A NEW HETEROCYCLIC RING CLOSURE IN FERRICYANIDE OXIDATION OF 2,4,6-TRIPHENYLPYRIDINIUM SALTS

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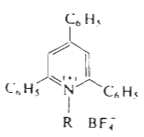
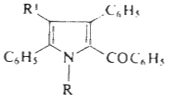
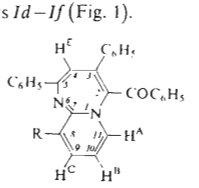
The quaternary pyridinium salts *Ia*–*Ic* react with alkaline solution of potassium ferricyanide to give the condensed heterocyclic derivatives *IIIa, b, IV*, whereas the salts *Id*–*If* give the pyrrole derivatives *IIa*–*IIc* under the same conditions. The diaza heterocycle *IIIa* reacts with methyl iodide to give methoiodide *V*, whereas by action of bromine it produces two monobromo derivatives *VIa, b*. The pyrrole derivatives *IIa, b* give monobromo derivatives *IId, e* on bromination. A probable mechanism of formation of the heterocyclic derivatives is discussed.

Oxidation of 1-substituted-2,4,6-triphenylpyridinium salts with aliphatic or aromatic 1-substituent by action of alkaline solution of potassium ferricyanide gives high yields of substituted pyrrole derivatives[1,2] type *II*. In the context of a systematical study of oxidation of substituted quaternary pyridinium salts it was interesting to find the oxidation course in the case of the quaternary salts *Ia*–*If* having heterocyclic substituent at 1-position. The obtained results are dealt with in the present communication. It was found that the ferricyanide oxidation of quaternary salts *Ia*–*Ic* gave the compounds *IIIa,b*, *IV* which differ considerably in their spectra from the pyrrole derivatives *IIa*–*IIc* formed from the salts *Id*–*If* (Fig. 1).





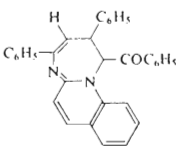


Ia, R = 2-pyridyl
Ib, R = 3-methyl-2-pyridyl
Ic, R = 2-chinolyl
Id, R = 3-pyridyl
Ie, R = 4-pyridyl
If, R = 3-chinolyl

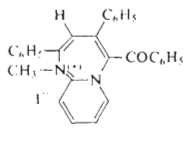
IIa, R = 3-pyridyl, R^1 = H
IIb, R = 4-pyridyl, ^{1} = H
IIc, R = 3-chinolyl, R^1 = H
IId, R = 3-pyridyl, R^1 = Br
IIe, R = 4-pyridyl, R^1 = Br

IIIa, R = H^D
IIIb, R = CH_3

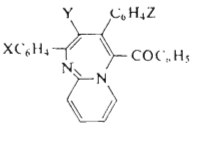
It is presumed generally[3,4] that, in the ferricyanide oxidation of quaternary salts, the primary substrate being oxidized is the 2-hydroxy-1,2-dihydro derivative (pseudobase) formed by addition of OH^- ion to α position of the pyridinium cation. Following this presumption, we assigned structure *IIIa* to the reaction product formed from salt *Ia*, and its formation through the intermediate *VIIa* is explained by the



