STRUCTURE AND PHOTOCHROMIC TRANSFORMATIONS OF FULGIDES OF THE INDOLE SERIES

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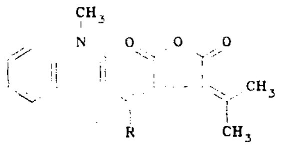
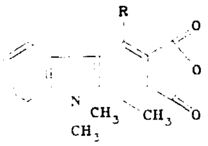
Previously undescribed fulgides of the indole series, viz., (1-methyl-3-indolylmethylene)- and (1-methyl-3-indolylethylidene) (isopropylidene)succinic anhydride, were synthesized. A Z conformation for (1-methyl-3-indolylmethylene) (isopropylidene)succinic anhydride and an E configuration for (1-methyl-3-indolylethylidene)-(isopropylidene) succinic anhydride were established by electronic and PMR spectroscopy and x-ray diffraction analysis. The photochromic properties of fulgides were observed and investigated. A scheme of photoinduced and thermal transformations of fulgides that includes a step involving Z → E isomerization in the excited state is proposed. An additional photoisomer was recorded by pulse photolysis and fluorescence.

Heterocyclic fulgides have practically valuable photochromic characteristics [1-3]. In view of this the expansion of the number of heterocyclic fulgides and the study of their photochemical properties are of undoubted interest. We have synthesized previously undescribed fulgides I and II of the indole series and studied their structure and photochromic transformations. See [4] for a preliminary communication regarding the photochromic properties of these compounds.



I Z, II Z



I E, II E

Synthesis and Structure of the Fulgides

(1-Methyl-3-indolylmethylene) (isopropylidene)succinic anhydride (fulgide I) and (1-methyl-3-indolylethylidene) (isopropylidene)succinic anhydride (fulgide II) were obtained via Scheme 1. The Stobbe condensation of 1-methyl-3-formyl(or acetyl)indole with diethyl isopropylidenesuccinate in the presence of sodium hydride was used [5]. Hydrolysis of the monoethyl esters (III, IV) of indolyl-substituted isopropylidenesuccinic acids (V, VI) with acetyl chloride in conformity with [1, 2] leads to the formation of fulgides I.

Fulgides I and II were isolated in the form of bright-yellow crystals. Characteristic bands of two carbonyl groups at 1790 and 1745 cm^{-1}, which correspond to an alkylidene-succinic anhydride [6], are present in the IR spectra of these compounds.

Fulgides I and II can exist in the form of Z or E isomers. An examination of the electronic absorption spectra and the PMR spectra makes it possible to choose between these structures. The electronic absorption spectra of fulgide I contain absorption bands at 400-417 nm, while the absorption bands of fulgide II show up at 369-395 nm (Table 1). It is

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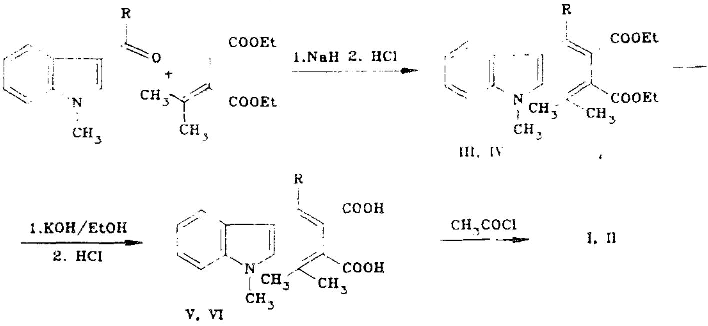
TABLE 1. Positions of the Maxima of the Absorption Bands ($S_0 \rightarrow S_1$) of Fulgides I and II and Their Colored Isomers

Solvent	λ_{max}, nm			
	I	II	IA	IIA
Hexane	400	369	530*	538
1,4-Dioxane	401	384	—	557
Toluene	408	384	—	557
2-Propanol	412	386	—	560
Ethanol	415	391	540*	566
DMSO	417	395	550*	580

*These data were obtained using pulse photolysis.

Scheme 1



I, III, V R=H; II, IV, VI R=CH_3

known that the Z isomers of fulgides absorb in the longer-wave region of the spectrum [2,7]; this makes it possible to assign the structure of a Z isomer to fulgide I and the structure of an E isomer to fulgide II. This conclusion is in good agreement with the data from the PMR spectra (Table 2). Singlet signals of $N-CH_3$ groups at 3.89 ppm and $C-CH_3$ groups at 2.81 ppm and of an isopropylidene fragment at 2.13 and 0.92 ppm are present in the spectrum of fulgide II in solution in $CDCl_3$. The signal at 0.92 ppm, as was previously substantiated in detail in [1], is related to the methyl group that is trans oriented with respect to the closer C=O group and is shifted to strong field because of the shielding effect of the indolyl fragment in the E configuration. On the other hand in the PMR spectrum of fulgide I the signals of the isopropylidene methyl groups are drawn together and are found at 2.52 and 2.37 ppm (Table 2). This is associated with the realization, in the case of fulgide I, of a Z configuration, in which the indolyl and isopropylidene residues are remote from one another.

