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Isoquinoline Syntheses *via* Δ^2-Oxazolines. Part VIII*. Cyclization of 2-Acetamido-1,2-diphenylethan-1-ol Derivatives into Isoquinoline Systems

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The results of the conversion of 2-acetamido-1,2-diphenylethan-1-ol derivatives (**1**) into 1-methyl-4-phenylisoquinoline derivatives (**2**) have been described. The mechanism proposed for these reaction assumes the existence of protonated Δ^2-oxazolines (**3**), carbonium ions (**4**), and unsaturated amides (**5** and **6**) as intermediates.

Key words: amino alcohols, isoquinoline, oxazoline

Earlier protonated Δ^2-oxazolines and unsaturated amides have been shown to be intermediates formed during of Pictet-Gams reaction [1,2]. A particularly interesting example of this reaction is cyclization of 2-acylamino-1,2-diphenylethan-1-ols. Heating of these compounds with phosphorus pentoxide in boiling decalin or with chlorophosphoric acid at 150°C yielded 4-phenyl- instead of the expected 3-phenylisoquinoline derivatives [3,4,5]. Moreover, 4,5-diphenyl-Δ^2-oxazoline derivatives isolated from the above-mentioned reaction media and treated with dehydrating agents under the same conditions as for hydroxyamides were also converted into 4-phenylisoquinoline derivatives. It was found that under the same conditions 1-benzamido-1-phenylalkan-2-ols and 5-alkyl-2,4-diphenyl-Δ^2-oxazolines were converted into 4-alkyl-1-phenylisoquinolines [6]. It was shown that in the above-mentioned reactions the phenyl group migration proceeds simultaneously with the opening of the protonated Δ^2-oxazolines [4]. The carbocation formed as a result of a rearrangement of the phenyl group is stabilized by proton abstraction, which most probably leads at first to N-styrylamide, further on undergoing cyclization to the isoquinoline system. Despite several attempts, the isolation of N-(2-phenylstyryl)benzamide from the reaction media on heating of *erythro*-2-benzamido-1,2-diphenylethan-1-ol with phosphorus pentoxide has been unsuccessful [2,4]. This could indicate that these compounds are easily converted to isoquinoline system [7,8]. We suppose that unsaturated amides undergo cyclization to isoquinoline derivatives immediately after formation from protonated Δ^2-oxazolines.

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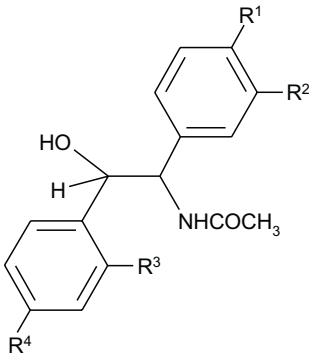
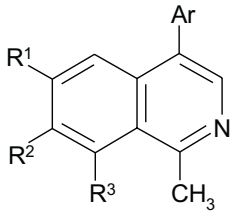
This paper describes the cyclization of 2-acetamido-1,2-diphenylethan-1-ol derivatives, in which hydrogen atom in one of two phenyl groups has been substituted with different substituents, to give the isoquinoline system.



1

	R^1	R^2	R^3	R^4
a:	H	H	H	H
b:	H	H	H	Me
c:	Me	H	H	H
d:	H	H	H	Cl
e:	Cl	H	H	H
f:	H	H	H	OMe
g:	OMe	H	H	H
h:	OMe	OMe	H	H
i:	OMe	OMe	Cl	H
j:	H	OMe	H	H
k:	OMe	H	Cl	H

In Scheme 1 the aryl group at the position C-2 in amide **1** was denoted as Ar^1, while that at the C-1 position as Ar^2.



2

	Ar	R^1	R^2	R^3
a:	Ph	H	H	H
b:	Ph	H	Me	H
c:	4-Me-C_6H_4	H	H	H
d:	Ph	H	Cl	H
e:	4-Cl-C_6H_4	H	H	H
f:	Ph	OMe	H	H
g:	Ph	H	H	OMe
h:	2-Cl-C_6H_4	H	OMe	H

The kind of substituent can be expected to have an essential influence on the reaction and the results can bring new information on the reaction mechanism.

