Reactions of 1,4-Dihydro-3-(2*H*)benzoisoquinolinones with Aldehydes in the Presence of a Strong Base. Condensation and Aromatization as Competing Reactions

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In reactions of 1-phenyl-1,4-dihydro-3-(2*H*)benzoisoquinolinones with benzaldehyde in the presence of a strong base, the final result can be ring substitution with aromatization or only aromatization of the starting isoquinolinone, depending on the position of the ring junction ([*f*] or [*h*]); in the 5-methyl derivative the latter process becomes predominating. In the system sodium hydride-dimethylformamide, containing no aromatic aldehyde, methylation at site 4 occurs. Using compounds labelled with deuterium, it has been established that the 4-benzyl or 4-methyl derivatives with aromatic structures are formed through hydride ion migrations.

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It is known that the C-4 methylene group in 1-aryl-1,4-dihydro-3-(2*H*)isoquinolinones can react as active methylene (1), and in reactions with aromatic aldehydes in the presence of strong bases, such as sodium hydride or the Avramoff reagent (2), 1-aryl-4-arylmethyl-3-(2*H*)isoquinolinones are formed through the 4-arylidene intermediates (3). An attempt has been made to extend this reaction to condensed isoquinolinone derivatives (4). First the reaction of 1-phenyl-1,4-dihydro-3-(2*H*)benzo[*f*]isoquinolinone and benzaldehyde was studied in dimethylformamide, in the presence of an equivalent amount of sodium hydride. The conversion was found to be very slow even at 100°; finally, the reaction was effected at 140° for 40 hours to obtain two products, besides many unidentifiable contaminants. As a result of the condensation reaction taking place at the C-4 methylene group, 4-benzyl-1-phenyl-3-(2*H*)benzo[*f*]isoquinolinone (**1**) formed; at the same time, aromatization of the starting material yielded 1-phenyl-3-(2*H*)benzo[*f*]isoquinolinone (**2**) (Figure 1).

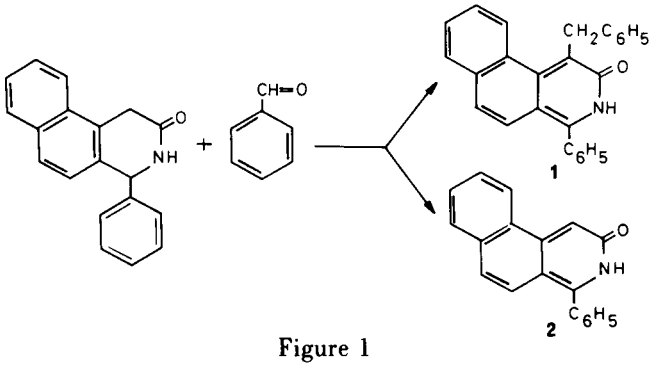
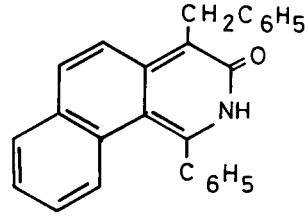


Figure 1

When the reaction was effected in the Avramoff reagent, the same result was obtained. According to nmr measurements, the ratio of **2** to **1** in the crude product was 4:1. When sodium hydride was used, compounds **1** and **2** were isolated in 10% and 20% yields, respectively; in the Avramoff reagent the corresponding values were 11% and 36%. The low yields are due to the poor crystallizability of the compounds and to the significant losses involved in the removal of the contaminants.

In the case of benzo[*h*]isoquinolinone only the 4-benzyl derivative (**3**) was isolated from the reaction mixture in 34% (sodium hydride) or 25% (Avramoff reagent) yield.



