Preparation of Compounds in the New Dipyrrolo[3,4-*b*:3′,4′-*e*]-Pyridine Series from 1-Benzylidene-2,3-dioxopyrrolidines. A Variation of the Hantzsch Synthesis.

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Treatment of easily prepared 1-substituted-4-benzylidene-2,3-dioxopyrrolidines with ammonium formate produces 1,2,4,6,7,8-hexahydro-2,6-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-diones (II), usually in yields of 50 to 60%. Aromatization of the dihydropyridine ring of the hexahydro derivatives II yields corresponding 1,2,6,7-tetrahydro-2,6-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-diones (III). These compounds appear to be the first to incorporate the dipyrrolo[3,4-*b*:3′,4′-*e*]pyridine ring system.

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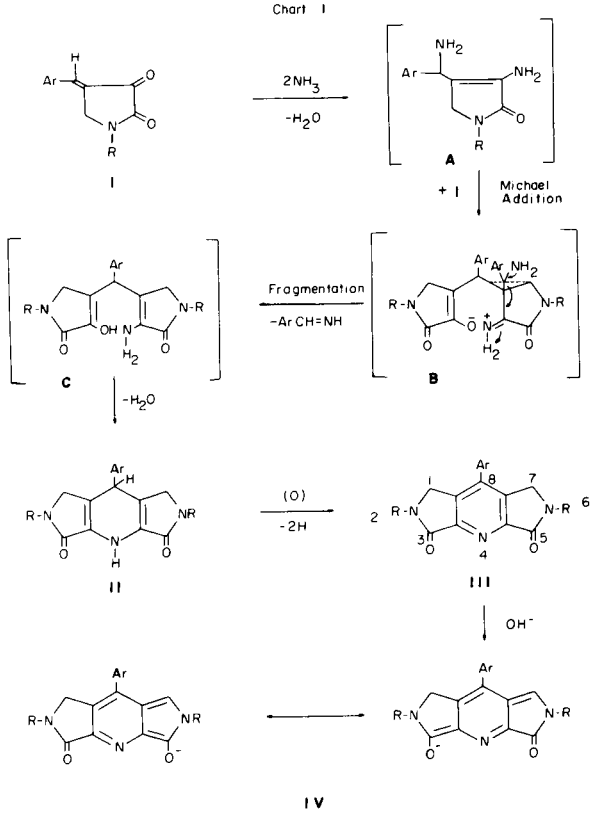
Apparently compounds containing the dipyrrolo[3,4-*b*:-3′,4′-*e*]pyridine ring system have not been described previously. We have found that one group of such compounds can be produced when 1-substituted-4-benzylidene-2,3-dioxopyrrolidines (I) (1) are treated with ammonium formate in refluxing ethanol. The products obtained from the reaction have been assigned structure II (Chart I) corresponding to a set of 2,6-disubstituted-1,2,4,6,7,8-hexahydro-8-phenyldipyrrolo[3,4-*b*:3′,4′,-*e*]-pyridine-3,5-diones on the basis of nuclear magnetic resonance, infrared and ultraviolet spectra. Chart I shows a possible sequence of intermediate steps for the reaction.

Chart I



Structure II, because of its symmetry, seemed to provide the only reasonable explanation for the simplicity of the observed nmr spectra. The distinguishing features of these spectra were a singlet of area 1 at *ca.* δ, 4.80 assigned to the proton at position 8, and a pair of doublets of the AB type (area 4; signals at 208, 230, 234, and 256 Hz downfield from TMS in IIa; J_{AB} 22 Hz) assigned to the geminal methylene protons at positions 1 and 7. The members of the geminal pairs are rendered nonequivalent by their *cis* or *trans* configuration relative to the phenyl at position 8 (2). All other signals were assignable to substituent R groups or the aryl group at C-8.

The infrared spectra of these compounds showed bands consistent with NH, lactam carbonyl and olefinic functions. The only aspect of the infrared data not in obvious accord with structure II was the presence of two bands rather than one in the carbonyl range (at *ca.* 5.9 and 6.0 μ). Hydrogen bonding between one lactam carbonyl group and the dihydropyridine NH probably accounts for this observation, since aromatization of the pyridine ring produced products with only one carbonyl band.

