

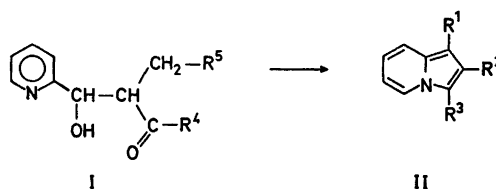
Indolizine Derivatives. III. Cyclization of the Aldol Product of 2-Pyridinecarbaldehyde and β -Dimethylamino- (or β -Hydroxy-)ketones

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A novel synthesis of 2-acylindolizines *via* cyclization of the aldol product of 2-pyridinecarbaldehyde and β -dimethylamino- (or β -hydroxy-) ketones is described. Cyclizations through reaction of the amino (or hydroxy) group or the carbonyl group are observed. Thus, 3-dimethylaminomethyl-4-hydroxy-4-(2-pyridyl)-2-butanone (Ia) gives, on treatment with acetic anhydride, several other indolizines in addition to 1-(2-indoliziny)ethanone (IIa), including those formed through reaction of the carbonyl carbon. 2-Dimethylaminomethyl-3-hydroxy-1-phenyl-3-(2-pyridyl)-1-propanone (Ib) behaves analogously. With 3-hydroxymethyl-4-hydroxy-4-(2-pyridyl)-2-butanone (Ic), IIa is the sole indolizine product. The divergent reactions of Ia and Ic are discussed on the basis of the finding that 3-dimethylaminomethyl-4-(2-pyridyl)-3-buten-2-one gives with acetic anhydride the same products as Ia. In boiling acetic acid, both Ia and Ic give 2-methyl-1-(2-pyridyl)-1,3-butanedione, which with acetic anhydride cyclizes to 1-acetoxy-3-methyl-2-indolizinylmethyl acetate.

known to give indolizine derivatives through cyclocondensation.³⁻⁵



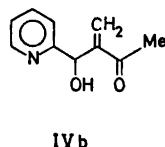
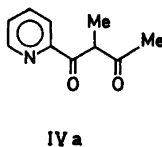
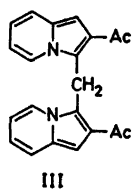
I/	R ⁴	R ⁵
a	Me	NMe ₂
b	Ph	NMe ₂
c	Me	OH

II/	R ¹	R ²	R ³
a	H	Ac	H
b	Ac	Ac	H
c	H	Ac	Ac
d	H	CHO	Me
e	OAc	Me	Me
f	H	PhCO	H
g	Ac	PhCO	H
h	H	PhCO	Ac
i	H	CHO	Ph
j	OAc	Me	Ph
k	OAc	CH ₂ OAc	Me
l	OAc	Me	Ac
m	OAc	Me	CH ₂ OAc
n	H	Ac	CH ₂ CH ₂ Ac

The cyclization of 3-*tert*-amino-1-(2-pyridyl)-1-alkanols or 3-*tert*-amino-1-(2-pyridyl)-1-alkenes on treatment with boiling acetic anhydride to afford indolizines was discussed by Barrett in detail.¹ Especially significant were his findings that pyridylalkenyl acetates cannot be intermediates and that the reaction of aminopyridyl-alkanols does not proceed through aminopyridylalkenes. Michalski *et al.* reported on the formation of 3-(2-pyridyl)indolizine from 1,3-di-(2-pyridyl)-1,3-propanediol when refluxed with acetic anhydride/sodium acetate.³ On the other hand, 3-(2-pyridyl)-1-propanones are

