REACTION OF ORGANOLITHIUM COMPOUNDS WITH 1-SUBSTITUTED 2,4,6-TRIPHENYLPYRIDINIUM PERCHLORATES

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The reaction of organolithium compounds with 1-substituted 2,4,6-triphenylpyridinium perchlorates *Ia—Ic* produces mixtures of 1,4-dihydropyridines *IIa—IIe* and 1,2-dihydropyridines *IIIa—IIIe*. Analogous reactions of phenylmagnesium bromide with compounds *Ia—Ic* proceed with very low conversions (less than 1%). Photochromism in visible range is observed only with the compounds *II* which have two aromatic substituents at 4-position, whereas compounds *III* and *IId* show no visible photochromism. The molecular spectra of the compounds newly prepared are discussed.

In the context of studies of photochromism of 1-substituted 2,4,4,6-tetraphenyl-1,4--dihydropyridines type *II* we were interested in the problem of the reasons of this phenomenon: whether it can be connected with the photoisomerization into the corresponding 1,2-dihydroderivatives type *III* with subsequent electrolytic opening of the heterocycle analogous to that of structurally similar 2*H*-pyranes[1,2]. As the 1,2-dihydroisomers *IIIa —IIIe* corresponding to the 1,4-dihydrocompounds *IIa —IIe* investigated by us[3,4] have not been described yet, we made an attempt at their preparation by the non-photochemical reaction of 1-substituted 2,4,6-triphenyl-pyridinium perchlorates $(Ia —Ic)$ with suitable organometallic reagents containing the R^1 substituent.

So far only one case of such transformation has been described[1], viz the reaction of 1-methyl-2,4,6-triphenylpyridinium perchlorate (Ia) with benzylmagnesium chloride giving the respective 4-benzyl-1,4-dihydropyridine derivative. Our preliminary attempts at transformations of salt *IIa* by action of other organomagnesium reagents led to extremely low conversions, the starting salt *IIa* being recovered from the reaction mixture almost quantitatively. We have found that much better results can be obtained by application of organolithium reagents (R^1Li) in ether solution. The results obtained are described in this present communication.

In order to obtain detailed information about the transformations taking place with the salts $Ia —Ic$, first of all we submitted the 1-methylpyridinium salt *Ia* to the reactions with three different reagents $(R^1 = \text{n-C}_4\text{H}_9, \text{C}_6\text{H}_5, \text{and } 4\text{-CH}_3\text{C}_6\text{H}_4)$,

and then we examined the reaction of phenyllithium alone with the salts *Ib* and *Ic*. In all the cases the reaction mixtures contained (according to their ^{1}H NMR spectra) both dihydroisomers (*II* and *III*) expected. From Table I it can be seen that the 1,4-dihydroisomers type *II* are predominating. This finding indicates that the regioselectivity of attack of the 1,2,4,6-tetrasubstituted pyridinium nucleus was affected, under the conditions chosen by us, by specific electronic effects of substituents in the substrate and/or the higher thermodynamic stability of 1,4-dihydropyridine isomers[5]

Ia, R = CH₃
Ib, R = CH₂C₆H₅
Ic, R = C₆H₅

IIa – IIe

IIIa – IIIe
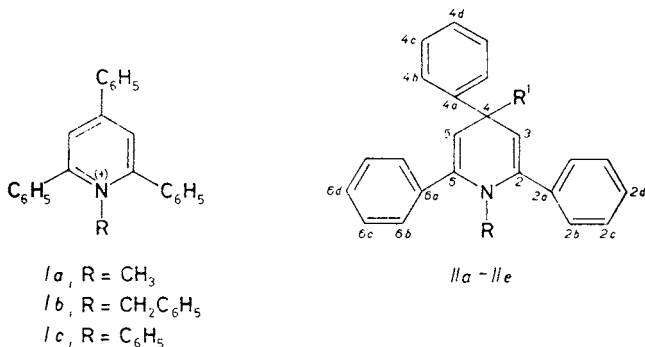
In formulae *II* and *III* : *a*, R = CH₃ ; R¹= C₆H₅   *b*, R = CH₂C₆H₅ ; R¹= C₆H₅
c, R = C₆H₅ ; R¹= C₆H₅   *d*, R = CH₃ ; R¹= n-C₄H₉
e, R = CH₃ ; R¹= 4-CH₃C₆H₄

made itself felt. The differences in ratios of 1,2 : 1,4-dihydroproducts formed from the salt *IIa* could most likely be ascribed to the steric effect of the attacking organolithium reagent: bulkier aryl groups R¹ tend to enter the sterically more accessible 4-position. On the other hand, the regioselectivity differences in attacks of various salts *Ia – Ic* by phenyllithium itself can hardly be interpreted only in terms of the above-mentioned steric interactions.

