  Bull. Chem. Soc. Jpn., 60, 1489—1495 (1987)

Cycloaddition of Pyridinium Methylides with Electron-Deficient Olefins and Silica-Gel Mediated Elimination of Pyridines from the Cycloadducts: A New Method of Alkylation or Hydroalkylidenation of Olefins

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(Received October 28, 1986)

Pyridinium methylides bearing an anion-stabilizing substituent at the ylide carbon react with a variety of olefins carrying two electron-withdrawing groups at the both carbons such as *N*-substituted maleimides, a citraconimide, dimethyl maleate, dimethyl fumarate, and 1,2-dibenzoylethene. The cycloadducts thus formed undergo a ready elimination of pyridines when treated with silica gel. This sequence is a new method for alkylation or hydroalkylidenation of olefins.

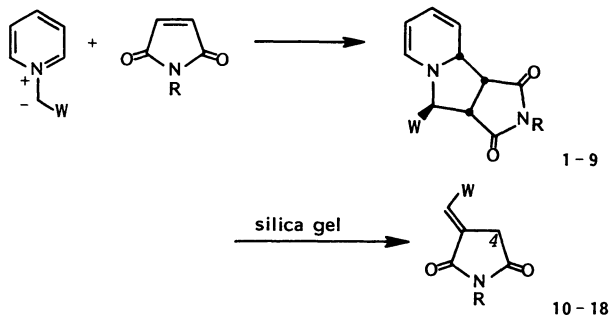
Heteroaromatic nitrogen ylides are readily accessible by the general procedure of *N*-alkylation of nitrogen-containing aromatic heterocycles and subsequent deprotonation with a base.[1] These ylides show high reactivity to a wide variety of olefins which are activated by electron-withdrawing substituents.[2] As a result, a fused pyrrolidine ring is added to the heterocycles and this cycloaddition reaction takes place in a highly stereo-, regioselective, and stereospecific manner.[2]

In the cycloaddition step, heteroaromatic ring of the ylides loses its aromaticity. Accordingly, the cycloadducts produced are often rather labile so as to undergo either a thermal retro cycloaddition going back to the ylides and olefins or a carbon-carbon bond cleavage into betaines.[2a,b] These reversible processes become visible only when they are accompanied by some further conversions leading to thermodynamically more stable compounds. A novel fragmentation reaction of the cycloadducts of pyridinium methylides via such betaine intermediates has been recently demonstrated.[3,4]

The present paper describes silica-gel mediated elimination reaction of pyridines from the olefin cycloadducts of pyridinium methylides. Part of the present results was previously reported as a preliminary communication.[4]

Results and Discussion

Pyridinium methylides bearing an anion-stabilizing group W such as benzoyl, 2-furoyl, acetyl, methoxy- and ethoxycarbonyl, cyano, or *p*-nitrophenyl moiety are easily generated in situ by treatment of the corresponding 1-alkylpyridinium halides with such a weak base as triethylamine. If a maleimide as a reactive olefinic dipolarophile is present, the pyridinium methylides are captured by the maleimide as soon as they are generated to give stereoselective cycloadducts **1—9** all in quantitative yields (Scheme 1).[2a]



1-9

10-18

1, 10: W=COPh, R=Me
2, 11: W=COPh, R=Ph
3, 12: W=COPh, R=p-tolyl
4, 13: W=2-furoyl, R=p-tolyl
5, 14: W=COMe, R=p-tolyl
6, 15: W=COOMe, R=p-tolyl
7, 16: W=COOEt, R=p-tolyl
8, 17: W=CN, R=p-tolyl
9, 18: W=p-$NO_2C_6H_4$, R=p-tolyl

Scheme 1.

These cycloadducts have quite different stability in an aprotic and a protic solvent. At room temperature in dry aprotic solvents such as benzene, toluene, dichloromethane, chloroform, tetrahydrofuran, and dimethyl sulfoxide, they stay stable. When warmed at 50—60 °C, they started to decompose slowly and changed into a mixture of complex and unidentified products after a long heating.[5] On the other hand, when heated under reflux in ethanol or treated with a catalytic amount of acetic acid in chloroform at room temperature, **1** underwent a clean decomposition leading to **10**. Use of strong acids such as hydrogen chloride, *p*-toluenesulfonic acid, trifluoroacetic acid, and titanium(IV) chloride, however, led to complex mixture of products. The most effective method of all employed so far is to treat the crude cycloadduct of **1** with silica gel in a glass column.

The procedure is very simple as shown below: A mixture of 1-phenacylpyridinium bromide and *N*-methylmaleimide in chloroform was treated with triethylamine (each 1 equivalent). After 10 min at room temperature, the mixture was poured into ice water and extracted in dichloromethane. The crude cycloadduct **1** thus obtained was charged in a silica-gel

Table 1. Cycloaddition of Pyridinium Methylides to Maleimides and Subsequent Elimination of Pyridines Leading to Itaconimides **10**—**18**

Ylide $Py^+-\bar{C}H_2-W$ W	Maleimide $(=CHCO)_2NR$ R	Reaction conditions: Cycloaddition[c]	Reaction conditions: Elimination[d]	Cycloadduct[a]	yield/%	Itaconimide[b]	yield/%
COPh	Me	rt, 10 min, CF	S	**1**	100	**10**	86
COPh	Ph	rt, 10 min, CF	S	**2**	100	**11**	85
COPh	*p*-Tolyl	rt, 10 min, DCM	S	**3**	100	**12**	82
2-Furoyl	*p*-Tolyl	rt, 10 min, CF	S	**4**	100	**13**	32
COMe	*p*-Tolyl	rt, 1 h, CF	S	**5**	93	**14**	46
COOMe	*p*-Tolyl	rt, 10 min, CF	S	**6**	100	**15**	87
COOEt	*p*-Tolyl	rt, 10 min, CF	S	**7**	100	**16**	72
CN	*p*-Tolyl	rt, 20 min, CF	S	**8**	87	**17**	51
p-$NO_2C_6H_4$	*p*-Tolyl	rt, 12 h, DMSO	S	**9**	100	**18**	59
		rt, 12 h, DMSO	A	**9**	100	**18**	52
3,5-Dimethylpyridinium phenacylide	*p*-Tolyl	rt, 10 min, DCM	S	**19**	100	**12**	100