The assignment of the configurations of the geometrical isomers (E and Z) that was made on the basis of the analysis of the spectral data was confirmed by the results of x-ray diffraction studies of fulgide II. Its molecule (Fig. 1) has a sterically strained conformation in which the 1-methylindolyl substituent is trans oriented with respect to the $C_{(1)}=O_{(1)}$ group relative to the $C_{(2)}=C_{(5)}$ bond. The $C_{(15)}$ methyl group and the benzene ring of the indole fragment are turned in the anti position with respect to one another relative to the $C_{(5)}-C_{(6)}$ bond. The resulting steric repulsion between the atoms of the indole and isopropylidene substituents gives rise to substantial distortions in the structure of the molecule. The $C_{(5)}$ and $C_{(16)}$ methylene atoms deviate to different sides of the average plane of the five-membered oxygen-containing heteroring by −0.47 Å and 0.53 Å, which leads to disruption of the planar orientation of the bonds of the sp^2-hybridized $C_{(2)}$ and $C_{(3)}$ atoms. The sums of the bond angles at these atoms are 359.1° and 358.1°. The indolylethylidene and isopropylidene fragments are twisted to the same side relative to the $C_{(2)}=C_{(5)}$ and $C_{(3)}=C_{(16)}$ double bonds by 24.3° and 24.5°. This twisting leads to lengthening of the bonds themselves to 1.367(2) Å and 1.350(2) Å. The indole fragment itself is turned about the $C_{(5)}-C_{(6)}$ bond

TABLE 2. Chemical Shifts of the Protons of the Methyl Groups of I and II

Compound	Solvent	δ. ppm			
		N—CH_3	R	=C(CH)₂	
				cis	*trans*
E-I	$CDCl_3$	3,89	—	2.42	1,58
Z-I	$CDCl_3$	3,93	—	2.52	2,37
E-I	C_6D_6	2,61	—	2.06	0,96
Z-I	C_6D_6	2,69	—	2.16	1,53
E-II	d_5-DMSO	3,90	2,78	2.06	0,83
Z-II	$CDCl_3$	3,89	2,81	2.13	0,92
E-II	C_6D_6	2,91	2,69	1.94	0,54

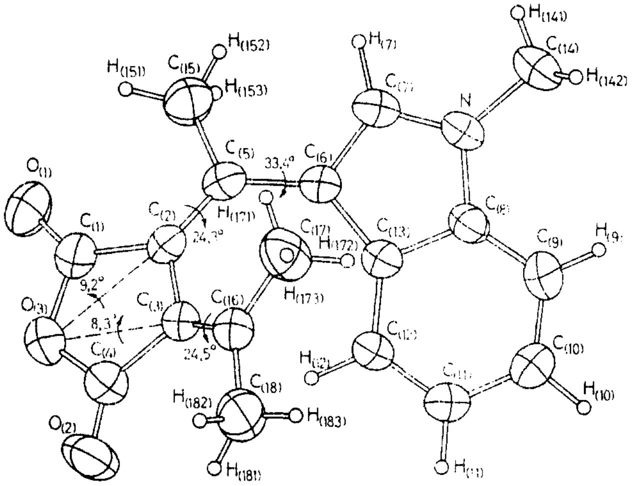


Fig. 1. Structure of the (1-methyl-3-indolylethylidene)-(isopropylidene)succinic anhydride (II) molecule.

on the same side by 33.4°. This structure leads to an increase in the intramolecular nonvalence distances between the atoms of the methylene substituents. Nevertheless, the $C_{(16)}\ldots C_{(12)}$, $C_{(17)}\ldots C_{(2)}$, $C_{(17)}\ldots C_{(5)}$,$C_{(17)}\ldots C_{(6)}$, $C_{(17)}\ldots C_{(13)}$, $H_{(171)}\ldots C_{(5)}$, $H_{(171)}\ldots C_{(6)}$ and $H_{(172)}\ldots C_{(13)}$, intramolecular contacts, which are, respectively, 3.28, 3.09, 3.35, 3.17, 3.30, 2.76, 2.72, and 2.79 Å, remain substantially shortened as compared with the sums of the van der Waals radii of the C atoms and the C and H atoms [8], which indicates that the molecule remains sterically strained.

