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GENERAL SYNTHETIC METHODS FOR THE PREPARATION OF 1-SUBSTITUTED-VINYL-2-PYRIDONES[a]

PATRICK S. MARIANO,*[b] EMIL KROCHMAL, RALPH BEAMER, PETER L. HUESMANN and DEBRA DUNAWAY-MARIANO

Department of Chemistry, Texas A&M University, College Station, TX 77843, U.S.A.

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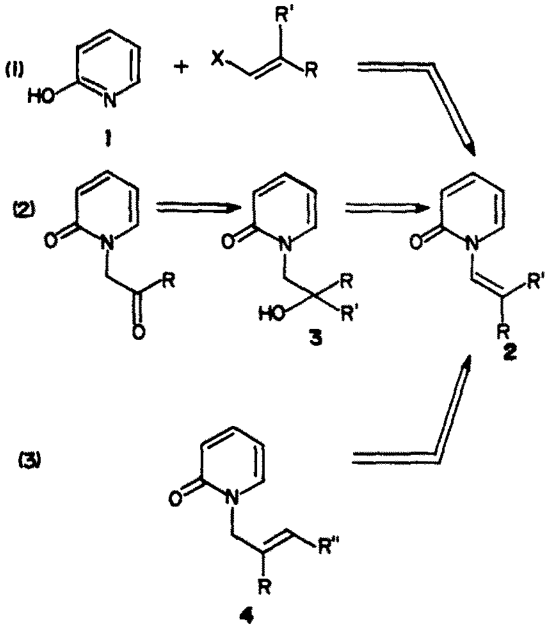
Abstract—General methods for the preparation of a variety of 1-substituted vinyl-2-pyridones are described. Synthetic routes followed involve (1) nucleophilic substitution reaction of the 2-hydroxy-pyridyl anion of haloolefins containing β-activating groups, such as carbonyl and phenyl, (2) elimination reactions of ester derivatives of 1-pyridonyl-2-ethanols and (3) base catalyzed isomerizations of 1-allyl-2-pyridones. The details involved with each of the synthetic methods and purification of the derived 1-vinyl-2-pyridones are described. Additionally, important spectroscopic properties of compounds in this series are discussed in terms of preferred conformations about the nitrogen-exocyclic vinyl carbon bond.

Our recent studies concerning the photochemistry of heterocyclic compounds containing the enamide (*N*-vinylamide) chromophore[2] and the development of novel synthetic methods for preparation of isoquinoline alkaloids[3] has stimulated the search for simple procedures to prepare a variety of 1-substituted vinyl-2-pyridones **2**. Additional interest in this class of compounds has been generated as a result of their importance as monomeric starting materials for the preparation of heterocycle containing polymers.[4] It is noteworthy to mention that few methods possessing sufficient generality for broad application to the synthesis of compounds in this class have been presented.[4,5] As a result of this, we have recently completed an investigation of several simple synthetic designs targeted at the 1-vinyl-2-pyridones which appear versatile enough to be of general utility.

The sequences studied fall into three broad categories: (1) nucleophilic substitution routes in which 1-vinyl-2-pyridones are generated directly from reactions of 2-hydroxypyridine **1** and haloolefins containing β-activating groups (eqn 1), (2) elimination routes in which 1-pyridonyl-2-ethanols **3**, prepared from the corresponding α-pyridonylketones, serve as key intermediates (eqn 2) and (3) isomerization routes starting with 1-allyl-2-pyridones **4** (eqn 3).



Direct substitution routes

Reaction of the 2-hydroxypyridyl anion, produced from **1** *in situ* using a number of bases, with β-halo-α,β-unsaturated ketones and esters results in generation of the corresponding 2-pyridones having the introduced vinyl-group as part of either a vinyl ketone or acrylic ester moiety. For example, 1-(5,5-dimethylcyclohex-2-en-1-on-3-yl)-2-pyridone **6** can be synthesized as a crystalline solid in 93% yield by the reaction of **1** with 3-chloro-5,5-dimethylcyclohex-2-en-1-one **5**[6] in the presence of potassium carbonate. In an analogous fashion, the reaction of the 2-hydroxypyridyl anion, generated in tetrahydrofuran from **1** and sodium hydride, with 3-chlorocyclohex-2-en-1-one **7**[6] or 4-chloropent-3-en-2-one (**9**)[6] proceeds in high yield to form the corresponding pyridonylenones **8** and **10** (59% and 46%, respectively). The reduced yields of these latter reactions can be directly attributable to slow aromatization of **7** and **8** under the reaction conditions and to a competitive dehydrohalogenation process followed by **9**.

Characteristic spectroscopic data accumulated for **6**, **8** and **10** (Tables 2 and 5) support fully their assignment as 1-vinyl-2-pyridones rather than vinyl-2-pyridyl ethers. Thus, these vinalogous acylation reactions contrast dramatically with simple acylations of 2-hydroxypyridine using acetic anhydride. McKillop *et al.*[7] have shown that competitive *O*- and *N*-acylations occur in this latter reaction. The 1-acetyl-2-pyridone formed predominantly at low temperature rapidly rearranges at room temperature to produce 1-acetoxypyridine exclusively (eq. 4). The facility of this rearrangement process is not matched by the vinalogous 1-pyridonylamides **5**, **8** and **10**. In none of the cases were products having the pyridyl enol ether structure detected.

Reaction of **1** with methyl 2,3-dibromo-2-methylpropanoate **11**[8] in refluxing dimethoxyethane containing potassium carbonate can be used to prepare the methacrylate ester derivative of 2-pyridone, **12** (46%). It

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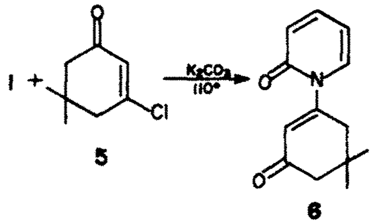
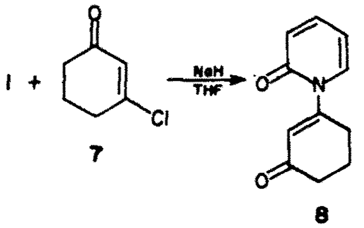
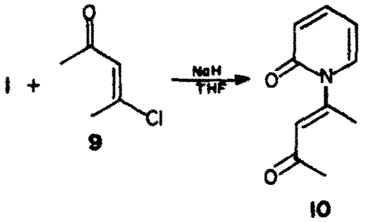
[a] A preliminary report of these results has been presented.[1]

[b] Camille and Henry Dreyfus Foundation Teacher-Scholar Grantee, 1975–80.







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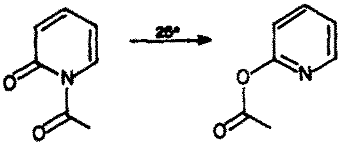
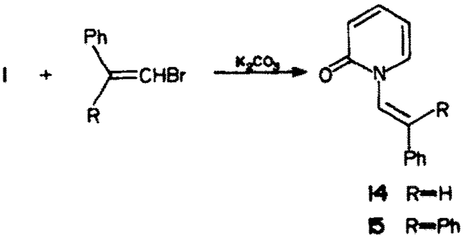


appears reasonable to conclude that this reaction follows the same general mechanistic course as in reaction of the 2-hydroxypyridyl anion with the β-haloenones, i.e. addition elimination, since under the reaction conditions methyl β-bromomethacrylate can be detected (NMR) in the medium at low conversions. Thus, it appears that dehydrohalogenation of **11** occurs prior to attack by the anion of **1**.

