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The Reactions of Pyridinium Bromides with Sulfenamides

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It was found that three different types of products, phenylthiomethylpyridinium bromide, ethoxy-bis(phenylthio)-methane and ethyl ethoxy-bis(phenylthio)acetate were obtained by the reactions of pyridinium bromides, such as phenacylpyridinium bromide, acetonylpyridinium bromide and ethoxycarbonylmethylpyridinium bromide, with sulfenamides in ethanol, depending on the nature of the carbonyl carbon of the starting pyridinium bromides.

Recently, it was reported that α-hydroxyimino-pyridinium bromides were obtained in good yields by the reactions of pyridinium bromides such as phenacylpyridinium bromide and acetonylpyridinium bromide with alkyl nitrite.[1] The results indicate that hydrogen atom attached to α-carbon of pyridinium bromide becomes acidic by the influence of both positively charged nitrogen atom and carbonyl group. It was also found that active methylene compounds react with sulfenamides to give mono- or di-sulfenylated products in good yields.[2]

In the present experiment, the reactions of pyridinium bromides with sulfenamides were investigated with the expectation that α-sulfenylated pyridinium bromides would be obtained as in the formation of α-hydroxyiminopyridinium bromide. When phenacylpyridinium bromide (I) was allowed to react with *N*-phenylthiophthalimide (II) in the presence of triethylamine (III) in ethanol for 2 hr, phenylthiomethylpyridinium bromide (VIII) and ethyl benzoate (VII) were obtained in quantitative and 64% yields, respectively, instead of the expected α-phenylthiophenacylpyridinium bromide. Similary, phenylthiomethylpyridinium bromide was obtained in quantitative yield by the reaction of phenacylpyridinium bromide with *N*-phenylthiosuccinimide and triethylamine or *N*,*N*-diethylbenzenesulfenamide in the absence of triethylamine.

The result indicates that pyridinium salt (VI) and ethyl benzoate are produced by way of a nucleophilic attack of ethoxide anion to carbonyl carbon of the initially formed intermediate (IV) with active carbonyl carbon induced by an electronegative phenylthio group attached to the α-carbon. The subsequent anion exchange between pyridinium salt (VI) and triethylammonium bromide (V) results in the formation of phenylthiomethylpyridinium bromide.

The reactions of acetonylpyridinium bromide with

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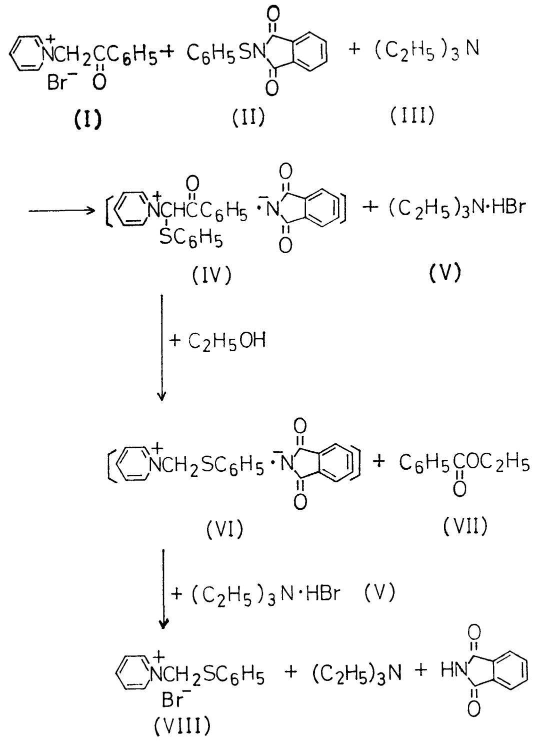
[1] T. Mukaiyama, K. Saigo, and H. Takei, This Bulletin, **44**, 190 (1971).

