

Synthesis of 4-Vinylquinoline: Pyrolytic Rearrangement of the 4-(1-Hydroxyethyl)quinoline and Related Derivatives

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The synthesis of 4-vinylquinoline has been carried out by means of the Wittig reaction between 4-quinolinecarbaldehyde and the methyl triphenylphosphonium ylide in dimethyl sulphoxide in good yield. Dehydration of the 4-(1-hydroxyethyl)quinoline and their xanthate derivative, give equimolar amounts of 4-ethylquinoline and 4-acetylquinoline while small amounts of 4-vinylquinoline were found. Dehydrochlorination of 4-(1-chloroethyl)quinoline in ethanol-sodium hydroxide provides 4-ethyl-3-ethoxyquinoline in good yield, but 4-vinylquinoline is a minor reaction product.

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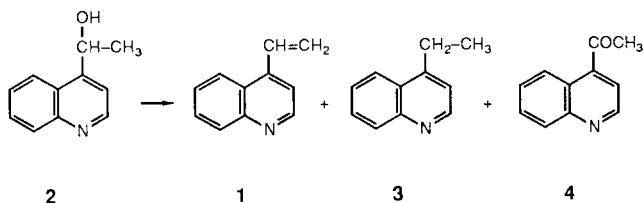
4-Vinylquinoline exhibits a particular stereoelectronic behaviour related to the 4-vinylpyridine which has been analyzed in the catalytic Ziegler-Natta polymerization [1]. The catalyst system used in this polymerization method, requires the preparation of 4-vinylquinoline in high purity. Two synthetic methods for the preparation of 4-vinylquinoline have been reported in the literature which require 4-methylquinoline as the synthon: a) condensation with formaldehyde and dehydration of the intermediate 4-hydroxyethylquinoline [2]; and b) Mannich condensation with formaldehyde and dimethyl amine in the presence of hydrochloric acid [3]. Both synthetic methods give very poor yields after the required purification. Several attempts have been developed to prepare the 4-vinylquinoline using 4-quinolinecarboxaldehyde as the common synthon, which was prepared by oxidation of the 4-methylquinoline with selenium oxide [4] in good yield.

Reaction between 4-quinolinecarboxaldehyde and methylmagnesium iodide occurs at room temperature to give the 4-(1-hydroxyethyl)quinoline in quantitative yield. Dehydration of 4-(1-hydroxyethyl)quinoline was proposed to produce the 4-vinylquinoline. Several dehydrating agents were employed such as: a) potassium bisulfate, b) phosphorus pentoxide, c) sodium hydroxide and d) dimethyl sulphoxide. Dehydration with sodium hydroxide (or pyrolysis in dimethyl sulphoxide) provides a residual oil resulting of the partial polymerization of the 4-vinylquinoline which contains the monomer in small amount.

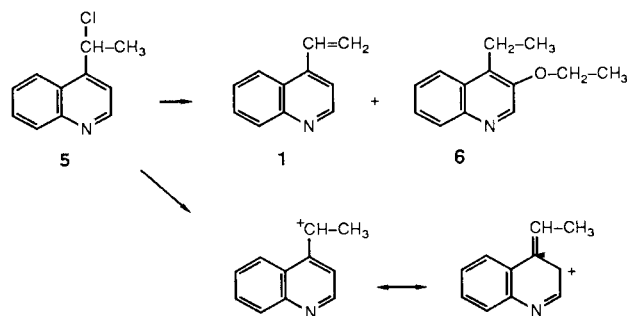
However, when dehydration was carried out in the presence of acids, cases a) and b), a mixture of 4-acetyl- and 4-ethylquinolines were obtained by distillation in a 1:1 molar ratio. Both products seem to be obtained by disproportionation of the 4-(1-hydroxyethyl)quinoline, Scheme 1.

To avoid the disproportionation reaction, the preparation of 4-vinylquinoline, was attempted by dehydrochlorination of the 4-(1-chloroethyl)quinoline. This chloroethyl derivative was obtained in good yield from 4-(1-hydroxyethyl)quinoline by nucleophilic substitution of the hydroxyl group with triphenylphosphine and carbon tetrachloride [5]. Dehydrochlorination of the 4-(1-chloroethyl)quinoline was carried out at 160° with potassium hydroxide in ethanol in the presence of *N*-phenyl-1-naphthylamine as an inhibitor of possible radical polymerization. Two main products were obtained, 4-vinylquinoline (16%) and 4-ethyl-3-ethoxyquinoline (72%). Formation of the 3-ethoxy derivative probably takes place by solvolysis of the chloroethyl derivative and *via* an unimolecular nucleophilic substitution mechanism. According to the resonance of the benzyl-type carbocation with the quinoline ring, the carbocation formulae on the position 3 of the quinoline ring, seems to be the main contributor, see Scheme 2. An alternative procedure was outlined starting

