Nitrogen Bridgehead Compounds. Part 6.[1] Ring Transformation. Part 3.[2] Thermal Cyclization of Diethyl 2-(2-Pyridylaminomethylene)-succinates and -glutarates

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The pyridylsuccinates (1) and pyridylglutarates (2), with various substituents on the pyridine ring, were cyclized in Dowtherm A at 250 °C. The succinates cyclized in two competing reaction routes, giving rise to pyrido[1,2-*a*]-pyrimidines (route A) and *N*-pyridylpyrrolinones (route B). The ratio of the two products varied with the nature of the substituent and its position. The *N*-pyridylpyrrolinones proved to be mixtures of the desmotropes (5) and (6) which were separated. The pyridylglutarates (2) gave only the pyrido[1,2-*a*]pyrimidines (4). The 6-substituted pyrido[1,2-*a*]pyrimidines underwent a ring-transformation reaction at or above 250 °C, forming the corresponding 1,8-naphthyridines (8) and (9).

We have previously reported [1] the cyclization of the succinates (1) and glutarates (2) in phosphoryl chloride–polyphosphoric acid at 120 °C. The succinates (1) formed cyclic products *via* ring closure onto the pyridine-nitrogen (route A) or onto the amino-nitrogen (route B), yielding the pyridopyrimidines (3) and the pyridylpyrrolinones (5) in competing reactions. The reaction conditions strongly favoured the formation of the pyridopyrimidines (yield 65—85%) over the pyridylpyrrolinones (yield 3—4%). A 6-Me substituent in the pyridine ring sterically hindered the ring closure onto the adjacent pyridine-nitrogen, rendering routes A and B roughly equivalent, while a 3-Me or 3-OH substituent hindered the ring closure onto the nearby amino-nitrogen, thus blocking route B. The glutarates (2) gave rise to only the pyridopyrimidines (4).

We have now carried out the cyclization of the above succinates (1) and glutarates (2) in Dowtherm A, at 250 °C. In addition to the cyclic products from routes A, B, and C (see Scheme 1), the 1,8-naphthyridines (8) and (9) could also be expected as products, as they were shown [2,3] to arise by heating the 6-substituted pyridopyrimidines.

RESULTS AND DISCUSSION

E—Z *Isomerization of the Starting Succinates* (1) *and Glutarates* (2).—The cyclic products in Scheme 1 can be derived from either the *E* or *Z* geometric isomer of the starting material. Under the $POCl_3$–PPA reaction conditions we found the isomerization to proceed much faster than the ring-closure reaction.

We investigated the thermal isomerization of some of the succinates (1a—f) and the glutarate (2e). The *E*-isomers, in 10% Dowtherm A solutions, were heated at various temperatures and the equilibration was followed by ^1H n.m.r. spectroscopy. The isomeric ratio of the succinates was determined on the basis of the $=C-CH_2-CO$ methylene singlet which appeared in Dowtherm A solution at δ 3.6 for the *E*-isomers, and δ 3.2 for the *Z*-isomers. The isomeric ratio of the glutarate was determined with the help of the $[CH_2]_2$ and NH signals. The former appeared as singlet at δ 2.56 for the *E* and δ 2.53 for the *Z*-isomer. The NH signal appeared as a doublet at δ 10.38 for the *Z*-isomer, while that of the *E*-isomer was covered by the solvent peak. Depending on the substituent, the equilibrium mixtures consisted of 18—25% *E*-isomer and 82—75% *Z*-isomer for the succinates, and of 65% *Z*- and 35% *E*-isomer for the glutarate. The time required for the equilibration decreased rapidly with increasing temperature. The *E*-isomers investigated attained equilibrium within 23 h at 115 °C, 7 h at 128 °C, 1 h at 143 °C, 10 min at 170 °C and 5 min at 200 °C. Thus, at 250 °C (the temperature at which ring-closure occurs) we expected fast isomerization and the presence of isomeric mixtures; this means that the same cyclic products should result whether the *E*- or *Z*-isomer of the succinate or glutarate is the starting

TABLE 1

Thermal cyclization of the succinates (1) and glutarates (2)