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Scheme 1

Assuming that suppression of the condensation reaction at C-4 is due to steric reasons, the reaction of 1-phenyl-5-methyl-1,4-dihydro-3-(2*H*)isoquinolinone (**4**) and benzaldehyde was studied, considering that the C-5 methyl

group represents, to a certain extent, a steric hindrance similar to the benzo[*f*] ring junction. In dimethylformamide, in the presence of sodium hydride, unchanged starting material was recovered. When using the Avramoff reagent, however, a homogeneous end-product was obtained, which proved to be the aromatized derivative **5** (Figure 2).

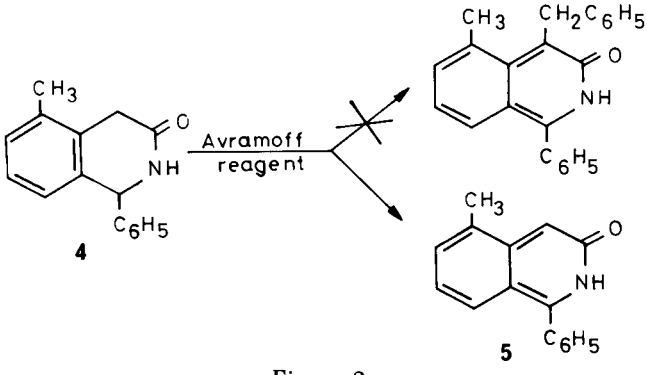
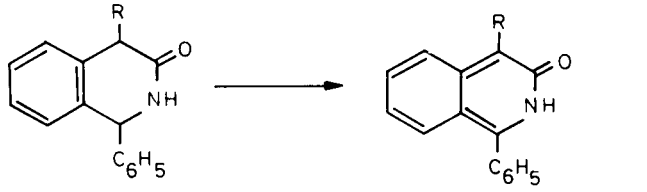


Figure 2

On the basis of these results it can be established that if there is a substituent at C-5 in the isoquinoline ring giving rise to steric hindrance in respect of the C-4 methylene group, the reaction with an aromatic aldehyde can follow two concurrent routes: carbonyl addition at the C-4 methylene group with subsequent dehydration and aromatization, or only aromatization of the starting compound. It is noteworthy that in the case of the 5-methyl derivative the former reaction path is completely blocked.

The formation of **5** was not unexpected, as it has been found earlier that C-4-monosubstituted 1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinones readily undergo aromatization in the Avramoff reagent or in the presence of sodium hydride in dimethyl formamide or dimethylsulfoxide, to yield the corresponding 3-(2*H*)isoquinolinone derivatives (Figure 3).



6: R = $CH_2C_6H_5$ (Avramoff reagent)
7: R = CH_3 (NaH/DMF or DMSO)
8: R = C_6H_5 (— " —)

Figure 3

If R = benzyl, the product is the isoquinolinone described by us earlier (1); compound R = C_6H_5 is also a known derivative (5).

It could be assumed that the system sodium hydride-dimethylformamide was responsible for the aromatization of the benzo[*f*]isoquinolinone derivative described above, giving compound **2** in addition to **1**. In order to test this assumption, 1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinone (**9**) was chosen as a relatively simple model compound (Figure 4).

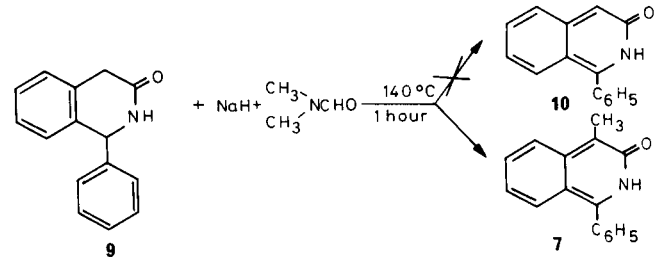
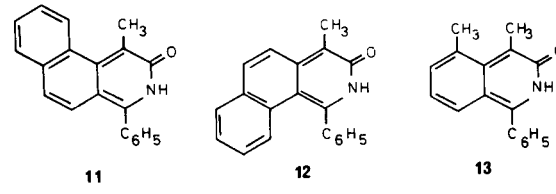


Figure 4

The reaction gave a homogeneous product, which was found to be 1-phenyl-4-methyl-3-(2*H*)isoquinolinone **7**, instead of the expected aromatized compound **10**. The reaction was also tried with the isoquinolinone derivatives described earlier: the benzo[*f*]-, benzo[*h*]- and 5-methylisoquinolinones were allowed to react with sodium hydride and dimethylformamide. The aromatic derivatives methylated at C-4 (**11**, **12**, **13**) were invariably obtained.