It was found that the dihydropyridine ring could be aromatized easily to yield products considered to be 1,2,6,7-tetrahydro-2,6-disubstituted-8-aryldipyrrolo[3,-4-*b*:3′,4′-*e*]pyridine-3,5-diones (III). Aromatization occured when the hexahydro derivatives (II) were refluxed in dimethylformamide for about 48 hours without precautions for the exclusion of air. The conversion could be conducted more rapidly by treatment with bromine and sodium acetate in acetic acid solution. The analytical, nmr and infrared data were entirely consistent with the assignment of structure III to the products. Aside from signals assignable to the substituents R or the aryl groups, only a 4-proton singlet at *ca.* δ 4.75 arising from the methylene protons at positions 1 and 7 was seen in the nmr spectra. Infrared spectra showed the expected lactam carbonyl absorption at *ca*, 5.8-5.9 μ and an aromatic ring absorption at *ca.* 6.2-6.29 μ.

There was some evidence suggesting anion formation when compounds of type III were dissolved in strongly basic solution. Concentrated alcoholic solutions of the dibenzyl derivative containing potassium hydroxide showed a deep purple color which was discharged upon

neutralization. Moreover, as evidenced by the data in Table 4, some changes in the ultraviolet spectra of the type III compounds were observed when comparisons were made between spectra determined in basic and neutral solutions. As indicated in Chart I, delocalization of the negative charge should be possible in an anion of type IV derived from the aromatized compounds III. Solubility was also increased in basic solutions (3).

The conversion of the 4-benzylidene-2,3-dioxopyrrolidine derivatives (I) to products of types II and III can be regarded as a new variation of the Hantzch pyridine synthesis (4). The intermediates postulated in Chart I resemble those which have been proposed to account for the results in previously known examples of the Hantzsch synthesis (4). As was the case with earlier variations of the Hantzsch method, 4-aryl-1,4-dihydropyridines and 4-arylpyridines can be obtained by this new method by means of a sequence of reactions beginning with an aromatic aldehyde. The outcome of the present synthesis is the formation of 4-arylpyridine derivatives having amide (lactam) fuctions at the 2 and 6 pyridine positions and lactam-incorporated aminomethyl functions at the 3 and 5-positions. By way of such transformations as hydrolysis of the lactam rings these compounds could presumably serve as precursors of a variety of other highly substituted 4-arylpyridine derivatives. The method could also provide access to derivatives substituted in the benzene ring, as demonstrated by the experiments starting from 4-methoxybenzylidene and 4-hydroxy-3-methoxybenzylidene compounds of type I which have yielded the dipyrrolo[3,4-*b*:3′,4′-*e*]pyridine derivatives IIg, IIh and IIIg.

EXPERIMENTAL

All melting points are corrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee and W-H-W Laboratories, Phoenix, Arizona. All infrared spectra were taken as Nujol mulls on a Perkin-Elmer Infracord spectrophotometer. All nmr spectra were determined on a Varian A-60 spectrometer in a variety of solvents with tetramethylsilane as the reference standard. Ultraviolet spectra were determined on Cary Model 11 or Perkin-Elmer Model 202 spectrophotometers. In nmr descriptions, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.

4-Benzylidene-2,3-dioxopyrrolidenes (I).

These starting materials were prepared from 4-carbethoxy-2,3-dioxopyrrolidines by use of several variations of the combined one-pot hydrolysis-decarboxylation-aldol condensation procedure of Southwick and Barnes (1). The starting materials used for products IIa, IIb, and IIc were described in reference (1), that for product IIe in reference (5). Directions for the preparation of the four other 4-benzylidene derivatives used are given below

Table 1

Preparation of 1,2,4,6,7,8-Hexahydro-2,6-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-diones

