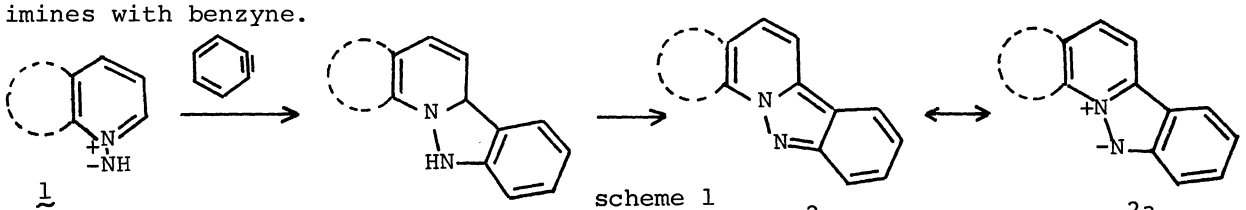
CHEMISTRY LETTERS, pp. 1133-1136, 1980.

REACTIONS OF SUBSTITUTED PYRIDINIUM N-IMINES WITH BENZYNE: SYNTHESES OF PYRIDO[1,2-b]INDAZOLES AND RELATED COMPOUNDS

Yoshiro YAMASHITA, Takashi HAYASHI, and Mitsuo MASUMURA*
Department of Applied Chemistry, Faculty of Engineering,
Tokushima University, Minami-Josanjima, Tokushima 770

Reactions of benzyne with several pyridinium N-imines were examined. 2-o-Aminophenylpyridine derivatives 6, pyrido[1,2-b]indazoles (7), indazolo[2,3-a]quinoline (17), and indazolo[3,2-a]isoquinoline (18) were obtained by the reactions of benzyne with the corresponding ylides 5, 10, 15, and 16, respectively.

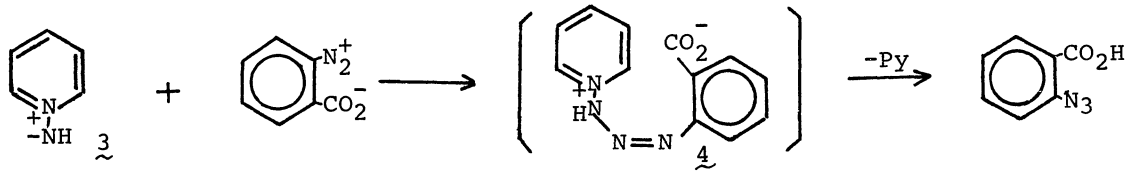
In recent years much attention has been focused on the 1,3-dipolar cycloaddition reactions of zwitterionic ylides of aza-aromatic heterocycles with dipolarphiles.[1] As for benzyne dipolarphile, interesting reactions with pyridazinium ylides have been reported.[2] However, no reaction of benzyne with pyridinium ylides except with pyridine N-oxide[3] has been reported yet. The reaction of the N-iminopyridinium ylides 1 with benzyne seems to provide a useful synthetic method to prepare pyrido[1,2-b]indazoles (2) and related compounds, which are novel aromatic heterocycles and of interest in chemical behavior due to the resonance structures of the ylides 2a.[4] Thus we have examined the reactions of several pyridinium N-imines with benzyne.



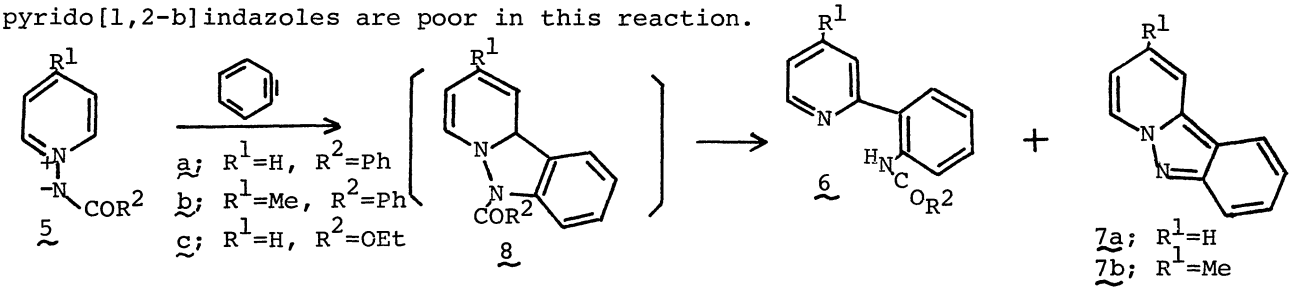
1 scheme 1 2 2a

When benzenediazonium-2-carboxylate[5] was added to a boiling acetonitrile solution of N-iminopyridinium ylide (3), prepared from the corresponding 1-aminopyridinium iodide with potassium carbonate in situ, o-azidobenzoic acid[6] was obtained in 32% yield. This reaction can be rationallized by the initial formation

