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BENZOYLATION OF DEACTIVATED COMPOUNDS OF THE THIOPHENE AND FURAN SERIES WITH PHENYLDICHLOROCARBENIUM TETRACHLOROALUMINATE*

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The reactions of benzotrichloride with methyl and ethyl esters and nitriles of 2-thiophenecarboxylic and 2-furancarboxylic acids, with 2-acetylthiophene, 2-acetylfuran, and 2-thiophenaldehyde in the presence of an excess of anhydrous aluminum chloride have been studied. The phenyldichloromethyl group enters into position 4 of the thiophene and position 5 of the furan ring and on treating the reaction mixture with water is converted to benzoyl group.

Keywords: 2-acetylthiophene, 2-acetylfuran, benzotrichloride, thiophene- and furan-2-carbonitriles, 2-thiophenaldehyde, 2-thiophene- and 2-furancarboxylic acid esters, benzoylation with phenyldichlorocarbenium tetrachloroaluminate.

The incomplete hydrolysis of trichloromethylarenes (TCMA) is used in industry to obtain the corresponding aromatic acid chlorides. In addition the Friedel–Crafts reaction between TCMA and arenes or heterenes with subsequent hydrolysis of the resulting diaryldichloromethanes or aryl(heteryl)dichloromethanes may serve as a preparative route for the synthesis of diaryl and aryl(heteryl) ketones. Our attention was drawn to the report [1] on phenyldichlorocarbenium tetrachloroaluminate $[PhCCl_2]^+AlCl_4^-$ (**1**) as an effective reagent for obtaining substituted benzophenones possessing high stability (the complex was conserved unchanged for two weeks at 25°C). It was concluded by the authors of [1] on the basis of ^{13}C NMR spectra that the phenyldichlorocarbenium carbocation has a substantially larger positive charge compared with the charge on the carbonyl carbon atom in the complex of benzoyl chloride with aluminum chloride $PhCOCl \cdot AlCl_3$. This also causes the complex **1** to be more reactive as an electrophile.

The use of benzotrichloride in the presence of $AlCl_3$ enables the corresponding ketones to be obtained at room temperature in high yield from various aromatic compounds, including anisole, naphthalene, thiophene, chlorobenzene, bromobenzene, and *o*-dichlorobenzene [2]. The benzoylation of acetanilide was studied in particular detail and is linked with the development of new methods of synthesis of 3,4-diaminobenzophenone as a key intermediate for obtaining the antihelmintic drug mebendazole [3]. The action of benzotrichloride in the presence of three-fold molar amount of aluminum chloride in 1,2-dichloroethane leads to 4-acetylaminobenzophenone in 72-98% yield. It is essential to note that acetanilide is not benzoylated by benzoyl chloride in the presence of $AlCl_3$. Only the initial acetanilide and benzoic acid were isolated from the reaction mixture [1].

* Dedicated to Professor M. A. Yurovskaya on her Jubilee.

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Consideration of the fairly wide range of aromatic compounds giving benzoylation products under the action of complex **1** [2], shows that there are no compounds amongst them with strong electron-withdrawing substituents possessing a –I–M effect. However our preliminary experiments showed that even methyl benzoate reacts with benzotrichloride in the presence of $AlCl_3$, although the yield of products was low. The problem of the present work is the investigation of the benzoylation with complex **1** of carbonyl compounds of furan **2a-d** and thiophene **3a-d** and also the corresponding nitriles **4** and **5**. The choice of subject was caused by the possibility of comparison with known data on their acylation by the traditional agents, the acid chlorides.

The benzoylation of 2-furancarboxylic acid methyl ester (**2a**) was described for the first time in 1964 by Galust'yan and Tsukervanik [4]. The reaction was carried out by the action of benzoyl chloride in the presence of ferric chloride (in catalytic amount) in CCl_4 at 80-90°C for 5-8 h. Later, the reaction of ester **2a** in benzene with X-substituted benzoyl chlorides catalyzed by ferric chloride was studied (X = H, NO_2, CH_3, Cl, CH_3O) [5]. A high yield of keto ester **6a** (as described in [4]) was no reached; it was only 41%.