IV

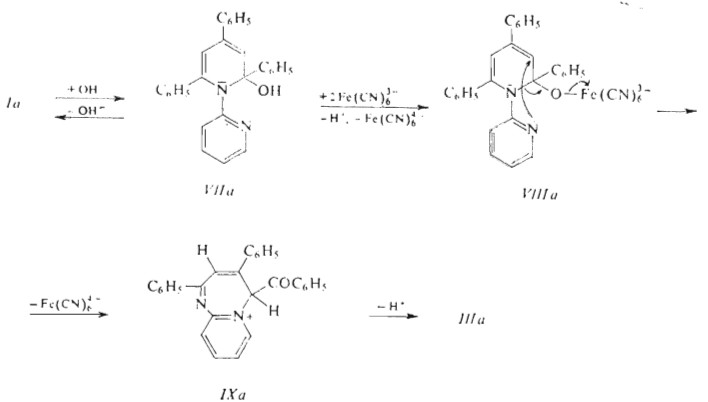


V



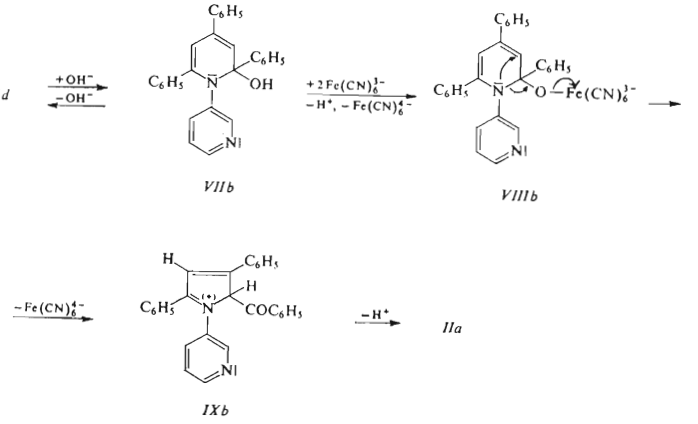
VIc, X = Y = H, Z = Br
VId, X = Z = H, Y = Br
VIe, Y = Z = H, X = Br

mechanism given in Scheme 1. The nitrogen atom of the 1-substituent acts here as a nucleophilic centre enabling subsequent cyclization of the intermediate *VIIIa* to the heterocycle *IXa* which gives compound *IIIa* on deprotonation. In the same way we also explain formation of the other condensed derivatives and assign to them the structures *IIIb* and *IV*. A different situation is encountered in the oxidation



SCHEME 1

of the quaternary salt *Id*. From Scheme 2 it is obvious that the distance between nitrogen atom of the 1-substituent and the electrophilic centre in the intermediate *VIIIb* is so great that the intramolecular cyclization analogous to the transformation *Ia* → *IIIa* cannot take place. Therefore, another mechanism makes itself felt in which nitrogen atom of the original pyridinium ion acts as the nucleophilic centre in the



SCHEME 2

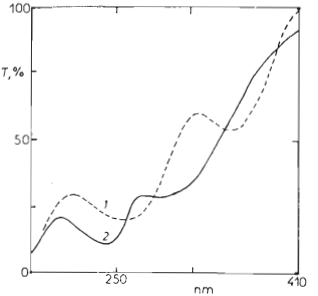


FIG. 1

Ultraviolet spectra of compounds *IIa* (*1*) and *IIIa* (2) in ethanol, $c = 2{\cdot}5 \cdot 10^{-5}$ mol l^{-1}

recyclization giving thus the pyrrole derivative *IIa via* the intermediate *IXb*. For similar reasons, the quaternary salts *Ie,f* give the expected pyrrole derivatives *IIb,c* on oxidation.

Compound *IIIa* reacts with methyl iodide to give the quaternary salt to which we ascribe the structure *V*. This assignment is supported by the presumption that the attacked homonuclear nitrogen atom in compound *IIIa* is one of pyridine type with nonconjugated electron pair, and, hence, it can represent the nucleophilic centre in the reaction with alkylating agent. On the contrary, the other nitrogen atom