The isomeric dihydropyridine derivatives type *II* and *III* were isolated by preparative column chromatography in all the cases given in Table I. The physico-chemical and

spectral characteristics of newly prepared compounds are summarized in Table II. The IR spectra of 1,2-dihydropyridines $IIIa-IIIe$ measured in chloroform show two bands of medium intensity in the regions of $1\,620-1\,626$ and $1\,595-1\,598\ cm^{-1}$, which is similar to the 1,4-dihydropyridines. However, in comparison with 1,4-dihydropyridines[3], the values of skeletal vibrations are somewhat shifted to lower frequences. The UV spectra of ethanolic solutions of compounds $IIIa-IIIe$ are also characterized by two bands lying in the regions of $254-256$ and $352-363$ nm, the absorption in the longer-wave region being characteristic of 1,2-dihydropyridines (in contrast to 1,4-dihydropyridines)[6]. The ^{1}H NMR spectra of compounds $IIIa$ to $IIIe$ were measured in deuteriochloroform (Table II): due to assymetry of the molecule the olefinic protons at 3- and 5-positions are no longer isochronous and exhibit two signals at the ratio $1:1$ in the region of δ $5\cdot01-6\cdot28$. In comparison with the isomeric 1,4-dihydropyridines[3,4] these protons show a downfield shift. When the above-mentioned region of chemical shifts was extended, it was possible to observe (due to the conjugated system of double bonds present) a splitting of these signals into doublets with the coupling constants ^{4}J in the interval of $1\cdot6-1\cdot8$ Hz. Similar splitting of olefinic protons at these positions was observed with N-unsubstituted dihydropyridines[4]. Due to strong paramagnetic deshielding the aromatic region exhibits distinctly separated signals of eight (six for the compound $IIId$) ortho-aromatic protons of all the phenyl groups in the 1,2-dihydropyridine skeleton. The other signals of aromatic protons form a complex multiplet out of which markedly separated are the signals of N-phenyl group of compound $IIIb$ and $IIIc$ which are shifted upfield.

Table III presents the ^{13}C NMR spectra of compounds $IIb-IId$ and $IIIa-IIIe$ (the spectra of compounds IIa and IIe were published elsewhere[4]). Due to the molecular symmetry of compounds II the carbon atoms at 2,6 and 3,5 positions are isochronous as are also the aromatic carbon atoms in phenyl groups at 2,6 and

TABLE I

Reaction of quaternary pyridinium salts $Ia-Ic$ with organolithium compounds

Starting salt (R)	Reagent	Products	II/III ratio[a]
$Ia\ (CH_3)$	C_4H_9Li	$IId, IIId$	$40:60$
$Ia\ (CH_3)$	C_6H_5Li	$IIa, IIIa$	$20:80$
$Ia\ (CH_3)$	$4\text{-}CH_3C_6H_4Li$	$IIe, IIIe$	$17:83$
$Ib\ (CH_2C_6H_5)$	C_6H_5Li	$IIb, IIIb$	$40:60$
$Ic\ (C_6H_5)$	C_6H_5Li	$IIc, IIIc$	$10:90$

[a] Determined in the raw reaction mixture by means of ^{1}H NMR.

TABLE II

Physico-chemical and spectral characteristics of dihydropyridines *IId* and *IIIa—IIIe*