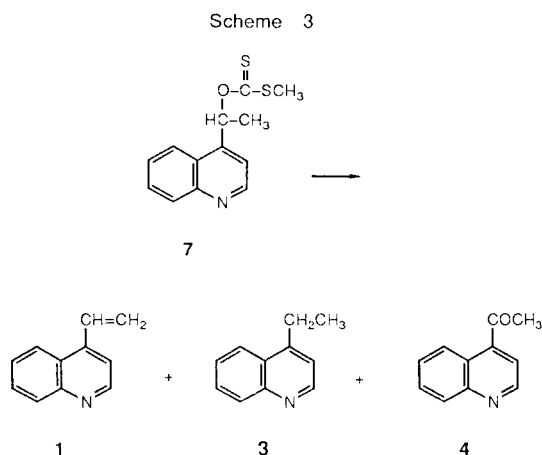
Scheme 1



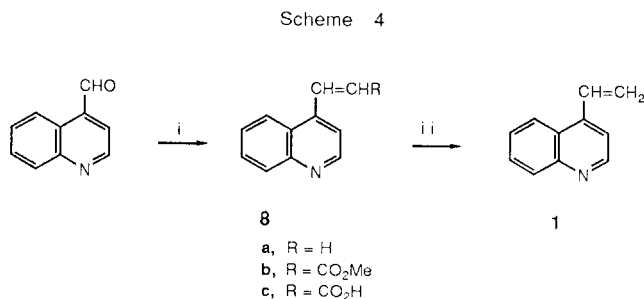
Scheme 2



with the methyl xanthate of the 4-(1-hydroxyethyl)quinoline, which was prepared in good yield following a general method [6], (See Experimental). Pyrolysis of the xanthate provides 4-vinylquinoline (15%) and two main products identified as 4-ethyl- and 4-acetylquinolines in an equimolar ratio, Scheme 3, in a similar manner as occurred in the above referred dehydration reaction of 4-(1-hydroxyethyl)quinoline.



The synthesis of the 4-vinylquinoline was finally carried out by means of the Wittig reaction between the 4-quinolinecarboxaldehyde and the convenient ylide. Two ylide reagents were employed, the carboxymethyl triphenylphosphonium and the methyl triphenylphosphonium ones. The former provides very good yields of 3-(4-quinoline)-methyl propenoate but hydrolysis and decarboxylation stages are required to obtain 4-vinylquinoline and decarboxylation proceeds in very low yield. The reaction between the 4-quinolinecarboxaldehyde and the methyl triphenylphosphonium ylide gives the best yields of 4-vinylquinoline. The ylide is generated "in situ" using dimethyl sulphoxide-sodium hydride as the base [7]. In this way, 4-vinylquinoline was isolated in 70% yield after column chromatography in high purity as required for the Ziegler-Natta catalyst [1]. Furthermore it allows recovery of the rest of the aldehyde that remains untransformed during the reaction for reuse, see Scheme 4.



i) (C₆H₅)₃P=CHR; ii) Hydrolysis, copper chromite, heat.

EXPERIMENTAL

Melting points were determined by using a Reichert stage microscope and are uncorrected. Infrared spectra were recorded using an SP 1100 Philips Pye Unicam Spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Bruker WM-200-SY spectrometer. Chemical shifts (δ), are given relative to internal tetramethylsilane. Elemental analysis were performed with a Perkin-Elmer 240 analyzer. Mass spectra were recorded on a Hewlett-Packard 5985 GC/MS system.

4-Vinylquinoline (1).

a. Preparation of 4-(1-Hydroxyethyl)quinoline (2).

To a mixture of wire magnesium (0.10 g, 0.0044 g-atom) and methyl iodide (0.6 g, 0.0044 mole) in diethyl ether, was added dropwise a solution of 4-quinolinecarboxaldehyde (0.7 g, 0.0044 mole) in diethyl ether, maintaining a moderate reflux. After the mixture was stirred for 3 hours, it was hydrolyzed with aqueous ammonium chloride and extracted with diethyl ether. The solvent was evaporated to provide the alcohol **2** in 90% yield, mp 115-117°.

Dehydration of 4-(1-Hydroxyethyl)quinoline (2).

Several dehydration agents were employed such as a) potassium bisulfate, b) phosphorus pentoxide, c) sodium hydroxide and d) dimethyl sulphoxide. In this experimental section, only optimal or representative results are considered.

The alcohol **2** (1.0 g, 0.0057 mole) was stirred with monobasic potassium sulfate in glycerine (or tetraethylglycol) at 180° and 2 mm Hg, in the presence of a small amount of *N*-phenyl-1-naphthylamine. The mixture was distilled and chromatographed on a silica gel column, eluted with ethyl acetate:*n*-hexane (2:1) to provide 4-ethylquinoline, **3**, (30%) as a colourless oil and 4-acetylquinoline, **4**, (30%) as a yellow oil. 4-Vinylquinoline was isolated in 15% yield.

