ORGANODIMAGNESIUM DERIVATIVES OF THIOPHENE.

4.* REACTION OF ORGANODIMAGNESIUM DERIVATIVES OF THIOPHENES THAT CONTAIN ARYL SUBSTITUENTS IN THE RING β POSITION WITH DIETHYL OXALATE

Yu. V. Shklyaev, Yu. P. Dormidontov,
and I. I. Lapkin

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It was established that 2,5-dibromo-3-R-4-arylthiophenes form organodimagnesium compounds in ether with the "accompaniment" of dibromoethane. It is shown that because of steric hindrance, only 2-ethoxalyl-3-R-4-arylthiophenes are formed in the reaction of the organodimagnesium compounds with diethyl oxalate. It was established that the bromomagnesiumethoxycarbinolates obtained from the indicated thiophenes and bromomagnesium ethoxide have high thermal stabilities. The IR and PMR spectra of the synthesized compounds were studied.

A rather large number of papers have been devoted to the problems of the reactions of sterically hindered Grignard reagents with various secondary components. The reactions of duryl-, mesityl-, α-naphthyl-, and o-tolylmagnesium halides and a number of other Grignard compounds with ketones, esters, chloromethyl ethers, oxalates, etc. have been studied [2-4]. However, such studies have not been made in the I series. It seemed of interest to study the reaction of symmetrical and unsymmetrical compounds Ia-e of the thiophene series and to ascertain the effect of steric (as well as electronic) factors on the direction and course of their reaction with diethyl oxalate (II).

Complete passivity of Ia was observed in a study of the reaction of II with Ia. In an attempt to carry out this reaction in diethyl (or dibutyl) ether at the boiling point of the solvent we isolated only 3,4-diphenylthiophene after hydrolysis. The desired result also was not obtained in the reaction of Ia with ethoxalyl chloride at the boiling point of dibutyl ether. Thus phenyl groups in the "ortho" positions create extremely great steric hindrance, by virtue of which the reaction of Ia with II does not occur.

The result of the reaction of Ib with diethyl oxalate, which leads to the formation of only ethyl 4-phenyl-2-thienylglyoxylate (IIIb), is also in complete agreement with the preceding fact.

According to [5], in the reaction described above one might have expected the formation of yet another reaction product, viz., bis(4-phenyl-2-thienyl)ethane-1,2-dione; however, it was not detected. A similar diketone, viz. bis[4-(p-anisyl)-2-thienyl]ethane-1,2-dione (V), was obtained along with ethyl 4-(p-anisyl)-2-thienylglyoxylate in the reaction of Ic with II. This is evidently associated with the greater nucleophilicity of the thiophene ring when there is a p-anisyl grouping rather than a phenyl group in the latter.

Only the formation of ethyl 3-methyl-4-aryl-2-thienylglyoxylates IIId,e was established in a study of the reaction of Id,e with II. The corresponding diketones are not formed because of the steric hindrance created by the methyl groups [6].

A study of the thermal stabilities of the bromomagnesiumethoxycarbinolates obtained from esters IIIb-e and bromomagnesium ethoxide showed that these carbinolates do not decompose with the liberation of an aldehyde even when they are heated in refluxing toluene for 6 h. Such high thermal stability of the carbinolates is evidently due to the following reasons. Considerable suppression of the δ^+ charge on the central carbon atom in the carbinolate occurs when methyl groups, which have a +I effect and a positive hyperconjugation effect, are present in the 3 position of the ring. It has been shown [7] that the increased stability of thienyl-

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[*] See [1] for Communication 3.