TABLE I
The oxidation products of salts *Ia—If*

Compound M.p., °C	Formula (mol. mass)	Calculated/Found % C	% H	% N	ν(C=O), cm^{-1} ($CHCl_3$)	δ, ppm C^2HCl_3
IIa 194—196	$C_{28}H_{20}N_2O$ (400·5)	83·97 83·96	5·03 5·36	6·99 6·71	1 630	6·60 s (1 H), 7·0—8·4 m (19 H)
IIb 200—202	$C_{28}H_{20}N_2O$ (400·5)	83·97 84·13	5·03 5·29	6·99 6·81	1 630	6·59 s (1 H), 6·9—8·6 m (19 H)
IIc 212—214	$C_{32}H_{22}N_2O$ (450·5)	85·31 85·07	4·92 4·92	6·22 6·07	1 625	6·64 s (1 H), 7·0—8·7 m (21 H)
IId 202—203	$C_{28}H_{19}BrN_2O$ (479·4)	70·16 70·33	3·99 3·81	5·84 5·76	1 635	7·0—8·5 m (19 H)
IIe 225—226	$C_{28}H_{19}BrN_2O$ (479·4)	70·16 70·45	3·99 4·30	5·84 5·89	1 635	6·9—8·5 m (19 H)
IIIa 163—165	$C_{28}H_{20}N_2O$ (400·5)	83·97 84·15	5·03 5·05	6·99 6·92	1 655	6·65 t (1 H) 7·0—7·7 m (19 H)
IIIb 68—70	$C_{29}H_{22}N_2O$ (414·5)	84·03 83·71	5·35 5·30	6·76 6·83	1 655	2·62 s (CH_3), 6·67 t (1 H), 6·8—7·7 m (18 H)
IV 218—219	$C_{32}H_{22}N_2O$ (450·5)	85·31 85·31	4·92 4·99	6·22 6·22	1 660	7·0—8·2 m (22 H)
V 185—186	$C_{29}H_{23}IN_2O$ (542·4)	64·21 64·02	4·27 4·25	5·16 4·81	1 660	4·9 s (CH_3), 7·2—7·5 m (20 H)
VIa[a] 182—184	$C_{28}H_{19}BrN_2O$ (479·4)	70·16 70·10	3·99 4·07	5·84 5·78	1 665	6·75 t (1 H), 7·0—7·5 m (18 H)
VIb[a] 189—191	$C_{28}H_{19}BrN_2O$ (479·4)	70·16 70·23	3·99 4·22	5·84 5·90	1 665	7·04 t (1 H), 7·13—7·8 m (18 H)

[a] Measured in hexadeuteriodimethyl sulphoxide.

of the *IIa* molecule is involved in delocalization of its free electron pair by interaction with p-orbitals of the adjacent carbon atoms (pyrrole type), which should suppress its nucleophilicity and, hence, also its reactivity to methyl iodide. Action of bromine on the pyrrole derivatives *IIa,b* produces exclusively the monobrominated derivatives *IId,e* substituted in the pyrrole ring. On the contrary, bromination of *IIIa* gave two monobromo derivatives *VIa,b* which we ascribe a probable structure corresponding to two out of three possible formulae *VIc,d,e*. Properties of all the compounds prepared are given in Table I.

Comparison of ^{1}H NMR spectra of compounds *IIIa,b* measured at 360 MHz in hexadeuteriodimethyl sulphoxide made it possible to assign the six-line signal at $\delta = 6{\cdot}65$ ppm of spectrum of *IIIa* to the proton H^B. The splitting of each component of the H^B triplet by interaction with H^D proton ($J_{BD} = 1{\cdot}4$ Hz) cannot take place in compound *IIIb* (R = CH_3), and, accordingly, the H^B signal in spectrum of *IIIb* is only a triplet formed by interaction with the H^A and H^C protons. The spectrum of *IIIa* also shows a singlet at $\delta = 7{\cdot}8$ ppm corresponding, by its integral intensity, to one H^E proton. Also the ^{13}C NMR spectrum of *IIIa* in deuteriochloroform agrees with the suggested structure (Table II). As in the 200 MHz spectra of compounds *VIa,b* (measured in dimethyl sulphoxide) the one-proton signal H^B shows the same multiplicity as that of compound *IIIa*, it is concluded that the bromination did not take place in the six-membered ring of the bicyclic molecule *IIIa*. Although the measurements of the mentioned ^{1}H NMR spectra of compounds *IIIa*, *VIa,b* were carried out at the same conditions, none of the derivatives *VIa,b* shows a one-proton signal analogous to that of H^E of compound *IIIa*. Besides the resolved H^B signal, the spectra of compounds *VIa,b* consist of a multiplet of 18 protons. In the mass spectra of the derivatives *VIa,b* bromine is only contained in the mole-

