REACTIVITIES OF DIANIONS OF PYRIDYL PHENYL KETONES*

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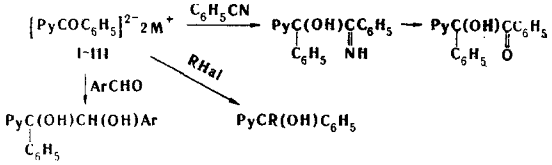
Substituted pyridylphenylcarbinols are formed in the reaction of the dianions of isomeric pyridyl phenyl ketones with alkyl halides, aldehydes, and benzonitrile. The reaction of the dianion of 3-pyridyl phenyl ketone with benzophenone, in contrast to the analogous reaction of the dianion of 2-pyridyl phenyl ketone, gives 5-benzoyl-2-diphenylhydroxymethyl-1,2-dihydropyridine. It is assumed that the observed reaction includes one-electron transfer and the formation of two anion radicals. Recombination of the anion radical of 3-pyridyl phenyl ketone leads to 5,5'-dibenzoyl-2,2'-di(1,2-dihydropyridyl).

In contrast to the dianions of the carbocyclic series, very little study has been devoted to the reactivities of the dianions of heterocyclic ketones. Only the preparation of the dianions of pyridyl phenyl ketones and their alkylation has been described [3]. It is also known that the reduction of isomeric pyridine derivatives containing electron-acceptor groups may proceed differently. Thus the reduction of 3-cyanopyridine with sodium borohydride gives di- and tetrahydropyridine derivatives, while the nitrile group is reduced in the analogous reaction of 2- and 4-cyanopyridines [4]. In this connection, it seemed of interest during a study of the reactivities of the dianions to compare the properties of the dianions and anion radicals of isomeric pyridyl phenyl ketones.

The reaction of all three isomeric pyridyl phenyl ketones with two equivalents of lithium or sodium in liquid ammonia gives dianions, the alkylation of which with alkyl halides leads to alkylpyridylphenylcarbinols, while reaction with aromatic aldehydes and benzonitrile leads to glycols and keto alcohols.



I Py=2-pyridyl II Py=3-pyridyl III Py=4-pyridyl

A difference in the reactivities of dianions I-III was observed in the reaction with benzophenone. While reaction of dianion I with benzophenone gave 1,1,2-triphenyl-2-(2-pyridyl)ethanediol, the analogous reaction of dianion II gave 5-benzoyl-2-diphenylhydroxymethyl-1,2-dihydropyridine (IV) in 93% yield. This same compound was obtained by reaction of two anion radicals – those of benzophenone and 3-pyridyl phenyl ketone (V) – and by reaction of the dianion of benzophenone with 3-pyridyl phenyl ketone. The structure of dihydropyridine IV was proved by spectral methods and also by chemical transformations. The UV spectrum of IV contains two bands, which is characteristic for 5-substituted 1,2-dihydropyridine [5]. Oxidation of IV gave 5-benzoyl-2-diphenylhydroxymethylpyridine (VI), the Haller cleavage [6] of which gave the known 2-pyridyldiphenylcarbinol.

The formation of dihydropyridine IV is possibly due to steric hindrance arising during the reaction of dianion II with benzophenone. It has been shown [7] that ambident character of the dianion is displayed in the reaction of the dianion of benzophenone with sterically hindered alkyl halides. Alkylation of dianion II with

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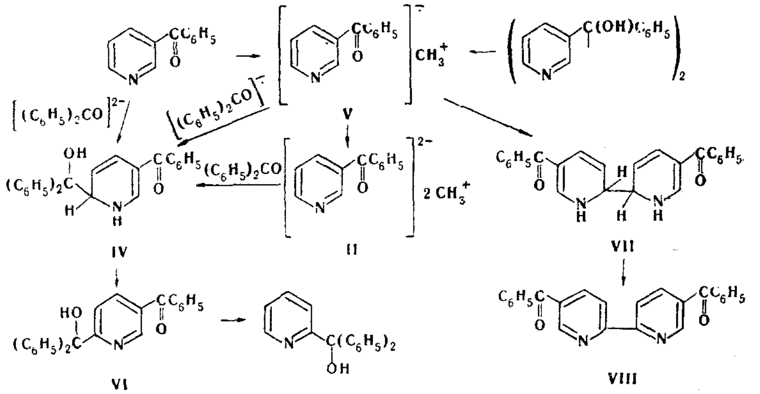

