

# 1,3-Dipolar Cycloaddition Reactions of Pyridinium Azomethine Ylides Containing 5,6-Dicyanopyrazines

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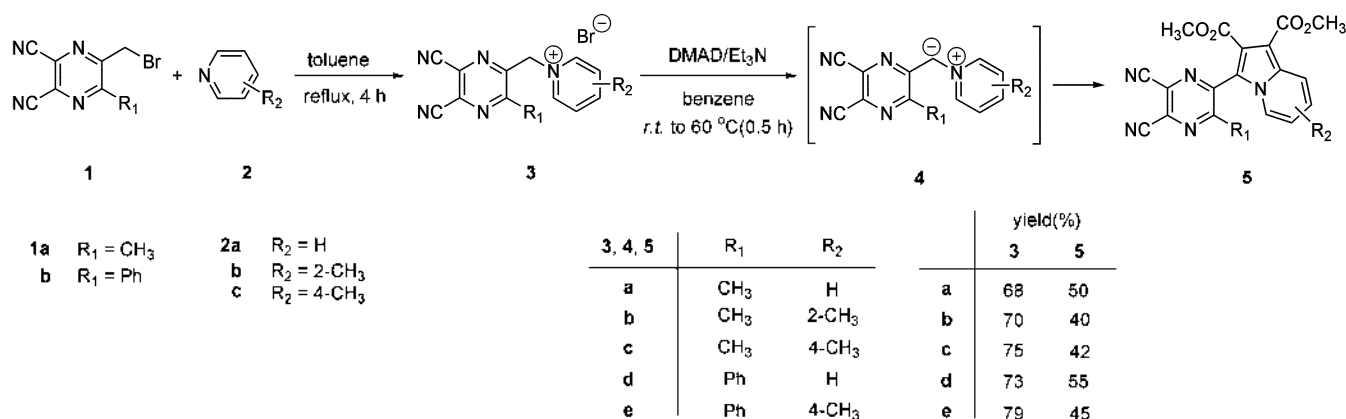
The intermolecular 1,3-dipolar cycloaddition reaction of azomethine ylides with carbon-carbon double or triple bonds represents an efficient and convergent method for the construction of heterocyclic structures containing a single nitrogen atom.<sup>1</sup> One of the most frequently employed methods for the generation of azomethine ylide involves the thermolysis of an aziridine.<sup>2</sup> However, the ring opening of aziridines to azomethine ylides is limited to those having substituent groups capable of stabilizing the dipole centers. Desilylation of  $\alpha$ -trimethylsilylium salts represents another convenient method of generating azomethine ylide.<sup>3</sup> More recently it has been found that nonstabilized azomethine ylides can be generated by the deprotonation of amine N-oxides.<sup>4</sup> Azomethine ylides are too unstable to be isolated, and are typically used *in situ*. Of the various types of azomethine ylides, the pyridinium azomethine ylides are among the most attractive synthetically because they are easily prepared from the appropriate N-alkylpyridinium salt with base and their cycloadducts, the indolizines, have been used as synthetic building blocks.<sup>5</sup>

In our continuing efforts to develop functional dyes based on dicyanopyrazine chromophores, we have become interested in pyridinium azomethine ylides containing dicyanopyrazines and their 1,3-dipolar cycloaddition reaction with dipolarophiles, because the indolizine cycloadducts, containing dicyanopyrazines, might meet our purpose. Dyes and pigments generally possess satisfactory color, and good color fastness properties against light and heat, and additional

properties such as near infrared absorption, pleochroism, and photoconductivity.<sup>6</sup> The majority of these properties are caused by intramolecular charge-transfer interactions involving  $\pi$ -electrons and intermolecular  $\pi$ - $\pi$  interactions of the dye chromophores.<sup>7</sup>

In this paper, we report the generation of pyridinium azomethine ylide intermediates and the results of 1,3-dipolar cycloaddition reactions of the ylides with dipolarophiles to provide indolizines containing 5,6-dicyanopyrazine. The preparation of methyl or phenyl substituted 2-bromomethyl-5,6-dicyanopyrazine **1** is described in a previous report.<sup>6b</sup> Treatment of methyl substituted pyridine **2** with 1.0 equiv of pyrazine methylbromide **1** under toluene reflux afforded (5,6-dicyanopyrazine) methyl pyridinium bromide **3** in 70-79% yield (Scheme 1).<sup>8</sup> The generation of ylide **4** *in situ* from **3** followed by the cycloaddition of **4** with dimethyl acetylenedicarboxylate (DMAD), one of the most reactive dipolarophiles, was attempted. To a mixture of the salt **3** with DMAD in benzene was added Et<sub>3</sub>N, and the mixture was turned to a dark purple and produced indolizines **5** in 40-55% yields.<sup>9</sup>

Although azomethine ylides are generally unstable species, which must be prepared and used *in situ*, we found that the ylides are quite stable in solution. Thus, the isolation of the ylide **4** was attempted. Treatment of **3** with aqueous sodium hydroxide in acetonitrile provided the dark red colored ylide **4** as a solid.<sup>8</sup> The formation of the ylide **4** was verified with <sup>1</sup>H NMR spectroscopy. For example, conversion of the