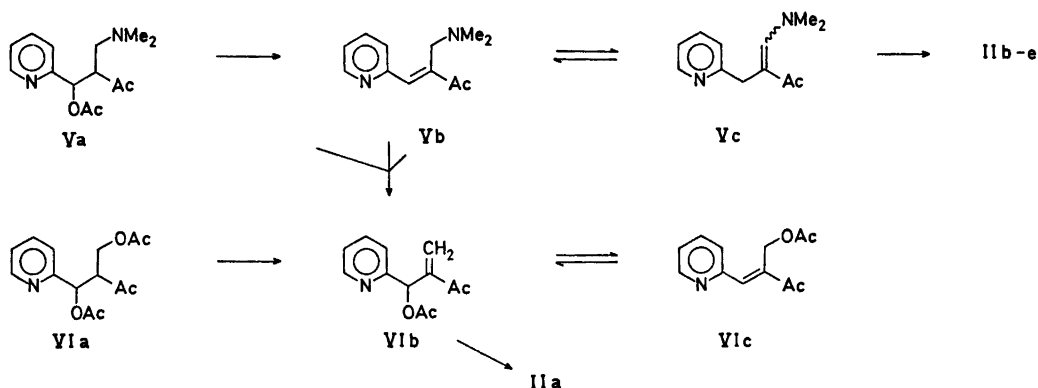
The multifunctional aldols I, possessing simultaneously 3-(2-pyridyl)-1-propanone and 3-*tert*-amino- (or 3-hydroxy-) 1-(2-pyridyl)-1-propanol properties, may be expected to cyclize to indolizines in two ways: the 3-carbon of the resultant indolizines could originate from the carbonyl carbon or from the carbon carrying the amino (or hydroxy) group. In this paper it is shown that in heating with acetic anhydride the β -aminoketones Ia and Ib are converted in both ways, whereas the β -hydroxyketone Ic is changed only through reaction of the hydroxymethyl group. Herewith a practical route to several new indolizines is demonstrated. Thus, the aldol Ia when refluxed with acetic anhydride gives rise to several indolizines, namely: IIa, IIb, IIc, and III through reaction of the carbon carrying the dimethylamino group, and IIId and IIe through reaction of the carbonyl carbon. The analogous products IIg, IIh, and III, IIj are obtained from Ib, whereas Ic yields only IIa and III. All three aldols Ia, Ib, and Ic produce some 2-pyridylmethyl acetate. In boiling acetic acid, neither Ia nor Ic give indolizines, but the pyridine IVa, probably through IVb. With boiling acetic acid, IVa in turn cyclizes to the indolizine IIIk.

At room temperature, with acetic anhydride, Ia is rapidly acetylated to Va, from which acetic acid is then eliminated to afford the unsaturated pyridineketone Vb. At early stages of the reaction of Ic with acetic anhydride the NMR monitoring suggests acetylation to VIa, but on further reaction the presence of any subsequent intermediates could not be demonstrated. In an acetic acid solution at 60 °C, Vb is soon partly isomerized. Comparison between the NMR

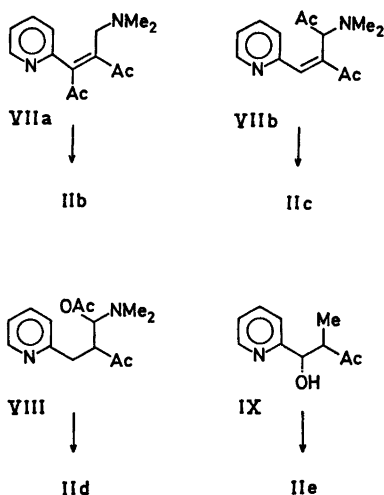


spectrum of the starting solution and that obtained after 0.5 h showed that Vb had been partly changed into another pyridine, probably Vc. The methylene peak of Vc appears at lower field (0.25 ppm) and the C-6 ring proton of Vc at higher field (0.35 ppm) than those of Vb, indicating that Vc cannot be a conjugated pyridine. On further heating with acetic acid, Vb yields only IIa and III. With boiling acetic anhydride, Vb gives the same products, IIa–e and III, in practically identical ratio as Ia. This strongly suggests that Vb is an intermediate in the formation of the indolizines IIb–e from Ia. No decomposition through the retroaldolization of the aldols I to 2-pyridinecarbaldehyde and β -amino- (or β -hydroxy) ketones occurs. This is proved (TLC) by the absence of the indolizinediketone IIIn in the product mixtures, as 2-pyridinecarbaldehyde and 4-dimethylamino- (or 4-hydroxy-) 2-butanone should give IIIn.⁶

The cyclization of *tert*-aminopyridylalkanol and *tert*-aminopyridylalkenes without an acyl group may be explained in terms of a simple



substitution on the carbon carrying the amino group. In the case of the aldols Ia, Ib, and Ic the possibility of such a substitution is not entirely ruled out, of course, since IIa is also formed when Ia is heated in water containing some oxalic acid. However, it is more plausible that the five-membered ring of IIa, for example, is formed through addition to the carbon-carbon double bond of the intermediate unsaturated ketone VIb, which in turn can be generated from Ia, Ic, Vb, and Vc by several means, as indirectly stated above. The exclusive cyclization of VIb to IIa hence accounts for the absence of the ketones VIb and VIc in the product mixtures.



