SYNTHESIS OF 4,5,6,6a-TETRAHYDRO-8-AZAFLUORANTHENES

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UDC 547.837.07:543.422

The partially hydrogenated condensed cyclohexano-8-azafluoranthene system is formed as a result of cyclodehydration of 3-methyl-9,9-di(2-carboxyethyl)-2-azafluorene. A substituted partially hydrogenated 8-azafluoranthene was obtained from the product by opening of the cyclohexane ring.

Cyanoethylation of 3-methyl-2-azafluorene gives 3-methyl-9,9-di(2-cyanoethyl)-2-azafluorene (in quantitative yield) [1], from which we have obtained a number of new 2-azafluorene derivatives containing two ω-substituted alkyl groups attached to C_9 (Table 1). Their synthesis was accomplished by the usual successive transformations of the functional groups or by replacement of the substituent in the ω position of the alkyl group.

It is known that the cyclodehydration of 9-(2-carboxyethyl)fluorene and 9,9-di(2-carboxyethyl)fluorene in the presence of sulfuric or polyphosphoric acid (PPA) leads, respectively, to 3-oxo-1,2,3,10b-tetrahydrofluoranthene and (4,4'-dioxo-1,2,3,4,1',2',3',4'-octahydro-8,8'-dinaphthyl)spiran [2]. Considering the electrophilic character of cyclodehydration, it might be assumed that the analogous cyclization of 3-methyl-9,9-di(2-carboxyethyl)-2-azafluorene (I) [1] should proceed differently without involvement of the pyridine ring of the 2-azafluorene system. The reaction was carried out in the presence of PPA at 150-160°. Three crystalline substances (in 63% yield) which differed with respect to their chromatographic mobilities and colors were isolated by means of chromatography on silica gel. Light-yellow crystals with mp 202-203°, which were found to be 9-methyl-4,13-dioxo-8-aza-4,5,6,6a-tetrahydro-5,6a-propanofluoranthene (XVI), were isolated constituting the major component of the mixture.

The UV spectrum of XVI is similar to the UV spectrum of 3-oxo-1-carboxy-1,2,3,3,10b-tetrahydrofluoranthene [3]. Two intense bands at 1683 and 1727 cm^{-1}, corresponding to the

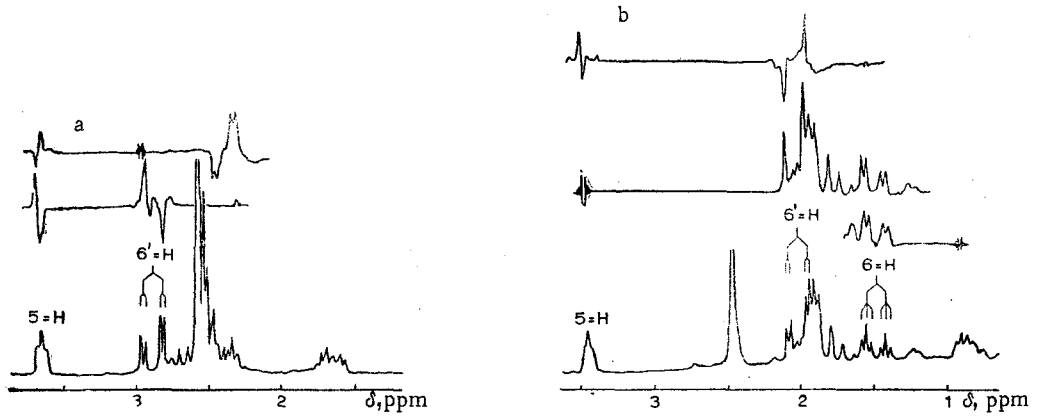
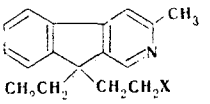


Fig. 1. Fragment of the PMR spectrum (single resonance, double resonance, and INDOR) of azafluoranthene XVI: a) in deuterochloroform; b) in deuterobenzene.

Patrice Lumumba International-Friendship University, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 215-219, February, 1976. Original article submitted October 8, 1974; revision submitted September 16, 1975.

