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# CONDENSATION OF 1-AMINO-4-AZAFLUORENE WITH α-DIKETONES AND α,β-UNSATURATED KETONES

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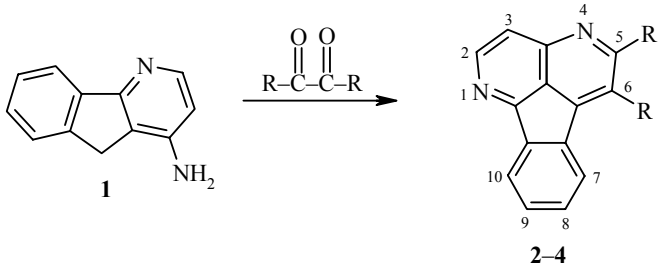
*Condensation of 1-amino-4-azafluorene with α-diketones and with unsaturated ketones in basic medium gives novel substituted 1,4-diazafluoranthenes and also dihydro-4-azafluoreno[9,9a,1-b,c]-cyclohexano[2',3'-e]- and indano[1',2'-e]azepines.*

**Keywords:** 4-azafluorenocyclohexanoazepines, 1-amino-4-azafluorene, diazafluoranthenes, α-diketone, unsaturated ketones.

We have previously used the Chichibabin reaction to prepare 1-amino-4-azafluorene (**1**) and studied some of its chemical reactions [1]. Azafluorene **1**, with an active methylene group in position 9 and an amino group in position 1, is a promising synthon for the construction of condensed nitrogen-containing compounds with a 4-azafluorene fragment, which are of interest for biological screening.

In this communication we report the results of a study of the condensation of the azafluorene **1** with α-diketones and chalcones, prepared from cyclic ketones.

Condensation of azafluorene **1** with benzil, furil, and *p*-anisil in alcoholic medium (KOH in alcohol or sodium ethylate in alcohol) gives the 1,4-diazafluoranthenes **2-4**.




**1** **2–4**

**2** R = Ph, **3** R = *p*-$MeOC_6H_4$, **4** R = 2-furyl

The low yields of diazafluoranthenes **2-4** (30-40%) are apparently associated with the fact that the α-diketones can undergo a benzil rearrangement in these reaction conditions. The use of an excess of the α-diketones does not have an effect on the yield of compounds **2-4** but complicates their separation.

A similar condensation of compound **1** with acenapthoquinone gives the acenaphthodiazafluoranthene **5**.

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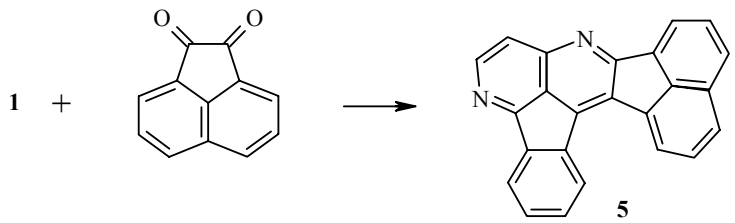
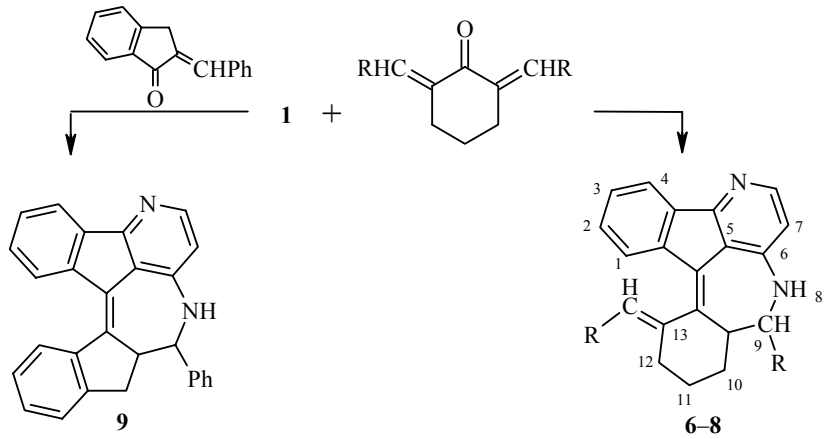



