CONDENSATION OF 4-AZAFLUORENE WITH γ-BUTYLENE GLYCOL AND GLYCERIN

N. S. Prostakov, V. P. Shalimov,
Galo B. Montenegro Cordova and E. V. Kruglyak

UDC 547.424.23'426.1'828.07:542.953

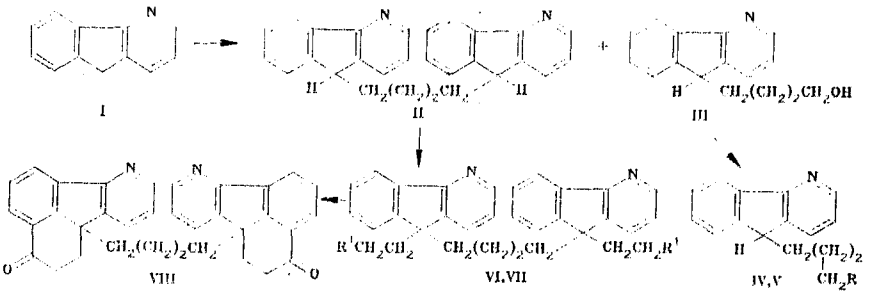
1,4-Di(4-azafluoren-9-yl)butane and 9-(δ-hydroxybutyl)-4-azafluorene were obtained by condensing 4-azafluorene with γ-butylene glycol. From the first of these products, 1,4-di(7-aza-3-oxo-1,2,3,10b-tetrahydrofluoranthen-10b-yl)butane was synthesized by a series of successive transformations (cyanoethylation, hydrolysis, dehydrocyclization). In the condensation of 4-azafluorene with glycerin, 1,2,3-tri(4-azafluoren-9-yl)propane was obtained.

In continuation of the work in [1] on the synthesis of heterocyclic compounds containing two azafluorene fragments bound by a polymethylene chain, and also of 9-ω-hydroxyalkyl derivatives of azafluorenes, we studied the condensation of 4-azafluorene (I) with γ-butylene glycol, which was carried out at 230°C in the presence of sodium. From the reaction products, two compounds were chromatographically isolated in more than 70% overall yield: 1,4-di(4-azafluoren-9-yl)butane (II) and 9-(δ-hydroxybutyl)-4-azafluorene (III). The second compound quantitatively predominates. With increase in the amount of γ-butylene glycol used in the reaction, the yield of compound III increases and the yield of compound II decreases.

The chemical reactions of compounds II and III carried out serve as a proof for their structure. The new compounds are also interesting as potentially biologically active compounds.

From alcohol III, 9-(δ-chlorobutyl)-4-azafluorene (IV) and 9-(δ-phenylcarbamoyloxybutyl-4-azafluorene) (V) were obtained in quantitative yields.

In the cyanoethylation of compound II carried out in the presence of an alcoholic solution of ethoxytrimethylphenylammonium (the Rodionov catalyst, cR), a dinitrile, 1,4-di[9-(β-cyanoethyl)-4-azafluoren-9-yl]butane (VI) was obtained, which was then converted into a dibasic acid, 1,4-di[9-(β-carboxyethyl)-4-azafluoren-9-yl]butane (VII).



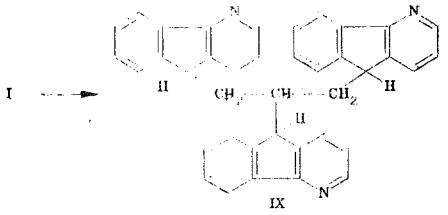
IV R=Cl; V R=$OCONHC_6H_5$; VI R^1=CN; VII R^1=COOH

In intramolecular dehydrocyclization of the dibasic acid VII, carried out by the action of polyphosphoric acid, 1,4-di(7-aza-3-oxo-1,2,3,10b-tetrahydrofluoranthen-10b-yl)butane (VIII) was obtained in a yield of more than 20%. It was a light-yellow crystalline compound, melting above 300°C.

A similar condensation of azafluorene I with glycerin was carried out.

P. Lumumba Peoples' Friendship University, Moscow 117923. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 810-812, June, 1986. Original article submitted January 24, 1985.

 0009-3122/86/2206-0640$12.50



1,2,3-Tri(4-azafluoren-9-yl)propane (IX) was obtained in a yield of 15%, and was isolated in the form of colorless high-melting crystals.

The structure of the compounds synthesized was confirmed by spectral and elemental analysis data.

EXPERIMENTAL

The IR spectra of the compounds were run on a UR-20 spectrophotometer in KBr tablets. The electronic absorption spectra were obtained on a Specord UV-VIS spectrophotometer in ethanol. The course of the reactions, the individuality and the separation of the compounds were controlled by TLC on aluminum oxide, grade II of activity. The molecular weights were determined on a LKV-2091 chromato-mass-spectrometer.