Compound No.	Ar	R	Reaction Time, Hours	Yield	Molecular Formula		Analysis Calcd.	Found	Melting Point (°C)
IIa	Ph-	$PhCH_2$-	24	50%	$C_{29}H_{25}N_3O_2$	C	77.85	78.02	283.285° dec (a)
						H	5.59	5.67	
						N	9.39	9.28	
IIb	Ph-	C_6H_{11}- (cyclo)	24	63%	$C_{27}H_{33}N_3O_2$	C	75.17	75.48	324° dec (a)
						H	7.65	7.88	
						N	9.74	9.69	
IIc	Ph-	CH_3-	1	26%	$C_{17}H_{17}N_3O_2$	C	68.89	69.09	> 370° (b)
						H	5.79	5.80	
						N	14.51	14.22	
IId	Ph-	$(CH_3)_3C$-	1.5	66%	$C_{23}H_{29}N_3O_2$	C	72.77	72.98	345-347° dec (c)
						H	7.71	7.70	
						N	11.07	11.01	
IIe	Ph-	*p*-Br-Ph-	8	54%	$C_{27}H_{19}Br_2N_3O_2$	C	56.15	56.15	> 3.80°
						H	3.29	3.43	
						N	7.27	7.05	
IIf	Ph-	*p*EtO_2C-Ph-	8	63%	$C_{33}H_{29}N_3O_6$	C	70.33	70.07	> 363°
						H	5.15	5.07	
						N	7.46	7.26	
IIg	*p*CH_3O-Ph-	$PhCH_2$-	25	53%	$C_{30}H_{27}N_3O_3$	C	75.45	75.68	309-310°
						H	5.70	5.86	
						N	8.80	9.00	
IIh	3(CH_3O-4-HO-Ph)	C_6H_{11}- (cyclo)	25	21%	$C_{28}H_{35}N_3O_4$	C	70.41	70.53	> 330°
						H	7.39	7.21	
						N	8.80	8.96	

(a) Recrystallized from dimethylformamide-water. (b) Recrystallized from 7:1 mixture of water and ethanol. (c) Recrystallized from 3:1 mixture of water and acetone.

Table 2

Preparation of 1,2,6,7-Tetrahydro-6,7-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-diones

Compound No.	Ar	R	Procedure	Yield	Molecular Formula		Analysis Calcd.	Found	Melting Point (°C)
IIIa	Ph	$PhCH_2$-	A,B	A, 58% B, 91%	$C_{29}H_{23}N_3O_2$	C H N	78.20 5.16 9.43	77.96 5.14 9.16	311-316° (a)
IIIb	Ph	C_6H_{11}-(cyclo)	A	58%	$C_{27}H_{31}N_3O_2$	C H N	75.52 7.22 9.79	75.66 7.18 9.66	313-320° dec (a)
IIIc	Ph	CH_3-	A,B	A, 50% B, 90%	$C_{17}H_{15}N_3O_2$	C H N	69.36 5.14 14.61	69.39 5.33 14.42	380° dec (a)
IIId	Ph	$(CH_3)_3C$-	A	54%	$C_{23}H_{27}N_3O_2$	C H N	73.16 7.22 11.13	73.32 7.07 11.01	343-353° dec (b)
IIIe	Ph	*p*-Br-Ph-	B	79%	$C_{27}H_{17}Br_2N_3O_2$	C H N	56.34 2.95 7.30	56.48 3.04 7.17	> 390°
IIIf	Ph	*p*-EtO_2C-Ph-	A	60%	$C_{33}H_{27}N_3O_6$	C H N	70.58 4.81 7.48	70.43 4.84 7.36	> 360°
IIIg	*p*-CH_3O-Ph-	$PhCH_2$-	B	78%	$C_{30}H_{25}N_3O_3$	C H N	75.77 5.30 8.84	76.04 5.26 8.82	303-304° dec (c)

(a) Recrystallized from dimethylformamide-water. (b) Recrystallized from ethanol-water. (c) Recrystallized from methylene chloride-ether.

Table 3

Spectra of 1,2,4,6,7,8-Hexahydro-2,6-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-diones (II).