The condensation of the unsaturated ketones of 2,6-bisarylidenecyclohexanone and 2-benzylideneindan-1-one with compound **1** was also carried out in basic medium in alcohol. The carbonyl group of the chalcone condensed with the methylene group of the azafluorene and the amino group adds to the double bond (Michael addition) to give the dihydroazepines **6-9** which are condensates of the 4-azafluorene with the cyclohexane or indane fragments.




**6** R = Ph, **7** R = *p*-MeOC$_6$H$_4$, **8** R = 2-furyl

The IR spectra of compounds **6-9** show a broad stretching band for the NH group in position 8 in the range 3400-3200 cm$^{-1}$ and this confirms the proposed cyclization scheme.

The $^1$H NMR spectra of compounds **2-9** (Tables 1 and 2) show signals for all of the protons present in these molecules and the absence of signals for the $C_{(9)}$ methylene protons found in the spectrum of the starting material **1**.

The mass spectra of compounds **2-9** show strong molecular ion peaks corresponding to their empirical formulae. In the mass spectra of the diazafluoranthenes **4** and **5** the $[M]^+$ ion peak is maximal whereas in the spectra of the 5,6-disubstituted compounds **2** and **3** it is the $[M\text{-}H]^+$ ion peak and this is a feature of the dissociation of α-phenyl-substituted azines [2]. The high aromaticity of the diazafluoranthene system is the reason of the small number of decomposition pathways. The basic route for fragmentation of the molecular ion peaks for compounds **3** and **4** is associated with the fission of methoxyphenyl and furyl radicals. For $[M]^+$, compound **3** is characterized by elimination of the radicals $CH_3$· and $OCH_3$· and the formation of the fragments 401 (30) and 385 (25) respectively*. Successive elimination in the ion $[M]^+$ of the radicals CHO· and CO· gives the fragments 307 (19) and 279 (34) respectively.

The dissociation of the acenaphthenyl-substituted diazafluoranthene **5** is characterized by the loss of HCN (301 (14)) and breakup of the $[M]^+$ in half to form the fragments 164 (40).

* Here and subsequently the values *m/z* ($I_{rel}$, %) are quoted for the molecular ion peaks.

TABLE 1. $^1$H NMR Spectra of Compounds **2-5**

| Compound | Chemical shift, δ, ppm (*J*, Hz)* | | | | |
|---|---|---|---|---|---|
| | 2-H, d | 3-H, d | 7-H – 9-H | 10-H | 5-R, 6-R*$^2$ |
| **2** | 8.81 ($J_{23}$ = 6.1) | 7.78 ($J_{32}$ = 6.1) | 7.0-7.5 | 8.06 | 7.0-7.5 |
| **3** | 8.79 ($J_{23}$ = 5.1) | 7.75 ($J_{32}$ = 5.1) | 7.0-7.5 | 8.06 | 7.36, 7.23 (*o*-H); 6.96, 6.79 (*m*-H); 3.89 (s, 2$CH_3O$); 3.80 s |
| **4** | 8.78 ($J_{23}$ = 6.1) | 7.77 ($J_{32}$ = 6.1) | 7.20-7.47, m | 8.03 (m, $J_{109}$ = 7.6) | 7.75 (d, $J_{23}$ = 1.5, 2-H); 6.73 (dd, $J_{34}$ = 3.1, 3-H); 6.44 (dd, $J_{34'}$ =3.7); 6.67 (d, $J_{34}$ = 3.1, 4-H); 6.05 (d, $J_{34'}$ = 3.7) |
| **5** | 8.83 ($J_{23}$ = 6.1) | 7.91 ($J_{32}$ = 6.1) | 7.65-8.74 | | 7.65-8.74 |

* The $^1$H NMR spectrum was recorded in $CDCl_3$ at 30°C (compounds **2-4**) and DMSO-$d_6$ at 40°C (compound **5**).
*$^2$ The furyl substituent signals are given for compound **4**.