The acetylation of methyl ester **2a** directed to position 5 by the action of acetic anhydride in the presence of $FeCl_3$ or $SnCl_4$ has been described [6]. The reaction however may be complicated by substitution in the acetyl group. On acylating the ethyl ester **2b** with acetic anhydride in benzene in the presence of $SnCl_4$ 5-acetoacetyl-2-ethylfuroate was formed and not 5-acetyl-2-ethylfuroate [7]. Acetylation of 2-acetyl-furan (**2c**) with acetic anhydride in the presence of zinc chloride was also directed to the side-chain, though the yield of 2-acetoacetylfuran was only 4.6% [8]. The reaction of 2-acetylfuran with acetyl chloride in the presence of aluminum chloride does not proceed even in the absence of solvent at 115°C and a large portion of the starting ketone was recovered unchanged [9]. Such a result is explained by deactivation of the furan ring, primarily position 5, by the modified substituting agent $MeCO{\cdot}AlCl_4$. Furfurol (**2d**) is acetylated unexpectedly readily [9]: 5-acetylfurfurol was formed in 45% yield by the action of 2 mole of acetyl chloride and 2.5 mole of $AlCl_3$ in chloroform even at a temperature of 50°C. This is probably caused by the conversion of furfurol into the corresponding chloroacetate under the reaction conditions [9].

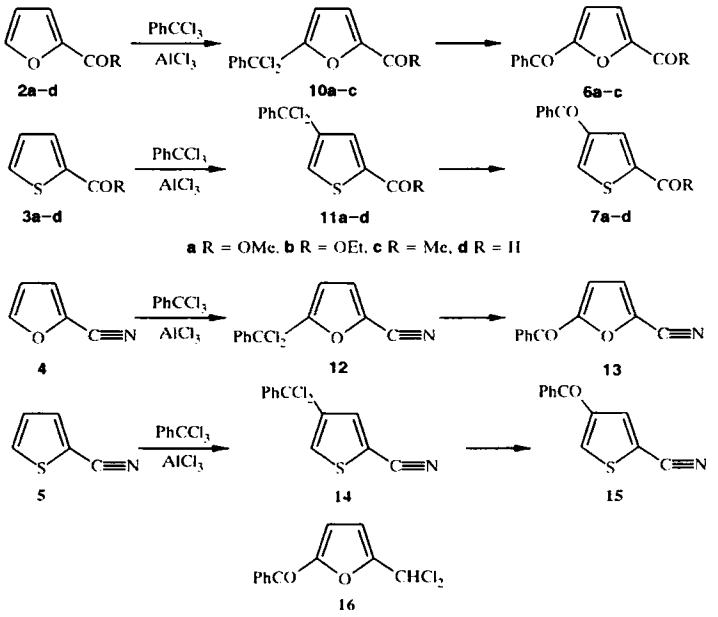
The thiophene analogs of the keto esters of type **6**, as far as we know, are not described in the literature, however acylation of ketones of thiophene series has been studied in comparative detail. In particular, under the usual conditions (using solvent) the presence of an alkyl group is a necessary condition for introducing a second acyl group into the thiophene nucleus [10]. Acetylation of 2-acetylthiophene (**3b**) was successfully carried out by the action of acetyl chloride in the presence of an excess of aluminum chloride at 100°C without solvent. In this way 2,4-diacetylthiophene was obtained in a yield of 50-70% on the reacted ketone, and contained about 5% contamination by the 2,5-isomer [11]. Benzoylation of ketone **3b** under the same conditions was complicated by overacylation so that a mixture of products was formed containing 2-benzoylthiophene, diacetyl-, acetylbenzoyl-, and dibenzoylthiophene [12]. It is essential to emphasize that on acylating 2-acylthiophenes diketones are formed preferentially with acyl residues in positions 2 and 4 of the thiophene ring [11,12]. Such an orientation is caused by the fact that complexes of monoacyl thiophenes with aluminum chloride react. These contain the very strong *meta* orientant, the modified acyl grouping $RCO{\cdot}AlCl_4$, which proved to be capable of overcoming the α-orienting effect of the hetero atom. In the case of the furan analogs complexation at the acyl substituent fails to overcome the more powerful orienting effect of the oxygen atom [13].