a) These cycloadducts were isolated when crude mixture from the cycloaddition was washed with water and then the dried solvent was evaporated in vacuo. b) These products were obtained when the crude cycloaddition product was subjected to a silica-gel chromatography or treated with acetic acid. The yields are all based on maleimides. c) CF: chloroform; DCM: dichloromethane; DMSO: dimethyl sulfoxide. d) S: silica-gel chromatography; A: treatment with acetic acid.

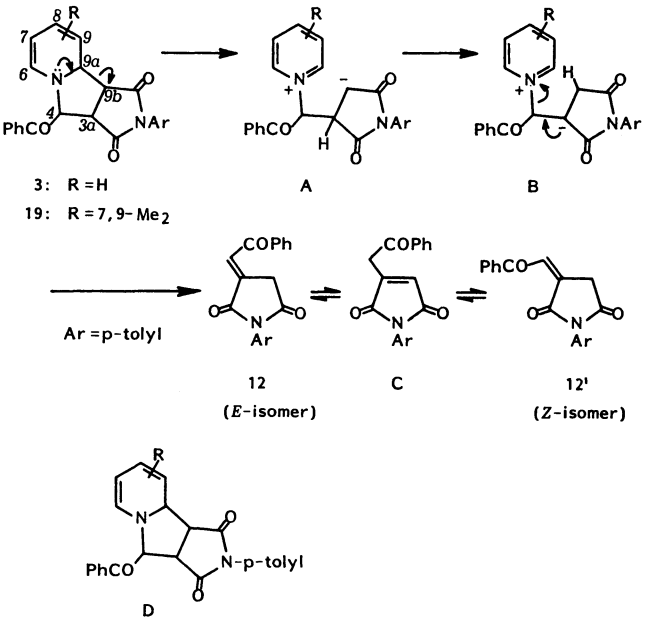
column and then eluted with chloroform to give a single product **10** in 86% yield.

The product **10** was assigned as (*E*)-3-benzoylmethylene-1-methyl-2,5-pyrrolidinedione on the basis of spectral data as well as elemental analysis. The E-geometry of olefin part of **10** was based on low chemical shifts of both the 4-methylene hydrogens (3.76 ppm) and the olefinic hydrogen (7.94 ppm), compared with those (4-H: 3.47 ppm; $=CH_2$: 5.70 and 6.43 ppm) of 3-methylene-1-(*p*-tolyl)-2,5-pyrrolidinedione (*N*-(*p*-tolyl)itaconimide).[3a]

The other cycloadducts **2**—**9** underwent similar silica gel-mediated elimination of pyridine to afford derivatives of itaconimides **11**—**18** (Scheme 1 and Table 1).

Scheme 2 illustrates a possible mechanism: The cycloadduct **3** as an example undergoes a reversible cleavage at the 9a,9b-bond into betaine intermediate **A**. This transformation is driven by the recovery of aromaticity. A 1,2-proton migration into **B** is followed by the β-elimination of pyridine to give itaconimide **12**.

The exclusive formation of (*E*)-itaconimide **12** was previously explained by a stereoselective elimination route from the sterically defined cycloadduct **3**.[4] However, this mechanism should be now renewed on the basis of the following observations: 1) 3-Methylene-1-(*p*-tolyl)pyrrolidine-2,5-dione (*N*-(*p*-tolyl)-itaconimide) readily isomerizes into 3-methyl-1-(*p*-tolyl)-3-pyrroline-2,5-dione (*N*-(*p*-tolyl)citraconimide) on treatment with triethylamine;[3a] 2) 4-Methyl derivative of **12** (or **12'**) is so unstable that it is isolated in a structure of 3,4-disubstituted 3-pyrroline-2,5-dione (see compound **39** in Scheme 5); 3) No isomerization occurs on treatment of **12** with butyllithium in THF.[6] Thus, the selective formation of (*E*)-itaconimide **12** has presumably resulted from the thermodynamic stability of



Scheme 2.

12 over either of its *Z*-isomer **12'** or citraconimide **C** (Scheme 2).[7]

Electron-donating substituents on the pyridine nucleus of cycloadducts were found to facilitate the elimination reaction of pyridines. For example, cycloadduct **19** bearing two methyls at the 7- and 9-positions underwent a quick elimination leading to **12** when chromatographed over silica gel.[8] However, cycloadducts **D** bearing an electron-withdrawing substituent (R is 8-CN, 7- or 9-CF_3, and 7- or 9-COOMe) were recovered unchanged under similar conditions. Presumably, the reversible 9a,9b-bond cleavage into betaine **A** was facilitated by the electron-donating substituents (Scheme 2).

