BULLETIN OF THE
KOREAN CHEMICAL SOCIETY

VOLUME 5, NUMBER 6, DECEMBER 20, 1984

# Reactions of Thianthrene Cation Radical Perchlorate with Free Radical. II. On the Reaction with *tert*-Butyl Peroxide[1]

**Jongheon Shin and Kyongtae Kim**†

*Department of Chemistry Seoul National University, Seoul 151, Korea* (*Received September 22, 1983*)

Reaction of thianthrene cation radical perchlorate (1) with *tert*-butyl peroxide (TBP) in acetonitrile gave thianthrene (2), thianthrene 5-oxide (3), *cis*-thianthrene-5,10-dioxide (4), 5-acetonylthianthrenium perchlorate (9), along with small amount of thianthrene-5, 5-dioxide (7) in some cases. Isolation of N-*tert*-butylacetamide indicated the formation of tert-butyl cation from TBP. The formation mechanisms of these products were proposed.

## Introduction

Some years ago, we investigated the reactions of thianthrene cation radical perchlorate (1) with azobisisobutyronitrile (AIBN)[2] and dibenzoyl peroxide (DBP)[3] in acetonitrile at reflux temperature. In contrast with the expectation of possible combination reactions between **1** and radicals derived from the radical initiators, any combination product, whatsoever, was not obtained. Instead, thianthrene (2), thianthrene 5-oxide (3), *cis*-thianthrene-5,10-dioxide (4), 5-thianthreniumyl thianthrene perchlorate (5), and usual decomposed products of the initiators were obtained.

One interesting observation in these reactions was the isolation of **4** because no formation of **4** was reported in many studies of reactions with a variety of nucleophiles.[4] Therefore, it was felt that oxygen dissolved in the solvent might be incorporated to be reactive intermediate and became the source of oxygen of disulfoxide.

The findings that no combination products were formed in the reactions of **1** and either AIBN or DBP at solvent reflux temperature raised a doubt about the speculation of radical-thianthrene cation radical combination mechanism. Recently, cyanomethylthianthrene (6) was isolated, inter alia, from the photolysis of **1** in acetonitrile using 450W Hanovia medium-pressure mercury lamp.[5]

The formation mechanism of **6** was uncertain. One may consider two possible routes. That is, cyanomethyl radical generated by the absorption of high energy[6] undergoes either $S_H2$ reaction with **2** or the combination reaction between a resonance form of **1** and cyanomethyl radical. In order to see if **6** can be formed by the former process, **2** was photolyzed in acetonitrile using the same light source. It has been unsuccessful to detect **6**. Therefore, it is hard to say that $S_H2$ reaction is involved in the photochemical decomposition of **1**. Nevertheless, there has not been reported a clear example on the combination reaction of **1** and any radical. It is felt that more relevant data about the reactions of **1** with radicals are needed. Herein are described the results of the reactions of **1** with *tert*-butyl peroxide (TBP).

## Experimental

Thianthrene was obtained from Merck (Art. 821109) and recrystallized from ethanol. Acetonitrile was Kanto Chemical Co. Extra pure and refluxed with phosphorous pentoxide for 3 h, followed by distilling twice. Dried acetonitrile was stored over molecular sieve (Merck 4Å, Art. 5708) in a septum capped bottle. *tert*-Butyl peroxide (TBP) was obtained from Matheson, Coleman and Bell and *tert*-butyl hydroperoxide (TBH) was obtained from Merck (Art. 820244). All solvents used for the chromatography were distilled before use. Thin layer chromatogphy(tlc) was performed on a glass plate (2×8 cm) with Merck kieselgel 60 $PF_{254}$ Silansiert (Art. 7751). The slurry of the adsorbent was made in a mixture of chloroform and methanol (2:1 v/v). The chromatogram was visualized by mineral UV lamp. Column chromatography was performed with Merck Silica gel, 70-230 mesh (Art. 7734). Ultraviolet spectra were obtained using Beckman Model 5270 spectrophotometer. Infrared spectra were obtained with Perkin-Elmer Model 283 spectrophotometer. $^1H$ nmr spectra were recorded using Varian EM-360A spectrometer. All chemical shifts were measured in ppm relative to an internal standard TMS. Melting points were taken with Fisher-Johns melting point apparatus and were not calibrated.