Assignment of the *E*-configuration to the olefinic center in **12** can be made unambiguously by comparison of the characteristic spectroscopic data (see below) for **12** with that obtained from the *Z*-isomer **13**, furnished by irradiation of **12** in degassed acetonitrile using flint-glass filtered light. Under these photolytic conditions, a photostationary state consisting of **13** (66%) and **12** (33%) can be reached after 6 h. The vinyl-proton resonances and allylic coupling constants (**12**, δ 7.86, $J = 2.0$ Hz; **13**, δ 7.07, $J = 1.5$ Hz) were particularly indicative of the configurational assignments.

The use of the direct displacement method for generation of 1-vinyl-2-pyridones is not restricted to members of this series having the exocyclic vinyl moiety as part of an α,β-unsaturated ketone or ester function. In earlier studies[2] we had demonstrated that the β-phenyl and diphenylvinyl-2-pyridones, **14** and **15**, can be easily obtained in high yield by reaction of 2-hydroxypyridine with β-bromostyrene or 1,1-diphenyl-2-bromoethene. However, as expected the utility of this simple route is limited to cases where the vinyl halide substrate contains a β-activating group (e.g. carbonyl or phenyl) needed for stabilization of the presumed, intermediate anions. Alternate methods appear more tailored to syntheses of 1-alkyl-substituted vinyl-2-pyridones.

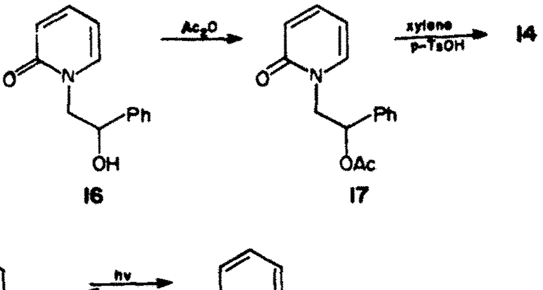


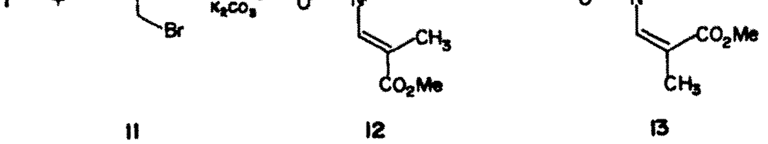
Elimination route

A more general method for preparation of 1-substituted vinyl-2-pyridones utilizes sequences in which elimination reactions of 2-pyridonylethanol derivatives serve as key steps. These procedures, although somewhat more lengthly than those presented above, appear to be more versatile in deriving members of this series with a greater range of structural variation.

1-(2-Phenyl-2-hydroxyeth-1-yl)-2-pyridone **16**,[9] prepared by sodium borohydride reduction of 1-phenacyl-2-pyridone,[10] can be smoothly dehydrated by pyrolysis of its acetate derivative **17** in refluxing xylenes containing catalytic quantities of p-toluenesulfonic acid. The β-styryl-2-pyridone **14** obtained in this way (93%) had spectroscopic and physical properties identical with those of material derived by the direct displacement route.[2]

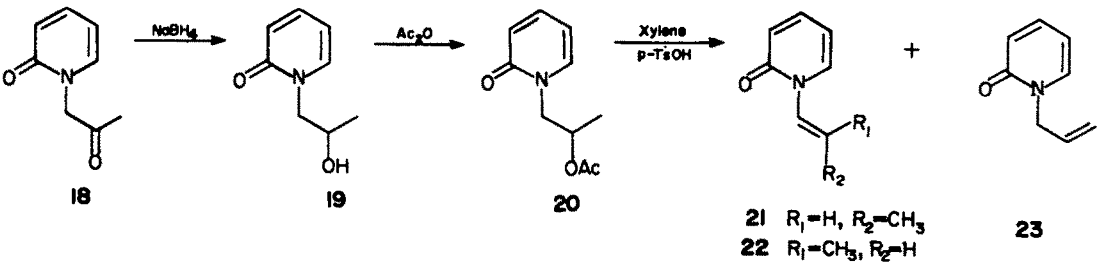
The application of this methodology to syntheses of simple 1-vinyl-2-pyridones is demonstrated by the preparation of the propenyl and isobutenyl pyridones starting with the known[11] 1-acetonyl-2-pyridone **18**. Reduction of **18** with sodium borohydride in ethanol gives the pyridonyl propanol **19** (58%) which can be converted in a

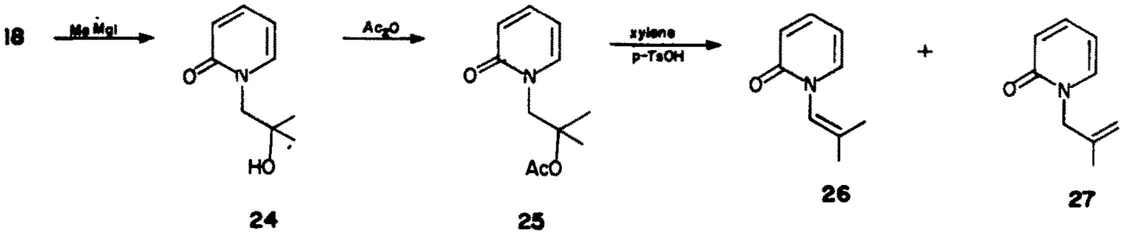




63% yield to its acetate derivative **20** by brief reflux in acetic anhydride containing potassium acetate. The pyrolytic conversion of **20** is induced by refluxing in xylenes containing *p*-toluenesulfonic acid and leads to production of a mixture containing the *trans*- and *cis*-1-propenyl-2-pyridines (**21** and **22**) and the regioisomeric 1-allyl-2-pyridone **23** in relative ratios of 5.6:2.7:1. The overall yield of this reaction is near quantitative when conversion of the acetate is kept low (*ca.* 40%). Assignment of the allylpyridone structure to **23** is based on a comparison of spectroscopic and physical data with those of the known compound.[12] The *cis*- and *trans*-propenylpyridones, **21** and **22**, are distinguished easily on the basis of spectroscopic properties (Tables 2–4); the most significant data being the UV (**21** λ_{max} 318 nm, **22** λ_{max} 309 nm) and vicinyl olefinic proton coupling constants (J = 12.0 Hz for **21** and 9.0 Hz for **22**). Further evidence supporting the stereoisomeric relationship between these substances comes from photoequilibration studies. Irradiation of **21** in degassed acetonitrile using Pyrex-filtered light leads to rapid conversion of **22** along with a 4+4 dimer.[2] Large quantities of **22** can be made available in this way by fractional distillation of the crude photolysate.

