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Synthesis of Pyrido[3,2,1-*de*]phenanthridine Derivatives*†

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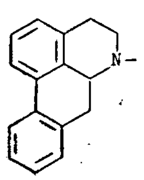
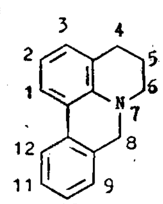
The title compounds have been prepared (i) by cyclization of N-acyl-8-phenyl-1,2,3,4-tetrahydroquinoline derivatives, and (ii) by a Pschorr reaction on N-(2-aminobenzoyl)-1,2,3,4-tetrahydroquinolines. In the Pschorr reaction the decomposition of the diazonium salts of the amines is shown to result in intramolecular diaryl coupling, affording the pyridophenanthridones and phenolic products, N-salicyloyltetrahydroquinolines. The structures of the various pyridophenanthridines synthesized by the two methods have been corroborated by NMR, IR and UV spectral data. A similar Pschorr reaction on N-(2-aminobenzenesulphonyl)-1,2,3,4-tetrahydroquinoline affords a tetracyclic sulphone analogue of phenanthridone. Results of attempts to prepare pyrrolophenanthridine derivatives are presented and rationalized. The NMR spectral data of N-acyltetrahydroquinoline derivatives used in the preparation of pyridophenanthridine by the cyclization method (i) show slow inversion of the tetrahydropyridine ring compared to tetrahydroquinoline or its 8-phenyl derivative. On the basis of NMR data structures (VIII) and (IX) have been assigned to N-acetyl- and N-chloroacetyl-8-phenyl-1,2,3,4-tetrahydroquinolines respectively.

ALKALOIDS incorporating the aporphine system (I) have been well investigated chemically and biologically[1]. A recent publication deals with the chemistry and biological properties of a number of purely synthetic aporphines[2]. Two syntheses of a comparatively much less known isoster, pyrido[3,2,1-*de*]phenanthridine (II)[3] involving (i) cyclization of N-β-carboxyethylphenanthridone[4] and (ii) a Pschorr reaction on N-(2-aminobenzyl)-1,2,3,4-tetrahydroquinoline[5], are recorded in literature. Two other synthetic routes developed by us are reported in this paper. Some of the properties of the ring system (II) are also discussed. In the first synthesis, reduction of 8-phenylquinoline afforded the 1,2,3,4-tetrahydro derivative which was converted to the N-acyl derivatives (III). These were subjected to a 'Morgan and Walls' type reaction[6] with $POCl_3$ to afford 8-substituted-5,6-dihydro-4H-pyrido[3,2,1-*de*]phenanthridinium salts isolated as the iodides (IV-VII) in 40-60% yields. These four derivatives were identified by analysis and by the highly characteristic phenanthridinium UV absorption spectrum.



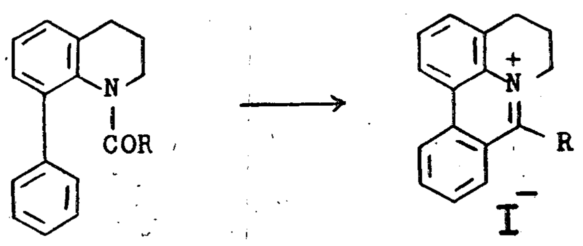
I



II

In order to make the route versatile and capable of yielding diverse compounds for biological evaluation, the cyclization of the chloracetyl (IX) as well as aminoacetyl, such as morpholinoacetyl derivatives, was attempted but this was unsuccessful. In the latter case, a crystalline iodide was obtained from the work up, but UV revealed it to be only the salt of the starting material.

A study of the NMR spectra of some N-acyl-8-phenyl-1,2,3,4-tetrahydroquinolines showed slow inversion of the tetrahydropyridine ring compared to tetrahydroquinoline and its 8-phenyl derivative[7]. Thus the methylene protons at positions 2, 3 and 4



IV R = Methyl
V R = Phenyl
VI R = p-Chlorophenyl
VII R = p-Nitrophenyl

III

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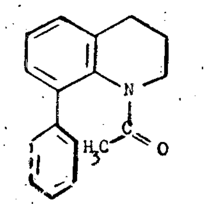
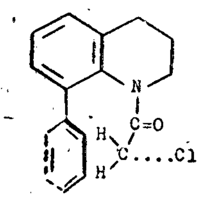
were seen as approximate triplet, quintet and triplet respectively at 3·07, 1·77 and 2·63 ppm in tetrahydroquinoline, at 3·30, 1·92 and 2·82 ppm in 8-phenyltetrahydroquinoline and at 3·80, 1·93 and 2·72 ppm in N-acetyltetrahydroquinoline. The pattern of the corresponding signals in VIII was very complex; particularly noteworthy was the fact that one of the methylene protons at position 2, presumably the equatorial one appeared as a complex multiplet at 4·78 ppm and that the acetyl methyl signal was seen at 1·43 ppm, 0·77 ppm higher field with respect to its position in N-acetyltetrahydroquinoline (2·20 ppm) and 0·49 ppm higher field relative to the methyl signal in 2-acetamidobiphenyl (1·92 ppm). These data allow one to deduce the structure of N-acetyl-8-phenyl-1,2,3,4-tetrahydroquinoline as shown in VIII, with the tetrahydropyridine ring undergoing slow or no inversion, and the methyl group held in the shielding region of the aromatic ring current.

The NMR spectrum of the N-chloracetyl derivative (IX) was again indicative of slow inversion of the hetero ring (signals of the methylene protons at C-3 and C-4 complex; equatorial proton at C-2, multiplet at 4·78 ppm; axial proton at C-2, multiplet at 3·17 ppm). Further, the methylene protons in the chloracetyl group were non-equivalent; one was a doublet at 3·73 ppm (J = 13 *cps*) and the other at 3·20 ppm (J = 13 *cps*). Both doublets were displaced to higher field, compared to the signal due to the methylene protons in N-chloracetyltetrahydroquinoline which was a singlet at 4·23 ppm. These data are accommodated by structure IX for N-chloracetyl-8-phenyl-1,2,3,4-tetrahydroquinoline with both methylene protons of the chloracetyl group held in the shielding region of the benzene ring current in such a way that one is more shielded than the other.



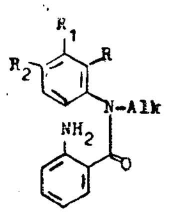
VIII



IX

The second synthesis of the pyrido[3,2,1-*de*]phenanthridine system II employed a Pschorr-type reaction[8] on N-(2-aminobenzoyl)tetrahydroquinolines (XVI), obtained from the nitro compounds XV. This study was of some theoretical interest, because of several reports in the literature on the course of the Pschorr reaction on 2-aminobenzoyl derivatives of nuclear substituted N-alkyl anilines. Whereas diazotization of the *meta*- or *para*-substituted amides X and XI, followed by decomposition, afforded phenanthridones XIII, similar treatment of amides XII carrying *ortho*-substituents, especially alkyl groups, yielded very little[9] or none[10,11] of the expected phenanthridone. The major product was XIV, arising from XII by deamination and dealkylation. Amides XVI can be considered to belong to type XII in which the *ortho*- and N-alkyl groups have been tied together in a strainless six-membered ring and were expected in our study to behave normally under the Pschorr reaction conditions. It was thus interesting to find that decomposition of the diazonium salts from XVI resulted in intramolecular diaryl coupling, affording 50-60% yields of the cyclic products XVII-XIX.

