Tetrahedron Vol 24, pp 2517 to 2525 Pergamon Press 1968 Printed in Great Britain

THE REACTION OF 1-β-ARYLETHYL-2-PYRIDONES AND OF 2-β-ARYLETHYLISOCARBOSTYRILS WITH PHOSPHORUS OXYCHLORIDE

D. W. BROWN, S. F. DYKE, W. G. D. LUGTON and (in part) A. DAVIS

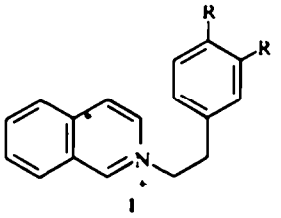
(*Received in the UK* 31 *August* 1967; *accepted for publication* 14 *September* 1967)

Abstract – The previously reported reactions of some 1-β-arylethyl-2-pyridones (**1a**) and 2-β-arylethylisocarbostyrils (**4**) with phosphorus oxychloride have been shown to yield, not the cyclized products, but the 2-chloropyridinium and 1-chloroisoquinolinium salts respectively.

IN A previous paper[1] we showed how the procedure established[2] for the cyclization of an N-(β-arylethyl)1,2-dihydroisoquinoline (**2**) to a berbine derivative **3** could be simplified and yields improved, and we also described a novel cyclization of an N-(β-arylethyl)isocarbostyril (**4**) to a 8-oxoberbine (**5**). All attempts to cyclize the parent 1,2-dihydroisoquinoline (**2a**) gave[3] instead a dimeric compound, whereas treatment of **4a** with mineral acid led only to recovered starting material. When, however, the isocarbostyril **4a** was dissolved in a mixture of HCl, H_3PO_4 and $POCl_3$ ("old" phosphorus oxychloride), allowed to stand for 1 hr, the excess $POCl_3$ removed and an aqueous solution of the residue was basified with ammonia, a 90% yield of a new base, $C_{17}H_{16}N_2$, m.p. 107° was obtained. The compound was further characterized as the hydrochloride and as the methiodide, $C_{18}H_{18}N_2I$. The base absorbed at 3320 and 1640 cm^{-1} in the IR and its NMR spectrum (in $CDCl_3$ soln) was found to be almost identical with that of **4a** itself; the only obvious difference was the presence, in the spectrum of the new base, of a concentration-dependant one proton singlet between 6·0–7·0 ppm, removable by deuteration. Reduction of the base with LAH followed by $NaBH_4$, or by catalytic hydrogenation, gave N-(β-phenethyl)1,2,3,4-tetrahydroisoquinoline (**6**). These facts are consistent with structures **7**, **8** and **9** for the base, the hydrochloride and methiodide respectively. Presumably $POCl_3$ converts **4a** into the 1-chloroisoquinolinium salt (**10**) which, with NH_3, gives **7**.

Previous reports in the literature suggest[4] that when N-alkylisocarbostyrils are treated with $POCl_3$ they are dealkylated, with the formation of 1-chloroisoquinolines, but in marked contrast to this Akahoshi[5] stated that **4a** undergoes cyclization to the 8,9-dihydrodibenzo[a,h]quinolizinium salt (**11a**) when heated with $POCl_3$. This formulation was supported by an elemental analysis, which corresponded to $C_{17}H_{14}N.3H_2O$, and by analogy with previous work on N-(β-arylethyl)α-pyridones (see later). Catalytic hydrogenation of the cyclization product gave[6] a tetrahydro compound, hydrochloride, m.p. 217°. Akahoshi reported when **11a** is treated with aqueous Na_2CO_3 or NaOH, the isocarbostyril (**4a**) is regenerated. It is difficult to provide a mechanistic interpretation of this ring-opening reaction, and in view also of our own results outlined above, Akahoshi's work was repeated.

Treatment of **4a** with $POCl_3$ as described gave an iodide m.p. 162 (Akahoshi reports m.p. 115°), whose UV spectrum is identical with that of **1a**. Treatment of this



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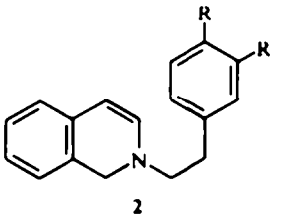

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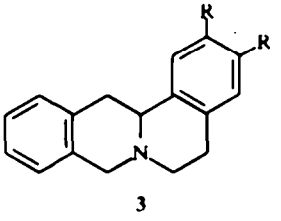