In a similar manner, the 1-isobutenyl-2-pyridone **26** is derived from 1-acetonyl-2-pyridone by a reaction sequence involving addition of methyl magnesium iodide to generate the tertiary alcohol **24** (69%) followed by acetylation giving the pyridonyl acetate **25** (55%) and pyrolysis using the above described conditions. The last reaction in this sequence affords a mixture of isobutenyl-**26** and methallyl-2-pyridones **27** (*ca.* 1:1) in near quantitative yield at 62% conversion of **25**.



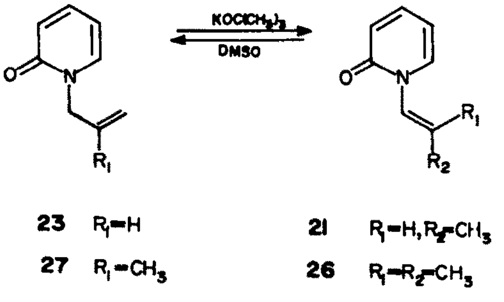


Isomerization route

Another synthetic design of high efficiency and convenience for generation of 1-substituted vinyl-2-pyridones, but limited to particular substitution patterns, involves isomerizations of 1-allyl-2-pyridones. This design is based upon earlier observations by Price[13] and others[14] which show that tertiary *N*-allylamines can be smoothly isomerized to corresponding enamines in the presence of strong bases and proton donors. We have found that this reaction is applicable to the preparation of 1-vinyl-2-pyridones in which non-tertiary alkyl-substitution at the terminal vinyl carbon is desired and base sensitive functionality is lacking. Exemplifying this route is the catalyzed isomerization of 1-allyl-2-pyridone **23** to *trans*-1-propenyl-2-pyridone **21** using potassium *t*-butoxide in dimethylsulfoxide at room temperature. Pure propenylpyridone can be separated from the equilibrium mixture, containing **21** and **23** in a 19:1 ratio, by fractional distillation (42%).

This method has also been employed to prepare 1-isobutenyl-2-pyridone **26** in high yields and purity from 1-methylallyl-2-pyridone **27**. The starting material is simply derived from 2-hydroxypyridine and methallyl chloride (79%). Accordingly, isomerization of **27** using the conditions described above gave an equilibrium mixture of **26** and **27** (*ca.* 2:1). Separation of reasonably large (*ca.* 2 g) quantities of pure isobutenyl pyridone can be accomplished using the newly developed Sephadex G-10 column chromatographic technique.[15] Typical results from chromatographic separation of a 3.81 g sample, containing a 2:1 ratio of **26** and **27** using a 3.5 × 163 cm column packed with Sephadex G-10 (fine) and eluting with 1:1 water-methanol, are recorded in Table 1.

An alternate separation procedure, of greater utility when larger quantities of the pure isobutenylpyridone are desired, is through preparation of a purifiable, crystalline methoxy chloromercurate salt **28**.[c] The crude isomerization reaction mixture containing **26** and **27** is reacted with



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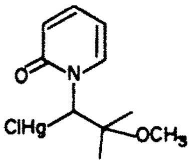
[c] The general procedure used for preparation of this salt follows that described by Marvel.[16]

methanolic mercuric acetate followed by ligand exchange using ethanolic sodium chloride producing a mixture from which **28** can be separated by fractional crystallization. This salt, characterized by NMR, can be converted to **26** by treatment with hydrochloric acid followed by neutralization and distillation.

Table 1. Sephadex G-10 chromatographic purification of a mixture of 1-isobutenyl-2-pyridone **26** and methallyl-2-pyridone **27**

Elution volume (ml)[a]	Weight (g)[b] isobutenylpyridone	Weight (g)[b] methallylpyridone
0–834	—	—
835–857	1.35	—
858–886	0.68	0.73
887–1038	—	0.25

[a]Void volume is 367 ml as determined by elution of blue-dextran. [b]Recovery of the pyridones are by extraction with chloroform.



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Spectroscopic and conformational properties of the 1-vinyl-2-pyridones.

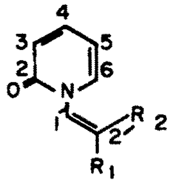
The spectroscopic properties of the 1-vinyl-2-pyridones require brief comment due to their relationship to preferred conformations about the nitrogen-exocyclic vinyl carbon bond. It appears reasonable to expect that in the absence of other perturbations conformations about the C–N bond which allow conjugation of the two π-chromophores in these systems would be of lowest energy. Evidence to support this postulate, discussed earlier by Kaye,[5] is found in the ultraviolet spectra of the

Table 2. UV spectroscopic data for a series of 1-vinyl-2-pyridones and related 1-substituted-2-pyridones

N-Substituent (compound)	λ_{max}(nm)[a]	Molar extinction coefficient
Methyl	301	5490
Vinyl[b]	322	6290
trans-Propenyl (**21**)	318	6270
cis-Propenyl (**22**)	309	5450
Isobutenyl (**26**)	309	5850
E-2-Methoxycarbonylethenyl (**12**)	317	6930
Z-2-Methoxycarbonylethenyl (**13**)	315	5910
5,5-Dimethylcyclohex-2-en-1-onyl (**6**)	315	5480
Cyclohex-2-en-1-onyl (**8**)	315	5930
Pent-3-en-2-onyl (**10**)	312	5090

[a]Spectra were recorded on ethanol solutions. [b]Reported earlier by Kay and Chang.[5]

Table 3. Characteristic proton-NMR resonances for selected 1-vinyl-2-pyridones and related 1-substituted-2-pyridones

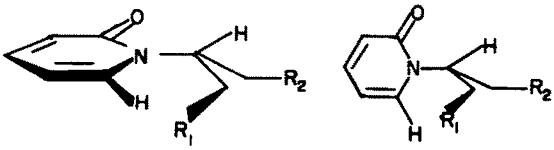


Compound	R_1	R_2	H-6[a]	H-4	H-1'	Cis H-2'	Trans H-2'	Cis 2'-CH$_3$	Trans 2'-CH$_3$
1-vinyl	H	H	7.48	7.26	7.46	5.25	5.06	--	--
21	CH$_3$	H	7.43	7.27	7.19	5.79	--	--	1.84
22	H	CH$_3$	7.21	7.32	6.68	--	5.71	1.69	--
26	CH$_3$	CH$_3$	7.13	7.30	6.46	--	--	1.66	1.87
12	CO$_2$CH$_3$	CH$_3$	7.19	7.35	7.86	--	--	1.95	--
13	CH$_3$	CO$_2$CH$_3$	7.17	7.33	7.07	--	--	--	2.08
23	--	--	7.23	7.33	--	--	--	--	--
27	--	--	7.27	7.31	--	--	--	--	--

[a] Proton-NMR spectra were run in $CDCl_3$ with TMS as internal standard. Chemical shifts were assigned on the basis of multiplicities and coupling constants.