Compound	IR (Microns) NH	H-bonded C=O	C=C	NMR (a) (δ, center of pattern) R	Ar	C-8 H	Pyrrolo CH_2	UV nm (ε × 10^{-3}) Ethanol
IIa	3.00	5.90 5.99	6.09	7.10 m (10H) 4.55 q (4H) J = 15 Hz	7.10 m (5H)	4.69 s (1H)	3.55 q (4H) J = 22 Hz	254 (7.6)
IIb	3.06	5.90 6.00	6.09	4.00 m (2H) 1.57 m (20H)	7.37 m (5H)	5.03 s (1H)	3.89 q (4H) J = 20.5 Hz	240 (9.1) 257 (7.6)
IIc	3.02	5.90 6.00	6.10	2.95 s (6H)	7.15 m (5H)	4.80 s (1H)	3.71 q (4H) J = 20 Hz	265 (5.3) 296 (0.9)
IId	2.95	5.89 5.99	6.04	1.23 s (18H)	7.08 m (5H)	4.79 s (1H)	3.80 q (4H) J = 21.5 Hz	240 (8.3) 250 (6.9)
IIe	2.98	5.95 6.01	6.08	(b)	(b)	(b)	(b)	250 (c)
IIf	2.98	5.90 6.00	6.08	7.89 q (8H) 4.45 q (4H) (d) 1.44 t (6H)	7.41 s (5H)	5.14 s (1H)	4.30 q (4H) (d)	290 (c)
IIg	3.05	5.90 6.00	6.07	7.30 m (10 H) 4.65 q (4H) (e) J = 15 Hz	7.05 q (4H) 3.85 s (3H) (CH_3O)	4.75 (1H) (e)	3.75 s (4H)	235 (c,f) 273 (c,f) 280 (c,f)
IIh	3.10	5.87 5.98	6.23	(g)	(g)	(g)	(g)	227 (19.9) (f) 251 (10.6) (h) 250 (15.8) (f) 270 (10.1) (h) 275 (12.9) (f) 389 (5.4) (h) 293 (12.8) 320 (8.1) (f)

(a) Spectra taken in deuteriochloroform-trifluoroacetic acid mixtures. (b) Suitable solvent for nmr analysis was not found. (c) Saturated solution. (d) Patterns from pyrrolo CH_2 and CH_2 of OCH_2CH_3 partly obscured by overlapping. (e) C-8 proton signal coincides with left inner signal of CH_2 quartet. (f) Inflection. (g) Nmr spectrum obtained on sample of IIh corresponded to that expected for aromatized product IIIh; see Table 4. (h) Spectrum in 0.1*N* protassium hydroxide in ethanol.

Table 4

Spectra of 1,2,6,7-Tetrahydro-2,6-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-diones (III)

	IR (Microns)		NMR (δ, center of pattern)			UV, nm (ε × 10^{-3})	
Compound No.	C=O	C=C	R	Aryl	Pyrrolo CH_2	ethanol	0.1*N* potassium hydroxide ethanol
IIIa	5.81	6.29	7.12 s (10H) 4.50 s (4H)	7.24 m (5H)	4.72 s (4H)	222 (25.0) 257 (15.0) 280 (13.6)	240 (19.4) 280 (7.0)
IIIb	5.90	6.28	4.17 m (2H) 1.7 m (20H)	7.67 m (5H)	4.77 s (4H)	255 (11.8) 287 (10.4)	240 (14.2) 280 (7.7)
IIIc	5.81	6.25	(b)	(b)	(b)	260 (15.7)	280 (7.6)
IIId	5.84	6.21	1.43 s (18H)	7.48 s (5H)	4.75 s (4H)	255 (16.0) 278 (13.9)	240 (23.0) 2.78 (7.9)
IIIe	5.80	6.20	(b)	(b)	(b)	2.60 (c)	244 (13.4)
IIIf	5.85	6.20	7.90 q (8H) 4.30 q (4H) 1.25 t (6H)	7.67 s (5H)	5.10 s (4H)	270 (c)	290 (c)
IIIg	5.84	6.20	7.27 s (10H) 4.65 s (4H)	7.22 m (4H) 3.88 s (3H) (OCH_3)	4.87 s (4H)	227 (12.8) 298 (9.7)	230 (10.2) 299 (7.8)
IIIh (d)			4.20 m (2H) 1.7 m (20H)	7.12 m (3H) 3.95 s (3H) (OCH_3)	4.70 s (4H)		

(a) Spectra taken in deuteriochloroform-trifluoroacetic acid mixtures. (b) Suitable solvents for nmr analysis were not found. (c) Saturated solution. (d) Spectrum taken on sample of IIh; nmr spectrum showed conversion of IIh to IIIh had occurred prior to or during preparation of deuteriochloroform-trifluoroacetic acid solution for nmr determination. IIIh not otherwise characterized.