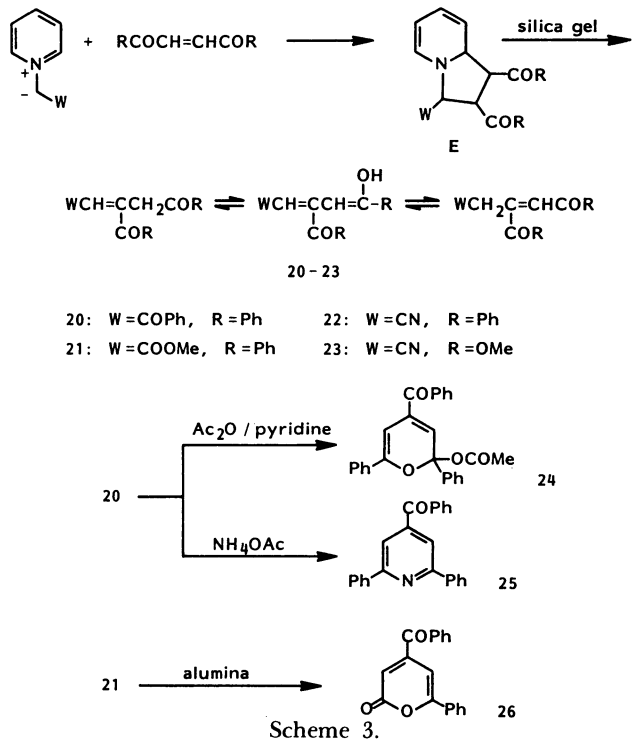
Table 2. Reaction of Pyridinium Methylides with Acyclic Olefinic Dipolarophiles Leading to **20—23**[a)]

Pyridinium methylide $Py^{+}-\bar{C}H_2-W$ W	Olefin	Reaction conditions	Product	Yield/%[b)]
COPh	PhCOCH=CHCOPh (*Z*)	rt, 10 min, DCM	**20**	61
	PhCOCH=CHCOPh (*E*)	rt, 20 min, DCM		100
COOMe	PhCOCH=CHCOPh (*E*)	rt, 1 h, CF	**21**	62
CN	PhCOCH=CHCOPh (*E*)	rt, 1 h, CF	**22**	38
	MeOOCCH=CHCOOMe (*Z*)	reflux, 3 h, CF	**23**	50
	MeOOCCH=CHCOOMe (*E*)	reflux, 22 h, CF		65

a) After the cycloaddition was over, the crude reaction mixture was chromatographed over silica gel by using chloroform or benzene as an eluent. b) All isolated yields based on the olefin.

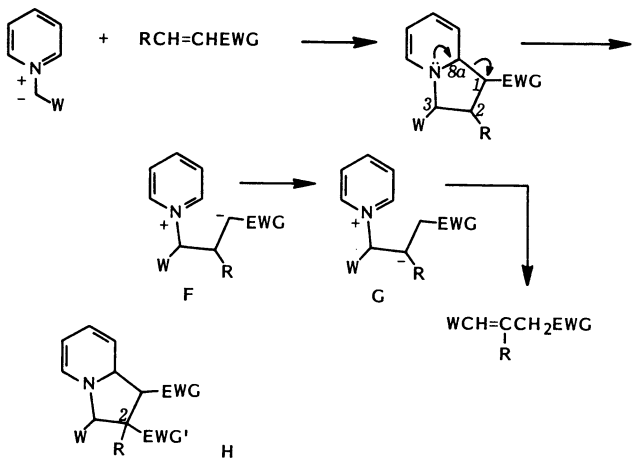
Reactions of pyridinium methylides with acyclic olefins such as (*E*)- and (*Z*)-1,2-dibenzoylethene and dimethyl fumarate and maleate formed unstable cycloadducts **E** which could not be isolated in pure forms. During the usual work-up or chromatographic operation on silica gel, the cycloadducts **E** eliminated pyridine to give olefins **20—23** (Scheme 3 and Table 2).

These products **20—22** were not single isomers but mixtures of several isomers and/or tautomers. As **20—22** belong to allyl systems bearing strongly electron-withdrawing substituents at every carbon, the stable structure of **20—22** depends upon the polarity of solvent in which they are dissolved. For example, **20** mainly takes propene structures (mixture of *E*- and *Z*-isomers) in chloroform, while 1,3-butadien-1-ol structure as an enol form is a major contributor in dimethyl sulfoxide. When electron-withdrawing property of the substituents is decreased, isomeric purity is increased as seen in the case of **23** which exclusively exists in one isomer form of propene structure, dimethyl 3-cyanopropene-1,2-dicarboxylate, in its chloroform solution.



Scheme 3.

Treatment of **20** with acetic anhydride in the presence of a catalytic amount of pyridine gave 2-acetoxy-4-benzoyl-2,6-diphenyl-2*H*-pyran (**24**) (Scheme 3). With ammonium acetate at room temperature, 4-benzoyl-2,6-diphenylpyridine (**25**) was obtained. The latter pyridine formation foregone by the ylide cycloaddition and the pyridine elimination presumably corresponds to a sequence of reactions which are involved in the pyridine synthesis discovered by Kröhnke.[9)] The ester group of **21** participated in a lactonization leading to 4-benzoyl-6-phenyl-2*H*-pyran-2-one (**26**) on its chromatography on alumina.



Scheme 4.

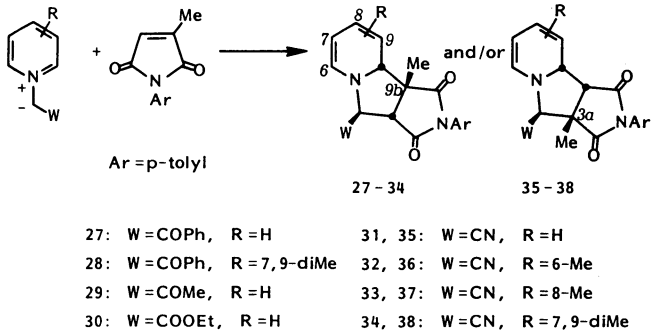
Since only olefins activated by electron-withdrawing moiety (EWG) can be successfully employed in the cycloaddition with pyridinium methylides, the cycloadducts carry an EWG at the 1-position (Scheme 4). Accordingly, every cycloadduct has a chance to undergo the 1,9a-bond cleavage leading to betaine **F**. When R is an anion-stabilizing moiety, 1,2-proton migration of **F** occurs to form another betaine **G** which is an inevitable intermediate in the pyridine elimination reaction. This means that the cycloaddition and pyridine elimination sequence can be performed only by use of the olefins in which the both olefinic carbons are attached by electron-withdrawing substituents. If

