# REACTIONS OF 3-QUINOLINECARBONITRILE AND 6-QUINOLINECARBONITRILE WITH METHYLMAGNESIUM IODIDE AND PHENYLMAGNESIUM BROMIDE*

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Reaction of methylmagnesium iodide with 3-quinolinecarbonitrile gave a product of the 1,4-addition (*IIa*), whereas that of phenylmagnesium bromide gave products of the 1,2-addition (*III*) and the 1,4-addition (*IIb*). 6-Quinolinecarbonitrile (*Va*) exposed to the two agents gave ketones *Vb* and *Vd*, as well as products of the 1,2-addition and the subsequent oxidation (*Vc* and *Ve*); with phenylmagnesium bromide one more product was formed, *viz.* ketone *Vf*.

In studying the reduction of ketones of the quinoline series[1] we paid attention to the reactions of Grignard agents with quinolinecarbonitriles, namely *Ia* and *Va*. The reaction of methylmagnesium iodide with 3-quinolinecarbonitrile (*Ia*) was reported[2] to produce an unstable 4-methyl-1,4-dihydro-3-quinolinecarbonitrile (*IIa*), which was oxidized with chloranil to a stable 4-methyl-3-quinolinecarbonitrile (*Ib*). We have reproduced this reaction and succeeded, by means of column chromatography, in isolation and characterization of the dihydroderivative *IIa*, which was then oxidized with nitric acid to the stable *Ib*. In reaction of phenylmagnesium bromide with the nitrile *Ia* we obtained, unlike Japanese authors[3], two products. One m.p. 230–232°C, was evidently 4-phenyl-1,4-dihydro-3-quinolinecarbonitrile (*IIb*), the other, m.p. 134–138°C, was 2-phenyl-1,2-dihydro-3-quinolinecarbonitrile (*III*). The dihydro derivative *III* underwent a spontaneous conversion to 2-phenyl-3-quinolinecarbonitrile (*IV*), which was also prepared, as an authentic sample, by condensation of 2-aminobenzaldehyde with benzoylacetonitrile. The structure assigned to compound *IIb* was corroborated by oxidation, which converted this dihydronitrile into the known 4-phenyl-3-quinolinecarbonitrile[9] (*Ic*).

The reaction of methylmagnesium iodide with 6-quinolinecarbonitrile (*Va*), followed by column chromatography, gave 6-acetylquinoline (*Vb*) and 2-methyl-6-quinolinecarbonitrile (*Vc*) as a by-product. Exposure of the nitrile *Va* to phenyl-

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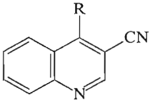
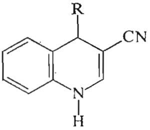
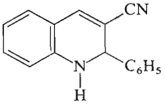
magnesium bromide produced three compounds: 6-benzoylquinoline (*Vd*), 2-phenyl-6-quinolinecarbonitrile (*Ve*) and 6-benzoyl-2-phenylquinoline (*Vf*). The structures of *Vc*, *Ve* and *Vf* were determined by $^1$H-NMR spectroscopy with *Va* and *Vd* as reference compounds. The $^1$H-NMR spectra of products *Vc*, *Ve* and *Vf* lacked the signal corresponding to the hydrogen at position 2 of the standards *Va* and *Vd*. The products with substituent at position 2, *i.e.* *Vc*, *Ve* and *Vf*, were evidently formed by spontaneous oxidation of the primary 1,2-dihydro compounds.



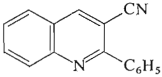
*Ia*, R = H
*Ib*, R = $CH_3$
*Ic*, R = $C_6H_5$



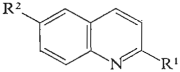
*IIa*, R = $CH_3$
*IIb*, R = $C_6H_5$



*III*



*IV*



*Va*, $R^1 = H$, $R^2 = CN$
*Vb*, $R^1 = H$, $R^2 = COCH_3$
*Vc*, $R^1 = CH_3$, $R^2 = CN$
*Vd*, $R^1 = H$, $R^2 = C_6H_5CO$
*Ve*, $R^1 = C_6H_5$, $R^2 = CN$
*Vf*, $R^1 = C_6H_5$, $R^2 = C_6H_5CO$

## EXPERIMENTAL

Thin-layer chromatography was carried out on Silufol UV 254 and 366 (macroporous silica gel Silpearl with a luminiscence indicator for wave lengths 254 and 366 nm on an aluminium plate and starch as binder). The spots were detected with a Universal-UV-Lampe Camag (Muttenz, Schweiz) for wave lengths 254 and 255 nm. The column chromatography was run on silica gel Silpearl UV 254. Infrared spectra were measured with a spectrophotometer Perkin–Elmer, Model 325. The absorption peaks are given in $cm^{-1}$. $^1$H-NMR spectra were measured with an apparatus Varian XL-100-15 (100·1 MHz) at 37°C using tetramethylsilane as internal standard. The chemical shifts are given in $\delta$ units (ppm.), and the interaction constants in Hz. The temperature data were not corrected.