Compound **3** had nmr (deuteriochloroform): 8.82 (d, 1H, Ar-H pos-2), 8.13 (m, 1H, Ar-H pos-8), 7.78-7.46 (m, 4H, Ar-H), 3.09 (q, 2H, CH₂, J = 6 Hz), 1.31 (t, 3H, CH₃, J = 6 Hz); ms: (70 eV) 157 (M⁺, base peak), 142 (M⁺-15, 51%), 128 (M⁺-29, 10%), 101 (5%), 75 (4%).

Anal. Calcd. for C₁₁H₁₁N: C, 84.04; H, 7.05; N, 8.91. Found: C, 83.87; H, 7.20; N, 8.85.

Compound **4** had ir (film): 1680 cm⁻¹; nmr (deuteriochloroform): 9.10 (d, 1H, Ar-H pos-2), 8.32 (m, 1H, Ar-H pos-8), 7.83-7.62 (m, 4H, Ar-H), 2.76 (s, 3H, CH₃); ms: (70 eV) 171 (M⁺, 71%), 156 (M⁺-15, 67%), 128 (M⁺, base peak), 101 (39%), 75 (29%).

Anal. Calcd. for C₁₁H₉ON: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.31; H, 5.26; N, 8.23.

b. Preparation of 4-(1-Chloroethyl)quinoline (5).

A mixture of dry carbon tetrachloride, 22 ml, and triphenylphosphine (8.5 g, 0.03 mole) was stirred and warmed at 50°. 4-(1-Hydroxyethyl)quinoline (5.0 g, 0.02 mole) was added and the mixture was refluxed during 3 hours. The mixture was treated with *n*-pentane and the triphenylphosphine oxide was filtered. The solvent was evaporated and **5** was obtained in 90% yield as an oil, which was submitted to dehydrochlorination.

Dehydrochlorination of the 4-(1-Chloroethyl)quinoline (5).

Compound **5** obtained above, was treated with potassium hydroxide (1.2 g, 0.021 mole) in 30 ml of ethanol, at 160° during 6 hours. A sample of the crude product was analyzed by gc/ms and two reaction products were detected, 4-vinylquinoline in 16% and 4-ethyl-3-ethoxyquinoline, **6**, in 72% yield. The crude product was purified by column chromatography on silica gel using ethyl acetate:hexane (1:1) as the eluent. Compound **6**, was a colorless liquid.

Compound **6** had nmr (deuteriochloroform): 8.82 (d, 1H, Ar-H pos-2), 8.10 (m, 1H, Ar-H pos-8), 7.84-7.72 (m, 3H, Ar-H), 3.91 (q, 2H, OCH₂, J = 6.3 Hz), 3.52 (t, 3H, CH₃, J = 6.3 Hz), 3.31 (q, 2H, CH₂, J = 6 Hz), 1.21 (t, 3H, CH₃, J = 6 Hz); ms: (70 eV) 201 (M⁺, 26%), 186 (M⁺-15, 35%), 157 (M⁺-44, base peak), 130 (M⁺-71, 55%), 101 (8%), 75 (5%).

Anal. Calcd. for $C_{13}H_{15}ON$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.22; H, 7.39; N, 7.15.

c. Preparation of the Methyl-4-(1-hydroxyethyl)quinoline Xanthate (7).

To a solution of 4-(1-hydroxyethyl)quinoline (2.8 g, 0.016 mole) in 20 ml of dry diethyl ether, was added sodium metal (0.44 g, 0.02 g-atom) freshly cut into small pieces. The mixture was stirred at room temperature for 30 hours and then carbon disulfide (2.19 g, 0.02 mole) was added in portions. Then, the excess sodium was removed and stirring was continued for 1 hour. Methyl iodide (6.3 g, 0.04 mole) was added and the mixture was stirred overnight. Methyl iodide (1 ml) was added and the reaction was continued for 1 hour longer. The inorganic salts were removed by filtration and the volatile material was evaporated under reduced pressure at room temperature to yield 97% of the methyl xanthate 7.

Compound 7 had mp 254°; nmr (deuteriochloroform): 8.90 (d, 1H, Ar-H pos-2), 8.12 (m, 1H, Ar-H pos-8), 7.74-7.43 (m, 4H, Ar-H), 7.31 (q, 1H, CH, J = 5.8 Hz), 2.55 (s, 3H, CH₃), 1.80 (d, 3H, CH₃, J = 5.8 Hz).

Anal. Calcd. for $C_{13}H_{15}NS_2$: C, 63.12; H, 5.38; N, 5.66; S, 25.92. Found: C, 63.44; H, 5.67; N, 5.79; S, 26.14.