It is currently assumed that the diacetylindolizines IIb and IIc are formed analogously to IIa through the cyclization of acetyl derivatives of Va or Vb, such as VIIa and VIIb, rather than through the acetylation of IIa; for the indolizines having electron-withdrawing substituents are very reluctantly acetylated.^{7,8}

The indolizinecarbaldehyde IIId is undoubtedly formed from Vb or Vc, but before the addition step to the carbonyl carbon giving rise to the five-membered ring can take place, the unsaturated ketone clearly has to change into a saturated one, probably VIII. The reduced indolizine product IIe can also be prepared by the cyclocondensation of the pyridylbutanone IX, and its origin is obviously analogous to that of the reduced indolizine derivatives from the Perkin reaction of 2-pyridinecarbaldehyde.⁹ The second reduced reaction product, 2-pyridylmethyl acetate, may have a similar origin. The formation of methylenebisindolizines, such as III, was discussed by Barrett.¹

The structure of IIk is consistent with the finding that IVa in the presence of acetic anhydride/potassium acetate yields as the main product IIk, which is stable on further reaction, accompanied by a small amount of the acetylindolizine III. It is assumed that acetic anhydride effects the cyclization of IVa to the pyridinium compound X, which rearranges into the indolizines IIk or IIIm. The latter indolizine, which was not isolated, gives III through the cleavage of formaldehyde and subsequent acetylation catalyzed by acetic anhydride/potassium acetate.

The structures of the new indolizines were unambiguously deduced from their analyses and spectral data. Especially informative are the NMR spectra, for the position and nature of the substituents of indolizines are in most cases easily determined by inspection of the chemical shifts of the indolizine ring protons.^{8,10} To facilitate comparison, the NMR data are collected in Table 1. The appearance of the C-1 proton of 2,3-diacetylindolizines (IIc, IIh) and C-3 proton of 1,2-diacetylindolizines (IIb, IIg) at higher field than those of 2-acetylindolizines (IIa, IIf) is due to the distortion of the 2-acetyl group of diacetylindolizines out of the ring plane.

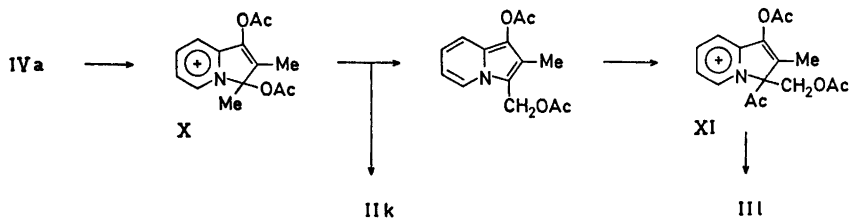


Table 1. NMR-Data of the new indolizines II and III. (δ -values, $J_{6,6} = J_{6,7} = ca. 7$ Hz, $J_{7,8} = ca. 9$ Hz).

	R ¹	R ²	R ³	H ⁵	H ⁶	H ⁷	H ⁸
IIa	6.76(s)	2.53(3 H s)	7.75(br s)	7.84	6.35—6.8		7.33
IIb	2.64 or (3 H s) 2.60	2.64 or (3 H s) 2.60	7.64(s)	7.96	6.65—7.25		8.17
IIc	6.55(s)	2.51 or (3 H s) 2.40	2.51 or (3 H s) 2.40	9.59	6.5 —7.1		7.32
IId	6.65(s)	10.04(1 H s)	2.73 (3 H s)	7.60	6.3 —6.75		7.27
IIe	2.10(3 H s)	2.31 or (3 H s) 2.26	2.31 or (3 H s) 2.26	7.40	6.15—6.65		7.09
IIf	6.69(br s)	7.8(2 H) and 7.35(3 H)	7.60(d 1.5)	7.73	6.2 —6.7		7.20
IIg	2.18(3 H s)	7.9(2 H) and 7.5(3 H)	7.35(s)	7.97	6.7 —7.25		8.29
IIh	6.45(s)	7.9(2 H) and 7.5(3 H)	2.24(3 H s)	9.92	6.7 —7.4		7.45
IIi	6.77(s)	9.79(1 H s)	7.37(5 H s)	7.81	6.15—6.75		7.26
IIj	2.09(3 H s)	2.28(3 H s)	7.36(5 H s)	7.83	6.05—6.65		7.06
IIk	2.34 or (3 H s) 2.28	5.04(2 H s) and 1.94(3 H s)	2.34 or (3 H s) 2.28	7.40	6.15—6.6		7.06
III	2.33(3 H s)	2.38(3 H s)	2.47(3 H s)	10.05	6.6 —7.4		7.15
III	6.78(s), 2.74(s), 5.50(s), 8.05(br d 7), 6.2—6.8(m), 7.22(br d 9), (1/3/1/1/2/1)						

