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Communications

Reaction of 1-Bromo-1-Nitropropane and Trimethyl Phosphite

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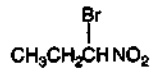
There have been reports on the reactions of α-halonitroalkanes with trialkyl phosphites.[1-3] Allen reported that trialkyl phosphites reacted with α-halonitroalkanes to form alkyl halides and oxime esters of the corresponding pentavalent phosphorus acids.[1] Stirling *et al.* reported that triethyl phosphite, on reaction with bromonitromethane, gave triethyl phosphate and hydrogen cyanide.[2] On the other hand, Donnelly *et al.* found that α-bromophenylnitromethane reacted with two molar equivalents of triethyl phosphite at 0 °C to afford benzonitrile as the major product, together with phenylnitromethane, ethyl bromide, and triethyl phosphate.[3] These earlier results on the reaction of α-halonitroalkanes with trialkyl phosphites are neither conclusive nor consistent. Therefore, we reinvestigated the reaction of α-bromonitroalkanes with trimethyl phosphite.

1-Bromonitropropane (**1**) was prepared by the reaction of the potassium salt of 1-nitropropane with bromine.[4] Reaction of compound **1** with 2.2 molar equivalents of trimethyl phosphite in chloroform at room temperature afforded a mixture of E- and Z-isomers of 1-(dimethylphosphonyl)propanal oxime (**2**)[5] in 58% yield[6] and trimethyl phosphate as well. NMR and IR spectral data indicated that the product was neither 1-(dimethylphosphonyl)-1-nitropropane nor 1-(dimethylphosphonyl)propanenitronic acid. IR spectrum of compound **2** showed a broad intense OH absorption near 3200 cm^{-1} and a C=N absorption at 1630 cm^{-1}. ^1H NMR spectrum of **2** showed a broad singlet at 9.54 ppm owing to a hydroxy proton. ^{13}C NMR spectrum of **2** showed a doublet at 153.9 ppm ($J_{P,C}$=212.0 Hz) for the major isomer and at 151.8 ppm ($J_{P,C}$=149.9 Hz) for the minor isomer attributable to the carbon of C=N. ^{31}P NMR spectrum of **2** showed a multiplet at 29.81 ppm owing to pentavalent phosphorus.

^{13}C NMR spectrum of compound **2** clearly indicated that



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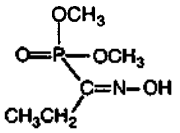
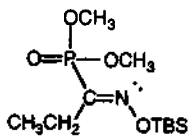
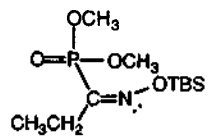


2

it was the mixture of E- and Z-isomers although they could not be separated. This E- and Z-isomerism is one of the evidences that the product is not a phosphonylpropanenitronic acid of which NMR spectral data would be quite similar with those of oxime **2**. For further identification of **2**, it was transformed into silylated derivative **3**. Silylation of compound **2** with *t*-butyldimethylsilyl (TBS) chloride in the presence of DBU at 0 °C in methylene chloride gave stable O-silyl oxime **3** in 90% yield. ^1H and ^{13}C NMR spectra clearly showed that it was a mixture of E- and Z-isomers. The ratio of E/Z was determined by NMR and HPLC and found

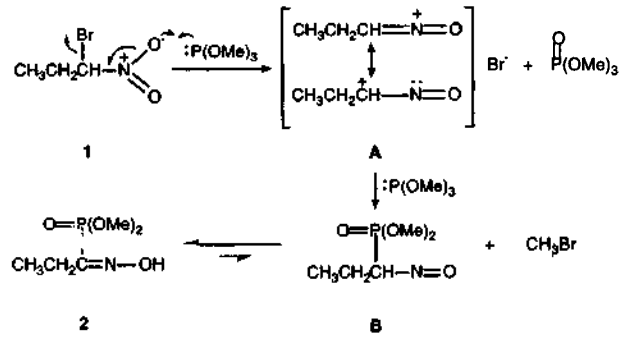


3a



3b

to be 4 : 1. Solvent change did not affect substantially the E/Z ratio but base was critical in the yield of O-silyl oxime. The reaction did not occur with pyridine and the yield of **3** was very low with triethylamine while LDA in THF at − 78 °C gave the almost same result as DBU in THF at room temperature. No appreciable isomerization between two isomers occurred in solution or in neat at room temperature although very slow decomposition of both isomers was ob-



Scheme 1.