Scheme 1

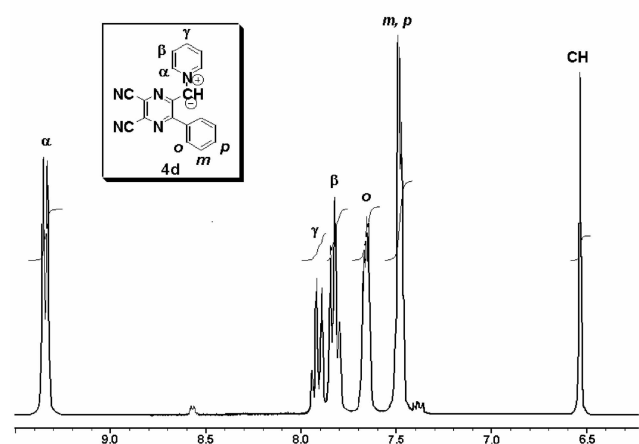
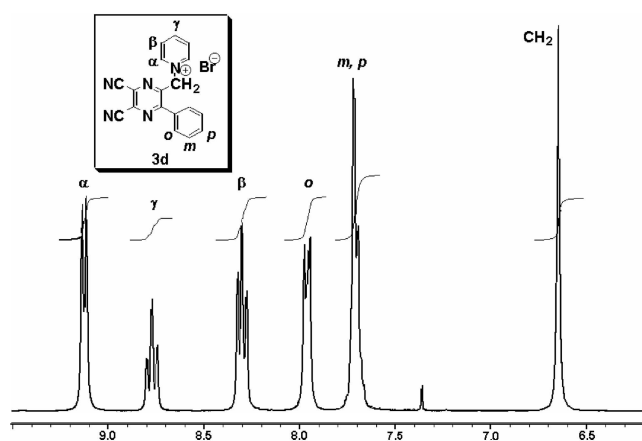
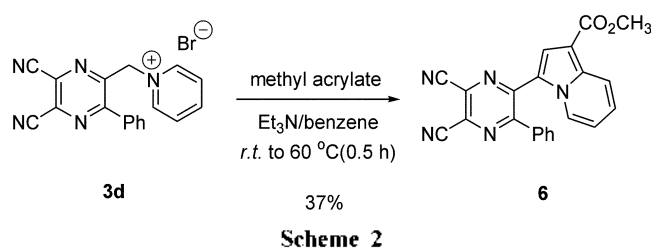


Figure 1

pyridinium bromide **3d** into the ylide **4d** causes a down field shift of  $\alpha$ -pyridine protons from  $\delta$  9.12 to  $\delta$  9.34, and up field shifts of  $\beta$ -pyridines from  $\delta$  8.29 to  $\delta$  7.82 and  $\gamma$ -pyridine proton from  $\delta$  8.76 to  $\delta$  7.91 (Figure 1). In the chemical shifts of C-H protons, the  $\text{CH}_2$  of **3d** and the CH of **4d** appear at  $\delta$  6.64 and  $\delta$  6.53, respectively. Similar observation of the chemical shifts in  $^1\text{H}$  NMR has been reported recently.<sup>10</sup>

Another 1,3-dipolar cycloaddition reaction of **4d** with methyl acrylate was attempted and indolizine **6** was obtained in 37% yield after flash column chromatography (Scheme 2). According with electronic factor, the cyclization reactions of **4d** proceeds to yield **6** instead of the other possible regioisomer. In the case of the preparations of **5** and **6**, the intermediates, dihydroindolizines and tetrahydroindolizine, were not stable enough to be isolated.

In summary, we carried out the 1,3-dipolar cycloaddition reactions of the pyridinium azomethine ylides with DMAD and methyl acrylate as dipolarophiles to provide indolizines containing 5,6-dicyanopyrazines in moderate yields. The pyridinium azomethine ylide **4d** was isolated and identified by  $^1\text{H}$  NMR.



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- These compounds will be candidate for nonlinear optical (NLO) materials because they produce a large dipole moment in the excited state. They have strong fluorescence in solution and some have strong fluorescence even on solid state. These characteristics are very important to evaluate their NLO and electroluminescence properties.
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- Typical procedure for 1,3-dipolar cycloaddition reactions of the pyridinium bromide **3** with DMAD: To a mixture of **3a** (37 mg, 0.11 mmol) and DMAD (25 mg, 0.17 mmol) in anhydrous benzene (3 mL) was added  $\text{Et}_3\text{N}$  (18 mg, 0.17 mmol), and the mixture was heated at 60 °C for 0.5 h. Concentration of the mixture under reduced pressure afforded a crude product, which was purified by flash chromatography (silica gel, hexane : EtOAc 2 : 1) to provide **5a** (21 mg, 50%) as a yellow solid. For analytical data, the solid was recrystallized from methanol to give **5a** as a yellow crystal, mp 192-193 °C;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  2.63 (s, 3H,  $\text{CH}_3$ ), 3.86 (s, 3H,  $\text{OCH}_3$ ), 3.94 (s, 3H,  $\text{OCH}_3$ ), 6.94 (ddd,  $J = 7.2, 6.8, 1.2$  Hz, 1H, ArH), 7.31 (ddd,  $J = 9.2, 6.8, 1.0$  Hz, 1H, ArH), 8.03 (dt,  $J = 7.2, 1.0$  Hz, 1H, ArH), 8.30 (dt,  $J = 9.2, 1.2$  Hz, 1H, ArH); EIMS  $m/z$  (rel. intensity) 375 ( $M^+$ , 87), 344 (100), 312 (90), 284 (31), 257 (46).
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