4-Benzylidene-1-*t*-butyl-2,3-dioxopyrrolidine (Id).

A mixture of 30.4 g (0.2 mole) of benzaldehyde, 45.4 g (0.2 mole) of 1-*t*-butyl-4-carboethoxy-2,3-dioxopyrrolidine (6), 1 ℓ of 10% hydrochloric acid and 200 ml of 95% ethanol was refluxed for 2 hours. The mixture was cooled to 10° and filtered to collect the product, yield, 24.4 g (56%). Recrystallization from 95% ethanol gave yellow plates, mp 208.5-210°; ir (Nujol): 5.82 (ketone C=O), 5.91 (lactam C=O), 6.15 (C=C), 6.27, 6.35, 7.14, 7.41, 7.83, 8.27, 8.61, 8.73, 9.64, 13.37, and 14.73 μ; uv λ max (95% ethanol) 239 sh (ε 4,960) and 327 nm (ε 24,170).

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.97; H, 7.09; N, 5.64.

1-Cyclohexyl-4-(4-hydroxy-3-methoxybenzylidene)-2,3-dioxopyrrolidine (Ih).

A mixture of1-cyclohexyl-4-carboethoxy-2,3-dioxopyrrolidine (50.6 g, 0.2 mole) (6), 30.4 g (0.2 mole) of vanillin, 1 ℓ of 20% hydrochloric acid and 400 ml of 95% ethanol was refluxed for 3 hours, than cooled to 10% and filtered to yield 38.9 g (62%) of 1h. Recrystallization from dimethylformamide-water gave yellow crystals, mp 254-255° dec; ir (Nujol): 3.21 (OH), 5.82 (ketone C=O), 6.00 (lactam C=O), 6.15 (C=C), 6.32, 7.60, 7.81, 7.95, 8.59, 8.90, 9.68 and 10.78 μ; uv λ max (95% ethanol, neutral), 268 (ε 7,190), 395 ((ε 19,800) and 515 nm (ε 2,100); (*ca.* 1 × 10^{-6} *M* ethanolic sodium hydroxide) 284 (ε 8,300) and 515 nm (ε 44, 100).

Anal. Calcd. for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.75; H, 6.45; N, 4.48.

1-Benzyl-4-*p*-methoxybenzylidene-2,3-dioxopyrrolidine (Ig).

A mixture of 5.2 g (0.02 mole) of 1-benzyl-4-carbethoxy-2,3-dioxopyrrolidine (6), 200 ml of 20% hydrochloride acid and 50 ml of 95% ethanol was refluxed with stirring for 1 hour. An anisaldehyde solution was prepared by dissolving 4.5 ml of anisaldehyde (0.03 mole) in 30 ml of 95% ethanol and *ca.* 20 ml of this solution was added dropwise to the refluxing mixture. The rate of addition was adjusted so that the 20 ml portion was added over a 1-hour period. After the 20 ml of the anisaldehyde solution has been added, the refluxing mixture was filtered, while hot, using a preheated Buchner funnel and filtering flask. The filtrate was returned to reflux temperature and the remainder of the anisaldehyde solution was added dropwise. The mixture was refluxed for an additional 1.5 hours (the total reflux period was 4 hours). After the reaction mixture had been cooled in an ice bath, all solids were collected by filtration and added to the previously filtered solids. These solids were recrystallized from and ethanol-water mixture to give 3.63 g (59%) of yellow, needle-like crystals, mp 188-189°; ir 5.81 and 5.88 (C=O), 6.13 (conj. C=C), 7.99 μ ($C_6H_4OCH_3$); nmr (CF_3CO_2H) δ 7.03 (s, 5, C_6H_5), 6.85 (q, 4, J = 9.0 Hz *p*-$CH_3OC_6H_4$), 4.54 (s, 2, C-5 CH_2 or $CH_2C_6H_5$), 4.20 (s, 2, C-5 CH_2 or $CH_2C_6H_5$), 3.57 (s, 3, *p*-$CH_3OC_6H_4$); uv (ethanol): max 244 nm (ε 9,210), 366 nm (ε 21,951).

Anal. Calcd. for $C_{19}H_{17}NO_3$: C, 74.27; H, 5.54; N, 4.56. Found: C, 74.52; H, 5.68; N, 4.62.

