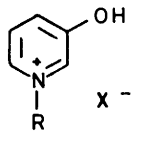
1,3-Dipolar Character of Six-membered Aromatic Rings. Part 52.[1] 2π + 8π Cycloaddition Reactions of 1-Substituted 3-Oxidopyridinium Betaines [2]

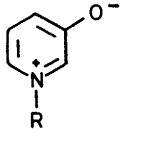
By **Alan R. Katritzky,* Alan T. Cutler, Nicholas Dennis, Gebran J. Sabongi,** and **Soheila Rahimi-Rastgoo,** School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ
Gerhard W. Fischer (in part), Research Centre for Chemical Toxicology, Academy of Sciences of the G.D.R., 705 Leipzig, G.D.R.
Ian J. Fletcher (in part), Ciba-Geigy Ltd., Basle, Switzerland.

Dichloroketen and a series of aryl(bromo)ketens react with various 1-substituted 3-oxidopyridiniums to give novel bicyclic compounds by addition across the C(4)–O and the C(2)–O positions. Frontier-MO theory is used to rationalise the orientation of these cycloadditions. Acid-catalysed hydrolysis of the C(2)–O adducts (9) yielded 3-hydroxy-2-benzylpyridines.

CYCLOADDITIONS have been reported in which 3-oxidopyridinium betaines (2) act as 4π-components (adding 2π [3] or 6π [4] addends across the 2,6-positions) or as 2π/6π-components (adding thermally 4π [5] or photochemically 2π/6π [6] addends across the 2,4-positions). We now describe cycloadditions in which they act as 8π components, adding 2π addends across the oxygen and C-4, and across the oxygen and C-2.

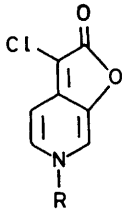


(1)



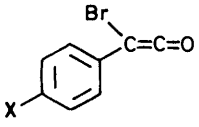
(2)

a; R = Me, X = I
b; R = Ph, X = Cl
c; R = CH_2Ph, X = Br
d; R = *p*-$ClC_6H_4COCH{=}CH$, X = Cl
e; R = $PhCH{=}CH$, X = Cl
f; R = 1-oxido-4-pyridyl, X = Cl
g; R = 4,6-dimethylpyrimidin-2-yl, X = Cl
h; R = 4,6-dimethoxy-1,3,5-triazin-2-yl, X = Cl
i; R = 3-oxocyclohex-1-enyl, X = Cl



(3)

a; R = Ph
b; R = CH_2Ph
c; R = 4,6-dimethoxy-1,3,5-triazin-2-yl
d; R = 4,6-dimethylpyrimidin-2-yl
e; R = 1-oxocyclohex-2-en-3-yl



(4)

a; X = H
b; X = NO_2
c; X = MeO
d; X = Br

RESULTS AND DISCUSSION

Dichloroketen Additions.—Dichloroketen generated *in situ* from dichloroacetyl chloride [7] or from chloral,[8] in the presence of 3-oxido-1-phenylpyridinium [9] (2b), 1-benzyl-[10] (2c), 1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-[11] (2h), 1-(4,6-dimethylpyrimidin-2-yl)-[12] (2g), and 1-(3-oxocyclohex-1-enyl)-3-oxidopyridinium (2i) gave the new bicyclic compounds (3a), (3b), (3c), (3d), and (3e),

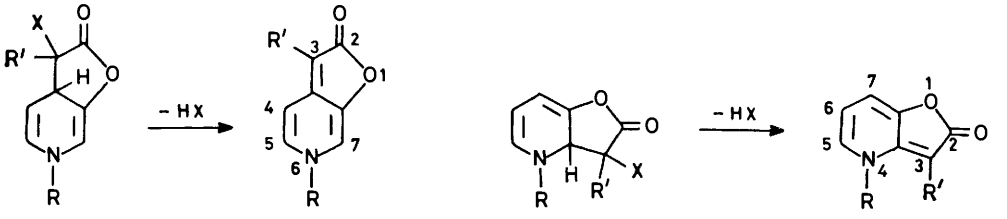
respectively. Neither monochloroketen nor dichloroketen was successfully reacted with 1-methyl-3-oxidopyridinium (2a), which is in keeping with the limited [13a] reactivity of this betaine in cycloadditions.

Aryl(bromo)ketens.—The aryl(bromo)ketens (4a—d) were prepared *in situ* from their corresponding α-bromoarylacetyl chloride which in turn had been derived from arylacetic acids using thionyl chloride–*N*-bromosuccinimide.* Aryl(bromo)ketens (4a—d) reacted with 1-benzyl-3-oxidopyridinium (2c), 3-oxido-1-phenylpyridinium (2b), 3-oxido-1-(1-oxido-4-pyridyl)pyridinium (2f), 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium (2g), and 3-oxido-1-styrylpyridinium (2e) betaines to yield isomeric mixtures of the corresponding 3,6-disubstituted-2-oxo-2,6-dihydrofuro[2,3-*c*]pyridines (6) and 3,4-disubstituted-2-oxo-2,4-dihydrofuro[3,2-*b*]pyridines (8). However, 1-[*trans*-3-(4-chlorophenyl)-3-oxoprop-1-enyl]-3-oxidopyridinium (2d) only gives the 2-oxo-2,4-dihydrofuro[3,2-*b*]pyridines. Moderate yields were obtained by generating the betaines and the ketens *in situ* using triethylamine as HCl scavenger at low temperature (0 °C) (see Table 1). 1-Methyl-3-oxidopyridinium (2a) failed to react with the aryl(bromo)ketens. No products could be isolated from attempted reaction of bromo(methyl)keten with any of these betaines.

I.r. and U.v. Spectra.—The i.r. spectra show ν(C=O) characteristic for α,β-unsaturated-γ-lactones [14] and ν(C=C) characteristic for an enamine double bond.[15] The doubling of the ν(C=O) at 1 730 and 1 770 cm^{-1} in $CHCl_3$ is characteristic of α,β-unsaturated-γ-lactones and is ascribed to Fermi resonance (*cf.* $\Delta^{\alpha,\beta}$-butenolide,[16] 1 745 and 1 778 cm^{-1}). The i.r. spectra for the isomeric 3,4-disubstituted-2-oxo-4*H*-furo[3,2-*b*]pyridines show corresponding ν(C=O) and ν(C=C) stretching frequencies. The ν(C=O) stretching frequencies of the furo[3,2-*b*]-pyridines are usually at higher wavelength than those for the ν(C=O) of the isomeric furo[2,3-*c*]pyridines [*cf.* (8a) > (6a)].

The 3-chloro-2-oxo-6-substituted-2,6-dihydrofuro-[2,3-*c*]pyridines exhibit consistently higher ν(C=O) stretching frequencies (1 730—1 740 cm^{-1}) characteristic of α-chloro-α,β-unsaturated-γ-lactones (*cf.* α-halogenoketones [17]).