TABLE II
^{13}C NMR spectrum of the derivative *IIIa*

δ, ppm[a]	$^2J_{CH}$, Hz	Atom	δ, ppm[a]	$^2J_{CH}$, Hz	Atom
112·4, d	45	C(10)	133·6, s	–	quart. C_6H_5 at C(3)
117·4, d	47	C(8)	137·7, s	–	C(3)
124·6, d	50	C(9)	138·0, s	–	quart. C_6H_5CO
125·0, d	45	C(11)	141·6, s	–	C(5)
127·6–129·2, m	[b]	tert-C_6H_5	145·7, s	–	C(2)
130·4, s	–	quart. C_6H_5 at C(3)	146·1, s	–	C(7)
132·3, d	45	C(4)	190·9, s	–	C=O

[a] d doublet, s singlet, m multiplet; [b] it could not be determined due to overlapped absorptions.

cular ions with m/z 478 and 480. The fragments with lower ratios m/z contain no bromine. As the base peak of the mass spectra of compounds *VIa,b* is the ion $m/z = 105$ ($C_6H_5CO^+$), it is presumed that bromination of *IIIa* could take place at the H^E atom or at some of the adjacent phenyl groups.

The obtained results show that the previously described[1,2] oxidation of 1,2,4,6-substituted pyridinium salts with ferricyanide can lead to heterocyclic systems type *III* and *IV* in the cases of suitable choice of the 1-substituent.

EXPERIMENTAL

The temperature data are not corrected. The melting points were measured with a Boetius apparatus. The UV spectra were measured with a Specord UV-VIS apparatus, the IR spectra were measured with a Perkin–Elmer 325 apparatus, the mass spectra were measured with an LKB 9000 apparatus at 70 eV, the NMR spectra were measured with a Varian XL-100 and XL-200 and with a Bruker HX-360 apparatus.

Quaternary Salts *I*

1-(2-*Pyridyl*)-2,4,6-*triphenylpyridinium tetrafluoroborate* (Ia): Mixture of 5·7 g 2,4,6-triphenylpyrylium tetrafluoroborate, 1·7 g 2-aminopyridine, and 15 ml ethanol was stirred at 20°C 4 h, After standing overnight and addition of 75 ml ether, 6·5 g (96%) salt *Ia* was collected by suction, m.p. 227—228°C (ethanol). For $C_{28}H_{21}BF_4N_2$ (472·1) calculated: 71·24% C, 4·48% H, 5·93% N; found: 71·04% C, 4·3% H, 6·02% N. ^{1}H NMR spectrum, $CDCl_3$, δ(ppm): 7·0—8·2 m, 21 H.

1-(3-*Methyl*-2-*pyridyl*)-2,4,6-*triphenylpyridinium tetrafluoroborate* (Ib): Mixture of 2·5 g 2,4,6-triphenylpyrylium tetrafluoroborate, 2·0 ml 2-amino-3-methylpyridine and 40 ml chloroform was boiled 8 h. After evaporation in vacuum, the residue was recrystallized from ethanol–ether mixture. Yield 0·4 g (13%), m.p. 132—134°C. For $C_{29}H_{23}BF_4N_2$ (486·1) calculated: 71·65% C, 4·77% H, 5·76% N; found: 71·63% C, 4·67% H, 5·81% N. ^{1}H NMR spectrum, heptadeuteriodimethylformamide, δ(ppm): 2·02 s CH_3, 7·3—8·6 m 18 H, 8·86 s 2 H.