### Reaction of Methylmagnesium Iodide with 3-Quinolinecarbonitrile (*Ia*)

To a stirred and boiling solution of methylmagnesium iodide, prepared from magnesium (1·82 g, 0·075 ml) and methyl iodide (10·6 g, 0·075 mol) in diethyl ether (25 ml), a solution of *Ia* (7·7 g, 0·05 mol) (ref.[4]) in a mixture of diethyl ether (150 ml) and tetrahydrofuran (75 ml) was added dropwise. The mixture was refluxed for 4 h, then the formed precipitate was collected on a filter, washed with diethyl ether (100 ml) and decomposed with a solution of ammonium chloride (16 g, 0·3 mol) in water (75 ml). The separated oil was extracted with diethyl ether (5 × 100 ml) and the extract was dried with magnesium sulphate. The solvent was distilled off and the residue (6·3 g) was identified by thin-layer chromatography (benzene–methanol 19 : 1) as a mixture containing *Ia*. Chromatography of the mixture (2 g) on a column of silica gel gave 1·5 g (55·4%) of 4-methyl-1,4-dihydro-3-quinolinecarbonitrile (*IIa*), m.p. 89—90°C (aqueous ethanol). For $C_{11}H_{10}N_2$ (170·2) calculated: 77·62% C, 5·92% H, 16·47% N; found: 77·56% C, 6·14% H, 16·34% N. IR spectrum ($CHCl_3$): 3460, 3430, $\nu$(NH); 2200, $\nu$(CH); 1643, $\nu$(C=C). $^1$H-NMR spectrum ($CDCl_3$): 1·43 (d, 3 H, $J = 7$) $CHCH_3$; 3·80 (q, 1 H, $J = 7$) $CHCH_3$; 6·30—6·54 (1 H, bs) NH; 6·55—7·27 (m, 5 H) benzene ring and CH(2). The ether-tetrahydrofuran fraction gave 2·9 g (37·6%) of the unreacted *Ia*, m.p. 103—107°C.

### 4-Methyl-3-quinolinecarbonitrile (*Ib*)

A solution of *IIa* (150 mg) in nitric acid (1 : 3, 3 ml) was heated to 70°C for 1·5 h. The mixture was diluted with water and precipitated with ammonia. The precipitated product was dried with $P_2O_5$ and sublimed at 130—135°C/1·6 kPa, m.p. 141—142°C (methanol); reported[5] m.p. 140 to 141°C.

### Reaction of Phenylmagnesium Bromide with *Ia*

The reaction and isolation of the products were analogous to the preceding experiment. Apart from the unreacted *Ia* (24%), chromatography identified: 4-phenyl-1,4-dihydro-3-quinolinecarbonitrile (*IIb*, 22%), m.p. 230—232°C, reported[3] m.p. 222—223°C. For $C_{16}H_{12}N_2$ (232·2) calculated: 82·73% C, 5·20% H, 12·05% N; found 82·61% C, 5·42% H, 11·70% N. IR spectrum ($CHCl_3$): 3455, $\nu$(NH); 2205, $\nu$(CN); 1640, $\nu$(C=C). $^1$H-NMR spectrum (pentadeuteropyridine): 5·14 (s, 1 H), CH(4); 6·80—7·60 (m, 10 H) benzene rings and CH (2); 10·3—10·6 (bs, 1 H) NH; (hexadeuterodimethylsulphoxide): 4·8 (s, 1 H) CH (4); 6·65—7·30 (m, 10) benzene rings and CH (2); 9·24—95·0 (1 H, bs) NH.

2-*Phenyl*-1,2-*dihydro*-3-*quinolinecarbonitrile* (III, 8%), m.p. 134—138°C. IR spectrum ($CHCl_3$) 3430, $\nu$(NH); 2215, $\nu$(CN); 1625, $\nu$(C=C). $^1$H-NMR spectrum ($CDCl_3$): 3·0—3·8 (bs, 1 H) NH 5·4 (s, 1 H) CH (2); 6·3—7·7 (m, 10 H) benzene rings and CH (4).

