BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 190—192 (1971) [Vol. 44, No. 1

Reactions of Sulfonium and Pyridinium Salts with Alkyl Nitrite

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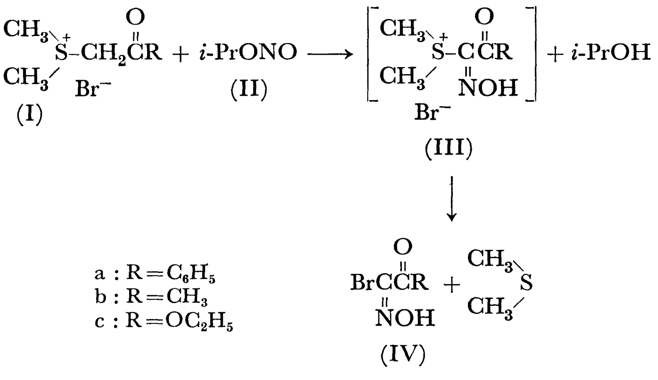
(Received July 18, 1970)

It was found that α-bromo-α-hydroxyimino compounds were obtained in good yields by the reactions of sulfonium bromides, such as dimethylphenacylsulfonium bromide, acetonyldimethylsulfonium bromide and ethoxycarbonylmethyldimethylsulfonium bromide, with isopropyl nitrite. On the other hand, (α-hydroxyiminophenacyl and -acetonyl)pyridinium bromides were obtained in quantitative yields by the reactions of pyridinium bromides, such as phenacylpyridinium bromide and acetonylpyridinium bromide, with isopropyl nitrite. Further, the reactions of α-bromo-α-hydroxyimino compound or (α-hydroxyiminophenacyl)pyridinium bromide, which were obtained by the above mentioned reactions, with several nucleophiles were studied.

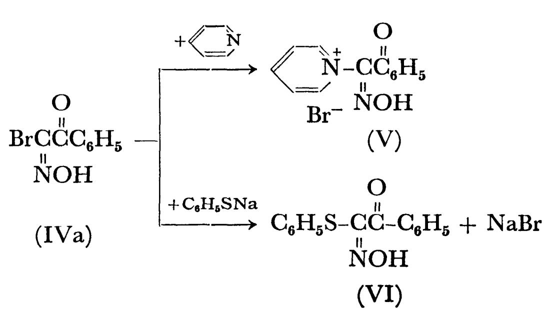
It is well known that dimethylphenacylsulfonium salt affords the corresponding stable ylide by treatment with alkali. The result indicates that hydrogen atom attached to α-carbon of the sulfonium salt becomes acidic by the influence of both positively charged sulfur atom and carbonyl group.

In the present experiment, the reactions of sulfonium salts with alkyl nitrite were tried in order to prepare hydroxyimino derivatives of the sulfonium compounds and to examine their reactions. When a mixture of phenacylsulfonium bromide (Ia) and isopropyl nitrite (II) in dichloromethane was stirred at room temperature, evolution of dimethyl sulfide was observed. After removal of the solvent, α-bromo-α-hydroxyiminoacetophenone (IVa) (93%) was unexpectedly obtained. It was identified by mixed melting point with authentic sample.[1] This result shows that the reaction proceeds by eliminating dimethyl sulfide from the initially formed α-hydroxyiminosulfonium salt by an intramolecular nucleophilic displacement with bromide ion. Similarly, α-bromo-α-hydroxyiminoacetone (IVb) and ethyl α-bromo-α-hydroxyiminoacetate (IVc) were obtained in quantitative yields from the reactions of the corresponding sulfonium salts, acetonyldimethylsulfonium bromide (Ib) and ethoxycarbonylmethyldimethylsulfonium bromide (Ic), with isopropyl nitrite. According to this method, α-bromo-α-hydroxyimino compounds can be prepared in higher yields than the previous methods.[1–3] Whereas, the reaction of benzyldimethylsulfonium bromide with isopropyl nitrite could not be observed and the starting materials were recovered quantitatively.



Then, the same reactions by the use of sulfonium tetrafluoroborates were tried with the expectation that the nucleophilic displacement by tetrafluoroborate anion at α-carbon of the sulfonium salts would be obstructed because of its lower nucleophilicity. But, α-hydroxyiminosulfonium tetrafluoroborates could not be obtained by the reactions of the sulfonium tetrafluoroborates, such as dimethylphenacylsulfonium tetrafluoroborate, ethoxycarbonylmethyldimethylsulfonium tetrafluoroborate and benzyldimethylsulfonium tetrafluoroborate, with isopropyl nitrite and the starting materials were recovered quantitatively.