(*a*) *General Procedure.* About 3-5 m*M* of **1** was dissolved in 40 m*l* of anhydrous acetonitrile, followed by the removal of oxygen by passing through the solution with dried nitrogen or argon gas for 20min. To this was added 3-5 m*M* of TBP using a hypoder mic syringe. The mixture was gently refluxed with vigorous stirring under inert gas atmosphere until dark purple color of **1** disappeared to become pale brown. The reaction mixture was checked by tlc, followed by the concentration using rotary evaporator. The residue was chromatographed. Eluting solvents are specified in each case. Compound **2** and **3** were identified by comparison of ultraviolet spectrum and $R_f$ value of authentic sample.

(*b*) *In the Air.* To the solution of 1.504 g (1.77 m*M*) of **1** in 40 m*l* of acetonitrile was added 0.657 g (4.50 m*M*) of TBP. After 1 h refluxing, the reaction mixture showed five spots ($R_f$=0.71, 0.45, 0.31, 0.26, 0) on tlc (benzene). $R_f$ values with 0.71 and 0.31 corresponded to **2** and **3**, respectively. The reaction mixture was worked up as described in the general procedure and the residue was chromatographed on silica gel column (1.5×15 cm). Elution with hexane (7×120 m*l*) gave 0.433g (2.00 m*M*) of **2**. Next hexane (1×120 m*l*) fraction gave 0.010g (0.04 m*M*) of white solids, identified as thianthrene-5,5-dioxide (**7**), whose UV absorption data was identical with that of the reported data.[7]

Elution with benzene (500 m*l*) gave 0.438g (1.89 m*M*) of **3**. Elution with ethyl ether (600 m*l*) gave 0.101g (0.408 m*M*) of white solids, identified as cis-thianthrene-5,10-dioxide (**4**), mp 283-284°C (*lit.*[8] 284-6°C); IR (KBr) 1420, 1080 ($SO_2$ stretch), 755 $cm^{-1}$; $^1$H nmr ($CDCl_3$) $\delta$ 7.67 (*m*, 4H), 8.11 (*m* 4H) UV $\lambda_{max}^{MeOH}$ 210 nm.

Elution with ethyl acetate (200 m*l*) gave 0.433g of yellow sticky materials which were extracted with ethyl ether to give 0.093g of yellow solids, identified as N-*tert*-butylacetamide hydroperchlorate (**8**)[9], mp 106.5-108°C; IR (KBr) 3200, 2960, 1600, 1100, 1080, 620 $cm^{-1}$; $^1$H nmr ($CDCl_3$) $\delta$ 1.41 (*s*, 9H), 2.29 (*s*, 3H), 8.14 (*s*, 1H), 12.86 (*s*, 1H); No UV absorption.

Elution with acetone (360 m*l*) gave 0.756 g of brown sticky materials from which 0.168 g (0.45 m*M*) of 5-acetonylthianthrenium perchlorate (**9**)[10] was obtained by washing with water.

(*c*) *Under $N_2$ Atmosphere.* To the stirred solution of 0.182 g (3.43m*M*) of **1** in 40 m*l* of acetonitrile was added 0.504 g (3.45 m*M*) of TBP. The mixture was refluxed under $N_2$ atmosphere and worked up as before. After the solvent was removed, the residue was chromatographed (1.5×15 cm). First six fractions of hexane (600 m*l*) gave 0.208 g (0.96 m*M*) of **2**, while next two fractions gave 0.006 g (0.02 m*M*) of **7**. Elution with benzene (800 m*l*) gave 0.374 g (1.61 m*M*) of **3**. First five fractions of ethyl ether (500 m*l*) gave 0.169 g (0.68 m*M*) of **4**. Next two fractions of ethyl ether (200 m*l*) gave 0.096g (0.83 m*M*) of pale yellow solids, identified as N-*tert*-butylacetamide (**10**), mp 97.5-98°C; IR (KBr) 3290, 3080, 2970, 1650, 1450, 1400, 1320 $cm^{-1}$; $^1$H nmr ($CDCl_3$) $\delta$ 1.37 (*s*, 9H, *tert*-Bu), 1.98 (*s*, 3H, Me), 5.7 (broad *s*, IH, NH); No UV absorption. Elution with ethyl acetate (200 m*l*) gave 0.195 g of yellow materials, which were consisted of inorganic perchlorates and unknown solids. Finally elution with acetone (200 m*l*) gave 0.416 g of brown sticky materials from which 0.008 g (0.02 m*M*) of **9** was obtained by the treatment with water.

