Synthesis of Triphenylphosphinbenzylimines by Deprotonation of Benzylaminotriphenylphosphonium Bromides: A Key Step for Preparation of Diphenyl *N*-Benzyl Ketenimines

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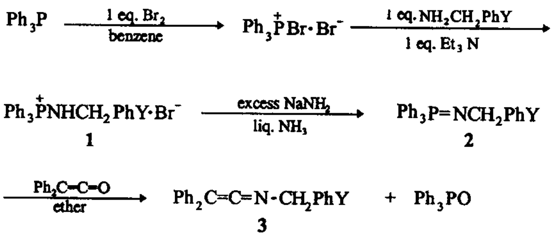
The thermal isomerizations of the ketenimines to the corresponding nitriles have been studied in recent years.[2] We employed $NaNH_2$/liq.NH_3 for the deprotonation of **1** leading to formation of **2** (Scheme 1). The reaction time was drastically reduced and the yield was improved.

Several alkylaminotriphenylphosphonium bromides[3] were prepared by addition of a primary amine and triethylamine to triphenylphosphine dibromide (refer to Table 1 of reference 3 for the yields and m.p.'s). The deprotonation of the phosphonium bromides was then achieved with $NaNH_2$/liq. NH_3. The yields ($\geq$ 93.0%) and m.p.'s of triphenyl-phosphinalkylimines[3] were tabulated. Benzylaminotriphenylphosphonium bromides[4] were also similarly[3] derived from triphenylphosphine dibromide. However the foregoing phosphonium bromides[4] underwent deprotonations by KOH/ether for 20-40 h at room temperature with yields in excess of 75% (refer to Table 1 of reference 4 for m.p.'s and NMR data of the benzylaminotriphenylphosphonium bromides and corresponding imines). In our own hand, **1** has been deprotonated at −78 °C by $NaNH_2$/liq. NH_3 to yield **2** for 2-4 h in excellent yields ($\geq$ 90%). Transformation of **2** into **3** followed the previous method[4] with better yields (70-80%). Table 1 contains m.p.'s and NMR data of **1** and **2**. In summary, we have discovered a mild reaction condition for synthesis of **2** with much shorter reaction time and improved yields.

Experimental

Materials and Method. All the reagents were purchased from the major suppliers. Liquids were distilled with center-cut collections and solids were recrystallized according to standard procedures[5] when necessary. A Varian Gemini 2000 NMR spectrometer was used for identification of the compounds.

Procedure for Conversion of 1 to 2. Dry powder of **1** (0.05 mol) was slowly added to a solution of liq. NH_3 (100 mL) containing $NaNH_2$ (0.05 mol) and the mixture was stirred for 2-4 h at −78 °C. After evaporation of NH_3, **2** was extracted with anhydrous ether. The evaporation of ethereal solution yielded crude **2**, which was recrystallized from cyclohexane.



(Y: *p*-Br, *p*-Cl, *p*-OCH_3, *m*-F, *m*-Cl, *p*-CH_3, *p*-F, H, *m*-OCH_3, *m*-CH_3, and *m*-Br)

Scheme 1. Preparation of diphenyl *N*-benzyl ketenimines.

Table 1. Properties of benzylaminotriphenylphosphonium bromides **1** and triphenylphosphinbenzylimines **2**

Y	$Ph_3{}^+PNHCH_2PhY\cdot Br^-$ [a]		Ph_3=P=NCH_2PhY [b]	
	m.p., °C	NMR ($CDCl_3$, δ)	m.p., °C	NMR ($CDCl_3$, δ)
p-Br	185-187	8.7(br, 1H) 7.1-7.8(m, 19H) 4.3(dd, 2H)	78-80	- 7.1-7.8(m, 19H) 4.3(d, 2H)
p-Cl	183-185	8.7(br, 1H) 7.1-7.8(m, 19H) 4.3(dd, 2H)	79-81	- 7.2-7.7(m, 19H) 4.3(d, 2H)
p-OCH_3	135-137	3.7 (s, 3H) 8.7(br, 1H) 7.0-7.8(m, 19H) 4.3(dd, 2H)	82-84	3.8(s, 3H) 7.1-7.8(m, 19H) 4.3(d, 2H)
m-F	169-170	8.9(br, 1H) 7.1-7.8(m, 19H) 4.3(dd, 2H)	81-83	- 7.1-7.7(m, 19H) 4.4(d, 2H)
m-Cl	138-140	8.8(br, 1H) 6.8-7.8(m, 19H) 4.3(dd, 2H)	78-79	- 7.0-7.8(m, 19H) 4.3(d, 2H)
p-CH_3	189-190	2.2 (s, 3H) 8.6(br, 1H) 6.9-7.8(m, 19H) 4.2(dd, 2H)	79-80	2.3(s, 3H) 7.1-7.8(m, 19H) 4.4(d, 2H)
p-F	167-168	8.7(br, 1H) 7.1-7.8(m, 19H) 4.3(dd, 2H)	81-83	- 7.1-7.7(m, 19H) 4.3(d, 2H)
H	195-197	8.6(br, 1H) 7.1-7.8(m, 20H) 4.3(dd, 2H)	137-138	- 7.1-7.8(m, 20H) 4.4(d, 2H)
m-OCH_3	139-140	3.7 (s, 3H) 8.7(br, 1H) 6.9-7.8(m, 19H) 4.3(dd, 2H)	81-83	3.8(s, 3H) 6.6-7.8(m, 19H) 4.4(d, 2H)
m-CH_3	140-142	2.2 (s, 3H) 8.7(br, 1H) 6.9-7.8(m, 19H) 4.2(dd, 2H)	84-86	2.3(s, 3H) 6.9-7.7(m, 19H) 4.3(d, 2H)
m-Br	142-144	8.7(br, 1H) 7.1-7.8(m, 19H) 4.3(dd, 2H)	98-100	- 7.0-7.8(m, 19H) 4.3(d, 2H)

