THE REDUCTION OF AZAFLUORENONES

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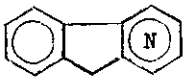
Treatment of 1- and 4-aza- as well as 1,5- , 1,8- , 2,5-, and 4,5-diazafluorenones with hydrazine hydrate at 160-170° C led to azafluorenes in the yield 33-90%. In the case of 4-aza-, 2,5- and 4,5-diazafluorenone, the dimerization products, 9,9'--bisazafluorenes were also formed under reduction conditions.

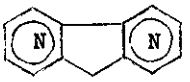
In connection with the considerable current interest in the chemistry and pharmacology of azafluorenone and azafluorene derivatives, many works have been reported recently[1]. Nevertheless, only little attention has been paid to unsubstituted compounds.

Although some azafluorenes have been known earlier, they were obtained by the application of complex procedures of cyclization or reduction[2-4].

As a part of our studies on tricyclic azines having potential pharmacological activity, we reported recently a convenient method of synthesis of azafluorenones starting from benzoquinolines and phenanthrolines[5]. We have also studied the synthesis of azafluorenes, and we report in this work simple general method based on the Wolff-Kishner reaction. We obtained 1- and 4-azafluorenes 1a,b and 1,5- , 1,8- , and 4,5-diazafluorenes 2a,b,d in the yields better than reported in literature[2-4], as well as previously unknown 2,5-diazafluorene 2c.

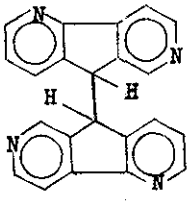


1a 1-N
1b 4-N



2a 1,5-N
2b 1,8-N

2c 2,5-N
2d 4,5-N



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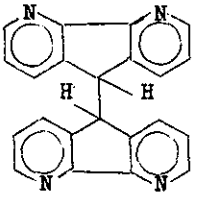

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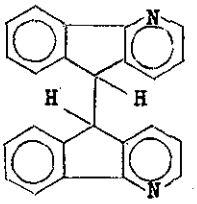

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When 2,5- and 4,5-diazafluorenones were reduced, the substantial amounts of 9,9'-bis-(2,5-diazafluorene) 3 and 9,9'-bis-(4,5-diazafluorene) 4 were also formed. A small amount of 9,9'-bis-(4-azafluorene) 5 was isolated after reduction of 4-azafluorenone, but when reaction was carried out in diethylene glycol according to Huang-Minlon procedure, the yield of 5 increased to 11%. No dimerization products were observed as a result of reduction of other azafluorenones.

Both ionic and free-radical mechanisms have been proposed for Wolff-Kishner reduction[6]. Weisburger and Grantham[7] found that fluorenone yielded besides fluorene also a product of dimerization, but dimer wasn't formed when six-fold excess of hydrazine was used. This fact was explained by the free-radical mechanism. Nevertheless, our investigation showed that some azafluorenes were dimerized even with very large excess of hydrazine. Further work on the determination of possible mechanism is in progress. The typical procedure is as follow: azafluorenone (4.55 g, 0.025 mole) and hydrazine hydrate (14.0 ml, 0.285 mole) were heated in autoclave to 160-170° C for 18 hours. After cooling, the crude azafluorene was filtered off and washed with water. The filtrate was extracted with chloroform. The combined extracts were dried ($MgSO_4$) and evaporated in vacuo to give addi-

tional portion of crude product. The crude azafluorenes were purified as follows:

1a was recrystallized from n-hexane, white needles, 84% yield, m.p.84-85°C (lit.[2,3] 79-85°C), NMR ($CDCl_3$) δ(ppm)8.67 (dd,2-H,J=5Hz and 1,5Hz), 8.10 (dd,4-H,J=8Hz and 1,5Hz), 7.94-7.85 (m,5-H), 7.75-7.69 (m,8-H), 7.58-7.49 (m,6-H,7-H), 7.40 (dd,3-H,J=8Hz and 5Hz), 4.05 (s,9-H).