EXPERIMENTAL

Acetic anhydride contained less than 3 % acetic acid. Silica chromatography columns were made up in benzene and eluted with benzene containing increasing amounts of methylene chloride. The fractionations were followed by TLC (silica, benzene containing 2–5 % of methanol). Melting points are uncorrected. Elemental analyses were performed by Mrs. M. Horko. The solid products were recrystallized from ethanol or light petroleum (b.p. 40–65 °C). UV spectra were obtained for solutions in ethanol. IR spectra were obtained for KBr-tablets or liquid films. NMR spectra were measured for solutions in CDCl₃ or CCl₄ at 60 MHz. Mass spectra were recorded at 70 eV through the cooperation of Mr. L. Hiltunen, Dipl. Eng.

Preparation of the aldols I

3-Dimethylaminomethyl-4-hydroxy-4-(2-pyridyl)-2-butanone, (Ia). Method A. 2-Pyridinecarbaldehyde (10.7 g, 0.10 mol), 4-dimethylamino-2-butanone (11.5 g, 0.10 mol), 2 ml of water and 0.5 g finely powdered Ca(OH)₂ were kept at –15 °C for 10 h with occasional shaking. The product was extracted with ether and dried

over Na₂SO₄. The remaining oil (19.0 g, 81 %) consisted of almost pure Ia, according to its NMR spectrum: δ 8.40 (1 H, br d), 7.9–6.95 (3 H, m), 5.5 (1 H, br s), 5.10 and 5.08 (1 H, d 6.5 and d 5), 3.7–2.3 (3 H, m), 2.3–2.15 (9 H). Method B. 2-Pyridinecarbaldehyde and 4-dimethylamino-2-butanone were allowed to stand at room temperature without any added catalyst for 3–4 days, giving a dark oil which contained, besides Ia, about 10 % unchanged starting materials.

2-Dimethylaminomethyl-3-hydroxy-1-phenyl-3-(2-pyridyl)-1-propanone, (Ib). From 2-pyridinecarbaldehyde (10.7 g, 0.10 mol) and 3-dimethylamino-1-phenyl-1-propanone (17.7 g, 0.10 mol) by the method A 24.1 g (85 %) almost pure Ib was obtained; NMR spectrum: δ 8.39 and 8.28 (1 H, d 5 and d 5), 6.20 (1 H, br s), 5.4–5.15 (1 H, d and d), 4.6–4.1 (1 H, m), 3.1–2.4 (2 H, m), 2.28 and 2.18 (6 H, s and s).

4-Hydroxy-3-hydroxymethyl-4-(2-pyridyl)-2-butanone, (Ic). 2-Pyridinecarbaldehyde (10.7 g, 0.10 mol), and 4-hydroxy-2-butanone (8.8 g, 0.10 mol) gave Ic (15.4 g, 79 %) by the method A; NMR spectrum: δ 8.43 (1 H, d), 7.9–7.0 (3 H, m), 5.20 and 5.07 (1 H, d 5.5 and 6.5), 4.7 (1 H, br s), 2.22 and 2.14 (3 H, s and s).

The aldols I were used without further purification.