[a] The yield is more than 95%. [b] The yield is over 90%.

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Tautomeric and *Ab initio* Studies of 3-Amino-4*H*-1,2,4-oxadiazolin-5-one

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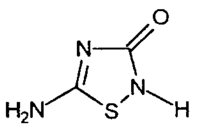
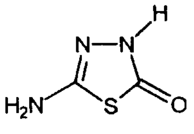
We have recently reported on the synthesis and tautomeric behavior of 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**)[1-5] and 5-amino-3*H*-1,3,4-thiadiazolin-2-one (**2**)[1,6] within the framework of our systematic studies of biologically active analogs of pyrimidines and their derivatives. Compound **1** is an analog of cytosine, in which the C=C bond of cytosine is replaced with sulfur. The analogy of the C=C bond in heterocyclic benzenoids (cytosine) and either the divalent sulfur or oxygen in their sulfur (oxygen) containing counterparts is well-known, both in benzenoid and also in heterocyclic chemistry. Compound **2** is an isomer of 5-amino-2*H*-1,2,4-thiadiazolin-3-one. Thus, compounds **1** and **2** can exist in equilibria of four possible tautomeric forms, as can cytosine. In order to understand their reactivity, it is necessary to determine the stable tautomeric structure. Particularly in biologically active compounds, investigation of the relative stability of tautomers is important in structure-biological activity relationship studies.



1

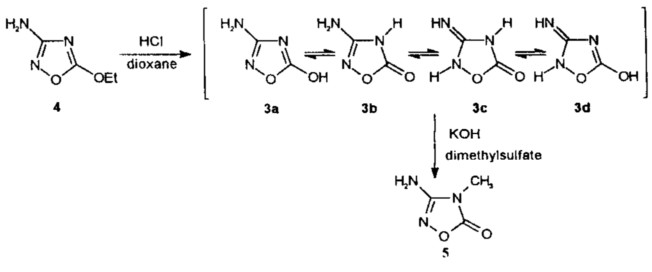


2

The spectroscopic study (^{13}C and ^{1}H nmr and ir) and theoretical calculations supported that compound **1**[4] and 5-acylamino-2*H*-1,2,4-thiadiazolin-3-ones[3] exist as lactam forms in solution. Compound **2**[7,8] and 5-acylamino-3*H*-1,3,4-thiadiazolin-2-ones[6] also exist as lactam forms, on the basis of ir, ^{13}C, ^{15}N and ^{1}H NMR[6-8] and theoretical calculations.[6] As an extension of these studies, we report our study of the tautomerism of 3-amino-4*H*-1,2,4-oxadiazolin-5-one (**3**) through spectroscopic investigation and theoretical calculations. By replacement of sulfur with oxygen, compound **3** is an analog of compound **1**. The study of 3-amino-4*H*-1,2,4-oxadiazolin-5-one only dealt with synthesis,[9] not with its structure and reactivity. Thus, we promptly studied the tautomeric structure of **3**.

3-Amino-4*H*-1,2,4-oxadiazolin-5-one (**3**) was obtained by cleavage of the ethyl group in 3-amino-5-ethoxy-1,2,4-oxadiazole (**4**)[9] with dioxane-hydrochloric acid, as shown in Scheme **1**. The melting point of **3** is higher than the reported value[9] by 15 °C, however, the spectroscopic results are identical with those previously reported.[9] In addition, the elemental analyses matched the theoretical values. The synthesis of **4** was achieved by following the reported procedure.[9] It was confirmed by comparing the melting point and spectroscopic results with those in the literature.[9] These, along with the elemental analyses, matched the theoretical values.

3-Amino-4*H*-1,2,4-oxadiazolin-5-one (**3**) can theoretically exist in four tautomeric forms, **3a-d**. The stable tautomeric form was determined by spectroscopic methods. The spectroscopic results are shown in Scheme 2. The ratio of peak areas between 6.22 and 11.39 ppm (2 : 1) in the ^{1}H NMR spectrum indicates that **3** exists as either the lactam or the lactim, among the four possible tautomers. In the ir, a strong diagnostic carbonyl band and the typical stretching bands of the amino group appeared at 1760 cm^{-1}, 3400 and 3250 cm^{-1} respectively. These data imply that **3** exists as the lactam form.



Scheme 1. Synthesis of 3-amino-4*H*-1,2,4-oxadiazolin-5-one and derivative.