OXIDATIVE ELIMINATION OF TERT-BUTYL GROUP FROM α POSITION OF QUATERNARY PYRIDINIUM SALTS

Petr NESVADBA and Josef KUTHAN

Department of Organic Chemistry,
Prague Institute of Chemical Technology, 166 28 Prague 6

Received February 5th, 1982

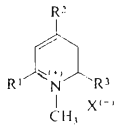
Ferricyanide oxidation of 1-methyl-2-tert-butyl-4,6-diphenylpyridinium tetrafluoroborate (*I*) and its 2,6-ditert-butyl analogue (*II*) is accompanied by elimination of the 2-substituent with formation of the corresponding 2-pyridones *VII* and *VIII*, respectively. On the contrary, oxidation of quaternary salt *III* with tert-butyl group at 4 position gives a complex reaction mixture from which a small amount of pyrrole derivative *IX* only could be isolated.

Oxidation of quaternary pyridinium salts having non-substituted α positions with alkaline ferricyanide solution is a standard method for preparation of 2-pyridones[1,2]. The reaction fails[3], if there are methyl groups at the both α positions, formation of less stable 2-methylene-1,2-dihydropyridine being preferred which undergoes fast decomposition reactions. If α and γ positions are substituted with phenyl groups, the reaction is smooth again, but the pyridine cycle is contracted to pyrrole derivatives[4,5].

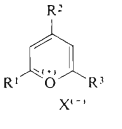
In connection with these findings we were interested in the ferricyanide oxidation of such derivatives which, having one or two tert-butyl groups at α positions, cannot be deprotonated to anhydrobases. For this purpose we investigated the oxidation of 1-methyl-2-tert-butyl-4,6-diphenylpyridinium tetrafluoroborate (*I*) and 1-methyl-2,6-ditert-butyl-4-phenylpyridinium tetrafluoroborate (*II*). For comparison we also oxidized a salt with the examined substituent at γ position, *i.e.* 1-methyl-4-tert-butyl-2,6-diphenylpyridinium perchlorate (*III*). The results obtained are dealt with in the present communication.

The starting 1-methylpyridinium salts *I*–*III* were prepared by reaction of methylamine[6] with pyrilium salts *IV*–*VI*, and the reaction with potassium hydroxide was carried out at mildly elevated temperatures in analogous way as in refs[4,5]. The products were isolated by crystallization or preparative column chromatography and were identified by IR and ^{1}H NMR and mass spectra.

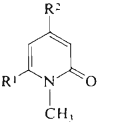
It is commonly accepted[1,2] that in the method used the primary oxidized substrate is not a pyridinium ion but its corresponding 2-hydroxy-1,2-dihydropyridine derivative (pseudobase). In the case of the asymmetrically substituted salt *I* we could expect



I–III



IV–VI



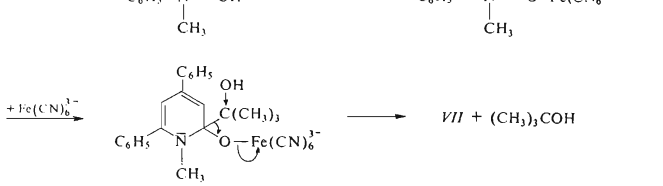
VII, VIII

I, $R^1 = R^2 = C_6H_5$, $R^3 = (CH_3)_3C$, X = BF_4
II, $R^1 = R^3 = (CH_3)_3C$, $R^3 = C_6H_5$, X = BF_4
III, $R^1 = R^3 = C_6H_5$, $R^2 = (CH_3)_3C$, X = ClO_4

IV, $R^1 = R^2 = C_6H_5$, $R^2 = (CH_3)_3C$, X = BF_4
V, $R^1 = R^3 = (CH_3)_3C$, $R^2 = C_6H_5$, X = BF_4
VI, $R^1 = R^3 = C_6H_5$, $R^2 = (CH_3)_3C$, X = ClO_4

