STUDY OF THE REACTIVITIES OF METHYL ESTERS OF FURAN-2-CARBOXYLIC AND THIOPHENE-2-CARBOXYLIC ACIDS BY THE METHOD OF COMPETITIVE NITRATION

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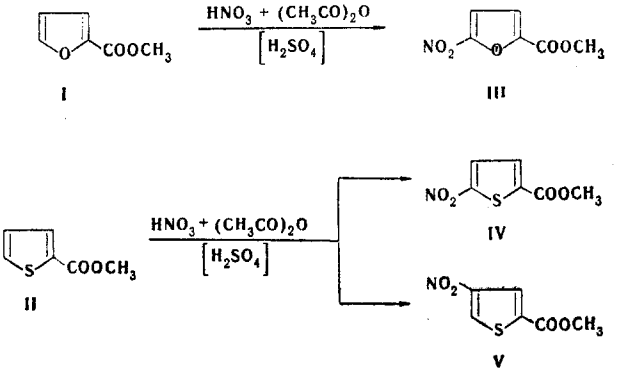
The reactivities of methyl esters of furan-2-carboxylic and thiophene-2-carboxylic acidswere studied by the method of competitive nitration. Methyl furan-2-carboxylate is more active in its reactions with a mixture of nitric acid and acetic anhydride (with sulfuric acid as the catalyst) and with a mixture of nitric and sulfuric acids (with acetic anhydride as the solvent).

A vast amount of experimental data on the relative reactivities of compounds of the furan and thiophene series in electrophilic substitution reactions has been accumulated [1]. However, up until now, data that make it possible to estimate the reactivities of furan and thiophene compounds in nitration have been virtually absent; this is evidently associated with the extremely low stabilities of unsubstituted furan and many of its derivatives in acidic media [2]. A qualitative estimate of both heterocycles, which provides evidence for the higher reactivity of the furan ring, is presented only in [3], in which the nitration of 2-furyl 2-thienyl ketone was studied.

In preliminary experiments we established that esters of furan-2-carboxylic acid (I) and thiophene-2-carboxylic acid (II) are convenient models for the quantitative estimate of the reactivities of furan and thiophene derivatives. These compounds have considerable stability with respect to acids and at the same time are nitrated by the action of nitric acid in the presence of a catalyst (sulfuric acid) in acetic anhydride by the method in [2] to give the corresponding mononitro derivatives — methyl 5-nitrofuran-2-carboxylate (III), methyl 5-nitrothiophene-2-carboxylate (IV), and methyl 4-nitrothiophene-2-carboxylate (V) (according to the PMR data, the IV:V ratio is 1.44) — in good yields.



Gas–liquid chromatography (GLC) was used for the separation, identification, and quantitative determination of the starting compounds (I and II) and their nitration products (III, IV, and V).

For comparison of the furan and thiophene rings in I and II we used the method of competitive nitration for the first time. Competitive nitration was carried out by two methods in which a) a previously prepared solution of acetyl nitrate containing the catalyst (sulfuric acid) in acetic anhydride, or b) nitric acid containing the catalyst (sulfuric acid) was added to a solution of equimolar amounts of I and II in acetic anhydride.

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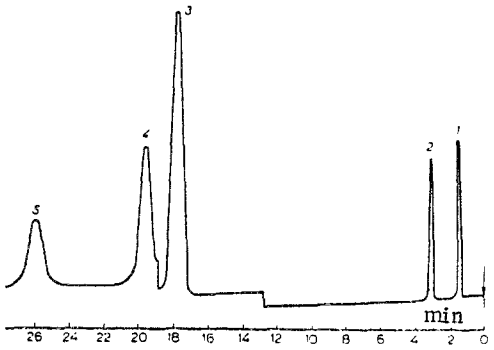
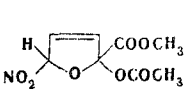


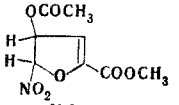
Fig. 1. Chromatogram of the separation of the products of competitive nitration of a mixture of I and II (the scale of recording of the peaks of I-V is indicated in parentheses): 1) I (1:3000); 2) II (1:3000); 3) III (1:100); 4) IV (1:30); 5) V (1:30).

Stable adducts of acetyl nitrate with the starting compound — methyl 5-nitro-2-acetoxy-2,5-dihydrofuran-2-carboxylate (VI) and methyl 5-nitro-4-acetoxy-4,5-dihydrofuran-2-carboxylate (VII) [4] — are formed in the nitration of I; treatment of the reaction mixture with a weakly alkaline reagent (sodium acetate) is required for the quantitative conversion of VI and VII to III. The formation of similar adducts is not observed in the nitration of II.

