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Reaction of 2,2-Dimethyl-1,3-dioxin-4-one Derivatives with Pyridinium (Isoquinolinium) Methylides and Cyano Compounds

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Cycloaddition of acylketenes (**2**) to 1,2- and 1,3-dipolar compounds was investigated. The thermal reaction of 1,3-dioxin-4-ones (**1**) with isoquinolinium phenacylide (**11**) gave the aromatized pyrrolo[2,1-*a*]isoquinolines (**12**—**15**). The reaction of **1** with pyridinium and isoquinolinium cyanomethylides (**3**—**5**) afforded the 1,3-oxazinylmethylides (**6**—**8**). The intermediate **2** likewise reacted with cyanamides and benzonitriles to give the corresponding 1,3-oxazin-4-one derivatives (**19**—**23**).

Keywords——1,3-cycloaddition; 1,4-cycloaddition; ring transformation; thermal fragmentation; acylketene; 1,3-dioxin-4-one; 1,3-oxazin-4-one; pyrrolo[2,1-*a*]isoquinoline

Recently, we have reported a facile and general method for the preparation of 1,3-dioxin-4-one derivatives (**1**) starting from β-keto acids.[1] By analogy with the diketene–acetone adduct (2,2,6-trimethyl-1,3-dioxin-4-one) (**1a**),[2] dioxinones **1** are expected to generate acylketenes **2** under heating. In order to study the reactivity of **2** and to utilize the masked acylketene **1** for the synthesis of nitrogen heterocycles, we have investigated the reaction of **1** with pyridinium and isoquinolinium methylides and some cyano compounds.

Reaction with Pyridinium and Isoquinolinium Methylides

Previously, we have found that on heating with **1a** ($R^1 = H$, $R^2 = Me$), pyridinium cyano(ethoxycarbonyl)methylide (**3**) is transformed to the 1,3-oxazinylmethylide **6a** ($R^1 = H$, $R^2 = Me$), while pyridinium phenacylide is converted to the indolizine derivative.[2d] The reaction involves cycloaddition of acetylketene (**2a**) with the 1,2- or 1,3-dipole. Thus, our interest was focused on the reaction of **2** with such heterocyclic methylides.

When the ylide **3** was heated at 165 °C with the 5,6-disubstituted dioxinones (**1e**—**g**), the 1,3-oxazinylmethylides (**6e**—**g**) were obtained. Similarly, pyridinium and isoquinolinium dicyanomethylides (**4** and **5**) reacted with **1e**, **1f**, and **1g** to give the corresponding bis(oxazinyl)methylides **7** and **8** in high yields. The structures of **6**, **7**, and **8** were confirmed by elemental analysis and spectral data. NMR spectral data showed that the oxazine nitrogen is protonated in a mixture of trifluoroacetic acid and deuteriochloroform. The reaction of dimethylsulfonium dicyanomethylide (**9**) also gave a similar bis-adduct (**10**) on heating with **1a**.

Though the above heterocyclic ylides are known to be 1,3-dipoles,[3] acylketenes **2** preferentially added to the C≡N moiety. In contrast, isoquinolinium phenacylide (**11**) underwent 1,3-dipolar cycloaddition with **2**. Namely, heating of 2,2-dimethyl-6-phenyl-1,3-dioxin-4-one (**1b**) with the ylide **11** gave the pyrroloisoquinoline derivative **12** in 25% yield.

Interestingly, the reaction of **11** with 5,6-disubstituted dioxinones also gave the pyrroloisoquinolines. Heating of **11** with the 5,6-dimethyldioxinone (**1e**) and the 5-methyl-6-phenyldioxinone (**1f**) gave low yields of the acetoxy compound (**13**) and the 2-benzoylpro-

