in Table 3 provide evidence that varying the heterene fragment has the greatest effect on the magnitude of the barrier of activation of the thermal reactions of spiropyrans.

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FORMATION OF 5-OXOINDENO[1,2-b]PYRAN DERIVATIVES IN CYCLIZATION OF 1,5-DIKETONES OF THE INDIAN-1,3-DIONE SERIES

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Indeno[1,2-b]pyrans, including 2-methylene and 2-acetoxy derivatives of 3-ethoxycarbonyl-4-phenyl-5-oxo-3,4-dihydroindeno[1,2-b]pyran, are formed in the cyclization of 4-(indan-1',3'-dion-2'-yl)-4-phenyl-2-butanone and its 3-ethoxycarbonyl derivative in acetic anhydride in the presence of sulfuric acid.

One method for the synthesis of pyrans is ring closing of pentane-1,5-dione derivatives with splitting out of water. The use of cycloaliphatic 1,5-diketones instead of aliphatic 1,5-diketones leads to condensed pyrans, including indenopyrans [1].

In the present research we investigated reactions involving the cyclization of 1,5-diketones of the indan-1,3-dione series, i.e., indan-1,3-dione derivatives that contain a CO group in the composition of the substituent attached to the $C_{(2)}$ atom, particularly the cyclization of 4-(indan-1',3'-dion-2'-yl)-4-phenyl-2-butanone (Ia) and its 3-ethoxycarbonyl analog Ib in an acidic medium.

In solution in acetic anhydride in the presence of catalytic amounts of sulfuric acid the above-mentioned 1,5-diketones readily undergo ring closing to give a pyran ring and form 5-oxoindeno[1,2-b]pyran derivatives. In the absence of an electron-acceptor substituent attached to the $C_{(3)}$ atom in the molecule of the starting compound, i.e., in the cyclization of 4-(indan-1',3'-dion-2'-yl)-4-phenyl-2-butanone (Ia), the only reaction product is 2-methyl-4-phenyl-5-oxo-4H-indeno[1,2-b]pyran (IIa).

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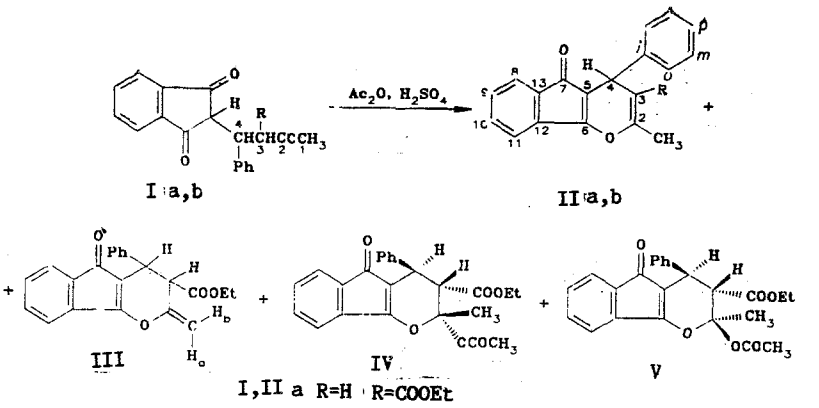
The presence of an electron-acceptor substituent attached to the $C_{(3)}$ atom of the starting indandionylbutanone leads to the formation of a mixture of dihydroindenopyrans. Thus 2-methylene derivative III and isomeric 2-acetoxyindenopyrans IV and V are formed in addition to 2-methyl-3-ethoxycarbonyl-4-phenyl-5-oxo-4H-indeno[1,2-b]pyran (IIb) in the cyclization of ethyl α-acetyl-β-(indan-1,3-dion-2-yl)-β-phenylpropionate (Ib).

It was established experimentally that under the reaction conditions 2-acetoxydihydroindenopyrans IV and V are not capable of splitting out acetic acid. Moreover, neither isomerization of 2-methylene derivative III to 4H-indenopyran IIb nor addition of acetic acid to pyrans IIb and III occurs under these conditions. This constitutes evidence that all of the compounds IIb and III-V obtained are the final products of the reaction.