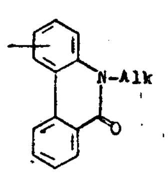
The reactions also partially led to the replacement of the diazonium group by hydroxyl, yielding N-salicyloyltetrahydroquinolines to the extent of 10-30%. Further, traces of deaminated products were detectable. Structures of products XVII-XIX were confirmed by analyses and characteristic phenanthridone UV absorption spectra. The NMR spectrum of XVII showed signals at 8·53, 8·17 and



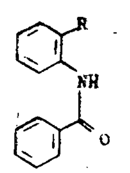
X : $R=R_2=H$; $R_1 = CH_3$, Cl

XI : $R=R_1=H$; $R_2 = CH_3$, Cl

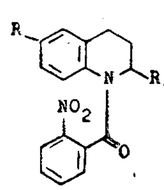
XII: $R_1=R_2=H$; $R = CH_3$, Cl



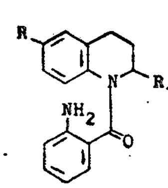
XIII



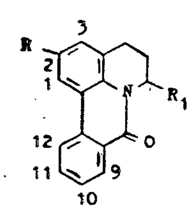
XIV : $R = CH_3$, Cl



XV



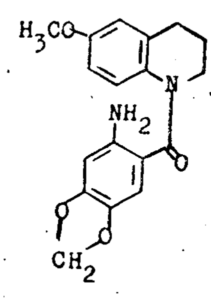
XVI



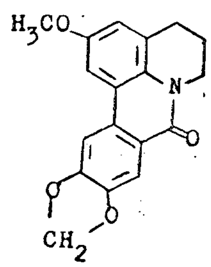
XVII $R = R_1 = H$

XVIII $R = H$; $R_1 = CH_3$

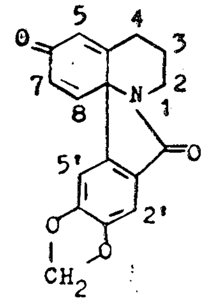
XIX $R = OMe$; $R_1 = H$.



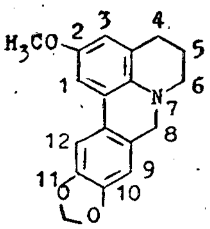
XX



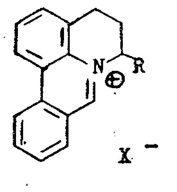
XXI



XXII

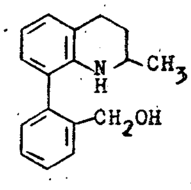


XXIII

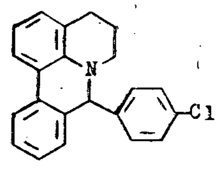


XXIV : R = H

XXV : R = CH_3



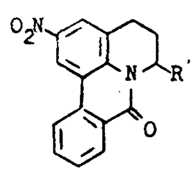
XXVI



XXVII

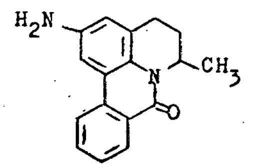
8·02 ppm respectively for the proton at C-9 in the carbonyl field and the two *peri*-protons at C-1 and C-12. The other four aromatic proton signals were spread between 7·05 and 7·83 ppm. The signals of the aromatic protons in XVIII had approximately the same locations and shapes. The NMR features of the alicyclic protons of the above two compounds have been discussed elsewhere[7]. Diazotization of N-(2-amino-4,5-methylenedioxybenzoyl)-6-methoxy-1,2,3,4-tetrahydroquinoline (XX) yielded the expected product XXI (57%) and the spirodienone XXII (30%). The structure of XXII followed from its analysis, lack of methoxyl group and UV and NMR spectra. In addition to indicating the absence of the methoxyl group, and the presence of the methylenedioxy function (singlet at 6·07 ppm), the NMR spectrum showed singlets at 6·52 and 7·20 ppm (protons at C-5′ and C-2′), a doublet for proton at C-8 at 6·62 ppm ($J = 10$ *cps*), a doublet of doublets for proton at C-7 at 6·35 ppm ($J = 10$ *cps*, $J_1 = 1·5$ *cps*) and a doublet for proton at C-5 at 6·32 ppm ($J = 1·5$ *cps*). Further the slowing down of inversion of the piperidine ring was revealed by the appearance of a multiplet corresponding to only one proton at about 4·25 ppm (equatorial proton on C-2), the axial one being lost in the complex at higher field. The formation of dienones in the Pschorr reaction has been recorded[12] and can be attributed to the activation of the *para*-position of an aromatic methoxyl group for diaryl coupling, with concomitant loss of the O-alkyl group. A similar dienone may have been formed in the reaction leading to XIX, but not in detectable amounts.

LAH reduction of the phenanthridone XXI gave a high yield of the expected XXIII which was obtained crystalline and analytically pure but had a bad m.p. behaviour and appeared to be unstable when exposed to air. Its NMR spectrum was consistent with the structure: C-12 H, singlet at 7·12, C-1 H, doublet at 6·98 ($J = 3$ *cps*), C-9 H, singlet at 6·60, C-3 H, doublet at 6·53 ($J_* = 3$ *cps*), $CH_2\langle^{O-}_{O-}$ singlet at 5·12, C-8 CH_2, singlet at 3·87, $-OCH_3$, singlet at 3·77, C-6 CH_2, triplet at 3·08, C-4 CH_2, triplet at 2·77 and C-5 CH_2, quintet at 2·0 ppm. The products from the LAH reduction of the phenanthridones XVII and XVIII were likewise unstable bases resisting proper isolation, but eventually yielded crystalline salts whose elemental analyses were equally compatible with the expected 7,8-dihydro products analogous to XXIII as well as the fully aromatic phenanthridinium structures XXIV and XXV, analogous to IV. The UV spectra of the salts indicated that the latter structures were more likely. The NMR spectra of these products provided conclusive evidence for the structural assignments. The spectrum of XXIV (X = perchlorate) in DMSO-d_6 showed a proton singlet at 10·17 ppm in addition to seven aromatic protons at higher field, while that of XXV (X=Cl) in D_2O (TMS external reference) had the C-8 proton singlet at 9·3 ppm. The spectra of both the salts significantly lacked the two proton singlets that would have been expected of the benzylic methylene at C-8 in the saturated structures. Obviously, the primary reduction products had undergone spontaneous oxidation prior to or during salt formation to the more aromatic structures. In the LAH reduction of XVIII, a significant amount of a byproduct, considered to have structure XXVI, was formed. Its formation can be visualized to occur via a carbinol amine intermediate, which in its aldehydic tautomeric form will suffer further reduction

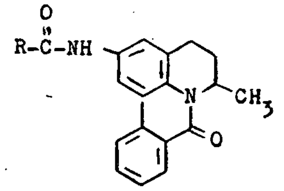


XXVIII : R = H

XXIX : R = CH_3

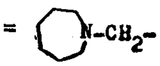


XXX



XXXI : R = Ph-NH-

R = $ClCH_2$-

R = 

to the observed product. One attempted conversion of the hydrochloride of XXVI to a hydriodide resulted in ring closure to give the salt of XXV (X=I).

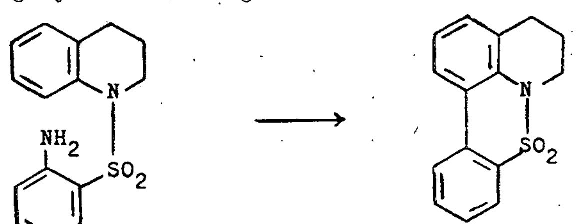
The perchlorate salt of XXIV had a different m.p. from the one reported for the product of Pschorr reaction on N-(2-aminobenzyl)-1,2,3,4-tetrahydroquinoline[5]. However, the structure of the latter product cannot be considered to have been established in the absence of spectral data and in view of the possibility of several different products being formed in a Pschorr reaction[8-11].