We have found that the esters of 2-furancarboxylic acid **2a,b** and of 2-thiophenecarboxylic acid **3a,b**, in the presence of an excess of $AlCl_3$ without solvent or in such solvents as 1,2-dichloroethane, chloroform, or dichloromethane, react with benzotrichloride. After the usual processing the esters of 5-benzoylfuran-2-carboxylic acid **6a,b** and 4-benzoylthiophene-2-carboxylic acid **7a,b** were obtained in 50-75% yield. The corresponding acids **8** and **9** were obtained by the alkaline hydrolysis of these esters. In difference to benzotrichloride, benzoyl chloride under the same conditions gave practically no reaction with ester **2b**, which is additional confirmation of the higher reactivity of phenyldichlorocarbenium tetrachloroaluminate **1** compared with the $PhCOCl{\cdot}AlCl_3$ complex.

Undoubtedly the direct reaction products are not keto esters **6**, **7** but the corresponding dichloro compounds, *viz.* the esters of 5-(α,α-dichlorobenzyl)furan-2-carboxylic acid **10a,b** and 4-(α,α-dichlorobenzyl)-thiophene-2-carboxylic acid **11a,b**. As a rule they are partially conserved on treating the reaction mixtures with water and are detected by ^1H NMR spectrum, mass spectrum, and elemental analysis results. The ratio keto ester : dichloride depends seemingly on the nature of the latter but changes from experiment to experiment so

that it is difficult to trace any regularity. Hydrolysis of the dichlorides to the esters **6** and **7** occasionally succeeds on contact with silica gel. Detection of the dichlorides **10** and **11** is not so unusual. The comparative stability of similar compounds may be used for preparative purposes. For example, dichlorodiphenylmethane is formed in 90% yield from benzene and benzotrichloride in the presence of $AlCl_3$ at 0°C in dichloroethane. The reaction of benzotrifluoride and its substituted derivatives proceeds under the same conditions and with the same high yields (the latter are initially converted into TCMA under the action of $AlCl_3$). Substrates studied included benzene, toluene, *p*-xylene, chloro- and bromobenzene, anisole, naphthalene, and thiophene [14].

Similar results were obtained in the reaction of benzotrichloride with nitriles, ketones, and aldehydes of the furan and thiophene series. The nitrile of 5-(α,α-dichlorobenzyl)furan-2-carboxylic acid (**12**) was formed from 2-cyanofuran (**4**). The reaction product was then partially converted into 5-benzoylfuran-2-carbonitrile (**13**). 4-(α,α-Dichlorobenzyl)thiophene-2-carbonitrile (**14**) and 4-benzoylthiophene-2-carbonitrile (**15**) respectively were obtained from 2-cyanothiophene (**5**). 2-Acetyl-5-(α,α-dichlorobenzyl)furan (**10c**) and 2-acetyl-5-benzoylfuran (**6c**) were obtained from 2-acetylfuran (**2c**). 2-Acetyl-4-(α,α-dichlorobenzyl)thiophene (**11c**) and 2-acetyl-4-benzoylthiophene (**7c**) were obtained from 2-acetyl-thiophene (**3c**). A multicomponent mixture was formed from furfurol (**2d**) in which compounds containing a formyl group were almost completely absent according to ^1H NMR data. On the other hand 2-dichloromethyl substituted furans were present. An insignificant quantity of 2-benzoyl-5-dichloromethylfuran (**16**) was successfully isolated by crystallization. 4-(α,α-Dichlorobenzyl)-thiophene-2-carbaldehyde (**11d**) and 4-benzoylthiophene-2-carbaldehyde (**7d**), with contamination by the corresponding dichloromethyl-substituted derivatives, were obtained from 2-thiophencarbaldehyde (**3d**).