TABLE 2. $^1$H NMR Spectra of Compound **6-9**

| Compound | Chemical shift, δ, ppm (*J*, Hz)* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1-H, m | 2-H, m | 3-H, m | 4-H, m | 6-H, d | 7-H, d | 9-H, d | 9a-H, d | 10-H; 11-H; 12-H | RCH=, s | R |
| **6** | 7.74*$^2$ ($J_{12}$ = 7.0) | 6.7-6.9 7.3-7.5 | | 7.89*$^2$ ($J_{34}$ = 7.0) | 8.20 ($J_{67}$ = 5.5) | 6.50 ($J_{67}$ = 5.5) | 4.48*$^2$ ($J_{99a}$ = 3.4) | 4.43*$^2$ ($J_{99a}$ = 3.4) | 1.6-1.9; 2.3-2.7; 2.9-3.0, m | 6.16 | 6.7-6.9, m; 7.3-7.5, m |
| **7** | 7.73*$^2$ ($J_{12}$ = 7.0) | 7.2-7.5 | | 7.91*$^2$ ($J_{34}$ = 7.0) | 8.19 ($J_{67}$ = 5.8) | 6.50 ($J_{67}$ = 5.8) | 4.42*$^2$ ($J_{99a}$ = 3.1) | 3.38*$^2$ ($J_{99a}$ = 3.1) | 1.2-3.0, m | 6.19 | R = *p*-$CH_3OC_6H_4$, 6.35 (m, *o*-H); 6. 93 (m, *m*-H); 6.05, m; 7.25, m |
| **8** | 7.8 | 7.80 | 7.80 | 7.80 | 8.12 ($J_{67}$ = 5.8) | 6.96 ($J_{67}$ = 5.8) | 5.20 ($J_{99a}$ = 3.1) | 4.63 ($J_{99a}$ = 3.1) | 1.6-1.8; 2.55-2.7, m | 5.93 | 7.41, 7.40 (dd, $J_{23}$ = 1.8, 2-H); 6.55 (dd, $J_{23}$ = 1.8, 3-H); 5.93 (dd, $J_{34'}$ = 3.4, 4-H) |
| **9** | 7.72*$^2$ ($J_{12}$ = 7.0) | 7.2-7.5 | | 7.84*$^2$ ($J_{34}$ = 7.0) | 8.32 ($J_{67}$ = 5.5) | 6.74 ($J_{67}$ = 5.5) | 4.94*$^2$ ($J_{99a}$ = 3.7) | 4.53 ($J_{99a}$ = 3.7) | 10-$CH_2$ 3.55, s | — | 6.7-6.9, m; 7.15-7.50, m |

* The $^1$H NMR spectrum was recorded in $CDCl_3$ at 30°C (compounds **6,7,9**) and DMSO-$d_6$ at 40°C (compound **8**).
*$^2$ Possible reversal of assignments.

The breakdown of the $[M]^+$ ions for the azepines **6-9** is characterized by the existence of several joint fragmentation routes (see Scheme 1) connected with the loss of the radicals H·, $\cdot CH_2R$, and ·R. Moreover, for the fission of $CH_2R$ and R, the charge is localized on both fragments. Hence the intensities of the ion peak for $[CH_2R]^+$ in the mass spectra of compounds **6-9** are 50, 100, 100, and 8% respectively.

