and II before the reaction; $[C_I]$ and $[C_{II}]$ are the concentrations of sulfides I and II after the reaction; $(S_I/S_{st})_0$ and $(S_{II}/S_{st})_0$ are the ratios of the areas of the chromatographic peaks of sulfide I to the standard and of sulfide II to the standard before the reaction; and (S_I/S_{st}) and (S_{II}/S_{st}) are the ratios of the areas of the chromatographic peaks of sulfide I to the standard and of sulfide II to the standard after the reaction.

Equation (2) is correct provided that the ratios $[C_I]/[S_I/S_{st})$ and $[C_{II}]/(S_{II}/S_{st})$ remain constant quantities over the range of concentrations studied. To fulfill this condition, we chose the concentrations of the reactants so that, in the GLC analyses, the peaks of the sulfides and the standard were comparable in area both before and after the reaction. To estimate the reproducibility of the determination of K_{rel}, we carried out several experiments to determine the relative activities of the same pairs of sulfides. In this way, we found that the error in the chromatographic results was no more than 2%, and in the value of K_{rel}, from 5 to 10%.

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PREPARATION OF SPIROAZIRIDINEFLUORENE, SPIROINDOXYL-FLUORENE, AND β-AMINOPROPIONIC ACID ESTER WITH A 4-AZAFLUORENE FRAGMENT

N. S. Prostakov, L. A. Gaivoronskaya, S. K. Sarkar, V. F. Zakharov, and N. M. Durbazheva

UDC 547.828'678.3'755' 466.2.07:543.42

It has been established that the reaction of 9-(p-methoxyphenylimino)fluorene with dichlorocarbene (conditions of phase-transfer catalysis) proceeds in two directions — the formation of spiroaziridinefluorene and of spiroindoxylfluorene, the structure of which has been demonstrated. Opening of the aziridine ring of spiroaziridine-fluorene has been accomplished. From the analagous azamethine, 4-aza-fluorene, an ester of N-substituted β-aminopropionic acid with a 4-azafluorene fragment was obtained by alkylation of its dianion with methyl chloroacetate.

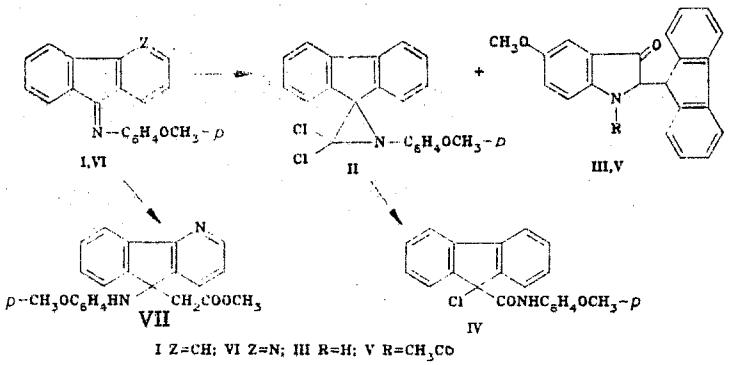
The cycloaddition of carbenes to imines is widely used as a contemporary preparative method for the synthesis of aziridines [1]. There is no published information on the preparation of spiro compounds containing aziridine fragments from a series of fluorene imines by such a method. We have carried out a study of the compounds which are formed by the reaction of 9-(p-methoxyphenylimino)fluorene (I) with dichlorocarbene under phase-transfer catalysis conditions [2] using triethylbenzylammonium chloride (TEBA) as catalyst. The reaction does not proceed in only one direction. The main product is 3',3'-dichloro-1'-(p-methoxyphenyl)spiro-[aziridine-2',9-fluorene] (II) (75% yield). In addition to this, a compound with the composition $C_{21}H_{15}NO_2$ is obtained in 10% yield; spectroscopic data indicate that this is 5'-methoxyspiro[indoxyl-2',9-fluorene] (III). The structure of compound II is confirmed by carbon-13 NMR studies carried out during the present work. On heating the spiroaziridinefluorene II with ethanol (rectified spirit), opening of the aziridine ring occurs. In this way, 9-chloro-9-(N-p-methoxyphenylcarbamoyl)fluorene (IV) is obtained in quantitative

Patrice Lumumba Peoples' University, Moscow 117293.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 895-897, July, 1986. Original article submitted February 27, 1985.