Reactions of the aldols I

Ia with Ac₂O. The aldol Ia (22.2 g, 0.10 mol) and Ac₂O (150 ml) were boiled under reflux for 2 h. Most volatile materials (AcOH, the excess of Ac₂O, *N,N*-dimethylacetamide) were removed *in vacuo*, the temperature not exceeding 40°C. The black tar was chromatographed on silica. The following components could be identified, listed in order of elution: *2,3-Dimethyl-1-indolizinyll acetate, (IIe)*, (0.8 g, 4%), m.p. 111°C. (Found C 70.85; H 6.60; N 6.95. Calc. for C₁₅H₁₃NO₂: C 70.90; H 6.45; N 6.90). UV, λ_{\max} (nm) and log ϵ : 361 (2.96), 301 (3.07), 289 (3.10), 279 (3.05), 239 (4.49). IR, ν_{\max} (cm⁻¹): 1760, 1745. MS, *m/e* (%): 203 (40), 161 (100), 160 (98), 78 (74), 53 (17), 52 (11), 51 (17), 43 (13). *3,3'-Methylenebis-1-(2-indolizinyll)ethanone, (III)*, (0.3 g, 1%), m.p. 218°C. (Found C 76.35; H 5.30; N 8.55. Calc. for C₂₁H₁₈N₂O₂: C 76.35; H 5.50; N 8.50). UV, λ_{\max} (nm) and log ϵ : 394 sh (3.31), 377 (3.48), 363 (3.43), 350 sh (3.31), 311 (2.41), 302 (3.36), 267 sh (4.13), 247 (4.67), 243 (4.68). IR, ν_{\max} (cm⁻¹): 1645. MS, *m/e* (%): 330 (27), 288 (24), 287 (100), 245 (16), 243 (25), 43 (15). *3-Methyl-2-indolizinecarbaldehyde, (IIId)*, (1.4 g, 9%), m.p. 75°C. (Found C 75.35; H 5.55; N 8.75. Calc. for C₁₅H₉NO: C 75.45; H 5.70; N 8.80). UV, λ_{\max} and log ϵ : 399 sh (3.09), 381 (3.17), 365 (3.11), 310 (2.40), 267 sh (3.75), 251 (4.31), 246 (4.27). IR, ν_{\max} (cm⁻¹): 2780, 2720, 2700, 1670, 1655, 1645, 1625. MS, *m/e* (%): 159 (77), 158 (60), 130 (100), 78 (18), 77 (15), 29 (40). *1-(2-Indolizinyll)ethanone, (IIa)*, (3.2 g, 20%), m.p. 127°C. (Found C 75.45; H 5.70; N 8.80. Calc. for C₁₀H₉NO: C 75.45; H 5.70; N 8.80). UV, λ_{\max} (nm) and log ϵ : 397 sh (2.64), 382 sh (3.08), 365 (3.30), 351 sh (3.30), 340 sh (3.20), 311 (3.15), 299 (3.08), 275 (3.82), 266 (3.97), 245 (4.55). IR, ν_{\max} (cm⁻¹): 1645, 1630. MS, *m/e* (%): 159 (65), 144 (93), 116 (100), 89 (37), 63 (31), 62 (15), 51 (21), 50 (15), 43 (50), 39 (29), 38 (15). *1,1'-(2,3-Indolizinediyl)bisethanone, (IIc)*, (0.6 g, 3%), m.p. 65°C. (Found C 71.60; H 5.50; N 7.20. Calc. for C₁₂H₁₁NO₂: C 71.60; H 5.50; N 6.95). UV, λ_{\max} (nm) and log ϵ : 375 (3.89), 261 (4.11), 237 (4.36). IR, ν_{\max} (cm⁻¹): 1670, 1610. MS, *m/e* (%): 202 (14), 201 (93), 187 (20), 186 (100), 144 (14), 130 (42), 116 (16), 43 (14). *2-Pyridylmethyl acetate*, (0.8 g, 5%). *1,1'-(1,2-Indolizinediyl)bisethanone, (IIb)*, (4.8 g, 24%), m.p. 123°C. (Found C 71.60; H 5.75; N 6.80. Calc. for C₁₂H₁₁NO₂: C 71.60; H 5.50; N 6.95). UV, λ_{\max} (nm) and log ϵ : 381 sh (3.58), 366 (3.64), 354 sh (3.63), 313 (3.43), 304 (3.38), 260 (3.65). IR, ν_{\max} (cm⁻¹): 1660, 1635, 1615. MS, *m/e* (%): 201 (26), 186 (100), 130 (16), 89 (16), 43 (68).