RESULTS AND DISCUSSION

The compounds *erythro*- and *threo*-2-acetamido-1,2-diphenylethan-1-ol (**1a**), after being heated with phosphorus pentoxide in boiling decalin, cyclise to 1-methyl-4-phenylisoquinoline with similar yields (about 65%).

Freshly distilled phosphorus oxychloride appeared to be ineffective dehydrating agent in these reactions. A heating of *erythro*-2-acetamido-1,2-diphenylethan-1-ol (**1a**) with phosphorus pentoxide in boiling toluene or xylene yielded *trans*-4,5-

diphenyl-2-methyl-Δ^2-oxazoline and trace amounts of isoquinoline. Ardabilchi and Fitton [9] have reported isolation of N-(2-phenylstyryl)benzamide from the reaction medium when heating *erythro*-2-benzamido-1,2-diphenylethan-1-ol under the same condition. Having repeated the reaction we obtained only *trans*-2,4,5-triphenyl-Δ^2-oxazoline and trace amount of 1,4-diphenyl-isoquinoline [2]. However, heating of amide **1a** with chlorophosphoric acid at 150°C gave 1-methyl-4-phenylisoquinoline in 61%. The use of chlorophosphoric acid instead of phosphorus pentoxide permitted carrying out the cyclization in milder conditions.

Yields of 1-methyl-4-phenylisoquinoline derivatives (**2**) obtained by cyclization of appropriate amides (**1**) are collected in Table 1.

It was found that heating of compounds **1b** and **1c** with phosphorus pentoxide in boiling decalin or with chlorophosphoric acid at 150°C yielded a mixture of 1,7-dimethyl-4-phenylisoquinoline (**2b**) and 1-methyl-4-(4-methylphenyl)isoquinoline (**2c**) in the ratio of about 1.6:1. The ratio of isoquinolines was assessed from ^{1}H-NMR spectrum of their mixtures, on the basis of a comparison of integrated absorption signals assigned to the hydrogen atoms from the methyl groups C-7CH_3, C-4′CH_3 and those from C-3H. The total yield of isoquinolines was 54–65%. The proposed mechanism of conversion of amides (**1**) to isoquinolines (**2**) is presented in Scheme 1.

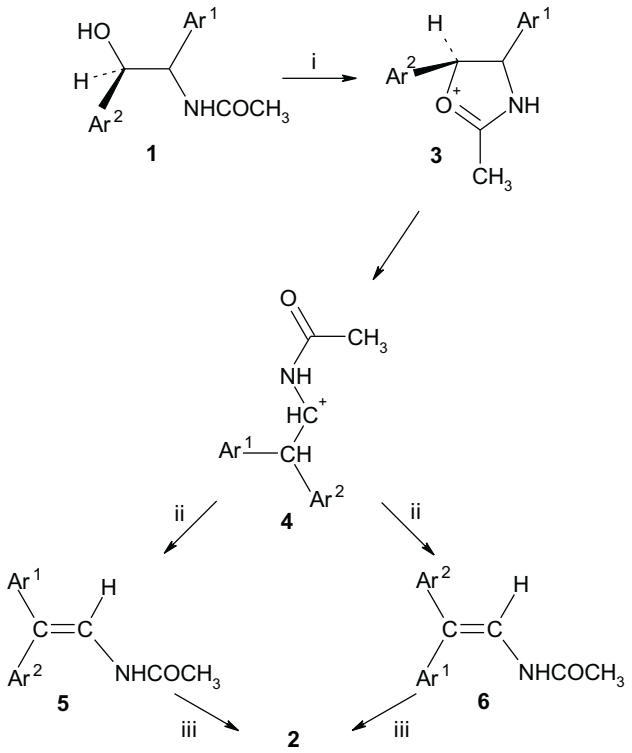
At the first stage of the reaction, each of the hydroxyamides (**1b** and **1c**) undergoes cyclization to protonated Δ^2-oxazoline (**3**). Below 150°C, compound **3** split forming a carbocation, which stabilises due to proton abstraction, leading to a mixture of isomeric N-styrylamides (**5**) and (**6**). The proportion of the isoquinolines obtained depends on the relative susceptibility to cyclization of the two unsaturated amides.