0009-3122/86/2207-0710$12.50

yield. An analogous conversion of aziridines has been described in [1].



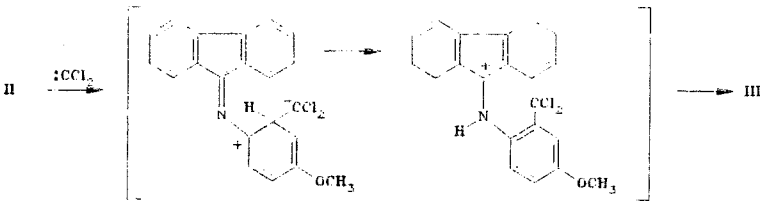
I Z=CH; VI Z=N; III R=H; V R=CH_3CO

In the IR spectrum of compound III (KBr) there is an intense band at 1720 cm^{-1} corresponding to the carbonyl group and a broad, very intense band at 3270 cm^{-1} of the NH group of the indoxyl fragment; bands at 3180 (broad) and 3425 cm^{-1} (narrow) (chloroform solution) correspond to associated and free secondary amine groups. All the signals of the carbon-13 NMR spectrum of compound III have been assigned; the signal at 64.6 ppm corresponds to the spirocarbon.

The structure of the spirocompound III was further confirmed by x-ray photoelectron spectroscopy; a signal N1s = 400.1 eV corresponds to a nitrogen atom of pyrrole type. A symmetrical signal with band halfwidth = 3.2 eV resulting from the overlapping of signals from two oxygen atoms in qualitative splitting gives two values for O is at 534.0 and 532.6 eV which are assigned respectively to the oxygens of the methoxy and carboxy groups [4].

Confirmation of the presence of a secondary NH group in the spirocompound III is provided by its conversion into 5'-methoxy-1'-acetylspiro-[indoxyl-2'9-fluorene] (V).

The formation of an indoxyl structure in the reaction under study is somewhat unexpected, there having been no analogous examples up to now. It could be conjectured that in proceeding in this direction the reaction of the imine I with dichlorocarbene takes place via an electrophilic addition of dichlorocarbene at the σ-position to the imino group of the methoxy-substituted benzene ring. Aromatization of the 1,3-dipole thus formed accompanied by migration of the proton to the nitrogen atom leads to a zwitterion which, in its turn, is cyclized and after hydrolysis of the *gem*-dihalide is converted into the spiroindoxylflorene III.



The study of the transformations of azomethines was also directed to the alkylation of 9-(p-methoxyphenylimino)-4-azafluorene (VI) with the object of preparing an ester of β-aminopropionic acid containing an azafluorene fragment.

The dianion which if formed from the azomethine VI by reaction with solidum was alkylated with methyl chloroacetate. Under appropriate reaction conditions (absence of moisture and oxygen, −50°C during the alkylation [5]), 9-(p-methoxyphenylamino)-9-(carbonylmethoxymethyl)-4-azafluorene (VII) was obtained in 22% yield.

The compounds reported in the present communication were prepared for evaluation as physiologically active substances.

EXPERIMENTAL

Proton and carbon-13 NMR spectra were run on a Bruker WP-80 instrument in $CDCl_3$ using TMS as reference. Photoelectron spectra were run on an ES-200 spectrometer from Kratos (England). A Specord UR-20 instrument was used for IR spectra with KBr, NaCl, and LiF prisms,

the samples being in the form of KBr discs. UV spectra were obtained on a Specord UV-Vis spectrophotometer in chloroform solution. Mass spectra were run on an MX-1303 instrument with direct injection of the samples into the ion source and an ionization potential of 70 eV.