Starting material	Products (yield %) Pyrido-pyrimidine [(3) or (4)]	Naphthyr-idine [(8) or (9)]	Pyridyl-pyrrolinone [(5) or (6)]
(1a)	54		28 [a]
(1b)	65		
(1c)	21		62 [a]
(1d)	50		32 [a]
(1e)	44		36 [a]
(1f)	12		70 [a]
(1g)	74		8 [b]
(1h)	57		22 [b]
(1i)	44		21 [c]
(1j)	70		
(1k)	28		
(1l)	66		
(1m)	7	6	57 [a]
(1n)	47		22 [a]
(1p)	66		6 [c]
(2a)	82		
(2e)	80		
(2m)	50	22	

M.p.s (°C) (for those not listed here see previous paper [1]); (5a) [a] 145—148; (5c) [a] 155—158; (5d) [a] 102—105; (5e) [a] 101—108; (5f) [a] 121—123; (5g) [b] 124—125; (3h) 298—302; (5h) [b] 153—155; (5i) [c] 132—134; (3m) 125—126; (5m) [a] 145—148; (8m) 280; (3n) 238—240; (5n) [a] 207—214; (5p) [c] 102—110; (4m) 133—135; (9m) 263—265.

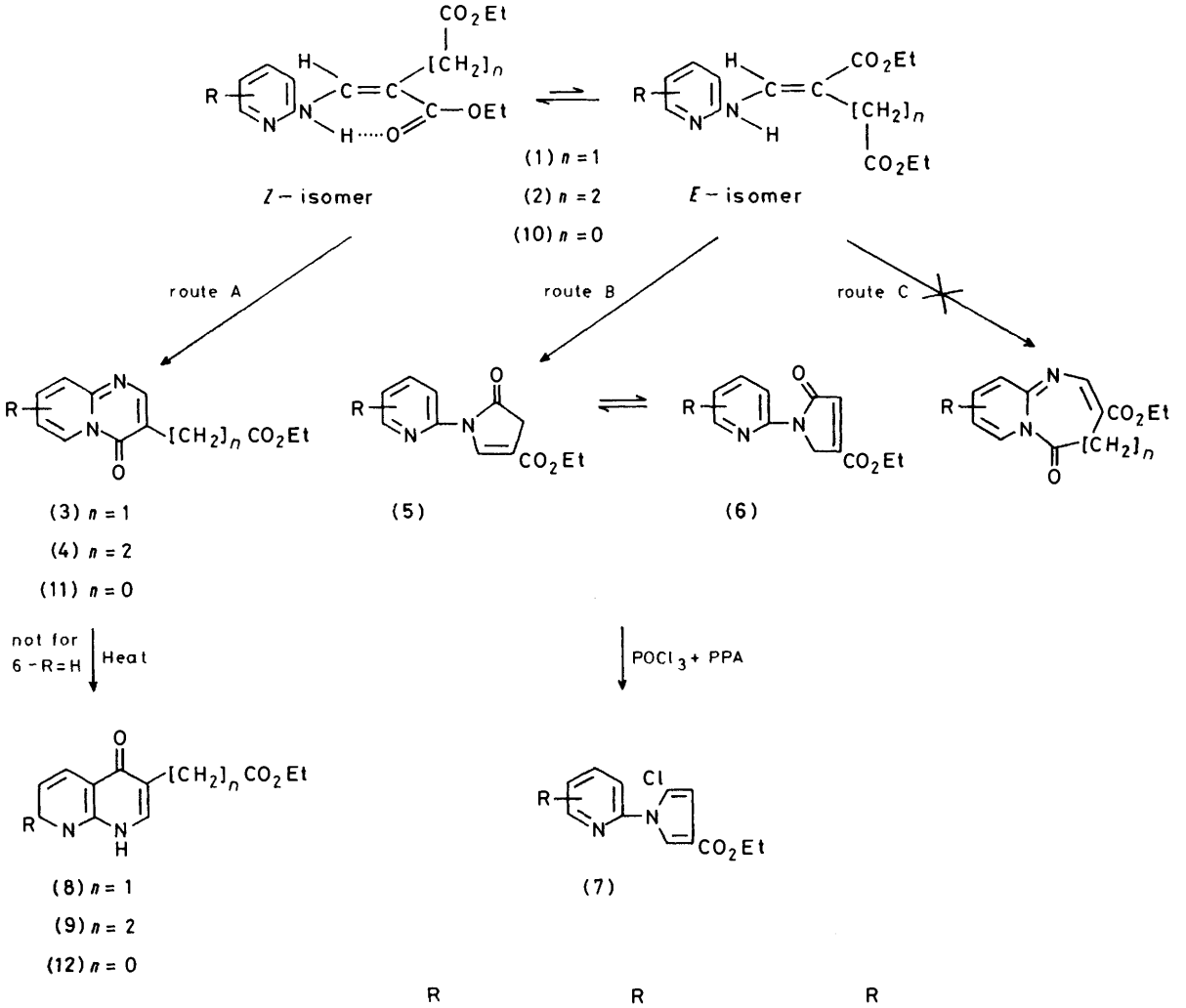
[a] (5) containing <10% (6).
[b] (5) containing 40–45% (6).
[c] (5) containing 25–30% (6).