Table 1. Yields of isoquinolines (**2**) obtained upon heating of *erythro*-2-acetamido-1,2-diphenylethan-1-ol derivatives (**1**) with condensing agent.

Substrate (**1**)	Dehydrating agent[a]	Total yield of isoquinolines (%) (2)	Isoquinolines (molar ratio)
1a	A	66	**2a**
1a	B	61	**2a**
1b	A	54	**2b**, **2c** (1.6:1)
1b	B	48	**2b**, **2c** (1.7:1)
1c	A	65	**2b**, **2c** (1.6:1)
1c	B	61	**2b**, **2c** (1.6:1)
1d	A	89	**2d**, **2e** (1:6)
1d	B	87	**2d**, **2e** (1:6)
1e	A	91	**2d**, **2e** (1:7)
1e	B	86	**2d**, **2e** (1:7)
1f	B	42	**2f**, **2g** (1:1)
1g	B	8	**2h**

[a]Reaction conditions: A – P_2O_5 (boiling decalin, 193°C); B – HPO_2Cl_2 (150°C).

The fact that 1,7-dimethyl-4-phenylisoquinoline (**2b**) was obtained in excess suggests that the methyl group from the Ar^1 (compound **6**) or Ar^2 (compound **5**) ring facilitates the closure of the isoquinoline ring.



Scheme 1. i: P_2O_5, boiling decalin or HPO_2Cl_2 (150°C); ii: $-H^+$; iii: $H^+ - H_3O^+$.

The heating of compounds **1d** and **1e** with phosphorus pentoxide in boiling decalin or with chlorophosphoric acid at 150°C was found to yield a mixture of 7-chloro-1-methyl-4-phenylisoquinoline (**2d**) and 4-(4-chlorophenyl)-1-methylisoquinoline (**2e**) in the ratio of about 1:1.6. The ratio of isoquinolines was assessed from the ^{1}H-NMR spectrum of their mixture, on the basis of a comparison of integrated absorption signals assigned to the hydrogen atoms from the methyl groups C-1CH_3 and from C-3H.

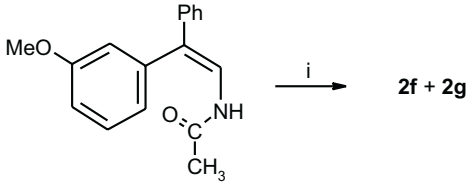
The total yield of the isoquinolines formation was 80–90%. A similar proportion of the isoquinoline systems obtained as a result of cyclization of compounds **1d** and **1e** testifies that the reaction occurs according to the mechanism presented in Scheme 1, so *via* formation of carbocation **4**. The excess of 4-(4-chlorophenyl)-1-methylisoquinoline (**2e**) indicates that the presence of the chlorine atom in the Ar^2 (compound **5**) or Ar^1 (compound **6**) ring hinders the closure of the isoquinoline ring. The chlorine atom deactivates the position C-2′, which otherwise would be subjected to the electrophilic attack of the carbon atom from the amide group.

An attempt was undertaken to synthesise the isoquinoline systems substituted with the methoxy group by the Pictet-Gams method. The procedure was as follows: 2-acylamino-1,2-diphenylethan-1-ol derivatives, containing the methoxy group in the phenyl ring were heated with chlorophosphoric acid at 150°C. Unfortunately, the use of phosphorus pentoxide as a condensing agent did not lead to formation of even traces of isoquinolines.

