OXIDATION OF POLYSUBSTITUTED PYRIDINIUM SALTS

Petr Nesvadba and Josef Kuthan

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

Oxidation of 1-substituted 2,4,6-triphenylpyridinium salts $Ia-Ij$ with potassium ferricyanide in an alkaline medium was accompanied by contraction of the pyridine ring and formation of 1,2,3,5-tetrasubstituted pyrroles II. The derivative IIf underwent facile electrophilic substitution in the position 4. Contrary to compounds $Ia-Ij$, the 1-substituted-2,6-diphenylpyridinium salts $IIIa, b$ were oxidized to give a complex reaction mixture containing 4-pyridones IVa, b.

Reaction of alkaline potassium ferricyanide solution with quaternary pyridinium salts in which at least one of the positions 2,6 is unsubstituted represents a method of preparation of 2-pyridones[1]. Only a few examples of 4-pyridone formation are known[2], all giving only negligible yields. We found no mention about action of alkaline potassium ferricyanide solution on pyridinium salts containing phenyl groups in positions 2,6 or 2, 4, 6. It has been found recently[3] that oxidation of salts $Ia-Ij$ with hydrogen peroxide afforded — according to the type of substituent on the nitrogen atom — 3-amino-1,3-diphenyl-2-propen-1-one, pyridinium-3-olate or 1-substituted-2,3,5-triphenylpyrrole. As we have shown in our preliminary communication[4] (and are presenting in more detail in this paper), the salts $Ia-Ij$ are oxidized with ferricyanide solution to give pyrroles II (Table I). The same reaction can be realized also by action of silver oxide. Whereas compounds $If-Ii$, containing an aryl group in the position 1, gave high yields, the 1-alkyl derivatives $Ia-Ie$ under the same experimental conditions afforded only small amounts of the products $IIa-IIe$. This is in agreement with the observation that ferricyanide oxidation of the salts I, containing aliphatic substituents, requires a longer reaction time.

Contrary to compounds $Ia-Ij$, the 1-substituted-2,6-diphenylpyridinium salts $IIIa, b$ on reaction with ferricyanide afforded a complex mixture in which we were unable to detect pyrrole derivatives, analogous to the mentioned products II. The reaction gives the corresponding 4-pyridones IVa, b in about 30% yield.

It is known[5] that the first step in the oxidation of quaternary salts with ferricyanide in an alkaline medium consists in addition of OH^- ion to the quaternary cation. Formation of the pyrroles $IIa-j$ from the primarily formed 2-hydroxy--1,2-dihydro derivative (pseudobase) V can be visualized as depicted in Scheme 1.

The fact that in oxidation of the salts III we did not detect any analogues of compounds II can then be explained by a secondary steric effect of the 3-phenyl