The five-membered oxygen-containing heteroring is also nonplanar and has bends along the $O_{(3)}\ldots C_{(2)}$ and $O_{(3)}\ldots C_{(3)}$ lines of 9.2° and 8.3° to the same side, which is associated with steric repulsion between the $O_{(1)}$ and $O_{(2)}$ atoms and the $C_{(15)}$ and $C_{(18)}$ methyl groups, the distances between which remain shortened: $O_{(1)}\ldots C_{(15)}$ 2.86 Å. $O_{(2)}\ldots C_{(18)}$ 2.91 Å, $O_{(1)}\ldots H_{(151)}$ 2.28 Å, and $O_{(2)}\ldots H_{(181)}$ 2.23 Å.

One's attention is drawn to the unusual distribution of the lengths of the bonds in the five-membered heteroring of the indole fragment, in which the $C_{(6)}=C_{(7)}$ double bond [1.392(2) Å] is substantially lengthened as compared with the normal value of the length of the C=C bond [1.335(5) Å]. This redistribution of the bond lengths indicates strong conjugation of the unshared electron pair of the nitrogen atom with the $C_{(6)}=C_{(7)}$ bond.

Photoisomerization in Solutions

When solutions of fulgides I and II are irradiated, one observes changes in their electronic absorption spectra, which are shown in Figs. 2, 4, and 5. The nature of these changes can be explained within the framework of general Scheme 2.

TABLE 3. Positions of the Maxima of the Absorption, Fluorescence-Excitation, and Fluorescence Bands in Toluene of the Isomers of Fulgides I and II

Compound	λ_{max}, nm		
	absorption	Fluorescence	
		excitation	emission
E-I	—	385	440
Z-I	408	410	490
IX	460*	460	515
E-II	384	385	440
Z-II	—	415	490
IIX	460*	460	520
IIA	557	560	700

*These data were obtained using photolysis.

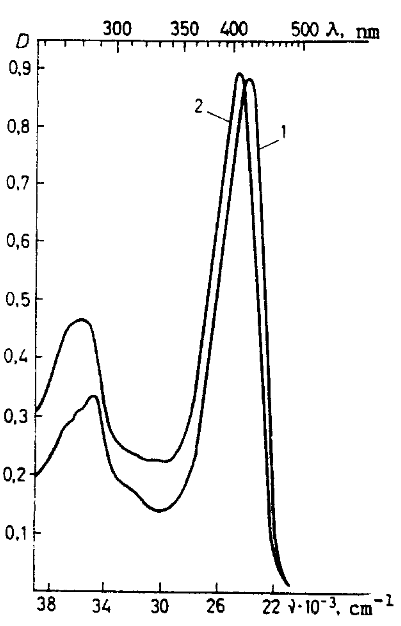


Fig. 2

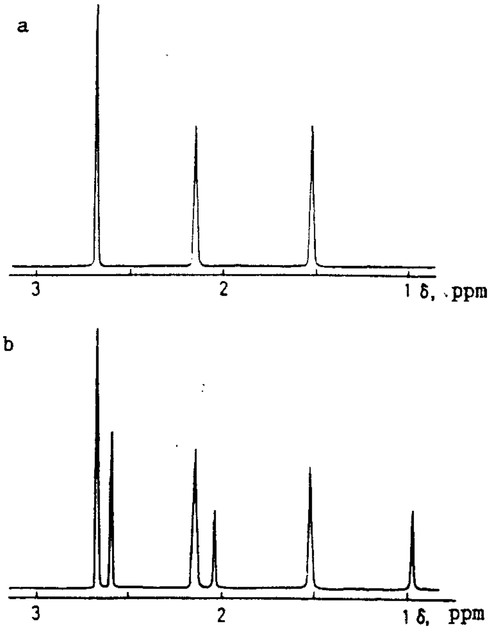
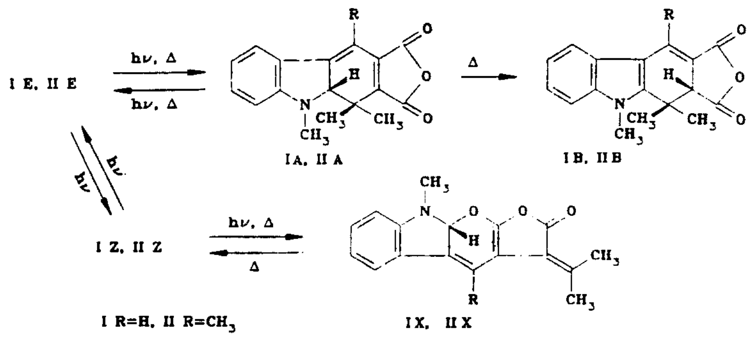


Fig. 3

Fig. 2. Electronic absorption spectra of fulgide I in ethanol ($c = 3.5 \cdot 10^{-5}$ mole/liter) before (1) and after (2) irradiation. The irradiation time was 60 sec at λ_{irr} 405 nm.

Fig. 3. PMR spectra of fulgide I in C_6D_6: a) before irradiation; b) after irradiation at λ_{irr} 405 nm.

