SYNTHESIS AND IONIZATION CONSTANTS OF 2-ARYLIMINOTETRAHYDROFURANS

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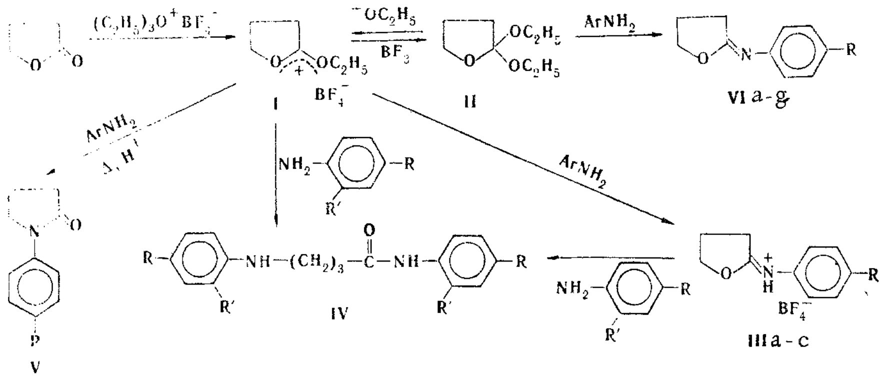
The tetrafluoroborates of 2-aryliminotetrahydrofurans were synthesized by the reaction of O-ethylbutyrolactonium tetrafluoroborate with aromatic amines, and a number of bases of imido esters with various substituents in the aromatic ring were synthesized by the reaction of aromatic amines with 2,2-diethoxytetrahydrofuran. The ionization constants of the products were measured.

A considerable number of publications have been devoted to the study of the chemistry of "activated amides," viz., complexes of amides and lactams with various alkylating and acylating agents, imido and lactim esters, and amide and lactam acetals [1-6]. On the other hand, information regarding the activation of the lactone carbonyl group is available only in [7]. In the latter study the possibility of alkylation of butyrolactone with a Meerwein reagent, as a result of which a complex (I), treatment of which with sodium ethoxide leads to a lactone acetal, viz., 2,2-diethoxytetrahydrofuran (II), was synthesized, is demonstrated. It was established that the reaction of complex I with primary aromatic amines (in the case of p-toluidine, p-chloroaniline, and 2,4-dichloroaniline) proceeds through a step involving the formation of an imido ester tetrafluoroborate (III), which then reacts with excess amine and undergoes ring cleavage to give a γ-arylaminobutyric acid arylamide (IV). N-Aryl-2-pyrrolidones are formed from I and arylamines under severe conditions [7]. The chemical transformations of the acetal II are limited to a study of its hydrolysis [7, 8], alkylation, and conversion to complex I under the influence of triethyloxonium tetrafluoroborate [7].



III a R=Me; b R=OMe; c R=Cl; IV R=Me or Cl, R′=H, R=R′=Cl; V R=Me, Cl; VI a R=H; b R=Me; c R=OMe; d R=Cl; e R=Br; f R=CO_2Et; g R=NO_2

The aim of the present research was to investigate the possibility of the synthesis of imido esters by reactions of complex I and acetal II with various aromatic amines and to study the structures of the resulting cyclic imido esters as compared with their aza analogs, viz., the cyclic amidines that were previously synthesized from N-methylbutyrolactam diethylacetal [9].

The reactions with complex I proceed under mild conditions and lead to imido ester tetrafluoroborates IIIa-c. The corresponding imido esters cannot be obtained in the case of

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TABLE 1. Constants of VI

Compound	R	pK_a (50% alcohol)[a]	ΔpK_a (nitromethane)[a]
VIa	H	4,28	4,83
VIb	Me	4,78	3,87
VIc	OMe	5,12	3,62
VId	Cl	3,65	5,60
VIe	Br	3,60[b]	5,90
VIf	COOEt	3,24[b]	6,33
VIg	NO_2	2,32[b]	7,40

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[a] The accuracy in the determination of the pK_a values was ± 0.05, as compared with ± 0.1 in the case of the ΔpK_a values. [b] Calculated values.