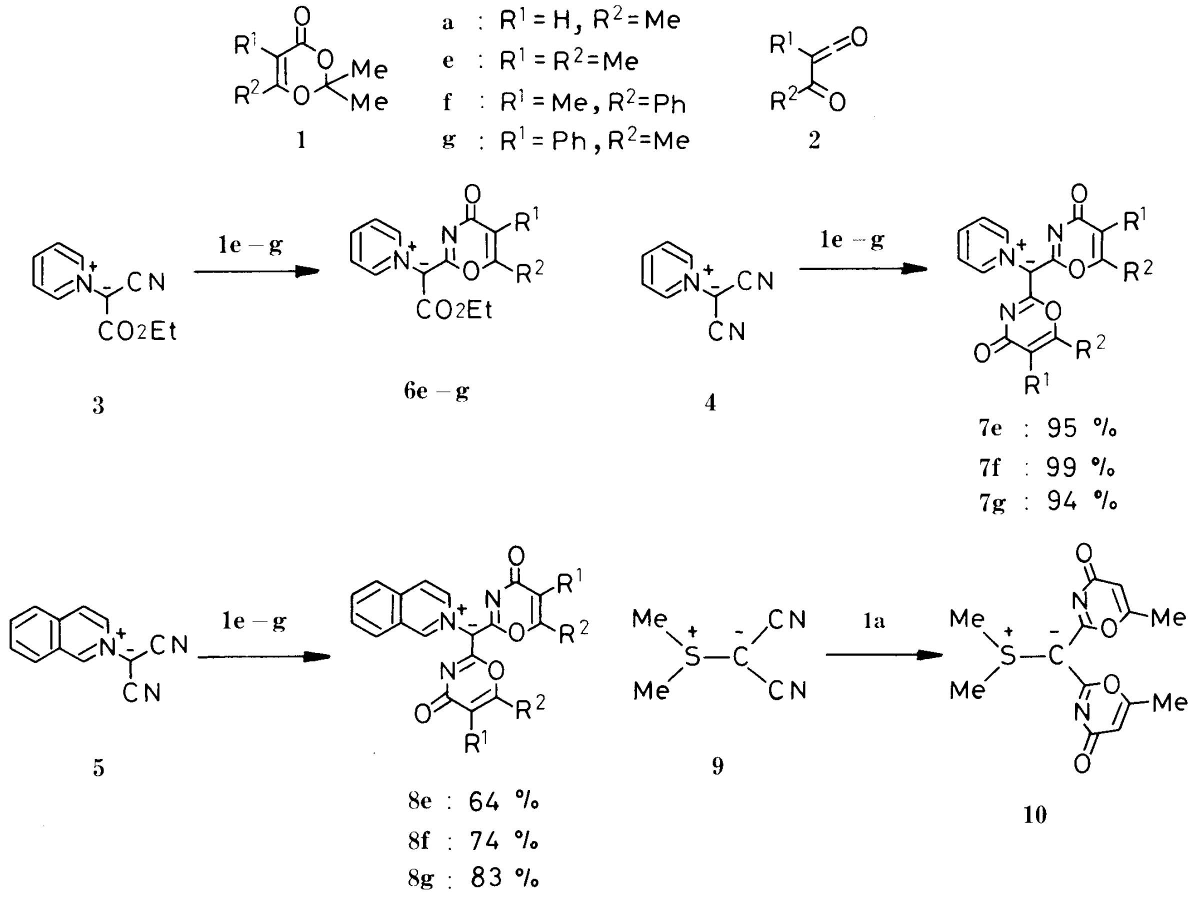

Chart 1

Table I. Melting Points and Analytical Data for Pyridinium and Isoquinolinium Bis(1,3-oxazinyl)methylides (**7e**—**g**, **8e**—**g**)

Compd. No.	Substituent		mp °C (dec.) Recryst. solvent	Formula	Analysis (%) Calcd (Found)		
	R1	R2			C	H	N
7e	Me	Me	300 MeOH	$C_{18}H_{17}N_3O_4$	63.71 (63.26	5.05 5.01	12.38 12.18)
7f	Me	Ph	286—287.5 MeOH	$C_{28}H_{21}N_3O_4$	72.56 (72.22	4.57 4.51	9.07 9.03)
7g	Ph	Me	261—263 EtOH	$C_{28}H_{21}N_3O_4$	72.56 (72.25	4.57 4.73	9.07 9.04)
8e	Me	Me	295—296 MeOH	$C_{22}H_{19}N_3O_4$	67.85 (67.72	4.92 4.91	10.79 10.76)
8f	Me	Ph	272.5—275 MeOH	$C_{32}H_{23}N_3O_4$	74.84 (74.62	4.51 4.54	8.18 7.95)
8g	Ph	Me	263 MeOH	$C_{32}H_{23}N_3O_4 \cdot 1/2H_2O$	73.54 (73.50	4.62 4.55	8.04 7.99)

pionyloxy compound (**14**), respectively. Similarly, the hexahydrobenzodioxinone (**1j**) reacted with **11** to give the oxocin derivative (**15**).

The structures **13**, **14**, and **15** were assigned to these products on the basis of their spectral data. For confirmation, compound **13** was treated with methanolic potassium hydroxide to

Table II. Spectral Data for Pyridinium and Isoquinolinium Bis(4-oxo-4H-1,3-oxazin-2-yl)methylides (**7e**—**g**, **8e**—**g**)

Compd. No.	IR (Nujol) cm^{-1}	NMR (50% CF_3CO_2H–$CDCl_3$) δ	MS m/e: M^+
7e	1670, 1628	2.14 (6H, s, 2×Me), 2.25 (6H, s, 2×Me), 8.03—9.20 (6H, m, Ar–H and –NHCO)	339
7f	1646, 1623	2.21 (6H, s, 2×Me), 7.16—9.13 (16H, m, Ar–H and –NHCO)	463
7g	1641 (sh), 1630	2.06 (6H, s, 2×Me), 7.10—9.05 (16H, m, Ar–H and –NHCO)	463 (FD)
8e	1670, 1626	2.12 (6H, s, 2×Me), 2.15 (6H, s, 2×Me), 7.82—8.77 (6H, m, Ar–H and –NHCO), 9.81 (1H, s, isoquinoline C_1–H)	389
8f	1638, 1622 (sh)	2.30 (6H, s, 2×Me), 7.05—8.88 (17H, m, Ar–H and –NHCO), 9.89 (1H, s, isoquinoline C_1–H)	513 (FD)
8g	1657 (sh), 1640	2.08 (6H, s, 2×Me), 7.15—8.80 (17H, m, Ar–H and –NHCO), 9.86 (1H, s, isoquinoline C_1–H)	513 (FD)

give the hydroxy compound **16**. On similar treatment, compound **14** afforded **16** and methyl α-methylbenzoylacetate, while compound **15** gave the methyl pentanoate **17**. These transformations support the acyloxy structures of **13**, **14**, and **15**.

Concerning the formation of these products, the most likely pathway is shown in Chart 2. A [2+3] cycloadduct **18b**, where R^1 is hydrogen, is unstable and easily oxidized to the product **12**. When R^1 is not hydrogen, the adduct **18** would be oxidized, accompanied with the migration of the acyl group to the neighboring oxygen to give the products, **13** and **15**. Compound **14** is presumably formed as follows; the first stage should be the formation of a 2-benzoxy-3-benzoyl-1-methylpyrrolo[2,1-*a*]isoquinoline such as **13**, with which excess benzoylmethylketene reacts to result in the exchange of the 2-acyl group, giving the product **14**.

The olefinic moiety of ketenes rarely acts as a dipolarophile toward 1,3-dipoles.[4] However, such [2+3] dipolar cycloadditions seem to occur generally in the reaction of acylketenes with 1,3-dipolar methylides such as isoquinolinium ethoxycarbonylmethylides[2d] and phenacylide.