Ia–j

IIa–j, R² = H
IIk, R² = Br
IIl, R² = CH₃CO
IIm, R² = NO₂

IIIa, R¹ = CH₃
IIIb, R¹ = C₂H₅

IVa, R¹ = CH₃
IVb, R¹ = C₂H₅

V

VII

VIII

XIV
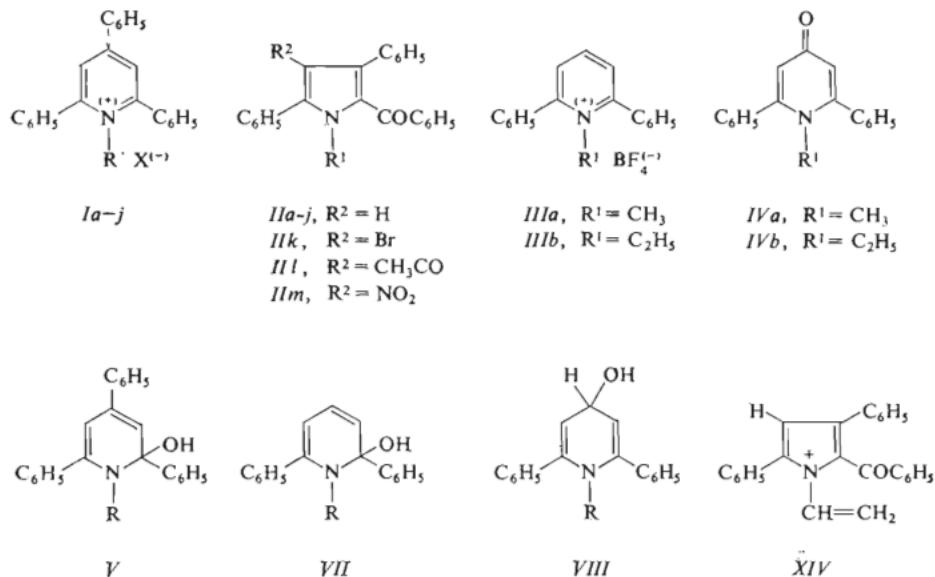
group in the intermediate *VI*, favouring (as seen on molecular models) pyrrole ring closure. The formation of an appreciable amount of 4-pyridones *IV* in the oxidation of the salts *IIIa* and *IIIb* can be caused by a steric hindrance in positions 2 and 6 by bulky phenyl groups as compared with the unsubstituted position 4. As a result,
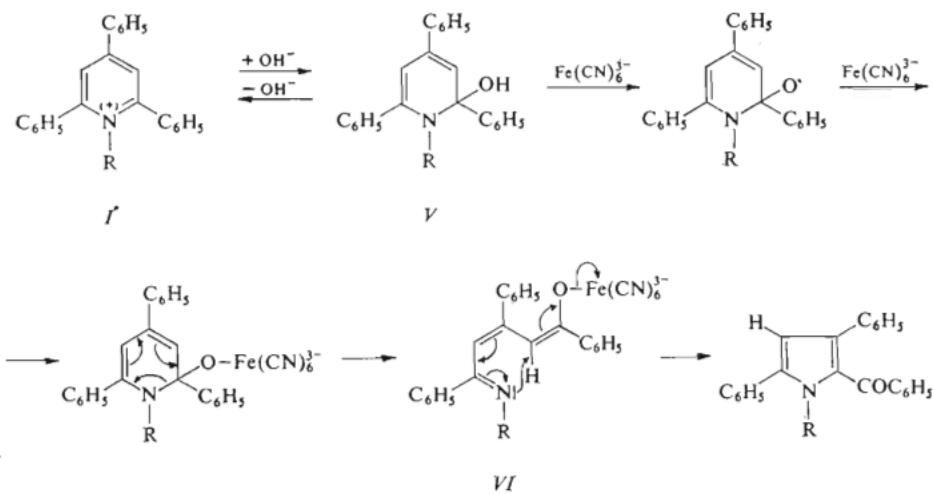
SCHEME 1

TABLE I
Pyrrole derivatives IIa—IIm, prepared from the quaternary salts Ia—Ij[a]

Compound (yield, %)	R¹ R²	Formula (mol. wt.)	M.p., °C	Calculated/Found			ν(C=O) cm⁻¹, in CCl₄	¹H NMR δ(ppm)
				% C	% H	% N		
IIa (71)	CH₃ H	C₂₄H₁₉NO (337.4)	163—165	85·43 85·41	5·67 5·59	4·15 4·13	1 630	3·88(CH₃), 6·3s(CH), 6·9—7·6(3 C₆H₅)
IIb (80)	C₂H₅ H	C₂₅H₂₁NO (351.5)	100—101	85·42 85·76	6·02 6·03	3·98 4·10	1 630	1·17t(CH₃), 4·37q(CH₂), 6·32s(CH), 6·9—7·8m(3 C₆H₅)
IIc (65)	CH₂CH₂OH H	C₂₅H₂₁NO₂ (367.5)	126—127	81·81 82·02	5·76 5·93	3·81 3·81	1 625	3·2—3·5m(OH), 3·6—3·72(CH₂), 4·45t(CH₂), 6·35s(CH), 6·8—7·7m(3 C₆H₅)
IId (71)	CH₂CH₂CH₃ H	C₂₆H₂₃NO (365.5)	60—62	85·43 85·33	6·34 6·38	3·83 4·02	1 630	0·65t(CH₃), 1·2—1·7m(CH₂), 4·32t(CH₂), 6·3s(CH), 6·9—7·8m(3 C₆H₅)
IIe (73)	CH₂C₆H₅ H	C₃₀H₂₃NO (413.5)	165—166	87·14 87·10	5·61 5·70	3·39 3·43	1 630	5·63s(CH₂), 6·44s(CH), 6·8—7·6m(4 C₆H₅)
IIf (75)	C₆H₅[b] H	C₂₉H₂₁NO (399.5)	177—178	87·19 87·42	5·22 5·42	3·51 3·66	1 640	6·65s(CH), 7·0—7·75m(4 C₆H₅)
IIg (97)	p-CH₃C₆H₄ H	C₃₀H₂₃NO (413.5)	200—201	87·14 86·91	5·61 5·57	3·39 3·65	1 643	2·28s(CH₃), 6·57s(CH), 6·9—7·8m(3 C₆H₅, C₆H₄)
IIh (91)	p-FC₆H₄ H	C₂₉H₂₀FNO (417.5)	190—191	83·43 83·48	4·83 4·98	3·35 3·31	1 640	6·58s(CH), 6·8—7·7m(3 C₆H₅, C₆H₄)