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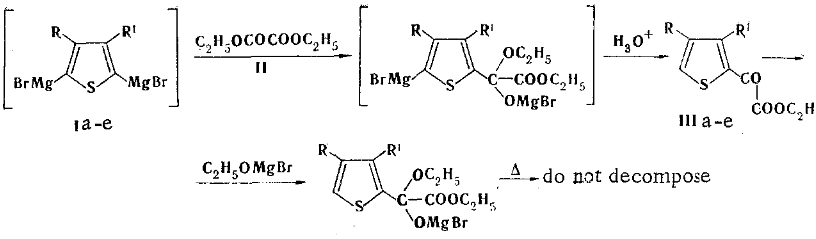

I, III a R=R¹=C_6H_5; b R=C_6H_5, R¹=H; c R=*n*-$CH_3OC_6H_4$, R¹=H; d R=C_6H_5, R¹=CH_3; e R=*n*-$CH_3OC_6H_4$, R¹=CH_3

containing carbinolates is due to suppression of δ^+ in the carbinolate by the π electrons of the thiophene ring, as a result of which an electron density deficit is created over the entire ring. The introduction of phenyl or p-anisyl groups, which have a +M effect, in the 4 position of the ring increases the electron density in the thiophene ring, as a result of which further suppression of δ^+ in the carbinolate occurs. An attempt to reduce esters IIIc-e with aluminum ethoxide led only to saponification of the esters to the corresponding acids IVc-e. The structures of the synthesized compounds were confirmed by the results of elementary analysis and the IR and PMR spectra.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in perfluorinated mineral oil were recorded with an IKS-22 spectrometer. The PMR spectra of solutions of the compounds in CCl_4 were recorded with a Tesla BS-487C spectrometer at 80 MHz with hexamethyldisiloxane as the internal standard. The SSCC of the protons of the ethoxy group was 7 Hz, while the SSCC of the protons of the anisyl group was 10 Hz; the SSCC between the 3 and 5 protons of the thiophene ring was 1.7 Hz [8].*

The purity of esters IIIc-e was proved by thin-layer chromatography (TLC) on Silufol plates in a CH_2Cl_2–hexane–ether system (1 : 1 : 1).

The starting thiophenes were obtained by the method in [9]. Bromination was carried out by the method in [10]. Data on the dibromothiophenes obtained are presented in Table 1.

Compounds Ia-e. A solution of 7.5 g (0.04 mole) of dibromoethane in 20 ml of ether was added dropwise to a mixture of 0.01 mole of the dibromothiophene and 1.44 g (0.06 mole) of magnesium in 100 ml of ether in such a way that the ether boiled uniformly. At the end of the addition, the mixture was heated on a water bath for 1 h. Compounds Ia-e were obtained in 87-95% yields (determined from the results of hydrolysis).

Esters IIIb-e. An ether solution of Ia-e was added dropwise to a solution of 6.8 g (0.05 mole) of diethyl oxalate in 100 ml of ether, and the mixture was stirred for 1 h. It was then decomposed with water and 10% HCl, and the ether layer was separated, washed successively with water, sodium bicarbonate solution, and water to neutrality, and dried with sodium sulfate. The ether was removed by distillation, the excess diethyl oxalate was removed in vacuo, and the residue was recrystallized from alcohol to give esters IIIb-e. Hydrolytic cleavage of esters IIIc-e gave acids IVc-e. The synthesized compounds are presented in Table 2.

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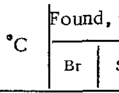
*The PMR spectra of IIIb,c were recorded and interpreted by M. I. Vakhrin, for which the authors express their gratitude.

TABLE 1. Starting Dibromothiophenes



R	R¹	mp, °C	Found, %		Empirical formula	Calc., %		Yield, %
			Br	S		Br	S	
C_6H_5	C_6H_5	149—151[a]	40,1	8,0	$C_{16}H_{10}SBr_2$	40,2	8,0	90
C_6H_5	H	37—39[b]	50,0	10,1	$C_{10}H_6SBr_2$	50,2	10,1	85
p-$CH_3OC_6H_4$	H	52—54	46,0	9,3	$C_{11}H_8OSBr_2$	45,9	9,2	85
C_6H_5	CH_3	51—52	48,2	9,6	$C_{11}H_8SBr_2$	48,1	9,7	95
p-$CH_3OC_6H_4$	CH_3	67—68	44,1	8,9	$C_{12}H_{10}OSBr_2$	44,1	8,9	92

[a] According to [11], this compound had mp 148-149°C. [b] In [12] this compound was described as a liquid with bp 110°C (0.5 GPa) and n_D^{20} 1.6754.