Reaction with Cyano Compounds

It has been reported that dioxinone **1a** and the cyclopenta analog (**1**: $R^1=R^2=(CH_2)_3$) reacts with cyano compounds such as cyanamides and cyanates to give the 1,3-oxazin-4-ones.[2a] Some 2-amino-1,3-oxazin-4-one derivatives have analgesic and fungicidal activities.[5] Thus, the reaction of cyanamides with various dioxinones **1** was carried out. When dioxinones **1** were heated with *N,N*-dimethyl- and *N,N*-diethyl-cyanamide without solvent, the corresponding 2-dialkylamino-1,3-oxazin-4-ones **19** and **20** were obtained in good yields. The results are summarized in Table III. This method for synthesis of 2-amino-1,3-oxazin-4-ones is more facile and general than the previous method,[5] which utilizes 3-hydroxyisoxazoles as starting materials.

As regards the cycloaddition of acylketenes with nitriles, only a few examples have been reported.[2a,6] Thus, we studied the reaction of dioxinones with benzonitriles. Though the reaction was sluggish, 5,6-disubstituted dioxinones gave 2-aryl-1,3-oxazin-4-ones (**21**—**23**) in 13—41% yields. The results are summarized in Table VI. The reaction of 6-phenyldioxinone **1b** with benzonitrile gave a complex reaction mixture, from which only the pyrone **24** was isolated in a low yield. This product is a dimer of benzoxylketene. Therefore, it is suggested