The 2-oxo-2,6-dihydrofuro[2,3-*c*]pyridines exhibit strong u.v. absorption due to π→π* transitions. The 2-oxo-6-phenyl-2,6-dihydrofuro[2,3-*c*]pyridines having con-



(5) (6) (7) (8)

a; R = R′ = Ph
b; R = Ph, R′ = BrC_6H_4-*p*
c; R = Ph, R′ = $NO_2C_6H_4$-*p*
d; R = Ph, R′ = $MeOC_6H_4$-*p*
e; R = CH_2Ph, R′ = Ph
f; R = CH_2Ph, R′ = BrC_6H_4-*p*
g; R = CH_2Ph, R′ = $NO_2C_6H_4$-*p*
h; R = CH_2Ph, R′ = $MeOC_6H_4$-*p*
i; R = PhCH=CH, R′ = Ph
j; R = 1-oxido-4-pyridyl, R′ = Ph
k; R = 4,6-dimethylpyrimidin-2-yl, R′ = Ph

TABLE 1

Percentage yields of O,4- and O,2-cycloadducts

Compounds (6) and (8)		Yields (%) *		
		Mixed	(6)	(8)
R	R′			
Ph	Cl	57	57	
Ph	Ph	38	11	12
Ph	BrC_6H_4-*p*	40	12	14
Ph	$MeOC_6H_4$-*p*	45	13	15
Ph	$O_2NC_6H_4$-*p*	35	10	
CH_2Ph	Cl	25	25	
CH_2Ph	Ph	25	9	9
CH_2Ph	BrC_6H_4-*p*	25	9	8
CH_2Ph	$MeOC_6H_4$-*p*	29	12	8
p-ClC_6H_4COCH=CH	Ph	61		61
p-ClC_6H_4COCH=CH	$O_2NC_6H_4$-*p*	83		83
p-ClC_6H_4COCH=CH	$MeOC_6H_4$-*p*	80		80
1-Oxido-4-pyridyl	Ph	20	10	10
Ph–CH=CH	Ph	43	9	29
4,6-Dimethoxy-1,3,5-triazin-2-yl	Cl	30	30	
4,6-Dimethylpyrimidin-2-yl	Ph	<3	2	<1
4,6-Dimethylpyrimidin-2-yl	Cl	85	85	
3-Oxocyclohex-1-enyl	Cl	30	30	

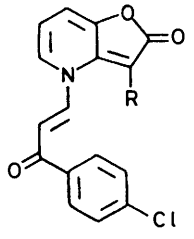
* Isolated yields are quoted: differences between the sum of (6) and (8) yields and the ' mixed ' yield represent separation losses.

* The aryl acid chlorides were prepared by the general method for 2-bromo-3-phenylacetyl chloride given in ref. 13*b*.

tinuous conjugation (*N*-phenyl substituent) generally absorb at longer wavelengths than their *N*-benzyl analogues [*cf.* (6a) > (6e)]. The extension of conjugation resulting from the replacement of the *N*-phenyl substituent group by an *N*-(1-oxidopyridyl) or *N*-styryl substituent group results in an enhanced bathochromic shift [(6i) > (6j) > (6a)].

As expected, *para*-substitution in the 6-phenyl moiety of the cycloadduct causes a bathochromic shift and intensification of absorption [*cf.* (6h) > (6e)]. Again, substitution by halogen causes a consistent bathochromic shift in both the *N*-phenyl [*cf.* (6b) > (6a)] and the *N*-benzyl [*cf.* (6f) > (6e)] series. In fact, the electronic effect of the NO_2 and MeO substituents in the *para*-position was sufficient to negate the loss of conjugation caused by disruption of conjugation by the imposition of a methylene between betaine nitrogen and the phenyl group [*cf.* (8d) ≈ (8h), (6c) = (6g), and (6d) = (6h)].

The 2-oxo-2,4-dihydrofuro[3,2-*b*]pyridine adducts also exhibited strong u.v. absorptions due to $\pi \rightarrow \pi^*$ transitions but, in general, absorbed at shorter wavelengths than the corresponding 2-oxo-2,6-dihydrofuro[2,3-*c*]-pyridines [*cf.* (8a) < (6a)]. The extension of conjugation resulting from the replacement of the *N*-phenyl group by the aroylvinyl substituent [*p*-$ClC_6H_4COCH{=}CH^-$] results in a bathochromic shift [*cf.* (9a) > (8a)]. Again, replacement of the *N*-phenyl group with the *N*-styryl group results in a substantial bathochromic shift [(8i) > (8a)].



(9)

a; R = Ph
b; R = Br C_6H_4-*p*
c; R = NO_2 C_6H_4-*p*
d; R = MeO C_6H_4-*p*

N.M.R. Spectra.—These spectra (Table 2) exhibited consistent and characteristic patterns for 4-H, 5-H, 6-H, and 7-H. Individual isomers were assigned structures based on the n.m.r. spectra; in the spectra of the adducts (6), the signal for 7-H appears as a fine doublet; 5-H as a finely split doublet coupled by 7—8 Hz with 4-H as a doublet or double doublet. By contrast, 5-H, 6-H, and 7-H for the adducts (8) form an ABC system of which 5-H is clearly seen as either a doublet (*J* 7—8 Hz) or a double doublet, whereas 6-H and 7-H are obscured by the benzene ring signals. The protons of the *para*-substituted aryl substituents at C-3 were generally observed as A_2B_2 patterns with further fine splitting (8.0 and 2.0 Hz). The chemical shifts varied with the electronic character of the 4-substituent.

Mass Spectra.—These all clearly exhibit the molecular ion $(M)^{+\cdot}$ attesting to the inherent stability of the cycloadducts. In the case of the *N*-oxide cycloadducts [(6j) and (8j)], the $M^{+\cdot}$ ions are absent but the $M^{+\cdot} - 16$ ions are the base peaks.

TABLE 2

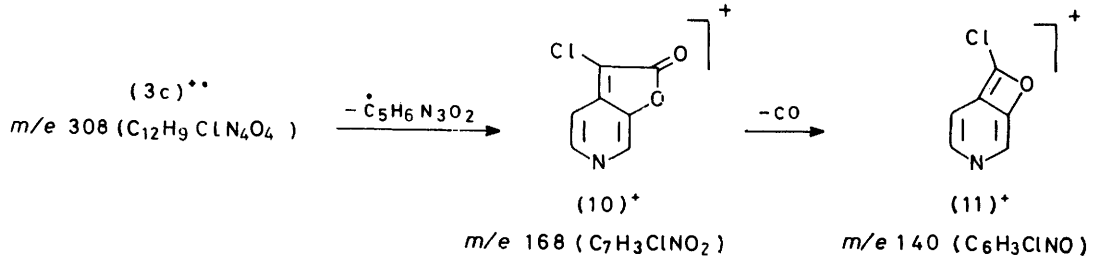
^{1}H N.m.r. spectra (δ values) of cycloadducts [a,b]