Scheme 2



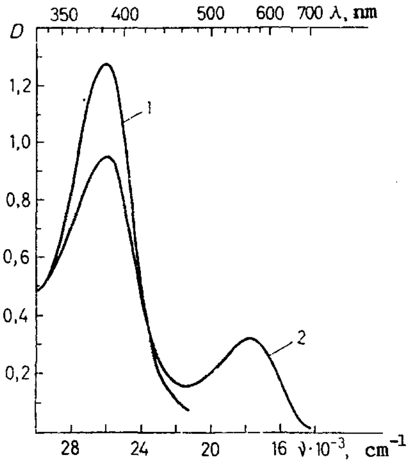


Fig. 4

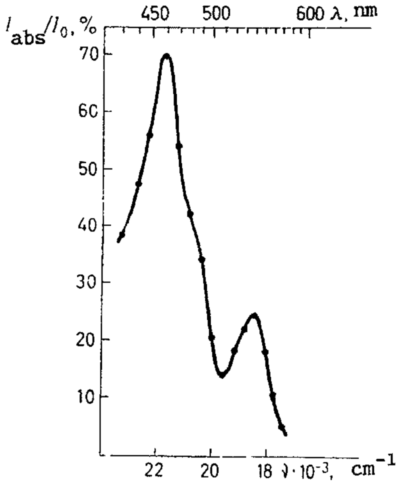


Fig. 5

Fig. 4. Electronic absorption spectra of fulgide II in toluene ($c = 4.2 \cdot 10^{-5}$ mole/liter) before (1) and after (2) irradiation. The irradiation time was 77 min at λ_{irr} 405 nm.

Fig. 5. Photoinduced absorption spectrum of fulgide I in ethanol ($c = 10^{-5}$ mole/liter) recorded 10^{-3} sec after the pulse of a photolytic lamp.

To make a detailed investigation of the mechanism of the phototransformations we studied the spectral properties of I and II under considerations of steady-state and pulse excitation in solvents with different polarities. A bathochromic shift of the maximum of the long-wave absorption of fulgides I and II is observed in the electronic absorption spectra with an increase in the polarity of the solvents (Table 1); in conformity with the data in [10], this constitutes evidence for the $\pi \rightarrow \pi^*$ nature of this electron transition.

As demonstrated above, fulgide I exists in the form of the Z isomer in unirradiated solutions, while fulgide II exists in the form of the E isomer. A shift in the absorption maximum from 412 to 405 nm occurs when an ethanol solution of fulgide I is irradiated (Fig. 2); this constitutes evidence for the development, upon irradiation, of a new isomeric structure of I (E-I), i.e., for Z → E isomerization (Scheme 2) [2, 7]. Signals of protons of methyl groups appear in the PMR spectrum of I under the same irradiation conditions in the strong-field region of the spectrum with respect to the signals corresponding to these protons prior to irradiation (Fig. 3, Table 2). A long-wave shift of the maximum of the absorption band of the starting form occurs upon irradiation of solution of II, which has an E configuration. These data constitute evidence for E → Z photoisomerization.

As a consequence of the substantial overlapping of the absorption bands of the Z and E isomers distinct separation of the bands can be carried out only by using the fluorescence and fluorescence-excitation spectra that are characteristic for these isomers (Table 3). The position of the maximum of the absorption band recorded as a result of the establishment of the photosteady state depends on the wavelength of irradiation, and the band recorded thus is the superimposition of the individual absorption bands of the Z and E isomers. Discontinuance of the irradiation and a subsequent change in the temperature of the solution (173-363°K) do not lead to modification of the absorption spectrum corresponding to this photosteady state. Thus $Z \rightleftarrows E$ isomerization occurs only in the excited state.

The development of cyclic photoisomer A in solutions of fulgides I and II is recorded from the development in the electronic absorption spectra of a band at 530-580 nm (Fig. 4, Table 1). This absorption is characteristic for the products of cyclization of fulgides [2]. Since the formation of the A isomer is possible only from the E-isomeric forms of I and II, this occurs in one step for II (E-II → IIA), whereas it occurs through an intermediate step involving Z → E isomerization (Z-1 → E-1 → IA) for I. The stability of structure A in the ground state differs for I and II, increasing sharply when $R = CH_3$ (II) and decreasing in both cases with an increase in the polarity of the solvent. Thus, whereas for fulgide I the short-lived A form with lifetime τ_A = 250-750 msec (depending on the polarity of the