Scheme 2

Further experiments have shown that the above reaction takes place also at 100° and the minimum amount of sodium hydride required is 2 equivalents.

The experiments afforded thus no unambiguous evidence for the aromatizing ability of the system sodium hydride-dimethylformamide in the absence of aromatic aldehyde, since the conditions favoured methylation at C-4, which became the predominating process.

On the basis of literature data on the sodium hydride-dimethylformamide reagent (6), the following mechanism of this reaction can be suggested. Under the given condi-

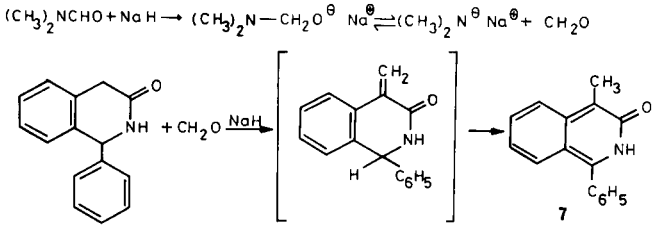


Figure 5

tions dimethylformamide and sodium hydride may give formaldehyde, which reacts with the isoquinolinone to yield the end-product **7** through a 4-methylene intermediate (Figure 5).

The above mechanism is supported by our experiments in which compounds labelled with deuterium were used. The isoquinolinone **14** containing deuterium at C-1 was prepared in polyphosphoric acid from benzyl cyanide and benzaldehyde labelled with deuterium, and this compound was allowed to react with dimethylformamide-sodium hydride. The product was examined by nmr and ms to find the deuterium indeed in the C-4 methyl group of the product **15** (Figure 6). Although the incorporation was not quantitative (its extent being dependent, *eg*, on the excess sodium hydride used), unambiguous evidence was obtained that the aromatic 4-methyl derivative is formed from the 4-methylene intermediate by inter- or intramolecular migration of the C-1 proton.

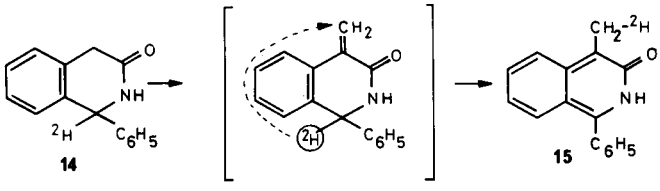


Figure 6

In order to decide between the inter- or intramolecular course of the reaction, the method of rearrangement of isotope isomers with benzaldehyde, described earlier (1,3), was used; in this reaction only a minimum excess of sodium hydride is needed. The two isotope isomers selected were **14** and **16**, labelled at different sites. After preparation of the derivative perdeuterated in the C-1 phenyl ring (**16**), the reaction with benzaldehyde was effected in the 1:1 mixture of the compounds **14** and **16** (Figure 7).

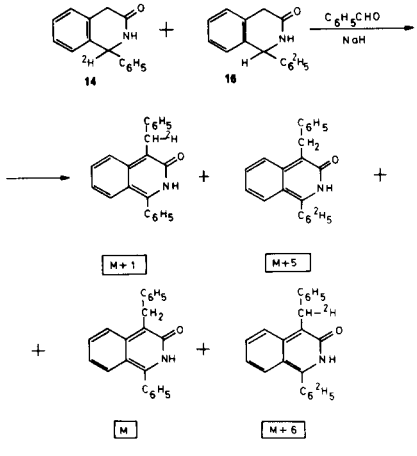


Figure 7

The product composition was examined by ms; the data of the mass spectrum are given in Table I.