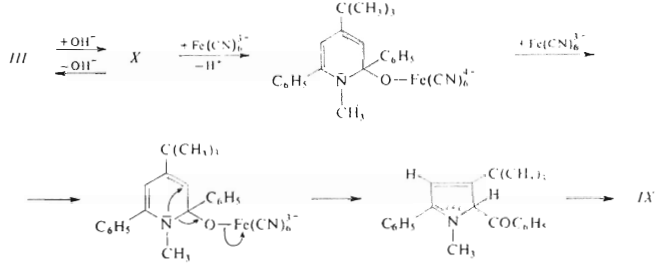
VII, $R^1 = R^2 = C_6H_5$
VIII, $R^1 = (CH_3)_3C$, $R^2 = C_6H_5$

two oxidation products from 2-hydroxy- and 6-hydroxyintermediate. From the reaction mixture it was possible to isolate 84% 1-methyl-4,6-diphenylpyridone (*VII*), wherefrom it follows that the 2-hydroxydihydroderivative predominantly underwent the oxidation with simultaneous elimination of tert-butyl group (as tert-butyl alcohol). The salt *II* also undergoes analogous oxidation to give 1-methyl-4-phenyl-6-tert-butyl-2-pyridone (*VIII*) which could be isolated in the yield 41%. The reaction can have a more general character; its postulated mechanism is given in Scheme 1. Similar CC bond splitting between a substituent and heterocyclic system, as far as we known, was observed in pyridine series in the cases of aromatization of dihydropyridine derivatives[7,8] and oxidative demethylation of quaternary pyridinium salts with alkyl



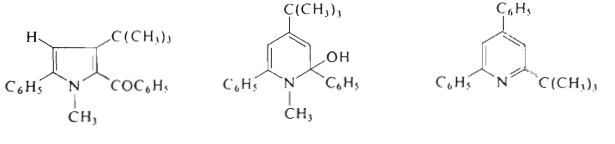
SCHEME 1

nitrites[9]. Behaviour of salt *III* was examined to verify whether analogous oxidative elimination of tert-butyl group can also take place at 4 position. In this case we could isolate only 18% 1-methyl-2-benzoyl-3-tert-butyl-5-phenylpyrrole (*IX*) from the complex reaction mixture. Hence it follows that the ferricyanide oxidation of compound *III* has similar course to that observed earlier[4,5] with 1-substituted 2,4,6-triphenylpyridinium cations. A likely mechanism of formation of compound *IX*, which is seen in Scheme 2, starts from primary formation of 2-hydroxy-1,2-dihydropyridine



SCHEME 2

derivative *X*. In this context it is worth mentioning that the 1-substituted 2,6-diphenylpyridinium cations, in which the formation of this type of intermediate could be still more significant, give very low yields of products of the ferricyanide oxidation[5]. Therefore is cannot be excluded that the participation of α position is significant from the point of view of reaction in ligand sphere of Fe ion. A condition of formation of the reactive complex is formation of the corresponding 2-hydroxy-1,2-dihydro derivative. This conclusion is also supported by our finding that the little electrophilic pyridine derivative *XI* (which does not form the respective 2-hydroxy-1,2-dihydro derivative under the reaction conditions) does not undergo the ferricyanide oxidation.



IX *X* *XI*

EXPERIMENTAL

The temperature data are not corrected. The melting points were determined on a Boetius apparatus; the ^{1}H NMR spectra were measured with a Varian XL-100 apparatus in deuteriochloroform with tetramethylsilane as internal standard (if not otherwise stated); the IR spectra were measured with a Perkin–Elmer 325 apparatus in chloroform; the mass spectra were measured with an LKB 9 000 apparatus at 70 eV. The gas chromatography was carried out with Chrom 3 apparatus.

Oxidation of Salt *I*

Solution of 7·7 g quaternary salt *I* in 250 ml ethanol was boiled and treated with solution of 19·6 g potassium ferricyanide and 10 g potassium hydroxide in 100 ml water. After 20 min boiling and stirring, the mixture was diluted with 300 ml water and extracted with 3 × 100 ml chloroform. The extract was dried with calcium chloride and evaporated to give 4·4 g (84%) pyridone *VII*, m.p. 89—91°C from benzene–light petroleum mixture. Ref.[10] gives m.p. 92°C. Mixed melting point with the authentic sample showed no depression. ^{1}H NMR spectrum, δ, ppm: 3·34 s (CH_3), 6·31 d (1 H, J = 2 Hz), 6·78 d (1 H, J = 2 Hz), 7·20—7·60 m (2 × C_6H_5).