1-*p*-Carbethoxyphenyl-4-benzylidene-2,3-dioxopyrrolidine (If) *via* 1-*p*-Carboxyphenyl-4-benzylidene-2,3-dioxopyrrolidine.

1-*p*-Carboxyphenyl-4-benzylidene-2,3-dioxopyrrolidine.

A mixture of 1.35 g (5 mmoles) of 1-*p*-carboxyphenyl-4-carbomethoxy-2,3-dioxopyrroline (7), 3 ml (30 mmole) of benzaldehyde, 50 ml of 88% of formic acid and 9 ml of water was refluxed for 5 hours. At the end of this reflux period, the reaction was filtered, while hot, using a preheated funnel and flask. The filtrate was refluxed for and additional 19 hours. At the end of this reflux period, the filtering process was repeated and the filtrate refluxed for an additional 24 hours. After the reaction had been cooled in an ice bath, all solids were filtered and combined with the previously filtered solids. Approximately 500 ml of water and crushed ice were added to the filtrate and the mixture was extracted three times with a 500-ml portion of chloroform. The yellow solid which formed a the interface was filtered and added to the previously filtered solids. The solids were recrystallized from a dimethyl formamide-water mixture to give 0.71 g (46%) of yellow, needle-like crystals of 1-*p*-carboxyphenyl-4-benzylidene-2,3-dioxopyrrolidine, mp 317° dec; ir 5.86 and 6.03 (C=O), 6.20 μ (C=C); nmr (trifluoroacetic acid/carbon tetrachloride): δ 7.84 (q, 4, J = 9.0 Hz *p*-HO_2C-C_6H_4), 7.30 (s, 5, C_6H_5), 4.86 (s, 2, C-5 CH_2); uv (ethanol): max 250 nm (ε 14,512), 338 nm (ε 25, 490).

Anal. Calcd. for $C_{18}H_{13}NO_4$: C, 70.36; H, 4.23; N, 4.56. Found: C, 70.16; H, 4.20; N, 4.65.

1-*p*-Carbethoxyphenyl-4-benzylidene-2,3-dioxopyrrolidine.

Dry hydrogen chloride gas was bubbled through a mixture of 1.54 g (5 mmoles) of 1-*p*-carboxyphenyl-4-benzylidene-2,3-dioxopyrrolidine and 100 ml of absolute ethanol for *ca.* 0.5 hours. After the mixture had been refluxed for 10 hours, the mixture was filtered using a preheated funnel and flask and the filtrate was refluxed for one additional hour. After the mixture had been cooled in an ice bath, all solids were filtered and combined with the previously filtered solids. Recrystallization from and acetone-water gave 1.23 g (73%) of yellow plates, mp 239-242°; ir: 5.80 and 5.88 (C=O), 6.13 μ (C=C); nmr δ 7.60 (m, 4, *p*-EtO_2C-C_6H_4), 7.07 (s, 5, C_6H_5), 4.60 (s, 2, C-5 CH_2), 4.00 (q, 2, J = 6.5 Hz *p*-$CH_3CH_2O_2C$-C_6H_4), 0.97 (t, 3, J = 6.5 Hz *p*-$CH_3CH_2O_2C_6H_4$); uv (ethanol): max 250 nm (ϵ 14,313), 338 nm (ϵ 23,754).

Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.64; H, 5.07; N, 4.18. Found: C, 71.89; H, 4.97; N, 4.12.

1,2,4,6,7,8-Hexahydro-2,6-disubstituted-8-aryldipyrrolo[3,4-*b*:3′,4′-*e*]-pyridine-3,5-diones.

The hexahydrodipyrrolopyridine derivatives were prepared by refluxing a 20:1 molar excess of ammonium formate with the 4-benzylidine-2,3-dioxopyrrolidine derivative in 95% ethanol. Reaction times and recrystallization procedures varied with the substitutent groups on the pyrrolo nitrogens. The precedures are illustrated by the preparation of the 2,6 dimethyl derivative, described below. Reaction times, yields, melting points and elemental analyses are given in Table 1. The infrared, nmr and ultraviolet spectra for these compounds are given in Table 3.