Next, the several reactions[4] of α-bromo-α-hydroxyiminoacetophenone (IVa), produced by the above mentioned reaction, with some nucleophiles were investigated. When pyridine was added to a solution of α-bromo-α-hydroxyiminoacetophenone (IVa) in ether at room temperature, (α-hydroxyiminophenacyl)pyridinium bromide (V) precipitated readily in a quantitative yield. Similarly, when a solution of sodium thiophenolate in ethanol was added to a solution of α-bromo-α-hydroxyiminoacetophenone (IVa) in ethanol at 0°C, the yellow crystals, α-hydroxyimino-α-phenylthioacetophenone (VI), was obtained in an almost quantitative yield after removal of the solvent under reduced pressure.



On the other hand, it was found that dibenzoylfuroxane (VIII) was obtained in 48% yield by treating α-bromo-α-hydroxyiminoacetophenone (IVa) with an equimolar amount of triethylamine in ether. This result indicates that benzoyl cyanide *N*-oxide (VII) is formed as an intermediate by the elimination of hydrogen bromide from α-bromo-α-hydroxyiminoaceto-

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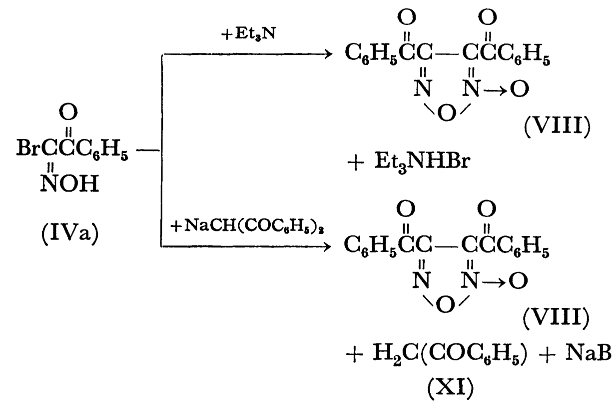
[1] G. C. Singhal and M. M. Bokadia, *J. Indian. Chem. Soc.*, **35**, 893 (1958).

[2] G. C. Singhal and M. M. Bokadia, *ibid.*, **35**, 898 (1958).

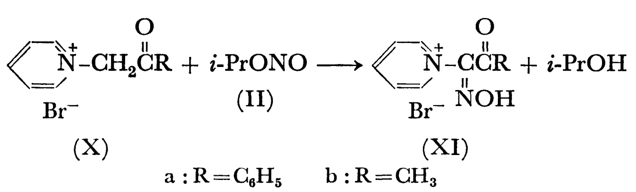
[3] M. Z. Jowitschitsch, *Ber.*, **39**, 785 (1906).

[4] There has been recently reported by Dornow that α-anilino-α-hydroxyiminoacetophenone was obtained in good yield by the reaction of α-bromo-α-hydroxyiminoacetophenone with aniline. A. Dornow and W. Sassenberg, *Ann. Chem.*, **594**, 185 (1955).

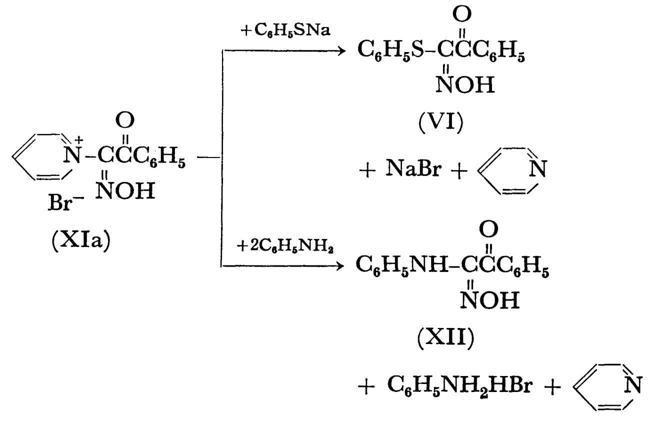
phenone when it is treated with base. Similarly, by the reaction of α-bromo-α-hydroxyiminoacetophenone (IVa) with sodium salt of dibenzoylmethane, dibenzoylfuroxane (VIII) and dibenzoylmethane (IX) were obtained in 62% and 90% yields. In this reaction, sodium salt of dibenzoylmethane behaved as a base to accept hydrogen bromide from α-bromo-α-hydroxyiminoacetophenone instead of a nucleophilic reagent.