TABLE I
(continued)

Compound (yield, %)	R^1 R^2	M.p., °C	Formula (mol. wt.)	Calculated/Found			$\nu(C=O)$ cm^{-1}, in CCl$_4$	^{1}H NMR δ(ppm)
				% C	% H	% N		
IIi (72)	2,4,6-(CH$_3$)$_3$C$_6$H$_2$ H	170—172	C$_{32}$H$_{27}$NO (441·6)	87·04 87·48	6·16 6·11	3·17 3·14	1 640	2·03s(2 CH$_3$), 2·26s(CH$_3$), 6·71s(CH), 6·75—7·7m(3 C$_6$H$_5$, C$_6$H$_2$)
IIj (36)	p-HOC$_6$H$_4$ H	225—227	C$_{29}$H$_{21}$NO$_2$ (415·5)	83·83 83·58	5·09 5·21	3·37 3·29	1 630	6·57s(CH), 6·5—7·7m(3 C$_6$H$_5$, C$_6$H$_4$)
IIk (94)^c	C$_6$H$_5$ Br	215—217	C$_{29}$H$_{20}$BrNO^d (478·4)	72·81 72·97	4·21 4·44	2·93 3·03	1 645	7·0—7·7m(4 C$_6$H$_5$)
IIl (96)^c	C$_6$H$_5$ CH$_3$CO	191—196	C$_{31}$H$_{23}$NO$_2$ (441·5)	84·33 84·34	5·25 5·20	3·17 2·85	1 645 1 680	1·95s(CH$_3$), 7·0—7·7m(4 C$_6$H$_5$)
IIm (45)^c	C$_6$H$_5$ NO$_2$	191—195	C$_{29}$H$_{20}$N$_2$O$_3$ (444·5)	78·36 78·22	4·54 4·59	6·30 6·29	1 655	7·6—8·6m(4 C$_6$H$_5$)

^{a} For *Ic—If* X = BF$_4$, for other compounds X = I; ^{b} ^{13}C NMR (CDCl$_3$), ppm: 188·15s(C=O), 138—126m. 111·0d(CH/4/); ^{c} prepared from *IIf* by electrophilic substitution (see Experimental); ^{d} calculated: 16·70% Br; found: 17·01% Br.

in an alkaline medium, in addition to 2-hydroxydihydropyridine *VII*, also 4-hydroxy-dihydropyridine *VIII* is formed which is then oxidized to give the 4-pyridone *IV*. The formation of complex reaction mixture in the oxidation of compound *III* can be due to subsequent transformations of the 4-pyridones *IVa*, *b*, as well as the instability of the pseudobase *VII* which, after ring opening, could undergo oxidative destruction.

A typical representative, compound *IIf*, underwent facile electrophilic substitution in the position 4. When treateds with bromine or acetyl chloride in the presence of anhydrous aluminium chloride, compound *IIf* gave the respective bromo and acetyl derivatives *IIk* and *IIl* in high yields. Reaction with nitric acid afforded, however, only 45% of the nitro compound *IIm*, the low yield being probably due to the instability of the pyrrole system in the acid medium.