the sterically hindered tert-butyl bromide gave a product of substitution of the pyridine ring in addition to tert-butyl-3-pyridylphenylcarbinol (in 70% yield). Although we were unable to isolate this compound because of its extreme instability, the spectral characteristics confirm that it has the dihydropyridine structure. However, in contrast to the quantitative yield of dihydropyridine IV, the yield of this compound was low. In addition, it can be assumed that the steric difficulties are identical in the reaction of benzophenone with dianions I and II, but, nevertheless, these reactions lead to completely different results.

In our opinion, the reaction of dianion II with benzophenone, in contrast to the reaction of II with alkyl halides, includes one-electron transfer. This sort of mechanism is observed in a number of anion reactions [8]. One-electron transfer is considered to be one of the alternative mechanisms for the reaction of benzophenone with azaheterocycles in the presence of lithium metal [9]. As a result of one-electron transfer, two anion radicals – those of benzophenone and 3-pyridyl phenyl ketone – which also interact, are formed in the investigated reaction. Anion radicals and dianions can differ substantially with respect to their reactivities [10]. Calculation of the distribution of the spin density in anion radicals of the similar compounds 3,3-dipyridyl ketone [11] and 3-pyridyl methyl ketone [12] leads to a maximum value of the density of the unpaired electron in the 6 position of the pyridine ring. Analysis of the ESR spectrum of the anion radical of 3-pyridyl phenyl ketone, which was performed by V. M. Kazakova and co-workers in the Department of Physical Chemistry of the Moscow Institute of Precision Chemical Technology, also showed that the maximum value of the spin density is in the 6 position of the pyridine ring.

In addition to the reactions of dianions I-III, we also studied the recombination reactions of the anion radicals of the three isomeric pyridyl phenyl ketones. Recombination of two anion radicals of 2-pyridyl phenyl ketone leads to 1,2-diphenyl-1,2-di(2-pyridyl)ethanediol. Only an equimolecular mixture of the corresponding carbinol and the starting ketone was isolated from the analogous reaction of 4-pyridyl phenyl ketone. Unsuccessful attempts to obtain pinacol from 4-pyridyl phenyl ketone are described in the literature

TABLE 1. $PyC(OH)RC_6H_5$

Py	R	mp, deg °C (solvent)	Empirical formula	N, %		petrol. ether
				found	yield, %	
2-Py	C_2H_5	78—79 (petroleum ether) [18]	$C_{14}H_{15}NO$	—	—	95
2-Py	i-C_3H_7	65 (hexane)[18]	$C_{15}H_{17}NO$	—	—	90
2-Py	t-C_4H_9	81—83 (2-propanol)	$C_{16}H_{19}NO$	5,8	5,8	97
2-Py	$CH(OH)C_6H_5$	167—169 (dioxane)	$C_{19}H_{17}NO_2$	4,7	4,8	75
2-Py	$C(OH)(C_6H_5)_2$*	113—115 (hexane)	$C_{25}H_{21}NO_2$	3,91	3,84	88
3-Py	C_2H_5	104—105 (cyclohexane [16]	$C_{14}H_{15}NO$	—	—	85
3-Py	i-C_3H_7	127—129 (hexane)	$C_{15}H_{17}NO$	—	—	96
3-Py	$C_6H_5CH_2$	153—154 (2-propanol) [16]	$C_{19}H_{17}NO$	—	—	94
3-Py	$CH(OH)C_6H_5$	184—186 (chloroform)	$C_{19}H_{17}NO_2$	4,7	4,8	50
3-Py	$CH(OH)(p$-$CH_3OC_6H_4)$	173—174 (chloroform)	$C_{20}H_{19}NO_3$	4,3	4,3	64
3-Py	$C(NH)C_6H_5$	140—141 (ethanol)	$C_{19}H_{16}N_2O$	9,8	9,7	50
3-Py	COC_6H_5 †	116—118 (2-propanol)	$C_{19}H_{15}NO_2$	4,7	4,8	98
4-Py	C_2H_5	152—153 (dichloroethane)[20]	$C_{14}H_{15}NO$	—	—	70
4-Py	i-C_3H_7	138 (heptane)[21]	$C_{15}H_{17}NO$	—	—	95

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* The reaction mass was poured into a solution of an excess of ammonium chloride in liquid ammonia for neutralization.