material. This was proved by performing reactions starting from pure (*E*)-(1e) or (*Z*)-(1e), and obtaining the same products in the same yields, or starting from the *E*-isomer of (2a, e), and obtaining (5a, e), which are the products derived from the *Z*-isomer.

Cyclization in Dowtherm A.—The reaction was performed by heating (1) or (2) in refluxing Dowtherm A for 30 min. Cyclic products were formed in good yield [except for (1k) which reacted slowly with tar formation]. Products from route C were never observed. The results are presented in Table 1.

Most of the succinates (1) formed cyclic products *via* both routes A and B. The ratio of the pyridopyrimidines (3) and the pyridylpyrrolinones (5) indicates that thermal ring-closure, in general, favours route A over route B; not as strongly, however, as was found for the $POCl_3$–PPA ring-closure. For (1c, f, and m) the pyridylpyrrolinone was the main product.

The steric effect of the substituents in the 3- and 6-positions of the succinates is not as marked in the thermal ring-closure as was found for the $POCl_3$–PPA ring-closure. For instance in the thermal ring-closure a 3-OH group hindered, but did not completely inhibit, the formation of the pyridylpyrrolinone; and a 6-Me group, which in the $POCl_3$–PPA ring closure had a very pronounced hindering effect on route A, has only very little, if any, effect under the conditions of thermal ring-closure [*cf.* the ratio of products obtained from (1e; R = 6-Me) with that of (1a; R = H) or (1d; R = 5-Me), in Table 1].



R	R	R
a ; H	f ; 4,6 - Me_2	k ; 3 - NO_2
b ; 3 - Me	g ; 3 - OH	l ; 5 - NO_2
c ; 4 - Me	h ; 6 - OH	m ; 6 - NHAc
d ; 5 - Me	i ; 5 - Cl	n ; 5 - $CONH_2$
e ; 6 - Me	j ; 3,5 - Cl_2	p ; 5,6 - $(CH{=}CH)_2$

SCHEME 1

TABLE 2

Ring transformation of the 6-substituted pyrido[1,2-*a*]pyrimidines into 1,8-naphthyridines

	Dowtherm A (250 °C, 0.5 h)		Liquid paraffin (300 °C, 0.5 h)		Liquid paraffin (350 °C, 5 min)	
Starting material	% Yield of (8) or (9)	Recovered (3) or (4)	% Yield of (8) or (9)	Recovered (3) or (4)	% Yield of (8) or (9)	Recovered (3) or (4)
(3e)	0	80	25	50	65	0
(3f)	0	78	Decomposition			
(3h)	0	75	0	70	Decomposition	
(3m)	50	16	Decomposition			
(3p)	0	78	Decomposition			
(4e)	0	85	85	0		
(4m)	30	60	80	0		

The glutarates cyclized only *via* route A and gave rise, in good yield, to the pyridopyrimidines (4).