Structure of the compounds *IIa–IIm* was confirmed by their elemental analyses and IR and ^{1}H NMR spectra. Also the ^{13}C NMR spectrum of *IIf* was consistent with its suggested structure. As an independent proof, *IIf* was synthesized from 1,2,4-triphenylpyrrole and benzoyl chloride in the presence of aluminium chloride. The suggested fragmentation of *IIa–IIj* on electron impact is based on comparison of their mass spectra (Scheme 2). Molecular ions *IX* of compounds *IIa–IIj* are
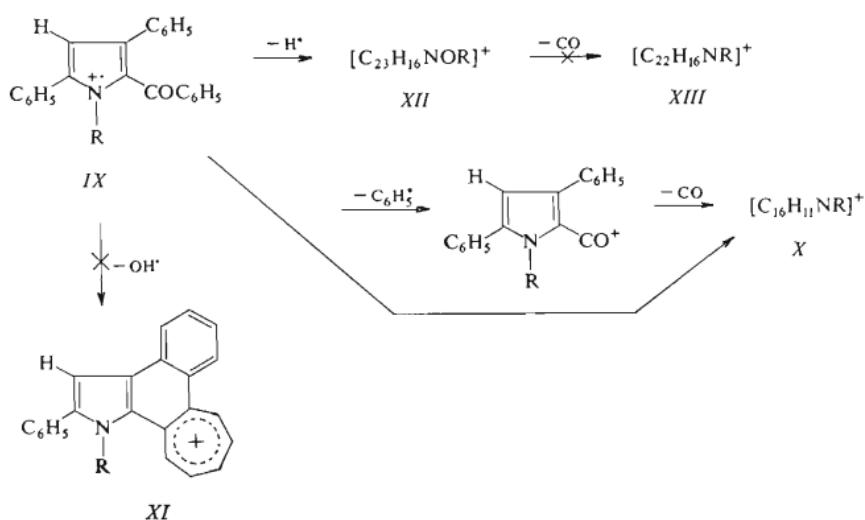
SCHEME 2

cleaved along three pathways. In the first the phenyl radical and the CO molecule are cleaved off to give the ion *X*. In the second pathway the OH radical is split off, giving rise to an ion of the possible structure *XI*. The direct transition *IX → XI* is confirmed by the occurrence of a metastable ion. In the third splitting process, the

ion M-1 loses a CO molecule under formation of the cation *XIII*. Also in this case metastable ions were observed in the spectra. Fragmentation of the molecular ion of *IIc* is accompanied by loss of water, and leads to the cation *XIV* which is split further by the above-described mechanism.

EXPERIMENTAL

Temperature data are uncorrected, spectral characteristics were measured on Perkin–Elmer 325 (IR), Varian XL-100 (^{1}H NMR), Jeol FX-60 (^{13}C NMR), and LKB 9 000 (70 eV; mass spectra) instruments. The ^{1}H NMR spectra were taken in deuteriochloroform with tetramethylsilane as internal standard. Purity of the synthesized compounds was checked by thin-layer chromatography on Silufol plates (Lachema, Brno); detection by UV. The quaternary salts *Ia—Ig*, *Ij* and *IIIa* were prepared by the described procedures[10–16].

1-Ethyl-2,6-diphenylpyridinium Tetrafluroborate (*IIIb*)

A solution of 2,6-diphenylpyridine[6] (27·6 g) in dichloroethane (50 ml) was added dropwise to a solution of triethyloxonium tetrafluoroborate (43 g) in 1,2-dichloroethane (50 ml). The mixture was refluxed for 4 h and after standing for 24 h methanol (10 ml) was added. After evaporation *in vacuo* the crude product was crystallized from ethanol, affording 34 g (98%) of crystals, m.p. 189—190°C. For $C_{19}H_{18}BF_4N$ (347·2) calculated: 4·03% N; found: 3·80% N. ^{1}H NMR spectrum, δ(ppm): 1·00 t(CH_3), 4·53 q (CH_2), 7·25—7·75 m (12 H), 8·45 t (γH).

Oxidation of Quaternary Fluoroborates *IIIa, b*

A solution of potassium ferricyanide (4 g) and potassium hydroxide (2 g) in water (40 ml) was added to a hot solution of the derivative *IIIa* (ref.[16]; 2 g) in water (120 ml). After heating to 90 to 100°C for 2 h the mixture was cooled and extracted with chloroform (3 × 50 ml). The combined extracts were dried over calcium chloride and taken down *in vacuo*. According to thin-layer chromatography on Silufol in chloroform (detection with UV light), the residue (1·6 g) consisted of 9 compounds, one of which (about 30%) was identified as the pyridone *IVa* (characteristic singlets[7] at δ 3·17 ppm (CH_3) and δ 6·40 ppm (βH)). Compound *IIIb* (2 g) was oxidized in the analogous manner. The presence of the pyridone *IVb* (30%) in the residue (1·6 g) was proved by ^{1}H NMR spectroscopy, using standard addition of the authentic[8] sample of *IVb*.

