Formation of 1,3-Oxazine and 2-Pyrone Derivatives from the Reaction of Pyridinium Ylides with Diphenylcyclopropenone[1]

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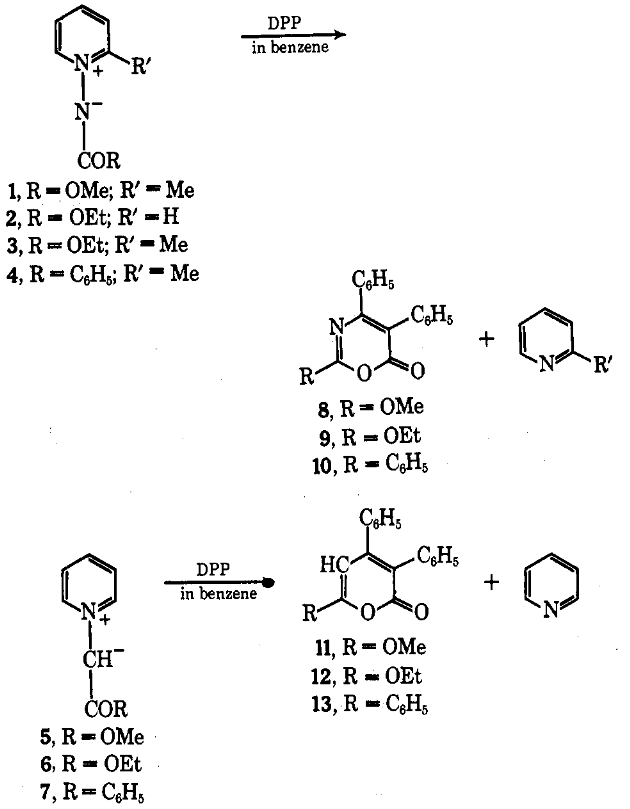
Reactions of iminopyridinium *N*-ylides (1–4) and pyridinium *N*-methylides (5 and 6) with diphenylcyclopropenone (DPP) gave 1,3-oxazine and 2-pyrone derivatives, respectively. Structural elucidation of the products was accomplished by spectral means. Some mechanisms for the formation of the products are discussed.

The utility of the 1,3-dipolar cycloaddition reaction of heteroaromatic nitrogen ylides with acetylenic dipolarophiles for the synthesis of bicyclic heterocyles is well documented.[2-4] As a continuation of work in this area, this paper deals with the reactions of *N*-iminopyridinium ylides with diphenylcyclopropenone (DPP). In addition, the reactions of *N*-alkoxycarbonylpyridinium methylides with DPP have been examined, since the related reactions of pyridinium phenacylide with DPP and methylenecyclopropene have been reported by Eicher and Hansen.[5] A variety of 2 + 3 cycloadditions of DPP to the azomethine ylides have been described. The reactions of DPP with 3-aroylaziridines to form 4-aroyl-4-oxazolines are plausibly interpreted to proceed by initial 2 + 3 cycloaddition of an azomethine ylide to the carbonyl bond of DPP, followed by rearrangement.[6] Another 2 + 3 cycloaddition to DPP is reported in which diazomethane adds to the carbon–carbon double bond.[7]

Results and Discussion

Reactions of the Pyridinium Ylides with DPP.—The reactions of the *N*-alkoxycarbonyliminopyridinium ylides (**1** and **2**) and *N*-benzoyliminopyridinium ylide (**4**) with DPP in benzene proceeded at room temperature or under reflux to give the corresponding stable compounds **8–10** in good yields together with the corresponding pyridine bases (by glpc inspection) as shown in Scheme I. When pyridinium *N*-ylide (**2**) was employed, the reaction solution became dark even at room temperature and gave the product **9** together with considerable amounts of tar. However, when there is a 2-methyl substituent (**3**) on the pyridine ring, the product **9** was obtained in 80% yield. Similar reactions of *N*-alkoxycarbonylpyridinium methylides (**5** and **6**), prepared *in situ* from alkyl bromoacetate adducts of pyridine and triethylamine, with DPP in benzene resulted in the formation of the adducts together with pyridine (by glpc inspection). The reaction mixture was then separated by column chromatography, but in each case a minor product could not be purified.

