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The Reactivity of Thiopyrylium Compound. Reduction of Thiopyrylium Cation by Alkali Metals—Evidence of Thiabenzene Radical

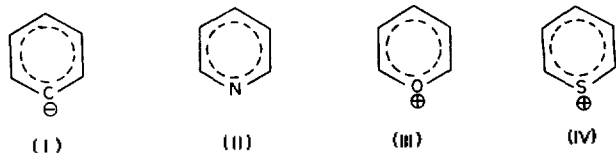
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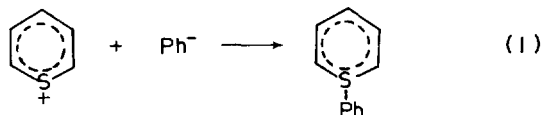
For the first time we have synthesized thiabenzene radical by the reaction of thiopyrylium cation with alkali metals. As might be expected for a free radical, ESR-spectrum of 2,4,6-triphenylthiabenzene radical shows the single signal with g -value of 2.0045. The proton signal of 2,4,6-triphenylthiabenzene radical in nmr spectrum shifts to the higher field than that of 2,4,6-triphenylthiopyrylium cation by *ca.* 0.5 ppm. From the UV-spectrum of thiabenzene radical the presence of 6 π non-benzenoid aromatic system was observed as in the case of thiopyrylium cation. The reactivity of alkali metals with thiopyrylium cation increases in the order of decreasing ionization energy, $\text{Li} < \text{Na} < \text{K}$.

Introduction

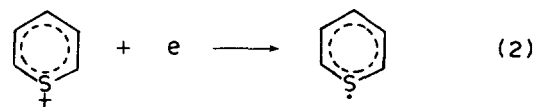
Six-membered heterocycles derived from phenyl anion C^- with heteroatom, N, O⁺, S⁺, differ markedly in reactivity from phenyl anion itself. This formal replacement of C^- of phenyl anion by N, O⁺ and S⁺ gives a non-benzenoid aromatic systems, pyridine, pyrylium cation and thiopyrylium cation respectively(I-IV)



Since thiopyrylium cation(IV) which is isoelectronic with phenyl anion(I), pyridine(II) and thiopyrylium cation(III) has been synthesized by Wizinger^{1,2} in 1956, attention has been focused on this non-benzenoid aromatic system and a good deal of works³⁻⁷ in this field were reported. Price *et al.*⁸ reported the thiabenzene derivatives formed by a nucleophilic attack on sulfur atom of thiopyrylium cation.



In the reaction (1) it is clear that thiopyrylium cation acts as an election acceptor. SCF MO calculations by Yoshida¹⁰ indicate that the contributions of the sulfonium ion structure and the carbonium ion structures to resonance hybrids are found to be 85.4 % and 14.6 % for thiopyrylium cation. Thiopyrylium cation acts as a π -acceptor in the CT-complex¹¹ formation from the reaction of thiopyrylium cation with olefins. From this point of view, when one electron is transferred to thiopyrylium cation, it is expected to form a thiabenzene radical analog of reaction (2).

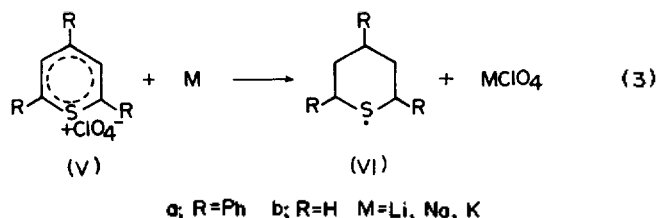


We are much interested in the synthesis of this thiabenzene radical which should be a very interesting chemical species in the non-benzenoid aromatic systems.

Results and Discussion

We have carried out our extensive works to synthesize thiabenzene radical and for the first time succeeded in obtaining it from the reaction of thiopyrylium cation with alkali metals.

The fact that sulfur atom of thiopyrylium cation has 3d vacant orbital might be responsible for the reactivity of this cation.

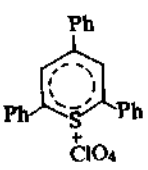
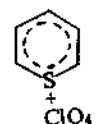


On the other hand, it is well known that alkali metals act as excellent reducing agents by donation of one electron.