TABLE 1



Compound	X	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
II	$CONH_2$	191—193	$C_{19}H_{21}N_3O_2$	—	—	12,9	—	—	13,0	80
III	COC_6H_5	153—155	$C_{31}H_{27}NO_2$	83,3	6,2	2,8	83,5	6,0	3,1	55
IV	$CH(OH)C_6H_5$	84—86	$C_{31}H_{31}NO_2$	82,8	7,1	3,1	82,9	6,9	3,1	80
V	$CON(C_2H_5)_2$	113—115	$C_{27}H_{37}N_3O_2$	—	—	9,4	—	—	9,4	78
VI	$CH_2N(C_2H_5)_2$[a]	Oily substance	$C_{27}H_{41}N_3$	80,1	10,2	10,0	80,0	10,0	10,0	92
VII	$CONHNH_2$	212—214	$C_{19}H_{23}N_5O_2$	—	—	19,8	—	—	19,8	43
VIII	CH_2OH b	132—134	$C_{19}H_{23}NO_2$	76,7	7,7	4.5	76,7	7,8	4,7	90
IX	$CH_2OCONHC_6H_5$	76—78	$C_{33}H_{33}N_3O_4$	—	—	8,1	—	—	7,9	37
X	$CH_2OCOC_6H_5$	128—130	$C_{33}H_{31}NO_4$	75,5	5,9	2,8	77,4	6,2	2,9	60
XI	CH_2Clc	97—98,5	$C_{19}H_{21}NCl_2$	68,0	6,3	3,9	68,4	6,3	4,2	86
XII	CH_2CN	139,5—140,5	$C_{21}H_{21}N_3$	80,0	6,7	12,9	80,0	6,7	13,3	79
XIII	CH_2COOH	308—310	$C_{21}H_{23}NO_4$	—	—	3,7	—	—	3,9	64
XIV	$CH_2CON(C_2H_5)_2$	111—113	$C_{29}H_{41}N_3O_2$	74,9	8,8	9,0	75,2	8,8	9,0	69
XV	$CH_2CH_2N(C_2H_5)_2$d	Oily substance	$C_{29}H_{45}N_3$	—	—	—	—	—	—	97

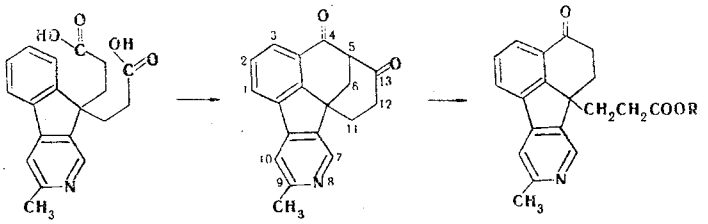
a) The trimethiodide had mp 260-263°. Found, %: N 5.4. $C_{30}H_{50}I_3N_3$. Calculated, %: N 5.0.
b) The hydrochloride had mp 222.5-225.5°. Found, %: Cl 10.5. $C_{19}H_{23}NO_3 \cdot HCl$. Calculated, %: Cl 10.3.
c) The perchlorate had mp 167-168°. Found, %: N 2.4. $C_{19}H_{21}ClN_2 \cdot HClO_4$. Calculated, %: N 2.6.
d) The trimethiodide had mp 154-156°. Found, %: C 44.8, H 6.0, N 4.7. $C_{32}H_{54}I_3N_3$. Calculated, %: C 44.6, H 6.3, N 4.8.

TABLE 2. Parameters of the PMR Spectra of Azafluoranthene XVI*

Solvent	δ, ppm (J, Hz)										
	1-H	2-H	3-H	5-H	6-H	6′-H	11-H	7-H	10-H	12-H	9-CH_3
$CDCl_3$	7,89 (q; 8,0; 1,3)	7,56 (t; 8,0)	7,99 (q; 8,0; 1,3)	3,71 (m)	2,94 (q; 13,0; 2,5)	2,36—2,56 (m)	1,60—1.90 (m)	8,58 (s)	7,53 (s)	2,50—2,80 (m)	2,63 (s)
C_6D_6	7,83 (q; 8,0; 1,3)		7,43 (q; 8,0; 1,3)	3,50 (m)	2,04 (q; 13,0; 2,5)	1,50 (sx; 13,0; 3,0; 3,5)	0,60—1,00 (m)	8,35 (s)		1,65—2,06 (m)	2,48 (s)