Table I

Isotope Distribution of 1-Phenyl-4-benzyl-3-(2*H*)isoquinolinone Obtained in the Reaction of a 1:1 Mixture of Compounds **14** and **16** with Benzaldehyde in the Presence of Sodium Hydride

^{2}H-content	m/e	d_1	d_5	d_1+d_5	Relative Intensity %
0	M	10		4	13
1	M+1	90		48	9
2					3
3			5	2	3
4			25	13	13
5	M+5		70	33	53
6	M+6				6

An entirely intramolecular rearrangement would give rise to the M+1 and M+5 isomers only; intermolecular rearrangement involving cross-reactions should yield the products with M, M+1, M+5 and M+6 molecular weights in the same proportion. According to the mass spectrum of the actual product, all the four isotope isomers are present, unambiguously confirming the occurrence of cross-reactions.

The relative amount of M+6 is significantly lower than that of M+5; however, this must not be regarded as evidence for the partially intramolecular character of the reaction, since M+1 and M are present in nearly identical amounts. The ratio of the products which can be derived from the starting material labelled with deuterium at C-1 (M, M+1 and M+6) is lower than the expected value. This indicates that the rearrangement takes place in such a manner that the deuterium can reach the benzyl carbon atom only partially, following the splitting of the C(1)-^{2}H bond, since hydrogen from the sodium hydride may also occupy this place in a competing reaction.

Since the rearrangement reaction can be effected in medium yield only and takes place only partially even after prolonged reaction periods, the possible role of the kinetic isotope effect must also be considered as a cause of the relatively low proportion of the isotope isomers formed by the rupture of the C(1)-^{2}H bond.

On the basis of the foregoing, the scheme shown in Figure 8 is suggested as the reaction mechanism.

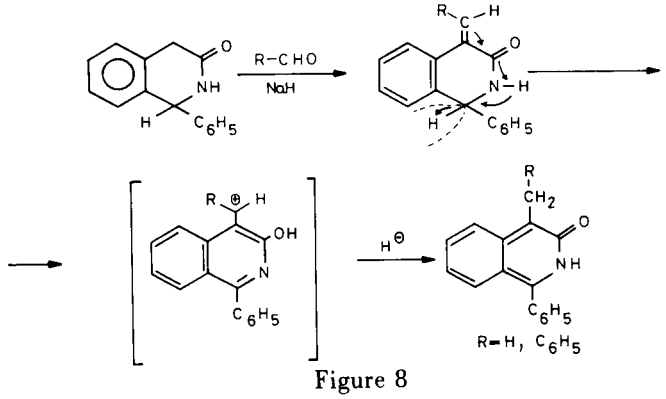


Figure 8

Since the migration of hydrogen as a proton in a medium containing sodium hydride is impossible, the reaction must involve hydride anion migration followed by an NH-CO proton shift and charge shift, resulting in a positive charge on the benzyl carbon atom. The hydride anion detached from C-1 is affixed to this site or, in a competing reaction, sodium hydride may also attack here, giving rise to the 4-methyl- or 4-benzyl-substituted aromatic 3-(2*H*)isoquinolinone.

EXPERIMENTAL

Melting points were determined on a Büchi-Tottoli apparatus and are uncorrected. Infrared spectra were determined in potassium bromide pellets (Perkin Elmer Model 457). Ultraviolet spectra were recorded in ethanolic solutions, nmr spectra were determined using a JEOL FX-100 spectrometer and chemical shifts δ are given in ppm relative to internal tetramethylsilane. Mass spectra were run on a Varian Mat spectrometer at 70 eV.

Reaction of 1-Phenyl-1,4-dihydro-3-(2*H*)benzo[*f*]isoquinolinone with Benzaldehyde.