The method developed in this research makes it possible to estimate the rate of attack of the active nitrating particle on the heterocyclic ring; in the case of II the deprotonation step does not affect the overall rate of nitration.



VI



VII

In the nitration of a mixture of I and II by method a, the corresponding nitro derivatives III, IV, and V are present in the reaction products in a molar ratio of 32.2:1.67:1, i.e., the furan compound is more reactive; this is in agreement with the results obtained during a study of these heterocycles in other electrophilic reactions [5]. The predominance of nitro derivative III is also observed in the reaction products in the case of nitration by method b, but in this case the amount of III in the mixture is somewhat lower (III:IV:V = 10.9:1.65:1). This can be explained by the fact that a small concentration of the nitrating agent is formed at the point of contact of the reagents when nitric acid (containing the catalyst) is added to a solution of I and II in acetic anhydride, and the difference in the reactivities of the furan and thiophene rings becomes less appreciable. This sort of phenomenon has been previously noted in a series of aromatic compounds when solutions of nitronium tetrafluoroborate in tetramethylene sulfone (sulfolane) are used as the highly active nitrating agent (see [6]).

EXPERIMENTAL

Compounds I [7], II [8], and III [2] were prepared by known methods. Compound IV [mp 75-76°C (petroleum ether)] was prepared from 2-formyl-5-nitrothiophene diacetate by a method similar to the procedure in [9]. According to the literature data, IV has mp 74-76°C (petroleum ether) [9] and 76°C (methanol) [10]. Compound V [mp 99-100°C (heptane)] was prepared from 4-nitro-2-acetothienone [11] by the method in [9]. According to the literature data, V has mp 99.5-100°C (heptane) [19] and 100-101°C (benzene) [12].

A reaction product with mp 66-67°C (ether) and an elementary composition corresponding to the composition $C_6H_5NO_4S$ was obtained in 86.5% yield in the nitration of II in acetic anhydride (the molar ratio of II to nitric acid, sulfuric acid, and acetic anhydride was 1:1.3:0.07:4 and the nitration temperature was —10 to —15°C). According to the results of thin-layer chromatography (TLC) [on Silufol UV-254 plates, elution with CCl_4—nitromethane (9:1), detection in UV light], the product was a mixture of IV (R_f 0.60) and V (R_f 0.46). According to the PMR spectra [obtained with a Perkin—Elmer R-12A spectrometer (60 MHz) with $CDCl_3$ as the solvent and tetramethylsilane as the internal standard], the ratio of IV [δ, ppm: 7.80 (3-H, d, $^3J_{H^3H^4}$ = 4.1 Hz), 8.11 (4-H, d, $^3J_{H^4H^3}$ = 4.1 Hz), and 3.93 (s, protons of the methyl group in $COOCH_3$)] and V [δ, ppm: 8.16 (3-H, d, $^4J_{H^3H^5}$ = 1.5 Hz), 9.02 (5-H, d,

$^4J_{H^3H^3}$ = 1.5 Hz), and 3.93 (s, protons of the methyl group in $COOCH_3$)] in the mixture was 1.44:1.*

The composition of the mixture and its yield (85.1%) remained virtually unchanged when the products of nitration of II were made alkaline to pH 4 and when they were treated as in [2] (at 50°C).

Competitive Nitration of I and II. A freshly prepared solution of acetyl nitrate containing the catalyst (sulfuric acid) in acetic anhydride, which was obtained by the addition of 2.2 mole of fuming nitric acid (sp. gr. 1.51) and 0.12 mmole of sulfuric acid (sp. gr. 1.84) to 21 mmole of acetic anhydride at 0-5°C, was added at −10 to −15°C to a solution of 6.25 mmole of I and 6.25 mmole of II in 29 mmole of acetic anhydride, and the mixture was stirred for 15 min. Cold (+4°C) water was then added, and the mixture was stirred for 15 min. A solution of 36.7 mmole of sodium acetate in 20 ml of water was then added, and the mixture was heated at 50°C for 1 h, after which it was cooled and extracted with four 15-ml portions of ether. The ether extract was analyzed by GLC.

Experiments in which nitric acid containing the catalyst (sulfuric acid) was used as the nitrating reagent were carried out as indicated above, the only difference being that the entire amount of acetic anhydride (50 mmole) was used to dissolve the mixture of I and II, and the above-indicated amount of fuming nitric acid in a mixture with sulfuric acid was added to the resulting solution at −10 to −15°C.

The composition of the products of competitive nitration was determined with an LKhM-8MD chromatograph (model 5) [14] with a flame-ionization detector under temperature-programming conditions from 140 to 185°C at 6 deg/min. Compounds I-V were used as standards.