1-(2-*Quinolyl*)-2,4,6-*triphenylpyridinium tetrafluoroborate* (Ie): Mixture of 0·4 g 2,4,6-triphenylpyrylium tetrafluoroborate, 0·2 g 2-aminoquinoline, and 10 ml toluene was boiled 2 h. The separated oil waw removed, washed with ether, and crystallized from ethanol. Yield 0·37 g (70%), m.p. 242—244°C. For $C_{32}H_{23}BF_4N_2$ (522·4) calculated: 73·58% C, 4·44% H, 5·36% N; found: 73·50% C, 4·44% H, 5·55% N. ^{1}H NMR spectrum, $CDCl_3$, δ(ppm): 7·0—8·0 m 21 H, 8·06 s 2 H.

1-(3-*Pyridyl*)-2,4,6-*triphenylpyridinium tetrafluoroborate* (Id): Mixture of 5·0 g 2,4,6-triphenylpyrylium tetrafluoroborate, 2·0 g 3-aminopyridine, and 30 ml ethanol was boiled 8 h. The crystalline solid precipitated on cooling was collected by suction, washed with ether, and recrystallized from methanol. Yield 4·0 g (67%), m.p. 284—286°C. For $C_{28}H_{21}BF_4N_2$ (472·1) calculated: 71·24% C, 4·48% H, 5·93% N; found: 71·40% C, 4·60% H, 5·86% N. ^{1}H NMR spectrum, heptadeuteriodimethylformamide, δ(ppm): 7·2—8·9 m 19 H, 8·76 s 2 H.

1-(4-*Pyridyl*)-2,4,6-*triphenylpyridinium tetrafluoroborate* (Ie): 50 ml ether was added to a mixture of 2·5 g 2,4,6-triphenylpyrylium tetrafluoroborate and 1·0 g 4-aminopyridine. After 24 h stirring with exclusion of moisture, the precipitated solid was collected by suction and recrystallized from methanol. Yield 2·5 g (84%), m.p. 310—313°C. For $C_{28}H_{21}BF_4N_2$ (472·1) calculated:

71·24% C, 4·48% H, 5·93% N; found: 71·15% C, 4·35% H, 5·71% N. ^{1}H NMR spectrum, heptadeuteriodimethylformamide, δ(ppm): 7·4—8·6 m (19 H), 8·79 s (2 H).

1-(3-*Quinolyl*)-2,4,6-*triphenylpyridinium tetrafluoroborate* (If): Mixture of 4·0 g 2,4,6-triphenylpyrylium tetrafluoroborate, 2·5 g 3-aminoquinoline, and 30 ml ethanol was boiled 2 h. The solid separated on standing overnight was collected by suction, washed with ether, and recrystallized from ethanol. Yield 3·5 g (66%), m.p. 345—348°C. For $C_{32}H_{23}BF_4N_2$ (522·4) calculated: 73·58% C, 4·44% H, 5·36% N; found: 73·50% C, 4·44% H, 5·55% N. ^{1}H NMR spectrum, heptadeuteriodimethylformamide, δ (ppm): 7·2—9·1 m (21 H), 8·86 s (2 H).

Oxidation of the Salts *I*

Ia: Solution of 5 g salt *Ia* in 200 ml ethanol was boiled and treated with solution of 10 g potassium ferricyanide and 2·5 g potassium hydroxide in 50 ml water. After 5 min boiling, the mixture was diluted with 400 ml water and extracted with 3 × 50 ml chloroform. The solvent was evaporated, and the residue was recrystallize from ethanol. Yield 3·0 g (71%) *IIIa*, orange crystals.

Ib: Solution of 0·6 g potassium ferricyanide and 0·3 g potassium hydroxide was added to the boiling solution of 0·3 g salt *Ib* in 20 ml ethanol. After 5 min boiling, the mixtue was diluted with 100 ml water and extracted with 3 × 50 ml chloroform. The solvent was evaporated, and the evaporation residue was submitted to column chromatography (silica gel, benzene + 5% methanol) to give 0·18 g (70%) *IIIb*.