Compound M.p., °C	Formula (M.w.)	Calculated/Found			IR: $\tilde{\nu}$, cm^{-1}	UV	^{1}H NMR: δ, ppm		
		% C	% H	% N	DHP-skeleton	λ_{max}, nm (log ε)	H-3 H-5	*ortho*-H_{Ar} H_{Ar}	N—R R^1
IId 67—70	C$_{28}$H$_{29}$N (379·6)	88·61 88·58	7·70 7·79	3·69 3·72	1 662 1 612	235 (4·35) 286 (3·71)	5·01 s 5·01 s	7·52—7·56 m 7·17—7·37 m	2·57 *a*
IIIa 115—117	C$_{30}$H$_{25}$N (399·5)	90·19 90·25	6·31 6·44	3·50 3·38	1 626 1 595	254 (4·41) 363 (3·66)	5·77 d (1·7) 5·39 d (1·7)	7·50—7·58 m 7·24—7·41 m	2·39 —
IIIb 126—130	C$_{36}$H$_{29}$N (475·4)	90·91 90·74	6·14 6·30	2·95 2·78	1 622 1 595	255 (4·29) 358 (3·66)	6·09 d (1·7) 5·58 d (1·7)	7·45—7·57 m 7·17—7·38 m	4·31^b —
IIIc 167—169	C$_{35}$H$_{27}$N (461·6)	91·07 91·21	5·90 6·06	3·03 2·99	1 620 1 598	256 (4·38) 352 (3·90)	6·28 d (1·6) 6·19 d (1·6)	7·39—7·68 m 7·10—7·37 m	6·65—6·77 m —
IIId oil	C$_{28}$H$_{29}$N (379·6)	88·61 88·50	7·70 7·81	3·69 3·71	1 625 1 595	255 (4·32) 356 (3·70)	5·18 d (1·7) 5·15 d (1·7)	7·49—7·68 m 7·10—7·37 m	2·46 *c*
IIIe oil	C$_{31}$H$_{27}$N (413·6)	90·03 90·00	6·58 6·61	3·39 3·35	1 622 1 597	254 (4·30) 357 (3·67)	5·77 d (1·8) 5·38 d (1·8)	7·47—7·56 m 7·15—7·42 m	2·39 2·35

^{a} The signals of butyl group are at δ 1·80 t (2 H, CH$_2$, $J = 4·2$ Hz), 1·25—1·33 m (4 H, 2× CH$_2$) and 0·87 t (3 H, CH$_3$, $J = 6·7$ Hz); ^{b} the signals of phenyl group are at δ 6·65—6·77; ^{c} the signals of butyl group are at δ 1·41—1·92 m (6 H, 3× CH$_2$) and 0·98 t (3 H, CH$_3$, $J = 6·8$ Hz).

4,4 positions in contrast to compounds *III* in which the carbon atoms at the positions given are not isochronous. The strong paramagnetic shift of the quaternary C-2 carbon atom in compounds *III* (as compared with the quaternary C-4 atom in compounds *II*) is caused by the close distance to the more electronegative heteroatom at 1-position. In analogy to the ^{1}H NMR spectra of compounds *III*, also their ^{13}C NMR spectra show (in comparison with compounds *II*) a paramagnetic shift of non-isochronous carbon atoms C-3 and C-5 which are observed at δ 117·08 to 121·83 and 99·83 − 108·18, respectively, whereas those of compounds *II* are observed at δ 112·32 − 114·13.

UV irradiation ($\lambda \sim 300$ nm) of the 1,2-dihydropyridines *III* in solid state revealed no photochromism, whereas out of the 1,4-dihydropyridines *II* only the derivatives

TABLE III

^{13}C NMR spectra of dihydropyridines *IIb—IId* and *IIIa—IIIe* in CDCl$_3$ (δ, ppm)

Carbon	IIb	IIc	IId	IIIa	IIIb	IIIc	IIId	IIIe
C-2	141·92	142·74	144·18	70·50	70·12	71·90	68·17	70·32
C-2a	138·03	138·54	138·33	145·47	146·11	145·69	157·56	145·71
C-2b	128·07	128·07	127·78	127·88	127·51	127·27	127·15	128·20
C-2c	128·32	128·77	128·25	128·61	128·84	129·42	129·11	128·60
C-2d	127·99	127·95	127·73	125·98	126·22	126·29	124·80	126·70
C-3	114·13	113·13	112·75	117·66	118·18	121·83	117·08	117·77
C-4	49·32	49·44	43·75	134·28	135·74	135·69	139·16	136·43
C-4a	151·18	151·24	151·75	139·82	140·01	144·11	146·74	139·86
C-4b	127·96	127·63	126·48	126·81	126·33	126·92	126·48	125·97
C-4c	128·20	128·27	128·22	128·29	128·03	128·49	128·69	128·45
C-4d	125·25	125·69	125·41	127·25	127·29	127·53	127·15	127·19
C-5	114·13	113·13	112·75	99·86	104·08	108·18	104·15	99·83
C-6	141·92	142·74	144·18	147·66	141·25	144·20	150·23	142·52
C-6a	138·03	138·54	138·33	138·54	138·14	138·04	139·65	138·58
C-6b	128·07	128·07	127·78	128·22	126·99	127·19	127·20	127·83
C-6c	128·32	128·77	128·25	128·48	128·38	128·51	129·03	128·48
C-6d	127·99	127·95	127·73	127·97	128·08	127·69	128·34	127·89
N–R	51·53[a]	144·59[b]	38·35	36·73	52·05[a]	139·60[b]	38·82	36·70
R, R^1	138·27[b]	127·52[b]	43·39[c]		147·02[b]	127·94[b]	43·76[c]	147·64[b]
R, R^1	127·69[b]	129·74[b]	27·97[c]		127·50[b]	129·77[b]	28·59[c]	128·27[b]
R, R^1	128·16[b]	126·62[b]	23·30[c]		128·75[b]	124·05[b]	23·82[c]	128·64[b]
R, R^1	126·90[b]		14·13[c]		125·86[b]		14·16[c]	134·16[b,d]

