Cyclization of Isomeric 2-Hydrazino-4-methylbenzo[*h*]quinoline and 3-Hydrazino-1-methylbenzo[*f*]quinoline. A Reinterpretation

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Synopsis. Cyclization of 2-hydrazino-4-methylbenzo[*h*]quinoline and 3-hydrazino-1-methylbenzo[*f*]quinoline with formic acid occurs on nitrogen rather than carbon to give 5-methylbenzo[*h*][1,2,4]triazolo[4,3-*a*]quinoline and 11-methylbenzo[*f*][1,2,4]triazolo[4,3-*a*]quinoline and not 7-methyl-10*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline and 11-methyl-8*H*-benzo[*f*]pyrazolo[3,4-*b*]quinoline, respectively, as it has been claimed before.

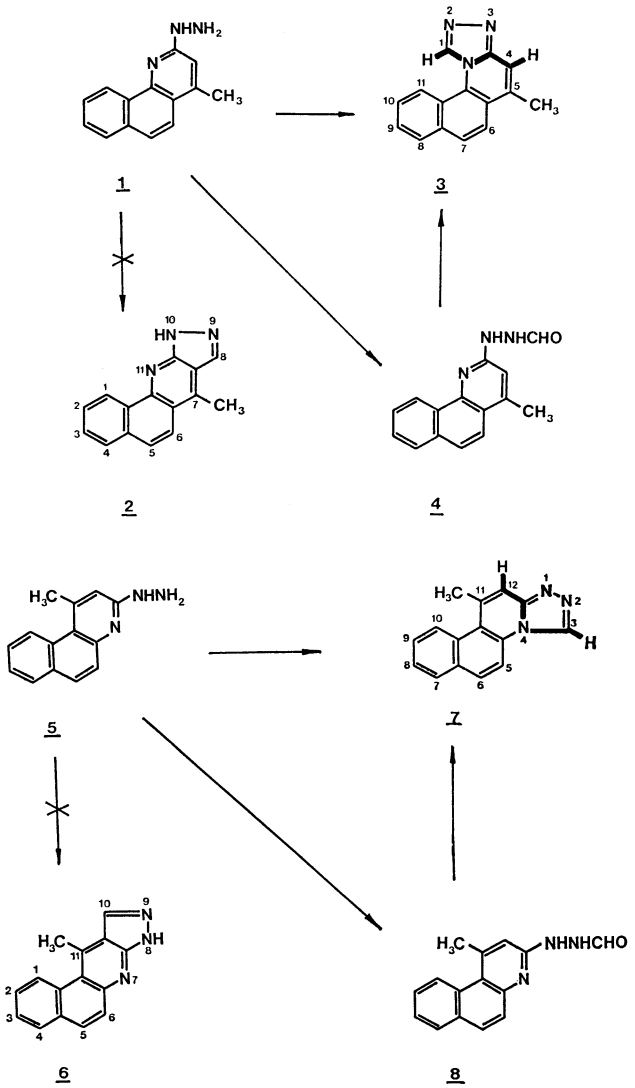
During our continuous interest in the field of polycyclic polyaza heterocyclic systems of "steroid" and "helicene" type,[1–9] a report by Tiagi and Yoshi[10] has attracted our attention. Namely, it has been claimed that the reaction of 2-hydrazino-4-methylbenzo[*h*]quinoline (**1**) and 3-hydrazino-1-methylbenzo[*f*]quinoline (**5**) with formic acid gave 7-methyl-10*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline (**2**) and 11-methyl-8*H*-benzo[*f*]pyrazolo[3,4-*b*]quinoline (**6**), respectively.

There are no other examples, known in the literature, in which cyclization of hydrazino group at α-position to ring nitrogen is taking place onto carbon atom. To the contrary, according to the common experience, cyclization of hydrazino group attached at α-position to ring nitrogen is taking place onto ring nitrogen to give *s*-triazolo[4,3-*x*]azines.[11–14] Therefore, it seems, that reinterpretation of the results reported by Tiagi and Yoshi is fully justified.