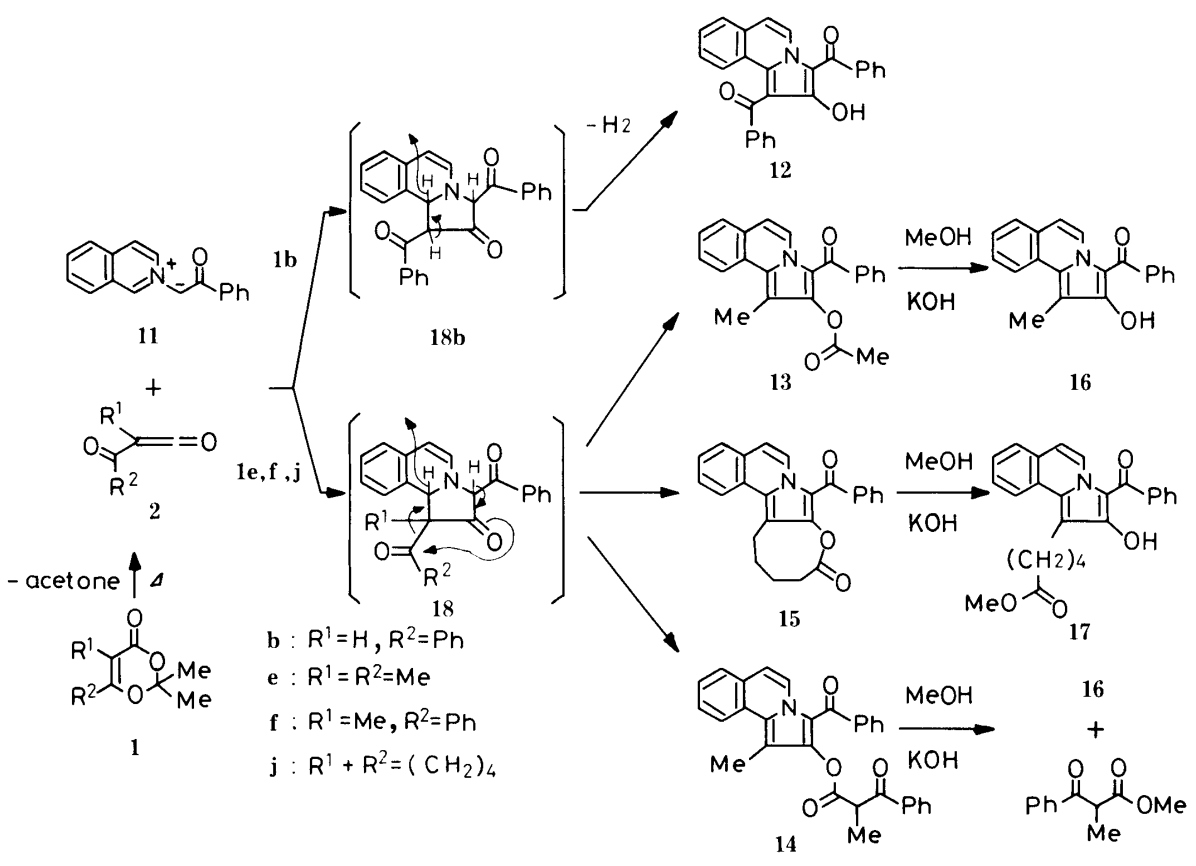

Chart 2

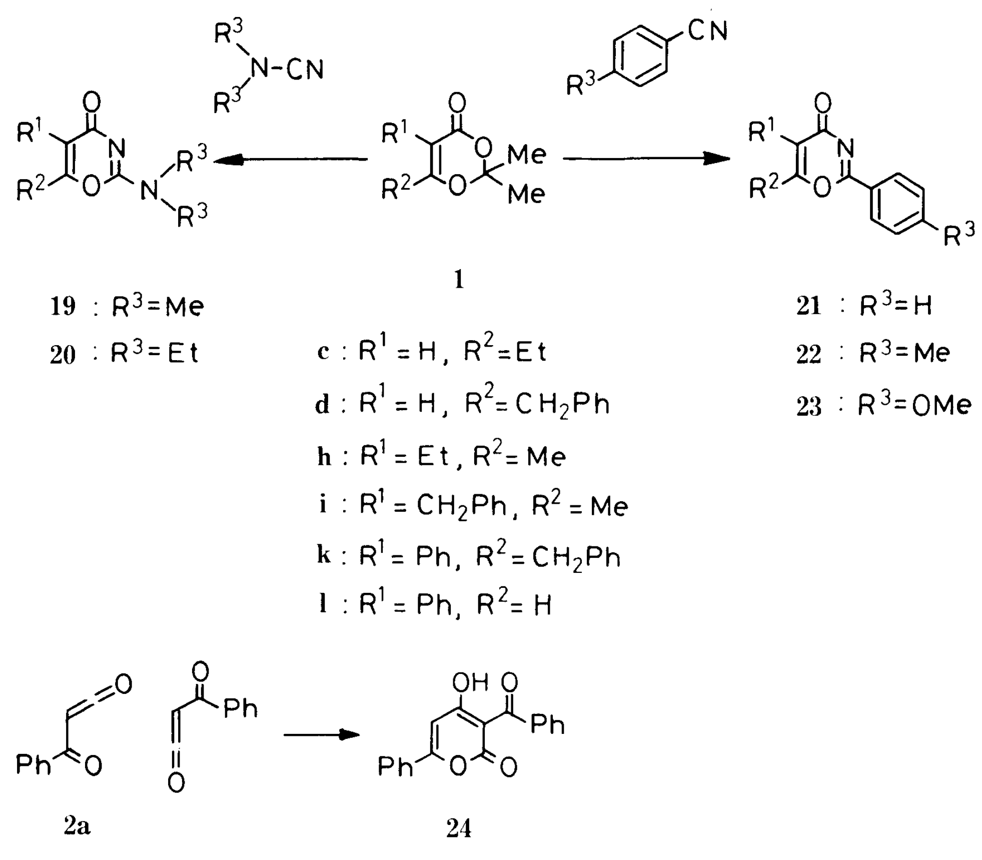

Chart 3

TABLE III. 2-Dialkylamino-4*H*-1,3-oxazin-4-ones (**19b**—**l**, **20b**—**g**, **j**)

Compd. No.	Substituent		Reaction condition[a]	Yield (%)	mp (lit.) (°C) or bp (°C/mmHg)	Recryst. solvent[b]	Formula	Analysis (%) Calcd (Found)		
	R^1	R^2						C	H	N
19b	H	Ph	A	88	199—201 (189—193)[c]	E	$C_{12}H_{12}N_2O_2$		—	
19c	H	Et	A	82	70—71[d]	F	$C_8H_{12}N_2O_2 \cdot 1/2H_2O$	54.22 (54.32	7.39 7.31	15.81 15.74)
19d	H	$PhCH_2$	B	84	127—127.5	G	$C_{13}H_{14}N_2O_2$	67.81 (67.53	6.13 5.98	12.17 12.02)
19e	Me	Me	D	64	129 (127.5—128.5)[c]	H	$C_8H_{12}N_2O_2$		—	
19f	Me	Ph	D	70	154—155.5	F	$C_{13}H_{14}N_2O_2$	67.81 (67.91	6.13 6.16	12.17 12.32)
19g	Ph	Me	D	86	111—113	G	$C_{13}H_{14}N_2O_2$	67.81 (67.56	6.13 6.09	12.17 12.11)
19h	Et	Me	C	50	73.5—75[d]	F	$C_9H_{14}N_2O_2$	59.32 (59.22	7.74 7.65	15.37 15.37)
19i	$PhCH_2$	Me	D	89	80—81	G	$C_{14}H_{16}N_2O_2$	68.83 (68.53	6.60 6.58	11.47 11.25)

19j	$-(CH_2)_4-$		D	83	147—149	H	$C_{10}H_{14}N_2O_2$	61.83 (61.87	7.27 7.32	14.42 14.48)
19k	Ph	$PhCH_2$	D	82	108—109.5	I	$C_{19}H_{18}N_2O_2$	74.49 (74.72	5.92 5.92	9.15 9.17)
19l	Ph	H	A	68	131—134	G	$C_{12}H_{12}N_2O_2$	66.65 (66.46	5.59 5.50	12.96 13.01)
20b	H	Ph	A	80	121—123 (123—124)[c]	G	$C_{14}H_{16}N_2O_2$		—	
20c	H	Et	A	83	Oil		$C_{10}H_{16}N_2O_2$	61.20 (60.98	8.22 8.51	14.28 13.99)
20d	H	$PhCH_2$	B	71	78.5—79.5	F	$C_{15}H_{18}N_2O_2$	69.74 (70.02	7.02 7.18	10.85 10.73)
20e	Me	Me	D	79	55—57[d]	J	$C_{10}H_{16}N_2O_2$	61.20 (61.14	8.22 8.23	14.28 14.22)
20f	Me	Ph	D	70	170/0.005		$C_{15}H_{18}N_2O_2$	69.74 (70.24	7.02 7.21	10.85 10.77)
20g	Ph	Me	D	89	129—130	G	$C_{15}H_{18}N_2O_2$	69.74 (69.57	7.02 7.07	10.85 10.58)
20j	$-(CH_2)_2-$		D	73	80—82	F	$C_{12}H_{18}N_2O_2$	64.84 (64.59	8.16 8.00	12.60 12.71)

a) A, 130 °C, 30 min; B, 130 °C, 1 h; C, 165 °C, 30 min; D, 165 °C, 1 h.
b) E, acetonitrile; F, ether; G, ethyl acetate; H, ethyl acetate–isopropyl ether; I, ethyl acetate–ether; J, ether–petroleum ether.
c) Reference 5.
d) The melting points were measured in a sealed tube.

TABLE IV. Spectral Data for 2-Dimethylamino-4*H*-1,3-oxazin-4-ones (**19c**—**d**, **f**—**l**)