TABLE 2. Characteristics of the Compounds Obtained

Compound	bp, °C (mm)	Found, %			Empirical formula	Calc., %			Yield, %	Excess acetal II (moles)
		C	H	N		C	H	N		
IIIc[a]	—[b]	42,4	3,7	4,9	$C_{10}H_{11}BF_4ClON$	42,3	3,9	4,9	82	—
IVb	173—178 (19)	75,4	7,3	8,2	$C_{11}H_{13}NO$	75,4	7,4	8,0	75	1,25
IVc	153—155 (1)	69,1	6,9	7,4	$C_{11}H_{13}NO_2$	69,1	6,8	7,3	80	1,25
IVd	150—152 (1)	61,5	5,1	6,7	$C_{10}H_{10}ClNO$	61,4	5,1	7,2	75	1,23
IVe[c]	168—169 (2)	50,3	4,3	5,5	$C_{10}H_{10}BrNO$	50,0	4,2	5,8	72	1,52
IVf	148—150 (1)	67,0	6,7	5,9	$C_{13}H_{15}NO_3$	67,0	6,4	6,0	73	1,88
IVg	191—193 (1)	58,0	5,2	13,6	$C_{10}H_{10}N_2O_3$	58,3	4,9	13,6	49	2,00

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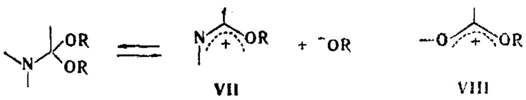
[a] Found: Cl 12.6%. Calculated: Cl 12.2%. [b] This compound had mp 142-143°C (from ethyl acetate). [c] Found: Br 32.9%. Calculated: Br 33.3%.

amines that have strong electron-acceptor substituents in the benzene ring. Thus, the reaction of I with p-nitroaniline leads to a mixture of amide IVa (R = NO_2, R' = H) and p-nitroanilinium tetrafluoroborate, which is probably formed via the same scheme by which the salts of amines are obtained in the reaction of amines with complexes of acid amides with phosphorus oxychloride [10]. Considerably more severe conditions (150-180°C) were required in the case of the reaction with acetal II; however, the reaction proceeds unambiguously, and imido esters VIa-g were generally obtained in good yields.

Imido esters VI are liquids or low-melting solids, the IR spectra of which contain an intense band of a C=N bond at 1670-1680 cm^{-1}, which is also characteristic for other cyclic imido esters, viz., lactim esters. It should be noted that tetrafluoroborates III readily underwent hydrolysis, and the preparation of imido esters VI from them was hindered.

Thus the reactivities of tetrafluoroborate complexes of lactams and lactones are generally similar, but the acetals of lactones are considerably less inclined to undergo reactions with nucleophilic reagents such as aromatic amines than the corresponding lactam acetals [5, 6]. This is understandable if one takes into account the fact that the high reactivities of amide and lactam acetals with respect to nucleophilic reagents are due to their dissociation in solutions to ambident cation VII and alkoxide anions [5, 6]. The stability of the oxa analog of this cation (of the VIII type), which could be formed from lactone acetals, is much lower.



VII VIII

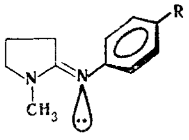
The constants of VI in alcohol and nitromethane were measured (Table 1).

Imido esters VI were found to be considerably (by approximately four orders of magnitude) less basic compounds than their amidine analogs [9], and this reflects the degree of stabilization by conjugation of the cations of the imido esters as compared with the amidinium cations. We were unable to obtain the ionization constants in 50% alcohol at all for the least basic VIf,g. Since there is a significant correlation between the pK_a values (50% alcohol) and the ΔpK_a values (CH_3NO_2), which is expressed by the equation $\Delta pK_a = 11.158 - 11.492pK_a$ ($r = 0.99$, $S_o = 0.025$), the pK_a values (50% alcohol) for imido esters VIf, g were calculated from this equation. The data obtained are presented in Table 1.

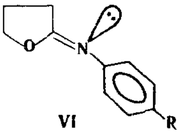
In contrast to amidines [9], in the case of the imido esters it was found that the basicity constants obtained in both 50% alcohol and nitromethane correlate satisfactorily with the σ_p constants:

$$pK_a = 4.30 - 2.97\sigma_p \quad (r = 0.999,\ S_0 = 0.03),$$
$$\Delta pK_a = 4.71 + 3.69\sigma_p \quad (r = 0.99,\ S_0 = 0.21).$$

The following conclusions can be drawn from the dependences obtained: 1) the closeness of the ρ values (50% alcohol) for the imido esters and amidines [9] confirms the previously drawn conclusion that protonation of amidines takes place at the exocyclic nitrogen atom; 2) since all of the points, including also those pertaining to the compounds with electron-acceptor substituents (which are capable of direct polar conjugation), fit into the correlation in nitromethane, it may be assumed that the benzene ring in this case lies in the plane of the C=N bond. This substantial difference between the stereochemistry of the investigated imido esters VI and amidines [9] (for which 49° rotation of the benzene ring was observed) can be explained on the basis of an examination of molecular models. The models show that, in contrast to amidines IX, a "planar" orientation of the benzene ring is possible for imido esters VI; whereas the aryl substituent in IX is anti-oriented relative to the heteroatom, a syn orientation of the ester oxygen atom and the N-aryl group is more favorable for the structure of imido esters VI.