† Obtained by saponification of the preceding compound with 5% hydrochloric acid at 50°C.

[13]. The recombination of two anion radicals V gave 5,5'-dibenzoyl-2,2'-di(1,2-dihydropyridyl) (VII). The structure of the latter was proved by spectral methods and also by oxidation to the known 5,5'-dibenzoyl-2,2'-dipyridyl (VIII) [14]. It is essential to note that dihydropyridyl VII is formed in the reaction of sodium amide in liquid ammonia with 1,2-diphenyl-1,2-di(3-pyridyl)ethanediol.

The recombination of two anion radicals of aromatic ketones can lead to the formation of three types of dimers – one with a new bond between the carbonyl carbons, one with a new bond between the carbonyl carbon and the ring carbon, and one with a new bond between two carbon atoms of different rings. Dimers of the first type – pinacols – are most often formed. The formation of dimers of the second type, which is associated with dearomatization of one aromatic ring, is considerably rarer [15, 16]. Finally, dearomatization of two rings and formation of a bond between two carbon atoms of these rings has been noted only in the case of electrochemical reduction [17]. This sort of recombination has been observed for the first time during the chemical reduction of ketones.

EXPERIMENTAL

Substituted Pyridylphenylcarbinols (Table 1). A solution of 0.01 mole of alkylating agent in 10 ml of ether was added to a violet solution of the dianion, prepared from 0.01 mole of pyridyl phenyl ketone and 0.022 g-atom of sodium in 50 ml of liquid ammonia via the method in [3]. After 10-15 min, 0.02 mole of ammonium chloride was added, and the ammonia was removed by distillation. The residue was diluted with water, and the reaction product was removed by filtration and crystallized. Alkyl bromides, benzyl chloride, benzaldehyde, p-methoxybenzaldehyde, benzonitrile, and benzophenone were used as reagents.

(3-Pyridyl)phenyl-tert-butylcarbinol. A 1.37 g (0.01 mole) sample of tert-butyl bromide was added to dianion II, obtained from 1.83 g (0.01 mole) of 3-pyridyl phenyl ketone in liquid ammonia. After 15 min, 1.1 g (0.02 mole) of ammonium chloride was added, and the ammonia was removed by distillation. Water was added to the residue, and the light-yellow precipitate was separated. Column chromatography (activity III aluminum oxide, ether) gave (3-pyridyl)phenyl-tert-butylcarbinol, with mp 153-154° (isopropyl alcohol), in 70% yield. IR spectrum ($CHCl_3$): 3620 cm^{-1} (OH). Found, %: N 6.0. $C_{16}H_{19}NO$. Calculated, %: N 5.8. In addition to the carbinol, 13% of a substance, the IR spectrum of which contained bands at 1670 (CO) and 3455 cm^{-1} (NH), was isolated.

5-Benzoyl-2-diphenylhydroxymethyl-1,2-dihydropyridine (IV). A. A 1.82 g (0.01 mole) sample of benzophenone was added to dianion II, obtained from 1.83 g (0.01 mole) of 3-pyridyl phenyl ketone in liquid ammonia. The usual workup gave IV, with mp 103-104° (from benzene), in 97% yield. IR spectrum ($CHCl_3$): 1650 (CO), 3435 (NH), 3550 and 3620 cm^{-1} (OH). UV spectrum in alcohol, λ_{max} nm (log ε): 304 (3.84), 360 (3.95). Found, %: C 82.0; H 6.1. $C_{25}H_{21}NO_2$. Calculated, %: C 81.7; H 5.8.

