REACTIONS OF AROMATIC AND HETEROAROMATIC COMPOUNDS THAT BEAR ELECTRON-ACCEPTOR SUBSTITUENTS

COMMUNICATION 19.* BROMINATION AND NITRATION OF 2-CYANOTHIOPHENE

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Previously it was shown that the complexing of 2-acylthiophenes [2, 3] and 2-alkylsulfonylthiophenes [4] with $AlCl_3$ or a strong protic acid makes it possible to overcome to some degree the α-orienting effect of the heteroatom and direct the electrophilic substitution either predominantly or almost completely in the 4 position of the thiophene ring. In the furan series a similar effect can be achieved only for 2-furaldehyde [5], while in the complex of 2-acetylfuran with $AlCl_3$ the activity of the 4 position only slightly exceeds the activity of the 5 position [6]. In a search for substituents with a stronger meta-orienting effect than that of the $RCO \cdot AlCl_3$ or $RCO \cdot HSbCl_6$ groupings (see [7]) we undertook a study of the reactions of the nitriles of the thiophene and furan series that were complexed with either a protic acid or $AlCl_3$.

Primarily we attempted to quantitatively estimate the meta-orienting ability of the substituents $CN \cdot AlCl_3$ and $CN \cdot HSbCl_6$ by studying the NMR spectra of benzonitrile and its complexes with $AlCl_3$ and $HSbCl_6$, similar to what we had done with respect to the substituents $RCO \cdot A$ (R = H, CH_3 or OCH_3, and A = $AlCl_3$ or $HSbCl_6$) [7]. Unfortunately, the difficulty of assigning the signals in the NMR spectra of benzonitrile and its complexes with $AlCl_3$ and $HSbCl_6$ did not permit us to characterize the modified nitrile group by the σ or σ^+ values (cf. [7]). Nevertheless, the values of the differences in the chemical shifts ($\Delta\delta$) of the nuclear protons in the NMR spectra of 2-cyanothiophene, 2-cyanofuran, and their complexes with $AlCl_3$ (Table 1) show that in its electron-acceptor capacity the $CN \cdot AlCl_3$ group is close to the $CH_3OCO \cdot AlCl_3$ group (cf. [7]). Approximately the same effect is mainfested by the $CN \cdot HSbCl_6$ grouping, which can be seen from the NMR spectrum of the complex of 2-cyanothiophene with $HSbCl_6$. The complexed methoxycarbonyl group, which in its electron-acceptor capacity is close to that of the analogously modified nitrile group, is, as was shown in [7], the weakest meta-orientant of the $RCO \cdot A$ type. Since in the furan series the directing of electrophilic substitution predominantly in the 4 position can be effected only in the complex of 2-furaldehyde with $AlCl_3$, it was impossible to expect the formation of 2,4-disubstituted furan derivatives using the 2-cyanofuran complexes, and consequently we limited ourselves to a study of the reactions of the 2-cyanothiophene complexes, and specifically, to nitration and bromination. In both cases certain peculiarities, which are caused by the nature of the nitrile group, are observed when comparison is made with the corresponding transformations of the carbonyl compounds. The nitration was run in H_2SO_4 by

TABLE 1. NMR Spectra of 2-Cyanothiophene, 2-Cyanofuran, and Their Complexes with $AlCl_3$ and $HSbCl_6$ in Dichloroethane

Compound	Chemical shifts, δ, ppm		
	H^3	H^4	H^5
C_4H_3SCN	7,62	7,10	7,62
$C_4H_3SCN \cdot AlCl_3$	8,24	7,37	8,24
	$\Delta\delta$ —0,62	—0,27	—0,62
$C_4H_3SCN \cdot HSbCl_6$	8,16	7,35	8,16
	$\Delta\delta$ —0,54	—0,25	—0,54
C_4H_3OCN	7,08	6,52	7,58
$C_4H_3OCN \cdot AlCl_3$	7,96	6,84	7,96
	$\Delta\delta$ —0,88	—0,32	—0,38

*See [1] for Communication 18.

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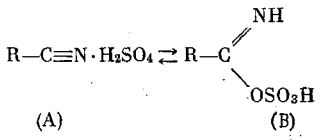
TABLE 2. NMR Spectra of Bromo Derivatives of 2-Cyanothiophene in CCl_4

Compound	Chemical shifts, δ, ppm			J_{34}, Hz
	H^3	H^4	H^5	
5-Bromo-2-cyanothiophene	7,32	7,02	—	4,0
4-Bromo-2-cyanothiophene	7,43	—	7,43	—
4,5-Dibromo-2-cyanothiophene	7,33	—	—	—

treatment with dry KNO_3. Hydrolysis of the nitrile group to the carboxyl group was observed during reaction and subsequent workup, in which connection this process goes only slightly in 60% H_2SO_4 solution, but already in 70% H_2SO_4 solution the starting nitrile is converted almost completely to 2-thiophenecarboxylic acid. The nitration practically does not go under these conditions. In 92% H_2SO_4 solution, the same as in the case of the carbonyl compounds (cf. [8]), 2-cyanothiophene gives the nitro derivatives in good yield. Treatment of the nitration products with methanol gave the methyl esters of the 4- and the 5-nitro-2-thiophenecarboxylic acid in a 60:40 ratio (GLC). Unfortunately, by itself this ratio cannot serve as a measure of the orienting ability of the protonated nitrile group, since an equilibrium probably exists under the reaction conditions between the protonated form (or correspondingly, the complex of the nitrile with the acid) and the iminosulfate, so that it is not known which of the forms (A, B) either predominantly or exclusively enters into the reaction.