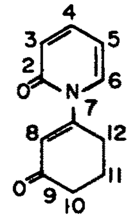
1-vinyl and 1-*trans*-propenyl-2-pyridones (Table 2). It is interesting to note, however, that the presence of bulky-substituents on the vinyl-moiety, *cis* to the pyridone ring could cause, twisting about the C–N bond and preferential adoption of an out-of-plane conformation. Indeed, the ultraviolet maximum for the 1-*cis*-propenyl- and 1-isobutenyl-2-pyridones (**22** and **26**) are substantially blue-shifted as compared to the vinyl and *trans*-propenyl analogs, a change consistent with deconjugation of the pyridone and olefinic chromophores.

Additional support for this conjecture arises from comparisons of key proton chemical shifts for the 1-vinyl-2-pyridones. Conformations for these compounds, which have the pyridone and vinyl groups in the same plane, orient the pyridone H-6 and vinyl H-1′ protons into deshielding regions of the adjacent chromophores.



On the otherhand, twisted conformations would either remove or reverse these magnetic anisotropic effects. Inspection of the data included in Table 3 demonstrates that the H-6 and H-1′ protons in the 1-vinyl and 1-*trans*-propenyl systems resonate at significantly higher fields than the corresponding protons in the *cis*-propenyl and isobutenylpyridones. Furthermore, chemical shifts for the terminal methyl protons in **21**, **22** and **26** again suggest that the presence of *cis*-alkyl substitution on the vinyl moiety of 1-vinyl-2-pyridones causes preferential adoption of the out-of-plane conformations. Accordingly, the dramatic upfield shifts of the *cis*-methyl protons in **22**

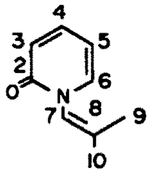
Table 5. ^{13}C NMR Resonances for selected 1-vinyl-2-pyridones



Carbons[a]	6	8	10
2	161.1	161.2	161.3
3	121.6	121.8	121.4
4	140.3	140.3	140.4
5	106.3	106.5	106.2
6	136.1	136.0	136.7
7	160.8	163.0	154.4
8	124.7	125.9	125.5
9	198.4	198.7	197.2
10	50.9	37.1	32.0
11	33.8	22.0	---
12	42.1	28.5	18.9
gem-CH_3	27.8	---	---

[a] ^{13}C-NMR spectra were run in $CDCl_3$ with TMS as internal standard. Chemical shifts were assigned on the basis of multiplicities obtained from proton-coupled spectra and by comparison with spectra of other compounds in this series.

Table 4. ^{13}C NMR Resonances for selected 1-vinyl-2-pyridones



Carbons[a]	1-Methyl-2-pyridone	1-Vinyl-2-pyridone	26	21	22	12	13
2	162.8	161.0	162.2	161.3	162.3	161.8	162.0
3	120.1	121.3	120.8	121.0	121.3	121.5	121.0
4	139.6	132.3	139.8	127.6	139.9	140.3	140.3
5	105.8	106.5	105.4	106.3	105.5	106.1	105.3
6	138.8	139.7	138.6	139.5	137.6	136.7	137.6
7	37.4	131.9	123.5	134.0	128.5	136.3	133.7
8	---	103.8	132.9	118.3	123.0	125.3	125.9
9	---	---	17.4	---	12.1	12.7	166.1
10	---	---	22.5	15.4	---	167.0	18.3
OCH_3	---	---	---	---	---	52.3	51.9

[a] ^{13}C-NMR spectra were run in $CDCl_3$ with TMS as internal standard. Chemical Shifts were assigned on the basis of multiplicities obtained from proton-coupled spectra and by comparison with spectra of other compounds in this series.

and **26** as compared to those of **21** appear to result from their location in the shielding region of the tilted pyridone ring.

EXPERIMENTAL

Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee. NMR spectra were recorded on a Varian HA-100 (proton) and Jeol PS-100 (carbon) spectrometers with tetramethylsilane as the internal standard. Infrared spectra were taken with a Beckman IR-8 or a Perkin Elmer-237 spectrophotometer using polystyrene film as reference, and ultraviolet spectra were measured using a Beckman Acta-III spectrophotometer (in 1-cm matched quartz cells). Gas chromatographic analyses were made using a Varian Model-940 chromatograph with a flame ionization detector. Mass spectra were recorded at 70 eV on a CEC-21-110 double-focusing, high resolution mass spectrometer. Melting points were measured using a MEL-TEMP apparatus and are reported uncorrected. Photolyses were conducted in a preparative apparatus consisting of a Hanovia 450 W medium pressure light source surrounded by a glass filter within a water-cooled quartz immersion well immersed in the solution irradiated and were monitored by UV using a Beckman DU and DK1 spectrophotometers. Sephadex G-10 (fine) was purchased from Pharmacia Fine Chemicals.

1 - (5,5 - *Dimethylcyclohex* - 2 - *en* - 1 - *on* - 3 - *yl*) - 2 - *pyridone* **6**. To a solution of 2-hydroxypyridine (60.0 g, 0.63 mol) and anhyd potassium carbonate (90.0 g, 0.65 mol) was quickly added (71.4 g, 0.45 mol) of 3 - chloro - 5,5 - dimethyl - cyclohex - 2 - en - 1 - one. The resulting mixture was heated at 110–120°C for 41 h. The solid obtained after cooling to room temp. was triturated with hot benzene. The triturates were combined and concentrated *in vacuo* yielding 1 - (5,5 - dimethylcyclohex - 2 - en - 1 - on - 3 - yl) - 2 - pyridone (90.8 g, 93%). A portion of this material was recrystallized from benzene to give the product as needles, m.p. 104.0–106.0°C. *Anal.* Calc. for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.86; H, 6.90; N, 6.40%). ^1H NMR ($CDCl_3$) δ 1.18 (s, 3H, methyl), 2.77 (s, 2H, α to nitrogen), 2.38 (d, 2H, α to carbonyl), 6.07 (m, 1H, vinyl), 6.27 (t, 1H, H-5), 6.36 (d, 1H, H-3), 7.23 (d, 1H, H-6), 7.42 (m, 1H, H-4): UV (95% ethanol) λ_{max} 315 nm (ϵ = 5484); IR (KBr) 1647(vs), 1626(vs), 1580(vs), 1520(s), 907(s), 875(s), 766(vs) cm^{-1}; MS (70 eV): frag (rel intens) P (3), P-28 (21), P-84 (100), P-138 (15), P-178 (25).

1-(*Cyclohex-2-en-1-on-3-yl*)-*2-pyridone* **8**. 2-Hydroxypyridine (4.0 g, 0.042 mol) in anhyd tetrahydrofuran was added to a suspension of 1.01 g (0.042 mol) of sodium hydride in anhyd tetrahydrofuran at room temp over a 30 min period. The resulting mixture was refluxed for 1 H and cooled to 0°C. 3-Chlorocyclohex-2-en-1-one (5.00 g, 0.038 mol) in tetrahydrofuran was then added dropwise over a 10 min period. The reaction mixture was stirred for 12 h at room temp. under an argon atmosphere, poured into ice-water and extracted with chloroform. The chloroform extracts were washed with 5% hydrochloric acid and water, dried and concentrated *in vacuo* giving 1.82 g of a crystalline solid. Recrystallization from carbon tetrachloride gave 1.72 g (59%) of the pure product, m.p. 106–108°C. High Resolution MS Calc. for $C_{11}H_{11}NO_2$: 189.07897. Found: 189.07940. ^1H NMR ($CDCl_3$) δ 2.16 (m, 2H, cyclohexenonyl-H-5), 2.86 (t, 2H, cyclohexenonyl H-4), 2.51 (t, 2H, cyclohexenonyl H-6), 6.01 (s, 1H, vinyl), 6.28 (td, 1H, H-5), 6.51 (d, 1H, H-3), 7.28 (m, 1H, H-6), 7.42 (m, 1H, H-4); UV (ethanol) λ_{max} 315 (ϵ = 5930); IR ($CHCl_3$) 1665(s), 1592(s) cm^{-1}; MS (70 eV): frag (rel intens) P (11), P-28 (90), P-56 (100).