TABLE 2. Characteristics of Esters IIIb-e and Acids IVc-e

Substance	mp, °C	R_f	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	S		C	H	S	
IIIb	94—96	—	64,4	4,3	12,4	$C_{14}H_{12}O_3S$	64,6	4,5	12,3	27
IIIc[a]	97—99	0,77	62,2	4,9	10,8	$C_{15}H_{14}O_4S$	62,0	4,8	11,0	37
IIId[b]	60—62	0,79	65,6	5,0	11,7	$C_{15}H_{14}O_3S$	65,7	5,1	11,7	32
IIIe[c]	46—48	0,80	63,4	5,1	10,3	$C_{16}H_{16}O_4S$	63,6	5,2	10,4	35
IVc	149—150	—	59,6	4,0	12,0	$C_{13}H_{10}O_4S$	59,5	3,8	12,2	—
IVd	116—118	—	63,3	4,0	12,8	$C_{13}H_{10}O_3S$	63,4	4,1	13,0	—
IVe	135—136	—	60,8	4,1	11,7	$C_{14}H_{12}O_4S$	60,9	4,3	11,6	—

[a] The dinitrophenylhydrazone had mp 167-168°C. Found: N 11.8%. $C_{21}H_{18}N_4O_7S$. Calculated: N 11.9%. [b] The dinitrophenylhydrazone had mp 123-124°C. Found: N 12.3%. $C_{21}H_{18}N_4O_7S$. Calculated: N 12.3%. [c] The dinitrophenylhydrazone had mp 128-129°C. Found: N 11.5%. $C_{22}H_{20}N_4O_7S$. Calculated: N 11.6%.

In the case of IIIc red crystals of V precipitated after removal of the ether by distillation and cooling. The crystals were separated and recrystallized from alcohol. The product, with mp 167-168°C and R_f 0.68, was obtained in 18% yield. Found: C 65.7; H 4.8; S 14.7%. $C_{24}H_{22}O_4S_2$. Calculated: C 65.8; H 5.0; S 14.6%.

Reduction of Esters IIIb-e with Bromomagnesium Ethoxide. A 1-ml sample of ethyl bromide was added to 0.24 g (0.01 mole) of magnesium in absolute ether, and 1 ml of absolute ethanol was then added at the end of the reaction. A 5-mmole sample of ester IIIb-e and 50 ml of absolute toluene were added to the solution of bromomagnesium ethoxide, and the diethyl ether was removed by distillation. The residue was refluxed for 6 h, decomposed with water and 10% HCl, and extracted with two 50-ml portions of ether. After the usual workup, the ether was removed by distillation. The resulting crystals were identified as unchanged esters IIIb-e. An increase in the heating time or the temperature led to pronounced resinification of the reaction mass.

Reduction of Esters IIIc-e with Aluminum Ethoxide. A 5-mmole sample of ester IIIc-e was added to a solution of 0.01 mole of aluminum ethoxide in diglyme, and the mixture was heated for 6 h. It was then decomposed with water and 10% HCl. After the usual workup, the solvent was removed by distillation, and the resulting crystals were identified as a mixture of esters IIIc-e and acids IVc-e (the saponification of the esters observed in this case did not go to completion).

Intense absorption bands at 1680 and 1730 cm^{-1}, which correspond to the stretching vibrations of ketone and ester carbonyl groups, were present in the IR spectra of esters IIIb-e. An intense band at 3480-3500 cm^{-1} was additionally observed in the IR spectra of acids IVc-e. The IR spectrum of V contained only one absorption band at 1640 cm^{-1} (ketone carbonyl group).