The 1,8-naphthyridines were also formed but only in the reaction of (1m) and (2m), where R = 6-NHAc (see later).

Ring Transformation of the 6-Substituted Pyrido[1,2-a-]*pyrimidines.*—The ring transformation of the 6-substituted pyridopyrimidines was studied by heating (3e, f, h, m, p) and (4e, m) at 250, 300 and 350 °C. Results are shown in Table 2. The reactivity of the pyridopyrimidines towards the ring transformation depended on the 6-substituent, and increased in the order OH < Me < NHAc, which is in accord with our earlier observation.[2]

Lappin [4] studied the cyclization of variously substituted pyridylmalonates (10) in Dowtherm A at 250 °C, and found that the malonates which contained the substituent in the 6-position of the pyridine ring gave rise to 1,8-naphthyridines (12), while the other substituted or unsubstituted pyridylmalonates yielded the pyridopyrimidines (11) (Scheme 1). He assumed that both (11), and (12) were formed directly from (10), and the reason why the 1,8-naphthyridines and not the pyridopyrimidines were formed was the presence of the 6-substituent, which sterically hindered the ring closure onto the pyridine-nitrogen.

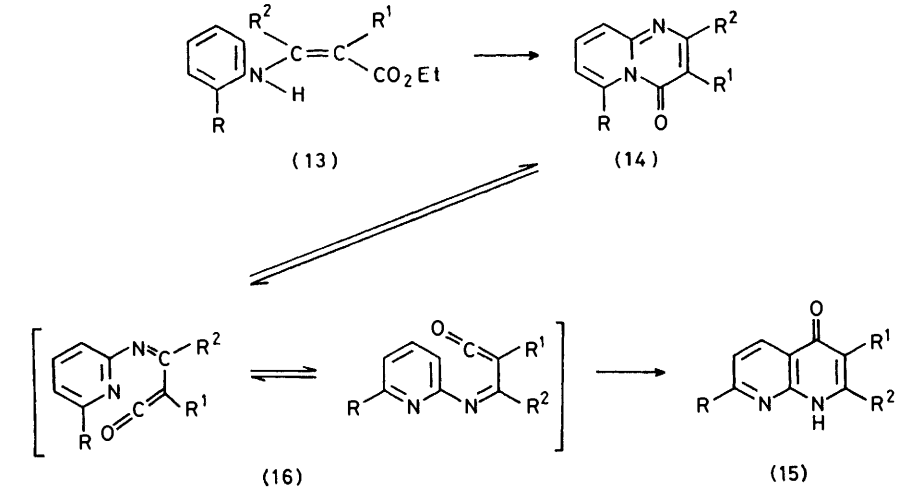
Later Hermecz and his co-workers proved [2,3] that the 1,8-naphthyridines (15) are not formed from (13) directly, but that ring-closure always takes place onto the pyridine nitrogen, and the resulting pyridopyrimidine (14) may transform into the thermodynamically more stable 1,8-naphthyridine (15) (Scheme 2).

The ring-closure of the succinates (1) represents an interesting example to support the above theory. The succinates (compared to the malonates) have an additional centre for the cyclization, *i.e.* the amino-nitrogen (route B).

In $POCl_3$–PPA, at 120 °C, the presence of a methyl group in 6-position of the succinates caused [1] a very significant fall in the yield of the pyridopyrimidines, in favour of the pyridylpyrrolinones. [(1a; R = H), (1c; R = 4-Me) and (1d; R = 5-Me) formed >80% pyridopyrimidine compared to 4% pyridylpyrrolinone, while (1e and f; R = 6-Me) formed the two products in 40% yield each.] This was explained in terms of the steric effect of the 6-Me group, causing *F*-strain, when the new bond is formed with the neighbouring pyridine nitrogen.

Such an effect (the 6-Me group hindering pyridopyrimidine formation) was not observed when we carried out ring-closure in Dowtherm A at 250 °C. (Lappin used similar conditions for his experiments.)