served. Isolation of E-isomer **3a** and Z-isomer **3b** was achieved by careful repeated flash column chromatography.[7] Assignment of E- and Z-isomers, **3a** and **3b** were made on the basis of ^{1}H-^{1}H 2D NOESY NMR spectra: NOE's were observed between methyl protons of TBS group and C-3 methyl protons in **3a** and between *t*-butyl protons of TBS group and methoxy protons of phosphonyl group in **3b**. The result of microanalysis of compounds **3a** and **3b** and the existence of E- and Z-isomerism of **3** definitely prove that the product of the present reaction is oxime **2** but not the nitronic acid because it has been well estabilished that silyl nitronates do not show E- and Z-isomerism.[8,9]

The plausible mechanism for the present reaction can be suggested as shown in Scheme 1. Deoxygenation of nitro group by trimethyl phosphite and concurrent elimination of bromide in compound **1** in the first step might produce an intermediate **A** and trimethyl phosphate. Additon of another trimethyl phosphite to **A** and the subsequent displacement of methyl group in the resultant phosphonium salt by bromide would give α-phosphonylnitroso compound **B**, which might readily tautomerize to more stable conjugate oxime **2**. One might argue that Arbuzov reaction occurs in the first step and the resulting α-phosphonylnitropropane is deoxygenated by trimethyl phosphite in the second step or that the deoxygenation of the nitro group by trimethyl phosphite occurs in the first step without elimination of bromide and Arbuzov reaction follows in the second step. However, the deoxygenation of aliphatic nitro compounds by trialkyl phosphites is not known. Moreover, 1-(phenylsulfonyl)-1-nitroethane, which we prepared as a model compound for the hypothetical intermediate, α-phosphonylnitropropane, did not react with trimethyl phosphite at all. Reaction of 1-bromo-1-nitroethane and 1-bromo-3-methyl-1-nitrobutane with trimethyl phosphite also provided 1-(dimehtylphophonyl)ethanal oxime in 55% yield and 1-(dimethylphosphonyl)-3-methylbutanal oxime in 48% yield, respectively. We are currently pursuing the asymmetric reduction of the phosphonylalkane oximes and their TBS ethers in order to prepare α-aminophosphonic acids.

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5. Compound **2**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.16 (t, *J*= 7.8 Hz, 3H), 2.40-2.54 (m, 2H), 3.81 (d, $3J_{P,H}$=11.5 Hz, 6H), 9.54 (brs, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 10.2 (minor isomer), 11.9 (major isomer), 19.8 (d, $J_{P,C}$=16.4 Hz, minor), 26.6 (d, $J_{P,C}$=18.6 Hz, major), 53.0 (d, $J_{P,C}$= 6.1 Hz, minor), 53.4 (d, $J_{P,C}$=6.1 Hz, major), 151.8 (d, $J_{P,C}$=149.9 Hz, minor), 153.9 (d, $J_{P,C}$=212.0 Hz, major); IR (neat) 3200, 1650 cm^{-1}; HRMS calcd for $C_5H_{12}NO_4P$ 181.050396, found 181.050541.
6. Less than two equivalents of trimethyl phosphite gave the same product but with lower yield. The ratio of E- and Z-isomers was varied with the reaction conditions and each isomer could not be separated as a pure form because of the rapid isomerization during chromatography. Although the HPLC yield reached 80%, the isolated yield was only 58% maybe because of the partial decomposition of the product during purification.
7. Compound **3a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.18 (s, 6H), 0.93 (s, 9H), 1.12 (t, *J*=7.6 Hz, 3H), 2.48-2.60 (m, 2H), 3.79 (d, $J_{P,H}$=11.1 Hz, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.6, 10.1, 17.9, 20.2 (d, $J_{P,C}$=16.2 Hz), 25.7, 53.3 (d, $J_{P,C}$=6.3 Hz), 160.4 (d, $J_{P,C}$=206 Hz); Anal. calcd for $C_{11}H_{26}NO_5PSi$: C, 42.44; H, 8.36; N, 4.50 found C, 44.25; H, 8.56; N, 4.58.
Compound **3b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 6H), 0.96 (s, 9H), 1.15 (t, *J*=7.4 Hz, 3H), 2.45-2.54 (m, 2H), 3.78 (d, $J_{P,H}$=11.5 Hz, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.3, 11.5, 18.4, 26.0, 26.8 (d, $J_{P,C}$=18.0 Hz), 52.8 (d, $J_{P,C}$=6.3 Hz), 158.0 (d, $J_{P,C}$=153 Hz); Anal. calcd for $C_{11}H_{26}NO_5PSi$: C, 42.44; H, 8.36; N, 4.50 found C, 43.39; H, 8.77; N, 4.63.
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