*Abbreviations: s is singlet, d is doublet, t is triplet, m is multiplet, q is quartet, and sx is sextet.

stretching vibrations of arylalkyl and dialkyl keto groups, are observed in the IR spectrum of this compound. The character of the splitting of the signals of the protons of the benzene ring in the PMR spectrum (Fig. 1 and Table 2) (two quartets with ortho and meta constants and a triplet with ortho constants) indicates substitution in the 3a position. Evidence for this is also provided by the diamagnetic shift of the 3-H signal ($\Delta\delta$ = 0.56 ppm) in the PMR spectrum of a C_6D_6 solution of the compound as compared with the spectrum of a $CDCl_3$ solution. A similar result was obtained for quinones [4]. The α position of the pyridine ring of I is not involved during cyclodehydration, as demonstrated by the signal at 8.58 ppm in the spectrum of cyclization product XVI. Signals of protons forming an AKX system are present in the strong-field region: a single-proton multiplet at 3.50 ppm, a doublet of doublets at 2.04 ppm (J_{AK} = 13.0, J_{AX} = 3.0 Hz), and a doublet of triplets at 1.50 ppm (J_{KA} = 13.0, J_{KX} = 3.0, and J_{KP} = 3.5 Hz). The character of the splitting of the latter signal



I XVI XVII, XVIII

XVII R = CH_3; XVIII R = H

shows that the AKX system is a part of a more complex multispin system of protons. Coupling of each of the A and K protons with the X proton is confirmed by the total double-resonance spectra (Fig. 1b). The existence of spin–spin coupling of the geminal protons follows from the INDOR spectrum obtained at the line of the 1.50-ppm signal. It may be concluded from the indicated data that XVI contains a CH_2–CH fragment, which is a structural element of the –CO–CH(CH_2)–CO– grouping. Additional splitting of the signal of one of the methylene protons attached to C_6 is due to spin–spin coupling with one of the protons attached to C_{11} (Fig. 1b), the signal of which is found at 0.60-1.00 ppm. Th indicated long-range spin–spin coupling of the protons through four σ bonds oriented in a W-shaped manner is characteristic for strained bicyclic systems [5].

Proof of the presence in XVI of two carbonyl groups is offered by the ^{13}C NMR spectrum, in which the signals at 191.77 and 201.57 ppm are due to arylalkyl keto and dialkyl keto groups, respectively [6]. According to the off-resonance data, the signal of a methylidyne carbon is observed at 63.49 ppm. The considerable paramagnetic shift of this signal ($\Delta\delta \approx$ 28 ppm) as compared with the signal of the methylidyne carbon in similar bridged compounds [7] is due to the deshielding effect of the two α-carbonyl groups.

9-Methyl-6a-(2-methoxycarbonylethyl)-4-oxo-8-aza-4,5,6,6a-tetrahydrofluoranthene (XVII) — the first representative of the previously unknown 8-azafluoranthenes — is formed when XVI is heated with methanol in the presence of sulfuric acid. The UV spectra of XVI and XVII are similar, and this indicates retention of the chromophore system. The absorption band of an arylalkylcarbonyl group (1687 cm^{-1}) is retained in the IR spectrum of ester XVII, and the intense band at 1740 cm^{-1} is related to the carbonyl group of the ester grouping. The presence in the PMR spectrum of XVII of a three-proton singlet at 3.37 ppm and the absence of the signal of a methylidyne proton indicate cleavage of the C_5–C_{13} bond to give the $-CH_2CH_2COOCH_3$ fragment. Compound XVI undergoes similar cleavage when it is heated in an alcohol solution of potassium hydroxide. In this case, 6a-(2-carboxyethyl)-9-methyl-4-oxo-8-aza-4,5,6,6a-tetrahydrofluoranthene (XVIII) was isolated. Esterification of acid XVIII gave ester XVII.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were measured with a UR-20 spectrometer. The UV spectra of ethanol solutions were recorded with a Hitachi EPS-3 recording spectrophotometer. The PMR spectra of $CDCl_3$ and C_6D_6 solutions were obtained with Varian HA-100D and T-60 spectrometers with hexamethyldisiloxane as the internal standard. The ^{13}C NMR spectra of $CDCl_3$ solutions were measured with an XL-100-15 spectrometer. The chemical shifts were measured relative to tetramethylsilane. The molecular weights were determined with an MKh-1303 mass spectrometer.