1b was recrystallized from n-hexane, colorless prisms, 88% yield, m.p.93°C (lit.[2] 96-97°C) NMR ($CDCl_3$) 8.72 (dd,3-H,J=5Hz and 1,8Hz), 8.34-8.24 (m, 5-H), 7.80 (dd,1-H,J=7,5Hz and 1,8Hz) 7.62-7.54 (m,6-H,7-H and 8-H), 7.23 (dd,2-H,J=7,5Hz and 5Hz), 3.78 (s,9-H).

2a was recrystallized from n-hexane, white needles, 85% yield, m.p. 108--109°C (lit.[5] 108°C) NMR ($CDCl_3$) 8.82-8.76 (m,2-H,6-H), 8.47 (dd,4-H,J=8Hz and 1,8Hz), 8.02 (dd,8-H,J=7,5Hz and 1,5Hz), 7.53 (dd,3-H,J=8Hz and 5Hz), 7.40 (dd,7-H,J=7,5Hz and 5Hz), 4.04 (s,9-H).

2b was recrystallized from water, white needles, 90% yield, m.p.174-175°C (lit.[5] 170°C) NMR ($CDCl_3$) 8.76 (dd,2-H,7-H,J=5Hz and 1,8Hz), 8.19 (dd,4-H, 5-H,J=8Hz and 1,8Hz), 7.51 (dd,3-H,6-H,J=8Hz and 5Hz), 4.24 (s,9-H).

2c was extracted from the crude product with chloroform and recrystallized from water, white prisms, 33% yield, m.p. 145-146°C NMR ($CDCl_3$) 9.04 (s,1-H), 8.88 (d,3-H,J=5Hz), 8.84 (dd,6-H,J=5Hz and 1,8Hz), 8.14 (d,4-H, J=5Hz), 8.08 (dd,8-H,J=8Hz and 1,8Hz), 7.50 (dd,7-H,J=8Hz and 5Hz), 4.08 (s,9-H).

2d was extracted from the crude product with n-hexane and recrystallized from mixture n-hexane - benzene, white prisms, 52% yield m.p.172°C lit.[5] 172°C) NMR ($CDCl_3$) 8.85 (dd,3-H,6-H,J=5Hz and 1,8Hz), 7.94 (dd,1-H, 8-H, J=7,8Hz and 1,8Hz), 7.38 (dd,2-H,7-H,J=7,8Hz and 5Hz), 3.80 (s,9-H).

3 was obtained from the residue after extraction of 2c. The residue was

washed with methanol to give pure 3, white prisms, 62% yield, m.p. 278-280°C (decompn.); insoluble in NMR solvents, m/e = 334 (M^+, 30 , UV (MeOH) $\lambda_{max.}$ 249, 289 and 302 nm (log ε 3.78, 4.08 and 4.09).

4 was obtained from the residue after extraction of 2d. The residue was recrystallized from mixture ethyl acetate-chloroform-methanol to give pure 4, white prisms, 42% yield, m.p. 318-320°C (decompn.); insoluble in NMR solvents, m/e = 334 (M^+, 40); UV (MeOH) $\lambda_{max.}$ 250, 300, 306 and 312 nm (log ε 3.76, 4.20, 4.21 and 4.31).

5 was isolated in a trace amount after crystallization of 1b. When reduction was carried out according to Huang-Minlon procedure, 5 was obtained in 11% yield. The crude 5 was recrystallized from acetic acid to give white prisms, m.p. 289-290°C, NMR (CF_3COOD) 8.88-7.40 (m, ring-H), 5.42 (s, 9-H, 9'-H); m/e = 332 (M^+, 17); UV (MeOH) $\lambda_{max.}$ 254, 283, 308 and 325 nm (log ε 3.54, 3.55, 3.77 and 3.47).

All the new compounds gave satisfactory elemental analyses.

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