In the ring-transformation reaction of the pyridopyrimidines however the 6-Me group, because of its steric effect, was found to play an important role. As the pyridopyrimidine ring is nearly planar,[5] the 6-methyl and 4-oxo-groups are near each other. The strain caused by their steric interaction is relieved when the N–C bond



SCHEME 2

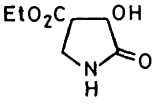
cleaves. Thus the 6-Me group, by causing *B*-strain in the molecule, sterically assists the ring transformation of the pyridopyrimidines.

We presume that the ring transformation takes place *via* a reactive keten intermediate (16). The proposed mechanism is outlined in Scheme 2.

Earlier [2] we also investigated the role of the R^1 substituent in the ring-transformation reaction of the pyridopyrimidines (14). The series can now be completed with two more substituents, $R^1 = CH_2CO_2Et$ (3), and $R^1 = [CH_2]_2CO_2Et$ (4), which proved to have a similar effect on the ring-transformation reaction as a methyl group.[2]

Prototropic Tautomerism of the Pyridylpyrrolinones.— The pyridylpyrrolinones obtained in the thermal ring-closure gave elementary analysis results supporting the formula, and they seemed to be pure on t.l.c. However, they did not have sharp m.p.s and their ^1H n.m.r. spectra indicated the presence of characteristic contamination. By repeated crystallization, the pyridylpyrrolinone resulting from the ring-closure of (1e) was separated into two pure components, with m.p.s 101—103 °C and 132—134 °C respectively. The ^1H n.m.r. spectra of the separated components suggested that they are double-bond isomers, the spectra differing mainly in the chemical shifts of the pyrrolinone ring protons.

The position of the double bond in pyrrolinones has been the subject of a number of studies.[6,7] For the parent compound, pyrrolin-2-one, the Δ^3 structure (18) was predicted [8] and found [9-11] to be energetically favourable. Alkyl-substituted pyrrolin-2-ones were also stable in the Δ^3-form, in contrast to pyrrolin-2-ones, bearing an ethoxycarbonyl group, or other electron-withdrawing substituent, in the 4-position, which were stable in the Δ^4-form.[12] Interchange and equilibrium between the tautomeric forms of pyrrolin-2-ones was also investigated. The Δ^4-pyrrolin-2-one (17) easily equilibrated with the more stable Δ^3-isomer (18), in the presence of acid or base. In some solvents the existence of a small



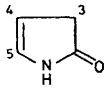
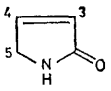
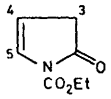
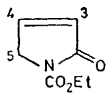
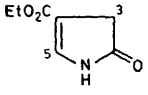
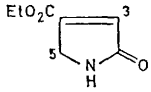
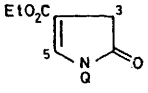
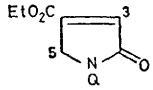
(23)

amount of the enol form has also been postulated.[10] The *N*-ethoxycarbonyl-Δ^4-pyrrolin-2-one (19) thermally isomerized rapidly to the Δ^3-isomer (20).[9] The 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one (21), however, failed to give any Δ^3-isomer (22) when treated with acid or base, and (22) could not be prepared by the dehydration of (23), the reaction leading to the Δ^4-isomer (21) only,[9] which was explained in terms of the instability of the Δ^3-isomer, if an electron-withdrawing substituent was present. The ^1H n.m.r. characteristics of the Δ^3- and Δ^4-pyrrolinones were studied in detail [9-11,13] and marked differences were found in the spectra of the isomers.

On the basis of the accumulated spectroscopic data we assigned the Δ^4-pyrroline-structure (5e) to the desmotrope melting at 103—105 °C, and the Δ^3-structure (6e) to the one melting at 132—134 °C (Table 3). The u.v. spectrum of the desmotropes differed remarkably too, as shown in Table 4. According to the ^1H n.m.r. spectra all the pyridylpyrrolinones were mixtures of the Δ^3- and Δ^4-isomers, the latter being the major product. On the basis of the CH_2 signals, the Δ^3-isomer content of the mixtures was estimated as <10% (6a, c, d, e, f, m, n); 25—30% (6i, p); and 40—45% (6g, h). The Δ^3-isomer (6) must have been formed from (5), by