Reactions with the nitrile, ketone, and aldehyde of furan series proceeded with worse yields than for their thiophene analogs, as might have been expected. This may be caused not only by the lower stability of the furan derivatives but also by their more general deactivation on complex formation with aluminum chloride [9]. The main characteristics of the products obtained are given in the Experimental and in Table 1. Conclusions on their structure were made on the basis of NMR spectra (see Experimental and Tables 2 and 3). We note that reactions with nitriles and aldehydes previously seemed of little promise, since aromatic nitriles on reaction with TCMA gave quaternary salts at the nitrogen atom of the nitrile group [15], but aldehydes react with TCMA in the presence of Lewis acids to give aryldichloromethanes [16]. However the higher reactivity of the heterocycle enables it to compete with the functional group in reactions with phenyldichlorocarbenium tetrachloroaluminate (**1**), although the yields of ring-substituted products were frequently low. The dichloromethyl-substituted derivatives in the case of aldehydes **2d** and **3d** are probably formed on reacting α,α-dichlorobenzyl- and benzoyl-substituted aldehydes

TABLE 1. Conditions for the Reaction of Furan and Thiophene Derivatives with Benzotrichloride in the Presence of Aluminum Chloride and the Characteristics of the Resulting Products

Expt. No.	Starting compound	Solvent	T, °C (duration, min)	bp, °C (mm)	Reaction products (ratio $PhCCl_2Het$: PhCOHet)	Yield, %
1	**2a**	$ClCH_2CH_2Cl$	84(25)	163 (2)	**10a**, **6a** (1:1)	49
2	**2a**	—	50-60 (15)	190-200 (4)	**6a**	65
3	**2b**	$CHCl_3$	40-42 (40)	176-180 (2)	**10b**, **6b** (1:1)	50
4	**2b**	$ClCH_2CH_2Cl$	50-55 (25)	205-207 (14)	**10b**, **6b** (2:1)*	53
5	**4**	—	75-110 (20)	164 (1.5)	**12**, **13** (5:1)	12
6	**2c**	—	55-80 (12)	174-185 (1)	**6c**	7*[2]
7	**2d**	—	70-100 (25)	170-173 (3)	**16**	Traces
8	**3a**	—	50-60 (15)	197 (5)	**11a**, **7a** (1:25)	57.5
9	**3a**	CH_2Cl_2	39-41 (105)	192 (3)	**11a**, **7a** (1.8:1)	74
10	**3b**	$CHCl_3$	40-43 (120)	224 (7)	**11b**, **7b** (1:1)	41
11	**3b**	$ClCH_2CH_2Cl$	60 (60)	*[3]	**9**	48
12	**5**	—	90 (35)	174-177 (1)	**14**, **15** (20:1)	42
13	**3c**	—	85-110 (15)	185-196 (1)	**11c**, **7c** (15:1)	40
14	**3c**	—	≤ 80 (17)		**11c**, **7c** (6:1)*	49
15	**3d**	—	80-100 (20)	188-192 (1)	**11d**, **7d** (1:10)*[4]	24

* The ratio of ethyl esters **10b** and **6b** was established from the elemental analysis data on the mixture obtained. Found, %: 60.90; 60.85; H 4.45; 4.53; Cl 16.13; 15.94. $C_{14}H_{12}Cl_2O_3$. Calculated, %: C 56.19; H 4.04; Cl 23.72. $C_{14}H_{12}O_4$. Calculated, %: C 68.84; H 4.95.