It was found that heating of 2-acetamido-1-(4-methoxyphenyl)-2-phenylethan-1-ol (**1f**), 2-acetamido-2-(4-methoxyphenyl)-1-phenylethan-1-ol (**1g**), 2-acetamido-2-(3,4-dimethoxyphenyl)-1-phenylethan-1-ol (**1h**) and 2-acetamido-1-(2-chlorophenyl)-2-(3,4-dimethoxyphenyl)ethan-1-ol (**1i**) with chlorophosphoric acid at 150°C led to formation of only traces of isoquinolines. Analysis of the ^{1}H and ^{13}C NMR spectra of the isoquinolines has shown that at the position C-7 they have a hydroxyl group instead of the methoxy one. Formation of the latter compounds resulted from splitting the ether bond by the applied condensing agent.

Kametani [10] and Zieliński [11] have also reported that the presence of the methoxy group in phenyl ring subjected to the electrophilic attack of the carbon atom from the amide group in Bischler-Napieralski reaction, hinders the closure of the isoquinoline ring.

However, heating of *erythro*-2-acetamido-2-(3-methoxyphenyl)-1-phenylethan-1-ol (**1j**) with chlorophosphoric acid at 150°C has been found to lead to a formation of a mixture of 6-methoxy-1-methyl-4-phenylisoquinoline (**2f**) and 8-methoxy-1-methyl-4-phenylisoquinoline (**2g**) with the former compound in slight excess. The ratio of isoquinolines was estimated from the ^{1}H-NMR spectrum of their mixture on the basis of a comparison of the integrated absorption signals assigned to the hydrogen atoms from the methyl groups C-1CH_3 and methoxy groups. The total yield of this reaction was 42%.



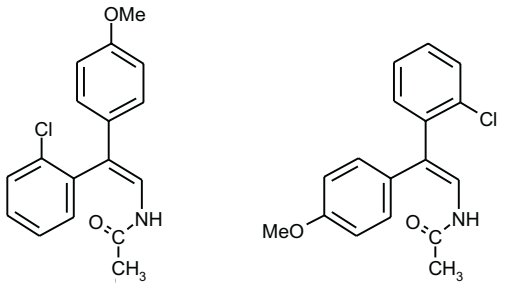
6j

Scheme 2. i: $H^+ - H_3O^+$

Neither 3-(3-methoxyphenyl)-1-methylisoquinoline nor 4-(3-methoxyphenyl)-1-methylisoquinoline have been detected among the reaction products, which means that the intermediates in this reaction are only compounds **3j** and **4j** and unsaturated amide **6j**.

On cyclization of the latter compound, the electrophilic attack of the carbon atom from the amide group takes place on the one of two possible positions in the phenyl group activated by the methoxy group (see Scheme 2).

Heating of *erythro*-2-acetamido-1-(2-chlorophenyl)-2-(4-methoxyphenyl)ethan-1-ol (**1k**) with chlorophosphoric acid at 150°C resulted only of 4-(2-chlorophenyl)-7-methoxy-1-methylisoquinoline (**2h**) in 8% yield.



5k **6k**

The post-reaction mixture contained neither 5-chloro-3-(4-methoxyphenyl)- nor 5-chloro-4-(4-methoxyphenyl)-1-methylisoquinoline. It means that of the two isomeric unsaturated amides **5k** and **6k**, which are most probable intermediates of this reaction, only the latter can undergo cyclization to the isoquinoline system. We suppose that methoxy group from compound **5k** positioned in the coplanar part of the molecule, reduces the electrophilicity of the carbon atom of the amide group through the mesomeric effect and thus hinders the closure of the ring. In compound **6k** the methoxy group is placed in the ring whose plane is deviated from the plane of the other part of the molecule. So its effect on the electrophilic character of the carbon atom from the amide group is insignificant. The low yield of the reaction can be related to the fact that the methoxy group in compound **6k** does not activate the position subjected to the electrophilic attack of the amide group carbon.

The above described reaction can be used for synthesis of 4-phenyl-1-methylisoquinoline derivatives substituted with the alkyl group or a halogen. The isoquinoline systems obtained (except **2a**) have not been synthesized yet by any other method. Synthesis of the methoxy derivatives of this heterocyclic system by the Pictet-Gams method is very difficult or impossible.