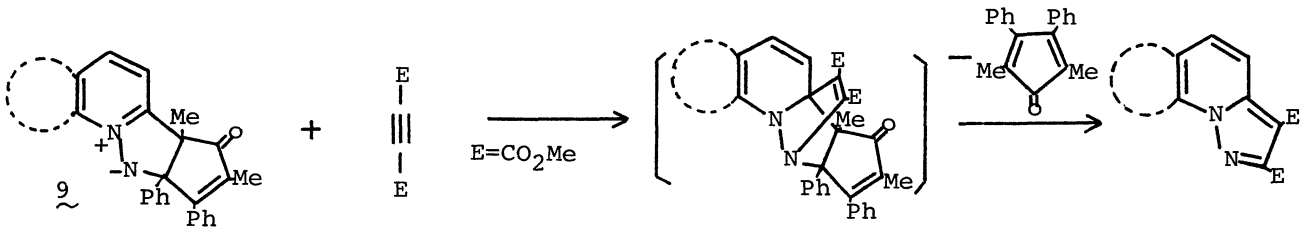
of the intermediate 4 followed by the pyridine elimination. This scheme indicates that benzenediazonium-2-carboxylate reacted with the ylide 3 before it decomposed to benzyne, probably due to the large nucleophilicity of the pyridinium ylides 3.[7]



In order to suppress the diazonium reaction, the pyridinium ylide 5 possessing an electron-withdrawing substituent at the imino position to diminish the nucleophilicity were chosen as the reactants for the benzyne reaction. When benzenediazonium-2-carboxylate was added to a boiling dichloroethane solution of the ylides 5, benzyne reacted with the ylides, as is to be expected. The reaction of the ylide 5a afforded a phenylpyridine derivative 6a [mp 110-112°C (ref,[8] 117°C)] and pyrido[1,2-b]indazole (7a) [mp 78-79°C (ref,[9] 78-79°C)] in 53 and 3% yields, respectively. Similarly, the reaction of the ylide 5b with benzyne afforded the phenylpyridine 6b (oil, 23%) and the pyridoindazole 7b (mp 116-121°C, 4%), and that of the ylide 5c gave 6c (oil, 53%) and 7a (13%). The structures of these products were determined on the basis of the spectral data and by comparison with the reported data.[8,9] They can be derived from the 1:1 adduct 8 which could not be isolated. This reaction may provide a useful method to prepare 2-o-aminophenylpyridine derivatives which are difficult to prepare by conventional routes, although the yields of the desired pyrido[1,2-b]indazoles are poor in this reaction.



In our previous paper,[10] we have reported that the novel polycyclic ylides 9, which could be easily obtained by the reactions of the corresponding N-iminopyridinium ylides with 2,5-dimethyl-3,4-diphenylcyclopentadienone, underwent the 1,3-dipolar cycloaddition reaction with dimethyl acetylenedicarboxylate followed by the retro-Diels-Alder reaction to give pyrazolopyridine derivatives as shown in the scheme 2. This interesting reaction seemed to be applied to prepare pyrido[1,2-b]indazoles and related compounds using benzyne instead of dimethyl acetylenedicarboxylate. Reaction of tricyclic ylides 10 with benzyne under the same conditions with those



scheme 2

of the ylides 5 afforded three products, pyrido[1,2-b]indazoles (7), a cyclopentadienone dimer 11, and a naphthalene 12 in the yields shown in Table 1. The structures of these products were determined by direct comparison with authentic samples.[11, 12] Their formation can be explained by the initial 1,3-dipolar cycloaddition reaction of the ylides with benzyne to give an adduct 13 followed by the retro-Diels-Alder reaction. The low yields of the pyrido[1,2-b]indazoles may be attributed to the concomitant formation of the adduct 14, which cannot undergo the retro-Diels-Alder reaction, at an initial stage of the 1,3-dipolar cycloaddition reaction.