	4-H	5-H	6-H	7-H	Aromatic protons
(3a) [c,d]	6.85 [ff]	8.10 [gg]		8.30 [ff]	7.60 [jj]
(3b) [c,e]	6.90 [ff]	7.85 [gg]		8.30 [ff]	7.05 [jj]
(3c) [c,f]	6.90 [ff]	8.75 [gg]		8.60 [ff]	
(3d) [c,g]	6.50 [ff]	8.50 [gg]		8.35 [ff]	6.90 [jj]
(3e) [c,h]	6.70 [ff]	7.95 [gg]		8.15 [ff]	
(6a) [c,i]	7.16 [gg]	8.00 [gg]		8.23 [ff]	7.12—7.64 [kk]
(6b) [c,i]	7.34 [ff]	8.06 [gg]		8.29 [ff]	7.3—7.68 [hh]
(6c) [c,k]	*hh*	*hh*		8.45 [ff]	7.46—7.7, 8.02—8.26 [kk]
(6d) [c,l]	7.24 [ff]	7.99 [gg]		8.22 [ff]	7.14—7.64 [kk]
(6e) [c,m]	7.09 [gg]	7.89 [gg]		8.04 [ff]	7.35 [kk]
(6f) [c,n]	7.27 [hh]	7.92 [hh]		8.10 [ff]	7.34 [kk]
(6g) [c,o]	*hh*	*hh*		8.31 [ff]	7.40 [kk]
(6h) [c,p]	*hh*	7.72 [ff]		7.94 [ff]	
(6i) [c,q]	7.10 [ff]	8.00 [gg]	6.59 [ii]	8.33 [ff]	7.18—7.56 [jj]
(6j) [c,r]	7.18 [ff]	8.15 [gg]		8.36 [ff]	7.14—7.86 [jj]
(6k) [c]	*hh*	*hh*		8.65 [ff]	
(8a) [s]		7.45 [ff]	6.52—7.14 [hh]	6.52—7.14 [hh]	6.52—7.14 [hh]
(8b)		7.50 [ff]	6.64 [ii]	7.12—7.2 [hh]	7.20 [kk]
(8d) [u]		7.41 [gg]	*hh*	*hh*	7.0—7.2 [kk]
(8e) [v]		7.50 [ff]	*hh*	*hh*	7.04—7.28 [kk]
(8f) [w]		7.53 [gg]	*hh*	*hh*	7.08 [kk]
(8g) [x]		7.56 [ff]	*hh*	*hh*	7.40 [kk]
(8h) [y]		7.40 [gg]	*hh*	*hh*	7.0—7.2 [kk]
(8i) [z]		7.73 [gg]	*hh*	*hh*	6.8—7.4 [jj]
(8j) [aa]		7.5 [gg]	*hh*	7.12 [ff]	
(8k) [bb]		7.76 [gg]	*hh*	*hh*	6.5—7.1 [jj]
(9a) [cc]		*hh*	*hh*	7.36 [ff]	7.72 [jj]
(9c) [dd]		8.10 [ff]	*hh*	7.92 [ff]	
(9d) [ee]		7.88 [ff]	*hh*	6.88 [ff]	

[a] In p.p.m. relative to $SiMe_4$ as internal standard. [b] In $(CD_3)_2SO$. [c] Numbering is systematic. [d] $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [e] CH_2 δ 5.05 (s); $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [f] OMe δ 4.00 (s); $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [g] CMe δ 2.10 (s); $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [h] $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [i] $J_{4,5}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [j] $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [k] A_2B_2, δ 8.02—8.28. [l] MeO δ 3.24 (s); $J_{4,5}$ 6.0 Hz; $J_{5,7}$ 1.0 Hz. [m] CH_2 δ 5.25 (s); $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [n] CH_2 δ 5.27 (s); $J_{5,7}$ 1 Hz. [o] CH_2 δ 5.40 (s); $J_{5,7}$ 1.0 Hz. [p] CH_2 δ 5.21 (s); OMe δ 3.70 (s); $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [q] HC=CH δ 7.08 (d); $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [r] $J_{4,5}$ 8.0 Hz; $J_{5,7}$ 2.0 Hz. [s] $J_{5,6}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [t] A_2B_2, δ 6.81; $J_{5,6}$ 7.0 Hz. [u] MeO δ 3.58 (s); $J_{5,6}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [v] CH_2 δ 5.13 (s); $J_{5,6}$ 7.0 Hz. [w] CH_2 δ 5.14 (s); $J_{5,6}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [x] CH_2 δ 5.40 (s). [y] CH_2 δ 5.10 (s); MeO δ 3.70 (s); $J_{5,6}$ 8.0 Hz. [z] $J_{5,6}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [aa] $J_{5,6}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [bb] Me δ 2.08 (s); $J_{5,6}$ 7.0 Hz; $J_{5,7}$ 1.0 Hz. [cc] 1′-H δ 8.24 (d), 2′-H δ 6.96 (d); $J_{6,7}$ 8.0 Hz; $J_{1',2'}$ 12.0 Hz. [dd] 2′-H δ 6.80 (d); $J_{1',2'}$ 12.0 Hz; $J_{5,6} = J_{6,7} = 8.0$ Hz. [ee] 2′-H δ 6.50 (d); OMe δ 3.70 (s); $J_{1',2'}$ 12.0 Hz; $J_{5,6} = J_{6,7} = 8.0$ Hz. [ff] Doublet. [gg] Double doublet. [hh] Overlap. [ii] Triplet. [jj] Complex. [kk] Complex singlet.

In the case of the 6-substituted-3-chloro-2-oxo-2,6-dihydrofuro[2,3-*c*]pyridines, the initial fragmentation of the molecular ion, *e.g.* $(3c)^{+\cdot}$ involves the loss of the nitrogen substituent yielding the ion $(10)^+$ which subsequently loses carbon monoxide forming the species $(11)^+$ (Scheme 1).

However, in the case of both the 3,6-disubstituted-2-oxo-2,6-dihydrofuro[2,3-*c*]pyridines and the isomeric 3,4-disubstituted-2-oxo-2,4-dihydrofuro[3,2-*b*]pyridines, the molecular ions fragment by the elimination of a molecule of carbon monoxide followed by the loss of the nitrogen substituent (Scheme 2). The expulsion of carbon monoxide from unsaturated lactones under electron impact has previously been observed and reported.[18]



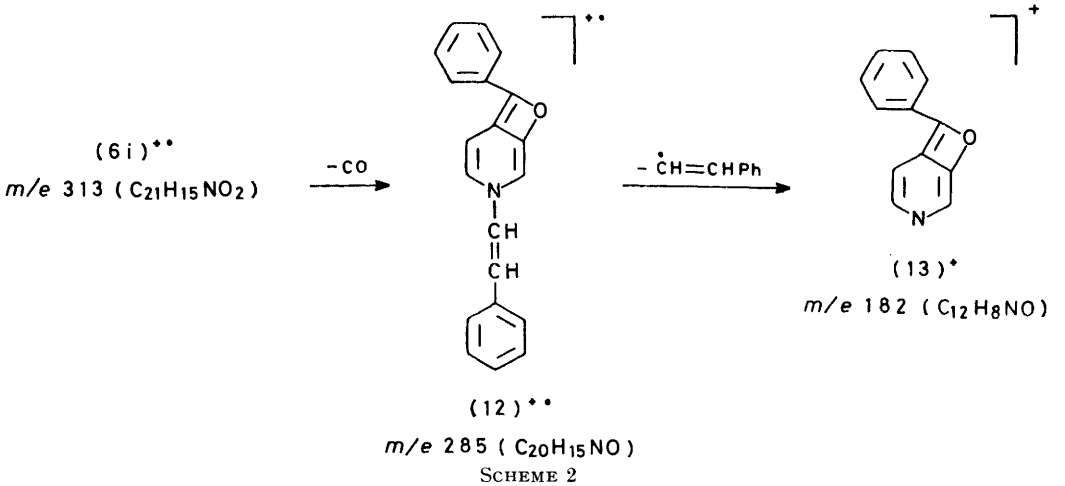
SCHEME 1

Keten Reactivity.—Dichloroketen and monochloroketen are very reactive and dichloroketen readily dimerises.[7,19] The apparent failure of bromo(methyl)-keten in this reaction may arise from the inductive effect of the alkyl group which renders the keten less electron deficient (see discussion later). The substituted phenylketens, while retaining sufficient reactivity, afford more stable 2π addends than dichloroketen.

In the series of reactions with the (4-substituted-phenyl)ketens, the proportion of O,4-orientation appears to increase somewhat from OMe to H to NO_2. The available calculations,[20] which were carried out on simple ketens, do not explain this variation.

