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Studies on Benzoquinolines [*f*] and [*h*]. Part I

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2-Chloro-4-methyl and 2-methyl-4-chloro-benzo[*h*]quinolines, 1-chloro-3-methyl- and 1-methyl-3-chloro-benzo[*f*]quinolines were converted into corresponding hydrazino derivatives. Structural studies of the hydrazino compounds and their derivatives were carried out. Chlorine atom in a position adjacent to nitrogen of the ring was found to be more reactive than in that away from nitrogen in benzo[*f*] and [*h*]quinolines. Cyclisation of hydrazino derivatives by nitrous and formic acids occurred at position 2 in 1-methyl-3-hydrazinobenzo[*f*]-quinoline and at position 3 in the case of 2-hydrazino-4-methylbenzo[*h*]quinoline, respectively, while in the case of 1-hydrazino-3-methylbenzo[*f*]quinoline, at position 10 and in 4-hydrazino-2-methylbenzo[*h*]quinoline, at position 5, respectively.

1-Methyl-3-chloro- and 1-chloro-3-methyl-benzo[*f*]-quinolines (IA and IB), and 2-chloro-4-methyl- and 2-methyl-4-chloro-benzo[*h*]quinolines (IC and ID) were prepared by the usual methods.[1-3] The chloro compounds IA—ID did not react with hydrazine hydrate (80%) when the reactions were carried out in low boiling solvents such as alcohol and dioxane. However, in hot glycerol the corresponding hydrazino derivatives (IIA—IID) were obtained. The hydrazino derivatives IIA and IIC were obtained under refluxing for 6—8 hr, while compounds IIB and IID were obtained when the time of refluxing was extended to 10—12 hr. This indicates the greater reactivity of chlorine at a position adjacent to nitrogen as compared to that away from nitrogen. Such differences in reac-

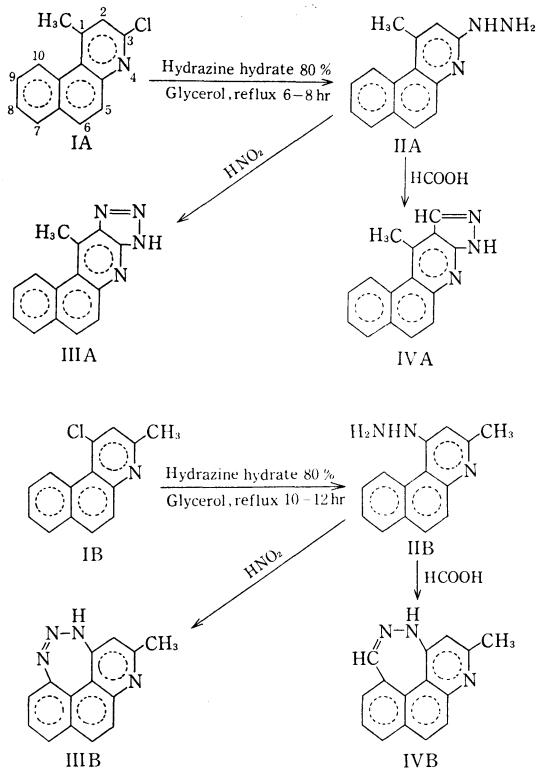
1) L. Knorr, *Ber.*, **17**, 540, (1884).
2) M. Conrad and L. Limpach, *ibid.*, **21**, 531 (1888); L. Limpach, *Ber.*, **64**, 969, (1931).
3) A. Albert, D. J. Brown, and H. Duewell, *J. Chem. Soc.*, **1948**, 1284.