A 3-m long stainless-steel column with an inner diameter of 3 mm was filled with Chemosorb AW-HDMS ground to a particle size of 0.200-0.360 mm and impregnated with GE-XE-60 siloxane rubber (5%). The carrier-gas (helium) flow rate was 30 ml/min, and the speed of the diagram ribbon was varied from 2400 to 600 mm/h. The scale of recording of the peaks of the substances ranged from 1:3000 to 1:30, depending on the concentrations of the compounds. The volume of the sample of the reaction mixture (after treatment with sodium acetate and extraction with ether) was 5 μliters; in this case I-V were eluted in the form of almost completely separated peaks (see Fig. 1), as also evidenced by the retention volumes (milliliters of He) of the corresponding substances (I 123, II 171, III 615, IV 669, and V 861). This made it possible to construct calibration graphs with the aid of artificial mixtures containing I-V over the range of hypothetical concentrations and to determine the quantitative composition of the reaction products. The ratio between the nitro derivatives of furan (III) and thiophene (IV and V) was determined from the areas of the peaks; this procedure gave the following numerical values (in moles): a) 0.58 III, 0.030 IV, and 0.018 V (when the nitrating reagent was a solution of acetyl nitrate in acetic anhydride containing the sulfuric acid catalyst); b) 0.35 III, 0.050 IV, and 0.032 V (when the nitrating reagent was nitric acid containing the sulfuric acid catalyst).

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*The nitration of II in a mixture of acetic anhydride and acetic acid was described in [13]. Gauthier and Maillard erroneously assigned structure IV to the product [mp 66-67°C (methanol)].

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SYNTHESIS AND ABSORPTION SPECTRA OF EPOXYDIARYLINDANONES AND THEIR PHOTOISOMERS

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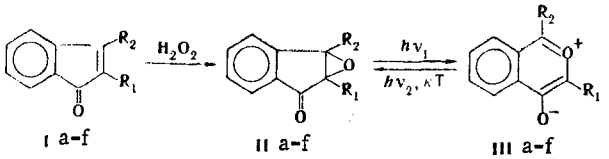
Some previously undescribed 2,3-epoxy-2,3-diarylindanones were obtained, and the spectral characteristics of their photoinduced forms were measured. A simple method for the determination of the molar extinction of benzopyrylium oxides is proposed.

The photochromic transformations of 2,3-epoxy-2,3-diphenylindanone have been studied in detail by Ullman and Henderson [1]. The available information regarding the synthesis and properties of other representatives of this series is extremely limited.

In the present research we obtained some previously undescribed epoxyindanones (EI) with various substituents in the 2 and 3 positions and measured some spectral characteristics of their photoinduced forms (III).



I—III a $R_1=R_2=C_6H_5$; b $R_1=C_6H_4OCH_3$-*p*, $R_2=C_6H_5$; c $R_1=C_6H_5$, $R_2=C_6H_4OCH_3$-*p*; d $R_1=\alpha$-$C_{10}H_7$, $R_2=C_6H_5$; e $R_1=C_6H_5$, $R_2=\alpha$-$C_{10}H_7$; f $R_1=C_6H_4NO_2$-*p*, $R_2=C_6H_5$

The starting indones (Ia-f) were synthesized by a known method [3] — by reaction of benzalphthalides with Grignard reagents — with simplification of the method in the case of Ia,e. Nitrophenylindone If was obtained by nitration of diphenylindone Ia with cupric nitrate in acetic anhydride. It is known that under the conditions of nitration of indone Ia with nitric acid [4] or oxides of nitrogen [5] the reaction does not stop with the formation of nitrophenylindone If because of the extremely easy subsequent addition of the nitrating agent to the double bond. In the case of nitration with cupric nitrate we were able to lower the yield of the addition product and isolate the nitrophenylindone directly from the reaction mixture.

The epoxidation of indones Ia-f was carried out in alkaline alcohol solutions of hydrogen peroxide at 65-70°C [6]. In the oxidation of 2-(p-nitrophenyl)-3-phenylindone (If) the pH of the medium was maintained at 8-9 to avoid side processes. The UV spectra of the synthesized epoxyindanones IIa-f are presented in Figs. 1 and 2.

All Ia-f form colored 1,3-disubstituted 2-benzopyrylium 4-oxides (IIIa-f) when benzene solutions of them are irradiated with UV light (λ 365 nm) because of photochemical valence tautomerization [1]. The reverse reactions take place under the influence of heat or visible light. The maxima of the long-wave absorption bands in the spectra of III are presented in Table 1.

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