Scheme I



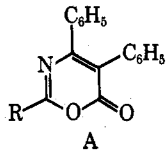
1, R = OMe; R' = Me
2, R = OEt; R' = H
3, R = OEt; R' = Me
4, R = C_6H_5; R' = Me

8, R = OMe
9, R = OEt
10, R = C_6H_5

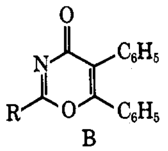
5, R = OMe
6, R = OEt
7, R = C_6H_5

11, R = OMe
12, R = OEt
13, R = C_6H_5

Structural Elucidation of the Products (8–12).—Several 1,3-dipolar cycloaddition reactions of the pyridinium ylides and DPP could be expected, since the carbonyl groups in both compounds are highly polarizable. On the basis of the reported chemistry of DPP[5-7] a variety of possible structures A–E for



A



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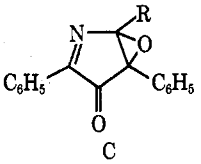
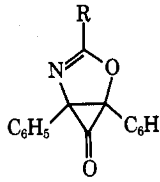
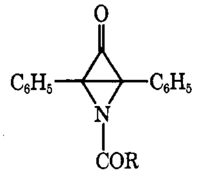


C



D



E

the adducts **8** and **9** could be postulated. The structural elucidation was based on spectral properties. The ir and uv data as well as the nmr spectral evidences indicated the absence of the pyridine moiety in these

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[1] Studies of Heteroaromaticity. LIII. For part LII of this series, see T. Sasaki and T. Yoshioka, *Bull. Chem. Soc. Jap.*, **44**, 803 (1971).

[2] For leading references, see (a) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes," S. Patai, Ed., Interscience, New York, N. Y., 1964, Chapter 11, p 739; (b) V. Boekelheide and N. A. Fedoruk, *J. Org. Chem.*, **33**, 2062 (1968).

[3] T. Sasaki, K. Kanematsu, and Y. Yukimoto, *J. Chem. Soc. C*, 481 (1970).

[4] T. Sasaki, K. Kanematsu, Y. Yukimoto, and S. Ochiai, *J. Org. Chem.*, **36**, 813 (1971).

[5] T. Eicher and A. Hansen, *Tetrahedron Lett.*, 1169 (1967).

[6] J. W. Lown, T. W. Maloney, and G. Dallas, *Can. J. Chem.*, **48**, 584 (1970).

[7] P. T. Izzo and A. S. Kende, *Chem. Ind. (London)* 839 (1964).

Table I

Ir, Uv, and Nmr Spectra of 1,3-Oxazine and 2-Pyrone Derivatives

Compd no.	Ir, cm^{-1} $\nu^{KBr}_{C=O}$	$\nu^{KBr}_{C=N}$	Uv, λ^{MeOH}_{max}, nm (ε)	Nmr,[a] τ (CDCl$_3$)
8	1735	1626	319 (8.82×10^3) 231 (1.66×10^4)	2.84 (10 H, s, 2 C_6H_5) 5.95 (3 H, s, OCH_3)
9	1732	1616	320 (8.38×10^3) 231 (1.90×10^4)	2.85 (10 H, s, 2 C_6H_5) 5.53 (2 H, q, J = 7.0 Hz, OCH_2) 8.54 (3 H, t, J = 7.0 Hz, OCH_2CH_3)
10	1727	1610	341 (1.19×10^4) 265 (2.17×10^4)	1.68 (2 H, m, ortho and ortho′ protons of C_6H_5) 2.60 (3 H, m, meta, meta′, and para protons of C_6H_5) 2.80 (10 H, s, 2 C_6H_5)
11	1710	1623	345 (8.27×10^3) 238 (1.45×10^3)	2.99 (10 H, s, 2 C_6H_5) 4.68 (1 H, s, ring proton) 6.13 (3 H, s, OMe)
12	1697	1623	348 (1.00×10^4) 237 (1.72×10^4)	2.98 (10 H, s, 2 C_6H_5) 4.67 (1 H, s, ring proton) 5.70 (2 H, q, J = 7.0 Hz, OCH_2) 8.55 (3 H, t, J = 7.0 Hz, OCH_2CH_3)
13	1695	1623	358 (1.53×10^4) 254 (1.88×10^4) 240 (shoulder)	2.20 (2 H, m, ortho and ortho′ protons of C_6H_5) 2.65 (3 H, m, meta, meta′, and para protons of C_6H_5) 2.95 (10 H, s, 2 C_6H_5 2) 3.32 (1 H, s, ring proton)