Ic: Solution of 4·0 g potassium ferricyanide and 1·0 g potassium hydroxide in 20 ml water was added to solution of 2·0 g salt *Ic* in 80 ml ethanol. After 5 min boiling, the mixture was diluted with 300 ml water and extracted with 3 × 50 ml chloroform. The extract was evaporated in vacuum, and the residue was recrystallized from ethanol to give 1·3 g (75%) crystalline *IV*.

Id: Solution of 5·0 g potassium ferricyanide and 2·5 g potassium hydroxide in 250 ml water was added to a boiling solution of 3·0 g salt *Id* in 250 ml ethanol. After 10 min boiling, the mixture was diluted with 250 ml water, cooled, and the precipitated yellow solid was collected by suction. Recrystallization from ethanol gave 2·5 g (98%) *IIa*.

Ie: Similar to above procedure (salt *Id*), we obtained 1·1 g (87%) *IIb* from 1·5 g *Ie* in 150 ml ethanol and 3·0 g potassium ferricyanide with 1·5 g potassium hydroxide in 150 ml water.

If: Solution of 3·0 g potassium ferricyanide and 1·5 g potassium hydroxide in 90 ml water was added to boiling solution of 1·5 g *If* in 90 ml ethanol. After 30 min boiling, the mixture was diluted with 200 ml water, extracted with 3 × 50 ml chloroform, the extract was evaporated, and the residue was recrystallized from ethanol to give 1·0 g (77%) *IIc*.

Reaction of *IIIa* with Methyl Iodide

Mixture of 0·5 g *IIIa*, 2 ml methanol, and 5 ml methyl iodide was boiled 11 h. After evaporation in vacuum, the residue was recrystallized from methanol to give 0·4 g (59%) V.

Reactions with Bromine

IIa: Bromine was added to solution of 0·8 g *IIa* in 10 ml chloroform until permanent brown colouration. After 1 h standing at room temperature, the mixture was evaporated in vacuum. The evaporation residue was dissolved in 30 ml chloroform, the solution was washed with sodium hydrogen carbonate and with water and evaporated in vacuum. The evaporation residue was recrystallized from ethanol to give 0·5 g (52%) *IId*.

IIb: The same procedure as with *IIa* was applied to 0·8 g *IIb* to give 0·8 g (84%) *IIe*.

IIIa: 1 ml bromine was added to solution of 1·5 g *IIIa* in 30 ml chloroform. After 2 h standing at room temperature, the mixture was evaporated in vacuum, and the residue was dissolved in 30 ml chloroform. The solution was extracted with 5% sodium hydrogen sulphite, washed with water, and evaporated. The residue was purified by column chromatography (silica gel, benzene with 5% ethyl acetate), to give 0·4 g starting *IIIa*, 0·55 g (42%) *VIa*, and 0·40 g (30%) *VIb*.

Mass spectra, *m/z* (% r.i.): *IIa*: 401 (100), 384 (5), 372 (4), 323 (28), 295 (5), 191 (14), 105 (38), 77 (24). *IIb*: 401 (100), 400 (20), 384 (2), 372 (5), 324 (10), 323 (39), 306 (4), 295 (3), 191 (17), 105 (26), 77 (22). *IIIa*: 401 (19), 400 (4), 322 (13), 295 (100), 218 (7), 200 (4), 191 (7), 105 (30), 77 (33). *IIIb*: 415 (27), 398 (1), 387 (1), 338 (8), 300 (100), 208 (6), 105 (13), 77 (12). *IV*: 451 (40), 374 (12), 345 (100), 322 (13), 267 (17), 204 (13), 128 (32), 105 (39), 77 (40). *VIa*: 480 (8), 478 (8), 400 (25), 399 (25), 346 (8), 321 (8), 294 (10), 293 (10), 292 (10), 291 (10), 105 (100), 77 (25). *VIb*: 480 (6), 478 (6), 400 (25), 399 (22), 321 (11), 294 (6), 293 (11), 292 (16), 291 (19), 105 (100), 77 (39).

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