EXPERIMENTAL

M.p.'s were determined on a Boetius hot stage and are uncorrected. IR spectra were measured using C. Zeiss Specord 80 spectrophotometer, whereas NMR spectra were measured on a Gemini Varian 300 VT spectrometer with tetramethylsilane as a internal reference. TLC was carried out with Merck Kieselgel 60 F_{254} (0.25 mm) plates using benzene–ethyl acetate mixture (3:1, v/v) as a developing system. Decalin and phosphorus oxychloride were refluxed over phosphorus pentoxide and then rectified immediately before use. Chlorophosphoric acid was obtained by reaction of phosphorus oxychloride with water (molar ratio from 1:1 to 1:2) at –10°C, according to the procedure of Goubeau and Schulz [12] or with commercial polyphosphoric acid. The mixture of isomeric isoquinolines (**2b**, **2c**) and (**2f**, **2g**) was separated by the fractional crystallization of their perchlorates from methanol, while the mixture of compounds **2d** and **2e** was separated by fractional crystallization from ethyl alcohol.

2-Acetamido-1,2-diphenylethan-1-ol derivatives (**1**) were obtained from appropriate ketones in a three-stage synthesis according to an earlier published procedure [6,8].

erythro-**2-Acetamido-1,2-diphenylethan-1-ol (1a)**: m.p. 197–198°C (*threo*-isomer: m.p. 154–154°C); IR (nujol): 3380, 3320, 1650 and 1540 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.69 (s, 3H, CH_3CO), 4.83 (t, 1H, C^2H), 4.92 (t, 1H, C^1H), 5.33 (d, 1H, OH), 7.04–8.02 (m, 10H, ArH), 8.20 (d, 1H, NH).

erythro-**2-Acetamido-1-(4-methylphenyl)-2-phenylethan-1-ol (1b)**: m.p. 186–187°C (*threo*-isomer: m.p. 142–145°C); IR (nujol): 3370, 3320, 1650 and 1550 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.70 (s, 3H, CH_3CO), 2.25 (s, 3H, CH_3), 4.77 (t, 1H, C^2H), 4.94 (t, 1H, C^1H), 5.31 (d, 1H, OH), 6.92–7.90 (m, 9H, ArH), 8.19 (d, 1H, NH).

erythro-**2-Acetamido-2-(4-methylphenyl)-1-phenylethan-1-ol (1c)**: m.p. 193.5–195°C (*threo*-isomer: m.p. 120–121°C); IR (nujol): 3350, 1650 and 1545 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.73 (s, 3H, CH_3CO), 2.23 (s, 3H, CH_3), 4.76 (t, 1H, C^2H), 4.94 (t, 1H, C^1H), 5.29 (d, 1H, OH), 7.01–7.68 (m, 9H, ArH), 8.25 (d, 1H, NH).

erythro-**2-Acetamido-1-(4-chlorophenyl)-2-phenylethan-1-ol (1d)**: m.p. 204.5–205°C (*threo*-isomer: m.p. 128–131°C); IR (nujol): 3310, 3300, 1645 and 1546 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.72 (s, 3H, CH_3CO), 4.82 (t, 1H, C^2H), 4.93 (t, 1H, C^1H), 5.51 (d, 1H, OH), 6.63–7.81 (m, 9H, ArH), 8.22 (d, 1H, NH).

erythro-**2-Acetamido-2-(4-chlorophenyl)-1-phenylethan-1-ol (1e)**: m.p. 214–216°C (*threo*-isomer: m.p. 127.5–128C°); IR (nujol): 3350, 1647 and 1540 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.72 (s, 3H, CH_3CO), 4.74 (t, 1H, C^2H), 4.93 (t, 1H, C^1H), 5.48 (d, 1H, OH), 7.00–7.62 (m, 9H, ArH), 8.28 (d, 1H, NH).