I.

1-Phenyl-1,4-dihydro-3-(2*H*)benzo[*f*]isoquinolinone (4) (5.16 g, 0.02 mole) was dissolved in anhydrous dimethylformamide (100 ml) at 50°, and a dispersion of sodium hydride in oil (1.06 g, 0.022 mole) was added in a stream of nitrogen. After stirring for half an hour, benzaldehyde (2.12 g, 0.02 mole) was added dropwise, and stirring was continued at 140° for 40 hours. The mixture was cooled to 60°, poured into water (1000 ml), and acidified with 20% hydrochloric acid (20 ml). A yellow precipitate separated, which was filtered off, washed with water, dried and subjected to fractional separation on a column of aluminium oxide. Elution with chloroform gave the following product:

4-Benzyl-1-phenyl-3-(2*H*)benzo[*f*]isoquinolinone (**1**).

The pure product (0.7 g 10%) had mp 269-270°; uv: λ max 411 nm (ϵ 5650), 344 nm (ϵ 3090), 327 nm (ϵ 4430), 302 nm (ϵ 8430), 290 nm (ϵ 7560), 274 nm (ϵ 10850); ir (potassium bromide): C=N 1615 cm^{-1}; ^{1}H-nmr (deuteriochloroform): 4.60 (s, 2H, $ArCH_2$), 7.03 (d, 1H, ArH), 7.15-7.50 (m, 14H), 8.21 (d, 1H).

Anal. Calcd. for $C_{26}H_{19}NO$: C, 86.40; H, 5.30; N, 3.88. Found: C, 86.43; H, 5.45; N, 3.70.

1-Phenyl-3-(2*H*)benzo[*f*]isoquinolinone (**2**).

This compound was crystallized from butanol. The pure product (1.1 g, 20.3%) had mp 256-257°; uv: λ max 410 nm (ϵ 4820), 337 nm (ϵ 2760), 322 nm (ϵ 4340), 310 nm (ϵ 5620), 299 nm (ϵ 7460), 277 nm (ϵ 8650); ir (potassium bromide): C=N 1640 cm^{-1}; ^{1}H-nmr (DMSO-d_6): 7.45-7.9 (m, 11H, ArH), 8.63 (1H), 10.35 (s, 1H, OH or NH).

Anal. Calcd. for $C_{19}H_{13}NO$: C, 84.11; H, 4.82; N, 5.16. Found: C, 84.18; H, 5.16; N, 5.20.

II.

1-Phenyl-1,4-dihydro-3-(2*H*)benzo[*f*]isoquinolinone (5.1 g, 0.01868 mole) was stirred with benzaldehyde (1.98 g, 0.01868 mole) in Avramoff reagent (98 ml) at 210° for 6 hours. After cooling, the reaction mixture was poured into a mixture of water (150 ml) and ether (300 ml), the organic phase was separated, the aqueous part was extracted with ether, the combined ethereal phases were dried over sodium sulfate, and the solvent and benzyl alcohol were removed by distillation. The residual oil was rubbed with ether, filtered and dried. Purification by column chromatography gave compound **1** (0.75 g) and compound **2** (0.6 g).

The aqueous phase was acidified with 2*N* hydrochloric acid, the oil which separated was extracted with chloroform, the solvent was evaporated and the residue rubbed with ether. The solid product was then crystallized from butanol to yield another crop of **2** (1.2 g), yield, 0.75 g of **1** (11.1%) and 0.6 + 1.2 g = 1.8 g of **2** (35.6%).

4-Benzyl-1-phenyl-3-(2*H*)benzo[*h*]isoquinolinone (**3**).

I.