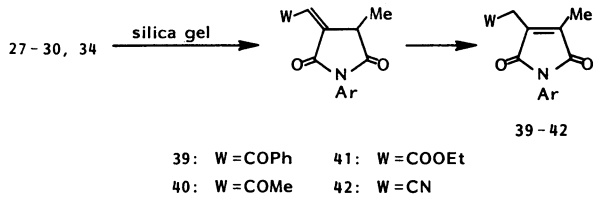
Table 3. Cycloaddition of Pyridinium Methylides to *N*-(*p*-Tolyl)citraconimide and Subsequent Elimination of Pyridines Leading to **39—42**

Pyridinium methylides W	R	Reaction conditions[a]	Cycloadduct	yield/%	Product[b]	Yield/%[c]
COPh	H	rt, 11 h, DCM	**27**	100	**39**	82
COPh	3,5-diMe	rt, 2 h, DCM	**28**	100	**39**	80
COMe	H	rt, 13 h, CF	**29**	94	**40**	37
COOEt	H	rt, 3 d, CF	**30**	d)	**41**	51
CN	H	rt, 24 h, CF	**31**+**35** (1:2)	100		
CN	2-Me	rt, 3 h, CF	**32**+**36** (1:3)	100		
CN	4-Me	rt, 5 h, CF	**33**+**37** (1:3)	100		
CN	3,5-diMe	rt, 19 h, CF	**34**+**38** (1:3)	100	**42**	20 (79)[e]

a) CF: chloroform; DCM: dichloromethane. b) Obtained after the crude cycloadduct was chromatographed over silica gel by using chloroform as an eluent. c) All isolated yields based on the citraconimide. d) Not isolated. e) Based on **34**.

the 2-position of cycloadduct is occupied by two substituents EWG′ and R as shown in **H**, such elimination should become impossible.





Scheme 5.

N-(*p*-Tolyl)citraconimide was allowed to react with a variety of pyridinium methylides (Scheme 5). When W is a bulky electron-withdrawing substituent such as benzoyl, acetyl, or methoxycarbonyl, single isomers of cycloadducts **27—30** were only produced. They were assigned as endo cycloadducts to the anti form of ylides with the methyl moiety at the 9b-position.[2b] On the other hand, when W is sterically small in size (W is CN), mixtures of two regioisomeric cycloadducts **31—34**+**35—38** were formed. Major regioisomers **35—38** carry the methyl moiety at the 3a-exo position.

The regioisomers with 9b-methyl were found to undergo a similar pyridine elimination when treated with silica gel. Thus, **27—30** and **34** were passed through a silica-gel column to give 3-methyl-4-(substituted methyl)-1-(*p*-tolyl)-3-pyrroline-2,5-diones **34—42**, respectively (Scheme 5 and Table 3). Exclusive isolation of **39—42** was presumably due to the ready isomerization of the intermediary 3-alkylidenepyrrolidine-2,5-diones under the reaction or work-up conditions.

As expected, such pyridine elimination reaction did not occur on the other regioisomers **35—38** bearing 3a-methyl. Instead, they decomposed into complex mixture of unidentified products when treated with silica gel. This instability was surprising. It is probable that cycloadducts **35—38** have taken an unassigned decomposition route via the corresponding betaine intermediates.

Experimental

General. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz) or a JEOL FX-100 instrument (100 MHz) and ^{13}C NMR on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. GC-Mass spectra as well as high-resolution mass spectra were also obtained on the same instrument. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck) or of aluminum oxide 60 F-254 type-E (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako), and Silicagel 60 (Merck) were employed. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20×180 mm) packed with Silicagel 60 (Merck, size: 0.04—0.063 mm). Preparative high-performance liquid chromatography (HPLC) was performed on a Kusano KHLC-201 apparatus with a UV-detector Uvilog-III using a column (22×300 mm)

packed with silica gel (Wakogel LC-50H). Gas liquid chromatography (GLC) was accomplished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization flame detector using a glass column (SE-30, 3×2000 mm) or a glass capillary column (Silicone GE, SE-30, 0.25×5000 mm). Micro vacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V at about 50 °C unless otherwise stated.

General Procedure for the Silica-Gel Mediated Pyridine Elimination from the Cycloadducts 1—9 and 19 Leading to 10—18. The reactions of pyridinium methylides with maleimides were carried out under the conditions previously reported[2a] giving quantitative yields of 1 : 1 cycloadducts **1**—**9** and **19**. The pyridine elimination was performed according to the following two methods: 1) The crude cycloadducts **1**—**9** were chromatographed over silica gel (Wako C-300) by using chloroform as an eluent to furnish the pyridine-eliminated products **10**—**18**. 2) The crude cycloadduct **9** was stirred in chloroform (20 ml/1 mmol) at room temperature for 24 h in the presence of a catalytic amount of acetic acid. The mixture was washed with water several times and then dried over anhydrous magnesium sulfate. The chloroform was evaporated in vacuo to give solid which was washed with a small amount of diethyl ether to afford **18** (52%). The results are summarized in Table 1.

10: Colorless needles (diethyl ether-petr. ether); mp 144 °C; IR (KBr) 1760, 1690, and 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.13 (3H, s, NMe), 3.76 (2H, d, J=3.0 Hz, 4-H), 7.3—7.7 (3H, m, Ph), 7.83 (1H, t, J=3.0 Hz, =CH-), and 7.9—8.1 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=24.95 (q, NMe), 34.65 (t, 4-C), 122.75 (d, =CH-), 128.45, 128.89, 133.86 (each d), 136.17, 139.76 (s, 3-C), 169.72, 174.01 (each s, 2- and 5-C), and 189.41 (s, CO); MS m/z (rel intensity, %) 229 (M^+, 45), 144 (18), 105 (base peak), 77 (69), and 51 (25). Found: C, 67.92; H, 4.80; N, 6.14%. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11%.