*[2] The yield of 2-acetyl-5-benzoylfuran (**6c**) is given approximately from the ^1H NMR spectrum of the product mixture. The content of 2-acetyl-5-(α,α-dichlorobenzyl)furan (**10c**) was not determined due to the presence of other contaminants.

*[3] The reaction mixture was subjected to hydrolysis without redistillation (see Experimental).

*[4] The mixture obtained contained about 20% of the corresponding 2-dichloromethyl-substituted derivatives (δ_{CHCl_2} 6.98 and 6.89, assignment was made by analogy with 2-benzoyl-5-dichloromethylfuran).

with benzotrichloride in the presence of $AlCl_3$. The alternative course for the reaction, the conversion of thiophene- and furanaldehydes into the dichloromethyl-substituted derivatives and their subsequent benzoylation, seems less probable due to the low yields of the main products and the formation of 2,4- and not 2,5-disubstituted derivatives from 2-thiophenecarbaldehyde.

TABLE 2. Chemical Shifts, δ, ppm (coupling constants, Hz) in the ^1H NMR Spectra of the Synthesized Furan Derivatives

Compound	Heterocycle 3-H, d; 4-H, d	Phenyl *o*-H, m; *m*-H and *p*-H, m	CH_3, s or OCH_2, q; CH_3, t
1	2	3	4
5-Benzoylfuran-2-carboxylic acid (**8**)	7.42; 7.44 (3.7)	8.08; 7.5-67.72	—
5-Benzoylfuran-2-carboxylic acid methyl ester (**6a**)	7.28; 7.30 (4)	8.07; 7.47-7.65	3.95
5-Benzoylfuran-2-carboxylic acid ethyl ester (**6b**)*	7.24; 7.28 (3.6)	8.06; 7.46-7.64	4.40; 1.42 (7)

TABLE 2 (continued)

1	2	3	4
2-Acetyl-5-benzoylfuran (**6c**)	7.31; 7.26 (3.75)	8.02 and 8.07;*[2] 7.48-7.70	2.60
5-(α,α-Dichlorobenzyl)furan-2-carboxylic acid methyl ester (**10a**)	7.12; 6.53 (3.5)	7.65; 7.35-7.46	3.95
5-(α,α-Dichlorobenzyl)furan-2-carboxylic acid ethyl ester (**10b**)*	7.09; 6.52 (3.4)	7.63; 7.33-7.43	4.32; 1.37 (7)
5-(α,α-Dichlorobenzyl)furan-2-carbonitrile (**12**)	7.06; 6.59 (3.6)	7.65; 7.42-7.48	
2-Benzoyl-5-(dichloromethyl)furan (**16**)*	7.20; 6.79 (3.6)	7.99; 7.46-7.65	6.77 s ($CHCl_2$)

* For ^{13}C NMR spectrum see Experimental, expt. 3.
*[2] Two dd, J_o = 7.85; J_m = 1.7; J_p = 0.9 Hz.

TABLE 3. Chemical Shifts, δ, ppm (coupling constants, Hz) in the ^1H NMR Spectra of the Synthesized Thiophene Derivatives