1-Phenyl-1,4-dihydro-3-(2*H*)benzo[*h*]isoquinolinone (1.8 g, 0.00658 mole) was dissolved in anhydrous dimethylformamide (40 ml), and a 50% dispersion of sodium hydride in oil (0.316 g, 0.00658 mole) was added in a stream of nitrogen at 50°. The mixture was stirred for a quarter of an hour, then benzaldehyde (0.7 g, 0.00658 mole) was added and stirring was continued at 50° for 12 hours. Pouring into water (400 ml) and acidification with 2*N* hydrochloric acid gave a solid which was filtered off, washed with water, dried, and recrystallized from dimethylformamide. The pure product (0.8 g, 33.7%) had mp 297-298°; uv: λ max 385 nm (ϵ 5619), 333 nm (ϵ 4205), 287 nm (ϵ 14470); ir (potassium bromide): C=N 1620 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid): 4.73 (s, 2H, $ArCH_2$), 7.2-8.3 (m, 16H, ArH), 12.7 (s, 1H, OH or NH).

Anal. Calcd. for $C_{26}H_{19}NO$: C, 86.33; H, 5.30; N, 3.88. Found: C, 86.30; H, 5.59; N, 4.13.

II.

A mixture of 1-phenyl-1,4-dihydro-3-(2*H*)benzo[*h*]isoquinolinone (1.5 g, 0.0055 mole) and benzaldehyde (0.585 g, 0.0055 mole) was stirred in Avramoff reagent (50 ml) at 210° for 6 hours. After cooling, the mixture was poured into a mixture of water (150 ml) and ether (150 ml). The precipitate was filtered off and recrystallized from dimethylformamide to obtain 0.5 g (25.3%) of the product (**3**).

1-Phenyl-5-methyl-3-(2*H*)isoquinolinone (**5**).

1-Phenyl-5-methyl-1,4-dihydro-3-(2*H*)isoquinolinone (7) (4.75 g, 0.02 mole) and benzaldehyde (2.12 g, 0.02 mole) were stirred in Avramoff reagent (100 ml) at 210° for 6 hours. After cooling, the reaction mixture was poured into a mixture of water (150 ml) and ether (300 ml). The aqueous phase was extracted with ether; the solvent and benzyl alcohol were then removed by distillation. The aqueous phase was acidified, extracted with chloroform, the solvent evaporated and the residue combined with the product obtained from the ethereal phase. Chromatographic separation on a column of aluminium oxide and crystallization from ethanol gave the pure product (2.3 g, 49%), mp 219-221°; uv: λ max 404 nm (ϵ 4559), 337 nm (ϵ 5848); ir (potassium bromide): C=O 1635 cm^{-1}, C=N 1620 cm^{-1}; ^{1}H-nmr (deuteriochloroform): 2.58 (s, 3H, ArMe), 6.9-7.6 (m, 9H, ArH), 9.7 (1H, OH or NH).

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.68; H, 5.79; N, 5.95.

Aromatization of 4-Benzyl-1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinone in Avramoff Reagent.

4-Benzyl-1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinone (3) (3.7 g, 0.0118 mole) was stirred in Avramoff reagent (100 ml) at 210° for 10 hours, then the reaction mixture was processed as described above. The residue obtained on evaporation of the ethereal phase was rubbed in gasoline, and the solid product was crystallized from benzene to give 4-benzyl-1-phenyl-3-(2*H*)isoquinolinone (**6**) (1.1 g, 29.9%), mp 233-235°.

1-Phenyl-4-methyl-3-(2*H*)isoquinolinone (**7**).

1-Phenyl-1,4-dihydro-3-(2*H*)isoquinolinone (7) (6.69 g, 0.03 mole) was dissolved in anhydrous dimethylformamide (90 ml), and a 50% dispersion of sodium hydride in oil (4.32 g, 0.09 mole) was added in a stream of nitrogen. The reaction mixture was stirred at 140° for 1 hour. After cooling it was poured into water (900 ml) and acidified with 2*N* hydrochloric acid. The solid product was filtered off, washed with water and dried. Crystallization from ethanol gave the pure product (2.1 g, 30%), mp 233-234°; uv: λ max 425 nm (ϵ 4060), 354 nm (ϵ 5210), 294 nm (ϵ 4700), 285 nm (ϵ 4820); ir (potassium bromide): C=N 1620 cm^{-1}; ^{1}H-nmr (deuteriochloroform): 2.51 (s, 3H, ArMe), 4-5 (broad, 1H, NH), 7.05-7.25 (m, 1H, ArH), 7.4-7.6 (m, 6H, ArH), 7.78 (d, 2H, ArH).