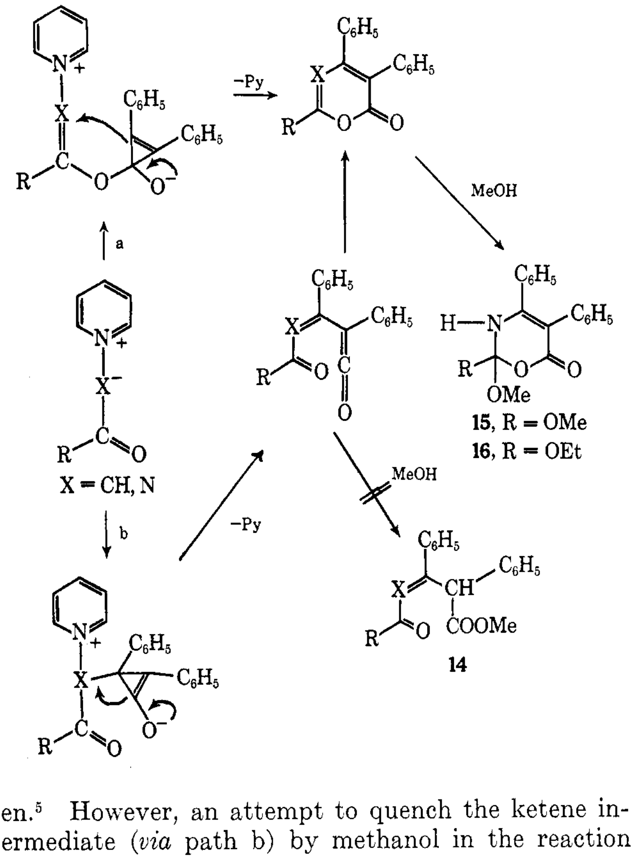
[a] s = singlet, t = triplet, q = quartet, m = multiplet.

adducts. In the ir, they showed absorptions at 1727–1735 cm^{-1} due to six-membered carbonyl bands rather than to those of carboxamide bands,[8,9] in comparison with a known structure of **10**, which has been prepared by the reaction of 2,3,5-triphenylpyrrole and hydrogen peroxide in acetic acid.[10] Furthermore, these compounds also gave a negative reaction with sodium thiosulfate reagent (oxiran ring test). Thus, the structures B–E could be ruled out from the possibilities for compounds **8** and **9**. On the other hand, compounds **11** and **12** showed absorptions at 1710 and 1697 cm^{-1}, respectively, attributable to carbonyl bands of the α-pyrone moiety, in comparison with a known structure of **13**, which has been prepared by the similar reaction of pyridinium *N*-phenacylide and DPP.[5] The nmr spectra of **8**, **9**, **11**, and **12** contained peaks at τ 2.80–2.99 (almost singlets) due to two phenyl protons. The uv absorption spectra showed two maxima at 231–265 and 319–358 nm.[11] Their ir, uv, and nmr spectra are summarized in Table I. The mass spectra of the oxazines and pyrones were characterized by fragment ion peaks (M − CO).[12]

On the basis of the above, spectral evidence, structures **8**, **9**, **11**, and **12** were assigned as 2-methoxy- and 2-ethoxy-4,5-diphenyl-1,3-oxazin-6-one and 6-methoxy- and 6-ethoxy-3,4-diphenyl-2-pyrone, respectively. Considering these results, the reactions seem to proceed *via* the cycloaddition reactions of DPP and acylnitrenes and acylcarbenes, generated from the corresponding pyridinium *N*-ylides. However, DPP proved to be inert to the reaction with ethyl azidoformate even under more drastic conditions.