Ib with Ac₂O. The aldol Ib (28.4 g, 0.10 mol) and Ac₂O (200 ml) gave analogously: *2-Methyl-3-phenyl-1-indolizinyll acetate, (IIj)*, (1.3 g, 5%), m.p. 42°C. (Found C 76.80; H 6.00; N 5.45. Calc. for C₁₇H₁₅NO₂: C 76.95; H 5.70; N 5.30). IR, ν_{\max} (cm⁻¹): 1765, 1740. *3-Phenyl-2-indolizinecarbaldehyde, (IIi)*, (1.8 g, 8%), m.p.

77°C. (Found C 81.60; H 5.25; N 6.05. Calc. for C₁₅H₁₁NO: C 81.45; H 5.00; N 6.35). UV, λ_{\max} (nm) and log ϵ : 382 (2.56), 324 (2.64), 269 sh (3.24), 251 (3.11). IR, ν_{\max} (cm⁻¹): 2820, 2790, 2730, 1660. MS, *m/e* (%): 221 (100), 220 (19), 192 (23), 191 (33). *2-Indolizinyllphenylmethanone, (IIf)*,¹⁰ (5.7 g, 26%), m.p. 95°C. (Found C 81.35; H 4.95; N 6.50. Calc. for C₁₅H₁₁NO: C 81.45; H 5.00; N 6.35). UV, λ_{\max} (nm) and log ϵ : 376 (3.01), 278 sh (4.38), 263 (4.55), 237 sh (4.05). IR, ν_{\max} (cm⁻¹): 1625, 1595. MS, *m/e* (%): 221 (100), 194 (44), 193 (17), 144 (49), 116 (30), 77 (17). *1-(2-Benzoyll-3-indolizinyll)ethanone, (IIh)*, (1.3 g, 5%), m.p. 81°C. (Found C 77.45; H 5.15; N 5.45. Calc. for C₁₇H₁₃NO₂: C 77.55; H 5.00; N 5.30). UV, λ_{\max} (nm) and log ϵ : 361 sh (3.78), 351 (3.80), 319 (3.71), 273 sh (4.04), 255 (4.22), 233 (4.13). IR, ν_{\max} (cm⁻¹): 1655, 1650, 1630, 1615. MS, *m/e* (%): 264 (15), 263 (100), 248 (89), 234 (19), 191 (21), 77 (45), 51 (20). *2-Pyridylmethyl acetate*, (0.8 g, 5%). *1-(2-Benzoyll-1-indolizinyll)ethanone, (IIg)*, (4.2 g, 16%), m.p. 114°C. (Found C 77.50; H 4.95; N 5.60. Calc. for C₁₇H₁₃NO₂: C 77.55; H 5.00; N 5.30). UV, λ_{\max} (nm) and log ϵ : 361sh (3.71), 352 (3.73), 320 (3.64), 274 sh (4.00), 255 (4.18), 232 (4.19). IR, ν_{\max} (cm⁻¹): 1650, 1630, 1610, 1590. MS, *m/e* (%): 263 (49), 249 (15), 248 (100), 191 (15), 77 (29).

Ic with Ac₂O. Similarly the aldol Ic (19.5 g, 0.10 mol) and Ac₂O gave: III (0.7 g, 2%) and IIa (6.7 g, 42%).

Ia or Ic with AcOH. The aldols Ia (22.2 g, 0.10 mol) or Ic (19.5 g, 0.10 mol) were refluxed with AcOH (100 ml) for 2 h. After evaporation the residue was put through a silica column and *2-methyl-1-(2-pyridyl)-1,3-butanedione, (IVa)*, (8.4 g, 47%), collected. Recrystallization from petroleum gave a white solid IVa, m.p. 35°C. (Found C 67.85; H 6.00; N 8.05. Calc. for C₁₀H₁₁NO₂: C 67.80; H 6.25; N 7.90). IR, ν_{\max} (cm⁻¹): 1720, 1695. NMR: δ 8.60 (1 H, br d 5), 8.1–7.6 (2 H, m), 7.6–7.3 (1 H, m), 4.82 (1 H, q 7), 2.28 (3 H, s), 1.35 (3 H, d 7). MS, *m/e* (%): 177 (2), 162 (3), 134 (54), 133 (24), 106 (40), 79 (73), 78 (100), 51 (25), 43 (55).