erythro-**2-Acetamido-1-(4-methoxyphenyl)-2-phenylethan-1-ol (1f)**: m.p. 176–177°C; ^{1}H-NMR (DMSO-d_6), δ: 1.71 (s, 3H, CH_3), 3.74 (s, 3H, OCH_3), 4.69–5.10 (m, 2H, C^1H and C^2H), 5.28 (d, 1H, OH), 6.72–7.15 (m, 9H, ArH), 8.19 (d, 1H, NH).

erythro-**2-Acetamido-2-(4-methoxyphenyl)-1-phenylethan-1-ol (1g)**: m.p. 183–185°C; IR (nujol): 3330, 1640 and 1530 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.70 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 4.65–4.99 (m, 2H, C^1H and C^2H), 5.34 (d, 1H, OH), 6.72–7.25 (m, 9H, ArH), 8.17 (d, 1H, NH).

erythro-**2-Acetamido-2-(3,4-dimethoxyphenyl)-1-phenylethan-1-ol (1h)**: m.p. 177– 178°C; IR (nujol): 3310, 1645 and 1540 cm^{-1}; ^{1}H-NMR ($CDCl_3$), δ: 1.72 (s, 3H, CH_3CO), 3.64 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 4.69 (t, 1H, C^2H), 4.94 (t, 1H, C^1H), 5.17 (d, 1H, OH), 6.77–7.32 (m, 8H, ArH), 8.23 (d, 1H, NH).

erythro-**2-Acetamido-1-(2-chlorophenyl)-2-(3,4-dimetoxyphenyl)ethan-1-ol (1i)**: m.p. 169–171°C; IR (nujol): 3320, 1645 and 1545 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.71 (s, 3H, CH_3CO), 3.64 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 4.71–4.86 (m, 2H, C^1H and C^2H), 5.31 (d, 1H, OH), 6.71–7.28 (m, 8H, ArH), 8.18 (d, 1H, NH).

erythro-**2-Acetamido-2-(3-methoxyphenyl)-1-phenylethan-1-ol (1j)**: m.p. 128–129°C; IR (nujol): 3350, 3335, 1647 and 1550 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.70 (s, 3H, CH_3CO), 3.74 (s, 3H, OCH_3), 4.86–5.01 (m, 2H, C^1H and C^2H), 5.50 (d, 1H, OH), 6.92–7.91 (m, 9H, ArH), 8.30 (d, 1H, NH).

erythro-**2-Acetamido-1-(2-chlorophenyl)-2-(4-methoxyphenyl)ethan-1-ol (1k)**: m.p. 72–73°C; IR (nujol): 3316, 1648 and 1535 cm^{-1}; ^{1}H-NMR (DMSO-d_6), δ: 1.80 (s, 3H, CH_3CO), 3.65 (s, 3H, OCH_3), 4.93–5.12 (m, 2H, C^1H and C^2H), 5.40 (d, 1H, OH), 6.67–7.36 (m, 8H, ArH), 8.33 (d, 1H, NH).

1-Methyl-4-phenylisoquinoline derivatives (2) were obtained by cyclization of hydroxyamides (**1**) according to the following procedures.

Procedure A: To a hot solution of amide (2 g) in the decalin (30 ml), 20 g of phosphorus pentoxide was added. The mixture was heated in an oil bath for 3 hrs and then cooled. The excess of dehydrating agent was decomposed very carefully with 100 g of crushed ice. The organic layer was separated and extracted with 5% hydrochloric acid. The combined aqueous layers were steam–distilled to remove traces of decalin and to hydrolyse unconverted oxazoline. The post–cooling solution was alkalized with 30% aqueous potassium hydroxide solution and then extracted several time with ether. The combined organic extracts were washed with water, dried (Na_2SO_4) and evaporated. The residue was distilled under reduced pressure and recrystallized from ethanol.

Procedure B: The mixture of amide (2 g) and chlorophosphoric acid (30 ml)* was heated in an oil bath for 3 hrs and then cooled. The excess of dehydrating agent was decomposed very carefully with 100 g of crushed ice and the solution obtained was heated for 10 minutes with charcoal. The cooled filtrate was alkalised with 30% aqueous potassium hydroxide solution with ether and then extracted several time with ether. The combined organic extracts were washed with water, dried (Na_2SO_4) and evaporated. The residue was distilled under reduced pressure and recrystallized from ethanol.