Table 1. NMR chart (Chemical shifts given in ppm (δ))

Compound	-NH Proton broad		Aromatic proton		Proton as singlet		N=CH proton		$-C-CH_3$ proton as singlet		$-NH-NH_2$ proton	
	Position	No. of proton	Position	No. of proton	Position	No. of proton	Position	No. of proton	Position	No. of proton	position	No. of proton
IIA	—	—	7.6 —8.05	6	7.05 at 2	1	—	—	2.50	3	1.55, 1.2	3
IIB	—	—	7.6 —8.05	6	7.05 at 2	1	—	—	2.60	3	1.6, 1.2	3
IIC	—	—	7.6 —8·05	6	7.05 at 3	1	—	—	2.50	3	1.55, 1.2	3
IID	—	—	7.6 —8.05	6	7.05 at 3	1	—	—	2.65	3	1.6, 1.2	3
IIIA	8.70	1	7.6 —8.05	6	—	—	—	—	2.50	3	—	—
IIIB	8.35	1	7.6 —8.05	5	7.05 at 2	1	—	—	2.65	3	—	—
IIIC	8.75	1	7.6 —8.05	6	—	—	—	—	2.50	3	—	—
IIID	8.30	1	7.6 —8.05	5	7.05 at 3	1	—	—	2.65	3	—	—
IVA	8.85	1	7.6 —8.05	6	—	—	6.5	1	2.50	3	—	—
IVB	8.40	1	7.6 —8.05	6	7.05 at 2	1	—	—	2.55	3	—	—
IVC	8.80	1	7.6 —8.05	6	—	—	6.5	1	2.50	3	—	—
IVD	8.25	1	7.45—8.05	6	7.05 at 3	1	—	—	2.60	3	—	—

tivities were observed in the quinoline compounds.[4]

4-Chloroquinaldine with hydrazine under drastic conditions gave 3-methyl-5-(*o*-aminophenyl)pyrazole, an isomer of 2-methyl-4-hydrazinoquinoline.[5] However, this was not observed in the case of the above compounds (IA—ID) wherein hydrazino derivatives (IIA—IID) were obtained.



Elemental analysis of the compounds IIA—IID suggested the formula $C_{14}H_{13}N_3$. NMR spectrum of IIB indicated the presence of six aromatic protons (δ 7.6—8.05 ppm) and one aromatic proton as singlet (δ 7.05 ppm). Protons at nitrogen were found at δ 1.6 and δ 1.2 ppm, while methyl protons ($C-CH_3$) as a singlet at δ 2.60 ppm. All the data supported hydrazino structure for IIB. The positions of various protons in compounds IIA, IIC, and IID were more or less similar to IIB.

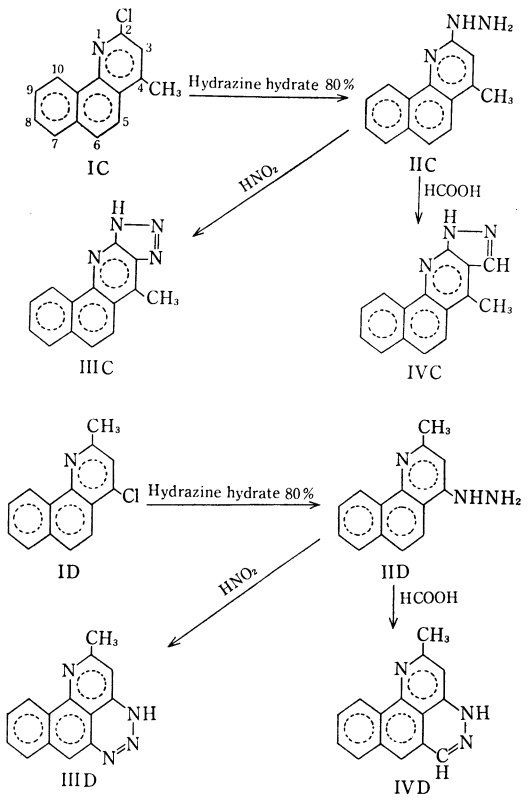
Hydrazino derivatives (IIA—IID) reacted with nitrous acid to give compounds IIIA—IIID ($C_{14}H_{10}N_4$). NMR studies of IIIB indicated the presence of methyl (δ 2.65 ppm), -NH(δ 8.35 ppm), five aromatic (δ 7.6—8.05 ppm) and one aromatic (δ 7.05 ppm) protons. The absence of the protons of $-NH-NH_2$ (δ 1.2, 1.6 ppm) as indicated in the NMR spectrum of IIB, along with the presence of a -NH proton at δ 8.35 ppm, indicated the formation of 3-methylbenzo[*f*]-1′,2′,3′-triazepino[4′,7′:1,10]quinoline.