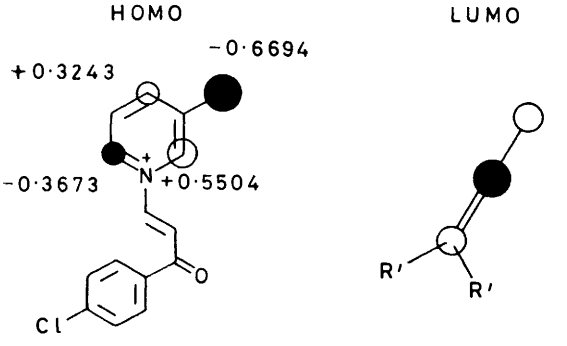
Periselectivity and Regioselectivity.—The synthesis of 2-oxo-2,6-dihydrofuro[2,3-*c*]pyridines involves a thermally allowed electrocyclic cycloaddition in which a keten, as a 2π component, reacts across the C-4 and oxygen positions of a 3-oxidopyridinium behaving as an 8π-component. In the case of the 2-oxo-2,4-dihydrofuro-[3,2-*b*]pyridines, the addition occurs across the C-2 and the oxygen positions of a 3-oxidopyridinium. The initially formed intermediates (5) and (7) spontaneously lose HX to yield the bicyclic compounds (6) and (8) respectively (*cf.* addition of dichloroketen to tropone [21]).

Ketens generally undergo $_{\pi}2_s + _{\pi}2_a$ cycloadditions,[22] although formal $2\pi + 4\pi$ addition of ketens as 4π components have been reported.[23] Cycloadditions of *N*-substituted-3-oxidopyridiniums with electron-deficient dipolarophiles are the result of the interaction of the highest-occupied molecular orbital (HOMO) of the former with the lowest-unoccupied molecular orbital (LUMO) of the latter. In the present case, the interaction presumably involves the low-lying LUMO [24] of the keten. The observed periselectivity can be rationalised by the frontier molecular orbital (FMO) approach [20] (CNDO/2 method). Since the addition is governed by



SCHEME 2

betaine-HOMO–keten-LUMO interaction and the keten LUMO has a high coefficient on the carbonyl carbon atom,[25] this carbon would be expected to interact with the oxygen atom of the betaine, which possesses the highest betaine-HOMO coefficient.[12] This is indeed found (see Scheme 3). The other bond is formed to either the 4-position or the 2-position. The FMO calculations [20] indicate that the 'covalent term' favours the O,2-orientation, while the 'steric term' favours the O,4-orientation: this explains why the betaine (2d) with the slender aroylvinyl substituent group yields only the O,2-isomers (9a,c,d). The addition of dichloroketen to

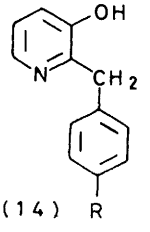


SCHEME 3

betaines (2b,c,g,h,i) with bulky *N*-substituent groups yields exclusively O,4-adducts (3a—e). The aryl-(bromo)ketens react at both the O,2- and O,4-positions of all betaines investigated other than (2d) (Table 1).

Transformations.—Electrophilic substitution of 3-hydroxypyridine is known [26] to yield predominantly 2- and 6-substitution products. Synthetically it would be advantageous to devise a synthetic method for 2- and 4-substituted 3-hydroxypyridines.

The complete removal of the N–R group and the opening of the lactone ring of 4-[*trans*-3-(4-chlorophenyl)-3-oxoprop-1-enyl]-2-oxo-3-phenyl 2,4-dihydrofuro[3,2-*b*]-pyridine (9a) with dilute HCl yielded 2-benzyl-3-hydroxypyridine (14a), m.p. 188 °C, in 50% yield. 2-Benzyl-3-hydroxypyridine was previously prepared by Leditschke [27] from benzyl 2-furyl ketone in low yields (26%). This last conversion represents a useful method for the specific substitution of 3-hydroxypyridine in 30% overall yield.



(14) R

a; R = H
b; R = NO_2
c; R = OMe

The corresponding acid hydrolyses of the cycloadducts (9c) and (9d) yielded 3-hydroxy-2-(4-nitrobenzyl)pyridine (14b) and 3-hydroxypyridine respectively. Presumably the hydrolysis of (9d) leads initially to the expected 3-hydroxy-2-(4-methoxybenzyl)pyridine (14c) which undergoes subsequent acid-catalysed debenzylation of the 4-methoxybenzyl group to form 3-hydroxypyridine.

EXPERIMENTAL

The m.p.s were determined with a Reichert apparatus. The spectra were recorded with a Perkin-Elmer 257 grating infrared spectrophotometer, a Unicam SP 800 ultraviolet spectrophotometer, a Hitachi–Perkin-Elmer RMU-6E mass spectrometer, and a Varian HA-100 n.m.r. spectrometer. Dichloromethane was purified by column chromatography on basic alumina, Brockmann Grade I. Compounds were purified until they were observed as single spots on t.l.c. using Kieselgel GF 254 (Type 60). Column chromatography was carried out on neutral alumina, Brockmann Grade I. The 2-acetyl-2-bromochlorides are extremely hygroscopic and yielded unsatisfactory analyses; therefore they were characterised by spectroscopic methods.

3-Hydroxy-1-phenylpyridinium chloride [28] (1b), 3-hydroxy-1-methylpyridinium iodide [29] (1a), 1-benzyl-3-hydroxypyridinium bromide [30] (1c), 1-(4,6-dimethylpyrimidin-2-yl)-3-hydroxypyridinium chloride [12] (1g), 1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-3-hydroxypyridinium chloride [11] (1h), 3-hydroxy-1-styrylpyridinium chloride [31] (1e), 3-hydroxy-1-(1-oxido-4-pyridyl)pyridinium chloride [32] (1f), 3-hydroxy-1-(3-oxocyclohex-1-enyl)pyridinium chloride [33] (1i), 1-[*trans*-3-(4-chlorophenyl)-3-oxoprop-1-enyl]-3-hydroxypyridinium chloride [34] (1d), and 2-bromo-2-phenylacetyl chloride [b.p. 65—67 °C at 1 mmHg (lit.,[13b] 100—102 °C at 5 mmHg) were prepared according to the literature methods.

3-*Chloro*-2-*oxo*-6-*phenyl*-2,6-*dihydrofuro*[2,3-c]*pyridine* (3a).—(*a*) Et_3N (10 g, 0.1 mol) was added dropwise during 5 min to a well-stirred cooled mixture of dichloroacetyl chloride (2 g, 0.013 mol) and 3-hydroxy-1-phenylpyridinium chloride (1b) (2 g, 0.01 mol) in CH_2Cl_2 (50 ml). The precipitated Et_3N·HCl was filtered off and the residue evaporated *in vacuo* to give a brown gum which was washed with water, Et_2O, and EtOH. The solid precipitate (1.5 g, 57%) was decolourised with charcoal from EtOH to give *compound* (3a) as fine yellow needles, m.p. 222—223 °C (EtOH) (Found: C, 63.2; H, 3.5; N, 5.6; Cl, 14.7. $C_{12}H_8ClNO_2$ requires C, 63.6; H, 3.3; N, 5.7; Cl, 14.4%); $\nu_{max.}$ ($CHBr_3$ film) 1 730 (α,β-unsaturated-γ-lactone C=O) and 1 660 cm^{-1} (enamine NC=C); $\lambda_{max.}$ (MeCN) 366 (log ε 4.70) and 235 nm (3.00); *m/e* 265 (12%).