In another approach to the synthesis of derivatives of type XXIII, the reduction of the salts of type IV was studied. While V was found to be stable to catalytic hydrogenation conditions, VI was reduced by $NaBH_4$ smoothly to XXVII. The product was crystalline and gave correct analytical data. The structure was supported by UV and NMR data (singlet for the benzhydrilic methine proton at 5·27 ppm). However, its m.p. behaviour was bad and resembled that of XXIII. Similar observations have been recorded by other authors[13,14] with molecules incorporating a dihydrophenanthridine ring system.

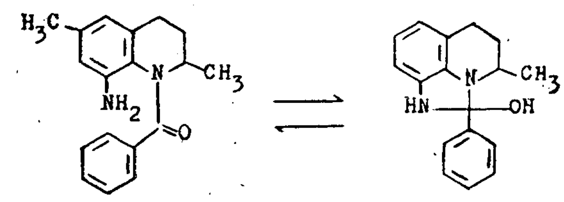
The phenanthridones XVII and XVIII were nitrated in high yield, to the 2-nitro derivatives XXVIII and XXIX. The NMR spectrum of XXVIII in CF_3CO_2H was consistent with the assigned orientation of the nitro group. XXIX was reduced to the amine XXX and a number of derivatives (XXXI) prepared therefrom.

An extension of the Pschorr reaction to N-(2-aminobenzenesulphonyl)tetrahydroquinoline XXXII afforded the tetracyclic sulphone analogue XXXIII of the phenanthridone XVII. Only in 1964, a report has appeared on the Pschorr reaction on 2-aminobenzenesulphonylanilines[15].

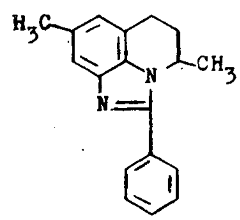
In a different approach to the synthesis of the ring system II, using the Pschorr reaction, the



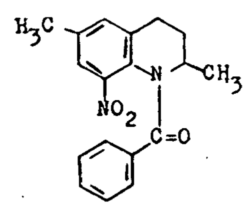
XXXII → XXXIII



XXXV



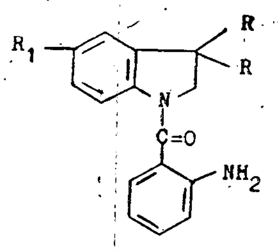
XXXVI



XXXIV

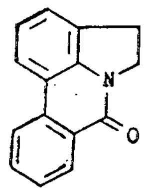
quaternization of 8-nitroquinoline and 8-nitroquinaldine with benzyl bromide was tried unsuccessfully. However, N-benzoyl-2,6-dimethyl-1,2,3,4-tetrahydroquinoline could be nitrated to the amide (XXXIV) which was reduced to the amine (XXXV), whose IR spectrum indicated it to exist largely as the carbinolamine. Under the Pschorr reaction conditions, nitrogen was not eliminated. An unexpected product, probably the benzimidazole (XXXVI), was obtained in high yield. This reaction has analogy in the literature[16].

The application of the Pschorr reaction to N-(2-aminobenzoyl)-indolines has been studied to a limited extent in the literature in connection with the synthesis of a degradation product of lycorine[13,14]. The desired internuclear cyclization to give (XXXIX), the lower ring homologue of (XVII), was achieved in poor yield. The major product was a N-benzoylindole. In spite of these discouraging reports, we were prompted to extend our studies to this area because of the successful synthesis of (XVII) and analogues reported in this paper. Commercially available 5-acetylindoline was converted to its 2-nitrobenzoyl derivative and thence to the amine (XXXVII). Diazotization, followed by the usual decomposition, afforded, besides the phenolic product 5-acetyl-N-salicyloylindoline (14%), only the indole derivative XL in

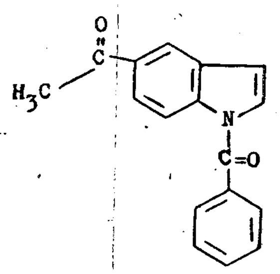


XXXVII : $R = H$; $R_1 = COCH_3$

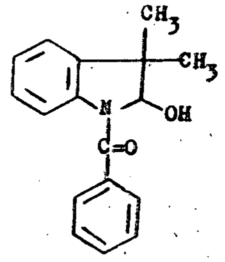
XXXVIII : $R = CH_3$; $R_1 = H$



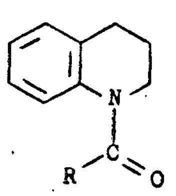
XXXIX



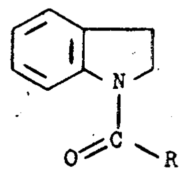
XL



XLI



XLII



XLIII

13% yield, which was identified by analysis, and characteristic UV and IR data.

The formation of an indole derivative in this reaction is considered to occur via abstraction of a hydrogen radical from the α-position of the indole nucleus by the phenyl radical generated by decomposition of the diazonium salt. Subsequent loss of a hydrogen radical from the β-position would lead to an indole derivative (an ionic mechanism can also be considered[10]). A total blocking of the β-position by methyl groups would render the aromatization impossible (unless methyl migration occurred) and may be expected to direct the reaction towards intramolecular diaryl coupling. Accordingly the amide (XXXVIII) was synthesized and subjected to the Pschorr reaction. N-Salicyloyl-3,3-dimethylindoline was isolated as the phenolic product in 50% yield. Besides traces of N-benzoyl-3,3-dimethylindoline, another neutral product was isolated in about 25% yield which was not the desired tetracyclic derivative. From analytical and UV, and IR spectral data, its structure was deduced to be (XLI). Its NMR spectrum in $CDCl_3$-CD_3SOCD_3 afforded conclusive corroborative evidence. Whereas in N-benzoyl-3,3-dimethylindoline, the two methyl groups were equivalent and appeared as a singlet at 1·30 ppm, those of (XLI) were non-equivalent, appearing as two singlets (3H each) at 1·13 and 1·33 ppm. The spectrum had the following further features: broad singlet (1H) at 4·12 ppm due to —OH, washed out by D_2O; singlet (1H) at 5·13 ppm due to methine proton at the α-position and multiplet (9H) at 7·00-7·92 ppm due to aromatic protons. Obviously, a hydrogen radical was abstracted from the α-position by the phenyl radical and its position taken by a hydroxyl group leading to XLI (an ionic mechanism is also feasible). It can be concluded from past[13,14] and present experience that diaryl coupling is not the favoured path in the decomposition of diazonium salts from N-(2-aminobenzoyl)-indolines. It is tempting to speculate that the difference in the behaviour of these compounds from that of N-(2-aminobenzoyl)tetrahydroquinolines may be due to a difference in the preferred configuration of the amide bond in the two molecules. It has been shown by us earlier[7,17] that, in general, N-acyltetrahydroquinolines exist in the form XLII, whereas N-acylindolines prefer to have the opposite configuration XLIII.

In the case of the diazonium salts of amides (XVI), configuration XLII would favour intramolecular diaryl coupling, whereas the diazonium salts from XXXVII and XXXVIII with the preferred configuration as shown in XLIII are better set up for attack at the α-position. It is also conceivable that structures of type XXXIX are more strained than of the type XVII and are correspondingly not easily formed.