IX



VI

EXPERIMENTAL

The ionization constants in 50% alcohol were determined by the method in [10], while the ionization constants in nitromethane were determined by the method in [11].

2-Ethoxybutyrolactonium tetrafluoroborate (I), 2,2-diethoxytetrahydrofuran, and 2-(4'-methylphenyl)iminotetrahydrofuran tetrafluoroborate (IIIa) were obtained by the Meerwein Method [7].

2-(4'-Methoxyphenyl)iminotetrahydrofuran Tetrafluoroborate (IIIb). A solution of 3.6 g (29.2 mmole) of p-anisidine in 30 ml of anhydrous methylene chloride was added dropwise to a solution of 6 g(29.7 mmole) of complex I in 50 ml of anhydrous methylene chloride, and the mixture was allowed to stand for 1 h. The solvent was removed by evaporation in vacuo, and the residue was triturated several times with anhydrous ether, removed by filtration, and dried to give 7.35 g (90%) of imido ester tetrafluoroborate IIIb with mp 129-131°C (from ethyl acetate). Found %: C 47.2; H 4.6; N 5.0. $C_{11}H_{14}BF_4NO_2$. Calculated %: C 47.3; H 5.0; N 5.0.

Imido ester tetrafluoroborate IIIc was similarly obtained (Table 2).

Reaction of Complex I with p-Nitroaniline. A solution of 8.5 g (61.6 mmole) of p-nitroaniline in 50 ml of methylene chloride was added to a solution of complex I, obtained from 11.7 g (61.6 mmole) of triethyloxonium tetrafluoroborate and 5.6 g (65.5 mmole) of butyrolactone, in 20 ml of anhydrous methylene chloride, and the mixture was allowed to stand for 3 h. The resulting precipitate was removed by filtration and dried to give 2.9 g [12.8 mmole (21%)] of p-nitroaniline tetrafluoroborate (the precipitate hydrolyzed to p-nitroaniline when it was treated with water). The filtrate was evaporated, the residual mobile oil was drenched with ether, and the mixture was allowed to stand in a refrigerator for 24 h. The precipitate was removed by filtration to give 0.9 g (8.7%) of γ-(p-nitrophenyl)aminobutyric acid p-nitrophenylanilide with mp 207-209°C (from DMF). Found %: C 55.7; H 4.6; N 16.3. $C_{16}H_{16}N_4O_5$. Calculated %: C 55.8; H 4.7; N 16.3.

2-Phenyliminotetrahydrofuran (IVa). A mixture of 5 g (31 mmole) of orthoester II and 2.5 g (27 mmole) of aniline was refluxed (with removal of the liberated alcohol) for 2 h, after which it was distilled to give 2.9 g (67%) of imido ester IVa with bp 175-176°C (2 mm). Found %: C 74.3; H 7.0; N 8.7. $C_{10}H_{11}NO$. Calculated %: C 74.5; H 6.8; N 8.7.

Imido esters IVb-g were similarly obtained (Table 2).

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^{14}N AND ^{15}N NMR SPECTRA OF 2-SUBSTITUTED 5-NITROFURANS

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The ^{14}N and ^{15}N NMR spectra of a number of 2-substituted 5-nitrofurans were studied. On the basis of experimental data it was concluded that there is considerable π-electron density on the nitrogen atom of the nitro group. A linear relationship between the chemical shifts in the ^{14}N NMR spectra and the frequencies of the asymmetrical deformation vibrations of the nitro group in the IR spectra was found for the series of investigated 5-nitrofurans. The observed ^{15}N–H spin–spin coupling constants showed that in the 5-nitrofuran molecule transmission of spin information through the ring oxygen atom to the H_2 nucleus is appreciably greater than through the carbon atom to the H_4 nucleus. It was established by measurement of the ^{15}N NMR spectra that the crude adduct formed in the nitration of furfural diacetate with acetyl nitrate is a mixture of trans and cis isomers of 5-nitro-2-acetoxy-2,5-dihydrofurfural diacetate in a ratio of 7:1.

In recent years ^{14}N and ^{15}N NMR spectroscopy has been successfully used for the study of the electronic effects in organic molecules, as well as for the identification of individual compounds; nevertheless, its possibilities as applied to in individual classes of compounds have not been fully ascertained. In the present research we were able for the first time to record the ^{14}N and ^{15}N NMR spectra of 2-substituted 5-nitrofurans.

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