1-Methyl-4-phenylisoquinoline (2a): m.p. 80–81°C, picrate m.p. 222–223°C; ^{1}H-NMR ($CDCl_3$), δ: 3.01 (s, 3H, CH_3), 7.24–8.22 (m, 9H, ArH), 8.36 (s, 1H, C-3H); ^{13}C-NMR ($CDCl_3$), δ: 22.49 (CH_3), 125.54 (C-5), 125.75 (C-7), 126.78 (C-8), 127.22 (C-10), 127.70 (C-4′), 128.52 (C-3′), 129.87 (C-6), 130.25 (C-2′), 131.99 (C-1′), 134.48 (C-4), 137.56 (C-9), 141.79 (C-3), 157.88 (C-1). Anal. Calcd. for $C_{16}H_{13}N$: C, 87.63; H, 5.98; N, 6.39. Found: C, 87.64; H, 5.97; N, 6.39.

1,7-Dimethyl-4-phenylisoquinoline (2b): b.p. 182–188°C (4 mm Hg), picrate m.p. 250–252°C, perchlorate m.p. 189.5–191.5°C; ^{1}H-NMR ($CDCl_3$), δ: 2.54 (s, 3H, C-7CH_3), 2.97 (CH_3), 7.25–7.92 (m, 8H, ArH), 8.29 (s, 1H, C-3H); ^{13}C-NMR, δ: 21.83 (C-7$\underline{C}H_3$), 22.43 (CH_3), 124.72 (C-5), 127.33 (C-10), 127.54 (C-4′ and C-8), 128.41 (C-3′), 130.14 (C-2′), 131.04 (C-6), 131.77 (C-1′), 132.53 (C-9), 134.31 (C-4), 136.57 (C-7), 140.87 (C-3), 157.13 (C-1). Anal. Calcd. for $C_{17}H_{15}N$: C, 87.54; H, 6.47; N, 5.99. Found: C, 87.52; H, 6.48; N, 6.00.

1-Methyl-4-(4-methyl)isoquinoline (2c): m.p. 80–83°C, picrate m.p. 229–230°C, m.p. perchlorate m.p. 205–207.5°C; ^{1}H-NMR ($CDCl_3$), δ: 2.43 (s, 3H, C-4′CH_3), 2.99 (s, 3H, CH_3), 7.30–8.15 (m, 8H, ArH), 8.34 (s, 1H, C-3H); ^{13}C-NMR ($CDCl_3$), δ: 21.19 (C-4′$\underline{C}H_3$), 22.43 (CH_3), 125.48 (C-5), 125.70 (C-7), 126.68 (C-8), 127.11 (C-10), 128.41 (C-1′), 129.17 (C-3′), 129.76 (C-6), 130.03 (C-2′), 134.42 (C-4), 136.59 (C-4′), 137.35 (C-9), 141.63 (C-3), 157.57 (C-1). Anal. Calcd. for $C_{17}H_{15}N$: C, 87.49; H, 6.49; N, 6.02. Found: C, 87.52; H, 6.48; N, 6.00.

7-Chloro-1-methyl-4-phenylisoquinoline (2d): m.p. 91–92°C, picrate m.p. 228–230°C; ^{1}H-NMR ($CDCl_3$), δ: 2.97 (s, 3H, CH_3), 7.35–8.20 (m, 8H, ArH), 8.35 (s, 1H, C-3H); ^{13}C-NMR ($CDCl_3$), δ: 22.40 (CH_3), 127.38 (C-5 and C-8), 127.92 (C-4′), 128.63 (C-3′ and C-10), 130.09 (C-2′), 130.74 (C-6), 131.71 (C-7), 132.64 (C-1′), 134.62 (C-4), 136.81 (C-9), 141.90 (C-3), 157.01 (C-1). Anal. Calcd. for $C_{16}H_{12}ClN$: C, 75.11; H, 4.77; N, 5.53. Found: C, 75.74; H, 4.77; N, 5.52.