Scheme 1

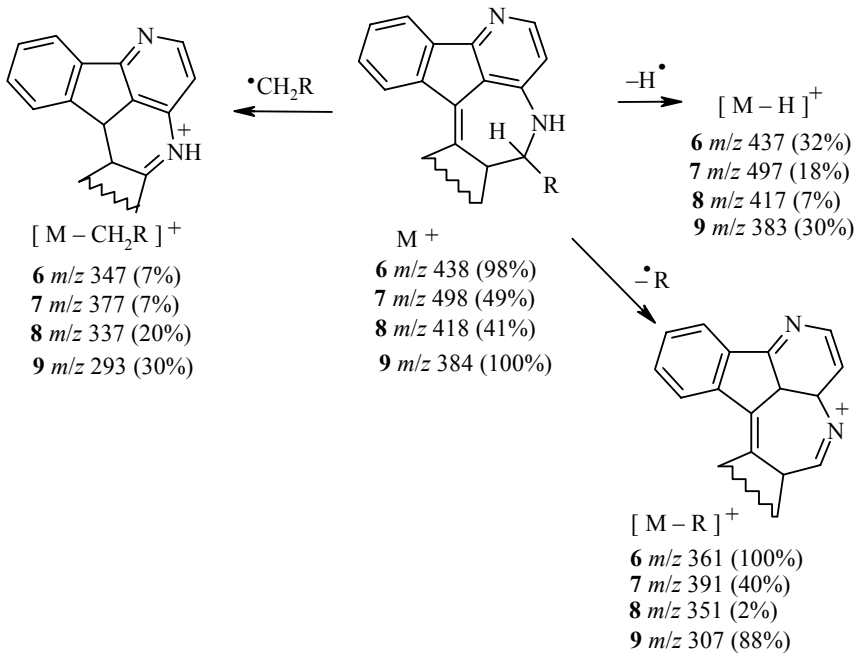



TABLE 3. Mass Spectra of Compounds **2-9**

| Compound | *m/z* ($I_{rel}$, %) |
|---|---|
| **2** | 365 $[M]^+$ (51), 355 (100), 354 (8), 353 (11), 327 (2), 251 (2), 250 (1), 224 (2), 178 (6), 177 (10), 176 (2), 108 (3), 107 (4), 88 (4), 77 (3), 32 (4), 28 (8) |
| **3** | 416 $[M]^+$ (80), 415 (100), 401 (30), 385 (25), 372 (30), 358 (10), 342 (100), 329 (40), 303 (10), 213 (25), 201 (20), 187 (18), 171 (31), 164 (35), 151 (20), 133 (15), 103 (20), 90 (25), 77 (5), 63 (15), 51 (3), 33 (2) |
| **4** | 336 $[M]^+$ (100), 333 (4), 320 (13), 319 (63), 307 (19), 279 (34), 278 (14), 251 (4), 250 (3), 226 (2), 210 (1), 196 (1), 187 (9), 186 (4), 185 (3), 181 (1), 140 (9), 139 (6), 126 (4), 111 (2), 99 (2), 94 (6), 91 (4), 87 (3), 86 (2), 77 (2), 76 (1), 75 (2), 74 (2), 65 (3), 63 (3), 51 (3), 50 (2), 45 (3), 44 (1), 43 (2), 40 (1), 39 (8), 38 (3) |
| **5** | 328 $[M]^+$ (100), 327 (15), 273 (5), 164 (40), 150 (21), 149 (20), 137 (20), 136 (21), 124 (5), 100 (2), 74 (1), 55 (2) |
| **6** | 438 $[M]^+$ (98), 437 (32), 361 (100), 360 (12), 347 (7), 319 (2), 269 (6), 242 (1), 219 (4), 165 (6), 138 (5), 115 (11), 91 (61), 77 (10), 57 (7), 43 (60) |
| **7** | 498 $[M]^+$ (49), 497 (18), 391 (40), 380 (1), 377 (7), 351 (1), 350 (10), 269 (3), 255 (5), 240 (5), 218 (10), 197 (11), 196 (21), 182 (11), 153 (21), 135 (70), 121 (100), 108 (20), 91 (30), 77 (37), 65 (5), 55 (7), 39 (5) |
| **8** | 418 $[M]^+$ (41), 417 (7), 389 (10), 375 (1), 351 (2), 337 (25), 321 (5), 309 (10), 293 (10), 281 (10), 269 (11), 255 (15), 242 (10), 231 (15), 218 (10), 196 (15), 181 (40), 165 (60), 153 (40), 138 (50), 127 (30), 115 (30), 107 (20), 91 (50), 81 (100), 65 (30), 53 (50), 39 (51) |
| **9** | 384 $[M]^+$ (100), 383 (35), 307 (88), 306 (25), 293 (30), 281 (3), 254 (4), 236 (3), 217 (1), 203 (20), 184 (10), 164 (8), 153 (30), 138 (10), 115 (2), 91 (5), 77 (4), 43 (2) |