Mechansitic speculation leads to consideration of paths a and b, with initial nucleophilic attack of the *N*-ylides to the carbonyl bond of DPP or to the carbon–carbon double bond, respectively, followed by rearrangement to give 1,3-oxazine and/or 2-pyrone derivatives (Scheme II), as suggested by Eicher and Hansen.[5] However, an attempt to quench the ketene intermediate (*via* path b) by methanol in the reaction of **2** and DPP gave compound **9** accompanied by a small amount of **16** instead of the expected compound **14**, as revealed by thin layer chromatography and nmr analyses. Upon treating **8** and **9** with refluxing methanol, compounds **15** and **16** were obtained in

Scheme II



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[8] *Cf.* $\nu_{C=O}$ 1730–1760 cm^{-1} in 1,3-oxazin-6-one; see H. B. Kogan, *Bull. Soc. Chim. Fr.*, 1819 (1966).

[9] *Cf.* $\nu_{C=O}$ 1750–1780 cm^{-1} in 1,3-oxazin-4-ones; see T. Kato and Y. Yamamoto, *Chem. Pharm. Bull.*, **15**, 1334 (1967).

[10] I. V. Sprio, *Gazz. Chim. Ital.*, **85**, 569 (1955).

[11] $\lambda^{dioxane}_{max}$ 340 nm in 2,5-diphenyl-1,3-oxazin-6-one; see F. Eiden and B. S. Nagar, *Naturwissenschaften*, **50**, 403 (1963).

[12] Mass spectral data for compounds **8–13**, **15**, and **16**, with a suggested fragmentation scheme, will appear immediately following this article in the microfilm edition of the journal. Single copies may be obtained from the Reprint Department, ACS Publication, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page number. Remit $3.00 for photocopy or $2.00 for microfiche.

quantitative yields, respectively. The nmr spectra indicate the two methoxyl groups as singlets at τ 6.36 and 6.44 and NH proton at τ −1.08 (broad singlet) in **15** and the ethoxyl protons at τ 5.91 (2 H, q, J = 7.0 Hz) and 8.82 (3 H, t, J = 7.0 Hz), the methoxyl protons at τ 6.46 (3H, s), and NH proton at τ −1.06 (broad singlet) in **16**. Thus compounds **15** and **16** were assigned as 2,2-dimethoxy- and 2-ethoxy-2-methoxy-4,5-diphenyl-2,3-dihydro-1,3-oxazin-6-one, respectively.

Attempts to effect the reactions of troponoids with *N*-alkoxycarbonyliminopyridinium ylides were unsuccessful even under more drastic conditions, although the similar reactions of troponoids with pyridinium phenacylide and sulfonium ylides have been reported to lead to a convenient one-step syntheses of azaazulene and 2,3-homotropone derivatives.[13]

Experimental Section[14]

2-Methoxy-4,5-diphenyl-1,3-oxazin-6-one (**8**).—To a solution of **1** (150 mg, 1 mmol) in benzene (30 ml), DPP (100 mg, 0.5 mmol) was added and the mixture was stirred overnight at room temperature. The mixture was concentrated *in vacuo* and the residue was purified by column chromatography (silica gel) using chloroform as eluent to give colorless crystals of **8** (110 mg, 79%, mp 111–112°) as the first fraction, which was recrystallized from carbon tetrachloride–*n*-hexane.

Anal. Calcd for $C_{17}H_{13}NO_2$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.08; H, 4.81; N, 4.92.

2-Ethoxy-4,5-diphenyl-1,3-oxazin-6-one (**9**).—(a) From **2** (500 mg, 1.5 mmol) and DPP (210 mg, 1 mmol) there was obtained colorless crystals **9** (180 mg, 61%, mp 94–95°). (b) From **3** (180 mg, 1 mmol) and DPP (100 mg, 0.5 mmol) there was obtained colorless crystals of **9** (120 mg, 82%, mp 94–95°).

Anal. Calcd for $C_{18}H_{15}NO_2$: C, 73.70; H, 5.15; N, 4.98. Found: C, 73.92; H, 5.24; N, 4.74.