11: Pale yellow needles (cyclohexane); mp 176 °C; IR (KBr) 1770, 1700, and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.93 (2H, d, J=3.0 Hz, 4-H), 7.2—7.6 (6H, m, ph), 7.37 (1H, t, J=3.0 Hz, =CH-), and 7.9—8.1 (4H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=34.94 (t, 4-C), 124.13 (d, =CH-), 126.48, 128.54, 128.77, 129.01, 129.19, 129.36, 134.25 (each d), 137.42, 139.60 (each s), 172.07, 173.25 (each s, 2- and 5-C), and 189.83 (s, CO); MS m/z (rel intensity, %) 291 (M^+, 5), 105 (74), 91 (15), 77 (base peak), 67 (20), and 51 (41). Found: C, 74.04; H, 4.58; N, 4.97%. Calcd for $C_{18}H_{13}NO_3$: C, 74.21; H, 4.50; N, 4.81%.

12: Pale yellow prisms (cyclohexane); mp 180—181 °C; IR (KBr) 1770, 1700, 1660, and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.38 (3H, s, p-Me), 3.92 (2H, d, J=2.8 Hz, 4-H), 7.0—7.4 (4H, m, Ar), 7.4—7.7 (3H, m, Ph), 7.8—8.1 (2H, m, Ph), and 7.94 (1H, t, J=2.8 Hz, =CH-); ^{13}C NMR ($CDCl_3$) δ=21.19 (q, p-Me), 34.87 (t, 4-C), 123.70 (d, =CH-), 125.99, 128.51, 128.93, 129.75, 133.98 (each d), 137.20, 138.85, 139.50 (each s), 168.79, 173.08 (each s, 2-and 5-C), and 189.52 (s, CO); MS m/z (rel intensity, %) 305 (M^+, 58), 199 (31), 105 (base peak), and 76 (43). Found: C, 74.55; H, 5.05; N, 4.77%. Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59%.

13: Colorless needles (diethyl ether-petr. ether); mp 172 °C; IR (KBr) 1780, 1710, and 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.37 (3H, s, p-Me), 3.93 (2H, d, J=3.0 Hz, 4-H), 6.58 (1H, dd, J=4.0 and 1.8 Hz, 4-H of furyl), 7.20 (4H, br s, Ar), 7.34 (1H, dd, J=4.0 and 1.0 Hz, 5-H of furyl), 7.62 (1H, dd, J=1.8 and 1.0 Hz, 3-H of furyl), and 7.72 (1H, t, J=3.0 Hz, =CH-); MS m/z (rel intensity, %) 295 (M^+, 43), 189 (17), and 89 (base peak). Found: C, 69.14; H, 4.45; N, 4.81%. Calcd for $C_{17}H_{13}NO_4$: C, 69.14; H, 4.44; N, 4.74%.

14: Colorless needles (diethyl ether-petr. ether); mp 128 °C; IR (KBr) 1780, 1710, and 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.37 (3H, s, p-Me), 2.40 (3H, s, COMe), 3.78 (2H, d, J=2.8 Hz, 4-H), 7.1—7.4 (4H, m, Ar), and 7.14 (1H, t, J=2.8 Hz, =CH-); MS m/z (rel intensity, %) 243 (M^+, base peak), 201 (29), 173 (20), 172 (14), 143 (23), 101 (16), 99 (38), 67 (15), and 43 (74). Found: C, 69.11; H, 5.42; N, 5.75%. Calcd for $C_{14}H_{13}NO_3$: C 69.12; H, 5.39; N, 5.76%.

15: Colorless needles (chloroform-diethyl ether); mp 146—147 °C; IR (KBr) 1776, 1720, and 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.37 (3H, s, p-Me), 3.80 (3H, s, COOMe), 3.80 (2H, d, J=3.0 Hz, 4-H), 6.86 (1H, t, J=3.0 Hz, =CH-), and 7.1—7.3 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=21.24 (q, p-Me), 34.52 (t, 4-C), 52.34 (q, COOMe), 122.46 (d, =CH-), 126.22, 129.10 (each d), 139.11, 140.67 (each s), 165.48, 168.26 (each s, 2- and 5-C), and 172.80 (s, COOMe); MS m/z (rel intensity, %) 259 (M^+, 91), 228 (19), 227 (72), 167 (33), 149 (base peak), 129 (38), 114 (25), 72 (25), 71 (28), 67 (22), and 57 (60). Found: C, 64.87; H, 5.08; N, 5.57%. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40%.

16: Colorless needles (diethyl ether); mp 121—122 °C; IR (KBr) 1777, 1700, and 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.34 (3H, t, J=7.0 Hz, Me of Et), 2.37 (3H, s, p-Me), 3.81 (2H, d, J=3.0 Hz, 4-H), 4.26 (2H, q, J=7.0 Hz, CH_2 of Et), 6.85 (1H, t, J=3.0 Hz, =CH-), and 7.2—7.4 (4H, m, Ar); MS m/z (rel intensity, %) 273 (M^+, base peak), 228 (26), 227 (85), and 67 (25). Found: C, 66.04; H, 5.56; N, 5.01%. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13%.

17: Colorless needles (chloroform-diethyl ether); mp 147 °C; IR (KBr) 2202, 1780, 1705, and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.37 (3H, s, p-Me), 3.66 (2H, d, J=3.0 Hz, 4-H), 6.43 (1H, t, J=3.0 Hz, =CH-), and 7.1—7.4 (4H, m, Ar); MS m/z (rel intensity, %) 226 (M^+, base peak), 198 (19), 87 (33), and 65 (40). Found: C, 68.97; H, 4.55; N, 12.38%. Calcd for $C_{13}H_{10}N_2O_2$: C, 69.01; H, 4.46; N, 12.38%.