Next, the reactions of pyridinium bromides with isopropyl nitrite were tried with the expectation that the nucleophilic displacement by bromide ion at α-carbon of pyridinium salt would not occur because of the lower activity of α-carbon of the pyridinium salts than that of the sulfonium salts described before. When a mixture of phenacylpyridinium bromide (Xa) and isopropyl nitrite (II) in ethanol was allowed to stand at room temperature, the crystalline, (α-hydroxyiminophenacyl)pyridinium bromide (XIa) was obtained in a quantitative yield. Similarly (α-hydroxyiminoacetonyl)pyridinium bromide (XIb) was quantitatively obtained by the reaction of acetonylpyridinium bromide (Xb) with isopropyl nitrite (II). They were identified by the IR spectra and the elemental analyses. Whereas, ethoxycarbonylhydroxyiminomethylpyridinium bromide could not be isolated by the reaction of ethoxycarbonylmethylpyridinium bromide with isopropyl nitrite and the starting materials were recovered quantitatively.



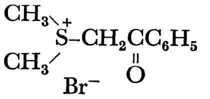
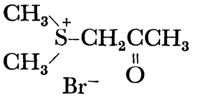
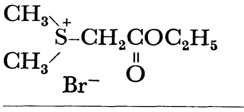
Then, the reactions of (α-hydroxyiminophenacyl)-pyridinium bromide, produced by the above mentioned reaction, with nucleophilic reagents were investigated. When a mixture of (α-hydroxyiminophenacyl)pyridinium bromide (XIa) and sodium thiophenolate in ethanol was allowed to stand at room temperature, α-hydroxyimino-α-phenylthioacetophenone (VI) was obtained in 71% yield. This was identical with that prepared by the reaction of α-bromo-α-hydroxyiminoacetophenone and sodium thiophenolate. Similarly, α-anilino-α-hydroxyiminoacetophenone (XII) was produced in 65% yield by the reaction of (α-hydroxyiminophenacyl)-pyridinium bromide (XIa) with two equimolar amounts of aniline in ethanol at room temperature. These reactions indicate that pyridine can be easily eliminated from the pyridinium salt by the nucleophilic displacement of the nucleophiles, such as aniline and sodium thiophenolate.



Experimental

Reaction of Dimethylphenacylsulfonium Bromide with Isopropyl Nitrite. A mixture of dimethylphenacylsulfonium bromide (1.31 g, 0.005 mol) and excess isopropyl nitrite (0.89 g, 0.01 mol) was stirred in dichloromethane (100 m*l*) for 12 hr at room temperature. The evolution of dimethyl sulfide was observed by its characteristic odor accompanied with disappearance of the crystals of the sulfonium salt. Evaporation of the solvent under reduced pressure gave white crystals, α-bromo-α-hydroxyiminoacetophenone (mp 138—139°C), 1.07 g (93%), recrystallized from cyclohexane. Similarly, various α-bromo-α-hydroxyimino compounds were obtained by the reactions of sulfonium bromides with isopropyl nitrite. The results are listed in Table 1. The α-bromo-α-hydroxyimino compounds were identified by their IR spectra and elemental analyses.

Table 1. The reaction of sulfonium bromides with isopropyl nitrite

Sulfonium bromide	Reaction time	Solvent	Yield	Mp, °C
 $\overset{CH_3\diagdown +}{\underset{CH_3\diagup\ Br^-}{S}}\text{-}CH_2\underset{\underset{O}{\|}}{C}C_6H_5$	12 hr	CH_2Cl_2	93%	138—139
 $\overset{CH_3\diagdown +}{\underset{CH_3\diagup\ Br^-}{S}}\text{-}CH_2\underset{\underset{O}{\|}}{C}CH_3$	1 day	CH_2Cl_2	quant.	119—120
 $\overset{CH_3\diagdown +}{\underset{CH_3\diagup\ Br^-}{S}}\text{-}CH_2\underset{\underset{O}{\|}}{C}OC_2H_5$	1 day	CH_2Cl_2	quant.	92—93

Reaction of α-Bromo-α-hydroxyiminoacetophenone with Pyridine. Into a solution of α-bromo-α-hydroxyiminoacetophenone (0.43 g, 0.0019 mol) in ether (50 m*l*), a solution of pyridine (0.15 g, 0.0019 mol) in ether (10 m*l*) was added drop by drop with stirring. After stirring for 30 min at room temperature, white precipitate deposited. The precipitate was collected by filtration and recrystallized from ethanol to give (α-hydroxyiminophenacyl)pyridinium bromide (mp 143.5°C (dec.)) in a quantitative yield.