## EXPERIMENTAL

$^1$H NMR spectra were recorded on a Bruker WP-200 spectrometer (200 MHz) with TMS as internal standard. IR spectra were obtained on an IR-75 spectrometer for KBr tablets. Mass spectra were recorded on a MAT-112 instrument with direct introduction of the sample into the ion source and an ionizing voltage of 70 eV. TLC was carried out on Silufol UV-254 plates (revealed using iodine vapor) and column chromatography on Woelm® grade 32-63 silica gel.

**5,6-Diphenyl-1,4-diazafluoranthene (2).** A solution of sodium ethylate, prepared from Na (0.5 g, 21 mmol), and the azafluorene **1** (0.2 g, 1 mmol) in absolute alcohol (20 ml) was heated to 60°C, benzil (0.21 g, 1 mmol) added, and refluxed for 2 h with monitoring by TLC. The alcohol was distilled off and the residue was transferred to a silica gel column (1.5 × 30 cm). A mixture of ethyl acetate and hexane (1:1) eluted the diazafluoranthene **2** (0.15 g, 42%), yellow crystals; mp 199-201°C (ethyl acetate–hexane), $R_f$ 0.58 (ethyl acetate). Found, %: C 87.61; H 4.53; N 7.84; $M^+$ 356. $C_{26}H_{16}N_2$. Calculated, %: C 87.60; H 4.50; N 7.80; M 356.

**5,6-Di(*p*-methoxyphenyl)-1,4-diazafluoranthene (3)** was prepared similarly from anisil (0.70 g, 2.75 mmol) and the aminofluorene **1** (0.5 g, 2.75 mmol) in the presence of sodium ethylate prepared from Na (1.0 g, 42 mmol). Yield 0.26 g (22%), yellow crystals; mp 220-221°C (ethyl acetate–hexane ), $R_f$ 0.57 (ethyl acetate). Found, %: C 80.71; H 4.81; N 6.74; $M^+$ 416. $C_{28}H_{20}N_2O_2$. Calculated, %: C 80.70; H 4.80; N 6.73; M 416.

**5,6-Di(2-furyl)-1,4-diazafluoranthene (4)** was prepared similarly from furil (0.53 g, 2.75 mmol) and the aminofluorene **1** (0.5 g, 2.75 mmol) in the presence of sodium ethylate prepared from Na (1.0 g, 42 mmol). Yield 0.21 g (24%), yellow crystals; mp 196-198°C (ethyl acetate–hexane), $R_f$ 0.50 (ethyl acetate). Found, %: C 78.61; H 3.61; N 8.35; $M^+$ 336. $C_{22}H_{12}N_2O_2$. Calculated, %: C 78.60; H 3.60; N 8.34; M 336.

**1,4-Diazaacenaphtho[1,2-*f*]fluoranthene (5)** was prepared similarly to that reported above from acetonaphthoquinone (0.5 g, 2.75 mmol) and the azafluorene **1** (0.5 g, 2.75 mmol) in the presence of sodium ethylate prepared from Na (1.0 g, 42 mmol). Yield 0.28 g (35%), yellow crystals; mp 277-279°C (ethyl acetate–hexane), $R_f$ 0.75 (ethyl acetate). Found, %: C 87.81; H 3.66; N 8.54; $M^+$ 328. $C_{24}H_{12}N_2$. Calculated, %: C 87.80; H 3.65; N 8.53; M 328.