9-Methyl-4,13-dioxo-8-aza-4,5,6,6a-tetrahydro-5,6a-propanofluoranthene (XVI). A mixture of 2 g (1.5 mmole) of acid I and 60 g of PPA (20 g of 85% orthophosphoric acid and 40 g of phosphorus pentoxide) was heated at 150-160° for 2 h, after which it was poured over 200 g of ice, and the mixture was neutralized with sodium carbonate. Workup gave initially 0.63 g (40%) of XVI as light-yellow crystals with mp 202-203° (from benzene–hexane) and R_f 0.6. Found, %: C 76.5*; H 5.2; N 4.6. M 289 (mass spectrometrically). $C_{19}H_{15}NO_2$. Calculated:

*The experimentally found percentage of carbon in XVI differed considerably from the calculated value, and the deviation was reproducible in many analyses. Compound XVI apparently contains strongly bonded crystallization water, as follows from its IR spectrum (3400 cm^{-1}). A similar conclusion was drawn [8] for 2-azafluoranthene derivatives.

C 78.9; H 5.2; N 4.8; M 289. The picrate had mp 220-222° (from alcohol). Found, %: C 57.3; H 3.5; N 10.7. $C_{19}H_{15}NO_2 \cdot C_6H_3N_3O_7$. Calculated, %: C 57.9; H 3.5; N 10.8. The methiodide had mp 264-268° (from a mixture with acetone). Found, %: N 2.9. $C_{20}H_{18}INO_2$. Calculated, %: N 3.2.

Subsequent elution gave 0.21 g (13%) of yellow crystals with mp 208-211° (from benzene–hexane) and R_f 0.5. At the end of the chromatography, 0.18 g (11%) of yellowish-orange crystals with mp 233-236° (from benzene–hexane) and R_f 0.3 was isolated. The structures of these two products have not yet been established.

9-Methyl-6a-(2-methoxycarbonylethyl)-4-oxo-8-aza-4,5,6,6a-tetrahydrofluoranthene (XVII). A mixture of 0.3 g (1 mmole) of diketone XVI, 7 ml of methanol, and 0.4 ml of sulfuric acid was refluxed for 10 h, after which the methanol was removed by distillation, the residue was neutralized with sodium carbonate solution, and the reaction products were extracted with ether. The residue remaining after removal of the ether by distillation was purified with a column filled with activity-II aluminum oxide with elution by ethyl acetate–hexane (1:1) to give 0.2 g (60%) of ester XVII as yellow crystals with mp 86-88.5° (from hexane) and R_f 0.4 [activity-II Al_2O_3, ethyl acetate–hexane (3:1)]. Found, %: C 74.4; H 6.2; N 4.3; M 321 (mass spectroscopically). $C_{20}H_{19}NO_3$. Calculated, %: C 74.8; H 5.9; N 4.4; M 321.

The hydrochloride of 9-methyl-6a-(2-ethoxycarbonylethyl)-4-oxo-8-aza-4,5,6,6a-tetrahydrofluoranthene (similarly obtained from XVI and ethanol) had mp 206-208° (from acetone–alcohol). Found, %: N 3.9. $C_{22}H_{21}NO_3 \cdot HCl$. Calculated, %: N 3.6.

A mixture of 0.2 g (0.7 mmole) of diketone XVI and 10 ml of a 20% alcohol solution of potassium hydroxide was refluxed for 2 h, after which it was neutralized with 70% sulfuric acid and worked up to give 0.02 g (10%) of acid XVIII as yellowish crystals with mp 238-240°. Found, %: N 4.4. $C_{19}H_{17}NO_3$. Calculated, %: N 4.5.

An 0.15-g (0.5 mmole) sample of acid XVIII was esterified with 5 ml of methanol and 0.2 ml of concentrated sulfuric acid to give 0.04 g (25%) of ester XVII.

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