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.54;

H, 5.69; N, 6.10.

Aromatization of 1-Phenyl-4-methyl-1,4-dihydro-3-(2*H*)isoquinolinone with Sodium Hydride-Dimethylformamide.

1-Phenyl-4-methyl-1,4-dihydro-3-(2*H*)isoquinolinone (8) (2.37 g, 0.01 mole) was stirred in the presence of sodium hydride (1.44 g, 0.03 mole) in anhydrous dimethylformamide (40 ml) in a stream of nitrogen at 140° for 1 hour. The reaction mixture was then poured into water (400 ml) and acidified with 2*N* hydrochloric acid. The solid which separated was filtered off, washed with water and dried. The pure product (1.1 g, 46.8%) had mp 234-236°; mixed mp with the product obtained from 1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinone, 234-236°.

1,4-Diphenyl-3-(2*H*)isoquinolinone (**8**).

1,4-Diphenyl-1,4-dihydro-3-(2*H*)isoquinolinone (9) (2.99 g, 0.01 mole) was stirred in anhydrous dimethylformamide (25 ml) in the presence of sodium hydride (1.44 g, 0.03 mole) at 140° in a stream of nitrogen for half an hour. The reaction mixture was then processed as above. Recrystallization from benzene gave the pure product (1.75 g, 59%), mp 229-231° (lit mp 226-227° (5)).

1-Phenyl-4-methyl-3-(2*H*)benzo[*f*]isoquinolinone (**11**).

1-Phenyl-1,4-dihydro-3-(2*H*)benzo[*f*]isoquinolinone (2.73 g, 0.01 mole) was stirred in anhydrous dimethylformamide (40 ml) in the presence of sodium hydride (1.44 g, 0.03 mole) in a stream of nitrogen at 140° for 2 hours. The reaction mixture was then poured into water (400 ml) and acidified with 2*N* hydrochloric acid. The solid which separated was filtered off, washed with water and crystallized from butanol. The pure product (0.4 g, 14.8%) had mp 244-246°; uv: λ max 411 nm (ε 7950), 326 nm (ε 5102), 298 nm (ε 17945); ir (potassium bromide): C=N 1630 cm^{-1}; ^{1}H-nmr (deuteriochloroform): 2.81 (s, 3H, ArMe), 7.0-7.7 (m, ArH), 8.55 (broad, 1H, OH).

Anal. Calcd. for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.36; H, 5.60; N, 4.97.

1-Phenyl-4-methyl-3-(2*H*)benzo[*h*]isoquinolinone (**12**).

1-Phenyl-1,4-dihydro-3-(2*H*)benzo[*h*]isoquinolinone (1.5 g, 0.0055 mole) was stirred in anhydrous dimethylformamide (25 ml) in the presence of sodium hydride (0.8 g, 0.0165 mole) in a stream of nitrogen at 140° for 4 hours. After cooling, the mixture was poured into water (250 ml). The precipitated material was extracted with chloroform, the organic phase dried over sodium sulfate and evaporated to dryness. The oily residue was rubbed with ether and the resulting solid, recrystallized from butanol. The pure product (0.45 g, 29%) had mp 271-273°; uv: λ max 394 nm (ε 6306), 331 nm (ε 2475); ir (potassium bromide): C=N 1620 cm^{-1}; ^{1}H-nmr (deuteriochloroform): 2.42 (s, 3H, ArMe), 6.9-7.65 (m, ArH).