It appeared that the intermediate $RNHN_2^+Cl^-$ from IIB to IIIB must have cyclised at position 10 instead of position 2 as there was still an indication of the aromatic proton as a singlet (δ 7.05 ppm) in IIIB which was also present in IIB. But in IIIA, no proton was found at position 2 as there was no indication of the aromatic proton at δ 7.05 ppm in the NMR spectrum. However, the positions of six aromatic protons (at positions 5, 6, 7, 8, 9, and 10), methyl and -NH protons were found to be more or less similar to those in IIA.

When the hydrazino derivatives (IIA—IID) were treated with formic acid, compounds of molecular formula $C_{15}H_{11}N_3$ (IVA—IVD) were obtained. NMR spectrum of IVA indicated the absence of the proton at 2 (as singlet at δ 7.05 ppm), along with the presence of methyl protons (δ 2.5 ppm singlet), -NH proton (δ 8.85 ppm) and N=CH (δ 6.5 ppm) proton. This also indicated the presence of methyl and six aromatic protons almost in similar positions as in IIA. In the NMR spectrum of IVB, the presence of methyl protons (δ 2.55 ppm singlet), one aromatic proton (δ 7.05 ppm), six aromatic protons (δ 7.5—8.05 ppm), NH proton (δ 8.4 ppm) and the absence of a proton at δ 6.5 ppm were evident. It appears that the cyclisation occurred at 10 and not at 2, since the aromatic proton at the position 2 was found as a singlet (δ 7.05 ppm).

4) R. J. Rowlett and R. E. Lutz, *J. Amer. Chem. Soc.*, **68**, 1288, (1946).

5) E. Koenigs and J. Freund, *Chem. Ber.*, **80**, 143, (1947).



Formation of IIIC, IIID, IVC, and IVD could be explained similarly.

Experimental

All the melting points are uncorrected. Micro analyses were performed by C.D.R.I., Lucknow. NMR spectra were made on a Varian A-60 model in $CDCl_3$ as a solvent and TMS as an internal indicator. Chemical Shifts are given in ppm (δ).

1-Methyl-3-hydrazinobenzo[f]*quinoline(IIA).* 2.27 g (0.01 mol) of 1-methyl-3-chlorobenzo[*f*]quinoline (IA) was dissolved in glycerol and the solution was refluxed. To the hot reaction mixture, hydrazine hydrate (80%, 0.06 g, 0.015 mol) was gradually added with constant stirring. After the addition of hydrazine hydrate was completed, the reaction mixture was refluxed for 6—8 hr. The mixture was cooled and poured into ice-cold water. The solid was filtered and dissolved in the least amount of methanol. The methanolic solution was filtered and was kept at 0°C for 24 hr. The compound (mp 141—142°C; yield, 1.36 g, 60%) thus obtained showed no chlorine. Tlc examination gave one spot (R_f, 0.54) using dioxane as a solvent and Silica Gel G as an adsorbent.

Found: C, 74.98%; H, 6.02%; N, 19.04%. Calcd for $C_{14}H_{13}N_3$: C, 75.33%; H, 5.82; N, 18.83%.

Similarly, IB yielded 1-hydrazino-3-methylbenzo[*f*]-quinoline (IIB) with a refluxing time of 10—12 hr. Yield 51%, mp 161—162°C (R_f, 0.72).