1,4-Di(4-azafluoren-9-yl)butane (II) and 9-(δ-hydroxybutyl)-4-azafluorene (III). A 0.58 g (25 mmoles) portion of sodium is dissolved in 1.62 g (18 mmoles) of 1,4-butanediol, 1 g (5.9 mmoles) of azafluorene I is added, and the mixture is heated for 22 h at 230°C. When cool, 20 ml of water are added, and the mixture is extracted by chloroform. The residue after the distillation of chloroform is chromatographed, using a 3:1 mixture of ether and hexane as eluent. Yield, 0.51 g (22%) of compound II, mp 138-140°C (from hexane). IR spectrum: 3065, 3010 (C_{ar}–H), 2950, 2930, 2860 cm^{-1} (C_{al}–H). Found, %: C 86.7; H 5.9; N 7.0; M^+ 388. $C_{28}H_{24}N_2$. Calculated, %: C86.6; H 6.1; N 7.2; M 388. The elution is then continued with ether. Yield 0.7 g (49%) of alcohol III, mp 123-124°C (from a 2:1 hexane–benzene mixture. IR spectrum: 3225-3235 cm^{-1} (OH). Found, %: C 80.6; H 7.1; N 5.8; M^+ 239. $C_{16}H_{17}NO$. Calculated, %: C 80.3; H 7.1; N 5.8; M 239.

9-(δ-Chlorobutyl)-4-azafluorene (IV). A solution of 10 ml of thionyl chloride in 5 ml of benzene is gradually added to a solution of 0.4 g (1.6 mmole) of alcohol III in 20 ml of anhydrous benzene. The mixture is heated at the boiling point for 5 h. After distillation of benzene and excess thionyl chloride, 20 ml of water and sodium carbonate are added to pH 10. The reaction products are extracted by ether. Ether is distilled off and the residue is passed through a chromatographic column (eluent, 3:1 mixture of ether and hexane). Yield, 0.35 g (81%) of chloride IV in the form of an oily, colorless compound, IR spectrum: 3060, 3030 (C_{ar}–H), 2999, 2950, 2870 cm^{-1} (C_{al}–H). Found, %: N 5.4; M^+ 257. $C_{16}H_{16}ClN$. Calculated, %: N 5.4; M 257.

9-(δ-Phenylcarbamoyloxbutyl)-4-azafluorene (V). A mixture of 0.2 g (0.8 mmole) of alcohol III and 0.2 g (1.6 mmole) of phenyl isocyanate in 20 ml of anhydrous benzene is heated for 3 h at 60°C. After the distillation of benzene, the residue is chromatographed, using a 3:1 mixture of benzene and hexane as eluent. Yield, 0.22 g (74%) of compound V in the form of an oily colorless compound. Found: M^+ 358. $C_{23}H_{22}N_2O_2$. Calculated, %: M 358. Hydrochloride: mp 95-96°C. Found, %: N 6.8. $C_{23}H_{22}N_2O_2 \cdot HCl$. Calculated, %: N 7.1.

1,4-Di[9(β-cyanoethyl)-4-azafluoren-9-yl)]butane (VI). In the reaction of 0.69 g (1.7 mmole of compound II, 4.8 g (90 mmoles) of acrylonitrile, 0.1 ml of cR and 30 ml of anhydrous toluene are used. The mixture is stirred for 3 h at 60°C. The toluene solution is shaken with water and dried over potassium carbonate. After the distillation of the solvent and recrystallization, 0.64 g (73%) of compound VI is isolated, mp 214-215°C (from 1:3 hexane–benzene mixture). IR spectrum: 3072 (C_{ar}–H), 2943, 2870 (C_{al}–H), 2254 cm^{-1} (CN). UV spectrum, λ_{max} (log ε): 262 (4.26); 278 (4.14); 286 (4.29); 305 nm (4.44). Found, %: C 82.4; H 5.8; N 11.5; M^+ 494. $C_{34}H_{30}N_4$. Calculated, %: C 82.6; H 6.0; N 11.3; M 494.

1,4-Di[9-(β-carboxyethyl)-4-azafluoren-9-yl]butane (VII). A solution of 1.75 g (3.5 mmoles) of dinitrile VI, 2.8 g (50 mmoles) of potassium hydroxide in 35 ml of ethanol is boiled for 18 h. The mixture is neutralized by 70% sulfuric acid to pH 7. The precipitate is washed with water and dried. Yield 1.1 g (58%) of dibasic acid VII, mp 222-224°C. IR spectrum: 3500 m, 3200, 2550 cm^{-1} (OH in COOH). UV spectrum, λ_{max} (log ε): 208 (4.68); 258 (4.24); 279 (4.08); 288 (4.28); 309 (4.51); 3.14 nm (4.54). Found, %: N 5.2; M^+ 532. $C_{34}H_{32}N_2O_4$. Calculated, %: N 5.3; M 532.