18: Pale yellow leaflets (chloroform-diethyl ether); mp 220—221 °C; IR (KBr) 1770, 1694; 1649, and 1598 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.38 (3H, s, p-Me), 3.72 (2H, d, J=2.6 Hz, 4-H), 7.1—7.8 (2H, m, ArH), 7.61 (1H, t, J=2.6 Hz, =CH-), 7.76 (2H, d, ArH), and 8.23 (2H, d, ArH); ^{13}C NMR ($CDCl_3$) δ=21.29 (p-Me), 34.13 (4-C), 125.41 (=CH-), 126.32, 127.73, 129.24, 130.12, 130.86, 132.52, 139.21, 140.33, 148.38, and 172.51 (2- and 5-C); MS m/z (rel intensity, %) 322 (M^+, base peak), 161 (85), 115 (32), and 76 (14). Found: C, 66.82; H, 4.38; N, 9.02%. Calcd for $C_{18}H_{14}N_2O_4$: C, 67.07; H, 4.38; N, 8.69%.

General Procedure for the Reaction of Pyridinium Methylides with Acyclic Olefins Leading to 20—23. To the mixture of a 1-alkylpyridinium bromide (1 mmol) and an olefin (1 mmol) in dichloromethane or chloroform was added triethylamine (1 mmol) at room temperature. The mixture was allowed to react under the conditions listed in Table 2, and then poured in ice water. The organic layer separated was dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel (Wako C-300) to give **20**—**23** (eluent for the chromatography: **20**: chloroform; **21**, **22**, and **23**: benzene). Only **23** could be purified by vacuum distilation. The results are summarized in Table 2.

20: (Mixture of several tautomers in solution): Orange

needles (acetone); mp 125—127 °C (lit,[10] mp 121—123 °C); IR (KBr) 3200, 1630, 1600, 1530, and 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.22 (4/11H, d, J=0.8 Hz, CH_2 of minor isomer), 4.88 (18/11H, d, J=1.4 Hz, CH_2 of major isomer), and 7.1—8.1 (16H, m, Ph); ^1H NMR (DMSO-d_6) δ=4.45, 4.65 (2/9H, each br s, CH_2 of two minor isomers), 6.56 (8/9H, br s, exchanged with D_2O, =CH- of major isomer), 7.2—8.0 (16H, m, Ph and =CH-), and 8.50 (8/9H, br s, exchanged with D_2O, OH of major isomer); ^{13}C NMR (DMSO-d_6) δ=99.86, 108.91 (each d), 110.85 (s), 124.94, 126.81, 127.46, 128.46, 128.75, 129.18 (each d), 131.75, 132.22, 138.91, 140.61 (each s), 164.15, 169.73, and 188.17 (each s); MS m/z (rel intensity, %) 354 (M^+, 14), 105 (base peak), 82 (26), 79 (32), and 78 (52). Found: C, 81.13; H, 5.13%. Calcd for $C_{24}H_{18}O_3$: C, 81.34; H, 5.12%.

This compound **20** was also available in 75% yield from a similar procedure using 3,5-dimethyl-1-phenacylpyridinium bromide (306 mg, 1 mmol), (*E*)-1,2-dibenzoylethene (236 mg, 1 mmol), and triethylamine (0.14 ml, 1 mmol) in dichloromethane (20 ml) at room temperature for 5 min.

21: (Mixture of several tautomers in solution): Yellow liquid; IR (neat) 1720, 1680, and 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.60, 3.65, 3.70 (each s, COOMe, integration area 18 (1 : 3 : 2)), 3.37 (s, area 1.2), 4.00 (br s, area 5.4), 4.15 (br s, area 0.7), 4.89 (br s, area 3.2), 6.35 (br s, area 1.7), 7.22 (br s, area 4.8), and 7.3—8.0 (area 72); ^{13}C NMR ($CDCl_3$) δ=50.73, 51.78 (each q, COOMe), 98.46, 104.91 (each d), 109.85 (s), 124.82, 126.58, 128.31, 128.63, 128.87, 128.98 (each d), 140.84 (s), 163.69, 166.50, 166.97 (each s). MS m/z (rel intensity, %) 308 (M^+, 33), 249 (18), 105 (base peak), and 77 (77). When chromatographed over alumina, this compound **21** changed into **26** which provided satisfactory elemental analysis as described below.

22: (Mixture of several tautomers in solution): Pale yellow liquid; IR (neat) 2250, 2200, 1740, 1680, 1660, 1600, and 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.32 (br s, integration area 5), 4.54 (br s, area 14), 5.80 (br s, area 7), and 7.0—8.2 (m, area 150); ^{13}C NMR ($CDCl_3$) δ=32.47, 41.98 (each t), 108.97 (d), 114.96 (s), 128.05, 128.22, 128.52, 128.69, 130.04 (each d), 133.33, 133.74, 135.27, 135.56 (each s), 155.17 (s), 189.34, 194.04, and 194.62 (each s); MS m/z (rel intensity, %) 167 (M^+ −108, 36), 127 (51), 105 (88), 79 (base peak), 78 (89), 92 (29), 51 (55), and 50 (37). This compound **22** was too labile to be purified as an authentic sample for elemental analysis.

23: Pale yellow liquid; IR (neat) 2220, 1750, 1740, 1720, and 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.66 (2H, d, J=0.8 Hz, CH_2), 3.72, 3.83 (each 3H, s, COOMe), and 6.48 (1H, d, J=0.8 Hz, =CH-); ^{13}C NMR ($CDCl_3$) δ=35.92 (t, CH_2), 52.48, 53.16 (each q, COOMe), 110.76 (d, =CH-), 114.81 (s, CN), 146.04 (s), 164.17, and 168.61 (each s, COOMe); MS m/z (rel intensity, %) 183 (M^+, 12), 152 (79), 139 (33), 124 (29), 113 (base peak), 82 (29), 81 (60), 59 (93), and 39 (22). Found: C, 52.33; H, 4.90; N, 7.57%. Calcd for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65%.