Experimental Procedure

Melting points are uncorrected. NMR spectra were obtained with a Varian A-60 spectrometer; chemical shifts are quoted in ppm from TMS internal standard; unless otherwise stated, $CDCl_3$ solutions were used. UV spectra are for 95% EtOH solutions. Silica gel (E. Merck) for chromatography had a particle size of 0·05-0·20 mm.

TABLE 1 — N-ACYL-8-PHENYL-1,2,3,4-TETRAHYDROQUINOLINES (III)

R	m.p. °C	Mol. formula	Found (%)		Calc. (%)	
			C	H	C	H
N-Acetyl	131-3	$C_{17}H_{17}NO$	80·93	6·69	81·24	6·82
N-Chloracetyl	116-18	$C_{17}H_{16}ClNO$	71·50	5·60	71·45	5·64
N-Dichloroacetyl	137-8	$C_{17}H_{15}Cl_2NO$	63·79	4·74	63·76	4·72
N-Benzoyl	171-3	$C_{22}H_{19}NO$	84·43	6·12	84·31	6·11
N-*p*-Chlorobenzoyl	212-14	$C_{22}H_{18}ClNO$	76·15	5·48	75·97	5·21
N-*p*-Nitrobenzoyl	170-72	$C_{22}H_{18}N_2O_3$	73·67	4·97	73·73	5·06
N-Morpholinoacetyl	141-2	$C_{21}H_{24}N_2O_2$	74·97	7·10	74·97	7·19
N-Piperidinoacetyl	116-18	$C_{22}H_{26}N_2O$	78·86	7·75	79·00	7·84
N-Pyrrolidinoacetyl (maleate)	145-6	$C_{25}H_{28}N_2O_5$	69·13	6·74	68·79	6·43
N-Diethylaminoacetyl (maleate)	154-6	$C_{25}H_{30}N_2O_5$	68·85	6·74	68·47	6·90
N-(4-Methylpiperazino)acetyl	112-13	$C_{22}H_{27}N_3O$	75·70	7·78	75·61	7·79
N-(N′-Ethyl-N′-β-hydroxyethyl-amino)acetyl	101-2	$C_{21}H_{26}N_2O_2$	74·47	7·78	74·52	7·74

TABLE 2 — 8-SUBSTITUTED-5,6-DIHYDRO-4H-PYRIDO[3,2,1-*de*]PHENANTHRIDINIUM IODIDES (IV-VII)

R	m.p. °C	Mol. formula	Found (%)		Calc. (%)		UV λ_{max}, mμ (log ε)
			C	H	C	H	
Methyl (periodide)	214-16	$C_{17}H_{16}I_3N$	33·28	2·68	33·20	2·62	
Methyl	189-91	$C_{17}H_{16}IN$	57·02	5·20	56·67	4·47	206 (4·46), 236† (4·32), 408 (3·74)
Phenyl	305*	$C_{22}H_{18}IN$	62·59	4·28	62·43	4·25	250 (4·57), 271† (4·30), 336 (4·05), 370† (3·78)
p-Chlorophenyl	>300	$C_{22}H_{17}ClIN$	57·38	3·93	57·71	3·74	250 (4·60), 270† (4·35), 335 (4·09), 370† (3·87)
p-Nitrophenyl	>300	$C_{22}H_{17}IO_2N_2$	56·40	3·95	56·40	3·60	214 (4·59), 252 (4·55), 272† (4·47), 340 (3·92), 380† (3·65)

*Decomposition with blackening about 200°.
†Inflexion.

8-Phenyl-1,2,3,4-tetrahydroquinoline — A solution of 8-phenylquinoline[18] (23 g) in MeOH (150 ml) and AcOH (10 ml) was hydrogenated at room temperature and atmospheric pressure using platinum oxide (1 g) catalyst. In 8 hr nearly theoretical uptake of hydrogen was observed. The reaction was stopped and the clear supernatant separated from the sludge containing a black gum and catalyst. This was extracted with MeOH and the combined extract concentrated. The residue was taken up in 1*N* HCl and the extract shaken with ether. The acid layer was basified with conc. NH_4OH and the liberated base extracted with ether and converted to the hydrochloride (17·7 g) which became crystalline with EtOH and was recrystallized from EtOH-ether; 16·1 g, m.p. 214-6° (d.) (Found: C, 72·90; H,6·50; Cl, 14·30. $C_{15}H_{16}ClN$ requires C, 73·31; H, 6·56; Cl, 14·43%).

N-Acyl-8-phenyl-1,2,3,4-tetrahydroquinolines — The N-acetyl derivative (VIII) was made by refluxing the free base from the above hydrochloride with acetic anhydride, and the N-benzoyl derivative under Schotten Baumann conditions. For the other derivatives, the following procedure was found convenient.

A suspension of 8-phenyl-1,2,3,4-tetrahydroquinoline hydrochloride (1 g) in 10% aq. $NaHCO_3$ (10 ml) was stirred with ether and with cooling treated with chloracetyl chloride (1 g) in ether (10 ml) added dropwise. Stirring was continued at room temperature till the ether evaporated off and the solid material filtered. It was washed successively with aq. $NaHCO_3$, water, 2*N* HCl and water. Recrystallization from ether afforded pure (IX) (1 g; 85%), m.p. 116-18°. The acyl derivatives are listed in Table 1. Yields of these derivatives were generally between 80 and 90%.

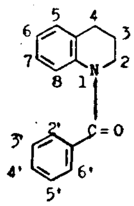
N-Aminoacyl-8-phenyl-1,2,3,4-tetrahydroquinolines — These were prepared by the following typical procedure and are listed in Table 1.

A mixture of N-chloracetyl-8-phenyl-1,2,3,4-tetrahydroquinoline (5 g) and morpholine (5 g) was heated at 150° for 5 hr. The mixture was cooled, rubbed with water and extracted with ether. The ether solution was shaken with 2*N* HCl. The solid basic product, recovered from the acid extract, was crystallized from aq. MeOH to give N-α-morpholinoacetyl-8-phenyl-1,2,3,4-tetrahydroquinoline (5·5 g; 90%), m.p. 141-2°.

8-Substituted-5,6-dihydro-4H-pyrido[3,2,1-*de*]*phenanthridinium salts* (IV-VII) — These are listed in Table 2 and are obtained by $POCl_3$ cyclization of the acyl derivatives as illustrated below.

A mixture of N-benzoyl-8-phenyl-1,2,3,4-tetrahydroquinoline (6·2 g) and $POCl_3$ (30 ml) was heated under reflux for 5 hr at 150°; excess $POCl_3$ was removed *in vacuo*, the residue digested with warm water and filtered from gummy matter. The aqueous solution was concentrated and treated with excess saturated KI solution, when 5,6-dihydro-8-phenyl-