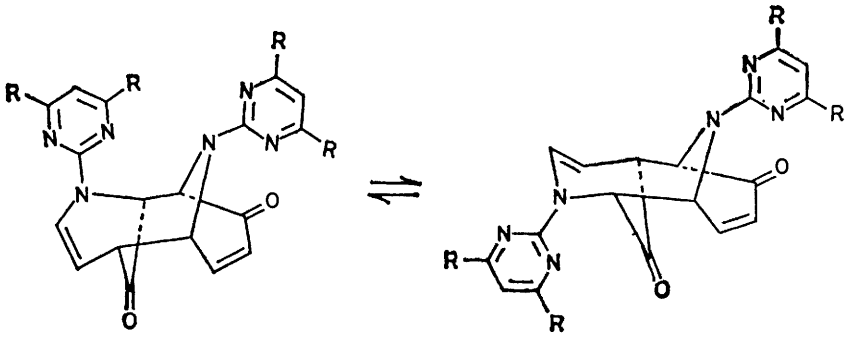
6-*Benzyl*-3-*chloro*-2-*oxo*-2,6-*dihydrofuro*[2,3-c]*pyridine* (3b).—Et_3N (12 g, 0.11 mol) was added dropwise during 10 min to a well-stirred cold (0 °C) mixture of dichloroacetyl chloride (2 g, 0.013 mol) and 1-benzyl-3-hydroxypyridinium bromide (1c) (2.6 g, 0.01 mol) in CH_2Cl_2 (100 ml). After being stirred for 20 min the reaction mixture was evaporated to dryness *in vacuo* and the residue chromatographed (EtOAc) to yield *compound* (3b) (0.5 g, 25%) as golden needles, m.p. 279—280 °C (EtOH) (Found: C, 64.8; H, 3.8; N, 5.4. $C_{14}H_{10}ClNO_2$ requires C, 64.9; H, 3.9; N, 5.4%); $\nu_{max.}$ ($CHBr_3$ film) 1 740 (α,β-unsaturated-γ-lactone, C=O) and 1 650 cm^{-1} (enamine NC=C); $\lambda_{max.}$ (MeCN) 408 (log ε 4.47), 396 (4.37), and 265 nm (3.80); *m/e* 259 (20%).

3-*Chloro*-6-(4,6-*dimethoxy*-1,3,5-*triazin*-2-*yl*)-2-*oxo*-2,6-*dihydrofuro*[2,3-c]*pyridine* (3c).—The dimer (15) [11] (0.2 g, 0.001 mol) and chloral (3 g, 0.02 mol) in THF (10 ml)–chlorobenzene (10 ml) were heated under reflux for 24 h. The mixture was evaporated *in vacuo* to yield a heavy syrup, which was eluted with Et_2O and refrigerated overnight. The crystalline precipitate (0.09 g, 30%) was recrystallised to give *compound* (3c) as red needles, m.p. 245—246 °C (Me_2SO) (Found: C, 46.3; H, 3.2. $C_{12}H_9ClN_4O_5$ requires C, 46.7; H, 2.9%); $\nu_{max.}$ ($CHBr_3$) 1 734 (α,β-unsaturated-γ-lactone C=O), 1 670 (enamine, NC=C), 1 570 (C=N), and 1 530 cm^{-1}; $\lambda_{max.}$ (EtOH) 398 (log ε 4.36), 378 (4.35), and 217 nm (3.56); *m/e* 308 (100%).

3-*Chloro*-6-(4,6-*dimethylpyrimidin*-2-*yl*)-2-*oxo*-2,6-*dihydrofuro*[2,3-c]*pyridine* (3d).—The dimer (16) [12] (0.2 g, 0.001 mol) and chloral (3 g, 0.02 mol) in THF (10 ml)–chlorobenzene (10 ml) were heated under reflux for 3 h. Et_3N (5 g, 0.05 mol) was added dropwise. After the mixture had refluxed for 12 h, the solvent was evaporated to dryness *in vacuo*. The residue was chromatographed (EtOAc) to yield *compound* (3d) (0.22 g, 85%), orange-red needles, m.p. 275—276 °C (EtOH) (Found: C, 56.3; H, 3.9; N, 14.9. $C_{13}H_{10}ClN_3O_2$ requires C, 56.6; H, 3.6; N, 15.3%); $\nu_{max.}$ ($CHBr_3$ film) 1 740 (α,β-unsaturated-γ-lactone C=O), 1 660 (enamine, NC=C), and 1 610 cm^{-1} (C=C); $\lambda_{max.}$ (MeCN) 396 (log ε 4.46), 374 (4.06), and 237 nm (3.08); *m/e* 275 (100%).

3-*Chloro*-6-(1-*oxocyclohex*-2-*en*-3-*yl*)-2-*oxo*-2,6-*dihydrofuro*-[2,3-c]*pyridine* (3e).—Et_3N (2 g, 0.02 mol) was added dropwise to a cooled stirred solution (0 °C) of dichloroacetyl chloride (4 g, 0.03 mol) and 3-hydroxy-1-(3-oxocyclohex-1-enyl)pyridinium chloride (1i) (0.20 g, 0.001 mol) in CH_2Cl_2 (20 ml). The dark reaction mixture was evaporated *in*

vacuo and the residue purified by preparative t.l.c. (Kieselgel GF 254, toluene–EtOAc, 15 : 1) to yield *isomer* (3e) (0.05 g, 30%) recrystallised as orange-yellow needles, m.p. 237—238 °C (EtOH) (Found: C, 59.1; H, 4.1; N, 5.3. $C_{13}H_{10}ClNO_3$ requires C, 59.2; H, 3.9; N, 5.3%); $\nu_{max.}$ ($CHBr_3$) 1 740 (lactone C=O) and 1 660 cm^{-1} (unsaturated C=O), *m/e* 230 (50%).



(15) R = MeO
(16a) R = Me

(16b) R = Me

2-*Bromo*-2-(4-*bromophenyl*)*acetyl Chloride*.—4-Bromophenylacetic acid (25 g, 0.12 mol), dry CCl_4 (30 ml), and $SOCl_2$ (57 g, 35 ml, 0.48 mol) were heated at 65 °C until the acid was converted to the acid chloride ($\nu_{max.}$ 1 720 cm^{-1} for acid carbonyl replaced by the acid chloride carbonyl, at 1 800 cm^{-1}). *N*-Bromosuccinimide (NBS) (24.92 g, 0.14 mol) in anhydrous CCl_4 (40 ml), and concentrated HBr (8 drops) were added to the acid chloride. The temperature was raised to 85 °C and the mixture heated and stirred for *ca.* 3—4 h (n.m.r. showed loss of the methylene singlet, δ 4.0, 2 H, and the appearance of a one-proton doublet, δ 5.62). The precipitated succinimide was filtered off, washed with CCl_4, and discarded. The solvent from the filtrate was removed *in vacuo* and the residue distilled (200 °C at 40 mmHg) to give the *bromo-acid chloride*, (18.15 g, 50%), b.p. 200 °C at 40 mmHg; $\nu_{max.}$ (film) 1 800 and 1 720 cm^{-1}; δ (CCl_4) 7.25 (4 H, A_2B_2 quartet) and 5.62 (1 H, d).

2-*Bromo*-2-(4-*nitrophenyl*)*acetyl Chloride*.—(4-Nitrophenyl)acetic acid (30 g, 0.17 mol), CCl_4 (40 ml), $SOCl_2$ (80.9 g, 50 ml, 0.68 mol), and NBS (33.8 g, 0.19 mol) in CCl_4 (40 ml) were reacted as described above to yield the *bromo-acid chloride* as an oil, b.p. 160—162 °C at 0.7 mmHg; $\nu_{max.}$ (film) 1 800 and 1 720 cm^{-1}; δ (CCl_4) 7.95 (4 H, A_2B_2 quartet) and 5.70 (1 H, s).