2-Acetoxy-4-benzoyl-2,6-diphenyl-2*H*-pyran (24): A solution of **20** (100 mg, 0.3 mmol) in acetic anhydride (6 ml) was heated at 50—60 °C under stirring for 1 h in the presence of a catalytic amount of pyridine. The mixture was poured into ice water (200 ml) and sodium hydrogencarbonate was added. After allowed to stand for 2 h, the mixture was extracted with chloroform (30 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using chloroform as an eluent to give **24** (78 mg, 66%): Pale yellow prisms (diethyl ether-petr. ether); mp 153—155 °C; IR (KBr) 1760, 1670, 1640, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.76 (3H, s, COMe), 6.70 (1H, s, 5-H), 7.2—7.7 (10H, m, 3-H and Ph), and 7.8—8.2 (6H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=19.83 (COMe), 115.78 (5-C), 125.28, 129.96, 133.03, 134.11, 136.10, 137.17, 151.11, 153.06, 167.88 (COMe), and 187.96 (COPh); MS m/z (rel intensity, %) 396 (M^+, 9), 337 (22), 250 (18), 249 (93), 105 (base peak), and 77 (78). Found: C, 78.77; H, 5.47%. Calcd for $C_{26}H_{20}O_4$: C, 78.77; H, 5.09%.

4-Benzoyl-2,6-diphenylpyridine (25). A mixture of **20** (187 mg, 0.5 mmol) and ammonium acetate (0.5 g, 0.5 mmol) in ethanol (20 ml) was allowed to stand at room temperature for a week. The precipitate was collected on a filter and washed with hexane to give **25** (141 mg, 84%): Beige leaflets (ethanol); mp 127—129 °C (lit,[9] mp125 °C); IR (KBr) 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.2—7.7 (9H, m, Ar), 7.8—8.0 (2H, m, Ar), 7.90 (2H, br s, 3- and 5-H), and 8.0—8.3 (4H, m, Ar); MS m/z (rel intensity, %) 336 (M^+ +1, 25), 335 (M^+, base peak), 334 (27), 306 (41), 127 (25), 105 (37), and 77 (49).

4-Benzoyl-6-phenyl-2*H*-pyran-2-one (26): The benzene solution of ester **21** (308 mg, 1 mmol in 0.5 ml) was charged in a column packed with activated alumina (Wako, 300 mesh) and eluted with benzene to give **26** (143 mg, 52%): Yellow prisms (diethyl ether); mp 135—137 °C; IR (KBr) 1720 and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.40 (1H, d, J=1.0 Hz, 5-H), 6.90 (1H, d, J=1.0 Hz, 3-H), and 7.3—8.1 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=99.75 (5-C), 114.72 (3-C), 125.70, 128.81, 128.93, 129.87, 131.22, 134.10, 134.62, 150.92 (6-C), 161.34 (2-C), and 192.92 (COPh); MS m/z (rel intensity, %), 276 (M^+, 19), 248 (19), 238 (17), 105 (base peak), and 77 (55). Found: C, 78.21; H, 4.43%. Calcd for $C_{18}H_{12}O_3$: C, 78.25; H, 4.38%.

General Procedure for the Cycloaddition of Pyridinium Methylides with *N*-(*p*-Tolyl)citraconimide Leading to 27—38. To a mixture of pyridinium halide and *N*-(*p*-tolyl)-citraconimide (each 1 mmol) in dry dichloromethane or chloroform (20—30 ml) was added triethylamine (1.1 mmol) at room temperature. The mixture was stirred at room temperature, poured into ice water, and extracted with dichloromethane (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo below room temperature to give **27—38** as unstable products. As cycloadducts **27—29**, **31+35**, and **34+38** are all known, they were prepared under the reported reaction conditions.[2b] The results are summarized in Table 3. Purification of these cycloadducts was unsuccessful because of their lability. The ^1H NMR spectra of regioisomeric mixture are separatedly assigned to each isomer as shown below.

32+36 (Inseparable mixture in a ratio of 1 : 3): Colorless solid; IR (KBr) 2220, 1780, 1720, 1705 and 1510 cm^{-1}; ^1H NMR ($CDCl_3$) **32**: δ=1.60 (3H, s, 9b-Me), 1.93 (3H, s, 6-Me), 2.37 (3H, s, *p*-Me), 3.20 (1H, d, J=0.6 Hz, 3a-H), 4.43 (t, J=2.0 Hz, 9a-H), 4.7—4.9 (1H, m, 7-H), 5.08 (d, 1H, J=0.6 Hz, 4-H), 5.52 (1H, br d, 9-H), 5.88 (1H, m, 8-H), and 6.9—7.3 (4H, m, Ar). **36**: δ=1.69 (3H, s, 3a-Me), 1.93 (3H, s, 6-Me), 2.37 (3H, s, *p*-Me), 3.10 (1H, d, J=8.2 Hz, 9b-H), 4.7—4.9 (2H, m, 7- and 9a-H), 5.00 (1H, s, 4-H), 5.52 (1H, br d, 9-H), 5.88 (1H, m, 8-H), and 6.9—7.3 (4H, m, Ar).