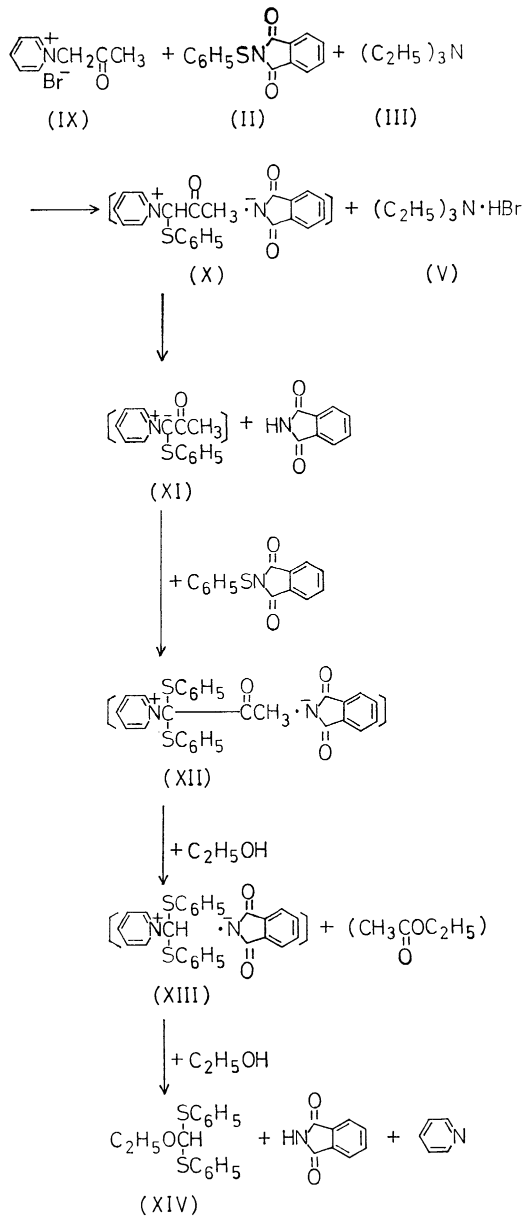
[2] T. Mukaiyama, S. Kobayashi, and T. Kumamoto, *Tetrahedron Lett.*, **1970**, 5115.



sulfenamides were tried. When an equimolar amount of acetonylpyridinium bromide (IX) was allowed to react with *N*-phenylthiophthalimide (II) and triethylamine (III), α-phenylthioacetonylpyridinium bromide could not be isolated and a tarry product resulted. On the other hand, when the same reaction was carried out in the presence of two equimolar amounts of *N*-phenylthiophthalimide, ethoxy-bis(phenylthio)methane (XIV) was obtained in 20% yield. Similarly, ethoxy-bis(phenylthio)methane (XIV) was isolated in 40% yield by the reaction of acetonylpyridinium bromide with two equimolar amounts of *N*-phenylthiosuccinimide.

This result can be explained as follows; the intermediate (X) is produced as expected from acetonylpyridinium bromide and *N*-phenylthiophthalimide. In this stage, deprotonation of X by imide anion predominates over the nucleophilic attack of ethoxide anion to the carbonyl carbon to form pyridinium ylide (XI), probably due to the slightly higher electron density of the carbonyl carbon of X in comparison with that of IV. XI reacts with another phenylthiophthalimide to give pyridinium salt (XII). The nucleophilic attack of ethoxide anion to the carbonyl carbon of XII followed by the nucleophilic attack by ethoxide anion to the α-carbon of pyridinium salt (XIII) gives ethoxy-bis(phenylthio)methane (XIV).