The first act in the formation of a pyran ring from 1,5-diketones in an acidic medium is protonation of the most basic CO group with subsequent intramolecular reaction of the carbonium ion of the protonated group with the oxygen atom of the other carbonyl function. Since data on the basicities of the CO groups of diketones Ia,b are not available, we feel that it is possible to be guided by the dissociation constants of the conjugate acids of similarly constructed ketones to determine the primary reaction center. The basicities of the CO groups of the indan-1,3-dione ring of Ia,b can be compared with the basicities of these groups in 2-monosubstituted indan-1,3-diones, which have pK_a −5.5 [2]. If the basicity of the CO group of the side chain of Ib is set equal to the basicity of acetoacetic ester, which has pK_a −4.0 [3, 4], and the basicity of the corresponding CO group of Ia is set equal to the basicity of acetone, for which pK_a −7.1 [5], it might be assumed that the intramolecular cyclization of Ia commences with protonation of the CO group of the indan ring and that the cyclization of Ib commences with protonation of the exocyclic carbonyl group. This assumption makes it possible to explain the substantial difference in the compositions of the products of cyclization of butanones Ia,b; however, according to the data in [2-5], the pK_a values were determined in media with different acidities and solvating capacities, and one must therefore have a cautious attitude toward their comparison.

Protonated carbonyl groups containing a hydrogen atom attached to the α-C atom are capable of enolization. The enol is always more basic than the starting ketone and, consequently, is converted quantitatively to an enolium cation in an acidic medium [4, 5]. The presence of the corresponding enolium cations in the reaction medium in the cyclization of I should also have led to the formation of products of substitution of $C_{(3)}$ [or $C_{(2')}$, respectively]. However, products with this structure were not detected in the reaction mixture. Consequently, only monoprotonation of the carbonyl groups occurs under the reaction conditions, and this makes it possible to conclude that the cyclization of Ib should be accomplished without a change in the configuration of the $C_{(3)}$ atom. The experimental observations also confirm this conclusion. Thus the starting triketone was isolated almost quantitatively after heating (100°C for 30 min) indandionylbutanone Ib in solution in acetic acid in the presence of catalytic amounts of concentrated sulfuric acid, as well as after refluxing this compound in an ethanol solution of hydrochloric acid (HCl, 0.4 M; 2 h). A product with a changed configuration of the $C_{(3)}$ atom was not detected under these conditions.

The structures of the compounds obtained were confirmed by a combination of spectral methods of investigation. The ^{13}C NMR spectra are presented in Table 1, and the PMR spectra and data from the IR and mass spectra are given in the experimental section.

TABLE 1. Chemical Shifts (ppm) in the ^{13}C NMR Spectra of Indeno[1,2-b]pyrans in $CDCl_3$

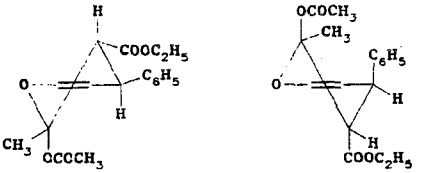
Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	$C_{(11)}$	$C_{(12)}$	$C_{(13)}$	2-CH_3	$C_{(Ph)}$				$COOC_2H_5$			$OCOCH_3$	
														C_i	C_o	C_m	C_p	CO	CH_2	CH_3	CO	CH_3
IIb	158,95	112,19	36,61	110,47	167,07	192,39	122,42	130,68	132,92	118,69	132,27	137,10	19,29	143,77	128,79	128,92	127,46	166,90	61,11	14,35	—	—
III	151,29	51,30	37,60	108,96	169,99	191,61	122,07	130,71	132,59	118,70	133,37	137,20	101,62 (=CH_2)	141.49	127,85	129,09	127,72	171,68	62,15	14,36	—	—
V	105,45	51,63	37,21	107,85	170,12	192,19	121,94	130,71	132,66	118,83	133,37	137,72	22,87	140,06	128,37	128,89	127,33	172,13	61,69	14,36	168,69	21,70
IV	102,79	58,38	37,15	110,58	169,21	191,35	121,94	130,58	132,72	118,63	133,05	137,40	23,84	139,15	128,63	128,89	127,72	170,77	61,50	14,30	168,30	22,15

The spatial orientations of the substituents of the isomeric 2-acetoxyindenopyrans IV and V were established on the basis of analysis of the ^1H and ^{13}C NMR spectra taking into account the ^1H-^1H and ^1H-^{13}C spin-spin coupling constants (SSCC).

The large $^3J_{H-H}$ value for isomer IV (11.5 Hz) indicates a trans orientation of the hydrogen atoms attached to the $C_{(3)}$ and $C_{(4)}$ atoms and, consequently, an equatorial orientation of the 4-C_6H_5 and 2-COOEt substituents. The low $^3J_{C-H}$ value (≤0.7 Hz) indicates a mutual cis orientation of the 3-H proton and the 2-methyl group; this is due to the equatorial orientation of the latter.