Thiopyrylium perchlorate(V) and a little excess of alkali metal were suspended in organic solvent under nitrogen atmosphere and refluxed for several hours. As the reaction (3) proceeded solid (V) disappeared leaving a dark red solution of thiabenzene radical (VI). MClO_4 produced from the reaction (3) was identified by IR and determined quantitatively. The reaction conditions were summarized in Table 1.

The reactivity of alkali metals with thiopyrylium cation increases in the order of decreasing ionization energy of metals, $\text{Li} < \text{Na} < \text{K}$ and in the order of increasing Lewis base character

TABLE 1: Reaction Condition of Thiopyrylium Cation with Alkali Metals

Reactant Cation	Metal	Solubility of reactant in the medium	Reaction temp (°C) (reflux)	Reaction hrs (time)	Solubility of product in the medium
	Li	Insoluble	66	30 hrs	Soluble
	Na	Insoluble	66	12 hrs	Soluble
	K	Insoluble	66	3 hrs	Soluble
	Li	Insoluble	66	60 hrs	Soluble
	Na	Insoluble	66	30 hrs	Soluble
	K	Insoluble	66	8 hrs	Soluble

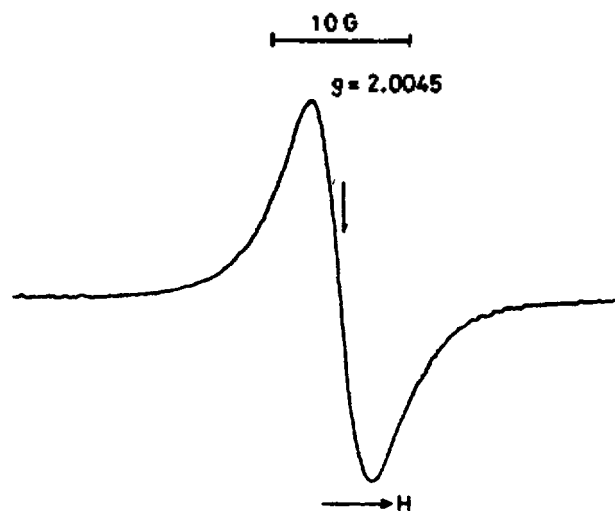


Figure 1. ESR spectrum of 2,4,6-triphenyl thiabenzene radical. Recorded on Varian E-9 with frequency of 9.51 GHz.

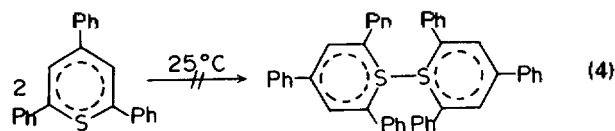
of organic solvents, dioxane > THF > diethylether > *n*-hexane.

The stability of thiabenzene radical might be related mainly with its substituent of the thiabenzene ring. From this point of view 2,4,6-triphenyl substituted thiabenzene radical, VI-a, is much favoured as compared to non-substituted thiabenzene radical, VI-b. In our observation, 2,4,6-triphenylthiabenzene radical, VI-a, is much stabler than non-substituted thiabenzene radical, VI-b. Therefore, although our spectroscopic studies of 2,4,6-triphenylthiabenzene radical, VI-a, have been carried out successfully, the analogous spectroscopic studies of non-substituted thiabenzene radical, VI-b, are now under investigation.

The free radical of VI-a was confirmed by ESR with the g -value of 2.0045 as a singlet by using DPPH as a standard ($G = 2.0023$). In ESR we have not found any hyperfine structures when the spectroscopy have been carried out in the temperature range from -195°C to room temperature and/or under the very diluted conditions. From these results it seems that the unpaired electron of the 2,4,6-triphenylthiabenzene radical might be localized largely at the sulfur atom of VI-a analogously to the positive charge of the thiopyrylium cation (Figure 1).