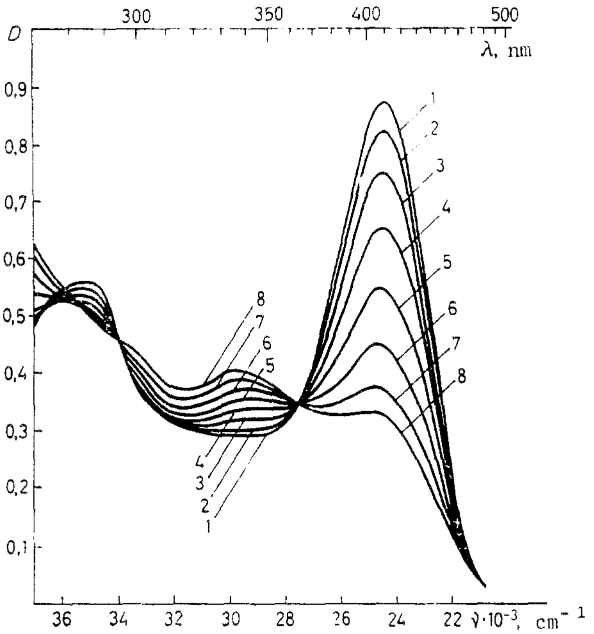


Fig. 6. Electronic absorption spectra of fulgide I in DMSO ($c = 3\cdot10^{-5}$ mole/liter) in the case of raising the temperature at a rate of 1°C/min from 293°K to 363°K: 1) 293°K; 2) 303°K; 3) 313°K; 4) 323°K; 5) 333°K; 6) 343°K; 7) 353°K; 8) 363°K.

solvent) is recorded only by pulse photolysis, for fulgide II the reverse dark reaction A → E takes place slowly and only in polar solvents (when T = 293°K, $\tau_A = 1.4\cdot10^3$ sec in DMSO, while $\tau_A = 6.6\cdot10^4$ sec in acetonitrile; the reaction does not take place in hexane, 1,4-dioxane, and toluene), and fluorescing photoproduct A is recorded not only in the case of pulse photolysis but also by steady-state absorption and fluorescence spectroscopy (Tables 1 and 3). A reverse photoreaction also takes place extremely efficiently in the case of excitation of reaction product A.

Attention should be directed to the fact that in [1, 11], which were accomplished using only steady-state methods of investigation, it is concluded that the photocyclization of molecules of fulgides obtained on the basis of aromatic or heterocyclic aldehydes, i.e., when R = H, is impossible, in contrast to fulgides of the II type (R = Alk, Ar), which contain quite bulky substituents. This conclusion is linked with the acoplanarity of the structure caused by steric interaction of the bulky R substituents. In fact, it follows from the x-ray diffraction data that II with R = CH_3 has an essentially acoplanar structure (Fig. 1). However, the results of our investigation using pulse photolysis provide evidence that photocyclization is realized in both types of molecules and that the impossibility of observing cyclic form A when R = H in steady-state methods of investigation is associated with the low stability of the latter.

In addition to isomer A, yet another short-lived form, viz., X, with an absorption maximum at 460 nm, the stability of which also decreases with an increase in the polarity of the solvent ($\tau_X \approx 250$-750 msec), is recorded by pulse photolysis (Fig. 5). In unirradiated solutions of fulgide I this form is also detected from the steady-state fluorescence spectra (Table 3). In the case of fulgide II prior photoactivation, which leads to the development of the Z isomers (E → Z isomerization), is necessary for the reliable recording of the weak signal of the X form. Since the structure of the Z isomer creates favorable steric conditions for the formation of cyclic form X, it may be assumed that precisely this structure is formed from both the ground and excited state of the Z isomer; in the latter case the equilibrium is shifted substantially to favor X.

Heating an unirradiated solution of fulgide I in DMSO from 293°K to 363°K does not lead to substantial changes in the absorption spectrum. At the same time, heating under similar conditions after prior irradiation ($\lambda_{irr} = 436$ nm), when the E-isomeric forms of fulgide I develop in solution, leads to irreversible spectral changes. As a result of raising the temperature, in addition to a decrease in the intensity of the absorption band of fulgides, one observes the development of absorption with a maximum at 336 nm (Fig. 6). According to [12], this constitutes evidence for the formation of form B as a result of the thermally permitted 1,5-sigmatropic shift of a hydrogen atom. The formation of structure B is possible only through cyclic intermediate A. The necessity for prior photoactivation, which leads to the development of ready-for-cyclization E-isomeric forms I, therefore confirms the assumption presented above.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were obtained with a UR-20 spectrometer. The electronic absorption spectra were recorded with a Specord UV-vis spectrophotometer and a Specord M-40 spectrophotometer with a device for smooth changing of the temperature of the samples. The PMR spectra of 10-15% solutions of the compounds were recorded with a Varian XL-100/15 radiospectrometer (100 Mhz) with hexamethyl disiloxane (HMDS) as the internal standard. The fluorescence and fluorescence-excitation spectra were recorded with a Fotolyum multislit apparatus produced by the Central Design Bureau of the Academy of Medical Sciences of the USSR. The method of homodyne detection, which makes it possible to increase the sensitivity of the apparatus by a factor of 10^2-10^4, was used to record the extremely weak and weak luminescence. The pulse-photolysis spectra were obtained with the lamp flash-photolysis apparatus described in [13]. The irradiating unit at the base of a DRSh-250 lamp with a set of light filters for isolation of the lines of the mercury spectrum was used to carry out the photochemical investigations.