TABLE 3 — 1-AROYL-1,2,3,4-TETRAHYDROQUINOLINES



Substituents	m.p. °C	Mol. formula	Found (%) C	Found (%) H	Found (%) N	Calc. (%) C	Calc. (%) H	Calc. (%) N
2′-Nitro	155-6	$C_{16}H_{14}N_2O_3$	68·34	5·14	10·16	68·07	5·00	9·92
2-Methyl-2′-nitro	124-8	$C_{17}H_{16}N_2O_3$	69·07	5·53	9·32	68·90	5·44	9·45
6-Methoxy-2′-nitro	147-9	$C_{17}H_{16}N_2O_4$	65·20	5·19	—	65·37	5·16	—
6-Methoxy-4′,5′-methylene-dioxy-2′-nitro	175-7	$C_{18}H_{16}N_2O_6$	60·99	4·83	—	60·67	4·53	—
2′-Amino	102-3	$C_{16}H_{16}N_2O$	75·54	6·69	11·53	76·16	6·39	11·10
2′-Amino-2-methyl	108-9	$C_{17}H_{18}N_2O$	76·95	7·03	10·60	76·66	6·81	10·52
2′-Amino-6-methoxy (HCl salt)	>300	$C_{17}H_{19}ClN_2O_2$	63·96	6·11	9·16	64·04	6·01	8·79
2′-Amino-6-methoxy-4′,5′-methylenedioxy	132	$C_{18}H_{18}N_2O_4$	66·54	5·72	8·83	66·24	5·56	8·58
2′-Methoxy-2-methyl	86-91	$C_{18}H_{19}NO_2$	76·78	6·61	4·69	76·80	6·81	4·98
6-Methoxy	85-87	$C_{17}H_{17}NO_2$	76·62	6·67	—	76·38	6·41	—
6-Methoxy-4′,5′-methylene-dioxy	94-95	$C_{18}H_{17}NO_4$	69·43	5·60	—	69·44	5·50	—
2,6-Dimethyl-8-nitro	161-2	$C_{18}H_{18}N_2O_3$	69·70	6·09	8·76	69·66	5·85	9·03

4H-pyrido[3,2,1-*de*]phenanthridinium iodide (V) was precipitated. This was filtered off, washed with water and crystallized from MeOH; 5·4 g (62%), m.p. about 305° (d.).

In the case of the N-acetyl derivative, cyclization and treatment with KI gave a quaternary iodide and a more sparingly soluble periodide.

Attempted cyclization of N-α-aminoacyl-8-phenyl-1,2,3,4-tetrahydroquinolines — Reaction of 8-phenyl-1-(α-*N*-piperidinoacetyl)-1,2,3,4-tetrahydroquinoline (1·7 g) with $POCl_3$ (15 ml) and isolation of the product as the iodide gave the colourless hydriodide (1·7 g) of starting material, m.p. 250-53° (Found: C, 56·02; H, 5·75. $C_{22}H_{27}IN_2O.\frac{1}{2}H_2O$ requires C, 56·00; H, 5·93%). Likewise attempted cyclization of 1-(α-N-morpholinoacetyl)-8-phenyl-1,2,3,4-tetrahydroquinoline gave, after the usual work up, its hydriodide, m.p. 258-61° (Found: C, 53·93; H, 5·22. $C_{21}H_{25}IN_2O_2$ requires C, 54·31; H, 5·44%).

N-(2-Nitrobenzoyl)tetrahydroquinoline derivatives (XV) — These were made by the following typical procedure and are listed in Table 3.

To a vigorously stirred mixture of 10% aq. $NaHCO_3$ (200 ml) and ether (100 ml) containing 1,2,3,4-tetrahydroquinaldine (22 g) was added (½ hr) in drops a solution of 2-nitrobenzoyl chloride (from 16·7 g acid and 25 ml thionyl chloride) in ether (30 ml). The mixture was stirred for another 3 hr, the ether layer separated and washed with 2*N* HCl when the amide crystallized out. This was filtered off and the ether filtrate concentrated to give some more of the amide. The total product (25 g) was recrystallized from aq. MeOH, m.p. 124-8°.

Similarly were prepared the 2-nitrobenzoyl derivatives of 5-acetylindoline (from acetone-MeOH), m.p. 167-8° (Found: C, 65·82; H, 4·66; N, 9·21. $C_{17}H_{14}N_2O_4$ requires C, 65·80; H, 4·55; N, 9·03%), and of 3,3-dimethylindoline (from MeOH), m.p. 129-31° (Found: C, 69·15; H, 5·46; N, 9·84. $C_{17}H_{16}N_2O_3$ requires C, 68·90; H, 5·44; N, 9·45%).

N-(2-Nitrobenzenesulphonyl)tetrahydroquinoline — 2-Nitrobenzenesulphonyl chloride (22 g) was added in portions to tetrahydroquinoline (26·6 g). Afterwards benzene (50 ml) was poured in and the mixture heated under reflux for 1 hr. It was then treated with water and the benzene layer worked up conventionally to give the neutral product (22 g), m.p. 127-9°, raised by one crystallization from CH_2Cl_2-MeOH to 132-3° (Found: C, 56·45; H, 4·63; N, 8·82. $C_{15}H_{14}N_2O_4S$ requires C, 56·60; H, 4·43; N, 8·80%).

The corresponding quinaldine derivative had m.p. 132-5° (from MeOH) (Found: C, 57·82; H, 5·02; N, 8·72. $C_{16}H_{16}N_2O_4S$ requires C, 57·83; H, 4·85; N, 8·43%).

N-(2-Aminobenzoyl)tetrahydroquinoline derivatives (XVI) — The following catalytic reduction is typical of the procedure for this class of compounds. The products are listed in Table 3. A solution of N-(2-nitrobenzoyl)tetrahydroquinaldine (20·7 g) in MeOH (300 ml) was shaken with hydrogen in an Ente apparatus in the presence of Adam's catalyst (0·25 g) at atmospheric pressure and 26°. At the end of 16 hr, hydrogen uptake was nearly theoretical. The solution was freed from the catalyst and concentrated *in vacuo* to give the product (18·5 g), m.p. 106-8°, raised to 108-9° by recrystallization from MeOH.

N-(2-Aminobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline gave a phenylthiourea, m.p. 156-7° (from MeOH) (Found: C, 71·93; H, 5·96; N, 10·18. $C_{24}H_{23}N_3OS$ requires C, 71·80; H, 5·78; N, 10·47%).

The following 2-amino acyl derivatives were similarly prepared from the nitro compounds by catalytic reduction: 5-acetyl-N-(2-aminobenzoyl)-indoline (XXXVII) (from MeOH), m.p. 139-40° (Found: C, 73·17; H, 5·97; N, 9·74. $C_{17}H_{16}N_2O_2$ requires C, 72·84; H, 5·75; N, 9·99%); N-(2-aminobenzoyl)-3,3-dimethylindoline (XXXVIII) (from MeOH), m.p. 127-8° (Found: C, 76·74; H, 6·79; N, 10·85. $C_{17}H_{18}N_2O$ requires C, 76·61; H, 6·81; N, 10·52%); and N-(2-aminobenzenesulphonyl)tetrahydroquinoline (XXXII) (from MeOH), m.p. 107-9° (Found: C, 59·24; H, 5·30; N, 8·88. $C_{15}H_{16}N_2O_2S.H_2O$ requires C, 58·78; H, 5·87; N, 9·14%).