Oxidation of Salt *II*

In analogy to the above experiment, solution of 1·85 g quaternary salt *II* in 100 ml ethanol was treated with solution of 3·34 g potassium ferricyanide and 5 g potassium hydroxide in 100 ml water. Yield of the isolated salt was 0·5 g (41%), m.p. 130—131°C (hexane). For $C_{16}H_{19}NO$ (241·3) calculated: 79·63% C, 7·94% H, 5·80% N; found: 79·93% C, 8·20% H, 5·67% N. ^{1}H NMR spectrum, δ, ppm: 1·51 s (C_4H_9), 3·61 s (CH_3), 6·48 d (1 H, J = 2 Hz), 6·70 d (1 H, J = 2 Hz), 7·40—7·70 m (C_6H_5). IR spectrum, ν(C=O), cm^{-1}: 1 653. Mass spectrum: *m/e* (r.i.): 241 (60), 226 (100), 199 (40), 198 (47), 185 (13), 184 (33), 116 (93), 82 (27).

Oxidation of Salt *III*

Boiling solution of 1 g salt *III* in 60 ml ethanol was treated with solution of 3·2 g potassium ferricyanide and 4 g potassium hydroxide in 60 ml water. After 3 h boiling and stirring the mixture was diluted with 400 ml water and extracted with 3 × 100 ml chloroform. The extract was evaporated and submitted to column chromatography on silica gel with chloroform as eluent to give 0·140 g (18%) pyrrole *IX*, m.p. 104—106°C (ethanol). For $C_{22}H_{33}NO$ (317·4) calculated: 83·24% C, 7·30% H, 4·41% N; found: 83·29% C, 7·53% H, 4·61% N. ^{1}H NMR spectrum, δ, ppm: 1·26 s (C_4H_9), 3·18 s (CH_3), 6·12 s (1 H), 7·20—7·85 m (2 × C_6H_5). IR spectrum, ν(C=O), cm^{-1}: 1 640. Mass spectrum: *m/e* (r.i. %): 317 (22), 316 (85), 302 (25), 301 (100), 297 (21), 296 (84), 273 (6), 272 (25), 271 (12), 270 (7), 233 (4), 144 (10), 129 (6), 115 (9), 105 (97), 91 (7), 77 (68), 51 (10).

1-Methyl-2,4-diphenyl-6-tert-butylpyridinium Tetrafluoroborate (*I*)

Suspension of 5·6 g pyrilium salt IV (ref.[11]) in 50 ml ethanol was treated with 4 ml 35% methylamine solution. After 7 h boiling and stirring the mixture was cooled and diluted with 300 ml ether to precipitate 5·2 g (89%) crystals, m.p. 238—239°C (ethanol). For $C_{22}H_{24}BF_4N$ (389·2) calculated: 67·88% C, 6·21% H, 3·60% N; found: 68·27% C, 6·19% H, 3·59% N. ^{1}H NMR spectrum (heptadeuteriodimethylformamide), δ, ppm: 1·80 s (t-C_4H_9), 4·28 s (CH_3), 7·60—8·50 m (12 H).

1-Methyl-2,6-ditert-butyl-4-phenylpyridinium Tetrafluoroborate (*II*)

Suspension of 7 g pyrilium salt *V* in 50 ml toluene was treated with 10 ml 20% methylamine solution in ether. After 10 h boiling and stirring the mixture was cooled and the precipitated crystals were collected by suction; yield 5·5 g (76%), m.p. 242–244°C (ethanol). For $C_{20}H_{28}BF_4N$ (369·2) calculated: 65·06% C, 7·64% H, 3·79% N; found: 65·45% C, 7·59% H, 3·79% N. ^{1}H NMR spectrum, δ, ppm: 1·72 s (2 × C_4H_9), 4·52 s (CH_3), 7·50–7·90 m (C_6H_5), 8·04 s (2 H).

1-Methyl-2,6-diphenyl-4-tert-butylpyridinium Perchlorate (*III*)

Suspension of 2 g perchlorate *VI* in 50 ml toluene was treated with 10 ml 20% metylamine solution in ether. After 5 h boiling and stirring the mixture was cooled, and the separated crystals were collected by suction; yield 1·5 g (73%), m.p. 212–214°C (ethanol). For $C_{22}H_{24}ClNO_4$ (401·9) calculated: 65·75% C, 6·02% H, 3·48% N, 8·82% Cl; found: 66·01% C, 6·02% H, 3·46% N, 8·80% Cl. ^{1}H NMR spectrum (heptadeuteriodimethylformamide), δ, ppm: 1·50 s (t-C_4H_9), 3·94 s (CH_3), 7·7–8·1 m (2 × C_6H_5), 8·14 s (2 H).