1-Methyl-2-benzoyl-3,5-diphenylpyrrole (*IIa*)

A solution of potassium ferricyanide (6·58 g) and potassium hydroxide (1·0 g) in water (60 ml) was added dropwise to a boiling solution of 1-methyl-2,4,6-triphenylpyridinium iodide (2·32 g) in ethanol (80 ml). The stirred mixture was refluxed for 2 h, cooled and extracted with chloroform (150 ml). The chloroform layer was dried over calcium chloride and taken down. Crystallization of the residue from aqueous methanol afforded 1·2 g (71%) of the yellow product *IIa*, m.p. 163—165°C. The derivatives *IIb—IIe* were prepared analogously, see Table I.

1-Phenyl-2-benzoyl-3,5-diphenylpyrrole (*IIf*)

a) A solution of potassium ferricyanide (3·95 g) and potassium hydroxide (1·0 g) in water (10 ml) was added to a boiling solution of *If* (2·36 g) in ethanol (80 ml). After 5 min chloroform

(50 ml) was added, the mixture filtered and the filtrate taken down *in vacuo*. The residue (1·5 g) was washed with water and crystalized from ethanol, affording yellow needles of *IIf*, m.p. 177 to 178°C. Compounds *IIg—IIj* were prepared in the analogous manner, see Table I.

b) Silver oxide (freshly prepared from 11 g of silver nitrate and 1·5 g of potassium hydroxide in 35 ml of water) was added to a solution of the quaternary salt (1·0 g) in ethanol (100 ml), the mixture was refluxed for 2 h and filtered. Upon cooling, the filtrate deposited 0·35 g of *IIf*. Compounds *IIg* and *IIi* were prepared analogously.

1-(4-Fluorophenyl)-2,4,6-triphenylpyridinium Iodide (*Ih*)

4-Fluoroaniline (1·5 g) was added to a suspension of the corresponding pyrylium salt (5 g) in ethanol (75 ml). After refluxing for 3 h the solution was saturated with water and set aside, depositing 4·2 g of yellow-orange crystals, m.p. 250—251°C (ethanol). For $C_{23}H_{21}FIN$ (529·4) calculated: 65·80% C, 4·00% H, 2·65% N; found: 65·68% C, 4·20% H, 2·66% N. ^1H NMR spectrum, δ (ppm): 7·97 s (2 H), 6·6—7·9 m (19 H).

1-(2,4,6-Trimethylphenyl)-2,4,6-triphenylpyridinium Iodide (*Ii*)

2,4,6-Trimethylaniline (2·36 g) was added to a suspension of the pyrylium salt (5 g) in ethanol (50 ml) and the mixture was refluxed for 18 h using a thimble with a molecular sieve (Nalsit). Crystallization afforded 4·6 g of *Ii*, m.p. 150—152°C (decomposition). The product crystallized from ethanol with one molecule of the solvent. For $C_{32}H_{28}IN \cdot C_2H_5OH$ (599·5) calculated: 68·11% C, 5·72% H, 2·33% N; found: 68·18% C, 5·59% H, 2·59% N. ^1H NMR spectrum, δ (ppm): 1·21 t (3 H, CH_3CH_2), 1·7—2·0 diff. (1 H, OH), 2·04 s (6 H, $2 \times CH_3$), 2·16 s (3 H, $1 \times CH_3$), 3·65 k (CH_3CH_2), 6·7—8·2 m (17 H), 8·25 s (2 H).

Synthesis of *IIf* from 1,2,4-Triphenylpyrrole

Anhydrous aluminium chloride (1·0 g) and benzoyl chloride (1·0 g) were added to a solution of 1,2,4-triphenylpyrrole[9] (1·0 g) in carbon disulfide (20 ml). After stirring for 10 min at room temperature water (50 ml) was added, the organic layer was washed with sodium hydrogen carbonate solution and water, dried over magnesium sulfate and taken down *in vacuo*. The residue was chromatographed on a silica gel column in a chloroform–hexane mixture (1 : 2), affording 0·7 g (52%) of compound *IIf*, m.p. 175—176°C. Crystallization from ethanol gave the product as yellow needles, m.p. 177—178°C. Its ^1H NMR spectrum was identical with that of compound obtained by oxidation of the salt *If*.