Pschorr reaction on the 2-aminobenzamides: *5,6-Dihydro-8-oxo-4H-pyrido*[3,2,1-*de*]*phenanthridine* (XVII) — To a solution of N-(2-aminobenzoyl)tetrahydroquinoline (5·05 g) in AcOH (80 ml) was added conc. H_2SO_4 (7·5 ml) and the mixture cooled to 0° to −5°. This was treated with a solution of sodium nitrite (1·55 g) in water (15 ml), added dropwise below the surface of the mixture with stirring during 15 min, the temperature being kept below 0°C. After being stirred at 0° for an additional 2 hr, the mixture was treated with urea (0·55 g) and 2*N* H_2SO_4 (125 ml); it was then heated with stirring on a boiling water-bath for 30 min, treated with zinc dust (10 g) and again heated with stirring for another ½ hr, when the orange coloured solution became practically colourless. The mixture was cooled, filtered and the insolubles extracted with $CHCl_3$. The extract was added to the aqueous filtrate which had been rendered basic with NH_4OH and the $CHCl_3$ layer separated, after thorough shaking. A few more $CHCl_3$ extracts were combined and evaporated. The residue was taken up in ether-CH_2Cl_2 mixture and shaken up with 10% NaOH till the phenolic product was completely extracted. The organic layer was washed with water, dried and evaporated. The residue became crystalline with MeOH; 2·4 g, m.p. 92-94° (51%). Recrystallization from MeOH afforded pure (XVII), m.p. 94-95° (Found: C, 81·47; H, 5·60; N, 6·25. $C_{16}H_{13}NO$ requires C, 81·68; H, 5·57; N, 5·95%); IR (CH_2Cl_2) 1620 cm^{-1} (C=O); λ_{max} 235, 263, 326, 340 mμ (log ε 4·63, 4·31, 3·88, 3·84). Chromatography of the mother liquors from this crystallization on silica gel afforded N-benzoyltetrahydroquinoline (100 mg), m.p. 78-79°, identical with a synthetic sample (Found: C, 81·36; H, 6·53; N, 6·29. $C_{16}H_{15}NO$ requires C, 80·98; H, 6·36; N, 5·90%).

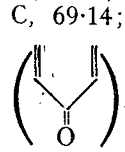
The phenolic product of the reaction was recovered from the NaOH layer by acidification. It was recrystallized from MeOH to afford N-(salicyloyl)-1,2,3,4-tetrahydroquinoline (1·5 g; 30%), m.p. 138° (Found: C, 75·60; H, 6·11; N, 5·48. $C_{16}H_{15}NO_2$ requires C, 75·87; H, 5·97; N, 5·53%). This was identical with a sample synthesized by treatment of tetrahydroquinoline with aspirin chloride, followed by saponification and further characterized as the acetate, m.p. 98-99° (from dil. MeOH) (Found: C, 73·57; H, 5·83; N, 5·16. $C_{18}H_{17}NO_3$ requires C, 73·20; H, 5·80; N, 4·74%).

5,6-Dihydro-6-methyl-8-oxo-4H-pyrido[3,2,1-*de*]*phenanthridine* (XVIII) — Treatment of N-(2-aminobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline as for the compound (XVII) afforded as the neutral product the pyridophenanthridine (XVIII) in about 60% yield; m.p. 96-97° (one preparation had m.p. 110-13° but was identified with the other form by TLC and IR) (Found: C, 82·20; H, 6·18; N, 5·63. $C_{17}H_{15}NO$ requires C, 81·90; H, 6·06; N, 5·62%); IR (CH_2Cl_2): 1625 cm^{-1} (C=O); λ_{max} 235, 263, 327, 342 mμ (log ε 4·68, 4·38, 3·91, 3·87). The phenolic product was obtained in 12% yield after crystallization from aq. MeOH, m.p. 100-105°, resolidifying and remelting at 114-15° and identified as N-(salicyloyl)-2-methyl-1,2,3,4-tetrahydroquinoline (Found: C, 76·52; H, 6·89; N, 5·43. $C_{17}H_{17}NO_2$ requires C, 76·38; H, 6·41; N, 5·24%). The m.p. was undepressed by a synthetic sample. The O-methyl ether, m.p. 86-91°, was likewise identical with synthetic N-(2-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline.

5,6-Dihydro-2-methoxy-8-oxo-4H-pyrido[3,2,1-*de*]-*phenanthridine* (XIX) — Treatment of N-(2-aminobenzoyl) - 6 - methoxy - 1,2,3,4 - tetrahydroquinoline under Pschorr condition gave about 60% neutral product, which on two crystallizations from methanol gave in 53% yield the pyridophenanthridone (XIX), m.p. 167-9° [Found: C, 76·68; H, 5·69; (O)CH_3, 5·72, 5·57. $C_{17}H_{15}NO_2$ requires C, 76·96; H, 5·70; (O)CH_3, 5·66%]; IR (nujol): 1625 cm^{-1} (C=O); λ_{max} 236, 268, 344, 356 (inflex.) mμ (log ε 4·68, 4·30, 3·95, 3·87). The presence of N-benzoyl-6-methoxy-1,2,3,4-tetrahydroquinoline in the mother liquor was detected by comparison with a synthetic sample on a silica TLC plate. The phenolic part (yield 13%) from the reaction was N-salicyloyl-6-methoxy-1,2,3,4-tetrahydroquinoline, m.p. 132-3° (from MeOH) (Found: C, 72·01; H, 6·30; N, 5·29. $C_{17}H_{17}NO_3$ requires C, 72·06; H, 6·05; N, 4·94%); IR (nujol): 3140 (OH), 1605 cm^{-1} (C=O).

5,6-Dihydro-2-methoxy-10,11-methylenedioxy-8-oxo-4H - pyrido[3,2,1 - *de*]*phenanthridine* (XXI) — The Pschorr reaction was carried out as usual on N-(2-amino-4,5-methylenedioxybenzoyl)-6-methoxy-1,2,3,4-tetrahydroquinoline except that the zinc dust treatment subsequent to decomposition of the diazonium salt was not carried out, as the product had crystallized out. There was very little phenolic product. The neutral product (5·4 g) was triturated with excess MeOH to give as the insoluble part, the pyridophenanthridone (XXI) (3·5 g; 57%), m.p. 258-60°, raised to 259-60° by crystallization from CH_2Cl_2-MeOH [Found: C, 70·18; H, 5·11; N, 4·48; (O)CH_3, 4·98, 5·07. $C_{18}H_{15}NO_4$ requires C, 69·89; H, 4·89; N, 4·53; (O)CH_3, 4·86%]. IR (nujol): 1625 cm^{-1} (C=O); λ_{max} 244, 284, 344, 358 mμ (log ε 4·65; 4·31, 3·84, 3·80).

The mother liquor contained 1·9 g material (~30%) which was almost pure dienone (XXII). This was crystallized once from MeOH and thrice from CH_2Cl_2-MeOH; m.p. 225-6° (Found: C, 69·02; H, 4·43; N, 4·83; OCH_3, 0·0. $C_{17}H_{13}NO_4$ requires C, 69·14; H, 4·44; N, 4·74%); IR (nujol): 1680



, 1660 cm^{-1} (—CO—N)<; λ_{max} 228, 302 mμ (log ε 4·65, 3·86). Silica TLC plates of the mother liquors showed that the deaminated product, 6-methoxy-N-(3,4-methylenedioxybenzoyl)-tetrahydroquinoline, was present in traces.

5,6-Dihydro-8-thia-4H-pyrido[3,2,1-*de*]*phenanthridine*-8,8-*dioxide* (XXXIII) — The Pschorr reaction was carried out on N-(2-aminobenzenesulphonyl)-1,2,3,4-tetrahydroquinoline (8·7 g) by the usual method to give 7 g neutral product. This was chromatographed on 50 g silica gel in benzene; the column was developed with the same solvent and fractions of 50 ml collected. Fractions 3-6 yielded 4·4 g crystalline material which was crystallized from CH_3COCH_3 to give 2·1 g (25%) of XXXIII, m.p. 131-3° (Found C, 66·76; H, 4·96; N, 4·97. $C_{15}H_{13}NO_2S$ requires C, 66·41; H, 4·83; N, 5·16%); λ_{max} 232, 270, 314 mμ (log ε 4·40, 4·13, 3·71).

The mother liquors showed on silica TLC plates, besides some of the cyclic product and minor impurities, a significant amount of N-benzenesulphonyl-1,2,3,4-tetrahydroquinoline, m.p. 65-67°.