When 2-hydrazino-4-methylbenzo[*h*]quinoline (**1**) was heated with formic acid as discribed by Tiagi and Yoshi,[10] a product with mp 167—168 °C (*cf.*[10] mp 204—205 °C) was obtained. Mass spectrum (M^+=251) together with elemental analysis gave molecular formula $C_{15}H_{13}ON_3$. IR absorption (1690 cm^{-1}) characteristic for a formyl group and a singlet at δ=7.63, a doublet for CH_3 group (δ=2.45) and a quartet for H-3 with a coupling constant ($J_{3\text{-H},4\text{-CH}_3}$ =1.0 Hz) characteristic for the coupling of a methyl group with an ortho proton in aromatic and heteroaromatic compounds in NMR spectrum suggest that the product is 2-(2-formylhydrazino)-4-methylbenzo[*h*]quinoline (**2**) and not the corresponding benzopyrazoloquinoline **2**, which presumably, according to the authors,[10] crystallizes with one half mole of water, in order to explain the low analysis for nitrogen.

On the other hand, the cyclization was effected by treatment of hydrazino compound **1** with triethyl orthoformate to give 5-methylbenzo[*h*][1,2,4]triazolo[4,3-*a*]quinoline (**3**), mp 299—300 °C, and not 7-methyl-10*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline (**2**) as reported by Tiagi and Yoshi.[10] That cyclization occured onto nitrogen rather than carbon is supported by the coupling of the methyl group at position 5 with 4-H ($J_{4\text{-H},5\text{-CH}_3}$=1.0 Hz) and by a long-range coupling of 1-H and 4-H ($J_{1\text{-H},4\text{-H}}$=0.9 Hz). This latter coupling is charasteristic for all 1,2,4-triazolo- and other azoloazines with bridgehead nitrogen atom.[15–17] The same tetracyclic compound was obtained also by prolonged heating of the 2-formylhydrazino compound **4**, however in lower yield.

3-Hydrazino-1-methylbenzo[*f*]quinoline (**5**) when treated with either triethyl orthoformate or formic acid gave a compound with mp 280—282 °C. Mass spectrum (M^+=233) and elemental analysis correspond to molecular formula $C_{15}H_{11}N_3$. A doublet for a methyl group ($J_{12\text{-H},11\text{-CH}_3}$=0.6 Hz) further supported by a long-range coupling between 3-H and 12-H ($J_{3\text{-H},12\text{-H}}$=0.6 Hz) are unambiguously consistent with 11-methylbenzo[*f*][1,2,4]triazolo[4,3-*a*]quinoline (**7**). On this basis, 11-methyl-8*H*-benzo[*f*]pyrazolo[3,4-*b*]quinoline (**6**) proposed by Tiagi and Yoshi[10] can be excluded. Furthermore, the compound obtained by Tiagi and Yoshi from hydrazino



compound **5** with formic acid is most probably the corresponding 2-formylhydrazino derivative **8** since the reported analysis for nitrogen (Found: 17.28%; Calcd: N, 16.72%) fits this much better than the cyclized products **6** or **7**. However, we have not been able to isolate this intermediate under reported conditions.

An analoguous reinterpretation for the products obtained from hydrazines **1** and **5** with nitrous acid has been reported recently.[18]

Experimental

2-Hydrazino-4-methylbenzo[*h*]quinoline (**1**) and 3-hydrazino-1-methylbenzo[*f*]quinoline (**5**) were prepared according to the procedure described in the literature.[10,18] ^{1}H NMR spectra were recorded on a JEOL JNM C60-Hl spectrometer, IR spectra on Perkin-Elmer 727B instrument, and mass spectra were obtained on a Hitachi-Perkin-Elmer RMU-6L instrument.