4-(4-Chlorophenyl)-1-methylisoquinoline (2e): m.p. 127–128°C, picrate m.p. 238– 239.5°C, ^{1}H-NMR ($CDCl_3$), δ: 3.03 (s, 3H, CH_3), 7.40–8.20 (m, 8H, ArH), 8.30 (s, 1H, C-3H); ^{13}C-NMR ($CDCl_3$), δ: 22.43 (CH_3), 125.10 (C-5), 125.86 (C-7), 126.89 (C-8), 127.03 (C-10), 128.73 (C-3′), 130.08 (C-6), 130.68 (C-1′), 131.44 (C-2′), 133.94 (C-4′), 134.15 (C-4), 135.89 (C-9), 141.52 (C-3), 158.31 (C-1). Anal. Calcd. for $C_{16}H_{12}ClN$: C, 75.72; H, 4.78; N, 5.50. Found: C, 75.74; H, 4.77; N, 5.52.

6-Methoxy-1-methyl-4-phenylisoquinoline (2f): m.p. 134.5–135.5°C, picrate m.p. 202–203°C; ^{1}H-NMR ($CDCl_3$), δ: 2.96 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 6.75–8.19 (m, 8H, ArH), 8.27 (s, 1H, C-3H); ^{13}C-NMR ($CDCl_3$), δ: 22.11 (CH_3), 55.26 (OCH_3), 103.75 (C-5), 119.14 (C-7), 122.88 (C-10), 127.70 (C-4′ and C-8), 128.57 (C-3′), 129.98 (C-2′), 131.44 (C-1′), 136.54 (C-4), 137.73 (C-9), 141.82 (C-3), 157.18 (C-1), 160.81 (C-6). Anal. Calcd. for $C_{17}H_{15}NO$: C, 82.21; H, 6.08; N, 5.66. Found: C, 82.23; H, 6.09; N, 5.64.

8-Methoxy-1-methyl-4-phenylisoquinoline (2g): picrate m.p. 212–215°C; ^{1}H-NMR ($CDCl_3$), δ: 3.15 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 6.80–8.20 (m, 8H, ArH), 8.26 (s, 1H, C-3H); ^{13}C-NMR ($CDCl_3$), δ: 28.93 (CH_3), 55.46 (OCH_3), 106.12 (C-7), 117.37 (C-5), 126.49 (C-4′), 127.24 (C-3′), 128.44 (C-10), 129.24 (C-2′), 130.15 (C-6), 131.16 (C-1′), 136.18 (C-9), 137.41 (C-4), 141.40 (C-3), 157.59, 157.98 (C-1 and C-8). Anal. Calcd. for $C_{17}H_{15}NO$: C, 82.23; H, 6.07; N, 5.65. Found: C, 82.23; H, 6.09; N, 5.64.

*Heating of chlorophosphoric acid, accompanied by release of hydrogen chloride, yielded the chloropolyphosphoric acids, which subsequently converted to cross – linked polymer [13].

4-(2-Chlorophenyl)-7-methoxy-1-methylisoquinoline (2h): ^{1}H-NMR ($CDCl_3$), δ: 2.91 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 7.18–7.34 (m, 7H, ArH), 8.13 (C-3H); ^{13}C-NMR ($CDCl_3$), δ: 29.70 (CH_3), 55.48 (OCH_3), 103.86 (C-8), 122.63 (C-6), 126.77 (C-4′), 127.25 (C-5), 128.13 (C-10), 129.43 (C-5′), 129.70 (C-3′), 132.32 (C-1′), 132.84 (C-9), 134.51, 134.54, 136.27, 140.02 (C-3), 157.03, 158.16 (C-1 and C-7). Anal. Calcd. for $C_{17}H_{14}ClNO$: C, 71.91; H, 5.00; N, 4.94. Found: C, 71.96; H, 4.97; N, 4.93.

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