33+37 (Inseparable mixture in a ratio of 1 : 3): Colorless solid; IR (KBr) 2250, 2200, 1780, 1720, 1705, and 1515 cm^{-1}; ^1H NMR ($CDCl_3$) **33**: δ=1.59 (3H, s, 1.72 (3H, br s, 8-Me), 2.34 (3H, s, *p*-Me), 3.23 (1H, s, 3a-H), 4.38 (1H, m, 9a-H), 4.6—5.0 (1H, m, 7-H), 5.30 (1H, m, 9-H), 6.28 (1H, br d,

6-H), and 6.9—7.3 (4H, m, Ar). **37**: δ=1.67 (3H, s, 3a-Me), 1.72 (3H, br s, 8-Me), 2.34 (3H, s, *p*-Me), 3.06 (1H, d, J=8.2 Hz, 9b-H), 4.76 (1H, s, 4-H), 4.6—5.0 (2H, m, 7- and 9a-H), 5.30 (1H, br s, 9-H), 5.94 (1H, br d, 6-H), and 6.9—7.3 (4H, m, Ar).

General Procedure for the Silica-Gel Mediated Elimination of Pyridines from the Citraconimide Cycloadducts 27—30 and 34 Leading to 39—42. The solution of cycloadducts **27—30** and **34** in chloroform (1 mmol in 0.5 ml) was charged in a column packed with silica gel (Wako C-300) and eluted with another portion of chloroform to give pyridine-eliminated products **39—42**. The results are summarized in Table 3.

39: Beige prisms (diethyl ether-petr. ether); mp 99—101 °C; IR (KBr) 1780, 1710, and 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.02 (3H, s, 4-Me), 2.34 (3H, s, *p*-Me), 4.13 (2H, s, CH_2), and 7.0—8.1 (9H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=9.22 (q, 4-Me), 20.96 (q, *p*-Me), 33.17 (t, CH_2), 125.52, 128.22, 128.65 (each d), 129.28 (s), 129.40, 133.63 (each d), 134.27, 135.80, 137.15, 140.91 (each s), 170.03, 170.32 (each s, 2- and 5-C), and 193.81 (s, COPh); MS m/z (rel intensity, %) 319 (M^+, 36), 105 (base peak), 77 (33), 74 (19), and 59 (37). Found: C, 75.06; H, 5.38; N, 4.46%. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39%.

40: Pale yellow needles (diethyl ether-petr. ether); mp 68 °C; IR (KBr) 1720, 1700, 1520, and 1390 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.00 (3H, s, 4-Me), 2.25 (3H, s, COMe), 2.34 (3H, s, *p*-Me), 3.56 (2H, s, CH_2), and 7.18 (4H, br s, Ar); ^{13}C NMR ($CDCl_3$) δ=9.28 (q, 4-Me), 21.08 (q, *p*-Me), 30.12 (q, COMe), 37.81 (t, CH_2), 125.64 (d), 129.05 (s), 129.52 (d), 133.68, 137.44, 140.73 (each s), 170.03, 170.32 (each s, 2- and 5-C), and 201.90 (s, COMe); MS m/z (rel intensity, %) 257 (M^+, 63), 216 (15), 215 (base peak), 53 (24), and 43 (55). Found: C, 69.84; H, 5.75; N, 5.35%. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44%.

41: Colorless liquid; IR (neat) 1770, 1740, 1710, 1510, and 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.33 (3H, t, J=7.0 Hz, Me of Et), 2.12 (3H, s, 4-Me), 2.40 (3H, s, *p*-Me), 3.52 (2H, s, CH_2), 4.20 (2H, q, J=7.0 Hz, CH_2 of Et), and 7.19 (4H, br s, Ar); MS m/z (rel intensity, %) 287 (M^+, 37), 202 (14), 201 (base peak), 157 (10), 132 (10), 117 (11), and 68 (12). HRMS Found: m/z 287.1130. Calcd for $C_{16}H_{17}NO_4$: M, 287.1156.

42: Pale yellow needles (diethyl ether-petr. ether); mp 106—107 °C; IR (KBr) 2250, 1710, 1520, and 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.20 (3H, s, 4-Me), 2.35 (3H, s, p-Me), 3.51 (2H, s, CH_2), and 7.19 (4H, br s, Ar); MS m/z (rel intensity, %) 240 (M^+, base peak), 213 (11), 169 (11), 156 (20), 132 (17), 104 (13), 91 (13), 79 (12), 78 (17), 77 (15), and 52 (28). Found: C, 69.25; H, 5.09; N, 11.43%. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66%.

References

1) As a review: I. Zugrăvescu and M. Petrovanu, "*N*-Ylid Chemistry," McGraw-Hill Internatl., New York (1976).

2) a) O. Tsuge, S. Kanemasa, and S. Takenaka, *Bull. Chem. Soc. Jpn.*, **58**, 3137 (1986); b) O. Tsuge, S. Kanemasa, and S. Takenaka, *ibid.*, **58**, 3320 (1986); c) The references cited in the above two papers.

3) a) O. Tsuge, S. Kanemasa, S. Kuraoka, and S. Takenaka, *Chem. Lett.*, **1984**, 281; b) Y. Miki, H. Hachiken, and S. Takemura, *Heterocycles*, **22**, 701 (1984).

4) O. Tsuge, S. Kanemasa, and S. Takenaka, *Chem. Lett.*, **1984**, 465.

5) Heating the cycloadducts at about 110 °C in the presence of a dipolarophile gives stereo- and regioselective biscycloadducts in fair yields (unpublished results).

6) When **12** was treated with an equimolar amount of butyllithium in THF at −78 °C, the mixture turned deep red. Quenching the anionic species with water, benzaldehyde, or iodomethane gave unchanged **12**.

7) The double bond of **12** is stabilized by conjugation with the benzoyl moiety. In addition, the benzoyl substituent of **12** is less sterically crowded than that of **12'**.

8) Cycloadducts **D** carrying one methyl (R is 6-Me, 8-Me, and 7- or 9-Me) undergo smooth elimination of pyridines as well.

9) As a review: F. Kröhnke, *Synthesis*, **1976**, 1 and references cited therein.

10) C. A. Henrick, E. Ritchie, and C. Taylor, *Aust. J. Chem.*, **20**, 2441 (1967).