Compd. No.	IR ($CHCl_3$) cm^{-1}	NMR ($CDCl_3$) δ		
		$-N\underline{Me}_2$	R^1	R^2
19c	1670, 1655	3.16	5.69 (1H, s)	1.22 (3H, t, $J=7.4$ Hz, $-CH_2C\underline{H}_3$), 2.50 (2H, q, $J=7.4$ Hz, $-C\underline{H}_2CH_3$)
19d	1671, 1652 (sh)	3.06	5.75 (1H, s)	3.71 (2H, s, $-C\underline{H}_2Ph$), 7.30 (5H, s, $-CH_2\underline{Ph}$)
19f	1659 (sh), 1646	3.17	2.07 (3H, s, Me)	7.52 (5H, s, Ph)
19g	1653, 1640 (sh)	3.11	7.30 (5H, s, Ph)	2.09 (3H, s, Me)
19h	1679, 1653	3.11	1.06 (3H, t, $J=7$ Hz, $-CH_2C\underline{H}_3$), 2.40 (2H, q, $J=7$ Hz, $-C\underline{H}_2CH_3$)	2.19 (3H, s, Me)
19i	1677, 1655	3.07	3.73 (2H, s, $-C\underline{H}_2Ph$), 7.18 (5H, s, $-CH_2\underline{Ph}$)	2.13 (3H, s, Me)
19j	1685, 1656	3.10	1.50—2.00 (4H, m, $C_{6,7}$-methylene), 2.23—2.57 (4H, m, $C_{5,8}$-methylene)	
19k	1670, 1655	3.03	7.19—7.43 (5H, m, Ph)	3.70 (2H, s, $-C\underline{H}_2Ph$), 7.34 (5H, s, $-CH_2\underline{Ph}$)
19l	1657, 1650	3.12	7.24—7.66 (6H, m, C_5–Ph and C_6–H)	

TABLE V. Spectral Data for 2-Diethylamino-4*H*-1,3-oxazin-4-ones (**20c**—**g**, **j**)

Compd. No.	IR ($CHCl_3$) cm^{-1}	$-N(CH_2CH_3)_2$		NMR ($CDCl_3$) δ	
		$2\times CH_3$	$2\times CH_2$	R^1	R^2
20c	1672, 1657 (sh)	1.23	3.53	5.73 (1H, s)	1.23 (3H, t, $J=7.4$ Hz, $-CH_2C\underline{H}_3$), 2.46 (2H, q, $J=7.4$ Hz, $-C\underline{H}_2CH_3$)
20d	1673, 1655 (sh)	1.10	3.45	5.81 (1H, s)	3.70 (2H, s, $-C\underline{H}_2Ph$), 7.29 (5H, s, $-CH_2\underline{Ph}$)
20e	1683, 1645	1.22	3.48	1.85 (3H, s, Me)	2.17 (3H, s, Me)
20f	1646	1.25	3.57	2.09 (3H, s, Me)	7.52 (5H, s, Ph)
20g	1672, 1654	1.23	3.55	7.31 (5H, s, Ph)	2.09 (3H, s, Me)
20j	1685, 1653 (sh), 1648	1.21	3.50	1.45—2.09 (4H, m, $C_{6,7}$-methylene), 2.18—2.59 (4H, m, $C_{5,8}$-methylene)	

that dimerization and polymerization precedes the cycloaddition with nitriles in the case of unsubstituted acylketenes such as benzoylketene (**2b**).

Generation of acylketenes from 1,3-dioxin-4-ones was generally recognized in this study. The reaction of the masked acylketene (**1**) with compounds having a cyano group provides a useful method for preparing a variety of 1,3-oxazin-4-ones. Further extensions of the cycloaddition of acylketenes are under investigation.

Experimental

Melting points are uncorrected. Infrared (IR) spectra were taken on a JASCO A-102 spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-PMX 60 with tetramethylsilane as an internal standard. Mass spectra (MS) were taken on JEOL JMS-01SG-2 (FD) and Hitachi M-52G spectrometers. All reactions of **1** were carried out in dry solvents. Dioxin-4-ones (**1**) were prepared according to the reported procedure[1)] except for 2,2,6-trimethyl-1,3-dioxin-4-one (**1a**),[7)] 6-ethyl-2,2-dimethyl-1,3-dioxin-4-one (**1c**),[8)] and 6-benzyl-2,2-dimethyl-1,3-dioxin-4-one (**1d**).

6-Benzyl-2,2-dimethyl-1,3-dioxin-4-one (1d)——Applying the reported procedure,[1,8)] a mixture of phenylacetyl Meldrum's acid[9)] (13.1 g) and acetone (1.45 g) in dry toluene (50 ml) was refluxed for 1 h. Concentration of the

Table VI. 2-Aryl-4*H*-1,3-oxazin-4-ones (**21e**—**g**, **22e**—**g**, **23e**—**g**)

Compd. No.	Substituent			Yield (%)	mp (°C)	Recryst. solvent[a]	Formula	Analysis (%) Calcd (Found)		
	R^1	R^2	R^3					C	H	N
21e	Me	Me	H	13	142—143	A	$C_{12}H_{12}NO_2$	71.62 (71.66	5.51 5.52	6.96 6.93)
21f	Me	Ph	H	18	129—130	B	$C_{17}H_{13}NO_2$	77.55 (77.32	4.98 5.01	5.32 5.17)
21g	Ph	Me	H	17	216—218	C	$C_{17}H_{13}NO_2$	77.55 (77.60	4.98 5.06	5.32 5.43)
22e	Me	Me	Me	22	155—157	A	$C_{13}H_{13}NO_2$	72.54 (72.24	6.09 6.15	6.51 6.39)
22f	Me	Ph	Me	16	125—127	B	$C_{18}H_{15}NO_2$	77.96 (77.84	5.45 5.55	5.05 4.99)
22g	Ph	Me	Me	18	205—206	A	$C_{18}H_{15}NO_2$	77.96 (77.70	5.45 5.53	5.05 4.83)
23e	Me	Me	OMe	33	156—158	D	$C_{13}H_{13}NO_3$	67.52 (67.25	5.67 5.77	6.06 6.06)
23f	Me	Ph	OMe	41	238—239	A	$C_{18}H_{15}NO_3$	73.70 (73.44	5.15 5.12	4.78 4.69)
23g	Ph	Me	OMe	35	168—169	A	$C_{18}H_{15}NO_3$	73.70 (73.50	5.15 5.12	4.78 4.68)

a) A, dichloromethane–hexane; B, ether; C, ethyl acetate; D, ethyl acetate–ether.