The non-benzenoid aromatic system of VI-a was confirmed by UV ($\lambda_{\text{max}} = 248 \text{ nm}$) and by nmr ($\delta = 6.86\text{--}7.72$, multiplet) as compared to the spectra of 2,4,6-triphenyl thiopyrylium cation, V-a.

The absorption band at the visible region ($\lambda = 300\text{--}360 \text{ nm}$, shoulder) seems to be responsible for the complement color of VI-a. The molecular weight of VI-a was determined to be 350 (theor. 325) by cryoscopic method. From this result we have concluded that dimerization of VI-a did not occur at room temperature. In Table 2 all of the spectroscopic result were summarized.



IR Spectra were recorded on Beckman Model 33, UV Spectra on Beckman Model 26 and nmr on Varian HA-100 using *i*-TMS as standard.

Experimental

2,4,6-Triphenylthiopyrylium perchlorate V-a² and thiopyrylium perchlorate, V-b⁹ were prepared according to Wizinger and Mislow. of V-a : $211\text{--}212^\circ\text{C}$ (lit: 211°C), m.p. of V-b, 336°C (lit: 336°C).

2,4,6-Triphenylthiabenzene Radical, VI-a. 2.3 mmole of 2,4,6-triphenylthiopyrylium perchlorate, V-a were suspended with a little excess of Li, Na or K in mole ratio in 75 ml abs. THF under nitrogen atmosphere and refluxed for 30, 12 and 3 hours, respectively. The suspended V-a disappeared as the reaction proceeded, forming initially a brown solution which became gradually dark-red THF-solution.

TABLE 2: Spectroscopic Data of IR, UV and ¹H-nmr

	2, 4, 6-triphenyl- thiopyrylium perchlorate V-a	2, 4, 6-triphenyl- thiabenzene radical VI-a	Thiopyrylium perchlorate V-b	Thiabenzene radical VI-b
IR (cm ⁻¹)				
C-H	3040(n)	3035(m)	3060(m)	2965(s)
C=S	1630(s)	1605(s)	1570(s)	—
C-H	1480(m)	1490(m)	1445(m)	—
	1450(m)	1450(m)	1410(m)	1420(w)
ClO ₄	1095(s)	—	1080(s)	—
ClO ₄	620(m)	—	620(m)	—
UV(nm)				
λ _{max} (log ε)	CH ₂ Cl ₂	CH ₂ Cl ₂	EtOH	EtOH
	251(1.21)		248(1.48)	244(1.66)
	275(1.04)	248(1.36)	288(1.15)	290(1.57)
	375(1.43)	300-360(shoulder)		298(1.38)
¹ H-nmr (ppm)				
	CD ₃ CN	CD ₃ CN	D ₂ O	
α -	8.08-7.92		10.69	
β -	8.76	7.72-6.86		
γ -	8.44-8.26		9.65-9.30	

After the completion of the reaction was confirmed by TLC the precipitate was filtered, washed with abs. THF and dried in vacuum at room temperature. This solid was identified as MClO₄ by IR, ν ClO₄ = 1140-1090 cm⁻¹, δ ClO₄ = 628 cm⁻¹. The quantity of MClO₄ was determined to be 2.23 mmole. From the filtrate the solvent THF was removed under reduced pressure.

The obtained residue was dissolved in 25 ml *n*-hexane and a trace of possible insoluble substances was filtered off by fine glassfilter. When this filtrate was left standing at -78 °C, 0.4 g reddish yellow crystalline -2,4,6-triphenylthiabenzene radical, VI-a were obtained. m.p 74-75 °C, yield 60 %. The ESR spectrum of VI-a indicated a single signal for this free radical with the *G*-value of 2.0045. The MW of VI-a was found cryoscopically in benzene to be 350 (calc. 325). In nmr the proton signal of VI-a showed in CD₃ CN a multiplet at 7.80 ppm, which was shifted to higher field by 0.5ppm as compared to 2,4,6-triphenylthiopyrylium perchlorate. The UV spectrum of VI-a in CH₂Cl₂ showed λ_{max} (log ε) = 248 nm(1.36).