2-(Formylhydrazino)-4-methylbenzo[h]*quinoline (4).* 2-Hydrazino-4-methylbenzo[*h*]quinoline (**1**) (800 mg) and formic acid (98—100%, 6 ml) were heated under reflux for two hours. The mixture was evaported to dryness and methanol (20 ml) was added to dry residue, followed by addition of water (20 ml). After cooling the precipitate was collected by filtration and recrystallized from a mixture of methanol and water (4:1) to give 2-(2-formylhydrazino)-4-methylbenzo[*h*]quinoline (**4**) (620 mg, 69%), mp 167—168 °C, *m/e* 252 (M^+), NMR (d_6-DMSO, 110 °C): 9.5—9.2 (2H, br, NHNH), 8.4 (1H, m, 10-H), 7.63 (1H, s, CHO), 7.50—6.95 (5H, m, 5-H, 6-H, 7-H, 8-H, 9-H), 6.38 (1H, q, 3-H), 2.45 (3H, d, 4-CH_3); $J_{3\text{-H},4\text{-CH}_3}=1.0$ Hz). Found: C, 71.35; H, 5.52; N, 16.97%. Calcd for $C_{15}H_{13}N_3O$: C, 71.69; H, 5.21; N, 16.72%.

5-Methylbenzo[h][*1,2,4*]*triazolo*[*4,3*-a]*quinoline (3).*
Method A: 2-Hydrazino-4-methylbenzo[*h*]quinoline (**1**) (800 mg) and triethyl orthoformate (4 ml) were heated under reflux for 1 h. After cooling ether (16 ml) was added and precipitate collected by filtration and recrystallized from ethanol to give 5-methylbenzo[*h*][1,2,4]triazolo[4,3-*a*]quinoline (**3**), (470 mg, 56%), mp 299—300 °C, *m/e* 233 (NMR (d_6-DMSO): 9.35 (1H, d, 1-H), 8.35—8.10 (1H, m, 11-H), 7.60—7.05 (6H, m, 4-H, 6-H, 7-H, 8-H, 9-H, 10-H), 2.57 (3H, d, 5-CH_3), $J_{4\text{-H},5\text{-CH}_3}=1.0$ Hz, $J_{1\text{-H},4\text{-H}}=0.9$ Hz. Found: C, 77.26; H, 5.14; N, 18.29%. Calcd for $C_{15}H_{13}N_3$: C, 77.23; H, 4.75; N, 18.02%.

Method B: 2-Hydrazino-4-methylbenzo[*h*]quinoline (**1**) (100 mg), sodium acetate (10 mg), dioxane (1 ml) and formic acid (98-100%, 1 ml) were heated under reflux for 6 h. After evaporation to dryness methanol (1 ml) and water (1 ml) were added to the residue, and the solid collected by filtration. Recrystallization from ethanol gave **3** (48%). The compound was identical in every respect to the compound described above.

11-Methylbenzo[f][*1,2,4*]*triazolo*[*4,3*-a]*quinoline (7).*
Method A: 1-Methyl-3-hydrazinobenzo[*f*]quinoline (**5**) (1,0 g) and triethyl orthoformate (5 ml) were heated under reflux for 1 h. After cooling ether (20 ml) was added, precipitate collected by filtration and recrystallized from ethanol to give 11-methylbenzo[*f*][1,2,4]triazolo[4,3-*a*]quinoline (**7**), (780 mg, 79%), mp 280—282 °C, *m/e* 233 (M^+), NMR (d_6-DMSO): 9.1 (1H, d, 3-H), 8.25—8.02 (1H, m, 10-H), 7.75 (1H, d, 5-H), 7.50 (1H, d, 6-H), 7.40—6.90 (4H, m, 7-H, 8-H, 9-H, 12-H), 2.82 (3H, d, 11-CH_3), $J_{3\text{-H},12\text{-H}}=0.6$ Hz, $J_{5\text{-H},6\text{-H}}=8.0$ Hz, $J_{12\text{-H},11\text{-CH}_3}=1.0$ Hz). Found: C, 77.41; H, 4.87; N, 18.05%. Calcd for $C_{15}H_{11}N_3$: C, 77.23; H, 4.75; N, 18.02%.

Method B: 1-Methyl-3-hydrazinobenzo[*f*]quinoline (**5**) (200 mg) and formic acid (98—100%, 1.5 ml) were heated under reflux for three hours. Ethanol (5 ml) was added and the mixture evaporated to dryness. Dry residue was suspended in ether (10 ml) and the solid collected by filtration and recrystallized from ethanol to give 11-methylbenzo[*f*][1,2,4]triazolo[4,3-*a*]quinoline (**7**), (81%). The compound was identical in every respect with the compound obtained from **5** and triethyl orthoformate as described above.

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