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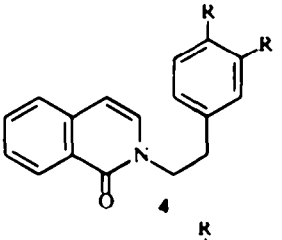

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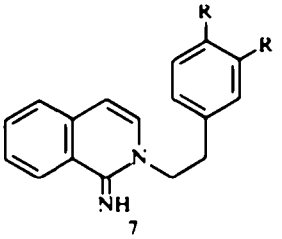

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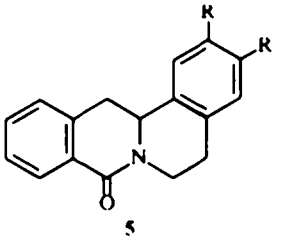

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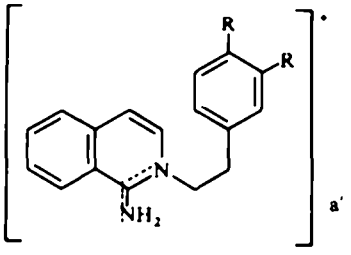

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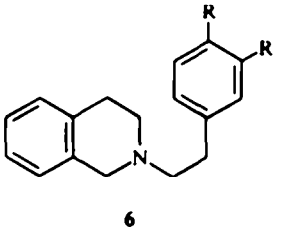

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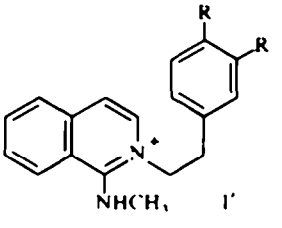

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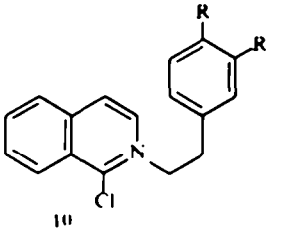

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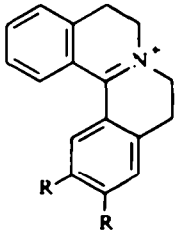

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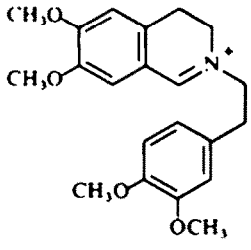
a: R = H.
b: R, R = CH_2O_2

compound with NH_3 gave the imine **7a** whereas catalytic hydrogenation yielded a tetrahydro compound, hydrochloride, m.p. 227° identical with **6a**, obtained by reducing **1a** with $NaBH_4$. The so-called cyclization product must, therefore, be the 1-chloroisoquinolinium salt (**10a**); its NMR spectrum is consistant with this, and in particular exhibits a five-proton singlet at 7·2 ppm attributed to a Ph group.

N-β-(3,4-Methylenedioxyphenylethyl)isocarbostyril (**4b**), on treatment with $POCl_3$ gave a product, m.p. 178° to which Akahoshi assigned the structure **11b**, without proof. Repetition of Akahoshi's procedure here yielded a substance, m.p. 166–168° which was not very stable, but whose UV spectrum is similar to that of **1b**, and whose NMR spectrum (Fig. 1) is diagnostic for the 1-chloroisoquinolinium salt (**10b**). Catalytic hydrogenation of **10b** gave a tetrahydro compound which was shown (IR spectra and mixed m.p. of the hydrochlorides) to be identical with **6b** obtained by reducing **1b** with $NaBH_4$.

The oxidation of the 3,4-dihydroisoquinoline (**12**) with pot.ferricyanide is reported[7] to yield the unstable dihydroisocarbostyril (**13**) which was not characterized, and this, with $POCl_3$ is claimed to cyclize to **14**; catalytic hydrogenation was then thought to lead to **15**, hydrochloride m.p. 236°, hydroiodide, m.p. 207°. We also found that the oxidation of **12** gave a red-brown oil, but on trituration with ethanol it gave some unchanged starting material together with a new base which we showed (IR spectra and mixed m.p.) to be identical with the tetrahydroisoquinoline (**16**) obtained by reducing **12** with $NaBH_4$. No neutral material corresponding to **13** could be found. When **16** was treated with $POCl_3$ the base was simply converted into the hydrochloride m.p. 231°. The hydroiodide, m.p. 207° was also characterized. Sugasawa,[7] then, did not form the dihydroisocarbostyril and his so-called cyclization product must be the tetrahydroisoquinoline (**16**).