(*d*) *Under Ar Atmosphere.* To the stirred solution of 1.407 g (4.47 m*M*) of **1** in 40 m*l* of acetonitrile was added 0.596 g (4.08 m*M*) of TBP. The reaction was run under Ar atmosphere and worked up as usual.

Elution with hexane (480 m*l*), followed by benzene (720 m*l*) gave 0.292 g (1.35 m*M*) of **2** and 0.489 g (2.11 m*M*) of **3**, respectively. Elution with ethyl ether (720 m*l*, 120 m*l*) gave 0.230 g (0.93 m*M*) of **4** and 0.014g (0.12 m*M*) of **10**. Ethyl acetate fractions (240 m*l*) gave 0.597 g of sticky materials which were extracted with ethyl ether to give 0.138 g of the unknown compound. Finally acetone fractions (240 m*l*) gave 0.499 g of brown solids from which 0.023 g (0.06 m*M*) of **9** was obtained by the same treatment as before.

In order to trap gaseous olefinic product, reaction vessel was connected into U tube containing $Br_2$ in $CCl_4$ and argon gas was used as a carrier gas. As reactants, **1** (1.614g, 5.12 m*M*) in 40 m*l* of acetonitrile and TBP (0.556 g, 3.81 m*M*) were used. Bromine solution turned pale yellow in 40 min. After carbon tetrachloride and excess bromine were removed using rotary evaporator, small amount of residue was obtained. $^1$H nmr ($CDCl_3$) spectrum showed two singlets at $\delta$ 1.89 and 3.81. The residue was assigned to be 1,2-dibromo-2-methylpropane. No further identification was attempted.

(*e*) *In the air at Room Temperature.* To the stirred solution of 1.188 g (3.77 m*M*) of **1** in 40 m*l* of acetonitrile was added 0.675 g (4. 62 m*M*) of TBP. The mixture was stirred at room temperature until the dark purple color of **1** disappeared completely. It took 4 days to obtain the same color of the reaction mixture as that obtained at reflux temperature. The reaction mixture was worked up as before (column, 1.5 ×12 cm). Elution with hexane (120 m*l*×6) gave 0.535 g (2.48 m*M*) of **2**, while benzene (120 m*l*×9) gave 0.231 g (1.00 m*M*) of **3**. Elution with ethyl ether (120m×5) gave 0.073 g (0.29 m*M*) of **4**. Elution continuously with ethyl ether (120 m×2) gave 0.044 g of unidentified compound. Next ethyl acetate fractions (120 m*l*×2) gave 0.476 g of yellow solids consisting of inorganic salts and unknown compounds. Finally acetone fractions (120 m*l*×2) gave 0.379 g of brown solids from which 0.015 g (0.04 m*M*) of **9** was obtained by the same treatment as before.

## Results

A mixture of TBP and **1** in acetonitrile was heated at reflux temperature for 1 h by which time dark purple color of **1** disappeared completely and dark brown solution was resulted. Consequenlty the complete color change was regarded as the end of the reaction. As described in the experimental part, reaction with TBP afforded, as isolable products, **2**, **3**, **4**, **9**, and **10** or protonated **10**. Apart from these products, **7** was isolated in some cases but in other