Compound	Heterocycle 3-H, d; 5-H, d	Phenyl *o*-H, m; *m*-H, m; *p*-H, m	CH_3, s or OCH_2 q; CH_3, t
4-Benzoylthiophene-2-carboxylic acid (**9**)	8.24 br.; 8.30 (1.2)	7.83; 7.53; 7.63	–
4-Benzoylthiophene-2-carboxylic acid methyl ester (**7a**)*	8.14 (1.2); 8.19 br.	7.83; 7.50; 7.61	3.93
4-Benzoylthiophene-2-carboxylic acid ethyl ester (**7b**)*[2]	8.11; 8.19 (1.2)	7.85; 7.42; 7.59	4.39; 1.42, t (7)
4-Benzoylthiophene-2-carbonitrile (**15**)	8.06 br.; 8.17 br.	7.84; 7.54; 7.62	
2-Acetyl-4-benzoylthiophene (**7c**)	7.81; 8.15 (1.4)	8.12 br. and 7.85 br.; 7.50; 7.63	2.60
4-Benzoylthiophene-2-carbaldehyde (**7d**)*[3]	8.20; 8.29 (1.1)	7.85 and 7.82; 7.51; 7.62	–
4-(α,α-Dichlorobenzyl)thiophene-2-carboxylic acid methyl ester (**11a**)	7.84; 7.61 (1.4)	7.66; 7.34; 7.39	3.38
4-(α,α-Dichlorobenzyl)thiophene-2-carboxylic acid ethyl ester (**11b**)*[2]	7.83; 7.59 (1.4)	7.63; 7.34; 7.42	4.35; 1.38 (7)
4-(α,α-Dichlorobenzyl)thiophene-2-carbonitrile (**14**)	7.64; 7.67 (1.4)	7.62; 7.38-7.47	
2-Acetyl-4-(α,α-dichlorobenzyl)-thiophene (**11c**)	7.62; 7.75 (1.4)	7.64; 7.35-7.42	2.52
4-(α,α-Dichlorobenzyl)thiophene-2-carbaldehyde (**11d**)*[4]	8.07 br.; 8.09 br.	7.35; 7.30-7.50	–

* For ^{13}C NMR spectrum see Experimental, expt. 8.
*[2] For ^{13}C NMR spectrum see Experimental, expt. 10.
*[3] CHO, δ: 9.97, s.
*[4] CHO, δ: 9.80, s.

It has been shown that phenyldichlorocarbenium tetrachloroaluminate is able to enter into electrophilic substitution reactions with carbonyl compounds and nitriles of the thiophene and furan series.

Some of the reactions described in the present paper, primarily with esters **2a,b**, **3a,b**, ketone **3c**, and nitrile **5** may be used preparatively to obtain the corresponding benzoyl-substituted derivatives.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 200 radiospectrometer in $CDCl_3$. The electron impact (EI) mass spectra were recorded on a Kratos MS-30 instrument with direct insertion of samples into the ion source.

Benzoylation of Carbonyl Compounds and Nitriles (General Procedure). A mixture obtained by the sequential addition of carbonyl compound (or nitrile) (15 mmol) and benzotrichloride (15 mmol) to anhydrous $AlCl_3$ (45 mmol) without solvent or with solvent (25 ml) was kept until evolution of HCl had ceased. The reaction mixture was then cooled [in experiments without solvent CH_2Cl_2 (20 ml) was added], and the solution poured onto ice. The organic layer was separated, the aqueous layer extracted with CH_2Cl_2, the extract was combined with the organic layer, washed with water, then with $NaHCO_3$ solution, with water once again, and dried over $MgSO_4$. After distilling off the solvent, the residue was distilled in vacuum. On attempting to benzoylate 2-thiophenecarboxylic acid methyl ester (**3a**) with benzoyl chloride in dichloroethane only the initial ester **3a** was isolated. The solvent, temperature, and duration and also the yields of mixtures of products and their compositions for individual experiments are given in Table 1. The ^1H NMR spectra of products are given in Tables 2 and 3. Samples of the products listed below were isolated by recrystallization of the mixtures from hexane (expt. 2, 3, 5, 7, 8, 12, 14, and 15) or a mixture (1 : 1) of hexane and aqueous ethanol (expt. 6).

Expt. 2. 5-Benzoylfuran-2-carboxylic Acid Methyl Ester (6a); mp 78-79.5°C, which corresponds to the data of [4,5].