Found: C, 51.07; H, 3.36; N, 9.31%. Calcd for $C_{13}H_{11}BrN_2O_2$: C, 50.83; H, 3.61; N, 9.12%.

Reaction of α-Bromo-α-hydroxyiminoacetophenone with Sodium Thiophenolate. A solution of sodium thiophenolate (0.66 g, 0.005 mol) in ethanol (50 m*l*) was added dropwise to a solution of α-bromo-α-hydroxyiminoacetophenone (1.14 g, 0.005 mol) in ethanol (50 m*l*) with stirring. After stirring for 12 hr at room temperature, solvent was evaporated. The residue was washed with water (100 m*l*) and extracted with ether (100 m*l*). Then, the solvent was evaporated under reduced pressure to give yellow crystals. Recrystallization from cyclohexane gave α-hydroxyimino-α-phenylthioacetophenone (mp 110—111°C) in an almost quantitative yield.

Found: C, 65.49; H, 4.56; N, 5.35; S, 12.20%. Calcd for $C_{14}H_{11}NO_2S$: C, 65.36; H, 4.31; N, 5.45; S, 12.44%.

Reaction of α-Bromo-α-hydroxyiminoacetophenone with Triethylamine. Into a solution of α-bromo-α-hydroxyiminoacetophenone (1.12 g, 0.005 mol) in ether (50 m*l*), an equimolar amount of triethylamine was added with stirring. The reaction mixture was stirred for 1 day at room temperature. After removal of the solvent, the residue was chromatographed on silica gel and elution with benzene gave dibenzoylfuroxane (mp 86—87°C, 48%).

Found: C, 65.51; H, 3.25; N, 9.27%. Calcd for $C_{16}H_{10}N_2O_4$: C, 65.30; H, 3.43; N, 9.52%.

Reaction of Phenacylpyridinium Bromide with Isopropyl Nitrite. A mixture of phenacylpyridinium bromide (2.78 g, 0.01 mol) and excess amount of isopropyl nitrite (1.78 g, 0.02 mol) in ethanol (50 m*l*) was stirred for 1 day at room temperature. After removal of the solvent, white crystals were obtained. Recrystallization from ethanol gave (α-hydroxyiminophenacyl)pyridinium bromide (mp 143.5°C (dec.)) in a quantitative yield. By a similar procedure, (α-hydroxyiminoacetonyl)-pyridinium bromide (mp 73.5—74.0°C) was obtained quantitatively.

Found: C, 39.48; H, 3.59; N, 11.36%. Calcd for $C_8H_9BrN_2O_2$: C, 39.20; H, 3.70; N, 11.43%.

Reaction of (α-Hydroxyiminophenacyl)pyridinium Bromide with Sodium Thiophenolate. To a suspension of (α-hydroxyiminophenacyl)pyridinium bromide (3.07 g, 0.01 mol) in ethanol (50 m*l*), a solution of sodium thiophenolate (1.32 g, 0.01 mol) in ethanol (20 m*l*) was added with stirring. After stirring for 12 hr, crystals of (α-hydroxyiminophenacyl)pyridinium bromide disappeared. The residue was chromatographed on silica gel after removal of the solvent under reduced pressure, and elution with dichloromethane gave yellow crystals, α-hydroxyimino-α-phenylthioacetophenone (mp 110—111°C), 1.82 g (71%).

Reaction of (α-Hydroxyiminophenacyl)pyridinium Bromide with Aniline. A mixture of (α-hydroxyiminophenacyl)pyridinium bromide (3.07 g, 0.01 mol) and two equimolar amounts of aniline (1.86 g, 0.02 mol) in ethanol (100 m*l*) was stirred for 5 days at room temperature. After removal of the solvent, the residue was washed with water (50 m*l*) and extracted with ether (50 m*l*). Then, the solvent was evaporated and crystalline solid of α-anilino-α-hydroxyiminoacetophenone (mp 145.0—146.5°C) was obtained in 65% yield after removal of the solvent under reduced pressure.