1-(*Pent-3-en-2-on-4-yl*)-*2-pyridone* **10** The same procedure used to prepare the cyclohexenonyl pyridone **8** was employed with the following quantities of reagents: sodium hydride (1.20, 0.05 mol), 2-hydroxypyridine (4.96 g, 0.05 mol), and 4-chloropent-3-en-2-one (5.00 g, 0.04 mol). Work up of the reaction mixture gave 3.35 g of an amber oil which was distilled yielding 2.11 g (29%) of pure product as a light green oil (b.p. 65°C, 0.05 mm). High Resolution MS Calc. for $C_{10}H_{11}NO_2$: 177.07965. Found: 177.07873. ^1H NMR ($CDCl_3$) δ 2.30 (s, 3H, CH_3), 2.50 (d, 3H, J = 0.5 Hz, allylic CH_3), 6.25 (m, 1H, vinyl), 6.20 (td, 1H, H-5), 6.50 (m, 1H, H-3), 7.20 (m, 1H, H-6), 7.35 (m, 1H, H-4); UV (ethanol) λ_{max} 312 (ϵ = 5090); IR ($CHCl_3$) 1684–1571(s), 1250(s) cm^{-1}; MS (70 eV) frag (rel intens) P (1), P-43 (100). The ^1H NMR spectrum of this compound indicated that it was contaminated with *ca.* 10% of a minor, unidentifiable component.

1 - (E - 2 - *Methyl* - 2 - *methoxycarbonylethen* - 1 - *yl*) - 2 - *pyridone* **12**. A solution of 2-pyridone (32.2 g, 0.34 mol) and anhydrous potassium carbonate (100.0 g, 0.72 mol) containing methyl 2,3-dibromo-2-methylpropanoate (88.1 g, 0.34 mol) and 200 ml 1,2-dimethoxyethane was refluxed for 15 h and cooled to room temp. The solution was poured into water and extracted with chloroform. The chloroform extracts were washed with saturated sodium chloride and concentrated to give 43.6 g of the crude product as a crystalline solid. Recrystallization from ethyl acetate gave 30.1 g (46.0%) of pure ester, m.p. 93.0–96.0°C. High resolution MS. Calc. for $C_{10}H_{11}NO_3$: 193.07388. Found: 193.07449. ^1H NMR ($CDCl_3$) δ 1.95 (d, 3H, CH_3), 3.81 (s, 3H, OCH_3), 6.22 (t, 1H, H-5), 6.58 (d, 1H, H-3), 7.19 (d, 1H, H-6), 7.35 (m, 1H, H-4), 7.86 (q, J = 2.0 Hz, 1H, vinyl); UV (95% ethanol) λ_{max} 317 nm (ϵ = 6930); IR (liquid film) 3096(s), 3003(s), 1719(vs), 1659(vs), 1583(vs), 1534(vs), 1442(s), 1301(s), 1151(s), 1017(s), 895(s), 872(s), 854(s), 766(vs), 748(vs), 732(vs), 700(s) cm^{-1}; MS (70 eV) frag (rel intens) P (2), P-59 (100), P-115 (13), P-154 (18).

1 - (Z - 2 - *Methyl* - 2 - *methoxycarbonylethen* - 1 - *yl*) - 2 - *pyridone* **13**. A solution of 5.04 g (26 mmol) of the *E*-isomer **12** in 2000 ml of degassed acetonitrile was irradiated in a preparative apparatus using a flint filter. The disappearance of the starting material was monitored by proton NMR spectroscopy on removed and concentrated aliquots of the photolysate during the irradiation. After 6 h the photolysate had reached a photostationary state of 66% *Z* and 33% *E* esters and the irradiation was terminated. The photolysate was concentrated *in vacuo* to give 4.50 g of the photostationary mixture. This was chromatographed on preparative silica-gel TLC (developed with chloroform) giving a band (R_f 0.30–0.728) containing 1.14 g (22.6%) of 1 - (*Z* - 2 - methyl - 2 - methoxycarbonylethen - 1 - yl) - 2 - pyridone. The addition of 10 ml of diethyl ether caused crystallization of 0.49 g (9.8%) of very pure *Z*-ester, m.p. 92.0–94.0°C. High resolution MS Calc. for $C_{10}H_{11}NO_3$: 193.07388. Found: 193.07429. ^1H NMR ($CDCl_3$) δ 2.08 (d, 3H, CH_3), 3.68 (s, 3H, OCH_3), 6.13 (t, 1H, H-5), 6.53 (d, 1H, H-3), 7.07 (q, 1H, J = 1.5 Hz, vinyl), 7.16 (d, 1H, H-6), 7.33 (m, 1H, H-4); UV (95% ethanol) λ_{max} 315 (ϵ = 5910); IR (liquid film) 1725(s), 1668(s), 1593(s), 765(s) cm^{-1}; MS frag (rel intens) P (2), P-59 (100), P-115 (15), P-154 (18).

1 - (2 - *Phenyl* - 2 - *acetoxyeth* - 1 - *yl*) - 2 - *pyridone* **17**. A solution of 1 - (2 - phenyl - 2 - hydroxyeth - 1 - yl) - 2 - pyridone (1.05 g, 4.9 mmol) in 30 ml of acetic anhydride was mixed with anhydrous sodium acetate (1.17 g, 14.0 mmol). The resulting mixture was refluxed for 6.5 h under a nitrogen atmosphere and then poured into cold H_2O and carefully neutrallized with potassium carbonate. This solution was extracted with chloroform. The combined chloroform extracts were concentrated *in vacuo* giving an oil which crystallized upon addition of ether. The crystals were filtered and dried yielding 1.10 g (87.7%) of tannish white needles, m.p. 90.0–93.5°C, characterized as the desired acetate. High resolution MS Calc. for $C_{15}H_{15}NO_3$: 257.10518. Found: 257.10581. ^1H NMR ($CDCl_3$) δ 4.17 (dd, 1H, CH–N), 4.23 (dd, 1H, CH–N), 6.02 (t, 1H, H-5), 6.16 (q, 1H, benzylic), 6.53 (d, 1H, H-3), 7.17 (m, 1H, H-6), 7.32 (br.m, 1H, H-4), 7.33 (br.m, 5H, aryl); UV (95% ethanol) λ_{max} 303 nm (ϵ = 2450); IR ($CHCl_3$) 1751(m), 1666(m), 1590(m), 1376(w), 1222(m), 1149(w), 1036(w), 1029(w), 946(w), 844(w), 699(m) cm^{-1}; MS frag (rel intens) P (7), P-57 (12), P-137 (11), P-152 (100), P-180 (24).