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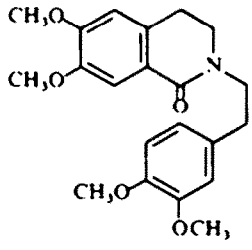

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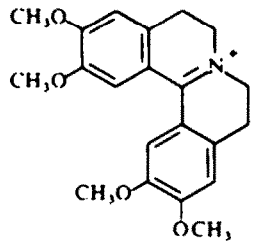

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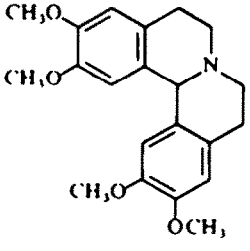

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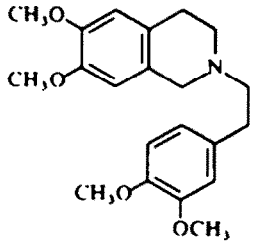

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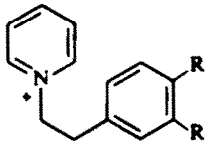
Now Akahoshi's structural assignments seem to have been made by analogy with previous reports on the behaviour of N-β-aryl ethyl-2-pyridones (**18**) when reacted with $POCl_3$; 6,7-dihydrobenzo[a]quinolizinium salts (**19**) were reported to be formed in most cases. The first cyclization reaction of this type appears to be due to Sugasawa and Sugimoto[8] who claimed, without proof that **19b** is formed from **18b**. Later this reaction was extended to the 8,9-dimethoxy-,[9] 8,11-dimethoxy-[9,10] and 8-methyl-10,11-dimethoxy-[9] derivatives, but again no proof of structure was offered. The parent system **19a** was reported in 1952 and catalytic hydrogenation to a hexahydro derivative (**20**) was described. When the methiodide of **20** was oxidized, phthalic acid was claimed to be among the products.*



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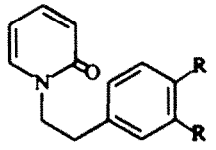

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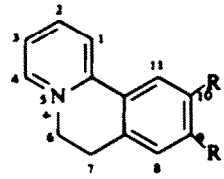

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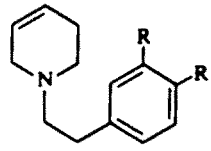
a: R = H
b: R, R = CH_2O_2
c: R = OMe.



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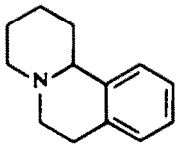

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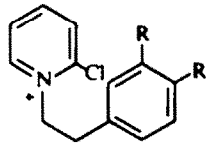

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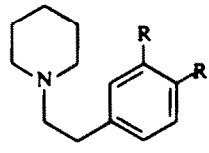

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We repeated the reaction of **18a** with $POCl_3$ and isolated a quarternary salt characterized as the iodide and picrate whose m.ps are the same as those described[11] for **19a**. However, the UV spectrum of our product is almost identical with that of **17a** and the NMR spectrum (Fig. 2) is consistant with structure **22a**; an elemental analysis (especially for chlorine *and* iodine) on the iodide supports this. Catalytic hydrogenation of the $POCl_3$ product was carried out as described[11] and a base, its hydrochloride, picrate and methiodide were obtained in agreement with the previous work. The product, however, was shown (superimposable IR spectra and mixed m.ps) to be identical with **23a**, which was obtained either directly from **17a** by catalytic hydrogenation, or by reducing **17a** with $NaBH_4$ to **24a**, followed by catalytic hydrogenation.

Sugasawa[8] was unable to prepare the pyridone **18c** from **17c**, but in our hands **18c** was easily prepared by oxidation of **17c** with pot. ferricyanide and on treatment with

* Since this paper was accepted for publication we have found a note by Sugasawa and Akahoshi (*Chem. Pharm. Bull.* 7, 263 (1959)) in which the previously claimed cyclizations of (**18a**) and (**18b**) were withdrawn, and the 2-chloropyridinium ion structures (**22a**) and (**22b**) respectively were proposed

$POCl_3$ it gave the quaternary salt **22c** and not a cyclized material. The identity of **22c** was established as described above for the parent series.

A whole series of closely related cyclizations of α-pyridones, carbostyrils and isocarbostyrils appear in the literature, especially from Sugasawa's group, and in view of the above findings the structures of the products described must remain in doubt until each cyclization reaction has been re-investigated. We are in the process of reviewing several examples and our findings will be reported in due course.