1,3,5-Triphenyl-2-benzoyl-4-bromopyrrole (*IIk*)

Bromine in chloroform (10% solution) was added dropwise at room temperature to a solution of *IIf* (0·8 g) in chloroform (30 ml) until the red-brown coloration persisted. After standing for 1 h the solution was taken down *in vacuo* and the residue was dissolved in chloroform (30 ml). The solution was washed with sodium hydrogen carbonate solution, water, dried over magnesium sulfate and taken down *in vacuo*. Crystallization of the residue from ethanol afforded *IIk*, m.p. 215—217°C. For $C_{29}H_{20}BrNO$ (478·4) calculated: 72·81% C, 4·21% H, 2·93% N, 16·70% Br; found: 72·97% C, 4·44% H, 30·03% N, 17·01% Br. ^1H NMR spectrum, δ (ppm): 7·0—7·7 m (20 H, aromatic H); IR spectrum (CCl_4): $\nu(C{=}O)$ 1 645 cm^{-1}.

1,3,5-Triphenyl-2-benzoyl-4-acetylpyrrole (*III*)

Anhydrous aluminium chloride (0·5 g) and acetyl chloride (1 ml) were added at room temperature to a solution of *IIf* (0·8 g) in carbon disulfide (30 ml). After standing for 2 h water (50 ml) and chloroform (60 ml) were added to the mixture, the organic layer was separated, washed with potassium hydrogen carbonate solution and water, dried over magnesium sulfate and taken down *in vacuo*. The residue was crystallized from ethanol, affording 0·85 g (96%) of *III*, m.p. 194 to 196°C. For $C_{31}H_{23}NO_2$ (441·5) calculated: 84·33% C, 5·25% H, 3·17% N; found: 84·34% C, 5·20% H, 2·85% N. ^1H NMR spectrum, δ (ppm): 1·95 s (3 H, CH_3), 7·0—7·7 m (20 H, aromatic H); IR spectrum (CCl_4): $\nu(C=O)$ 1 645, 1 680 cm^{-1}.

1,3,5-Triphenyl-2-benzoyl-4-nitropyrrole (*IIm*)

Nitric acid (65%, 2 ml) was added at room temperature to a solution of compound *IIf* (0·8 g) in acetic acid (100 ml). After 2 h water (200 ml) was added and the mixture was extracted with two 50 ml portions of chloroform. The chloroform extract was washed with potassium hydrogen carbonate solution and water, dried over magnesium sulfate and taken down *in vacuo*. The residue was chromatographed on a column of silica gel with chloroform as eluant, affording 0·4 g (45%) of compound *IIm*, m.p. 194—195°C. For $C_{29}H_{20}N_2O_3$ (444·5) calculated: 78·36% C, 4·5% H, 6·30% N; found: 78·22% C, 4·59% H, 6·29% N. ^1H NMR spectrum, δ (ppm): 7·6—8·6 m (20 H, aromatic H); IR spectrum (CCl_4): $\nu(C=O)$ 1 655 cm^{-1}.

Mass Spectra (ions and relative %)

IIa: 337 (100), 336 (97), 320 (46), 308 (11), 260 (68), 232 (8), 191 (43), 105 (16), 77 (32).

IIb: 351 (100), 350 (100), 334(78), 322 (27), 274 (38), 246 (22), 191 (32), 105 (76), 77 (78).

IIc: 367 (86), 366 (55), 350 (45), 349 (88), 348 (52), 338 (10), 332 (5), 320 (45), 290 (21), 262 (52), 234 (2), 191 (50), 105 (100), 77 (88).

IId: 365 (97), 364 (97), 348 (92), 336 (97), 288 (74), 260 (97), 191 (97), 105 (100), 77 (97).

IIe: 413 (97), 412 (97), 396 (92), 384 (13), 336 (89), 332 (92), 308 (97), 191 (97), 105 (100), 77 (95).

IIf: 399 (100), 398 (100), 397 (100), 382 (11), 370 (14), 322 (86), 294 (27), 191 (76), 105 (97), 77 (95).

IIg: 413 (100), 412 (28), 396 (6), 385 (6), 384 (1), 336 (5), 308 (16), 191 (36), 105 (97), 77 (56).

IIh: 417 (100), 416 (100), 415 (54), 400 (3), 399 (14), 398 (30), 388 (8), 340 (92), 191 (49), 105 (97), 77 (46).

IIi: 441 (100), 440 (18), 424 (18), 412 (2), 364 (30), 336 (65), 191 (35), 105 (71), 77 (47).

IIj: 415 (100), 414 (11), 398 (3), 386 (3), 338 (17), 310 (14), 191 (14), 105 (97), 77 (29).

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