Thermal Decomposition of the Methyl-4-(1-hydroxyethyl)quinoline Xanthate (7).

The xanthate 7 (4.0 g, 0.01 mole) was placed in a 50 ml round-bottomed flask fitted with a Claisen head for distillation. The flask was immersed in a silicone bath and the temperature was gradually increased. A slight decomposition began when the bath temperature reached 165° and at 180°/2 mm Hg was distilled. Three main products were identified; 4-ethyl-, 3, 4-acetyl-, 4, 84% (1:1 equimolar mixture) and 4-vinyl-, 1, quinolines (15%). Spectral analyses are indicated above.

d. Wittig Reaction Between 4-Quinolinecarboxaldehyde and Carboxymethyl Triphenylphosphonium Ylide.

A solution of 4-quinolinecarboxaldehyde (0.5 g, 0.0032 mole) and carboxymethyl triphenylphosphonium ylide (1.6 g, 0.0048 mole) in 30 ml of benzene were refluxed during 19 hours in the presence of benzoic acid as a catalyst. Solvent was evaporated and the crude product chromatographed on a silica gel column, eluting with ethyl acetate:n-hexane (1:1). The methyl ester of the 3-(4-quinoline)propenoic acid, 8, was obtained in 83% yield.

Compound 8 had mp 48-50°; nmr (deuteriochloroform): 8.65 (d, 1H, pos-2), 7.7 (m, 5H, Ar-H), 6.21 and 6.37 correspond to H_a and H_b vinylic protons, J = 15.9 Hz (trans), 3.66 (s, 3H, methyl ester).

Anal. Calcd. for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.45; H, 5.33; N, 6.84.

Decarboxylation of the 3-(4-Quinoline)propenoic Acid (9).

The methyl ester 8, obtained above, was hydrolyzed with a solution of

sodium hydroxide (15%) at 90° during 3 hours. After acidification, the 3-(4-quinoline)propenoic acid, was obtained in 90% yield, mp 150° dec. Finally, the 3-(4-quinoline)propenoic acid was submitted to pyrolysis at 200°, in presence of copper chromite, during 5 hours to provide 4-vinylquinoline in 10% yield.

Preparation of 4-Quinolinecarboxaldehyde.

A mixture of selenium oxide (38.8 g, 0.35 mole) recently sublimed in 209 ml of dioxane, was stirred at 60° until the dissolution was completed. Then, 4-methylquinoline (50.0 g, 0.35 mole) was added and the mixture was stirred during 30 minutes and finally, refluxed during 4 hours. After selenium was filtered and dioxane distilled, the crude product was chromatographed on a silica gel column, eluting with ethyl acetate:n-hexane (1:1) to provide the 4-quinolinecarboxaldehyde in 78% yield as an orange solid, mp 50-51°, lit [4] 49-50°.

Wittig Reaction Between 4-Quinolinecarboxaldehyde and Methyl Triphenylphosphonium Ylide.

A mixture of sodium hydride (0.56 g, 0.02 mole) and 20 ml of dimethyl sulphoxide was warmed at 70-75° until the evolution of hydrogen ceased. Then a solution of methyl triphenylphosphonium bromide (8.56 g, 0.02 mole) in 20 ml of dimethyl sulphoxide was added. The mixture, which takes on an orange color, was stirred during 15 minutes, and then 4-quinolinecarboxaldehyde (2.0 g, 0.01 mole) in 15 ml of dimethyl sulphoxide was added, stirring at room temperature during 12 hours. Finally it was hydrolyzed with water and extracted with hexane. The crude product was purified by chromatography on silica gel by using ethyl acetate:n-hexane (2:1) as the eluent. The 4-vinylquinoline, 1, was obtained as a slightly yellow liquid in 70% yield, bp 120-123°/3 mm Hg.

Compound 1 had ir (film): 1615 (CH=CH₂, conj), 1000-950 (=CH₂); nmr (deuteriochloroform): 8.87 (d, 1H, Ar-H pos-2), 8.13 (m, 1H, Ar-H pos-8), 7.71-7.42 (m, 4H, Ar-H), ABX system of the vinyl rest; $\nu_A = 5.98$, $\nu_B = 5.66$, $\nu_X = 7.42$, $J_{AX} = 1.2$, $J_{BX} = 17.2$, $J_{AB} = 11.0$ Hz; ms: (70 eV) 155 (M⁺, 57%), 154 (base peak), 128 (M⁺-27, 16%), 127 (M⁺-28, 35%), 101 (17%), 77 (50%).

Anal. Calcd. for $C_{11}H_9N$: C, 85.23; H, 5.85; N, 9.03. Found: C, 85.35; H, 5.73; N, 9.01.

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