[a] The signal of CH$_2$ group; [b] the signals of phenyl group; [c] the signals of butyl group; [d] the signal of CH$_3$ group is at δ 21·03.

containing tetraarylsubstituted dihydropyridine skeleton (*IIa−IIc, IIe*) exhibited photochromism. The 4-alkylsubstituted 1,4-dihydroderivative *IId* shows no visual photochromism. This fact makes it possible to eliminate the presumption that the visual photochromism of 1,4-dihydropyridines *II* could be caused by photochemical isomerization into 1,2-dihydropyridines *III*.

EXPERIMENTAL

The temperature data were not corrected. The melting points were determined with a Boetius apparatus. The IR spectra were measured with a Perkin–Elmer 325 apparatus in chloroform, the UV spectra were measured with a Specord M-40 apparatus in ethanol, the NMR spectra were measured with a Bruker AM-400 apparatus in deuteriochloroform and related to tetramethyl-silane as the internal standard. The experimental parameters: for ^{1}H NMR (400·134 MHz), digital resolution 0·184 Hz/point, pulse width 4 μs (45°), temperature 297 K; for ^{13}C NMR (100·61 MHz) digital resolution 0·9 Hz/point, temperature 297 K, APT technique.

Preparation of Starting Compounds

The quaternary salts *Ia−Ic* were obtained by the reaction[7] of corresponding amines with 2,4,6--triphenylpyrylium perchlorate[8].

1-*Methyl*-2,4,6-*triphenylpyridinium perchlorate* (Ia) was obtained in the yield of 87% with m.p. 216−217°C (methanol). For $C_{24}H_{20}ClNO_4$ (421·9) calculated: 68·33% C, 4·78% H, 8·40% Cl, 3·32% N; found: 68·22% C, 4·89% H, 8·47% Cl, 3·44% N.

1-*Benzyl*-2,4,6-*triphenylpyridinium perchlorate* (Ib) was obtained in the yield of 41% with m.p. 203−205°C (methanol) (ref.[9] gives m.p. 180−182°C, ref.[10] gives m.p. 196−198°C). For $C_{30}H_{24}$·.$ClNO_4$ (498·0) calculated: 72·36% C, 4·86% H, 7·12% Cl, 2·81% N; found: 72·40% C, 5·02% H, 7·15% Cl, 2·81% N.

1,2,4,6-*Tetraphenylpyridinium perchlorate* (Ic) was obtained in the yield of 77% with m.p. 267°C (methanol) (ref.[8] gives m.p. 260°C). For $C_{29}H_{22}ClNO_4$ (484·0) calculated: 71·97% C, 4·58% H, 7·33% Cl, 2·89% N; found: 71·84% C, 4·71% H, 7·13% Cl, 2·80% N.

Reactions of Organolithium Compounds with Pyridinium Perchlorates *Ia−Ic*

A solution of 20 mmol organolithium compound in 20 ml ether was added dropwise (with stirring under nitrogen) to 2 mmol pyridinium perchlorate in 30 ml anhydrous ether at room temperature. The reaction mixture was stirred at room temperature 1 h, whereupon it was decomposed by addition of 30 ml water. The organic layer was separated and the aqueous layer was extracted with 3× 20 ml benzene. The combined organic portions were washed with water until neutral and dried with sodium sulfate, whereupon the solvent was evaporated. The resulting oil was analyzed by means of ^{1}H NMR spectroscopy and submitted chromatography on 100 g silica gel with the bellow-given solvents as eluents. The individual fractions were identified by means of TLC (Silufol, tetrachloromethane), detection in iodine vapours and in UV light ($\lambda \sim 360$ nm.) The hydrocarbon formed by the Wurtz reaction of the organometallic reagent was isolated from the first fraction in some cases. From the subsequent fractions it was possible to isolate the 1,4-dihydropyridines *II* whose identity was confirmed by comparison of their spectral charac-teristics with those of authetic substances[3,4] prepared earlier. The last fractions gave the 1,2-

-dihydropyridines *III*. The physico-chemical and spectral characteristics of the newly prepared compounds *IId* and *IIIa*—*IIIe* are given in Table II and the ^{13}C NMR spectra of compounds *IIb*—*IId* and *IIIa*—*IIIe* are presented in Table III.