**TABLE 1: Summary of the Reaction of 1 with *tert*-Butyl Peroxide (TBP)**

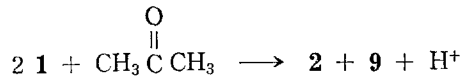
| Reactants (m$M$) | | Temp. | Reac. Atm, | Products $\left(\frac{\text{m}M}{\%\ \text{yield}}\right)$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **1** | TBP | | | **2** | **3** | **7** | **4** | **9** | Total |
| 4.77 | 4.50 | reflux | Air | 2.00 | 1.89 | 0.04 | 0.41 | 0.45 | 4.79 |
| | | | | 41.9 | 39.6 | 0.8 | 0.86 | 9.4 | 100.4 |
| 3.77 | 4.62 | r t | Air | 2.48 | 1.00 | — | 0.29 | 0.04 | 3.81 |
| | | | | 65.8 | 26.5 | — | 7.7 | 1.1 | 101.1 |
| 3.43 | 3.45 | reflux | $N_2$ | 0.96 | 1.61 | 0.02 | 0.68 | 0.02 | 3.29 |
| | | | | 28.0 | 46.9 | 0.6 | 19.8 | 0.6 | 95.9 |
| 4.47 | 4.08 | reflux | Ar | 1.35 | 2.11 | — | 0.93 | 0.02 | 4.45 |
| | | | | 30.2 | 47.2 | — | 20.8 | 1.3 | 99.6 |
| 5.12 | 3.81 | reflux | Ar | 1.27 | 2.82 | — | 0.93 | 0.02 | 5.04 |
| | | | | 24.8 | 55.1 | — | 18.2 | 0.4 | 98.4 |
| 4.79 | 4.90 | reflux | Ar | 2.08 | 1.87 | 0.02 | 0.39 | 0.25 | 4.59 |
| | | | | 43.4 | 39.0 | 0.4 | 8.1 | 5.2 | 95.8 |

cases identified only on thin layer chromatogram. Table 1 summarizses the amount of the reactants and products. Among the products, **3**, **4**, and **7** are the oxides of **2** but their formation mechanisms are not known.

## Discussion

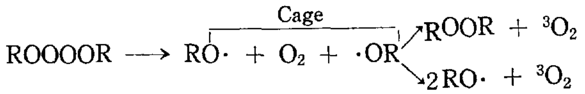
It has been well known that TBP undergoes thermal decomposition to give *tert*-butoxy radicals and a half-life of TBP at 100 C°is 218 h.[12] In spite of such a long half-life, color of **1** in acetonitrile containing TBP disappeared after 1 h refluxing or 4 days stirring at room temperature. TBP is fairly stable at room temperature. Nevertheless, disappearance of dark purple color of **1** in the presence of TBP dissolved in acetonitrile indicates that TBP reacts with **1** without forming *tert*-butoxy radical at the initial stage.

Compound **9**[10] has been reported to be the reaction product of **1** with acetone of which stoichiometry is the following.



$$2\ \mathbf{1} + \mathrm{CH_3}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{CH_3} \longrightarrow \mathbf{2} + \mathbf{9} + \mathrm{H^+}$$

Therefore, isolation of **9** of which yield is shown to be variable in each reaction suggests strongly the formation of acetone. Since *tert*-butoxy radical is unlikely to be formed from TBP at room temperature, the formation of acetone may not be due to $\alpha$-cleavage of *tert*-butoxy radical generated directly from TBP. Most probable precursor of acteone is therefore *tert*-butyl peroxy radical. Chain termination reaction of peroxy radical involves the reversible formation of a dimer; which is generally formulated as a tetroxide. This subsequently decomposes to give products, the nature of which depends on the type of peroxy radical. In the case of di-*tert*-alkyltetroxides, decomposition occurs involving 0-0 cleavage with formation of *tert*-alkoxy radicals and oxygen. The oxygen generated in this process is likely to be in the triplet ground state.[13] The *tert*-alkoxy radicals either dimerize within the solvent cage or diffuse away:



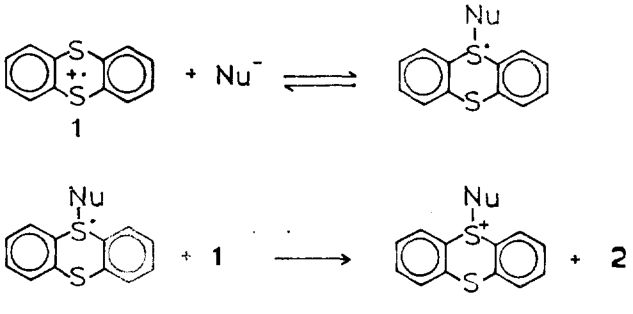
$$\mathrm{ROOOOR} \longrightarrow \overbrace{\mathrm{RO\cdot} + \mathrm{O_2} + \mathrm{\cdot OR}}^{\text{Cage}} \begin{cases} \nearrow \mathrm{ROOR} + {}^3\mathrm{O_2} \\ \searrow 2\mathrm{RO\cdot} + {}^3\mathrm{O_2} \end{cases}$$