1,4-Di(7-aza-3-oxo-1,2,3,10b-tetrahydrofluoranthen-10b-yl)butane (VIII). A mixture of 1 g (1.88 mmole) of diacid VII and 64 g of polyphosphoric acid are allowed to stand for 2 h at 160°C. The reaction mixture is poured onto ice (150 g) and neutralized by ammonia. The mixture is extracted by chloroform, and the extract is dried over potassium carbonate. After the distillation of chloroform, the residue is chromatographed, using ethyl acetate as eluent. Yield, 0.21 g (23%) of compound VIII, light-yellow crystals, mp 304-305°C (from a 1:2 benzene–hexane mixture). IR spectrum: 2944, 2875 (C_{al}–H), 1690 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 207 (4.69); 262 (4.48); 284 (4.14); 294 (4.25); 326 nm (4.19). Found, %: C 82.1; H 5.8; N 5.3; M^+ 496. $C_{34}H_{28}N_2O_2$. Calculated, %: C 82.2; H 5.6; N 5.6; M 496.

1,2,3-Tri(4-azafluoren-9-yl)propane (IX). A 0.14 g portion (6 mmoles) of sodium is dissolved in 3 g (32 mmoles) of glycerin, 1 g (5.9 mmoles) of azafluorene I are added, and the mixture is heated for 24 hours at 230°C. When cool, 20 ml of water are added, and the mixture is extracted by chloroform. After distillation of chloroform, the residue is chromatographed, using ether as eluent. Yield of compound IX 15%, mp 277-278°C (from a 2:1 hexane–benzene mixture). IR spectrum: 3050 (C_{ar}–H), 2910, 2860 (C_{al}–H), 1580 m, 1570 m, 1560 m, 1500 w (C=C, skeleton), 1450, 1410 cm^{-1} (C_{al}–H), 740 cm^{-1} (C_{ar}–H). UV spectrum, λ_{max} (log ε): 200 (4.93); 255 (4.55); 282 (4.4); 288 (4.57); 314 nm (4.76). Found, %: C 86.5; H 5.4; N 7.9; M^+ 539. $C_{39}H_{29}N_3$. Calculated, %: C 86.3; H 5.3; N 7.7; M 539.

LITERATURE CITED

1. N. S. Prostakov, V. P. Shalimov, and Galo B. Montenegro Cordova, Khim. Geterotsikl. Soedin., No. 11, 1525 (1984).

SYNTHESIS STARTING FROM 3-METHYL-2-PHENYL-5-(3-METHYL-2-PHENYL-3,4-DEHYDROPIPERIDYL-6)PYRIDINE. 2-PHENYLDINICOTINIC AND 4-AZAFLUORENONE-2-CARBOXYLIC ACIDS

N. S. Prostakov, I. V. Eliseeva, H. Bu Habib, L. M. Kirillova, and A. É. Aliev

UDC 547.829'826.2'836:543.422

N-Methyl (ethyl, benzoyl, trifluoroacetyl)-substituted 3-methyl-2-phenyl-5-(3'-methyl-2'-phenyl-3',4'-dehydropiperidyl-6')pyridines and di(N-oxide) of the correspondingly substituted α,β-dipyridyl were prepared. A method for synthesizing 2-phenyldinicotinic acid was developed. Cyclodehydration of this acid gave 4-azafluorenone-2-carboxylic acid. Transformations of this acid were carried out with respect to two functional groups.

We used the structural analog of anabasine, 3-methyl-2-phenyl-5-(3'-methyl-2'-phenyl-3',4'-dehydropiperidyl-6')pyridine (I), in the syntheses of its derivatives, potentially physiologically active compounds, for the preparation of 2-phenyldinicotinic acid, and also for developing a new path for building up of a 4-azafluorene system.

The syntheses which we carried out served as an additional proof of the structure of α-dehydropiperidyl-β-pyridine I, described in [1]; its N-alkyl substituted derivatives were obtained by two paths. 3-Methyl-2-phenyl-5-(1',3'-dimethyl-2'-phenyl-3',4'-dehydropiperidyl-6') pyridine (II) was synthesized by the Leuckart method. The N-ethyl-substituted derivative III was obtained by reducing the analogous N-acetyl-substituted derivative IV with lithium aluminum hydride [1].

P. Lumumba Peoples' Friendship University, Moscow 117923. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 813-817, June, 1986. Original article submitted March 12, 1985.

 0009-3122/86/2206-0642$12.50