Pschorr reaction on 5-acetyl-N-(2-aminobenzoyl)-indoline (XXXVII) — Diazotization and subsequent attempted cyclization of the amine XXXVII (2·8 g) yielded as the neutral crystalline product, 5-acetyl-N-benzoylindole (XL) (0·35 g, 13%), m.p. 115-16° (Found: C, 77·65; H, 4·94; N, 5·59. $C_{17}H_{13}NO_2$ requires C, 77·55; H, 4·98; N, 5·32%); IR (nujol): 1665 ($COCH_3$), 1680 cm^{-1} (—CO—N<); λ_{max} 236, 260, 312 mμ (inflex.) (log ε 4·45, 4·44, 3·67). The phenolic product, 5-acetyl-N-salicyloylindoline (0·4 g, 14%) was crystallized from MeOH, m.p. 138-40° (Found: C, 72·50; H, 5·68; N, 5·27. $C_{17}H_{15}NO_3$ requires C, 72·58; H, 5·37; N, 4·98%); IR (nujol); 3060 (OH), 1670 ($COCH_3$), 1620 cm^{-1} (—CO—N<) λ_{max} 220 (inflex.), 296 (inflex.), 316 mμ (log 4·25, 4·25, 4·39).

Pschorr reaction on N-(2-aminobenzoyl)-3,3-dimethylindoline (XXXVIII) — Diazotization and attempted ring closure of the amine (XXXVIII) (5·3 g) gave XLI in the neutral part, about 1·3 g, which crystallized from MeOH, m.p. 201-3° (Found: C, 76·55, 76·53; H, 6·56, 6·57; N, 5·15. $C_{17}H_{17}NO_2$ requires C, 76·38; H, 6·41; N, 5·24%); IR (nujol): 3160 (OH), 1610 cm^{-1} (C=O); λ_{max} 258, 284 (inflex.) mμ (log ε 4·15, 3·99).

The phenolic product (about 2·6 g, 50%) was N-salicyloyl-3,3-dimethylindoline which crystallized from dil. MeOH, m.p. 132-4° (Found: C, 76·15; H, 6·29. $C_{17}H_{17}NO_2$ requires C, 76·38; H, 6·41%). The mother liquor from the crystallization of the neutral part showed on silica plate the presence of N-benzoyl-3,3-dimethylindoline. An authentic sample for comparison was made by Schotten-Baumann benzoylation of 3,3-dimethylindoline and crystallized from MeOH, m.p. 113-14° (Found: C, 81·55; H, 7·17; N, 5·85. $C_{17}H_{17}NO$ requires C, 81·24; H, 6·82; N, 5·57%).

N-Benzoyl-2,6-dimethyl-8-nitro-1,2,3,4-tetrahydroquinoline (XXXIV) — Schotten-Baumann benzoylation of 2,6-dimethyltetrahydroquinoline (16·1 g) gave the N-benzoate (26·1 g), m.p. 98-102°. The benzoate (5·3 g) was added in small lots to 40 ml ice-cold conc. HNO_3 during 15 min. The resultant solution was left at 0° for ½ hr and poured into excess ice-water. The precipitate was collected, washed with hexane, and crystallized from MeOH (5·2 g), m.p. 159-61°, raised to 161-2° (Found: C, 69·70; H, 6·00; N, 8·76. $C_{18}H_{18}N_2O_3$ requires C, 69·66; H, 5·85; N, 9·03%).

8-Amino-N-benzoyl-2,6-dimethyl-1,2,3,4-tetrahydroquinoline (XXXV) — A solution of the above nitro compound (15·5 g) in MeOH (400 ml) was shaken in an Ente apparatus with hydrogen at 1 atm pressure and 50° in the presence of Adam's catalyst (0·2 g). Hydrogen uptake ceased in 68 hr and corresponded only to 70%. The solution was filtered from catalyst and concentrated to a small volume, when crystals (~1 g), m.p. 195-200°, separated. This could not be identified and was discarded. The mother liquor was evaporated, the residue taken up in EtOAc and saturated with HCl gas. The gummy product became crystalline with EtOH and recrystallized from EtOH-ether to give the desired amine hydrochloride (11·4 g), m.p. 200-205° (d.) (Found: C, 68·10; H, 6·48; N, 9·16. $C_{18}H_{21}ClN_2O$ requires C, 68·23; H, 6·68; N, 8·84%); IR (nujol): negligible C=O peak; λ_{max} 208, 242, 298 mμ (log ε 4·46, 4·35, 4·15). The free base was crystallized from benzene-ether; m.p. 127-30° (Found: C, 76·69; H, 7·56. $C_{18}H_{20}N_2O$ requires C, 77·11; H, 7·19%); IR (nujol): 3060, 3300 cm^{-1} (OH, NH), negligible C=O.

Attempted Pschorr reaction on (XXXV) — The reaction was carried out as usual on the hydrochloride of XXXV (6·4 g). Negligible neutral and phenolic products were obtained. Instead, an oily base (3·5 g) was isolated which gave a crystalline hydrochloride (3 g), m.p. 255-8°. The product (XXXVI) was recrystallized from alcohol-ether, m.p. 259-60° (Found: C, 71·94; 6·78; N, 8·90. $C_{18}H_{19}ClN_2$ requires C, 72·36; H, 6·41; N, 9·28%); IR: no C=O peak; λ_{max} 208, 244, 298 mμ (log ε 4·48, 4·18, 4·19).

5,6-Dihydro-2-nitro-8-oxo-4H-pyrido[3,2,1-*de*]*phenanthridine* (XXVIII) — Addition of 5,6-dihydro-8-oxo-4H-pyrido[3,2,1-*de*]phenanthridine (2·2 g) to ice-cold conc. HNO_3 gave an oil which was left for 15 min at room temperature. Upon warming on the water-bath for 5 min, the oil became crystalline. The mixture was cooled, diluted with water and filtered. The precipitate was recrystallized from CH_2Cl_2-CH_3COCH_3 to yield the nitro compound XXVIII (2·4 g); m.p. 224-7° (Found: C, 68·76; H, 4·54; N, 9·74. $C_{16}H_{12}N_2O_3$ requires C, 68·56; H, 4·32; N, 10·00%).

The methyl analogue XXIX was likewise obtained (from CH_2Cl_2-MeOH), m.p. 252-4° (Found: C, 69·44; H, 4·76; N, 9·20. $C_{17}H_{14}N_2O_3$ requires C, 69·37; H, 4·80; N, 9·52%).

2-Amino-5,6-dihydro-6-methyl-8-oxo-4H-pyrido[3,2,1-*de*]*phenanthridine* (XXX) — A suspension of the above nitro compound XXIX (2·4 g) in MeOH (100 ml) was charged into a Paar apparatus and hydrogenated at 50 lb/sq. in. and at 50°, using palladium-charcoal catalyst (10%; 0·5 g), for 4 hr. The filtered solution was concentrated to a small volume, diluted with ether and saturated with dry HCl gas. The resultant hydrochloride (1·9 g) was crystallized twice from EtOH-EtOAc, m.p. 292-8° (d.) (Found: C, 67·57; H, 5·74; N, 8·94. $C_{17}H_{17}ClN_2O$ requires C, 67·89; H, 5·70; N, 9·32%).

XXX yielded a phenylurea (from MeOH), m.p. 218-20° (Found: C, 75·00; H, 5·63; N, 11·28. $C_{24}H_{21}N_3O_2$ requires C, 75·17; H, 5·52; N, 10·96%).