3',3'-Dichloro-1'-(p-methoxyphenyl)spiro[aziridine-2',9-fluorene] (II) and 5'-Methoxyspiro[indoxyl-2',9-fluorene] (III). To a solution of 1.3 g (4.56 mmole) of the azomethine I and 0.09 g (0.4 mmole) TEBA in 15 ml chloroform, 5 ml of a 50% solution of NaOH heated to 60°C was added with vigorous stirring. This was stirred for 0.5 h at 40°C. Water at 0°C (20 ml) and chloroform (30 ml) were added and the chloroform solution dried over $MgSO_4$. The chloroform was removed under reduced pressure without heating. The residue was chromatographed on an aluminum oxide column 46 cm by 2.3 cm; a 2:1 mixture of petroleum ether and ether was used to elute 1.26 g (75%) compound II, yellow crystals, mp 114-115°C (from ether). Carbon-13 spectrum: 55.79 (OCH_3), 139.19, 122.51, 114.26, 157.99 (respectively $C_{(1')}$, $C_{(2')}$ and $C_{(6')}$, $C_{(3')}$ and $C_{(5')}$, $C_{(4')}$ of $-NC_6H_4OCH_3-p$, 147.50 (CCl_2), 74.76 (C-spiro), 125.33, 120.60, 130.47, 128.67 (doubled signals $C_{(1)}$–$C_{(4)}$ and $C_{(5)}$–$C_{(8)}$, 144.86 and 140.20 ppm (respectively doubled signals of $C_{(8a)}$ and $C_{(9a)}$, $C_{(4a)}$ and $C_{(4b)}$. UV spectra, λ_{max} (lgε): 208 (4.46), 240 (4.50), 278 (4.04) 338 nm (inflection) (2.60). Found: C 68.6, H 4.1, Cl 19.3, N 3.8%; M^+ 367. Calc. for $C_{21}H_{15}Cl_2NO$; C 68.7, H 4.1, Cl 19.1, N 3.8%; M 367. Ethanol was then used to elute 0.13 g (10%) compound III, colorless crystals, mp 230-232°C (from ethanol). Carbon-13 spectrum: 129.26, 127.56, 128.04 120.08 (respectively doubled signals of $C_{(1)}$–$C_{(4)}$ and $C_{(5)}$–$C_{(8)}$), 145.50 and 141.66 (respectively doubled signals of $C_{(8a)}$ and $C_{(9a)}$, $C_{(4a)}$ and $C_{(4b)}$), 64.16 (C-spiro), 136.68, 109.98, 155.28, 110.23, 113.63, 132.34 (respectively $C_{(3'a)}$, $C_{(4')}$–$C_{(7')}$, $C_{(7'a)}$), 176.66 ($C_{(3')}$, 55.17 ppm (C-methoxy). Proton NMR spectrum: 8.90 broad (s, 1H, N-H), 7.85-6.85 (m, H(arom.)), 6.24 (d, 1H, 4'-H), 3.60 ppm (s, 3H, OCH_3). UV spectrum, λ_{max} (lgε): 214 (4.78), 233 (4.44), 266 (4.55), 297 (3.92), 308 nm (4.00). Found: C 81.1, H 4.5, N 4.3%; M^+ 313. Calc. for $C_{21}H_{15}NO_2$: C 80.5, H 4.8, N 4.5%; M 313.

9-Chloro-9-(N-p-methoxyphenylcarbamoyl)fluorene (IV). A solution of 0.22 g (0.6 mmole) spiroaziridinefluorene II in 5 ml ethanol (rectified spirit) was heated at bp for 6 h. The residue after evaporation of the alcohol was recrystallized from 1:1 benzene–petroleum ether. Compound IV (0.17 g, 81%) was obtained as colorless crystals, mp 137-138°C. Proton NMR spectrum: 7.90 (broad, s, 1H, N-H), 7.80-7.20 (m, H(arom.)), 7.28 and 6.90 (two d, system AA'BB', 4H, p-C_6H_4), 3.75 ppm (s, 3H, OCH_3). IR spectrum: 3410 (N–H), 1683 (C=O), 1255 (C–O), 752 and 632 cm^{-1} (C–Cl). Found: N 3.8%; M^+ 349. Calc for $C_{21}H_{16}ClNO_2$: N 4.0%; M 349.

5'-Methoxy-1'-acetylspiro[indoxyl-2',9-fluorene] (V). A solution of 0.31 g (1 mmole) compound III and 5.4 g (52.5 mmole) acetic anhydride in 20 ml dry benzene was heated at bp for 2 h. After removing the solvent the residue was recrystallized from benzene yielding 0.2 g (56%) compound V, mp 211-213°C. Proton NMR spectrum: 8.25 (d, 1H, 7'-H), 7.86-6.80 (m, H(arom.)), 6.19 (d, 1H, 4'-H), 3.60 (s, 3H, OCH_3), 2.60 ppm (s, 3H, $COCH_3$). IR spectrum: 1750 (C_3'=O), 1707 ($CH_3CON<$), 1271 cm^{-1} (C–O). Found: N 3.8%; M^+ 355. Calc. for $C_{23}H_{17}NO_3$: N 4.0%; M 355.