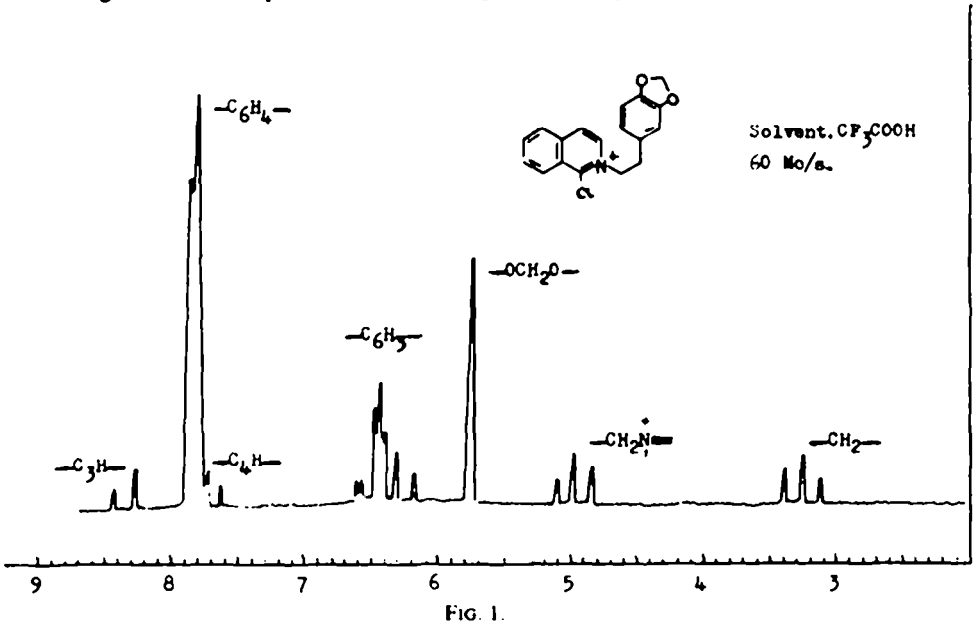

FIG. 1.

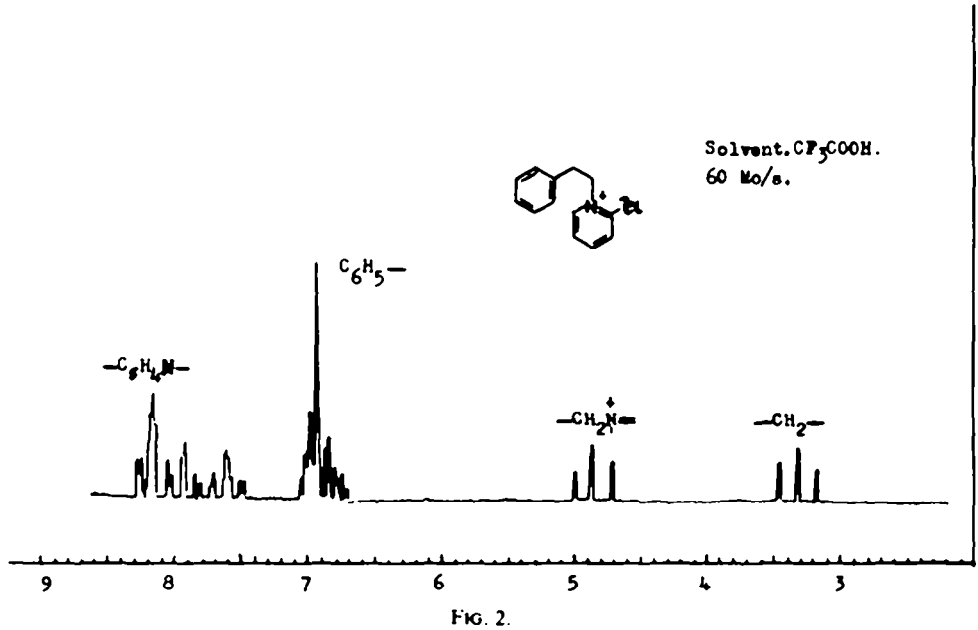

FIG. 2.

EXPERIMENTAL

M ps are uncorrected.