Anal. Calcd. for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.22; H, 5.50; N, 5.07.

4,5-Dimethyl-1-phenyl-3-(2*H*)isoquinolinone (**13**).

5-Methyl-1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinone (7) (2.37 g, 0.01 mole) was stirred in anhydrous dimethylformamide (25 ml) in the presence of sodium hydride (1.056 g, 0.022 mole) in a stream of nitrogen at 100° for 2 hours. The reaction mixture was poured into water (300 ml), acidified with 2*N* hydrochloric acid, and the product which separated was filtered off, washed with water and dried. Recrystallization from ethanol gave the pure product (0.6 g, 24%), mp 217-219°; uv: λ max 413 nm (ε 3315), 344 nm (ε 4301); ir (potassium bromide): C=N 1615 cm^{-1}; ^{1}H-nmr (deuteriochloroform): 2.74 (s, 3H, ArMe), 2.92 (s, 3H, ArMe), 6.94 (d, 1H, ArH), 7.26 (d, 1H, ArH), 7.61 (d, 1H, ArH), 7.45 (s, 5H, ArH).

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.73; H, 6.25; N, 5.66.

1-Phenyl-1,4-dihydro-3-(2*H*)isoquinolinone-1-*d* (**14**).

Benzyl cyanide (1.29 g, 0.011 mole) was added to 1:1 polyphosphoric acid (15 g) and the reaction mixture was stirred at 90° for half an hour. α-*d*-Benzaldehyde-sodium bisulfite adduct (10) (2.11 g, 0.01 mole) was then added and the mixture was stirred at 120° for 3 hours. After cooling it was poured into water (150 ml), made alkaline with concentrated ammonium hydroxide and brought to a boil. The solid was filtered off, washed with hot water and dried. The pure product (0.2 g, 10%) had mp 167-169°. In the ^{1}H-nmr spectrum recorded in deuteriochloroform, the H-1 band (5.60) did not appear, hence the compound can be regarded as at least 90% deuterated at C-1; this was also confirmed by the mass spectrum.

1-Pentadeuteriophenyl-1,4-dihydro-3-(2*H*)isoquinolinone (**16**).

A solution of the Grignard reagent prepared from pentadeuteriobromobenzene (4.1 g, 25 mmole) in ether (20 ml) was added dropwise to an ethereal solution (30 ml) of triethyl orthoformate (3.7 g, 25 mmole) at room temperature in 2 hours. After stirring for 1 hour, 2*N* hydrochloric acid (30 ml) was added to the solution and the ethereal phase was separated. The aqueous phase was extracted with ether, the combined ethereal phases were washed with water, dried over sodium sulfate, and the solvent was evaporated. Fractionation under vacuum gave pentadeuteriobenzaldehyde (0.7 g), which was allowed to react with benzyl cyanide according to the procedure given for 1-phenyl-1,4-dihydro-3-(2*H*)isoquinolinone deuterated at C-1 to obtain the product (**16**).

Reaction of Isoquinolinones Labelled with Deuterium in Sodium Hydride-Dimethylformamide Reagent.

1-Phenyl-1,4-dihydro-3-(2*H*)isoquinolinone-1-*d* (**14**) (0.4 g, 0.001785 mole) and sodium hydride (0.26 g, 0.00536 mole) were stirred in anhydrous dimethylformamide (10 ml) at 100° for 2 hours. The reaction mixture was processed as described for the non-labelled compound to obtain the product **15** (0.1 g, 23.7%), in which the 4-Me band (2.50, s) had 2H intensity; according to the mass spectroscopic measurement, the incorporation of deuterium in the C-4 methyl group was 54%.

A 1:1 mixture of **14** and **16** was allowed to react with benzaldehyde in the presence of sodium hydride according to (1) to obtain the mixture of isotope isomers, the data of which are shown in Table I.

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