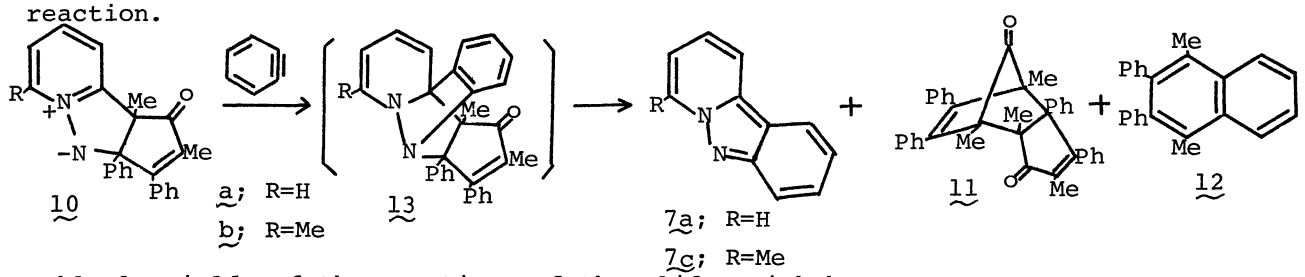
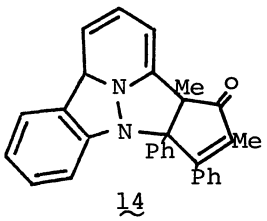
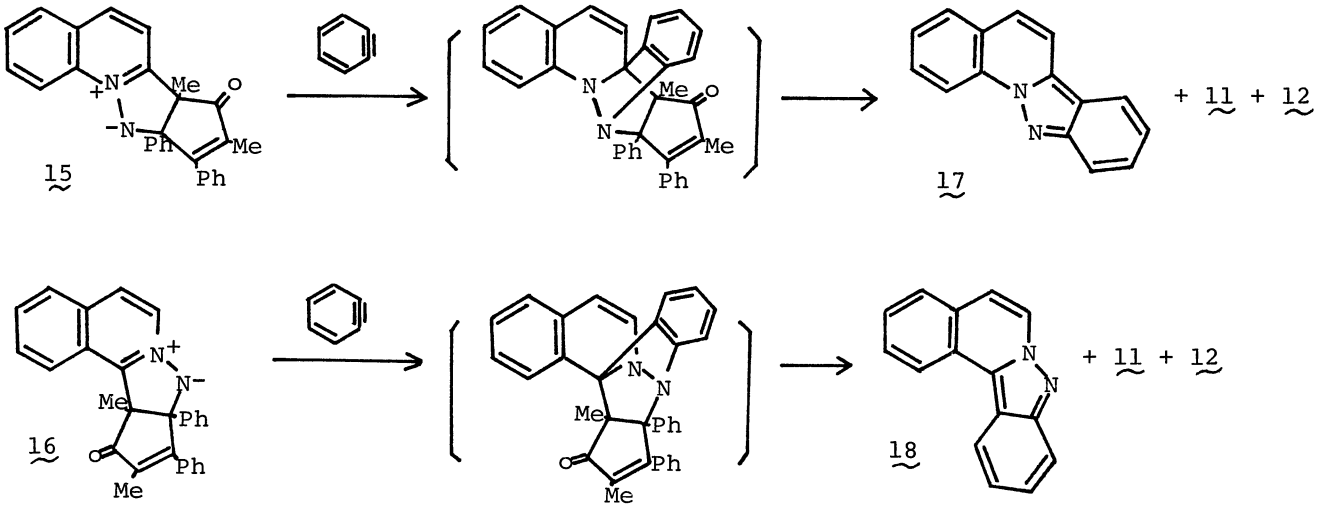


Table 1 Yields of the reactions of the ylides with benzyne

Starting Ylides	Heterocycles (%)	11, %	12, %
10a	7a (38)	14	11
10b	7c (20)	21	24
15	17 (57)	9	49
16	18 (59)	42	33



On the other hand, the corresponding N-iminoquinolinium ylide 15 and isoquinolinium ylide 16 are expected to undergo the 1,3-dipolar cycloaddition in one direction. In fact, reactions of the ylides 15 and 16 with benzyne under the same conditions with those of the ylides 10 gave the corresponding heterocycles, indazolo[2,3-a]quinoline (17) [mp 107-109°C (lit,[13] 109-110°C)] and indazolo[3,2-a]isoquinoline (18) [mp 90-91°C (lit,[14] 89°C)], respectively, in high yields as shown in Table 1. The reactions described here provide a simpler method to synthesize the heteroaromatics than the previous methods.[4, 13, 14]



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11. The product 7a produced in this reaction was identical with the product from the reaction of the ylide 5a. 7c; mp63-64°C. Satisfactory elemental analyses were obtained for all new compounds.
12. The authentic sample of the naphthalene derivative 12 was obtained by the reaction of 2,5-dimethyl-3,4-diphenycyclopentadienone with benzyne.
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(Received June 26, 1980)