Vb with Ac₂O. The aldol Ia (22.2 g, 0.10 mol) was treated with Ac₂O (51 g, 0.5 mol) at 20°C. After 1 h the mixture was neutralized with NaHCO₃, the precipitated oil extracted with ether and dried over Na₂SO₄. The residue (14.1 g, 69%) consisted of rather pure *3-dimethylaminomethyl-4-(2-pyridyl)-3-buten-2-one, (Vb)*. UV, λ_{\max} (nm) and log ϵ : 286 (4.11), 253 (4.09). IR, ν_{\max} (cm⁻¹): 1690–1650, 1615. NMR: δ 8.55 (1 H, br d 5), 7.65 (2 H, m), 7.34 (1 H, s), 7.3–6.9 (1 H, m), 3.69 (2 H, s), 2.32 (3 H, s), 2.12 (6 H, s). The unsaturated pyridylamino-ketone, Vb (20.4 g, 0.10 mol) without further purification was boiled with Ac₂O (150 ml) for 2 h giving the same products as Ia with Ac₂O: IIe (0.6 g, 3%), III (0.15 g, 0.5%), IIId (1.75 g, 11%), IIa (2.9 g, 18%), IIc (1.0 g, 5%), 2-pyridylmethyl acetate (0.8 g, 5%), IIb (5.4 g, 27%).

Vb with AcOH. The unsaturated pyridyl-aminoketone Vb (20.4 g, 0.10 mol) and AcOH (100 ml) were kept overnight at 60 °C yielding only III and IIa.

IVa with Ac₂O. The pyridinediketone IVa (17.7 g, 0.10 mol) and Ac₂O (150 ml) were refluxed for 1 h. After evaporation *in vacuo* the residue was purified by column chromatography giving *1-acetoxy-3-methyl-2-indolizinylmethyl acetate*, (IIk), (12.3 g, 47 %), m.p. 96 °C. (Found C 64.05; H 5.80; N 5.45. Calc. for C₁₄H₁₅NO₄: C 64.35; H 5.80; N 5.35). UV, λ_{\max} (nm) and log ϵ : 360 (3.06), 300 (3.21), 288 (3.17), 279 (3.06), 237 (4.39). IR, ν_{\max} (cm⁻¹): 1775, 1755, 1720. MS, *m/e* (%): 261 (10), 160 (21), 159 (100), 158 (23), 130 (15), 78 (23), 43 (15). Similar amounts of IVa and Ac₂O together with AcOK (50 g, 0.5 mol) yielded IIk (11.7 g, 45 %) and *1-(1-acetoxy-2-methyl-3-indolizinylo)ethanone*, (III), (1.8 g, 7), m.p. 75 °C. (Found C 67.35; H 5.85; N 6.00. Calc. for C₁₃H₁₃NO₃: C 67.50; H 5.65; N 6.05). UV, λ_{\max} (nm) and log ϵ : 365 (4.10), 297 (3.22), 269 (3.32), 263 sh (4.28), 226 (4.33). IR, ν_{\max} (cm⁻¹): 1750, 1735, 1600. MS, *m/e* (%): 231 (24), 189 (100), 188 (36), 174 (36), 159 (23), 146 (15), 105 (15), 78 (48), 43 (15).

IX with Ac₂O. 2-Pyridinecarbaldehyde (10.7 g, 0.10 mol), 2-butanone (14.4 g, 0.20 mol), K₂CO₃ (1.4 g, 0.1 mol) and 100 ml of water were stirred at 10 °C for 12 h. The precipitated oil was extracted with ether and dried over Na₂SO₄. Evaporation delivered a mixture (12.1 g) consisting mainly of *4-hydroxy-3-methyl-4-(2-pyridyl)-2-butanone*, (IX) and *1-(2-pyridyl)-1-penten-3-one* (XII) (NMR). The treatment of this mixture with Ac₂O gave after evaporation and chromatography IIe (12.3 g, 11 %, based on 2-pyridinecarbaldehyde) and XII, m.p. 13 °C. NMR: δ 8.56 (1 h, br d 5), 7.8–7.0 (3 H, m), 7.34 (1 H, d 15.7), 7.14 (1 H, d 15.7), 2.62 (2 H, q 7.5), 1.08 (3 H, t 7.5).

Acknowledgements. The author thanks Professor J. Gripenberg for his valuable comments and The Finnish Academy for a research grant.

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Received March 26, 1975.