2-*Bromo*-2-(4-*methoxyphenyl*)*acetyl Chloride*.—(4-Methoxyphenyl)acetic acid (16.62 g, 0.10 mol), CCl_4 (30 ml), $SOCl_2$ (30 ml, 0.40 mol), and NBS (21.4 g, 0.12 mol) in CCl_4 (40 ml) were reacted as above to yield the *bromo-acid chloride* as an oil, b.p. 125—128 °C at 1.4 mmHg (17.25 g, 65%); $\nu_{max.}$ (film) 1 800 and 1 720 cm^{-1}; δ (CCl_4) 7.15 (4 H, A_2B_2 quartet), 5.55 (1 H, s), and 3.80 (3 H, s).

2-*Bromo*-2-*propionyl Chloride*.—Propionic acid (14.8 g, 0.2 mol), $SOCl_2$ (28.8 ml, 0.4 mol), and NBS (42.5 g, 0.24 mol) in CCl_4 (40 ml) were reacted as described above to yield the bromo-acid chloride as an oil (12.82 g, 37%), b.p. 36—40 °C at 40 mmHg; $\nu_{max.}$ (film) 1 785 cm^{-1}; δ (CCl_4) 4.68 (3 H, q) and 2.00 (1 H, d).

General Procedure for the Formation of the Mixture of O,2- *and* O,4-*Adducts*.—Et_3N (6.1 g, 0.06 mol) was added dropwise to a cooled (ice-bath at 0 °C) stirred mixture of 2-aryl-2-bromoacetyl chloride (0.01 mol) and 1-substituted-3-oxidopyridinium salt (0.01 mol) in CH_2Cl_2 (100 ml). The dark reaction mixture was stirred for 20 min at 0 °C followed by a further 30 min at room temperature. The mixture was then extracted with water (4 × 30 ml) and the organic layer evaporated to dryness *in vacuo* to yield the crude mixture of the products as a dark gum. The two fluorescent regioisomers (6) and (8) [appearing on t.l.c. (toluene–EtOAc; (8 : 3) as yellow and blue fluorescent bands respectively] were isolated using preparative t.l.c. (Kieselgel, GF 254, in toluene–EtOAc; 14—16 : 1 unless indicated otherwise).

2-*Oxo*-3,6-*diphenyl*-2,6-*dihydrofuro*[2,3-c]*pyridine* (6a) *and* 2-*Oxo*-3,4-*diphenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8a).—2-Bromo-2-phenylacetyl chloride (2.3 g, 0.01 mol) was reacted with 3-hydroxy-1-phenylpyridinium chloride (1b) (2.1 g, 0.01 mol) as above, to give after purification the isomer (6a) (0.32 g, 11%) as yellow needles, m.p. 206 °C (EtOH) (Found: C, 79.3; H, 4.8; N, 4.9. $C_{19}H_{13}NO_2$ requires C, 79.4; H, 4.6; N, 4.9%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 392 (log ε 4.50), 267 (3.98), and 211 nm (4.35); *m/e* 287 (100%). The *isomer* (8a) (0.33 g, 11%) crystallized as yellow-green prisms, m.p. 232 °C (EtOH) (Found: C, 79.0; H, 4.6; N, 4.6. $C_{19}H_{13}NO_2$ requires C, 79.4; H, 4.5; N, 4.9%); $\nu_{max.}$ ($CHBr_3$) 1 720 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 304 (log ε 3.96), 292 (3.81), 252 (3.96), and 207 nm (4.15); *m/e* 287 (100%).

6-(4-*Bromophenyl*)-2-*oxo*-3-*phenyl*-2,6-*dihydrofuro*[2,3-c]-*pyridine* (6b) *and* 3-(4-*Bromophenyl*)-2-*oxo*-4-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8b).—2-Bromo-2-(4-bromophenyl)acetyl chloride (3.1 g, 0.01 mol) was reacted with 3-hydroxy-1-phenylpyridinium chloride (1b) (2.1 g, 0.01 mol) as above to yield after purification the *isomer* (6b) (0.4 g, 11%) as yellow needles, m.p. 201 °C (EtOH) (Found: C, 62.5; H, 3.7; N, 4.0. $C_{19}H_{12}BrNO_2$ requires C, 62.3; H, 3.3; N, 3.8%); $\nu_{max.}$ ($CHBr_3$) 1 695 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 395 (log ε 4.42), 280 (3.95), 239 (3.95), and 210 nm (4.37); *m/e* 367 (100%). The *isomer* (8b) (0.5 g, 13%) crystallised as yellow plates, m.p. 240—241 °C (EtOH) (Found: C, 62.7; H, 3.5; N, 3.7. $C_{19}H_{12}BrNO_2$ requires C, 62.3; H, 3.3; N, 3.8%); $\nu_{max.}$ ($CHBr_3$) 1 700 (lactone C=O) and 1 640 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 384 (log ε 4.22), 292 (4.04), 255 (4.25), and 210 nm (4.40); *m/e* 367 (100%).

6-(4-*Nitrophenyl*)-2-*oxo*-3-*phenyl*-2-6-*dihydrofuro*[2,3-c]-*pyridine* (6c) *and* 3-(4-*Nitrophenyl*)-2-*oxo*-4-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8c).—2-Bromo-2-(4-nitrophenyl)-acetyl chloride (2.8 g, 0.01 mol) was reacted with 3-hydroxy-1-phenylpyridinium chloride (2.1 g, 0.001 mol) as above to

yield after purification *isomer* (6c) (0.33 g, 10%) as red needles, m.p. 267—268 °C (EtOH) (Found: C, 67.2; H, 4.0; N, 8.3. $C_{19}H_{12}N_2O_4 \cdot \frac{1}{2}H_2O$ requires C, 66.9; H, 3.8; N, 8.2%); $\nu_{max.}$ ($CHBr_3$) 1 730 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 432 (log ε 4.36), 242 (4.04), and 208 nm (4.30); *m/e* 332 (100%). The *isomer* (8c) was detected in the crude isomeric mixture by ^1H n.m.r., but could not be isolated pure.

6-(4-*Methoxyphenyl*)-2-*oxo*-3-*phenyl*-2,6-*dihydrofuro*-[2,3-c]*pyridine* (6d) *and* 3-(4-*Methoxyphenyl*)-2-*oxo*-4-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8d).—2-Bromo-2-(4-methoxyphenyl)acetyl chloride (2.6 g, 0.01 mol) was reacted with 3-hydroxy-1-phenylpyridinium chloride (2.1 g, 0.01 mol) as described above to give after purification the *isomer* (6d) (0.4 g, 13%) as yellow plates, m.p. 249—250 °C (EtOH) (Found: C, 75.5; H, 5.0; N, 4.4. $C_{20}H_{15}NO_3$ requires C, 75.7; H, 4.8; N, 4.4%); $\nu_{max.}$ ($CHBr_3$) 1 705 (lactone C=O) and 1 655 cm^{-1} (C=CN); $\lambda_{max.}$ 398 (log ε 4.40), 268 (3.98), and 212 nm (4.34); *m/e* 317 (100%). The *isomer* (8d) (0.5 g, 15%) crystallised as yellow rods, m.p. 219—220 °C (EtOH) (Found: C, 75.4; H, 5.1; N, 4.7. $C_{20}H_{15}NO_3$ requires C, 75.7; H, 4.8; N, 4.4%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 388 (log ε 3.94), 294 (3.89), 250 (4.03), and 210 nm (4.24); *m/e* 317 (100%).