1-Imino-2-β-phenylethyl-1,2-dihydroisoquinoline **7**

Compound **4a** (9·5 g) was dissolved in $POCl_3$ (30 ml) and allowed to stand for 1½ hr at room temp. Excess $POCl_3$ was distilled, the residue poured into hot water and the cooled soln extracted with ether. The aqueous phase was basified with 0·880 NH_4OH and the organic material extracted into CH_2Cl_2. The dried extracts were evaporated to give a brown residue which was extracted by heating with successive portions (4 × 50 ml) of pet. ether (60–80°). The combined extracts were evaporated to a low bulk and on cooling **7** (8·1 g) was obtained as white plates m.p. 102–104°. Recrystallization from pet. ether raised this to 106–107°; ν_{max} (Nujol) 3320, 1635, 1610 cm^{-1} (Found: C, 82·5; H, 6·5; N, 11·15. $C_{17}H_{16}N_2$ requires: C, 82·2; H, 6·5; N, 11·3%.) **7** methiodide was obtained as stout yellow needles from EtOH m.p. 158–159°; ν_{max} (Nujol) 3200 (broad), 1645, 1615 cm^{-1}. (Found: C, 55·4; H, 4·85; N, 7·05; I, 32·6. $C_{17}H_{16}N_2 \cdot MeI$ requires: C, 55·4; H, 4·9; N, 7·2, I, 32·5%.)

1-Amino-2-β-phenylethylisoquinolinium chloride (**8**)

The base **7** (1·0 g) was dissolved in acetone (10 ml) and conc HCl (0·5 ml) added. The oil which separated yielded a white solid on scratching which separated from EtOH acetone as chunky prisms (0·9 g) m.p. 215–217° ν_{max} (Nujol) 3320, 3000, 1660, 1640 cm^{-1}. (Found: C, 71·3; H, 5·9; N, 9·55; Cl, 12·3. $C_{17}H_{16}N_2 \cdot HCl$ requires: C, 71·7; H, 6·0; N, 9·85, Cl, 12·4%.)

Reductions of 1-imino-2-β-phenylethyl-1,2-dihydroisoquinoline (**7a**) *to 2-β-phenylethyl-1,2,3,4-tetrahydroisoquinoline* (**6a**)

(i) The imine **7a** (0·4 g) was dissolved in ether (20 ml), treated with LAH (0·2 g) and the mixture stirred and heated under reflux for 10 hr. Excess LAH was decomposed with water when a strong smell of NH_3 was detected. The wet ethereal layer was decanted and evaporated to yield a pale yellow oil (λ_{max} 330 mμ) which was immediately dissolved in aqueous EtOH (10 ml) and treated with $NaBH_4$ (0·2 g) and the mixture heated on a steam bath for 30 min. The EtOH was allowed to evaporate and the aqueous residue was extracted with ether, the ethereal layer was evaporated and the residual oil treated with acetone (4 ml) and conc HCl (3 drops), when a white solid was obtained which separated from EtOH as white needles (0·2 g) m.p. 227 (Lit.[3] m.p. 227°). This material is identical to that obtained by $NaBH_4$ reduction of **1a**.

(ii) The imine **7a** (0·4 g) was dissolved in EtOH (20 ml) and shaken with Adams' catalyst (50 mg) under H_2 at 30 psi for 16 hr. The soln was filtered and evaporated. The residual oil was dissolved in acetone (10 ml) and treated with conc HCl (3 drops). The white solid so produced was collected and recrystallized from EtOH as white needles of **6a** hydrochloride (0·3 g) m.p. 227°. By an identical procedure **6a** hydrochloride (0·2 g) was obtained from **9a** (0·4 g).

Reaction of 2-β-phenylethylisocarbostyril with $POCl_3$

The isocarbostyril **5a** (1·5 g) was converted by the method of Akahoshi[5] to a quaternary iodide (1·5 g) which on rapid recrystallization from MeOH by the addition of ether (3 vol) yielded bright yellow needles of **10a** m.p. 161–162°; λ_{max} 232, 274, 343 mμ (ε 50,000; 6000; 6000) in EtOH; NMR (CF_3COOH) ppm 3·9 (2H, tr),* 5·3 (2H, tr), 7·3 (5H, broad s), 8–8·5 (5H, complex) 9·3 (1H, ½AB, 7 c/s). (Found: Cl, 7·6; I, 37·3. $C_{17}H_{15}NClI$ requires: Cl, 9·0; I, 32·1%.) Compound **1a** λ_{max} 234, 276, 343 (broad) mμ (ε 57500; 4600; 4600).