PMR spectra: IIIb: 7.50 (1H, d,α-H), 7.17 (5H, m, C_6H_5), 6.92 (1H, d,β-H), 3.55 (2H, q, OCH_2), 0.92 (3H, t, CH_3); IIIc: 7.20 (1H, d, α-H), 6.80 (2H, d, anisyl o-H), 6.60 (1H, d, β-H), 6.40 (2H, d, anisyl m-H), 3.54 (5H, m, OCH_2, OCH_3), 0.77 (3H, t, CH_3); IIId: 7.37 (1H, s, α-H), 7.20 (5H, s, C_6H_5), 4.25 (2H, q, OCH_2), 2.40 (3H, s, β-CH_3), 1.32 (3H, t, CH_3CH_2O); IIIe: 7.15 (1H, s, α-H), 7.00 (2H, d, anisyl o-H), 6.75 (2H, d, anisyl m-H), 3.65 (5H, m OCH_2, OCH_3), 1.92 (3H, s, β-CH_3), 0.80 (3H, t, CH_3CH_2O); V (in CH_2Cl_2): 7.35 (1H, s, α-H), 6.35-6.75 (5H, m, β-H+C_6H_4), 3.55 ppm (3H, s, OCH_3).

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MASS SPECTRA OF ISOMERIC THIENO[2,3-b]- AND THIENO[3,2-b]PYRIDINES

N. A. Klyuev, P. I. Abramenko,
I. S. Shpileva, and L. D. Pinkin

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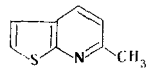
The mass spectra of six isomeric thieno- and thionaphthenopyridines were studied for the first time, and the pathways of fragmentation of the molecular ions, which made it possible to isolate the peaks of the fragment ions that characterize the destruction of the pyridine and thiophene rings, were traced. It is shown that the character and type of conjugation of the heterorings can be distinguished by analyzing the mass-spectral data. The relationship between the intensity of the peak of the doubly charged molecular ion and the number of π electrons in the system and the π-donor character of the heteroring was illustrated by means of the literature data on the mass spectrometry of heteroaromatic systems with one heteroatom.

Methyl-substituted thieno- and benzothienopyridines (I-VI) were previously obtained [1, 2] as starting materials in the synthesis of spectral sensitizers for silver halide photographic emulsions.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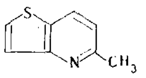
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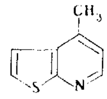
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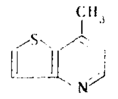
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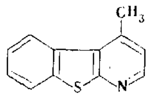
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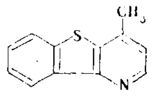
VI

In the present research for the first time we undertook a mass-spectrometric study of the indicated heterocyclic systems in order to elucidate those relationships between their structure and dissociative ionization processes that could be used in the solution of analytical problems, particularly with respect to distinguishing isomers.

Compounds I-VI are condensed aromatic systems, and their stability with respect to electron impact (W_M) is therefore quite high (see Table 1). As expected, the highest W_M values are reached in the case of benzothienopyridines V and VI; the selectivity of the fragmentation of the molecular ion increases markedly (the $S_{1/2}$ value decreases sharply). The differences in the W_M values for V and III (20.3) and VI and IV (13.4) are substantially greater than for naphthalene and benzene (4.8 [3]). This is explained by the fact that in our case the p and d electrons of the heteroatoms participate, in addition to the π electrons of the aromatic system, in the redistribution of the electron density on passing from III to V (or from IV to VI).

Compounds I-VI undergo fragmentation under electron impact in the same way, and the principal pathways are similar to those in the fragmentation of methylpyridines [4] and thiophenes [5].

A comparison of the ion currents due to dissociative ionization of the compounds of the type peculiar to pyridine or thiophene (Σ_1 and Σ_2 in Table 1, respectively) makes it possible to assume a structure with localization of the charge on the nitrogen atom of the pyridine ring for the molecular ion. Quantum-chemical calculations made for I [6] indirectly confirm this assumption. They show that the greatest electron density is concentrated on the nitrogen atom. It is therefore natural to assume that in the formation of the molecular ion

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