Compound II crystallized in the form of yellow crystals of parallelepiped form with monoclinic syngony. The principal crystallographic data are as follows: $C_{18}H_{17}NO_3$, a = 20.253(3), b = 10.304(7), c = 7.132(3) Å, 89.37(3)°, V = 1488(2) Å^3, M = 295.30, d_{calc} = 1.259(3) g/cm^3, Z = 4, space group $P2_1/a$. The intensities of 1714 independent nonzero reflections with $I \geq 2\sigma(I)$ in the region $0.049 \leq \sin\theta/\lambda \leq 0.550$ were measured with a DAR-UM automatic diffractometer in Cu K_α emission with a crystal fragment with dimensions of 0.50 by 0.75 by 0.45 mm^3. The structure was decoded by the direct method by means of a complex of Rentgen-75 programs [14] and was refined by the total matrix method of least squares within the anisotropic approximation (the nonhydrogen atoms). The hydrogen atoms were localized objectively in differential Fourier synthesis, and only the position parameters were refined for them. The final value of the R factor was 0.051. The coordinates of the atoms are presented in Table 4.

Diethyl isopropylidenesuccinate was obtained in analogy to the method in [15] and had bp 100-102°C; 1-methyl-3-formylindole and 1-methyl-3-acetylindole were synthesized in accordance with [16]. The results of elementary analysis for C, H, and N of I-VI were in agreement with the calculated values.

Monoethyl (1-Methyl-3-indolylmethylene)(isopropylidene)succinate (III, $C_{19}H_{21}NO_4$). A mixture of 15.9 g (0.1 mole) of 1-methyl-3-formylindole and 21.4 g (0.1 mole) of diethyl isopropylidenesuccinate in 50 ml of toluene was added dropwise to a stirred susension of 6 g (0.2 mole, 85% dispersion in paraffin) of sodium hydride in 80 ml of toluene in the presence of several drops of absolute ethanol as the initiator, after which it was stirred at room temperature for 3 h (until hydrogen evolution had ceased). It was then poured over crushed ice, and the aqueous layer was separated and acidified with 5 M HCl. The resulting resinous product solidified. It was purified by repeated reprecipitation to give 22 g (68%) of a pale yellow powder with mp 170-172°C (from diethyl ether—pentane).

(1-Methyl-3-indolylmethylene)(isopropylidene)succinic Acid (V, $C_{17}H_{17}NO_4$. A 2-g (6 mmole) sample of monoethyl ester III was hydrolyzed with a solution of 1.2 g (20 mmole) of KOH in a mixture of 1.5 ml of water and 3 ml of alcohol by refluxing for 4 h. The solvent was then removed by distillation with a rotary evaporator, the dry residue of the dipotassium salt of acid V was dissolved in the minimum amount of water, and the solution was acidified with cooling to pH 1. The precipitated acid V was washed successively on the filter with a small amount of ethanol and ether to give 1.7 g (94%) of a pale-yellow powder with mp 245°C.

(1-Methyl-3-indolylmethylene)(isopropylidene)succinic Anhydride (Fulgide I, $C_{17}H_{15}NO_3$). This compound was obtained by refluxing 4.5 g (15 mmole) of acid V in 115 ml of freshly distilled acetyl chloride for 2 h. Workup gave 4.05 g (96%) of bright-yellow crystals with mp 253-255°C (from o-dichlorobenzene). IR spectrum: 1790, 1745 cm^{-1}. PMR spectrum ($CDCl_3$): 2.37 (s, CH_3), 2.52 (s, CH_3), 3.93 (s, NCH_3), 7.21-7.86 (5H, m), 9.06 ppm (s, CH).

TABLE 4. Coordinates of the Nonhydrogen Atoms ($\cdot 10^4$) and Hydrogen Atoms ($\cdot 10^3$) in the Fulgide II Molecule