Table VII. Spectral Data for 2-Aryl-4*H*-1,3-oxazin-4-one Derivatives (**21e**—**g**, **22e**—**g**, **23e**—**g**)

Compd. No.	IR ($CHCl_3$) cm^{-1}	NMR ($CDCl_3$) δ[a]
21e	1658	2.01 (3H, s, Me), 2.35 (3H, s, Me), 7.36—7.60 (3H, m), 8.10—8.27 (2H, m)
21f	1667, 1640	2.18 (3H, s, C_5-Me), 7.33—7.72 (8H, m), 8.17—8.33 (2H, m)
21g	1680, 1660 (sh), 1650	2.26 (3H, s, C_6-Me), 7.15—7.67 (3H, m), 7.33 (5H, s, C_5-Ph), 8.08—8.43 (2H, m)
22e	1660, 1656 (sh)	2.00 (3H, s, Me), 2.33 (3H, s, Me), 2.41 (3H, s, -C_6H_4-Me), 7.26 (2H, d, J=8.4 Hz), 8.08 (2H, d, J=8.4 Hz)
22f	1600 (sh), 1642	2.18 (3H, s, C_5-Me), 2.43 (3H, s, -C_6H_4-Me), 7.30 (2H, d, J=8.2 Hz), 7.43—7.70 (5H, m, C_6-Ph), 8.15 (2H, d, J=8.2 Hz)
22g	1670, 1655 (sh), 1648	2.27 (3H, s, C_6-Me), 2.41 (3H, s, -C_6H_4-Me), 7.20—7.35 (7H, m), 8.15 (2H, d, J=8.2 Hz)
23e	1659	1.97 (3H, s, Me), 2.32 (3H, s, Me), 3.86 (3H, s, -OMe), 6.93 (2H, d, J=8.6 Hz), 8.13 (2H, d, J=8.6 Hz)
23f	1658 (sh), 1640	2.25 (3H, s, C_5-Me), 3.93 (3H, s, -OMe), 7.05 (2H, d, J=8.8 Hz), 7.65 (5H, s, C_6-Ph), 8.22 (2H, d, J=8.8 Hz)
23g	1653 (sh), 1648	2.26 (3H, s, C_6-Me), 3.84 (3H, s, -OMe), 6.95 (2H, d, J=8.8 Hz), 7.33 (5H, s, C_5-Ph), 8.19 (2H, d, J=8.8 Hz)

a) The NMR spectrum of compound **23f** was taken in CF_3COOH–$CDCl_3$ (9 : 1).

mixture *in vacuo* gave crude **1d** as a yellowish oil. Yield, 10.8 g (99%). This oil was used without purification for subsequent reactions. A portion of the crude **1d** was chromatographed on a silica gel column with a mixture of hexane–ethyl acetate (4 : 1, v/v) to give pure **1d** as a colorless oil, which solidified in a freezer. Recrystallization from pentane gave prisms of mp 38.5—40.5 °C. *Anal.* Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.26; H, 6.43. IR ($CHCl_3$): 1720, 1631 cm^{-1}. NMR ($CDCl_3$) δ: 1.60 (6H, s, C_2–Me_2), 3.49 (2H, s, $-C\underline{H}_2Ph$), 5.17 (1H, s, C_5–H), 7.24 (5H, $-CH_2\underline{Ph}$).

Pyridinium Ethoxycarbonyl(5,6-dimethyl-4-oxo-4*H*-1,3-oxazin-2-yl)methylide (6e)——A mixture of **3**[10] (0.57 g, 3 mmol) and **1e** (0.94 g, 6 mmol) in mesitylene (6 ml) was heated at 165 °C for 30 min, then cooled. Separated crystals were collected by suction, washed with ether and dried to give **6e**, yellow needles, mp 262—263 °C (dec.), 0.74 g (86%). Recrystallization from methanol gave an analytical sample, which decomposed at the same temperature. *Anal.* Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.51; N, 9.72. Found: C, 62.36; H, 5.54; N, 9.52. IR (Nujol): 1668, 1630 cm^{-1}. NMR (50% CF_3COOH–$CDCl_3$) δ: 1.19 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 1.94 (3H, s, oxazine ring C_5–Me), 2.05 (3H, s, oxazine ring C_6–Me), 4.33 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.93—9.06 (6H, m, Ar-H and –NHCO). MS *m/e*: 288 (M^+).

Pyridinium Ethoxycarbonyl(5-methyl-4-oxo-6-phenyl-4*H*-1,3-oxazin-2-yl)methylide (6f)——A mixture of **3** (0.19 g) and **1f** (0.44 g, 2 mmol) in mesitylene (2 ml) was heated at 165 °C for 30 min, then cooled. Separated crystals were collected by suction, washed with ether, and dried to give **6f**, yellow needles, mp 272—274 °C (dec.), 0.33 g (93%). Recrystallization from ethanol gave an analytical sample, which decomposed at the same temperature. *Anal.* Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.36; H, 5.20; N, 7.90. IR (Nujol): 1626 cm^{-1}. NMR (50% CF_3COOH–$CDCl_3$) δ: 1.24 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.13 (3H, s, oxazine ring Me), 4.37 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.07—9.05 (11H, m, Ar-H and –NHCO). MS *m/e*: 350 (M^+).

Pyridinium Ethoxycarbonyl(6-methyl-4-oxo-5-phenyl-4*H*-1,3-oxazin-2-yl)methylide (6g)——A mixture of **3** (0.19 g) and **1g** (0.44 g) in mesitylene (2 ml) was heated at 165 °C for 1 h, then cooled. Ether (10 ml) was added to the reaction mixture, and precipitates were collected by suction, washed with ethyl acetate, and recrystallized from benzene–ethyl acetate to give **6g**, yellow needles, mp 222—224 °C (dec.). Yield, 0.11 g (30%). *Anal.* Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.17; H, 5.12; N, 7.80. IR (Nujol): 1678, 1640 cm^{-1} NMR (50% CF_3COOH–$CDCl_3$) δ: 1.17 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 1.94 (3H, s, oxazine ring Me), 4.29 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.96—8.90 (11H, m, Ar-H and –NHCO). MS *m/e*: 350 (M^+).