Reduction of 1-chloroisoquinolinium iodide **10a**

The quaternary salt (0·29) obtained above by the method of Akahoshi[5] was dissolved in air free EtOH (50 ml) and shaken with Adams' catalyst (50 mg) under H_2 at 45 psi for 20 hr. The soln was filtered, basified with ammonia and evaporated. The residue was dissolved in ether and filtered and the filtrate evaporated, the resulting oil was treated with acetone (5 ml) and conc HCl (2 drops) and the solid material so obtained filtered. Recrystallization from EtOH yielded *N-β-phenylethylisoquinoline*(**6**)*hydrochloride* (0·1 g) m.p. 226–227°. (Found: C, 74·8; H, 7·2; N, 4·9. Calc. for $C_{17}H_{20}NCl$: C, 74·6; H, 7·3; N, 5·1%.)

* tr (triplet); s (singlet); m (multiplet).

2-β-(3,4-*Methylenedioxy*) *ethylisocarbostyril* (**4b**)

The salt **1b** (3·0 g) was dissolved in water (40 ml) and heated on a water bath. A soln of KOH (10 g) and $K_3Fe(CN)_6$ (4 g) in water (40 ml) was added dropwise with stirring and reaction mixture maintained at 90° for a further 30 min. The organic material was extracted into ether. The combined ether extracts were dried and evaporated and the residual solid recrystallized from benzene–pet. ether (60–80°) to yield the isocarbostyril as colourless cubes (1·5 g) m.p. 89·91° (Lit.[5] 91 92°).

Reaction of 2-β-(3,4-*methylenedioxyphenyl*) *ethylisocarbostyril* (**4b**) *with* $POCl_3$

Compound **4b** (1·2 g) was reacted with $POCl_3$ according to the method of Akahoshi.[5] The product was recrystallized from EtOH (1 vol) by the addition of ether (3 vol) giving **10b** (1·1 g) m.p. 166–168°; λ_{max} 236, 288, 340 mμ. Analysis as perchlorate (Found: C, 52·8; H, 4·1; N, 3·2 $C_{18}H_{15}NO_2Cl\cdot ClO_4$ requires: C, 52·45; H, 3·7; N, 3·45%.) Compound **1b** λ_{max} 236, 285, 336 mμ.

Reduction of 1-*chloro*-2-β-(3,4-*methylenedioxyphenyl*) *ethylisoquinolinium iodide* (**10b**)

The quaternary salt (0·2 g) obtained above by the method of Akahoshi[5] was dissolved in air free EtOH (50 ml) and hydrogenated at 45 psi in the presence of Adams' catalyst (50 mg) for 20 hr. The work up employed was as described for the unsubstituted **6a**. **6b** Hydrochloride (80 mg) was obtained as white needles from EtOH, m.p. 220–221°.

2-β-(3,4-*Methylenedioxyphenyl*) *ethyl*-1,2,3,4-*tetrahydroisoquinolinium* (**6b**) *hydrochloride*

The salt **1b** (1·0 g) was dissolved in 20% aqueous EtOH (25 ml). $NaBH_4$ (0·25 g) was added and the soln heated for 1 hr on the steam bath. The soln was poured into water (100 ml) and extracted with ether. The combined extracts were dried and evaporated and the resulting oil treated with a few drops of conc HCl.

The bromide **12** (1·0 g) was reduced with $NaBH_4$ (0·3 g) in the usual way to yield **16** hydrochloride C, 68·0; H, 6·3; N, 4·4, Cl, 11·2. $C_{18}H_{20}NO_2Cl$ requires: C, 67·9; H, 6·4; N, 4·55; Cl, 11·4%.) This material was identical, mixed m.p. and IR, with that obtained by catalytic reduction of **10b**.

The reaction of 2-β-(3,4 *dimethoxyphenyl*) *ethyl*-3,4-*dihydro*-6,7-*dimethoxyisoquinolinium bromide* (**12**) *with* $K_3Fe(CN)_6$

The salt **12** was reacted with $K_3Fe(CH)_6$ using the procedure of Sugasawa *et al.*[7] when an oily product (3·0 g) was obtained. Trituration of the product yielded a base which recrystallized from EtOH to give **16** as white plates (1·0 g) m.p. 113°; hydrochloride; white needles from EtOH m.p. 233°. (Found: C, 63·7; H, 7·3; N, 3·35; Cl, 8·8. $C_{21}H_{23}NO_4Cl\cdot\frac{1}{2}C_2H_5OH$ requires: C, 64·2; H, 7·15; N, 3·55; Cl, 9·05%; Sugasawa's[7] **15** hydrochloride– Found: C, 63·7; H, 7·0; N, 3·3%). Hydroiodide: white needles from EtOH m.p. 208°.