Thus the formation of acetone can be explained by $\alpha$-cleavage of *tert*-butoxy radical generated from di-*tert*-butyl tetroxide. This explanation is supported by the findings: Table 1 shows that **4** is formed regardless of the reaction atmosphere. If triplet state of oxygen is involved, yield of **4** must increase when the reaction was carried out in the atmosphere. Likewise, decreased yield of **4** expected under the inert gas atmosphere. This is in contrast with the results although the trend of variable yield is not always consistent with the expectation. In fact, the yields of **3**, **4** and **7** are not affected by the oxygen content on the solvent. If this view is correct, two oxygen atoms of *tert*-butyl peroxy radical must originate from oxygens of TBP.

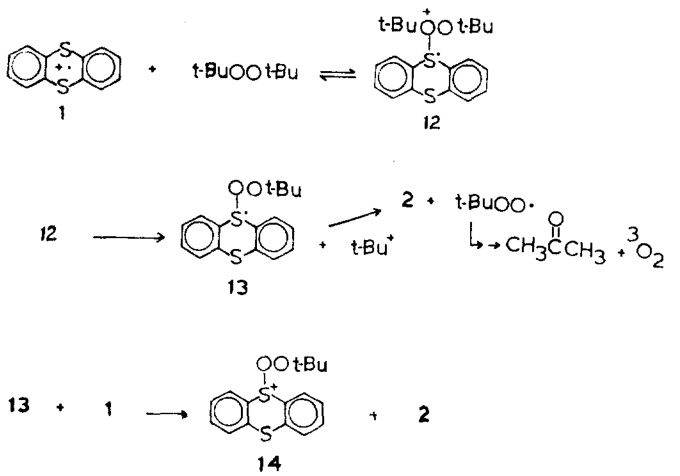
How is the *tert*-butyl peroxy radical generated ? Peroxides possessing an orbital of the donor type may interact with cationoids reagents (Lewis acids).[14] For example, TBP and iodine shows a slight shift for iodine band,[15] indicating a weakly interacting CT effect. In order to see any band shift at 546 nm, which is an absorption band of monomer of **1**, TBP was added to **1** in acetonitrile and visible spectrum was recorded. However, no band shift was observed.

Mechanism considered in various reactions of **1** with nucleophiles has been the so-called half-regeneration sequence shown in Scheme 1.[16] It has been found that this sequence describes all cases thus for studied.

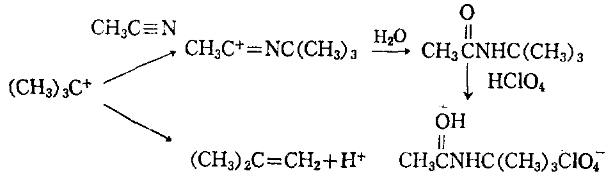
If the half-regeneration mechanism is applied to the reaction with TBP, the following scheme is obtained.



**Scheme 1**



**Scheme 2**



**Scheme 3**

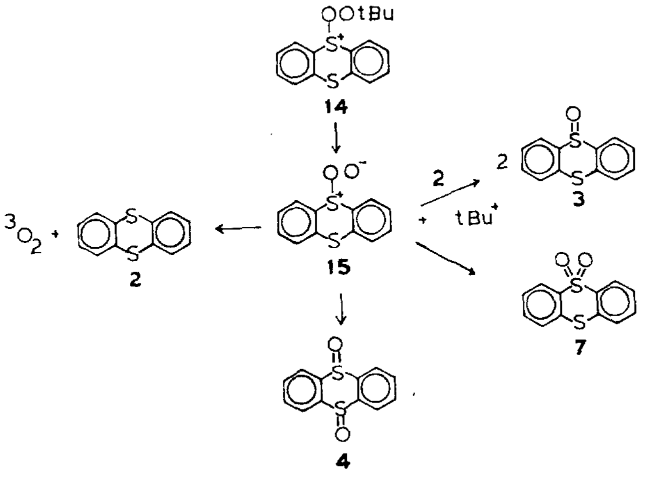
Nonbonding electrons on oxygen atoms of TBP attack **1** to give **12** which is a new cation radical. **12** either dissociates to go back to **1** and TBP or loses stable *tert*-butyl cation yielding **13** which is then oxidized by another molecule of **1** to give **14** and **2**. In the meantime, **13** seems to be unstable radical and decompose to give **2** and *tert*-butyl peroxy radical which then undergoes a sequence reaction shown in Scheme 2 to generate acetone.