The ^1H-^1H and ^1H-^{13}C SSCC are small in the case of isomer V ($^3J_{H-H}$ = 4.2 Hz, $^3J_{C-H}$ ≤ 0.7 Hz); this constitutes evidence for a mutual cis orientation of the protons attached to the $C_{(3)}$ and $C_{(4)}$ atoms and a cis orientation of the 3-H proton relative to the 2-CH_3 group. This situation is possible both in the case of an axial orientation of the 4-phenyl substituent and the 3-ester group and in the case of their ae orientation (and ea orientation, respectively). An axial-equatorial orientation of these substituents is impossible, since this requires a change in the configuration of the $C_{(3)}$ or $C_{(4)}$ atom in the starting substrate, which was not observed under the reaction conditions. A significant (0.54 ppm) strong-field shift of the signal of the CH_3 protons of the 2-$OCOCH_3$ group as compared with the corresponding resonance signal of isomer IV is observed in the PMR spectrum of V. This shift is evidently caused by significant spatial 1,3-drawing together of the 2-acetoxy group and the 4-C_6H_5 group and confirms their axial orientation.

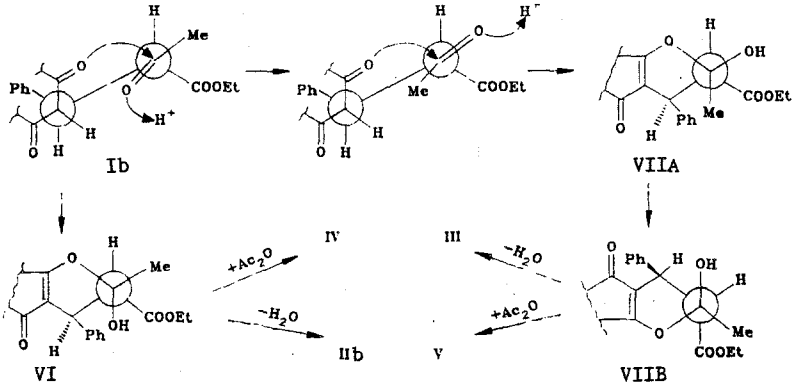
Thus the primary conformation of the pyran ring of IV and V can be represented in the form



IV V

The establishment of the conformations of the substances obtained gives an idea regarding the course of the reaction.

According to the NMR spectral data, starting indandionylbutanone Ib exists only in one diastereomeric form in which the hydrogen atoms attached to the $C_{(3)}$ and $C_{(4)}$ atoms exist in a trans orientation ($^3J_{34}$ = 11.5 Hz) and the proton attached to the $C_{(2)}$ atom of the indan ring exists in a cis orientation relative to the proton attached to the $C_{(4)}$ atom of the aliphatic chain ($^3J_{2'4}$ = 4.5 Hz). A conformation with a C–C or C–H bond eclipsed by the carbonyl oxygen atom is characteristic for the carbonyl group [6]. The exocyclic carbonyl group of substrate Ib exists in an eclipsed conformation relative to the $C_{(3)}$–$C_{(4)}$ bond, as evidenced by the small $^3J_{C-H}$ value (1.5 Hz) between the carbon atoms of the CH_3 group and the proton attached to the $C_{(3)}$ atom. Approximately the same SSCC could be observed in the case of eclipsing of the $C_{(3)}$–COOEt bond by the carbonyl oxygen atom; nevertheless, this conformation is unlikely because of repulsion of the electronegative centers – the oxygen atoms.



The approach of a nucleophile, particularly the carbonyl oxygen atom of the indan ring, to the 2-carbonyl carbon atom from the side of the 3-H atom turns out to be sterically con-

venient in the case of this orientation of the substituents in the Ib molecule. This interaction of the reaction centers leads to the formation of intermediate 2-hydroxyindenopyran IV, which has an axially oriented OH group and retains the trans orientation of the protons attached to the $C_{(3)}$ and $C_{(4)}$ atoms and, consequently, the equatorial orientation of the C_6H_5 and COOEt substituents. The proton attached to the $C_{(3)}$ atom and the 2-OH group of intermediate VI exist in a trans orientation, which favors splitting out of these substituents and the formation of a double bond between the $C_{(3)}$ and $C_{(2)}$ atoms of the pyran ring, i.e., the formation of 2-methyl-3-ethoxycarbonyl-4-phenyl-5-oxo-4H-indeno[1,2-b]pyran (IIb). The acylation of VI in turn leads to its acetoxy isomer IV – 2-methyl-2-acetoxy-3-ethoxycarbonyl-4-phenyl-5-oxo-3,4-dihydroindeno[1,2-b]pyran.