1-(trans-2-*Phenylethen*-1-*yl*)-*2-pyridone* **14**. A solution of 0.83 g (3.2 mmol) of the acetate **17** in 400 ml of xylene containing 0.10 g (3.7 mmol) of *p*-toluenesulfonic acid was refluxed under argon for 3 days. The solvent was removed *in vacuo* giving an oil which was dissolved in water and extracted with isopentylalcohol. The alcoholic extracts were concentrated *in vacuo* to yield 0.59 g (82%) of the desired pyridone. The spectroscopic and physical properties of this material matched those previously reported.

1-(*2-Hydroxyprop*-1-*yl*)-*2-pyridone* **19**. To a solution of 30.3 g (0.2 mol) of 1-acetonyl-2-pyridone in 600 ml of absolute methanol was added solid sodium borohydride (6.56 g, 0.17 mol) slowly in two portions. The temperature of the solution quickly rose to 56°C. The mixture was then allowed to rapidly stir for 2 days at room temp. Concentration of the reaction mixture *in vacuo* gave a solid which was dissolved in 500 ml of absolute ethanol and perculated through a silica gel column (300 g, Davison grade 9.23, 100-200 mesh). The ethanolic eluant was concentrated *in vacuo* and short-path distilled using a bulb-to-bulb apparatus b.p. 143–145°C (0.6 mm) giving 17.9 g (58%) of the desired alcohol which crystallized upon standing, m.p. 95.0–96.5°C. High resolution MS Calc. for $C_8H_{11}NO_2$: 153.07897. Found: 153.07958. ^1H NMR ($CDCl_3$) δ 1.28 (d, 3H, methyl), 3.89 (dd, 1H, CH–N), 3.96 (dd, 1H, CH–N), 4.06 (br.s, 1H, OH), 4.13 (br.m, 1H, CHO), 6.16 (t, 1H, H-5), 6.51 (d, 1H, H-3), 7.31 (m, 2H, H-4) and H-6); UV (95% ethanol) λ_{max} 303 nm ($\epsilon = 5681$); IR (liquid film) 3333(vs), 1650(vs), 1581(vs), 1556(vs), 1532(vs), 1463(s), 1423(s), 1374(s), 1352(s), 1166(s), 1139(vs), 1066(vs), 938(s), 848(s), 768(vs) cm^{-1}; MS frag (rel intens) P (5), p-44 (18), p-57 (100), P-72 (45), P-100 (17), P-114 (15), P-138 (2).

1-(*2-Acetoxyprop-1-yl*)*-2-pyridone* **20**. A solution of the pyridonyl alcohol **19** (10.0 g, 0.065 mol), 3.00 g (0.031 mol) of anhydrous potassium acetate in 200 ml of acetic anhydride was refluxed for 5 h under an argon atmosphere. The hot reaction mixture was slowly poured into ice-cold absolute ethanol and the resulting solution cooled to 0°C for 10 h. Concentration *in vacuo* of this mixture gave an oil which was then added to icecold aqueous saturated potassium carbonate. The resulting aqueous solution was extracted with chloroform. The chloroform extracts were combined, washed with saturated sodium chloride, and concentrated *in vacuo* giving an oil which was subjected to short path distillations using a bulb-to-bulb apparatus. This procedure gave 8.08 g (63) of the desired acetate as a clear liquid, b.p. 137.0–138°C (2.1 mm). High resolution MS Calc. for $C_{10}H_{13}NO_3$: 195.08953. Found: 195.08987. ^1H NMR ($CDCl_3$) δ 1.29 (d, 3H, methyl), 1.98 (s, 3H, methyl), 4.04 (dd, 1H, CH–N), 4.10 (dd, 1H, CH–N), 4.29 (m, 1H, CHO), 6.16 (t, 1H, H-5), 6.55 (d, 1H, H-3), 7.36 (m, H-4 and H-6); UV (95% ethanol) λ_{max} 303 nm ($\epsilon = 5000$); IR (liquid film) 1731(vs), 1659(vs), 1581(vs), 1532(s), 1370(s), 1238(vs), 1152(s), 1141(s), 1127(s), 1061(vs), 1019(s), 959(s), 771(vs) cm^{-1}; MS frag (rel intens) P (20), P-75 (16), P-86 (81), P-99 (100), P-114 (16), P-115 (16), P-152 (57).

Elimination reaction of 1 - (2 - *acetoxyprop* - 1 - *yl*) - 2 - *pyridone. Preparation of* cis- *and* trans - 1 - (*prop* - 1 - *en* - 1 - *yl*) - 2 - *pyridones* (21 *and* 22) *and* 1 - (*prop* - 2 - *en* - 1 - *yl*) -2 - *pyridone* 23

A solution of 0.83 g (4.3 mmol) of the acetate 20 in 50 ml of xylene containing 0.10 g (0.53 mmol) of *p*-toluenesulfonic acid was stirred at reflux for 2 days. The crude reaction mixture was quantitatively analyzed for product by GLC (1.5% OV-101, 60/70 ABS Anakrom, 120°) giving the following results: **21** 22.2%, **22** 10.9%, **23** 4.0%, recovered **20** 62.9%. Spectroscopic properties of these compounds are given below.

1 - (2 - *Hydroxy* - 2 - *methylprop* - 1 - *yl*) - 2 - *pyridone* **24**. A solution of 1-acetonyl-2-pyridone (30.6 g, 0.20 mol) in 500 ml of anhydrous tetrahydrofuran was slowly added over a 1.5 h period to a previously prepared solution of methyl magnesium iodide (made from magnesium (17.84 g, 0.73 g-at) and methyliodide (104.3 g, 0.73 mol) in 970 ml of anhydrous ether). The resulting solution was stirred for 10 h, cooled in an ice-ethanol bath to −15°C, and added slowly to a saturated ammonium chloride solution. The separated ethereal layer was washed with water. The aqueous layer was extracted with chloroform, made basic with 15% potassium hydroxide, and extracted again with chloroform. The combined organic extracts were concentrated *in vacuo* giving 23.5 g of the desired alcohol as a crystalline solid. Recrystallization from benzene gave the pure alcohol as white needles, m.p. 118.0–11.5°C, (11.38 g, 33.6%). High resolution MS Calc. for $C_9H_{13}NO_2$: 167.09462. Found: 167.09412. ^1H NMR ($CDCl_3$) δ 1.24 (s, 6H, CH_3), 4.02 (s, 2H, CH_2N), 4.42 (s, 1H, alcoholic), 6.28 (t, 1H, H-5), 6.58 (d, 1H, H-3), 7.34 (m, 2H, H-4 and H-6); UV (95% ethanol) λ_{max} 304 nm ($\epsilon = 5720$); IR ($CHCl_3$) 1672(s), 1583(s) cm^{-1}; MS frag (rel intens) P (13), P-58 (100), P-86 (56), P-87 (19), P-108 (34), P-114 (13), P-124 (9), P-128 (11).