Thiabenzene Radical (Non Substituted). 4.2 mmole of thiopyrylium perchlorate V-b were suspended with a little excess of L, Na or K in mole ratio in 75 ml abs. THF under nitrogen atmosphere and refluxed for 60, 30 or 8 hours, respectively. The suspended V-b disappeared giving a dark-red THF-solution. After completion of the reaction was confirmed by TLC, the precipitate was filtered, washed with abs. THF and dried in vacuum at room temperature. This

solid was identified as MClO₄ by IR and the quantity was determined to be 4.0 mmole. From the filtrate the solvent THF was removed under reduced pressure. The residual viscous darkbrown liquid was dissolved in abs. 50 ml ether and the ether solution was filtered. Ether was evaporated under reduced pressure. The isolation of pure VI-b from this viscous raw product was not successful because thiabenzene radical VI-b was very unstable at room temperature. The UV spectrum of VI-b in abs. EtOH which is the only one spectrum taken successfully showed λ_{max} (log ε) = 244 nm(1.66) and 290 nm(1.57).

The analogous reaction has been carried out with sodium in dioxane, THF and/or ether. It was confirmed that the reaction had been completed in 3, 12 and/or 40 hours in dioxane, THF and/or ether, respectively.

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Sequential Copolypeptides (III). Synthesis and Characterization of Poly (γ -benzyl-*L*-glutamyl)- γ -benzyl-*L*-glutamyl-glycine)

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A sequential copolypeptide with repeating unit sequences, in which a glycyl residue is flanked progressively by two γ -benzyl-*L*-glutamyl residues, has been synthesized by polymerizing *p*-nitrophenyl ester of γ -benzyl-*L*-glutamyl- γ -benzyl-*L*-glutamyl-glycine. Polymers obtained were characterized by viscosity and infra-red spectral data. The highest molecular weight obtained was 21,000. Molecular conformation in solid state was found to be a mixed form of α and β -structure. Polymers obtained were insoluble in the most of the organic solvents except in a strong acid like dichloroacetic acid, but in binary mixtures of solvents such as dichloroacetic acid-ethylene dichloride or dichloroacetic acid-chloroform, they were soluble within certain ranges of solvent compositions.

Introduction

It is well known that the helical conformation of polypeptide is stabilized by intramolecular hydrogen bonds formed between pairs of peptide residues separated by three residues along the backbone. In the conformation of copolypeptides the arrangement of peptide residues in the main chain becomes the most important factor. For both theoretical and experimental studies on the conformational behavior of copolypeptides, one has to face the complexity of two additional factors influencing their conformation. These factors are the composition of different peptide residues and their geometrical arrangement in the polymer chain. To approach the problem of copolypeptides it is therefore desirable to find systems with least complexities. One of these systems is an alternating sequential copolymer consisting of two peptide residues *A* and *B*, which may be schematically represented by $(A-B)_n$ or $(A_m-B)_n$. In this case, the composition and arrangement of the constituent residues are fixed not only in a particular chain but also among all the individual chains in the system.

The alternating sequential copolypeptide chosen for the present study was poly (γ -benzyl-*L*-glutamyl- γ -benzyl-*L*-

glutamyl-glycine), poly [Glu(OBzl)-Glu(OBzl)-Gly]. The choice was made since detailed investigations are available on conformational characteristics of the homopolypeptides of its constituent residues.¹⁻⁴ It was thus hoped that when compared with data for the parent polymers, the measurements on the copolypeptide would provide information about interactions between neighbouring different peptide units, which is usually difficult to obtain.

Present work deals primarily with the synthesis of the *p*-nitrophenyl ester of the corresponding tripeptide monomer unit and its polycondensations. Polymers obtained were characterized by viscosity data, infrared spectra, and solubility tests.

Experimental

1. Reagents and Solvents

Carbobenzoxyglycine(Z-Gly-OH), γ -benzyl-*L*-glutamate [Glu(OBzl)], and dicyclohexylcarbodiimide (DCCI) were obtained from the Protein Research Foundation, Osaka, Japan, and used without further purification. *p*-Nitrophenol(HONp) was recrystallized from toluene. 1-Hydroxybenzotriazol (HOBt) was synthesized⁵ from *o*-nitrochlorobenzene and