3-*Benzyl*-2-*oxo*-6-*phenyl*-2,6-*dihydrofuro*[2,3-c]*pyridine* (6e) *and* 4-*Benzyl*-2-*oxo*-3-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8e).—2-Bromo-2-phenylacetyl chloride (2.3 g, 0.01 mol) was reacted with 1-benzyl-3-hydroxypyridinium bromide (1c) (2.7 g, 0.01 mol) as described above to yield after purification the *isomer* (6e) (0.27 g, 9%) as yellow plates, m.p. 188—189 °C (EtOH) (Found: C, 79.5; H, 5.2; N, 4.7. $C_{20}H_{15}NO_2$ requires C 79.7; H 5.0; N, 4.7%); $\nu_{max.}$ ($CHBr_3$) 1 705 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 380 (log ε 4.39) and 273 nm (3.92); *m/e* 301 (95%). The isomer (8e) (0.27 g, 9%) was isolated as yellow prisms, m.p. 237 °C (EtOH) (Found: C, 79.8; H, 5.1; N, 4.6. $C_{20}H_{15}NO_2$ requires C, 79.7; H, 5.0; N, 4.7%); $\nu_{max.}$ ($CHBr_3$) 1 720 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 374 (log ε 4.10), 293 (3.99), and 212 nm (4.32); *m/e* 301 (95%).

3-*Benzyl*-6-(4-*bromophenyl*)-2-*oxo*-2,6-*dihydrofuro*[2,3-c]-*pyridine* (6f) *and* 4-*Benzyl*-3-(4-*bromophenyl*)-2-*oxo*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8f).—2-Bromo-2-(4-bromophenyl)-acetyl chloride (3.1 g, 0.01 mol) was reacted with 1-benzyl-3-hydroxypyridinium bromide (2.7 g, 0.01 mol) as described above to yield, after purification, the *isomer* (6f) (0.3 g, 8%) as yellow plates, m.p. 171—172 °C (EtOH) (Found: C, 62.9; H, 3.9; N, 3.6. $C_{20}H_{19}BrNO_2$ requires C, 63.2; H, 3.7; N, 3.7%); $\nu_{max.}$ ($CHBr_3$) 1 690 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 382 (log ε 4.34), 281 (3.88), 240 (3.79), and 211 nm (4.29); *m/e* 381 (95%). The *isomer* (8f) (0.3 g, 8%) was isolated as pale yellow flakes, m.p. 135—136 °C (EtOH) (Found: C, 62.8; H, 3.8; N, 3.6. $C_{20}H_{19}BrNO_2$ requires C, 63.2; H, 3.7; N, 3.7%); $\nu_{max.}$ ($CHBr_3$) 1 700 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 370 (log ε 3.64), 281 (3.80), and 208 nm (4.05); *m/e* 381 (42%).

3-*Benzyl*-6-(4-*nitrophenyl*)-2-*oxo*-2,6-*dihydrofuro*[2,3-c]*pyridine* (6g) *and* 4-*Benzyl*-3-(4-*nitrophenyl*)-2-*oxo*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8g).—2-Bromo-2-(4-nitrophenyl)acetyl chloride (2.3 g, 0.01 mol) was reacted with 1-benzyl-3-oxidopyridinium (2.7 g, 0.01 mol) as described above to yield a mixture of the *isomers* (6g) and (8g) (1.0 g, 30%) which could not be separated by preparative t.l.c. The mixture was recrystallised as red needles, m.p. 225—227 °C (EtOH) (Found: C, 69.0; H, 4.2; N, 7.8. $C_{20}H_{14}N_2O_4$ requires C, 69.4; H, 4.1; N, 8.1%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 432 (log ε 4.53), 356 (4.05), and 225 nm (4.18); *m/e* 346 (13%).

3-*Benzyl*-6-(4-*methoxyphenyl*)-2-*oxo*-2,6-*dihydrofuro*[2,3-c]-*pyridine* (6h) *and* 4-*Benzyl*-3-(4-*methoxyphenyl*)-2-*oxo*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8h).—2-Bromo-2-(4-methoxyphenyl)acetyl chloride (3 g, 0.01 mol) reacted with 1-benzyl-3-hydroxypyridinium bromide (2.7 g, 0.01 mol) to yield after purification (eluant toluene–EtOAc, 12 : 1) the *isomer* (6h) (0.4 g, 12%) as bright yellow plates, m.p. 219—220 °C (EtOH) (Found: C, 75.9; H, 5.4; N, 4.1. $C_{21}H_{17}NO_3$ requires C, 76.1; H, 5.1; N, 4.2%); $\nu_{max.}$ ($CHBr_3$) 1 705 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 400 (log ε 4.53), 266 (4.21), and 220 nm (4.33); *m/e* 331. The *isomer* (8h) (0.27 g, 8%) was obtained as yellow flakes, m.p. 190—191 °C (EtOH) (Found: C, 76.0; H, 5.3; N, 4.2. $C_{21}H_{17}NO_3$ requires C, 76.1; H, 5.1; N, 4.2%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 395 (log ε 4.16), 264 (4.40), and 212 nm (4.16); *m/e* 331 (43%).

2-*Oxo*-6-*phenyl*-3-(trans-*styryl*)-2,6-*dihydrofuro*[2,3-c]*pyridine* (6i) *and* 2-*Oxo*-3-*phenyl*-4-(trans-*styryl*)-2,4-*dihydrofuro*-[3,2-b]*pyridine* (8i).—2-Bromo-2-phenylacetyl chloride (2.3 g, 0.01 mol) was reacted with 3-hydroxy-1-*trans*-styrylpyridinium chloride (1 g, 0.01 mol) (1e) as above and after purification (eluant toluene–EtOAc, 7 : 1) the *isomer* (6i) (0.1 g, 9%) was isolated as orange-yellow plates, m.p. 238—240 °C (EtOH) (Found: C, 80.4; H, 5.0; N, 4.5. $C_{21}H_{15}NO_2$ requires C, 80.5; H, 4.8; N, 4.6%); $\nu_{max.}$ ($CHBr_3$) 1 680 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 419 (log ε 4.49), 275 (3.98), and 214 nm (4.08); *m/e* 313 (100%). The *isomer* (8i) (0.5 g, 29%) was isolated as orange-yellow plates, m.p. 157—177 °C (EtOH) (Found: C, 80.7; H, 5.0; N, 4.2. $C_{21}H_{15}NO_2$ requires C, 80.5; H, 4.8; N, 4.5%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 640 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 410 (log ε 4.18), 278 (4.41), and 217 nm (4.20); *m/e* 313 (100%).

2-*Oxo*-3-(1-*oxido*-4-*pyridyl*)-6-*phenyl*-2,6-*dihydrofuro*-[2,3-c]*pyridine* (6j) *and* 2-*Oxo*-4-(1-*oxido*-4-*pyridyl*)-3-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8j).—2-Bromo-2-phenylacetyl chloride (1.4 g, 0.01 mol) was reacted with 3-hydroxy-1-(1-oxido-4-pyridyl)pyridinium chloride (0.8 g, 0.01 mol) (1f) as described above to yield after purification (eluant toluene–EtOAc, 3 : 2) the *isomer* (6j) (0.9 g, 10%) as yellow plates, m.p. 258—262 °C (decomp.) (MeCN) (Found: C, 70.8; H, 4.3; N, 9.2. $C_{18}H_{12}N_2O_3$ requires C, 71.1; H, 4.0; N, 9.2%); $\nu_{max.}$ ($CHBr_3$) 1 715 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 405 (log ε 4.26), 255 (3.76), and 216 nm (3.97); *m/e* 288 ($M^{+\cdot}$ — 16, 100%). The *isomer* (8j) (0.9 g, 10%) was isolated as yellow plates, m.p. 268 °C (decomp.) (MeCN) (Found: C, 70.8; H, 4.3; N, 9.2. $C_{18}H_{12}N_2O_3$ requires C, 71.1; H, 4.0; N, 9.2%); $\nu_{max.}$ 1 705 (lactone C=O) and 1 650 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 391 (log ε 3.99), 291 (3.93), 250 (4.01), and 216 nm (4.11); *m/e* 288 ($M^{+\cdot}$ — 16, 100%).