It has often been noted [6] that in addition reactions the carbonyl group in the transition state occupies a conformation that differs from the conformation of the ground state. The carbonyl oxygen atom in this case exists in a hindered conformation between the two groups with the smallest volumes. In this case this change in the orientation of the 2-carbonyl group of the Ib molecule and the subsequent addition of the oxygen atom of the indan carbonyl group on the side of the least steric hindrance (on the 3-H side) leads to the formation of intermediate 2-hydroxy derivative VIIA with an equatorially oriented OH group. This is followed by a change in the conformation of the pyran ring due to the anomeric effect [7], and the 2-hydroxy derivative takes on conformation VIIB with an axial orientation of the substituents. The proton attached to the $C_{(3)}$ atom and the 2-OH group of the VIIB molecule exists in a cis orientation, which is unfavorable for splitting out of water, and the elimination of water therefore proceeds with the participation of a proton of the 2-methyl group, as a result of which 2-methylene-3-ethoxycarbonyl-4-phenyl-5-oxo-3,4-dihydroindeno[1,2-b]pyran (III) with an exocyclic double bond is formed. Acylation of intermediate VIB leads to isomer V – 2-methyl-2-acetoxy-3-ethoxycarbonyl-4-phenyl-5-oxo-3,4-dihydroindeno[1,2-b]pyran.

EXPERIMENTAL

The PMR spectra were recorded with a WH-90 spectrometer, and the ^{13}C NMR spectra were obtained with a WM-360 spectrometer with tetramethylsilane as the internal standard. The IR spectra were recorded with a PE 580 B spectrometer. The mass spectra were obtained with an MS-50 AEI spectrometer at an ionizing-electron energy of 70 eV; the substances were admitted through a direct-introduction system. 4-(Indan-1',3',-dion-2'-yl)-4-phenyl-2-butanone (Ia) was obtained by the method in [8]. Ethyl α-acetyl-β-(indan-1,3-dion-2-yl)-β-phenylpropionate was obtained by the method in [9]. PMR spectrum of Ib ($CDCl_3$): 0.94 (3H, t, OCH_2CH_3), 2.46 (3H, s, $COCH_3$), 3.51 (1H, d, $J_{2-\beta}$ = 4.5 Hz, 2-H), 3.91 (2H, q, OCH_2CH_3), 4.35 (1H, m, β-H), 5.04 (1H, d, $J_{\alpha-\beta}$ = 11.5 Hz, α-H), 7.00-7.21 (5H, m, β-C_6H_5), 7.64-7.98 ppm (m, 4H, aromatic H of the indan fragment).

2-Methyl-4-phenyl-5-oxo-4H-indeno[1,2-b]pyran (IIa). Two drops of concentrated H_2SO_4 were added to 1.46 g (5 mmole) of Ia in 5 ml of acetic anhydride, and the mixture was heated on a boiling-water bath for 10 min. It was then poured into 60 ml of hot water. The aqueous mixture was cooled, and the resulting yellow precipitate was removed by filtration and recrystallized from ethanol to give 1.02 g (73%) of a product with mp 122-124°C (after repeated crystallization) (mp 123-125°C [1]). PMR spectrum ($CDCl_3$): 2.04 (3H, s, 2-CH_3), 4.23 (1H, d, 4-H), 4.96 (1H, d, J_{34} = 3.5 Hz, 3-H), 7.29 ppm (m, 9H, aromatic).

Cyclization of Ethyl α-Acetyl-β-(indan-1,3-dion-2-yl)-β-phenylpropionate (Ib). A 1.8-g (5 mmole) sample of ester Ib was dissolved in 30 ml of acetic anhydride, three drops of concentrated H_2SO_4 were added, and the mixture was heated on a boiling-water bath for 15 min. It was then poured slowly into 150 ml of hot water, and the aqueous mixture, after decomposition of the acetic anhydride, was extracted with chloroform (three 60-ml portions). The chloroform extracts were combined, washed with water until the wash water was neutral, dried, and evaporated to give a yellow viscous mass containing 19.4%, 11.0%, 45.1%, and 13.7% IIa, III, V, and IV, respectively.

The composition of the mixture (in percent) was determined by means of high-performance liquid chromatography: the column was 4.6 by 250 mm, the support was Zorbax Sil, the eluent was ethyl acetate–hexane (3:7), the rate of elution was 2 ml/min, detection was accomplished with a UV detector at 330 nm, and the rate of recording of the chromatogram was 1 cm/min.