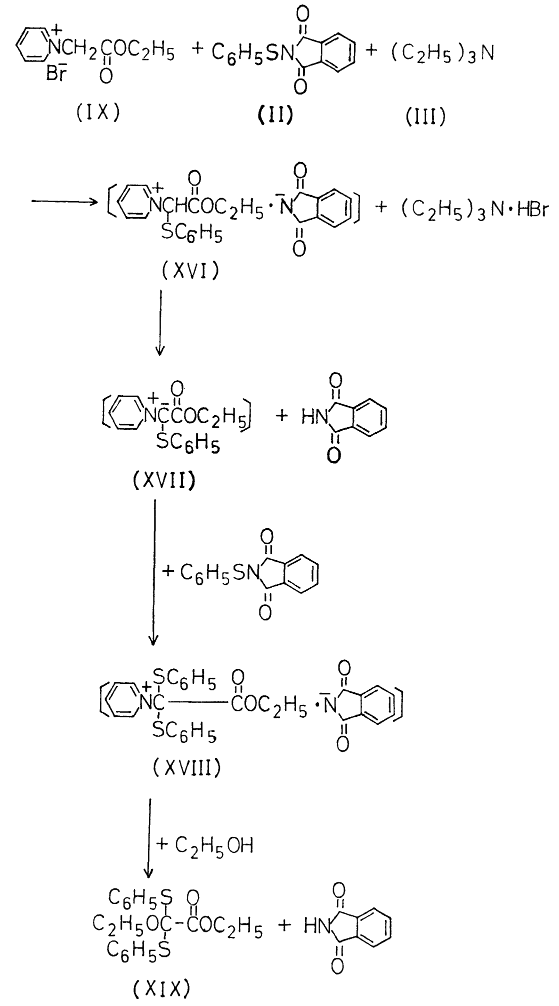
It was found that the reaction of ethoxycarbonylmethylpyridinium bromide (XV) with two equimolar amounts of *N*-phenylthiophthalimide (II) in the presence of triethylamine (III) gave ethyl ethoxy-bis(phenylthio)acetate (XIX) in 84% yield. In a similar way, ethyl ethoxy-bis(phenylthio)acetate was obtained in 77% yield by the reaction of ethoxycarbonylmethylpyridinium bromide with two equimolar amounts of *N*-phenylthiosuccinimide in the presence of triethylamine.

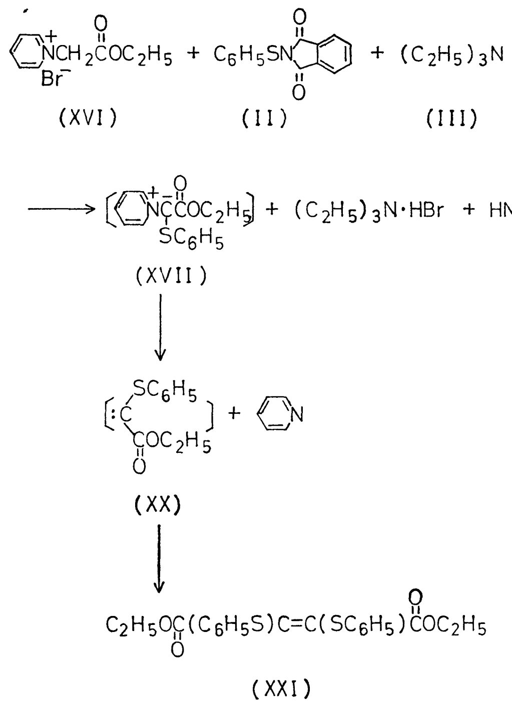


This result may be explained by considering the initial formation of intermediate (XVIII) in a similar manner to the case of the reaction of acetonylpyridinium bromide with sulfenamide. The nucleophilic displacement of ethoxide anion to the α-carbon of XVIII predominates over the nucleophilic attack to carbonyl carbon to form ethyl ethoxy-bis(phenylthio)-acetate.

The different types of products, phenylthiomethylpyridinium bromide, ethoxy-bis(phenylthio)methane and ethyl ethoxy-bis(phenylthio)acetate were obtained according to the nature of the carbonyl carbon of the starting pyridinium salts, by the reactions of phenacylpyridinium bromide, acetonylpyridinium bromide and ethoxycarbonylmethylpyridinium bromide, respectively, with sulfenamide.

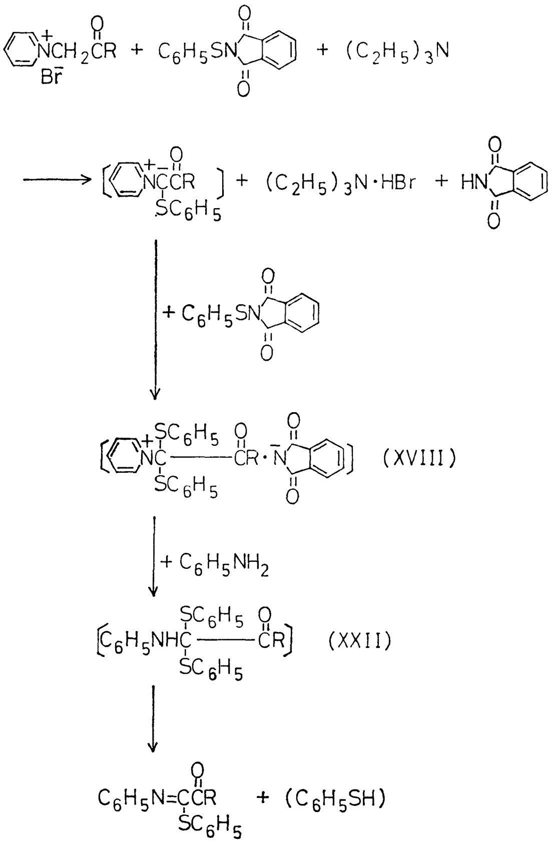
The reaction of ethoxycarbonylmethylpyridinium bromide with *N*-phenylthiophthalimide and triethylamine in dichloromethane was investigated in order