2-*Chloracetylamino*-5,6-*dihydro*-6-*methyl*-8-*oxo*-4*H*-*pyrido*[3,2,1-*de*]*phenanthridine* — Amine (5·3 g) was refluxed with chloracetyl chloride (2·3 g) and triethylamine (5 ml) in $CHCl_3$ (100 ml) for 6 hr and left overnight. The solvents were removed *in vacuo* and the residue washed with water and ether. Recrystallization from MeOH afforded the desired chloracetyl derivative (5·5 g), m.p. 226-8° (Found: C, 66·96; H, 5·26; N, 8·48. $C_{19}H_{17}ClN_2O_2$ requires C, 66·95; H, 5·03; N, 8·22%).

5,6 - *Dihydro* - 2 - (α- *N* - *hexamethyleneiminoacetyl*) - 6-*methyl*-8- *oxo*-4*H* - *pyrido*[3,2,1-*de*]*phenanthridine* — A mixture of the above chloracetyl derivative (3·4 g) and hexamethyleneimine (4 g) became warm. After ½ hr, $CHCl_3$ (100 ml) was added and the mixture heated under reflux for 4 hr. After thorough washing with water, the $CHCl_3$ solution was evaporated and triturated with hexane to give the desired compound, 3·6 g, m.p. 165-70°; 172-4° after two crystallizations from methanol (Found: C, 74·36; H, 7·15; N, 10·23. $C_{25}H_{29}N_3O_2$ requires C, 74·41; H, 7·24; N, 10·41%).

Reduction of 5,6-*dihydro*-8-*oxo*-4*H*-*pyrido*[3,2,1-*de*]-*phenanthridine* (XVII) — To a stirred suspension of lithium aluminium hydride (2·5 g) in dry THF (50 ml) was added (XVII, 2·1 g) in THF (10 ml). The mixture was heated under reflux for 6 hr, left overnight at room temperature, diluted with ether and decomposed with water. The dried organic layer was evaporated to give the crude product (1·9 g) which was chromatographed on a column of silica gel (25 g) using benzene-$CHCl_3$ (1:1) for elution. Evaporation of the eluate gave a waxy, unstable base (1·7 g). The perchlorate salt of XXIV upon crystallization from MeOH melted at 231-3° (Found: C, 59·65; H, 4·78; N, 4·52. $C_{16}H_{16}ClNO_4$ requires C, 59·72; H, 5·01; N, 4·36; and $C_{16}H_{14}ClNO_4$ requires C, 60·09; H, 4·42; N, 4·40%); λ_{max} 212, 247, 330 mμ (log ε 4·42, 4·56, 3·94); NMR (DMSO-d_6): C-8H, 10·17 (*s*); aromatics 7H, 7·9-9·2 (*m*); C_6-CH_2, 5·05 (*t*), C-4 CH_2 3·40 (*t*) C_5-CH_2 2·5 ppm (*m*).

The iodide on crystallization from MeOH had m.p. 266-8° (d.); λ_{max} 216, 244, 330, 360 mμ (inflex.) (log ε 4·51, 4·56, 3·94, 3·49) (Found: C, 55·22; H, 4·54; N, 4·06. $C_{16}H_{14}IN$ requires C, 55·34; H, 4·06; N, 4·03; and $C_{16}H_{16}IN$ requires C, 55·03; H, 4·61; N, 4·01%).

Reduction of 5,6-*dihydro*-6-*methyl*-8-*oxo*-4*H*-*pyrido*[3,2,1-*de*]*phenanthridine* — The phenanthridone (XVIII, 3·8 g) was reduced as before with lithium aluminium hydride (1·5 g). The total crude product (2·2 g) was converted to the hydrochloride and crystallized from absolute EtOH. The first crop (1·5 g) had m.p. 179-85°. After recrystallization from EtOH, washing with EtOAc and ether and drying at 80° *in vacuo* overnight, the chloride A (XXV) had m.p. 255-60° (sintering above 228°) (Found: C, 74·78; H, 7·17; N, 5·04. $C_{17}H_{18}ClN$ requires C, 75·11; H, 6·67; N, 5·15%); λ_{max} 212, 248, 334, 368 (inflex.) mμ (log ε 4·35, 4·51, 3·89, 3·49); NMR (D_2O): C_8-H 9·30 (*s*); aromatics 7H 7·0-8·0 (*m*), C_6-H 5·0 (unresolved *m*), C_4-CH_2 2·9 (unresolved, *m*), C-5 CH_2 2·1 (unresolved *m*) and CH_3 1·35 ppm (*d*, *J* = 7 *cps*). The mother liquor from the original crystallization was concentrated to a small volume and treated with ether to give a crop (1·5 g), m.p. 107-15°, which was triturated with EtOH to remove the hydrochloride A. The filtrate was treated with ether to give a second product B (XXVI), m.p. 277-9°, raised to 282-4° (d.) by a second crystallization from EtOH-ether (Found: C, 70·39; H, 6·99; N, 4·98. $C_{17}H_{20}ClNO$ requires C, 70·46; H, 6·96; N, 4·83%).

In a second reduction, the crude product (4·7 g) was chromatographed over 25 g silica. The product eluted by benzene-$CHCl_3$ (1:1) weighed 3 g and gave a salt corresponding to the product XXV. The fraction (0·9 g) eluted by EtOAc gave the hydrochloride of XXVI, m.p. 282-4° (d.).

The iodide from A had m.p. 272-5° (d.) (from MeOH) (Found: C, 56·69; H, 4·77; N, 3·70%) and was identical with the iodide from B, m.p. 272-5° (d.) (from MeOH) (Found: C, 56·78; H, 4·96; N, 3·70. $C_{17}H_{16}IN$ requires C, 56·52; H, 4·47; N, 3·88; and $C_{17}H_{18}IN$ requires C, 56·15; H, 4·99; N, 3·88%).

5,6-*Dihydro*-2-*methoxy*-10,11-*methylenedioxy*-4*H*, 8*H*-*pyrido*[3,2,1-*de*]*phenanthridine* (XXIII) —Reduction of the phenanthridone (XXI, 2·8 g) with lithium aluminium hydride (2 g) in THF (100 ml) as above, using moist ether for subsequent decomposition, gave the ether-sparingly soluble product (XXIII, 2·4 g) which crystallized from MeOH. The substance was homogeneous on silica TLC, but melted with a wide range, m.p. 135-60° (Found: C, 73·29, 73·00; H, 5·87, 5·75; N, 4·61. $C_{18}H_{17}NO_3$ requires C, 73·20; H, 5·80; N, 4·74%); IR: no OH, NH, C=O peaks; λ_{max} 210, 262, 280, 368 mμ (log ε 4·53; 4·48, 4·34, 4·05).

NaBH$_4$ *reduction of the phenanthridinium salt* (VI) — A solution of the iodide (0·2 g) in 5 ml MeOH was treated with $NaBH_4$ (50 mg) during 1 hr. The crystalline product that separated was filtered off, washed with water and recrystallized from EtOH; yield 80 mg; m.p. 130°, discolouring and softening above 110° (Found: C, 79·50; H, 5·76; N, 4·63. $C_{22}H_8ClN$ requires C, 79·62; H, 5·47; N, 4·22%); λ_{max} 226, 254, 365 mμ (log 4·38, 4·40, 3·67); NMR: Aromatics 11H, 6·5-8·0 (*m*); C_8-H, 5·27 (*s*), C_6-CH_2 3·15 (*t*), C_4-CH_2 2·68 (*t*) and C_5-CH_2 1·93 ppm (unresolved *m*).

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