) (0.01 mole) and ethyl hydrazinecarboxylate (0.01 mole) was refluxed in ethyl alcohol (50 ml.) for 8 hours. The reaction mixture was concentrated, and the precipitated solid was crystallized from ethyl alcohol to give ω-benzoyl-*N*-ethoxycarbonylacetophenone hydrazone (XI) as colorless needles, m.p. and mixed m.p. 159-161° (1), yield = 76%. This gave 1-ethoxycarbonyl-3,5-diphenylpyrazole (XII), m.p. and mixed m.p. 105-106°, when refluxed with acetic anhydride (1), yield = 78%.

Determination of the Amount of Ammonium Thiocyanate Produced During the Reaction of Ammonium Dithiocarbamate with Benzoylphenylacetylene.

This was based on the maximum absorption at 450 nm shown by a solution of ammonium thiocyanate after treatment with aqueous ferric perchlorate-perchloric acid solution (23).

Procedure.

A solution of ammonium dithiocarbamate (0.29 g., 0.0026 mole) in dioxane-water mixture (60%) (10 ml.) was added to a stirred solution of benzoylphenylacetylene (0.54 g., 0.0026 mole) in the same solvent (20 ml.) at 15°. The precipitated solid was filtered off and the filtrate was divided into two equal parts. The first part was treated with 1 *M* aqueous ferric perchlorate in 1 *M* perchloric acid (5 ml.) and the deep red colored turbid solution was left overnight at room temperature in order to obtain a clear solution. The solution was filtered from the precipitated solid and the filtrate completed with water to 100 ml. (solution a). The second part was treated with 1 *M* aqueous perchloric acid (5 ml.), left overnight at room temperature in order to obtain a clear solution and filtered. The filtrate was completed with water to 100 ml., and 3 ml. of this solution was completed with water to 25 ml. and then used as reference for the spectrophotometric determination. Solution (a) was shown to obey Beer's law, and ammonium dithiocarbamate was found to be stable in perchloric acid solution and no thiocyanate was formed on leaving the mixture overnight.

In order to determine the ammonium thiocyanate liberated in the reaction, solutions of known concentrations of ammonium thiocyanate were prepared and the concentrations were plotted versus the corresponding absorbances at λ max 450 nm. The straight line obtained was used for calculating the concentration of ammonium thiocyanate in the reaction mixture. Determination of the absorbance of solution (a) showed that the total amount of ammonium thiocyanate produced from the reaction = 0.197 g. (0.00259 mole), which is 98.85% of the stoichiometric amount.

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