9-(p-Methoxyphenylamino)-9-(carbonylmethoxymethyl)-4-azafluorene (VII). A solution of 2.86 g (10 mmole) azomethine VI in 75 ml THF (distilled over lithium aluminum hydride) and 0.5 g (20 mmole) finely divided sodium was heated at bp for 3 h with vigorous stirring in an atmosphere of dry, oxthen-free nitrogen. To the resulting balck-colored mixture, 3.7 g (15 mmole) methyl chloroacetate was added at –50°C and stirred for 0.5 h. Methanol (15 ml) was then added, the solvent distilled off and the residue extracted with boiling benzene (eight 10 ml portions). The solution was concentrated to 20 ml and passed through a layer of aluminum oxide (h = 5 cm, d = 3 cm). The benzene was distilled off and the residue (1.47 g) recrystallized from 100 ml ether. The yield of the aminoester VII was 0.8 g (22%); mp 136-137°C (from 1:5 benzene/hexane). Proton NMR secptrum: 8.55 (d.d, 1H, 3-H), 7.70-7.10 (m, H(arom.)), 6.40 and 6.05 (two d, system AA'BB'; 4H, p-C_6H_4), 5.70 (broad, s, 1H, N-H), 3.67 and 3.55 (s, 3H, two CH_3O), 2.92 and 2.67 (system AB, 2H, CH_2). IR spectrum: 3382 (free N-H), 1725 (C=O), 1250 cm^{-1} (C–O). Found: C 75.6, H 5.9, N 6.9%; M^+ 360. Calc for $C_{22}H_{20}N_2O_3 \cdot {}^1/_2C_6H_6$: C 75.3, H 5.8, N 7.0; M 399.

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MECHANISM OF THE FISCHER INDOLE SYNTHESIS. QUANTUM-CHEMICAL INTERPRETATION OF THE REARRANGEMENT OF SUBSTITUTED CYCLOHEXANONE ARYLHYDRAZONES TO TETRAHYDROCARBAZOLES

Yu. B. Vysotskii, N. M. Przheval'skii, B. P. Zemskii, I. I. Grandberg, and L. Yu. Kostromina

UDC 547.751:541:127

Calculations of a number of model structures within the scheme of the Fishcer indole synthesis were made on the basis of a bonding variant of perturbation theory in the self-consistent-field (SCF) MO LCAO method. A quantum-chemical interpretation of the effect of substituents on the course of the thermal process is given. The kinetics of the thermal and acid-catalyzed indolization of substituted cyclohexanone arylhydrazones to tetrahydrocarbazoles were studied by spectrophotometry. It was shown that the experimental data are in satisfactory agreement with the calculated values. It was concluded that a concerted mechanism (a [3,3]-sigmatropic shift) for the step involving the formation of a carbon–carbon bond in the Fischer reaction is preferred.

The mechanism of the Fischer indole synthesis continues to attract the interest of chemists [1-7]. To ascertain the details of this mechanism ^{15}N [8] and ^{13}C NMR [9] spectroscopy, mass spectrometry [10], and kinetic investigations [6, 11] have been used in recent years. However, some aspects of this reaction, viz., the effect of electronic factors on the rate of the process, the ratios of the resulting isomers, and the hydrazone–enehydrazine tautomerism, continue to remain unclear.

We assumed that a quantum-chemical investigation of the Fisccher reaction, in conjunction with kinetic and other experimental data, might give additional information with respect to these questions.

The calculations were made on the basis of a bonding variant of perturbation theory in the self-consistent-field (SCF) MO LCAO method (for example, see [12]). The indicated approach has been previously used to interpret the mechanisms of a number of processes [13] and to predict [14] the subsequently experimentally confirm [15] the effect of substituents on the recyclization of heterocyclic anhydro bases.

In the present study, as in [16], this approach was used to examine the step involving the formation of a C–C bond in the Fischer synthesis of indoles, which reduced to description of the interaction of the unbonded (or weakly bonded) π-electron systems of II-V (Scheme 1).

K. A. Timiryazev Moscow Agricultural Academy, Moscow 127550. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 898-907, July, 1986. Original article submitted April 29, 1985.

0009-3122/86/2207-0713$12.50