2,6-Ditert-butyl-4-phenylpyrilium Tetrafluoroborate (*V*)

Solution of 10 g 3,3-dimethyl-2-butanone and 37·2 g 1-phenyl-4,4-dimethyl-1-pentene-3-one in 50 ml 1,2-dichloroethane was treated with 40 ml 52% tetrafluoroboric acid solution in ether. After 4 h boiling the mixture was cooled and diluted with 300 ml ether to precipitate salt *V*, yield 8 g (22%), m.p. 227–230°C (ethanol). For $C_{29}H_{25}BF_4O$ (356·2) calulated: 64·07% C, 7·07% H; found: 64·14% C, 7·25% H. ^{1}H NMR spectrum, δ, ppm: 1·54 s (2 × t-C_4H_9), 7·70–8·20 m (7 H).

2,6-Diphenyl-4-tert-butylpyrilium Perchlorate (*VI*)

The Grignard reagent prepared from 3·86 g magnesium, 14·4 g tert-butyl chloride and 100 ml ether was treated with 7·5 g 2,6-diphenylpyrilium perchlorate[12]. After 1 h the mixture was poured onto 200 ml water. The organic layer was washed with water and evaporated in vacuum, the evaporation residue was dissolved in 25 ml acetic anhydride and treated with 3·7 g 1,3-diphenyl-2-propene-1-one and 5 ml 72% perchloric acid whereupon the mixture was left to stand at room temperature 24 h. The separated precipitate of 3·4 g (39%) raw salt *VI*, m.p. 230–231°C after repeated crystallizations from 1,2-dichloroethane and aqueous ethanol (charcoal). For $C_{21}H_{21}ClO_5$ (388·8) calculated: 64·87% C, 5·44% H, 9·12% Cl; found: 64·86% C, 5·43% H, 8·94% Cl. ^{1}H NMR spectrum (heptadeuteriodimethylformamide), δ, ppm: 1·65 s (t-C_4H_9), 7·75–8·75 m (2 × C_6H_5), 8·88 s (2 H).

Identification of Tert-Butyl Alcohol in Mixture after Oxidation of Salt *I*

Solution of 1 g salt *I* in 10 ml ethanol was refluxed and treated with solution of 4 g potassium ferricyanide and 1·25 g potassium hydroxide in 10 ml water. After 10 min boiling, 0·5 ml distillate was obtained in which tert-butyl alcohol was proved by gas chromatography.

Attempts to Oxidize Pyridine *XI*

Boiling solution of 0·17 g derivative *XI* (ref.[13]) in 10 ml ethanol was treated with solution of 0·42 g potassium ferricyanide and 0·5 g potassium hydroxide in 10 ml water. After 10 min boiling

the mixture was diluted with 50 ml water and extracted with 3 × 20 ml chloroform. TLC on Silufol could prove only the unchanged base *XI* in the chloroform extract.

The authors are indebted to workers of Central laboratories of the Institute for carrying out the elemental analyses and spectral measurements.

REFERENCES

1. Meislich H. in the book: *Pyridine and Its Derivatives* (M. Klingsberg, Ed.). Part 3, p. 596. Interscience, New York 1962.
2. Tieckelmann: *Pyridine and Its Derivatives*, Vol. 14, Supplement (R. A. Abramovitch, Ed.). Part 3, p. 706. Interscience, New York 1974.
3. Shaw E. N.: *Pyridine and Its Derivatives* (M. Klingsberg, Ed.). Part 2, p. 36. Interscience, London 1961.
4. Nesvadba P., Kuthan J.: Tetrahedron Lett. *21*, 3727 (1980).
5. Nesvadba P., Kuthan J.: This Journal *47*, 1494 (1982).
6. Katritzky A. R.: Tetrahedron *36*, 679 (1980).
7. Locv B., Snader K. M.: J. Org. Chem. *30*, 1914 (1965).
8. Giam Ch. S., Goodwin T. E., Rion K. F., Abbott S. D.: J. Chem. Soc., Perkin Trans. *1*, 1979, 3082.
9. Katritzky A. R., Patel R. C., Shanta M.: J. Chem. Soc., Perkin Trans. *1*, 1980, 1888.
10. El-Kholy I. E., Rafla F. K., Mishrikey M. M.: J. Chem. Soc., C, *1970*, 1578.
11. Dimroth K., Neubauer G., Möllenkamp H., Oosterloo G.: Chem. Ber. *90*, 1668 (1957).
12. Dorofeenko G. N., Lopatina N. A.: Khim. Geterosikl. Soedin. *1971*, 160.
13. Katritzky A. R., Thind S. S.: J. Chem. Soc., Perkin Trans. 1, *1980*, 1895.

Translated by J. Panchartek.