Pyridinium and Isoquinolinium Bis(4-oxo-4*H*-1,3-oxazin-2-yl)methylides (7e—g and 8e—g): General Procedure——A mixture of **4**[3a)] or **5**[3a)] (0.5 mmol) and **1** (1.5 mmol) in mesitylene (3 ml) was heated at 165 °C for 2 h, then cooled. The precipitates were collected by suction, washed with ether and dried to give **7** or **8**. The melting points (dec.) were unchanged on further purification by recrystallization. Melting points and analytical data for **7** and **8** are listed in Table I, and spectral data are summarized in Table II.

Dimethylsulfonium Bis(6-methyl-4-oxo-4*H*-1,3-oxazin-2-yl)methylide (10)——A mixture of **9**[3a)] (0.63 g, 5 mmol) and **1a** (2.13 g, 15 mmol) in xylene (15 ml) was heated at 130 °C for 20 min, then cooled. The precipitates were collected by suction, washed with ether, and recrystallized from acetonitrile to give **10**, needles, mp 201—203 °C (dec.). Yield, 1.23 g (84%). IR (Nujol): 1669, 1635 cm^{-1}. NMR (10% CF_3COOH–$CDCl_3$) δ: 2.52 (6H, s, 2×Me), 3.38 (6H, s, S–Me_2), 6.38 (2H, s, oxazine ring H). MS *m/e*: Calcd for M^+: 294.067. Obsd: 294.063; Calcd for (M – acetylketene)$^+$: 210.046. Obsd: 210.046.

1,3-Dibenzoyl-2-hydroxypyrrolo[2,1-*a*]isoquinoline (12)——A mixture of **11**[11)] (0.25 g 1 mmol) and **1b** (0.41 g, 2 mmol) in diglyme (4 ml) was heated at 130 °C for 1 h. After removal of the solvent *in vacuo*, the residue was subjected to silica gel (13 g) column chromatography. Elution with hexane–ether (5 : 1, v/v) gave a crystalline substance, which was recrystallized from benzene–ether to give **12**, yellow prisms, mp 164—166 °C. Yield, 0.10 g (25%). *Anal.* Calcd for $C_{26}H_{17}NO_3$: C, 79.78; H, 4.38; N, 3.58. Found: C, 80.06; H, 4.42; N, 3.64. IR ($CHCl_3$): 1637, 1610, 1597 cm^{-1}. NMR ($CDCl_3$) δ: 6.85—7.91 (15H, m, Ar-H), 9.22 (1H, d, J=7.6 Hz, C_5–H), 10.90 (1H, s, OH). MS *m/e*: 391 (M^+).

2-Acetoxy-3-benzoyl-1-methylpyrrolo[2,1-*a*]isoquinoline (13)——A mixture of **11** (0.49 g) and **1e** (0.63 g) in mesitylene (4 ml) was heated at 165 °C for 4.5 h. The reaction mixture was subjected to silica gel (33 g) column chromatography. Elution with benzene gave a crystalline substance, which was recrystallized from benzene–hexane to give **13**, yellow needles, mp 167—167.5 °C. Yield, 0.06 g (9%). *Anal.* Calcd for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 76.75; H, 5.00; N, 4.20. IR ($CHCl_3$): 1778 (sh), 1760, 1603 cm^{-1}. NMR ($CDCl_3$) δ: 1.60 (3H, s, acetyl), 2.37 (3H, s, C_1–Me), 6.97 (1H, d, J=7.2 Hz, C_6–H), 7.29—7.88 (8H, m, Ar-H), 8.05—8.46 (1H, m, C_{10}–H), 9.34 (1H, d, J=7.2 Hz, C_5–H). MS *m/e*: 343 (M^+).

3-Benzoyl-2-(2-benzoylpropionyloxy)-1-methylpyrrolo[2,1-*a*]isoquinoline (14)——A mixture of **11** (0.25 g) and **1f** (0.44 g) in mesitylene (4 ml) was heated at 165 °C for 1 h. The reaction mixture was purified by a procedure similar to that described for **13** to give **14** as yellow needles of mp 173.5—174 °C. Yield, 0.07 g (15%). *Anal.* Calcd for $C_{30}H_{23}NO_4$: C, 78.07; H, 5.02; N, 3.04. Found: C, 78.29; H, 5.10; N, 2.86. IR ($CHCl_3$): 1770, 1681, 1599 cm^{-1}. NMR ($CDCl_3$) δ: 1.17 (3H, d, J=7.6 Hz, Me), 2.34 (3H, s, C_1–Me), 3.67 (1H, q, J=7.6 Hz, methine-H), 6.99 (1H, d, J=7.6 Hz, C_6–H), 7.30—7.90 (13H, m, Ar-H), 8.10—8.43 (1H, m, C_{10}–H), 9.30 (1H, d, J=7.6 Hz, C_5–H). MS *m/e*: 461 (M^+).

7-Benzoyl-5-oxo-1,2,3,4-tetrahydro-5*H*-oxocino[3′,2′;3,4]pyrrolo[2,1-*a*]isoquinoline (15)——A mixture of **11**

(0.74 g) and **1j** (1.09 g) in mesitylene (6 ml) was heated at 165 °C for 3.5 h. The reaction mixture was subjected to silica gel (36 g) column chromatography. Elution with benzene gave a crystalline substance, which was recrystallized from dichloromethane–hexane to give **15**, yellow needles, mp 212—213.5 °C. Yield, 0.08 g (7%). *Anal.* Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 77.93; H, 5.19; N, 3.68. IR ($CHCl_3$): 1760, 1602 cm^{-1}. NMR ($CDCl_3$) δ: 1.74—2.74 (6H, m, $CH_2(C\underline{H}_2)_3CO_2$), 2.81—3.19 (2H, m, $C\underline{H}_2(CH_2)_3CO_2$), 7.04 (1H, d, J=7.6 Hz, C_{10}–H), 7.32—7.79 (8H, m, Ar-H), 8.14—8.31 (1H, m, C_{14}–H), 9.32 (1H, d, J=7.6 Hz, C_9–H). MS *m*/*e*: 369 (M^+).