The resulting mixture in the form of a concentrated chloroform solution was applied to a column (500 cm^3) packed with silica gel (L 100/160) and eluted with chloroform–hexane (1:1). The first yellow fraction contained 0.30 g of 2-methyl-3-ethoxycarbonyl-5-oxo-4H-indeno[1,2-

b]pyran (IIb) with mp 123-125°C (from methanol). PMR spectrum ($CDCl_3$): 1.09 (3H, t, OCH_2CH_3), 2.53 (3H, s, 2-CH_3), 4.03 (2H, q, OCH_2CH_3), 4.74 (1H, s, 4-H), 7.26 ppm (9H, m, aromatic). IR spectrum: 1705 (3-CO), 1672 (5-CO), 1623 cm^{-1} (C=C). Mass spectrum, m/z (%): 346 (100) $[M]^{+\cdot}$, 317 (57) $[M-C_2H_5]^+$, 300 (14) $[M-C_2H_5OH]^{+\cdot}$, 289 (19) $[M-C_2H_5-CO]^+$, 269 (80) $[M-C_6H_5]^+$, 241 (27) $[M-C_6H_5-CO]^+$, 223 (17) $[M-C_6H_5-C_2H_5OH]^+$. Found: C 76.0; H 5.4%. $C_{22}H_{18}O_4$. Calculated: C 76.3; H 5.2%.

The second fraction (also yellow) contained primarily III-V, which were separated by means of preparative TLC on plates with silica gel (loose layer of silica gel L 40/100, thickness 2 mm) with chloroform–hexane (3:1) as the eluent. All of the bands were yellow. The first contained another small amount of 4H-indenopyran IIb. The second band contained 2-methylene-3-ethoxycarbonyl-4-phenyl-5-oxo-3,4-dihydroindeno[1,2-b]pyran (III) with mp 115-117°C (from methanol). PMR spectrum ($CDCl_3$): 1.23 (3H, t, OCH_2CH_3), 3.54 (1H, d, 3-H), 4.17 (2H, q, OCH_2CH_3), 4.39 (1H, d, $J_{3,4}$ = 2.0 Hz, 4-H), 4.56 (1H, d, a-H), 5.18 (1H, d, J_{a-b} = 2.0 Hz, b-H), 7.26 (5H, s, 4-C_6H_5), 7.32 ppm (4H, m, H of the indene fragment). IR spectrum: 1736 (3-CO), 1702 (5-CO), 1641 cm^{-1} (C=C). Mass spectrum, m/z (%): 346 (10) $[M]^{+\cdot}$, 273 (100) $[M-COOC_2H_5]^+$, 245 (5) $[M-COOC_2H_5-CO]^+$, 233 (14). Found: C 76.1; H 5.0%. $C_{22}H_{18}O_4$. Calculated: C 76.3; H 5.2%.

The third and fourth bands contained isomeric 2-methyl-2-acetoxy-3-ethoxycarbonyl-4-phenyl-5-oxo-3,4-dihydroindeno[1,2-b]pyrans V and IV, respectively.

Compound V. This compound had mp 176-178°C (from methanol). PMR spectrum ($CDCl_3$): 1.20 (3H, t, OCH_2CH_3), 1.57 (3H, s, 2-$COCH_3$), 1.91 (3H, s, 2-CH_3), 4.11 (1H, d, 3-H), 4.12 (2H, q, OCH_2CH_3), 4.14 (1H, d, $J_{3,4}$ = 4.25 Hz, 4-H), 7.27 ppm (7H, m, aromatic). IR spectrum: 1745 (sh) (2-CO), 1734 (3-CO), 1701 (5-CO), 1641 cm^{-1} (C=C). Found: C 70.6; H 5.3%. $C_{24}H_{22}O_6$. Calculated: C 70.9; H 5.5%.

Isomer IV. This compound had mp 135-137°C (from methanol). PMR spectrum ($CDCl_3$): 1.06 (3H, t, OCH_2CH_3), 2.07 (3H, s, 2-CH_3), 2.11 (3H, s, 2-$COCH_3$), 2.82 (1H, d, 3-H), 4.02 (2H, q, OCH_2HC_3), 4.23 (1H, d, $J_{3,4}$ = 11.5 Hz, 4-H), 7.24 ppm (9H, m, aromatic). IR spectrum: 1761 (2-CO), 1741 (3-CO), 1701 (5-CO), 1644 cm^{-1} (C=C). Found: C 70.7, H 5.7%. $C_{24}H_{22}O_6$. Calculated: C 70.9; H 5.5%.

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