to isolate α-sulfenylated pyridinium ylide. When ethoxycarbonylmethylpyridinium bromide (XV) was allowed to react with *N*-phenylthiophthalimide (II) in the presence of triethylamine (III), 1,2-bis(ethoxycarbonyl)-1,2-bis(phenylthio)ethylene (XXI) was unexpectedly obtained in 50% yield. In contract to the above mentioned reaction at 0°C, carbene (XX) was formed by the thermal decomposition of unstable pyridinium ylide (XVII) at a temperature above 20°C. Carbene (XX) might be dimerized to form 1,2-bis(ethoxycarbonyl)-1,2-bis(phenylthio)ethylene (XXI).[3]

The reaction of ethoxycarbonylmethylpyridinium bromide, triethylamine and two equimolar amounts of *N*-phenylthiophthalimide in dichloromethane was tried with the purpose of isolating α,α-di-sulfenylated pyridinium bromide. It was found that under the above mentioned conditions, ethoxycarbonyl-bis(phenylthio)methylpyridinium salt could not be obtained but only a tarry product. When aniline was added the above mentioned reaction mixture, ethyl α-phenylimino-α-phenylthioacetate (XXIII, R=OC_2H_5) was obtained in 49% yield accompanied by the elimination of benzenethiol from the intermediate (XXII), formed by the nucleophilic displacement of aniline to the α-carbon of ethoxycarbonyl-bis(phenylthio)methylpyridinium salt (XVIII). Similarly, α-phenylimino-α-phenylthioacetophenone (XXIII, R=C_6H_5) was obtained in 48% yield by the reaction of phenacylpyridinium bromide.



Experimental

Reaction of Phenacylpyridinium Bromide with N-*Phenylthiophthalimide in the Presence of Triethylamine.* Into a solution of

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[3] The compound is assigned to a mixture of *trans* and *cis* isomers by gas-liquid phase chromatography.

phenacylpyridinium bromide (2.78 g, 0.01 mol) and *N*-phenylthiophthalimide (2.55 g, 0.01 mol) in ethanol (100 m*l*), triethylamine (1.01 g, 0.01 mol) in ethanol (10 m*l*) was added drop by drop under ice cooling and the reaction mixture was stirred for 2 hr. After removal of the solvent, a mixture of water and ether (1:1) was poured into the residue and resulting crystals, phthalimide, were filtered off. The filtrate was separated into water and ether layers. From the water layer, white crystals, phenylthiomethylpyridinium bromide (mp 121.5—123.0°C) were obtained in quantitative yield after removal of the solvent.

Found: C, 51.59; H, 4.30; N, 4.92; S, 11.20%. Calcd for $C_{12}H_{12}BrNS$: C, 51.81; H, 4.29; N, 4.96; S, 11.34%.

The ether layer was evaporated under reduced pressure to give oily residue. Distillation *in vacuo* gave ethyl benzoate (bp 88—90°C/15 mmHg), 0.96 g (64%), identified by IR spectrum.