3-Benzoyl-2-hydroxy-1-methylpyrrolo[2,1-*a*]isoquinoline (16)——a) Methanolic potassium hydroxide (0.1 M, 1.4 ml) was added to a solution of **13** (50 mg) in methanol (4 ml) and tetrahydrofuran (2 ml). After being stirred for 10 min at room temperature, the mixture was concentrated under reduced pressure. The residue was neutralized with 10% hydrochloric acid, and the solution was extracted with dichloromethane. The organic layer was dried over magnesium sulfate and concentrated. Recrystallization of the residue from methanol gave **16**, yellow needles, mp 159—159.5 °C. Yield, 38 mg (90%). *Anal.* Calcd for $C_{20}H_{15}NO_2$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.42; H, 5.14; N, 4.59. IR ($CHCl_3$): 1592 cm^{-1}. NMR ($CDCl_3$) δ: 2.51 (3H, s, Me), 6.53 (1H, d, J=7.2 Hz, C_6–H), 7.46—7.62 (9H, m, Ar-H), 8.17—8.36 (1H, m, C_{10}–H), 10.13—10.63 (1H, br, OH). MS *m*/*e*: 301 (M^+).

b) Methanolic potassium hydroxide (0.1 M, 2.2 ml) was added to a solution of **14** (100 mg) in methanol (7 ml) and tetrahydrofuran (3 ml). After being stirred for 30 min at room temperature, the mixture was evaporated under reduced pressure. The residue was neutralized with 10% hydrochloric acid, and the solution was extracted with dichloromethane. The dichloromethane layer was dried over magnesium sulfate and concentrated. The resulting semi-solid was extracted with hexane. The residue was recrystallized from methanol to give **16**. Yield, 53 mg (80%). Concentration of the hexane solution gave methyl 2-benzoylpropionate as an oil. Yield, 36 mg (85%).

Methyl 3-Benzoyl-2-hydroxy-1-pyrrolo[2,1-*a*]isoquinolinepentanoate (17)——Methanolic potassium hydroxide (0.1 M, 1.6 ml) was added to a solution of **15** (60 mg) in methanol (3 ml) and tetrahydrofuran (5 ml). After being stirred for 30 min at room temperature, the reaction mixture was purified by applying the procedure given for **16** to furnish **17**, yellow needles, mp 111.5—112.5 °C (recrystallized from hexane). Yield, 56 mg (87%). *Anal.* Calcd for $C_{25}H_{23}NO_4$: C, 74.79; H, 5.78; N, 3.49. Found: C, 74.95; H, 5.78; N, 3.42. IR ($CHCl_3$): 1726, 1590 cm^{-1}. NMR ($CDCl_3$) δ: 1.68—2.03 (4H, m, $CH_2(C\underline{H}_2)_2CH_2$), 2.30—2.60 (2H, m, $-CH_2CO_2$), 2.85—3.28 (2H, m, $C\underline{H}_2(CH_2)_3CO_2$), 3.65 (3H, s, –OMe), 6.54 (1H, d, J=7.6 Hz, C_6–H), 7.47—7.66 (9H, m, Ar-H), 8.12—8.32 (1H, m, C_{10}–H), 9.90—10.70 (1H, br, OH). MS *m*/*e*: 401 (M^+).

2-Dimethylamino- and 2-Diethylamino-4*H*-1,3-oxazin-4-ones (19 and 20): General Procedure——A mixture of the dioxinone **1** and 1.25 eq of *N*,*N*-dimethylcyanamide[12] or *N*,*N*-diethylcyanamide[12] was heated at 130 °C (**1b**—**d**, **l**) or 165 °C (**1e**—**k**). The reaction period is shown in Table III. Precipitated crystals were collected by suction, washed with a small amount of ether, and treated, if necessary, with charcoal in ethyl acetate. Purification by recrystallization afforded **19** or **20**. Product **20c** was purified by alumina (20 g) column chromatography of the reaction mixture using ether–ethyl acetate (3 : 2, v/v) as an eluent. Product **20f** was purified by silica gel (12 g) column chromatography with ether–ethyl acetate (2 : 1, v/v). The results are summarized in Tables III—V.

2-Phenyl-4*H*-1,3-oxazin-4-ones (21): General Procedure——A mixture of **1** (3 mmol) and benzonitrile (18 mmol) was heated at 165 °C for 10 h. Excess benzonitrile was distilled off under reduced pressure. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (3 : 2, v/v) gave a crystalline substance, which was purified by recrystallization to give **21**.

2-(*p*-Tolyl)-4*H*-1,3-oxazin-4-ones (22) and 2-(*p*-Anisyl)-4*H*-1,3-oxazin-4-ones (23): General Procedure——A mixture of **1** (3 mmol) and *p*-tolunitrile or *p*-anisonitrile (18 mmol) was heated at 165 °C for 10 h. The reaction mixture was subjected to silica gel column chromatography. Elution with hexane–ether (3 : 1, v/v) gave the starting nitrile. Subsequent elution with hexane–ethyl acetate (3 : 2, v/v) gave a crystalline substance, which was recrystallized to give **22** or **23**. Yields, melting points, and analytical data are listed in Table VI, and spectral data are summarized in Table VII.

3-Benzoyl-4-hydroxy-6-phenyl-2*H*-pyran-2-one (24)——A mixture of **1b** (0.612 g) and benzonitrile (1.85 g) was heated at 120 °C for 4 h. Excess benzonitrile was distilled off under reduced pressure. The residue (0.47 g) was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (4 : 1, v/v) gave a crystalline substance. Recrystallization from ethyl acetate gave **24**, needles, mp 168—169 °C (lit.[13] mp 171 °C). Yield, 35 mg (4%). The IR spectrum was identical with that of an authentic sample prepared according to the literature.[13]

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