TABLE 3

^1H N.m.r. data of some pyrrolin-2-ones (δ in p.p.m., J in Hz)

	Δ^4-Isomer	3-H_2	4-H	5-H	$^4J_{3,5}$	Δ^3-Isomer	5-H_2	3-H	4-H	$^4J_{3,5}$	Solvent	Ref.
(17)		3.2				(18)		4.2				*a*	9
		3.12	5.46	6.56	2.3			4.17	6.16	7.44	1.9	*a*	10
		2.99	5.30	6.51	2.2			4.08	6.11	7.33	1.9	*b*	10
		2.91	5.19	6.59	2.23			4.07	6.10	7.30	1.95	*c*	13
(19)		3.1	5.3	6.9		(20)		4.2	6.1	7.2		*d*	9
(21)		3.4		7.5		(22)						*d*	9
(5e)		3.57		8.62	1.9	(6e)		4.8	6.88		1.9	*d*	

Q = 6-methyl-2-pyridyl (m.p. 101-103°C)

Q = 6-methyl-2-pyridyl (m.p. 132-134°C)

[a] D_2O. [b] CD_3OD. [c] $(CD_3)_2CO$. [d] $CDCl_3$.

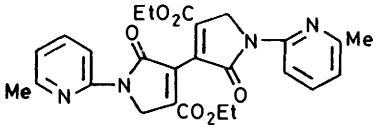
secondary isomerization, under the reaction conditions of the thermal ring-closure. Further isomerization could take place during the separation process, when the products were treated with acid, although the ratio of (5) to (6) did not change significantly during this process. A slow isomerization of the Δ^4-isomer (5) into the Δ^3-isomer (6) was, however, observed in acidic media ($CDCl_3$–CF_3COOH) in contrast to results for (21).[9] We have not yet studied the isomerization and equilibrium between (5) and (6) and, apart from the separation of (5e) and (6e), we did not separate the desmotropes.

TABLE 4

I.r. and u.v. characteristics of the isomeric cyclic compounds

	$\nu_{C=O}/cm^{-1}$	$\lambda_{max.}$(log ε)/nm
(3e)	1 730, 1 680	360 (3.99), 248 (3.99)
(8e)	1 738, 1 615	333 (3.90), 286 (3.40), 276 (3.46), 247 (4.23)
(5e)	1 732, 1 710	294 (4.15), 249 (4.07)
(6e)	1 730, 1 700	305 (3.88), 229 (4.16)

In addition to (5e) and (6e) a pyridylpyrrolinone dimer (24e) was also separated, in low yield, from the



(24e)

cyclization reaction mixture of (1e). The dimer structure was suggested by mass-spectrometry (M^+ 490, $C_{26}H_{26}N_4O_6$). The Δ^3-structure is supported by ^1H n.m.r.; δ(CH_2) 5.02 ($CDCl_3$). Compound (24e) must have been formed by the oxidative dimerization of (6e) under the conditions of the Dowtherm A ring-closure.

We have shown [14] for (5), based on spectral data and quantum-chemical calculations, that the pyridylpyrrolinone molecule is planar, and the oxo-group of the pyrrolinone ring is located as far as possible from the nitrogen atom of the pyridine ring. *X*-Ray analysis [15] gave similar results.

EXPERIMENTAL

I.r. spectra were measured for KBr pellets with a Zeiss UR-20 spectrometer, u.v. spectra for ethanolic solutions with a Unicam SP 800 spectrometer, and n.m.r. spectra with a Perkin-Elmer R 12 spectrometer ($SiMe_4$ as internal standard, $CDCl_3$ solution). Analyses for the products agreed with calculated figures; details of these are given in Supplementary Publication No. SUP 22633 (2 pp.).*

Cyclization in Dowtherm A.—To Dowtherm A (300 ml) (1) or (2) (0.1 mol) was added at 230 °C. The solution was stirred at 250 °C for 30 min, while the ethanol distilled out, then it was cooled to room temperature. The products were separated by one of the methods (*A*)—(*F*) below, and they were purified by crystallization from ethanol or from the solvent given. Each pyridylpyrrolinone (5), obtained in this way, contained a variable amount of (6), as shown in Table 3.