1 - (2 - *Acetoxy* - 2 - *methylprop* - 1 - *yl*) - 2 - *pyridone* **25**. A solution of the tertiary alcohol **24** (14.0 g, 84 mmol) and sodium acetate (4.65 g, 57.0 mmol) in 70 ml of acetic anhydride was refluxed for 6 h. The reaction mixture was cooled to room temp., poured in ice water and carefully neutrallized by the addition of solid sodium bicarbonate. The resulting solution was extracted with chloroform. The chloroform layer was washed with saturated potassium carbonate, dried over potassium carbonate, concentrated *in vacuo*, and subjected to shortpath distillation using a bulb-to-bulb apparatus. This procedure gave 9.70 g (55.2%) of the desired acetate as a clear liquid, b.p. 116.0–117.0°C (0.2 mm). High resolution MS Calc. for $C_{11}H_{15}NO_3$. 209.10519. Found 209.10397. ^1H NMR ($CDCl_3$) δ (1.51 (s, 6H, CH_3), 2.01 (s, 3H, CH_3), 4.30 (s, 2H, CH_2N), 6.18 (t, 1H, H-5), 6.56 (d, 1H, H-3), 7.34 (m, 2H, H-4 and H-6); UV (95% ethanol) λ_{max} 300 nm ($\epsilon = 4200$); IR (liquid film) 1733(vs), 1661(vs), 1592(vs), 1538(s), 1429(s), 1399(vs), 1370(vs), 1277(s), 1250(vs), 1238(vs), 1215(vs), 1170(vs), 1136(vs), 1022(s), 768(s) cm^{-1}; MS frag (rel intens) P(22), P-59 (31), P-75 (28), P-100 (100), P-166 (53).

Elimination reaction of 1 - (2 - *aceioxy* - 2 - *methylprop* - 1 - *yl*) - 2 - *pyridone. Preparation of* 1 - (2 - *methylprop* - 1 - *en* - 1 - *yl*) - 2 - *pyridone* **26**, *and* 1 - (2 - *methylprop* - 2 - *en* - 1 - *yl*) - 2 - *pyridone* **27**

A solution of 0.75 g (5.0 mmol) of the acetate **25** ml of xylene containing 0.10 g (0.53 mmol) of *p*-toluenesulfonic acid was refluxed for 2 days under an argon atmosphere. The crude reaction mixture was quantitatively analyzed by GLC (1.5% OV-101, 60/70 ABS Anakrom, 120°C) giving the following results: 26, 37.9%, 27, 36.3%, recovered 25, 25.9%.

The spectroscopic data for these compounds are given below.

1 - (trans - *Prop* - 1 - *en* - 1 *yl*) - 2 - *pyridone* **21**. 1 - (Prop - 2 - en - 1 - yl) - 2 - pyridone **23** (2.30 g, 1.6 mmol) was slowly added over a 10 min period to a previously prepared solution of potassium *t*-butoxide (from 61.6 g, 1.58 g-at, potassium and 900 ml of anhydrous tertiaryl butyl alcohol) in 1300 ml of anhydrous dimethylsulfoxide held at 0°C. After addition was complete, the solution was allowed to warm to room temp. and stirred for a 5 h period. The reaction mixture was poured into ice-cooled water and extracted with ether. The ethereal layer was washed with saturated sodium chloride, dried (potassium carbonate) and concentrated *in vacuo* to give the desired pyridone (108.1 g). Vacuum distillation using a bulb-to-bulb apparatus gave 90.1 g (42.0%) of pure material, b.p. 105.5°C (0.5 mm). High resolution MS Calc. for C_8H_9NO: 135.06841. Found: 135.06782. ^1H NMR ($CDCl_3$) δ 1.84 (d, 3H, CH_3), 5.79 (sextet, 1H, $J = 12.0$ Hz, vinyl), 6.15 (t, 1H, H-5), 6.51 (d, 1H, H-3), 7.19 (octet, 1H, $J = 12.0$ Hz, vinyl), 7.27 (m, 1H, H-4), 7.43 (d, 1H, H-6); UV (95% ethanol) λ_{max} 318 nm ($\epsilon = 6270$); IR (liquid film) 1668(vs), 1588(vs), 1534(s), 1270(vs), 1187(s), 1142(s), 951(vs), 762(vs) cm^{-1}; MS frag (rel intens) P(29), P-1 (18), P-15 (100), P-29 (14), P-96 (25).

1-(*cis-Prop-1-en-1-yl*)*-2-pyridone* **22**. A solution of 7.45 g (55 mmol) of the *trans*-propenylpyridone **21** dissolved in 850 ml of degassed acetonitrile was irradiated in a preparative apparatus using a Pyrex filter for 1 h. The disappearance of the *trans*-isomer was monitored by UV spectroscopy on removed and diluted aliquots of the photolysate during the irradiation. When disappearance of **21** had ceased the irradiation was terminated and the photolysate concentration *in vacuo* to give 7.31 g of crude reaction mixture. The addition of ether caused the precipitation of 0.89 g of the 4 + 4 dimer. The remaining 6.57 g was subjected to bulb-to-bulb distillation giving 3.40 g (46%) of the pure *cis*-propenylpyridone, b.p. 80–81°C (0.2 mm). High resolution MS Calc. for C_8H_9NO: 135.06841. Found: 135.06821. ^1H NMR ($CDCl_3$) δ 1.69 (d, 3H, CH_3), 5.71 (octet, 1H, $J = 9.0$ Hz, vinyl), 6.17 (t, 1H, H-5), 6.54 (d, 1H, H-3), 6.68 (octet, 1H, $J = 9.0$ Hz, vinyl), 7.21 (d, 1H, H-6), 7.42 (m, 1H, H-4); UV (95% ethanol) λ_{max} 309 nm ($\epsilon = 5450$); IR (liquid film) 1743(s), 1659(vs), 1588(vs), 1530(vs), 1173(s), 1142(vs), 930(s), 768(vs), 716(s), 649(m) cm^{-1}; MS frag (rel intens) P (27), P-1 (25), P-15 (100), P-68 (20), P-83 (20), P-94 (20), P-96 (45).

1-(*2-Methylprop-2-en-1-yl*)*-2-pyridone* **27**. A solution of 100.0 g (1.05 mol) of 2-hydroxypyridine, 29.9 g (1.44 mol) of methallylchloride, 350 g (2.5 mol) of potassium carbonate in 400 ml of anhydrous dimethoxyethane was refluxed for 12 h under an argon atmosphere. The resulting solution was filtered and concentrated *in vacuo* giving an oil which was distilled using a bulb-to-bulb apparatus giving 153.5 g (98%) of the desired methallyl pyridone as a clear oil, b.p. 130–131°C (0.12 mm). High resolution MS Calc. for $C_9H_{11}NO$: 149.08406. Found: 149.08360. ^1H NMR ($CDCl_3$) δ 1.73 (s, 3H, CH_3), 4.52 (br.s, 2H, CH_2N), 4.73 (br.s, 1H), 4.93 (m, 1H), 6.14 (t, 1H, H-5), 6.53 (d, 1H, H-3), 7.23 (d, 1H, H-6), 7.33 (m, 1H, H-4); UV (95% ethanol) λ_{max} 302 nm ($\epsilon = 4976$); IR (liquid film) 1663(vs), 1589(vs), 1535(s), 1463(s), 1432(s), 1168(s), 1146(s), 768(vs) cm^{-1}; MS frag (rel intens) P (54), P-1 (86), P-15 (100), P-17 (29), P-70 (30), P-71 (24), P-110 (38).