**13-Benzylidene-9-phenyl-4-aza-9,9a-dihydrofluoreno[9,9a,1-*b,c*]cyclohexano[2',3'-*e*]azepine (6).** A solution of the azafluorene **1** (0.3 g, 1.65 mmol), 2,6-dibenzylidenecyclohexanone (0.42 g, 1.65 mmol), and NaOH (0.3 g, 7.5 mmol) in ethanol (20 ml) was refluxed for 2 h with TLC monitoring. The alcohol was distilled off and the residue was chromatographed on a silica gel column (1.5 × 30 cm). A mixture of ethyl acetate and hexane (1:2) eluted the azepine **6**. Yield (0.17 g, 25%), yellow crystals; mp 216-217°C (ethyl acetate–hexane), $R_f$ 0.50 (ethyl acetate). IR spectrum, ν, cm$^{-1}$: 3210 (NH). Found, %: C 82.01; H 5.51; N 6.34; $M^+$ 438. $C_{32}H_{26}N_2$. Calculated, %: C 82.00; H 5.50; N 6.42; M 438.

**9-Anisyl-13-(*p*-methoxybenzylidene)-4-aza-9,9a-dihydrofluoreno[9,9a,1-*b,c*]cyclohexano[2',3'-*e*]-azepine (7)** was prepared similarly from the azafluorene **1** (0.3 g, 1.65 mmol), 2,6-di(*p*-methoxybenzylidene)-cyclohexanone (0.55 g, 1.65 mmol), and NaOH (0.3 g, 7.5 mmol) in ethanol (20 ml). Yield 0.12 g (15%), yellow crystals; mp 158-160°C (ethyl acetate–hexane), $R_f$ 0.45 (ethyl acetate). IR spectrum, ν, cm$^{-1}$: 3350 (NH). Found, %: C 81.91; H 6.10; N 5.61; $M^+$ 498. $C_{34}H_{30}N_2O_2$. Calculated, %: C 81.90; H 6.0; N 5.6; M 498.

**13-Furfurylidene-9-(2-furyl)-4-aza-9,9a-dihydrofluoreno[9,9a,1-*b,c*]cyclohexano[2',3'-*e*]azepine (8)** was prepared similarly from the azafluorene **1** (0.3 g, 1.65 mmol), 2,6-difurfurylidenecyclohexanone (0.42 g, 1.65 mmol), and NaOH (0.3 g, 7.5 mmol) in ethanol (20 ml) as described in the above method. Yield 0.19 g (27%), yellow crystals; mp 132-135°C (ethyl acetate–hexane), $R_f$ 0.48 (ethyl acetate). IR spectrum, ν, cm$^{-1}$: 3380 (NH). Found, %: C 76.71; H 5.4; N 6.71; $M^+$ 418. $C_{28}H_{22}N_2O_2$. Calculated, %: C 76.70; H 5.30; N 6.70; M 418.

**9-Phenyl-4-aza-9,9a-dihydrofluoreno[9,9a,1-*b,c*]indeno[1',2'-*e*]azepine (9)** was prepared similarly from the azafluorene **1** (0.3 g, 1.65 mmol), 2-benzylideneindanone (0.4 g, 1.65 mmol), and NaOH (0.3 g,

7.5 mmol) in ethanol (20 ml) as described in the above method. Yield 0.19 g (33%), yellow crystals; mp 182-184°C (ethyl acetate–hexane), $R_f$ 0.78 (ethyl acetate). IR spectrum, ν, $cm^{-1}$: 3200 (NH). Found, %: C 87.48; H 5.18; N 7.28; $M^+$ 384. $C_{28}H_{20}N_2$. Calculated, %: C 87.50; H 5.20; N 7.30; M 384.

## REFERENCES


1. A. V. Varlamov, A. N. Levov, F. Toze, A. N. Chernyshev, V. V. Davydov, M. A. Ryabov, and O. A. Egorova, *Khim. Geterotsikl. Soedin.*, 1682 (2002).
2. Q. N. Porter and A. Balcas, *Mass Spectrometry of Heterocyclic Compounds*, Wiley, New York (1971), p. 376.