Found: N, 19.28%. Calcd for $C_{14}H_{13}N_3$: N, 18.83%.

2-Hydrazino-4-methylbenzo[*h*]quinoline(IIC) was prepared from IC mp 116—117°C, yield 58% (R_f 0.79).

Found: N, 19.32%. Calcd for $C_{14}H_{13}N_3$: N, 18.83%.

ID yielded 2-methyl-4-hydrazinobenzo[*h*]quinoline (II-D) with a refluxing time of 10—12 hr in 48% yield mp 170—171°C (R_f, 0.68).

Found: N, 19.02%. Calcd for $C_{14}H_{13}N_3$: N, 18.83%.

1-Methylbenzo[f]*-1,2,3-triazolo[4,5-*b]*quinoline (IIIA).* 0.5 g of 1-methyl-3-hydrazinobenzo[*f*]quinoline(IIA) was dissolved in dilute hydrochloric acid. The ice-cold solution was kept at 0—2°C. The ice-cold saturated solution of sodium nitrite was added cautiously till brown fumes were evolved. The reaction mixture was shaken well during the course of addition, and was then decomposed with cold water. The solid was filtered and washed 3—4 times with water (till washings gave no positive test for ionic chlorine). It was crystallized from ethanol (mp 214—215°C).

Found: C, 71.5; H, 4.52; N, 23.62%. Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.27; N, 23.93%.

Similarly, IIB yielded 3-methyl-1′-*H*-benzo[*h*]-1′,2′,3′-triazepino[4′,7′ : 1, 10]quinoline (IIIB) (mp 180—181°C).

Found: N, 23.62%. Calcd for $C_{14}H_{10}N_4$: N, 23.93%. IIC yielded 4-methylbenzo[*h*]-1,2,3-triazolo[4,5-*b*]quinoline (IIIC) (mp 160—161°C).

Found: N, 23.68%. Calcd for $C_{14}H_{10}N_4$: N, 23.93%. and IID, yielded 2-methyl-1′-*H*-benzo[*h*]-1′,2′,3′-triazino-[4′, 6′ : 4, 5]quinoline (IIID): (mp 189—190°C).

Found: N, 23.58%. Calcd for $C_{14}H_{10}N_4$: N, 23.93%.

1-Methylbenzo[f]*-1,2-pyrazolo[4,5-*b]*quinoline (IVA).* To a well stirred hot solution of 0.5 g of 1-methyl-3-hydrazinobenzo[*f*]quinoline in redistilled dioxane (with a little sodium acetate), formic acid in excess was cautiously added. The mixture was then refluxed for 4—5 hr on a sand bath. The reaction mixture was cooled and poured into ice-cold water and kept overnight at 0°C. The solid obtained was filtered, washed 3—4 times with water and was crystallised from acetone (mp 260—261°C).

Found: C, 74.07%; H, 4.82%; N, 17.28%. Calcd for $C_{15}H_{11}N_3 \cdot 1/2H_2O$; C, 74.38%; H, 4.95%, N, 17.35%. Similarly, IIB yielded 3-methyl-1′-*H*-benzo[*f*]-1′,2′-diazepino[4′, 7′ : 1, 10]quinoline (IVB), mp (215—216°C).

Found: N, 17.02%. Calcd for $C_{15}H_{11}N_3 \cdot 1/2H_2O$: N, 17.35%. IIC yielded 4-methylbenzo[*h*]-1,2-pyrazolo-[4,5-*b*]quinoline(IVC) (mp 204—205°C).

Found: N, 16.88%. Calcd for $C_{15}H_{11}N_3 \cdot 1/2H_2O$: N, 17.35%, IID, yielded 2-methyl-2′-*H*-benzo[*h*]-1′,2′-pyrazino[3′,5′:4,5]quinoline (IVD) (mp 224—225°C).

Found: N, 16.82%. Calcd for $C_{15}H_{11}N_3 \cdot 1/2H_2O$: N, 17.35%.

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