Reaction of Acetonylpyridinium Bromide with Two Equimolar Amounts of N-*Phenylthiophthalimide in the Presence of Triethylamine.* Into a solution of acetonylpyridinium bromide (1.06 g, 0.005 mol) and *N*-phenylthiophthalimide (1.28 g, 0.005 mol) in ethanol (100 m*l*), triethylamine (0.51 g, 0.005 mol) in ethanol (10 m*l*) was added dropwise and the reaction mixture was stirred for 30 min under ice cooling. Another one mol of *N*-phenylthiophthalimide (1.28 g, 0.005 mol) was added to the reaction mixture with stirring. After a few minutes, the color of the reaction mixture changed from red brown to yellow and the precipitate of phthalimide increased in amount rapidly. The reaction mixture was stirred for additional 3 hr under ice cooling. After the solvent was evaporated under reduced pressure, the residue was extracted with ether. Removal of the ether gave oily residue. The residue was chromatographed on silica gel. Elution with benzene gave ethoxy-bis(phenylthio)methane (mp 88.0—89.5°C), 0.28 g (20%), recrystallized from cyclohexane, and identified by IR and NMR spectra.

Found: C, 65.49; H, 5.93; S, 22.98%. Calcd for $C_{15}H_{16}OS_2$: C, 65.21; H, 5.84; S, 23.16%.

Similarly, by the reaction of ethoxycarbonylmethylpyridinium bromide (1.23 g, 0.005 mol) with two equimolar amounts of *N*-phenylthiophthalimide (2.55 g, 0.01 mol) in the presence of triethylamine (0.51 g, 0.005 mol), ethyl ethoxy-bis(phenylthio)acetate was obtained, 1.47 g (84%), mp 54.0—54.5°C, identified by IR and NMR spectra.

Found: C, 61.87; H, 5.84; S, 17.88%. Calcd for $C_{18}H_{20}O_3S_2$: C, 62.02; H, 5.79; S, 18.37%.

Reaction of Ethoxycarbonylmethylpyridinium Bromide with N-*Phenylthiophthalimide in the Presence of Triethylamine in Dichloromethane.* Into a solution of ethoxycarbonylmethylpyridinium bromide (2.46 g, 0.01 mol) and *N*-phenylthiophthalimide (2.55 g, 0.01 mol) in dichloromethane (100 m*l*), triethylamine (1.01 g, 0.01 mol) in dichloromethane (10 m*l*) was added at room temperature and the reaction mixture was stirred for 3 hr. After removal of the solvent, the residue was extracted with ether. The ether layer was evaporated under reduced pressure and the resulting oily product was chromatographed on silica gel. Elution with benzene, gave 1,2-bis(ethoxycarbonyl)-1,2-bis(phenylthio)ethylene, 0.82 g (50%).

Found: C, 65.33; H, 5.96; S, 19.58%. Calcd for $C_{18}H_{20}O_2S_2$: C, 65.05; H, 6.07; S, 19.26%.

Formation of Ethyl α-Phenylimino-α-phenylthioacetate. By a similar procedure as in the formation of ethoxy-bis(phenylthio)methane, ethoxycarbonylmethylpyridinium bromide (1.23 g, 0.005 mol) was allowed to reacted with triethylamine (0.51 g, 0.005 mol) and two equimolar amounts of *N*-phenylthiophthalimide (2.55 g, 0.01 mol) in dichloromethane (100 m*l*). After stirring for 30 min under ice cooling, aniline (0.47 g, 0.005 mol) in dichloromethane (10 m*l*) was added to the reaction mixture. The solvent was evaporated under reduced pressure after stirring for additional 6 hr under ice cooling, and the residue was extracted with ether. After removal of ether, the resulting oily product was chromatographed on silica gel. Elution with benzene gave ethyl α-phenylimino-α-phenylthioacetate (mp 78—79°C), 0.70 g (49%), identified by IR and NMR spectra.

Found: C, 67.58; H, 5.54; N, 5.19; S, 11.33%. Calcd for $C_{16}H_{15}O_2NS$: C, 67.36; H, 5.30; N, 4.91; S, 11.21%.

Similarly, in the reaction of phenacylpyridinium bromide, α-phenylimino-α-phenylthioacetophenone was obtained in 48% yield, mp 75—76°C, identified by IR and NMR spectra.

Found: C, 75.40; H, 4.58; N, 4.52; S, 10.18%. Calcd for $C_{20}H_{15}ONS$: C, 75.69; H, 4.76; N, 4.41; S, 10.09%.

We thank Dr. H. Takei and Dr. T. Kumamoto for valuable discussions.