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
$O_{(1)}$	580(1)	3235(1)	3922(2)	$C_{(16)}$	761(1)	7349(2)	898(3)
$O_{(2)}$	−633(1)	6374(2)	1406(3)	$C_{(17)}$	1468(1)	7529(2)	438(3)
$O_{(3)}$	−127(1)	4669(1)	2695(2)	$C_{(18)}$	293(1)	8271(2)	−48(3)
N	2689(1)	8027(1)	5439(2)	$H_{(7)}$	287(1)	611(2)	482(3)
$C_{(1)}$	507(1)	4306(2)	3306(3)	$H_{(9)}$	241(1)	1055(2)	644(3)
$C_{(2)}$	938(1)	5435(1)	3134(3)	$H_{(10)}$	135(1)	1155(2)	645(3)
$C_{(3)}$	557(1)	6394(1)	2048(3)	$H_{(11)}$	45(1)	1027(2)	572(3)
$C_{(4)}$	−126(1)	5913(2)	2000(3)	$H_{(12)}$	56(1)	804(2)	492(3)
$C_{(5)}$	1512(1)	5527(2)	4132(3)	$H_{(141)}$	347(1)	917(2)	527(3)
$C_{(6)}$	1843(1)	6723(2)	4598(3)	$H_{(142)}$	362(1)	780(2)	589(3)
$C_{(7)}$	2519(1)	6818(2)	4918(3)	$H_{(143)}$	336(1)	876(2)	742(3)
$C_{(8)}$	2123(1)	8786(2)	5531(3)	$H_{(151)}$	168(1)	353(2)	441(3)
$C_{(9)}$	2055(1)	10073(2)	6072(3)	$H_{(152)}$	228(1)	440(2)	466(3)
$C_{(10)}$	1431(1)	10611(2)	6093(3)	$H_{(153)}$	193(1)	439(2)	603(3)
$C_{(11)}$	890(1)	9859(2)	5619(3)	$H_{(171)}$	174(1)	680(2)	80(3)
$C_{(12)}$	951(1)	8577(2)	5100(3)	$H_{(172)}$	164(1)	827(2)	111(3)
$C_{(13)}$	1586(1)	8013(2)	5005(2)	$H_{(173)}$	158(1)	778(2)	−78(3)
$C_{(14)}$	3350(1)	8460(2)	5937(3)	$H_{(181)}$	−17(1)	823(2)	51(3)
$C_{(15)}$	1828(1)	4313(2)	4930(4)	$H_{(182)}$	16(1)	800(2)	−125(3)
				$H_{(183)}$	52(1)	902(2)	−27(3)

Monoethyl (1-Methyl-3-indolylethylidene)(isopropylidene) succinate (IV, $C_{20}H_{23}NO_4$). This compound was synthesized via the method presented above by condensation of 17.3 g (0.1 mole) of 1-methyl-3-acetylindole and 21.4 g (0.1 mole) of diethyl isopropylidenesuccinate in 25 ml of toluene in the presence of a suspension of 6 g (0.2 mole, 85% dispersion in paraffin) of sodium hydride in 300 ml of toluene and several drops of absolute ethanol. The caramel-like dark-brown product was isolated. Extraction of the aqueous solution with diethyl ether or chloroform gave an additional 1.5 g of crude product. Final workup gave 24.89 g (73%) of a pale-yellow powder with mp 157-158°C (from benzene—hexane).

1-Methyl-3-indolylethylidene(isopropylidene)succinic Acid (VI, $C_{18}H_{19}NO_4$). A 6.5-g (0.02 mole) sample of ester IV was hydrolyzed with a solution of 3.92 g (0.07 mole) of KOH in a mixture of 4.75 ml of water and 9.5 ml of ethanol by refluxing. Workup gave 4.8 g (80%) of a pale-yellow powder with mp 213-214°C (from chloroform—hexane).

1-Methyl-3-indolylethylidene(isopropylidene)succinic Anhydride (Fulgide II, $C_{18}H_{17}NO_3$). This compound was obtained by refluxing 4.3 g (0.014 mole) of acid VI in 115 ml of freshly distilled acetyl chloride for 2 h. The excess acetyl chloride was removed with a rotary evaporator, and the resinous residue was solidified by the addition of a small amount of hexane. Workup gave 3.67 g (90%) of bright-yellow crystals with mp 140-142°C (from CCl_4). IR spectrum: 1785, 1745 cm^{-1}. PMR spectrum ($CDCl_3$): 0.92 (s, CH_3), 2.13 (s, CH_3), 2.81 (s, CH_3), 3.89 (s, NCH_3), 7.02-7.62 ppm (m, 5H).