1-(2-*Methylprop*-1-*en*-1-*yl*)-2-*pyridone* **26**. A procedure similar to that used for the conversion of **23** to **21** was used starting with 23.7 g (16 mmol) of the methallylpyridone **27**, potassium *t*-butoxide (from 3.70 g potassium and 100 ml of anhydrous *t*-butyl alcohol) in 500 ml of anhydrous dimethylsulfoxide. Work up in the manner described above gave 10.1 g of a mixture of the isobutenyl **26** and methallylpyridones **27** in a ratio of 2:1. A 3.81 g sample of this mixture was subjected to column chromatography on Sephadex G-10 (fine) (3.5 × 163 cm). Elution was with 1:1 water-methanol. Fractions were monitored by GCL (1.5% OV-101 on ABS Anakrom, 153°C). Results of this method of separation are given in Table 1. Pure isobutenyl-2-pyridone was obtained by this method. High resolution MS Calc. for $C_9H_{11}NO$: 149.08406. Found: 149.08375. ^1H NMR ($CDCl_3$) δ 1.66 (d, 3H, E–CH_3), 1.87 (d, 3H, Z–CH_3), 6.13 (t, 1H, H-5), 6.46 (m, 1H, vinyl), 6.55 (d, 1H, H-3), 7.13 (d, 1H, H-6), 7.30 (m, 1H, H-4); UV (95% ethanol) λ_{max} 309 nm ($\epsilon = 5850$); IR ($CHCl_3$) 1694(vs), 1619(vs) cm^{-1}; MS frag (rel intens) P (25), P-1 (21), P-15 (100), P-110 (11).

An alternate procedure is useful for purification of large quantities of the isobutenyl-2-pyridone **26**. Representative of this is the following experiment starting with 235.0 g (1.58 mol) of the methallylpyridone **27**. Short path distillation of the crude mixture of **26** and **27** gave (b.p. 135–140°, 2.6 mm) 68.6 g of a 3:1 mixture of the regioisomers. This material was added to 149.4 g (0.47 mol) of mercuric acetate in 2 l. of absolute methanol and the resulting solution was stirred for 2 days. Concentration of the mixture *in vacuo* gave a solid, containing methoxy acetoxy mercurate salt, which was not purified but dissolved in 2 l. of 95% ethanol containing 120 g (3 mol) of sodium chloride and stirred at room temp. for 21 h. The resulting solution was diluted with methylene chloride, filtered and concentrated *in vacuo* giving a crude mixture of methoxy chloromercurates. Repeated recrystallization from methanol gave 81.3 g (64%) of pure 1 - (1 - chloromercurato - 2 - methoxy - 2 - methylprop - 1 - yl) - 2 - pyridone **28** as a white crystalline solid, m.p. 129–131°C. ^1H NMR ($CDCl_3$) δ 1.25 (s, 6H, CH_3), 3.24 (s, 3H, OCH_3), 4.30 (s, 1H, CHN), 6.19 (t, 1H, H-5), 6.61 (d, 1H, H-3), 7.36 (m, 1H, H-4), 7.49 (d, 1H, H-6); ^{13}C NMR ($CDCl_3$) ppm relative to TMS 163.7 (s, C-2), 121.2 (d, C-3), 140.4 (d, C-4), 106.4 (d, C-5), 139 (d, C-6), 75.3 (d, CHN), 79.3 (s, quart), 24.4 (q, CH_3), 49.9 (q, OCH_3).

The methoxy chloromercurate was then subjected to conditions for hydrolysis of the carbon-mercury bond. This material was dissolved in concentrated hydrochloric acid (500 ml) and stirred for 0.5 h. Chloroform (500 ml) and 100 g of potassium carbonate were added. The chloroform layer was separated, concentrated *in vacuo* and distilled to give 18.0 g (57% from mercurate salt) of the pure isobutenyl pyridone.

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REFERENCES

[1] A preliminary report of these studies has been presented at the 169th National ACS Meeting, Philadelphia, Pennsylvania (1975), Orgn 56.

[2] *Abstracts of Papers*, 173rd National ACS Meeting, New Orleans, Louisiana (1977), Orgn 107; P. S. Mariano, A. Leone and E. Krochmal, *J. Org. Chem.* **42**, 1122 (1977); P. S. Mariano, A. Leone and E. Krochmal, *Tetrahedron Letters* 2227 (1977).

[3] P. S. Mariano, R. Beamer, P. Huesmann and D. Dunaway-Mariano, *Tetrahedron Letters* 4299 (1977).

[4] H. Kaye and S. H. Chang, *Tetrahedron* **26** 1369 (1970).

[5] H. Kaye, *J. Polymer Sci. Part B* **7**, 1 (1969); N. Neda, K. Kondo, M. Kono and K. Takemoto, *Makromol. Chem.* **120**, 13 (1968).

[6] A. W. Crossley and H. R. LeSuer, *J. Chem. Soc.* **110** (1903); R. D. Clark and C. H. Heathcock, *J. Org. Chem.* **41**, 636 (1976).

[7] A. McKillop and M. J. Zelesko, *Tetrahedron Letters* 4945 (1968).

[8] M. C. Ford and W. A. Waters, *J. Chem. Soc.* 1851 (1951).

[9] E. Alberti, *Gazz. Chim. Ital.* **86**, 1181 (1956).

[10] F. Krönke and W. Heffe, *Ber.* **70B**, 864 (1937).

[11] C. K. Bradsher and M. K. Zinn, *J. Heterocyclic Chem.* **4**, 66 (1967).

[12] B. I. Mikhant'ev, E. I. Fedorov, A. I. Kucherova, and V. P. Potapova, *Zhur. Obschei. Khim.* **29**, 1874 (1959); L. A. Paquette, U. S. patent 3,432,507 (*Chem. Abst.* **70**, 96834μ (1969)).

[13] C. C. Price and W. H. Snyder, *J. Am. Chem. Soc.* **83**, 1773 (1961).

[14] T. Cunningham, R. Gigg and C. D. Warrne, *Tetrahedron Letters* 1191 (1964); J. A. Montgomery and H. J. Thomas, *J. Org. Chem.* **30**, 3235 (1965).

[15] P. S. Mariano, G. I. Glover and S. Cheowtirakul, *Separation Science* **11**, 147–157 (1976).

[16] L. T. Sanborn and C. S. Marvel, *J. Am. Chem. Soc.* **48**, 1409 (1926); E. Griffith and C. S. Marvel, *Ibid.* **53**, 789 (1931).