The formation of *tert*-butyl cation was established by the isolation of N-*tert*-butylacetamide, its protonated form, and bromine test for isobutylene. Their formation mechanism are depicted in Scheme 3.

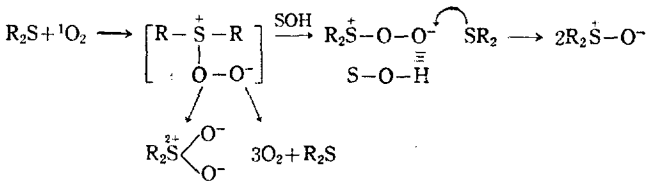
*tert*-Butyl cation is also assumed to be formed form **14** (vide infra). Table 1 shows that only **4** of the isomers is obtained from every reactions with TBP. It has been found that the isolation only **4** is due to the isomerization of *trans* form (**11**) either at room or reflux temperature under the reaction medium. So isomerization of **11** to **4** occurs not only at 200 to 300°C[8] but also under the conditions adapted in these reactions.

There has been no direct experimental evidence for the formation mechanism of *cis* and *trans* disulfoxides. However, in view of the inertness of **2** in the presence of TBP either at room or reflux temperature and the reactivity of **1** to TBP at room temperature, we prefer the involvement of persulfoxide formation from **14** to the direct reaction of peroxy radical with either **1** or **2**.

Foot *et al.*[17] suggested persulfoxide as an intermediacy of an oxidizing species for the sensitized photooxidation of alkyl sulfides. The persulfoxide undergoes different reactions depending on the solvent, the concentration of sulfide, and the reaction temperature. Their results are shown in the following.



**Scheme 4**



One interesting thing is the interpretation in which the formation of *cis*-disulfoxide from 1,4-dithiane is due to the result of trapping of the persulfoxide intramolecularly. Very similar effects are expected from **15** if **15** is formed from **14**. The following scheme 4 illustrates the formations of *tert*-butyl cation, **2**, and the oxides.

It is conceivable that the conformation of **4** may be *syn* form when it is formed but it is believed to undergo rapid inversion to more stable anti form.[18] The scheme 4 is essentially the same as those proposed for the reaction of **1** with superoxide by Ando *et al.*[19] except for the formation of **4** and **7**. We have not attempted to find the state of oxygen produced in this reaction.

*Acknowledgement.* Financial support from the Korea Science and Engineering Foundation is gratefully acknowledged.

## References

(1) Portions of this work are abstracted from M.S. Thesis of J.H Shin, SNU. 1982.
(2) K. Kim, *Proc. Coll. Natur. Sci., SUN*, **2**, 53 (1977).
(3) K. Kim and N.C. Jeong, STF-77-38 (1977).
(4) The formation of **4** has been isolated from the reaction of **1** with diethylmercury in Prof. H.J. Shine's laboratory, *J. Org. Chem*, **28**, 143 (1982).
(5) H-J. Lee and K. Kim, *Bull. Korean Chem. Soc.*, **1**, 114 (1980).
(6) D. E. McElcheran, M. H. J. Wijnen and E. W. R. Steacie, *Can. J. Chem.* **36**, 321 (1958).
(7) E. T. Kaiser and D. H. Eargle, Jr., *J. Phys. Chem.*, **69**, 2108 (1965).
(8) K. Mislow, P. Schneider and A. L. Ternay, *Jr., J. Amer. Chem. Soc.*, **86**, 2957 (1964).
(9) Infrared data of O-protonated propionamide are reported:

R. Stewart and L. J. Muenster, *Chem. and Ind.*, 1906 (1961).
(10) K. Kim, S. R. Mani and H. J. Shine, *J. Org. Chem.*, **40,** 3857 (1975).
(11) E. Bergman and M. Tschudnowshy, *Ber.*, **65,** 457 (1932).
(12) E. S. Huyser, in Free-Radical Chain Reactions, wiley-Interscience, New York, p. 287, 1970.
(13) J. A. Howard and K. U. Ingold, *J. Amer. Chem. Soc.*, **90,** 1056 (1968).
(14) K. Tokumaru and O. Simmamura, *Bull. Chem. Soc. Jap.*, **36,** 333 (1963).
(15) H. Tsubomura and R. P. Lang, *J. Amer. Chem. Soc.*, **83,** 2085 (1961).
(16) H. J. Shine, in The Chemistry of the Sulphonium Group, (Ed C. J. M. Stirling), Part 2, Chap. 14, Interscience. New York, p. 523, 1981.
(17) C. S. Foote and J. W. Peters *J. Amer. Chem. Soc.*, **93,** 3795 (1971).
(18) K. F. Purcell and J. R. Berschied, *Jr., J. Amer. Chem. Soc.*, **89,** 1579 (1967).
(19) W. Ando, Y. Kabe, S. Kobayashi, C. Takyu, A Yamagishi, and H. Inaba, *J. Amer. Chem. Soc.*, **102,** 4526 (1980).

# Synthesis of Nuclophilic Adducts of Thiols (VI). Addition of L-Cystein to $\beta,\beta$-Diethoxycarbonylstyrene Derivatives

**Tae-Rin Kim[†] and Bong Rae Cho**

*Department of Chemistry, Korea University, Seoul 132, Korea*

**Sung-Yong Choi**

*Department of Chemisty, Junju University, Junju 520, Korea*

**Won-Sik Choi**

*Department of Chemistry, Kangreung National University, Kangreung 210, Korea* (*Received March 26, 1984*)

A series of S-(2,2-diethoxycarbonyl-1-phenylethyl)-L-cysteine derivatives (10a-e) were synthesized from the reaction of $\beta,\beta$-diethoxycarbonylstyrene with L-cysteine in 1:1 aqueous methanol. Thus, S-(2,2-diethoxycarbonyl-1-phenylethyl)-L-cysteine(10a), S-[2,2-diethoxycarbonyl-1-(3′,4′-methylendioxyp) phenylethyl]-L-cysteine (10b), S-[2,2-diethoxycarbonyl-1-(3′,4′,5′-trimethoxy)phenylethyl]-L-cyseine (10c), S-[2,2-diethoxycarbonyl-1-(*p*-hydroxy) phenylethyl]-L-cysteine (10d), S-[2,2-diethoxycarbonyl-1-(*p*-methoxy) phenylethyl]-L-cysteine (10e) were obtained in moderate to excellent yields. The structure of the adducts was characterized by analytical and spectral data. The effects of pH upon the product yields were also briefly examined.

## Introduction

There have been growing interests in the synthesis of cysteinyl peptide derivatives with biological activities.[1–5] We reported the synthesis of S-(2-nitro-1-phenylethyl)-L-cysteine[6] and S-(2-nitro-1-phenylethyl)-L-glutathione derivatives.[7] In each case, the product was obtained in excellent yields from the reaction of $\beta$-nitrostyrene[8–10] with cysteine or glutathione under mild condition. The major advantage of this synthesis is that biologically important products can be obtainde in good yields by simple addition reactions without protecting the functional groups.[11–15]

In this work, we have synthesixed a series of S-(2,2-diethoxycarbonyl-1-phenylethyl)-L-cysteine derivatives from the reaction of $\beta,\beta$-diethoxycarbonylstyrene derivatives with L-cysteine. The effects of pH upon the product yields were also briefly examined.

## Experimental

*General.* Melting points were determined on a Fisher Johns melting point apparatus. Infrared spectra were obtained with a JASCO IRA-2 spectrophotometer. UV spectra were recored on a Beckman Model 26 spectrophotometer. Proton nmr spectra were obtained with a Varian Model EM-360 spectrometer in DMSO-$d_6$. Elemental analyses were conducted with MOO-1106 Model Carlo Erba, Italy. All of the reagents were commercially available and used without further purification.

*Synthesis of $\beta,\beta$-Diethoxycarbonylstyrene.* $\beta,\beta$-Diethoxycarbonylstyrene derivatives were prepared from substituted