LITERATURE CITED

1. H. G. Heller and S. N. Oliver, J. Chem. Soc., Perkin 1, No. 2, 197 (1981).
2. A. P. Glazo, S. A. Harris, H. G. Heller, W. Johncock, S. N. Oliver, P. J. Strydom, and J. Whittall, J. Chem. Soc., Perkin 1, No. 5, 957 (1985).
3. British Patents Nos. 1464603, 1600615, and 2104539; Ref. Zh. Khim., 18N275P (1977), 18N230P (1981), and 1N268P (1984).
4. V. I. Minkin, E. A. Medyantseva, O. T. Lyashik, A. V. Metelitsa, I. M. Andreeva, M. I. Knyazhanskii, and N. V. Volbushko, Khim. Geterotsikl. Soedin., No. 11, 1569 (1986).
5. U. S. Johnson and G. H. Dob, Organic Reactions [Russian translation], Vol. 6, Inostr. Lit., Moscow (1953), p. 7.
6. K. Nakanishi, Infrared Spectra and the Structures of Organic Compounds [Russian translation], Mir, Moscow (1965), p. 51.
7. R. Paetzold and H.-D. Ilge, J. Signalaufz., 3, 93 (1975).
8. Yu. V. Zefirov and P. M. Zorkii, Zh. Strukt. Khim., 17, 994 (1976).
9. L. E. Sutton, Tables of Interatomic Distances, Chem. Soc. Spec. Publ., London (1965), No. 18.
10. C. Lenoble and R. S. Becker, J. Phys. Chem., 90, 2651 (1986).
11. P. J. Darcy, H. G. Heller, S. Patharakorn, R. D. Piggot, and J. Whittall, J. Chem. Soc., Perkin 1, No. 2, 315 (1986).

12. H. G. Heller and M. Szewczyk, J. Chem. Soc., Perkin 1, No. 8, 1487 (1974).
13. I. M. Andreeva, E. M. Bondarenko, N. V. Volbushko, M. I. Knyazhanskii, E. A. Medyantseva, A. V. Metelitsa, V. I. Minkin, and B. Ya. Simkin, Khim. Geterotsikl. Soedin., No. 8, 1035 (1980).
14. V. I. Andrianov, Z. Sh. Safina, and B. A. Tarnopol'skii, "Rentgen-75": An Automated System of Programs for Decoding the Structures of Crystals [in Russian], Izd. Inst. Khim. Fiz. Akad. Nauk SSSR, Chernogolovka (1975), p. 82.
15. C. G. Overberger and C. W. Roberts, J. Am. Chem. Soc., 71, 3618 (1949).
16. G. I. Zhungietu, V. A. Budylin, and A. N. Kost, The Preparative Chemistry of Indole [in Russian], Shtiintsa, Kishinev (1975), p. 186.

SYNTHESIS OF 1-ARYL-5-CHLOROPYRAZOLES

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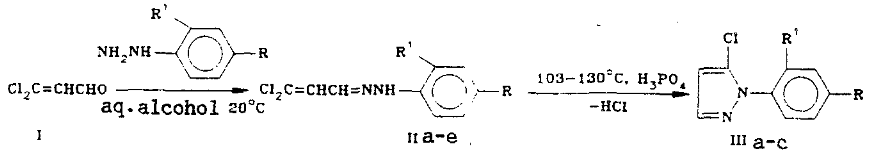
A method for obtaining 1-aryl-5-chloropyrazoles with vacant 3 and 4 positions by cyclization of 3,3-dichloro-2-propenal arylhydrazones is proposed.

1-Arylpyrazole derivatives are widely used as biologically active substances [1-3]. 1-Aryl-5-chloropyrazoles, the chlorine atom in which is capable of undergoing nucleophilic substitution [2, 4], while the vacant 4 position ensures the case of electrophilic substitution [3], are interesting intermediates for obtaining them.

1-Aryl-5-chloropyrazoles are usually obtained from other pyrazole derivatives. Thus 1-phenyl-5-chloropyrazole was obtained by decarboxylation of the corresponding 4-carboxylic acid or by treatment of 1-phenyl-5-pyrazolone with phosphorus oxychloride [5]. In [2, 4] 1-aryl-5-chloropyrazoles were obtained by nonaqueous diazotization of 5-amino-1-arylpyrazoles by means of butyl nitrite or nitrosyl chloride.

It seemed expedient to us to investigate the possibility of the synthesis of 1-aryl-5-chloropyrazoles with vacant 3 and 4 positions by cyclization of arylhydrazones of the accessible 3,3-dichloro-2-propenal (I) via the scheme



II III a R=H, b R=Me, c, d R=NO_2; a–c R'=H, d R'=NO_2, e R'=COOH

This sort of reaction has been realized only in the cyclization of 2,3,3-trichloro-2-propenal phenylhydrazone, as a result of which 1-phenyl-4,5-dichloropyrazole was obtained in 4.2% yield [6].

Aldehyde I was obtained by the method in [7] on the basis of the free-radical addition of CCl_4 to vinyl butyl ether. Hydrazones II (Table 1) were obtained in > 80% yields (the products darken under the influence of light and on contact with air oxygen).

The cyclization of hydrazones II to 1-aryl-5-chloropyrazoles (Table 1) was carried out in 85% phosphoric acid at 103-130°C, and the products were obtained in 22-39% yields. Xylene, DMSO, DMF, sulfolane, ethanol, aqueous ethanol (in pure form or with added acidic or basic catalysts such as potassium carbonate, sodium hydrocarbonate, and p-toluenesulfonic acid), acetic acid, a mixture of acetic anhydride with acetic acid, and 30% aqueous methane-

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