(*A*) The reaction mixtures of (1a—f, i, p) and (2a, e) were diluted with benzene (600 ml), and extracted with 5% hydrochloric acid solution (3 × 100 ml). The separated aqueous layer was neutralized with $NaHCO_3$ and extracted with chloroform. The chloroform extract was dried and evaporated, to obtain the pyrido[1,2-*a*]pyrimidines (3a—e, i, p) and (4a, e).

Compound (3e), 3-(ethoxycarbonylmethyl)-6-methyl-4-oxopyrido[1,2-*a*]pyrimidine; δ 1.30 (3 H, t, Me), 3.07 (3 H, s, 6-Me), 3.60 (2 H, s, CH_2CO), 4.26 (2 H, q, OCH_2), 6.63—6.88 (1 H, m, 7-H), 7.40—7.58 (2 H, m, 8-H and 9-H), and 8.19 (1 H, s, 2-H); see also Table 4.

Compound (4e), 3-(2-ethoxycarbonylethyl)-6-methyl-4-oxopyrido[1,2-*a*]pyrimidine: $\nu_{max.}$ 1 730 and 1 680 cm^{-1}; $\lambda_{max.}$ 360 (log ε 4.00) and 248 nm (4.02); δ 1.26 (3 H, t, Me), 2.50—3.00 (4 H, m, $[CH_2]_2CO$), 3.08 (3 H, s, 6-Me), 4.18 (2 H, q, OCH_2), 6.58—6.80 (1 H, m, 7-H), 7.34—7.52 (2 H, m, 8-H and 9-H), and 8.10 (1 H, s, 2-H).

The pyridylpyrrolinones (5a, c—f, i, p) were extracted from the Dowtherm A–benzene layer with 20% hydrochloric acid (3 × 50 ml). The aqueous layer was then treated as described above. The pyridylpyrrolinones were purified by crystallization or by column chromatography on silica gel (0.063—0.125 mm mesh) (eluant benzene).

(*B*) The reaction mixtures of (1g, j—l) were diluted with light petroleum (b.p. 60 °C) (600 ml) to precipitate the pyridopyrimidines (3g, j—l), which were then crystallized; (3k) was a tarry precipitate, which was dissolved in refluxing ethanol, the insoluble tar filtered off, and the filtrate evaporated to give pure (3k). The pyridylpyrrolinone (5g) was obtained from the Dowtherm A–light petroleum filtrate by extraction with 5% hydrochloric acid, and treating the aqueous layer as described under (*A*).

(*C*) From the cooled reaction mixture of (1h), compound (3h) precipitated and was filtered off and crystallized from dioxan. On diluting the filtrate with light petroleum (600 ml), the pyridylpyrrolinone (5h) precipitated.

(*D*) From the reaction mixture of (1m) the naphthyridine (8m) crystallized and was filtered off. The filtrate was diluted with light petroleum (500 ml), to precipitate the pyridylpyrrolinone (5m). The pyridipyrimidine (3m) was extracted from the Dowtherm A–light petroleum filtrate with 5% hydrochloric acid solution, and the aqueous layer was treated as described under (*A*).

(*E*) From the reaction mixture of (1n) both (3n) and (5n) crystallized. The crystals were collected, and dissolved in boiling chloroform. The insoluble (3n) was filtered off, the filtrate was evaporated, and the residue was dissolved in benzene. A second crop of the insoluble (3n) was filtered off. The filtrate was evaporated to give (5n). Compound (3n) was crystallized from methanol.

(*F*) From the reaction mixture of (2m) the naphthyridine (9m) precipitated. The filtrate was diluted with light petroleum (600 ml), and extracted with 5% hydrochloric acid. The aqueous layer was treated as described under (*A*) to obtain (4m).