The salt **12** (5·0 g) was again reacted with $K_3Fe(CN)_6$ to yield a red oil (3·0 g) which was immediately treated with $POCl_3$ according to the method of Sugasawa.[7] The salt (2·0 g) obtained was dissolved in water basified with ammonia and the base liberated, extracted into ether. The combined extracts were dried and evaporated and the residue was recrystallized from EtOH to yield white plates (1·0 g) m.p. 113° undepressed on mixture with **16** obtained directly from the $K_3Fe(CN)_6$ oxidation; hydrochloride m.p. 233°.

2-β-(3,4-*Dimethoxyphenyl*) *ethyl*-1,2,3,4-*tetrahydro*-6,7-*dimethoxyisoquinoline* (**16**)

The bromide **12** (1·0 g) was reduced with $NaBH_4$ (0·3 g) in the usual way to yield **16** hydrochloride (0·75 g) from EtOH m.p. 234–235°. **Base 16** from EtOH m.p. 113° (Found: C, 70·6; H, 7·65; N, 4·0. $C_{21}H_{26}NO_4$ requires: C, 70·75; H, 7·35; N, 3·95%.) The free base and its hydrochloride were identical (mixed m.p., IR superimposible) with those obtained from $Fe(CN)_6^{4-}$ treatment of **12** and from $Fe(CN)_6^{4-}$–$POCl_3$ treatment of **12**.

1-β-*Phenylethyl*-2-*pyridone* (**18a**)

The pyridone **18a** (6·2 g) m.p. 103–105° (Lit[11] 104–105°) was prepared from **17a** by the method of Sugasawa;[11] ν_{max} (Nujol) 1665, 1595, 1545 cm^{-1} NMR (CF_3COOH) ppm. 3·05 (2H, tr), 4·4 (2H, tr), 6·7–7·3 (8H, m), 7·6–7·9 (1H, m, C_3).

Reaction of 1-β-*phenylethyl*-2-*pyridone* (**18a**) *with* $POCl_3$

Compound **18a** (3 g) was reacted with $POCl_3$ (12 g) according to the method of Sugasawa[11] to yield a white solid (4·7 g) m.p. 188–189° which crystallized from MeOH as clusters of small white needles of 1-β-phenylethyl-2-chloropyridinium iodide m.p. 193–194° [Lit.[11] "(22)" 191–192°]; picrate, yellow needles,

EtOH m.p. 135–137° (Lit.[11] m.p. 137°); λ_{max} 276 mμ (ε 6600) in EtOH ν_{max} (Nujol) 1610, 1560, 1500, 1490 cm^{-1}; NMR (CF_3COOH) ppm 3·3 (2H, tr), 4·9 (2H, tr), 6·75–7·1 (5H, m) 7·5–8·3 (4H, m, pyridyl). (Found: C, 45·35; H, 3·85; N, 4·22; Cl, 10·5; I, 36·5. $C_{13}H_{13}NClI$ requires: C, 45·15; H, 3·80; N, 4·05; Cl, 10·25; I, 36·7%.)

Reductions of 1-β-*phenylethyl-2-chloropyridinium iodide* (**22a**)

The iodide (3·0 g) in MeOH (240 ml) was hydrogenated:

(i) At 30 psi over a sample of Adam's catalyst (50 mg) of very low activity for 16 hr. The soln was filtered and concentrated to low bulk when 1-β-phenylethylpyridinium iodide (2·1 g) m.p. 162–163° was obtained identical (mixed m.p. and IR comparison) with authentic material.

(ii) The iodide (0·5 g) in EtOH (250 ml) was hydrogenated over Adam's catalyst at 45 psi for 16 hr. The soln was filtered and the solvent evaporated under vacuum. The residue was triturated with acetone and the brown solid (0·38 g) so obtained was recrystallized from EtOH to yield 1-β-phenylethylpiperidine hydroiodide m.p. 196–198° (Lit.[11] "(20)" hydroiodide m.p. 193–195°) identical with the material obtained by the $NaBH_4$ followed by Pt/H_2 reduction of **17a**.