2,4,5-Triphenyl-1,3-oxazin-6-one (**10**).—To a solution of **4** (210 mg, 1 mmol) in benzene (20 ml), DPP (100 mg, 0.5 mmol) was added, and then the mixture was refluxed for 4 days. The mixture was concentrated *in vacuo* and the residue was worked up as described above. Pale yellow crystals were obtained as the first fraction, which was recrystallized from carbon tetrachloride–*n*-hexane to give **10** (130 mg, 80%, mp 207–208°). Compound **10** was also identified by the comparison of a mixture melting point with the melting point of an authentic sample.[10]

6-Methoxy-3,4-diphenyl-2-pyrone (**11**).—To a solution of pyridine–methyl bromoacetate adduct (300 mg) in benzene (30 ml) in the presence of triethylamine (0.5 ml), DPP (100 mg, 0.5 mmol) was added and stirred overnight at room temperature. The reaction solution was removed *in vacuo*, and the residue was separated by column chromatography using benzene as eluent; the product was recrystallized from benzene to give colorless crystals of **11** (90 mg, 67%, mp 134–135°).

Anal. Calcd for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.75; H, 5.10.

6-Ethoxy-3,4-diphenyl-2-pyrone (**12**).—From pyridine–ethyl bromoacetate adduct (300 mg), triethylamine (0.3 ml), and DPP (100 mg, 0.5 mmol) there was obtained **12** (60 mg, 41%) as colorless crystals, mp 104–106°.

Anal. Calcd for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 78.10; H, 5.50.

2,2-Dimethoxy-4,5-diphenyl-2,3-dihydro-1,3-oxazin-6-one (**15**).—A solution of **8** (50 mg) and methanol (30 ml) was refluxed for about 2 days and the solvent was removed *in vacuo*. The residue was recrystallized from ether–*n*-hexane to give colorless crystals, mp 166–169°, in quantitative yield; $\nu_{C=O}^{KBr}$ 1750 cm^{-1}; λ_{max}^{MeOH} 290 nm (ϵ 1.34 × 10^4); nmr τ (CCl_4) 6.44 (s, 3), 6.36 (s, 3), 3.03 (m, 10), −1.08 (NH).

Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.89; N, 4.31. Found: C, 69.50; H, 5.59; N, 4.58.

2-Ethoxy-2-methoxy-4,5-diphenyl-2,3-dihydro-1,3-oxazin-6-one (**16**).—(1) A solution of **9** (50 mg) and methanol (20 ml) was refluxed for about 2 days and the solvent was removed *in vacuo*. The residue was recrystallized from ether–*n*-hexane to give colorless crystals, mp 136–139°, in quantitative yield: $\nu_{C=O}^{KBr}$ 1756 cm^{-1}; λ_{max}^{MeOH} 289 (ϵ 1.16 × 10^{-4}); nmr τ (CCl_4) 8.84 (t, 3), 6.46 (s, 3), 5.91 (q, 2), 3.10 (m, 10), −1.06 (NH). (2) A solution of **2** (50 mg), DPP (30 mg), and methanol (30 ml) was stirred for 2 days at room temperature. The solvent was concentrated *in vacuo* and the residue was confirmed to be a mixture of **9** (as a major product) and **16** (minor) by tlc and nmr inspections. However, the reaction mixture was difficult to separate by means of column chromatography. Further treatment of the mixture with methanol under the refluxing condition afforded **16** in quantitative yield.

Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.25; H, 5.89; N, 4.20.

Registry No.—**8**, 30237-76-4; **9**, 30237-77-5; **10**, 30237-78-6; **11**, 30237-79-7; **12**, 30237-80-0; **13**, 14961-31-0; **15**, 30237-82-2; **16**, 30237-83-3; DPP, 886-38-4.

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[13] Y. Sugimura, I. Kawamoto, K. Ihno, and N. Soma, Abstracts of Papers, "International Symposium of the Chemistry of Non-benzenoid Aromatic Compounds," Sendai, Japan, 1970, p 67.

[14] All melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. The microanalyses were performed on a Perkin-Elmer 240 elemental analyzer, while the ir and uv spectra were obtained on JASCO Models IR-S and ORD/UV-5 spectrometers, respectively. The nmr spectra were recorded with a JEOL Model C-60-XL spectrometer with tetramethylsilane as an internal standard. The glpc was done isothermally with an Hitachi K-23 gas chromatograph on a 3-ft, 5 wt % SE 30 (Chromosorb GNAW) column (flame-ionization detector). The mass spectra were obtained on a Hitachi RMU-D double-focusing mass spectrometer operating at an ionization potential of 70 eV. The solid samples were ionized by electron bombardment after sublimation directly into the electron beam at 100–150°.