B. A 0.01 mole sample of 3-pyridyl phenyl ketone was added to 0.01 mole of the dianion of benzophenone in liquid ammonia. The usual workup gave IV, with mp 103-104° (from benzene), in 92% yield.

C. A solution of anion radical V, obtained from 1.83 g (0.01 mole) of 3-pyridyl phenyl ketone and 0.25 g (0.011 g-atom) of sodium in liquid ammonia, was added to a solution of the anion radical of benzophenone, obtained from 1.82 g (0.01 mole) of benzophenone and 0.25 g (0.011 g-atom) of sodium in liquid ammonia. The usual workup gave IV, with mp 99-101°, in 98% yield.

5-Benzoyl-2-(diphenylhydroxymethyl)pyridine (VI). A solution of 0.37 g (1 mmole) of IV and 0.11 g (1 mmole) of p-benzoquinone in 20 ml of benzene was refluxed for 4 h, after which it was cooled and washed with 10% sodium hydroxide solution, 5% hydrochloric acid, and water. The benzene was then removed by distillation to give 0.28 g (75%) of VI with mp 123-124° (from heptane). IR spectrum ($CHCl_3$): 1670 (CO), 3240 and 3620 cm^{-1} (OH). Found, %: C 81.8; H 5.3; N 3.8. $C_{25}H_{19}NO_2$. Calculated, %: C 82.2; H 5.2; N 3.8.

Diphenyl(2-pyridyl)carbinol. A solution of 1 g (2.7 mmole) of VI in 10 ml of toluene was added to a suspension of sodium amide in 40 ml of toluene. The mixture was cooled, and 1 ml of alcohol and 20 ml of water were added. The toluene layer was separated and washed with water. Removal of the solvent by distillation gave 0.3 g of diphenyl(2-pyridyl)carbinol with mp 102-105° (from ethanol); the product did not depress the melting point of an authentic sample [18].

1,2-Diphenyl-1,2-di(2-pyridyl)ethanediol. A 1.83 g (0.01 mole) sample of 2-pyridyl phenyl ketone was added to 0.23 g (0.01 g-atom) of sodium in liquid ammonia. The resulting blue solution of the anion radical was poured, after 15 min, into a solution of 3 g of ammonium chloride in liquid ammonia. The ammonia was evaporated, and water was added. The precipitate was removed by filtration to give 1,2-di(2-pyridyl)-ethanediol, with mp 138-139°, in 80% yield [23].

5,5'-Dibenzoyl-2,2'-di(1,2-dihydropyridyl) (VII). A. A 1.83 g (0.01 mole) sample of 3-pyridyl phenyl ketone was added to 0.23 g (0.01 g-atom) of sodium in 50 ml of liquid ammonia. The resulting green solution of anion radical V was neutralized with ammonium chloride, and the ammonia was removed by distillation. Water was added, and the yellow precipitate was removed by filtration to give VII, with mp 86-89° (from benzene), in 98% yield. IR spectrum ($CHCl_3$): 1665 (CO) and 3430 cm^{-1} (NH). Found, %: N 7.2. $C_{24}H_{20}N_2O_2$. Calculated, %: N 7.6.

B. A 0.9 g (2.5 mmole) sample of 1,2-diphenyl-1,2-di(3-pyridyl)ethanediol, obtained photochemically [22], was added to a suspension of sodium amide in 30 ml of liquid ammonia, obtained from 0.12 g (5 mg-atom) of sodium. The green solution that formed during the addition was neutralized with ammonium chloride. The usual workup gave VII, with mp 69-75°, in 90% yield. The IR spectra of the compounds obtained by methods A and B were identical.

5,5'-Dibenzoyl-2,2'-dipyridyl (VIII). A solution of 0.5 g (1.4 mmole) of VII and 0.15 g (1.4 mmole) of p-benzoquinone in 10 ml of benzene was refluxed for 2 h. It was then cooled and washed with 10% sodium hydroxide solution, 5% hydrochloric acid, and water. Removal of the benzene by distillation gave VIII, with mp 211-212° (from alcohol–benzene), in 40% yield [14].

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