Sodium borohydride reduction of 1-β-*phenylethyl pyridinium bromide* (**17a**)

The bromide **17a** (3·6 g) in EtOH (35 ml) was added dropwise with stirring to a soln of $NaBH_4$ (1·1 g) in water (15 ml) containing 5N NaOH (3 drops). The soln was stirred for 14 hr and the EtOH then removed under vacuum. The residue was treated with water (100 ml) and extracted with ether. The combined extracts were water washed, dried and evaporated leaving **24a** as a colourless oil (2·1 g). The methiodide was obtained from EtOH as broad white needles m.p. 181–182°. (Found: C, 51·2; H, 5·9; N, 4·0; I, 39·0. $C_{14}H_{20}NI$ requires: C, 51·1; H, 6·1; N, 4·25; I, 38·55%.) The hydrochloride was obtained as colourless hygroscopic needles from EtOH m.p. 204–206°; NMR (CF_3COOH) ppm contained 5·4, 5·6, 5·75, 5·95 (2H, broad absorptions). The hydroiodide was obtained from EtOH as cream plates m.p. 182–184°.

The above hydroiodide of **24a** (0·5 g) was hydrogenated over Adams' catalyst in EtOH (200 ml) for 16 hr. The soln was filtered and evaporated to a low bulk when **23** hydroiodide (0·4 g) separated as cream plates m.p. 196–198°. The hydrochloride of **23** (0·3 g) was obtained from **24** hydrochloride (0·5 g) by the same reduction procedure as colourless needles m.p. 226–228° [Lit.[11] "(20)" hydrochloride 214–216° hygroscopic]. The methiodide was obtained as long colourless needles from MeOH m.p. 182° (Lit.[11] "(20)" methiodide m.p. 180°). (Found: C, 51·0; H, 7·0; N, 3·95; I, 37·9. $C_{14}H_{22}NI$ requires: C, 50·8; H, 6·7; N, 4·25; I, 38·3%.) The picrate was obtained as bright yellow needles from MeOH m.p. 149–150° [Lit.[11] "(20)" picrate 148–148·5°].

1-β-(3,4-*Dimethoxyphenyl*) *ethyl-2-pyridone* (**18c**)

Compound **17c** (13·6 g) dissolved in water (50 ml) was treated rapidly under N_2 with $K_3Fe(CN)_6$ (60 g) in water (140 ml). The dark brown soln was stirred for 30 min. KOH (73 g) in water (60 ml) was then added dropwise so that the temp of the reaction mixture remained below 40°. The temp of the reaction mixture was then raised to 65° and there maintained for 1 hr, cooled shaken with benzene ((200 ml), filtered and the organic layer separated. The aqueous layer was extracted with benzene and the combined extracts dried and evaporated to leave a dark oil (9·5 g), which solidified after some days. A portion was recrystallized from benzene petrol (60–80°) giving **18c** as pale brown needles m.p. 67–68°. λ_{max} (Nujol) 1663, 1580, 1510 cm^{-1} NMR (CF_3COOH) ppm 3·1 (2H, tr), 3·75 (3H, s), 3·78 (3H, s), 4·55 (2H, tr), 6·55 (1H, s), 6·4 and 6·55 (1H, ½AB broad), 6·65 and 6·8 (1H, ½AB), 6·9–7·6 (3H, m), 7·85–8·05 (1H, m, C_3). (Found: C, 69·55; H, 6·75; N, 5·7. $C_{13}H_{17}NO_3$ requires: C, 69·5; H, 6·6; N, 5·4%.)

Reaction of 1-β-(3,4-*dimethoxyphenyl*) *ethyl-2-pyridone with* $POCl_3$

A soln of the crude pyridone (3 g) and the $POCl_3$ (8 ml) was heated at 120° for 1½ hr. Excess $POCl_3$ was distilled under vacuum and the dark residue was triturated with pet. ether (60–80°) (2 × 15 ml) and then acetone (10 ml) to yield a grey hygroscopic solid 3·6 g which was dried *in vacuo* at 50°. This material was dissolved in water (90 ml) filtered and excess KI added to the soln when **22c** (2·1 g) was precipitated. This yielded small yellow needles from EtOH m.p. 167–168°; λ_{max} (Nujol) 1607, 1588, 1565, 1500 cm^{-1}; NMR (CF_3COOH) ppm 3·3 (2H, tr), 3·8 (6H, s), 5·0 (2H, tr), 6·4 and 6·55 (1H, ½AB, 7·5 c/s, meta-split 1·5 c/s), 6·7 (1H, d, 1·5 c/s), 6·65 and 6·8 (1H, ½AB, 7·5 c/s), 7·5–8·4 (4H, m). (Found: C, 44·65; H, 4·15; N, 3·35; Cl, 8·55; I, 31·55. $C_{13}H_{17}NO_2ClI$ requires: C, 44·4; H, 4·20; N, 3·45; Cl, 8·75; I, 31·3%.)

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