Reaction of pyridinium salt Ia *with phenyllithium*. The chromatography of 1·2 g oil (gradient elution: benzene–cyclohexane 1 : 2 — benzene) gave 0·45 g (48%) 1,4-dihydroderivative *IIa*, R_F 0·56, m.p. 181—183°C (acetone), identical with the substance prepared earlier[3]. On increasing polarity of the eluent until 1% methanol in benzene it was possible to isolate (from the last fractions) 0·15 g (16%) 1,2-dihydroderivative *IIIa*, R_F 0·16, which was recrystallized from an acetone––methanol mixture.

Reaction of pyridinium salt Ib *with phenyllithium*. The chromatography of 1·0 g oil with benzene as the eluent gave 0·42 g (45%) 1,4-dihydroderivative *IIb*, R_F 0·47, m.p. 176—178°C (acetone) which was identical with the substance prepared earlier[3]. Subsequent fractions gave 0·28 g (30%) 1,2-dihydroderivative *IIIb*, R_F 0·19, which was recrystallized from acetone.

Reaction of pyridinium salt Ic *with phenyllithium*. The chromatography of 1·1 g oil with benzene as the eluent gave 0·75 g (80%) 1,4-dihydroderivative *IIc*, R_F 0·34, m.p. 166—168°C (acetone––methanol), which was identical with the substance prepared earlier[3]. Subsequent fractions gave 0·05 g (5%) 1,2-dihydroderivative *IIIc*, R_F 0·23, which was recrystallized from acetone.

Reaction of pyridinium salt Ia *with butyllithium*. The chromatography of 1·0 g oil with benzene as the eluent gave 0·45 g (48%) 1,4-dihydroderivative *IId*, R_F 0·65, which was recrystallized from an acetone–methanol mixture. Subsequent fractions gave 0·22 g (25%) oily 1,2-dihydroderivative *IIId*, R_F 0·23.

Reaction of pyridinium salt Ia *with p-tolyllithium*. The chromatography of 1·3 g oil with cyclohexane as the eluent gave (in the first fractions) 0·20 g *p,p'*-dimethylbiphenyl, m.p. 120—121°C (hexane) (ref.[11] gives m.p. 121°C) whose ^{1}H and ^{13}C NMR spectra were consistent with its structure. Subsequent fractions gave 0·57 g (60%) 1,4-dihydroderivative *IIe*, R_F 0·69, m.p. 156 to 160°C (acetone–methanol), which was identical with the authetic substance[4]. The gradient elution (hexane–benzene) gave (in the last fractions — benzene) 0·09 g (10%) 1,2-dihydroderivative *IIIe*, R_F 0·20, whose crystallization was unsuccessful.

Reaction of Pyridinium Salts *Ia*—*Ic* with Phenylmagnesium Bromide

A suspension of 2 mmol pyridinium perchlorate *Ia*—*Ic* in 10 ml anhydrous ether was stirred at room temperature under nitrogen, and 3·63 g (20 mmol) phenylmagnesium bromide in 15 ml ether was added thereto. During the reaction the pyridinium salt dissolved. After 1 h stirring the reaction mixture was decomposed by addition of 10 ml water and neutralized with dilute hydrochloric acid. The separated solid was isolated and identified with the starting substance by comparison of melting points and IR spectra; after recrystallization from acetone the yields of the recovered starting substance varied within the limits 80—90% in the individual cases. The organic layer of the filtrate was separated, and the aqueous layer was extracted with benzene. The combined organic portions were washed with water and dried with sodium sulfate. The solvent was evaporated and the oily residue (0·4—0·5 g) was submitted to ^{1}H NMR spectral measurement which showed that the dihydropyridines *II* and *III* are formed in the yields lower than 1% (related to the starting pyridinium perchlorate).

The same result was obtained from the inverse procedures when the pyridinium perchlorates *Ia*—*Ic* were added to phenylmagnesium bromide in ether.

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Translated by J. Panchartek.