A mixture of 2.01 g (0.01 mole) of 1-methyl-4-benzylidene-2,3-dioxopyrroline, 12.6 g (0.2 mole) of ammonium formate and 120 ml of 95% ethanol was refluxed for one hour and then cooled in an ice bath. After the addition of 1 liter of water an orange solid precipitated which was removed by filtration and washed thoroughly with acetone. The resultant white powder was recrystallized from 500 ml of a 7:1 mixture of water and ethanol to give 0.37 g (26%) of a white, microcrystalline solid.

1,2,6,7-Tetrahydro-2,6-disubstituted-8-penyldipyrrolo[3,4-*b*:3′,4′-*e*]-pyridine-3,5-diones.

The oxidation of the hexahydrodipyrrolopyridine derivatives was accomplished by two procedures: a) refluxing the hexahydrodipyridine derivatives in a dimethylformamide solution, and b) treating an acetic acid solution of the hexahydro-dipyrrolopyridine derivative with bromine and sodium acetate. The two procedures are illustrated below using the 2,6-dimethyldipyrrolopyridine derivative as the starting material. Yields, melting points and elemental analyses are presented in Table 2. The infrared, nmr and ultraviolet spectra of these compounds are presented in Table 4.

Procedure A.

A solution of 0.30 g (1 mmole) of 1,2,4,6,7,8-hexahydro-2,6-dimethyl-8-phenyldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-dione dissolved in 75 ml of dimethylformamide was refluxed for 48 hours. The reaction mixture was concentrated to 25 ml by heating under reduced pressure. Precipitated solids were removed by filtration and washed thoroughly with acetone and ether to give 0.15 g (50%) of white, microcrystalline solid.

Procedure B.

A solution of 0.20 g (0.67 mmole)of 1,2,4,6,7,8-hexahydro-2,6-dimethyl-8-phenyldipyrrolo[3,4-*b*:3′,4′-*e*]pyridine-3,5-dione, (0.2 g, 1 mmole) of bromine and 0.16 g (2 mmoles) of sodium acetate in 50 ml of acetic acid was refluxed for two hours. The solution was concentrated to near dryness by heating under reduced pressure. Water (60 ml) was added and the resultant precipitate removed by filtration and washed thoroughly with acetone and ether to give 0.18 g. (90%) of a white, microcrystalline solid.

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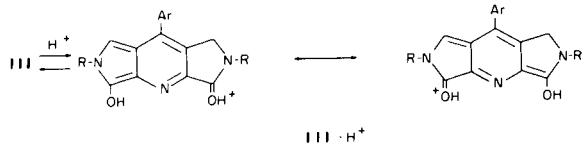
REFERENCES AND NOTES

(1) P. L. Southwick and E. F. Barnes, *J. Org. Chem.*, **27**, 98 (1962).

(2) In the case of the 2,6-dibenzyl derivatives IIa and IIg, the AB patterns for CH_2's of the pyrrolidine ring have collapsed virtually (IIa) or completely (IIg) to a singlet, but the benzyl methylene protons appeared as AB quartets, J_{AB} = 15 Hz.

(3) Integration of signal areas of nmr spectra for some of the type III compounds gave values closer to 3 than to 4 for the total number of protons in the 1 and 7 ring positions, suggesting existence of an equilibrium III + H^+ ⇌ III′•H^+ in the trifluoroacetic acid solutions used for nmr spectra.



(4) *Cf.* for example (a) H. S. Mosher in "Heterocyclic Compounds", R. C. Elderfield, ed., John Wiley & Sons, Inc, New York, 1950, Vol I, p 422 ff; (b) L. A. Paquette, "Principles of Modern Heterocyclic Chemistry", W. A. Benjamin, Inc, New York, 1968, p 226-229.

(5) R. Madhav, C. A. Snyder and P. L. Southwick, *J. Heterocyclic Chem.*, **17**, 1231 (1980).

(6a) P. L. Southwick and R. T. Crouch, *J. Am. Chem. Soc.*, **75**, 3413 (1953); (b) P. L. Southwick, E. P. Previc, J. Casanova, Jr., and E. H. Carlson, *J. Org. Chem.*, **21**, 1087 (1956).

(7) R. Madhav, M. D. Frishberg, C. A. Snyder and P. L. Southwick, *J. Heterocyclic Chem.*, **12**, 585 (1975).