2-*Phenyl*-3-*quinolinecarbonitrile* (IV) was formed from *III* by standing in contact with the air, m.p. 197—197·5°C (chloroform–methanol), reported[6] m.p. 193—194°C.

### 2-Phenyl-3-quinolinecarbonitrile (*IV*)

A mixture of 2-aminobenzaldehyde[7] (3·1 g), benzoylacetonitrile[8] (3·7 g), ethanol (50 ml) and 10 drops of pyridine was refluxed for 5 h. The separated product (2·9 g) was collected on a filter, m.p. 196—197·5°C (ethanol–benzene); the mother liquor gave another crop of *IV*, the total yield being 5·2 g (88%). The product proved identical with an authentic sample, obtained by oxidation of *III* (undepressed m.p., identity of IR spectra).

### 4-Phenyl-3-quinolinecarbonitrile (*Ic*)

A mixture of *IIb* (0·54 g) and chloranil (0·6 g) was boiled in a chloroform solution, then shaken with 10% potassium hydroxide and with water. The chloroform layer was separated and dried ($MgSO_4$). The solvent was distilled off; yield 410 mg, m.p. 181—183°C (methanol–chloroform), reported[9] m.p. 179—181°C.

### Reaction of Methylmagnesium Iodide with 6-Quinolinecarbonitrile (*Va*)

The reaction with *Va* (prepared from 6-bromoquinoline[10] in analogy to *Ia* (ref.[4]) was carried out like that with 3-quinolinecarbonitrile (*Ia*). Chromatography on a column of silica gel (10% of acetone in tetrachloromethane) gave two products: 6-Acetylquinoline (*Vb*, 42%), m.p. 73 to 73·5°C (n-hexane–ethyl acetate), rep.[11] m.p. 74—75°C. For $C_{11}H_9NO$ (171·2) calculated: 77·17% C, 5·30% H, 8·18% N; found: 77·03% C, 5·47% H, 8·06% N. 2-Methyl-6-quinolinecarbonitrile (*Vc*, 15·8%), m.p. 172—174°C (methanol). For $C_{11}H_8N_2$ (168·2) calculated: 78·56% C, 4·79% H, 16·65% N; found: 78·46% C, 5·00% H, 16·41% N. IR spectrum ($CDCl_3$): 2240, ν(CN). $^1$H-NMR spectrum ($CDCl_3$): 2·80 (s, 3 H) $CH_3$; 7·25—8·20 (m, 5 H) benzene ring and CH (3·4).

### Reaction of Phenylmagnesium Bromide with 6-Quinolinecarbonitrile (*Va*)

The reaction and isolation of the products were carried out as with *Ia*. Column chromatography on silica gel (2% of methanol in chloroform) gave: 6-Benzoylquinoline (*Vd*, 71·5%), m.p. 59—60°C (light petroleum–diethyl ether), reported[12] m.p. 59—60°C. IR spectrum ($CHCl_3$): 1 660 ν(C=O). $^1$H-NMR spectrum, ($CDCl_3$): 7·35—8·35 (m, 10 H) benzene rings and CH (3·4); 9·00—9·09 (m, 1 H) CH (2). The picrate melted at 223—224°C (ethanol–acetone) reported[12] m.p. 217 to 218°C. 6-Benzoyl-2-phenylquinoline (*Vf*, 2·2%), m.p. 163—166°C (methanol–benzene). $^1$H-NMR spectrum ($CDCl_3$): 7·42—8·38 (m, 15 H) benzene rings and CH (3·4). For $C_{22}H_{15}NO$ (309·4) calculated: 85·41% C, 4·89% H, 4·53% N; found: 85·35% C, 5·08% H, 4·49% N. 2-Phenyl-6-quinolinecarbonitrile (*Ve*, 9·5%), m.p. 142—143°C (methanol). For $C_{16}H_{10}N_2$ (230·3) calculated: 83·46% C, 4·38% H, 12·16% N; found: 83·48% C, 4·54% H, 12·10% N. IR spectrum ($CHCl_3$): 2 240 ν(CN). $^1$H-NMR spectrum ($CDCl_3$): 7·50—8·30 (m, 10 H) benzene rings and CH (3·4).

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