3-(4,6-*Dimethylpyrimidin*-2-*yl*)-2-*oxo*-6-*phenyl*-2,6-*dihydrofuro*[2,3-c]*pyridine* (6k) *and* 4-(4,6-*Dimethylpyrimidin*-2-*yl*)-2-*oxo*-3-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (8k).—2-Bromo-2-phenylacetyl chloride (1 g, 0.01 mol) was reacted with 1-(4,6-dimethylpyrimidin-2-yl)-3-hydroxypyridinium chloride (0.5 g, 0.002 mol) (1g) as described above to yield after purification by column chromatography (eluant toluene–EtOAc, 12 : 1) the *isomer* (6k) (0.2 g, 2%), recrystallised as yellow needles, m.p. 256 °C (EtOH) (Found:

C, 71.5; H, 4.9; N, 13.3. $C_{19}H_{15}N_3O_2$ requires C, 71.9; H, 4.9; N, 13.2%); $\nu_{max.}$ ($CHBr_3$) 1 705 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 407 (log ε 4.52), 253 (4.02), and 217 nm (4.13); *m/e* 317 (100%). The *isomer* (8k) (<1%) recrystallised as yellow plates, m.p. 226—227 °C (EtOH) (Found: C, 71.9; H, 4.9; N, 13.3. $C_{19}H_{15}N_3O_2$ requires C, 71.9; H, 4.8; N, 13.2%); $\nu_{max.}$ ($CHBr_3$) 1 720 (C=O) and 1 655 cm^{-1} (C=CN); $\lambda_{max.}$ (EtOH) 402 (log ε 4.20), 285 (4.11), 250 (4.40), and 217 nm (4.28); *m/e* 317 (100%).

General Procedure for the Preparation of the O,2-*Regioisomers only*.—Et_3N (0.02 mol) was added dropwise to a cooled (0 °C) stirred mixture of 1-[*trans*-3-(4-chlorophenyl)-3-oxoprop-1-enyl]-3-hydroxypyridinium chloride (1d) (0.003 mol) and 2-aryl-2-bromoacetyl chloride (0.009 mol) in CH_2Cl_2 (100 ml). The orange mixture was then left to stir for 15 min at 0 °C and a further 2 h at room temperature. The reaction mixture was evaporated to dryness *in vacuo* and the residual crude solid extracted with water (3 × 40 ml) to remove all salts. The organic solid showed one spot on t.l.c. using toluene–EtOAc (8 : 3). The solid was recrystallised from EtOAc to give the O,2-isomer as the sole product.

4-[trans-3-(4-*Chlorophenyl*)-1-*oxoprop*-2-*en*-3-*yl*]-2-*oxo*-3-*phenyl*-2,4-*dihydrofuro*[3,2-b]*pyridine* (9a).—2-Bromo-2-phenylacetyl chloride (2.1 g, 0.01 mol) was used, and after purification the reaction mixture yielded *isomer* (9a) (0.3 g, 27%) as red needles, m.p. 224—226 °C (EtOAc) (Found: C, 70.1; H, 4.1; N, 3.6. $C_{22}H_{14}ClNO_3$ requires C, 70.3; H, 3.7; N, 3.7%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ ($CHCl_3$) 450 (log ε 4.20) and 283 nm (4.52); *m/e* 375 (48%).

4-[trans-3-(4-*Chlorophenyl*)-1-*oxoprop*-2-*en*-3-*yl*]-3-(4-*nitrophenyl*)-2-*oxo*-2,4-*dihydrofuro*[3,2-b]*pyridine* (9c).—2-(4-Nitrophenyl)acetyl chloride (5.0 g, 0.02 mol) was used and after purification the mixture yielded *isomer* (9c) (2.1 g, 83%), recrystallised as orange-brown prisms, m.p. 258—260 °C (EtOAc) (Found: C, 62.4; H, 3.5; N, 6.2. $C_{22}H_{13}ClN_2O_5$ requires C, 62.8; H, 3.1; N, 6.6%); $\nu_{max.}$ ($CHBr_3$) 1 720 (lactone C=O) and 1 610 (C=CN); $\lambda_{max.}$ ($CHCl_3$) 450 (log ε 4.03) and 280 nm (4.19); *m/e* 420 (90%).

4-[trans-3-(4-*Chlorophenyl*)-1-*oxoprop*-2-*en*-3-*yl*]-3-(4-*methoxyphenyl*)-2-*oxo*-2,4-*dihydrofuro*[3,2-b]*pyridine* (9d).—2-Bromo-2-(4-methoxyphenyl)acetyl chloride (4.7 g, 0.02 mol) was used as described above, and the reaction mixture after purification yielded *isomer* (9d) (2.0 g, 80%), recrystallised as red flakes, m.p. 186—188 °C (EtOH) (Found: C, 67.7; H, 4.1; N, 3.1. $C_{23}H_{16}ClNO_4$ requires C, 68.1; H, 4.0; N, 3.5%); $\nu_{max.}$ ($CHBr_3$) 1 710 (lactone C=O) and 1 660 cm^{-1} (C=CN); $\lambda_{max.}$ ($CHCl_3$) 460 (log ε 3.86) and 285 (4.20); *m/e* 266 (90%).

Hydrolysis of Adducts (9a, c, d).—A solution of the cycloadduct (9a, c or d) (2 g, *ca.* 0.006 mol) in 50% HCl was heated under reflux for 24 h. The cooled reaction mixture was extracted with $CHCl_3$ (3 × 10 ml) and the aqueous layer evaporated to dryness. The residue was dissolved in water (5 ml), cooled with ice, and basified with $NaHCO_3$. The adduct (9a) yielded 2-benzyl-3-hydroxypyridine (14a) (0.4 g, 50%) which precipitated out of the basic water solution and was recrystallised from EtOH as colourless *prisms*, m.p. 188 °C (Found: C, 77.7; H, 5.8; N, 7.5. $C_{12}H_{11}NO$ requires C, 77.8; H, 6.0; N, 7.6%); $\nu_{max.}$ ($CHBr_3$) 2 000 (OH), 1 575, and 1 600 cm^{-1} (C=C ring); $\lambda_{max.}$ ($CHCl_3$) 282 nm (log ε 3.89); *m/e* 185 (100%). The adduct (9c) yielded 3-hydroxy-2-(4-nitrobenzyl)pyridine (14b) (65%) which precipitated from the basic aqueous solution, and was recrystallised as yellow flakes, m.p. 224—225 °C (EtOH–H_2O) (Found: C, 62.4; H, 4.5; N, 12.0. $C_{12}H_{10}N_2O_3$ requires C, 62.6; H, 4.4; N, 12.2%); $\nu_{max.}$ ($CHBr_3$) 3 350, 2 600 (OH), 1 600, and 1 580 cm^{-1} (C···C); $\lambda_{max.}$ ($CHCl_3$) 340 nm (log ε 4.12); *m/e* 230 (M^+, 100%). Adduct (9d) yielded 3-hydroxypyridine after evaporation of the basic aqueous solution and extraction of the residue with hot EtOAc.

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