Separation of the Pyridylpyrrolinone Desmotropes (5e) *and* (6e) *and the Dimer* (24e).—The pyridylpyrrolinone (6 g), obtained from (1e) as described under (*A*), was heated in refluxing light petroleum (b.p.: 100—120 °C) for 30 min. The insoluble crystals (0.8 g) were filtered off, and heated in refluxing 96% ethanol (4 ml). From the hot mixture the insoluble crystals (0.19 g) were filtered off and washed with

* For details see Notice to Authors No. 7, *J.C.S. Perkin* I, 1978, Index issue.

ethanol; (24e), 4,4′-bi[ethyl 1-(6-methyl-2-pyridyl)-5-oxo-3-pyrroline-3-carboxylate], m.p. 205—206 °C; $\nu_{max.}$ 1 725 and 1 703 cm^{-1}; $\lambda_{max.}$ 314 (log ε 4.04), 281 (4.14), and 225 nm 4.45; δ 1.3 (6 H, t, 2 × Me), 2.58 (6 H, s, 2 × 6-Me), 4.35 (4 H, q, 2 × OCH_2), 5.02 (4 H, s, 2- and 2′-CH_2), 7.01 (2 H, d, 2 × 5-H), 7.7 (2 H, t, 2 × 4-H), and 8.31 (2 H, d, 2 × 3-H).

The light petroleum filtrate was evaporated, and the residue was crystallized four times from ethanol, to obtain pure (6e) (0.2 g); ethyl 1-(6-methyl-2-pyridyl)-5-oxo-3-pyrroline-3-carboxylate, m.p. 132—134 °C; δ 1.40 (3 H, t, Me), 2.50 (3 H, s, 6-Me), 4.39 (2 H, q, OCH_2), 6.39 (1 H, d, 5-H), 7.64 (1 H, m, 4-H), and 8.28 (1 H, d, 3-H); see also Tables 3 and 4. Evaporation of the filtrate of the first crystallization gave pure (5e) (3.0 g); ethyl 1-(6-methyl-2-pyridyl)-5-oxo-2-pyrroline-3-carboxylate, m.p. 101—103 °C; δ 1.35 (3 H, t, Me), 2.52 (3 H, s, 6-Me), 4.33 (2 H, q, OCH_2), 7.09 (1 H, d, 5-H), 7.72 (1 H, m, 4-H), and 8.05 (1 H, d, 3-H); see also Tables 3 and 4.

Ring Transformation of the Pyrido[1,2-a]*pyrimidines.*—(a) *In Dowtherm A.* The 6-substituted (3) or (4) (1 g) was added to hot Dowtherm A (50 ml), and heated at 250 °C for 30 min. On cooling the mixture the naphthyridine (8) or (9) precipitated. The unchanged pyridopyrimidine was recovered by the methods outlined above.

(b) *In liquid paraffin.* Compound (1) or (2) was added to liquid paraffin at 300 and 350 °C, and heated at this temperature for 30 and 5 min, respectively. After cooling the naphthyridine was filtered off.

Compound (8e), 3-(ethoxycarbonylmethyl)-7-methyl-1,8-naphthyridin-4(1*H*)-one, m.p. 212; δ 1.25 (3 H, t, Me), 2.60 (3 H, s, 7-Me), 3.53 (2 H, s, CH_2CO), 4.16 (2 H, q, OCH_2), 7.12 (1 H, d, 6-H), 7.78 (1 H, m, 2-H), 8.56 (1 H, d, 5-H), and 10.4 (1 H, br, NH); see also Table 4.

Compound (9e), 3-(2-ethoxycarbonylethyl)-7-methyl-1,8-naphthyridin-4(1*H*)-one, m.p. 192 °C; $\nu_{max.}$ 1 730, 1 620, and 3 160 cm^{-1}; $\lambda_{max.}$ 335 (log ε 3.91), 274 (3.32), and (4.27) 247 nm; δ 1.22 (3 H, t, Me), 2.71 (3 H, s, 7-Me), 2.50—3.10 (4 H, m, 3-$[CH_2]_2$), 4.15 (2 H, q, OCH_2), 7.18 (1 H, d, 6-H), 7.95 (1 H, m, 2-H), 8.73 (2 H, d, 5-H), and 11.70 (1 H, br, NH).

We thank Miss Anikó Pajor for the preparative work.

[8/2022 *Received*, 20*th November*, 1978]

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