(A) (B)

The above mentioned difficulties do not arise when the complex of 2-cyanothiophene with $AlCl_3$ is brominated. Under these conditions, as was shown previously on the example of benzonitrile [9], the reaction products are the corresponding bromonitriles. A peculiarity of the process, caused by the low activity of the thiophene ring in 2-cyanothiophene and the stability of its complex with $AlCl_3$, is displayed in the impossibility of accomplishing the bromination in the absence of $AlCl_3$ or with a catalytic amount of it. Practically the same results are obtained in the presence of either 1.5 or 2.5 moles of $AlCl_3$ per mole of nitrile in chloroform (cf. [4]): based on the GLC data, the mixture of bromination products contains ~ 70% of 4-bromo-2-cyanothiophene, which can be isolated by distillation and crystallization; in addition, ~ 2% of 5-bromo-2-cyanothiophene and 10% of 4,5-dibromo-2-cyanothiophene are formed. Samples of the 5-bromo- and 4,5-dibromo-2-cyanothiophenes were obtained by us from the corresponding bromoaldehydes via their oximes; the 4-bromo-2-cyanothiophene that was isolated from the bromination products of 2-cyanothiophene (see above) had mp 45°C (cf. [10]). The bromonitriles were also characterized by the NMR spectra, which confirm their structure (Table 2).

EXPERIMENTAL METHOD

The NMR spectra were taken on a Varian DA-60-IL radiospectrometer (60 MHz), with HMDS as the internal standard or (in the case of the complexes) without the HMDS, and were measured relative to the signal of the solvent (cf. [7]). The chemical shifts are given relative to TMS.

The GLC was run on an LCM-8 M chromatograph, using a flame-ionization detector, nitrogen as the carrier gas, a flow rate of 20 ml/min, a 1.5 × 1500 mm stainless steel column packed with 15% poly(ethylene glycol adipate) deposited on Chromosorb P, and a temperature of 155° when analyzing the bromides, and 180-190° when analyzing the nitro derivatives.

The starting 2-cyanothiophene was obtained by heating the oxime of 2-thiophenecarboxaldehyde in Ac_2O as described in [11]. 2-Cyanofuran [12] and 5-bromo-2-cyanothiophene [10] were obtained in a similar manner. 4,5-Dibromo-2-cyanothiophene was obtained in 90% yield, mp 117-117.3° (from heptane). Found: C 22.55; H 0.37; Br 59.64; N 5.10; S 11.97%. C_5HBr_2NS. Calculated: C 22.49; H 0.38; Br 59.87; N 5.25; S 12.01%.

Nitration of 2-Cyanothiophene. To a stirred solution of 1.7 g of 2-cyanothiophene in 15 ml of 92% H_2SO_4 solution was added 1.97 g of KNO_3 in small portions, the mixture was allowed to stand at 20° for 20 h, 40 ml of CH_3OH was added under ice cooling, the mixture was refluxed for 5 h, poured into water,

extracted with chloroform, and the extract was washed in succession with water, sodium carbonate solution, and again with water. After removal of the solvent we obtained 2.6 g (89%) of the mixed methyl esters of the 4- and 5-nitro-2-thiophenecarboxylic acids in a 60:40 ratio. See [7] for the preparation of authentic samples of the mentioned esters for the GLC. In addition, the methyl ester of 4-nitro-2-thiophenecarboxylic acid was obtained from the 4-nitro-2-cyanothiophene, isolated from the nitration products of 2-cyanothiophene in Ac_2O as described in [13], by refluxing with methanol in the presence of H_2SO_4.

Bromination of 2-Cyanothiophene. To 15.5 g of anhydrous $AlCl_3$ in 10 ml of $CHCl_3$ was added 5 g of cyanothiophene in 10 ml of $CHCl_3$, and then 8 g of bromine ($AlCl_3$—nitrile—Br_2 mole ratio = 2.5:1:1). The mixture was stirred at 20° for 6 h, let stand 20 h, and poured on ice. After the usual workup and removal of the chloroform we obtained 9 g of an oil, which represented (based on the GLC data) a mixture of the starting nitrile and the 4-bromo-, 5-bromo-, and 4,5-dibromo-2-cyanothiophenes in a 16:70:2:12 ratio. By distillation we isolated 5 g of a fraction with bp 115-130° (15 mm), and 1.9 g of a fraction with bp 130-140° (15 mm). The first fraction was 4-bromo-2-cyanothiophene that was contaminated slightly with the 5-isomer and had mp 38-43°, while the second fraction was a mixture of the 4-bromo- and 4,5-dibromo-2-cyanothiophenes. Recrystallization of the latter from heptane gave 1.2 g of the mono- and 0.4 g of the dibromide. The total yield of 4-bromo-2-cyanothiophene was 6.2 g (71%). Additional recrystallization from heptane enabled us to isolate a 4-bromo-2-cyanothiophene sample with mp 45° (cf. [10]) and a 4,5-dibromo-2-cyanothiophene sample with mp 117°.

When the bromination was run in the presence of 1.5 moles of $AlCl_3$ per mole of the nitrile the ratio of the products differed but slightly from that given above, and was 18:72:2:8. In the presence of 1.1 moles of $AlCl_3$ ~ 80% of the starting 2-cyanothiophene is recovered unchanged, and the main product is 4-bromo-2-cyanothiophene, containing traces of the 5-isomer; the dibromide was not detected. The bromination does not go in the presence of a catalytic amount of $AlCl_3$.

CONCLUSIONS

A study was made of the bromination of the complex of 2-cyanothiophene with $AlCl_3$, which leads predominantly to the 4-bromo derivative. In the nitration of 2-cyanothiophene in H_2SO_4 and subsequent workup the nitrile group is converted to the carboxyl group, and consequently the reaction products are the 4- and 5-nitro derivatives of 2-thiophenecarboxylic acid.

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