Expt. 3. 5-Benzoylfuran-2-carboxylic Acid Ethyl Ester (6b); mp 52°C. ^{13}C NMR spectrum, δ, ppm: 181.9 (CO); 158.0 (COO); 153.6 ($C_{(2)}$); 147.0 ($C_{(5)}$); 136.1 (*ipso*-C); 133.1 (*o*-C); 129.4 (*p*-C); 128.6 (*m*-C); 119.9 ($C_{(4)}$); 118.2 ($C_{(3)}$); 61.5 (CH_2O); 14.1 (CH_3). Found, %: C 69.17; H 4.95. $C_{14}H_{12}O_4$. Calculated, %: C 68.84; H 4.95. The ^{13}C NMR spectrum of **5-(α,α-dichlorobenzyl)-furan-2-carboxylic acid ethyl ester (10b)** was adduced from the spectrum of the mixture with ester **6b**, δ, ppm: 155.9 (COO); 145.8 ($C_{(2)}$); 140.5 ($C_{(5)}$); 128.6 (*ipso*-C); 128.4 (*o*-C); 128.2 (*m*-C); 126.6 (*p*-C); 117.7 ($C_{(3)}$); 112.1 ($C_{(4)}$); 82.2 (CCl_2); 61.1 (CH_2O); 14.1 (CH_3).

Expt. 5. 5-(α,α-Dichlorobenzyl)furan-2-carbonitrile (12); mp 98-100°C. Found, %: C 57.89; H 3.12; Cl 26.63; N 6.64. $C_{12}H_7Cl_2NO$. Calculated, %: C 57.17; H 2.80; Cl 28.13, N 5.56. The EI mass spectrum contained peaks $[M\text{-}Cl]^+$ with *m/z* (I_{rel}, %): 216 (100) and 218 (35.5).

Expt. 6. 2-Acetyl-5-benzoylfuran (6c); mp 103-105°C. Found, %: C 72.27; H 5.36. $C_{13}H_{10}O_3$. Calculated, %: C 72.89; H 4.71.

Expt. 7. 5-Benzoyl-2-(dichloromethyl)furan (16) was isolated in insignificant amount by two recrystallizations from hexane of the complex mixture of reaction products; mp 110-112°C. ^{13}C NMR spectrum, δ, ppm: 182.1 (CO); 154.2 ($C_{(2)}$); 152.5 ($C_{(5)}$); 136.6 (*ipso*-C); 133.0 (*o*-C); 129.4 (*p*-C); 128.6 (*m*-C); 120.4 ($C_{(3)}$); 111.2 and 111.1 ($C_{(4)}$); 62.0 and 61.9 ($CHCl_2$). The doubling of the ^{13}C signals of the substituent in the position and the β carbon of the furan ring is caused by the high rotation barrier relative to the $C_{(2)}$–$C_{(CHCl_2)}$ bond (see [17]). An analytically pure sample of compound **16** was not obtained.

Expt. 8. 4-Benzoylthiophene-2-carboxylic Acid Methyl Ester (7a); mp 83-85°C. ^{13}C NMR spectrum, δ, ppm: 189.2 (CO); 162.1 (COO); 141.5 (*ipso*-C); 138.7 (*o*-C); 137.9 ($C_{(4)}$); 134.6 ($C_{(2)}$); 134.3 (*p*-C); 132.8 (*m*-C); 129.4 ($C_{(5)}$); 128.6 ($C_{(3)}$); 52.6 (CH_3O). Found, %: C 63.42 H 4.18; S 12.87. $C_{13}H_{10}O_3S$. Calculated, %: C 63.40; H 4.09; S 13.02.

Expt. 12. 4-Benzoylthiophene-2-carbonitrile (15); mp 78-80°C. Found, %: C 67.86; H 3.45; N 6.29; S 14.72. $C_{12}H_7NOS$. Calculated, %: C 67.59; H 3.31; N 6.57; S 15.01.

Expt. 14. 2-Acetyl-4-benzoylthiophene (7c); mp 123°C. Found, %: C 67.44; H 4.36; S 13.55. $C_{13}H_{10}O_2S$. Calculated, %: C 67.80; H 4.38; S 13.90.

Expt. 15. 4-Benzoylthiophene-2-carbaldehyde (7d); mp 74-75°C. Found, %: C 66.11; H 3.69; S 15.02. $C_{12}H_8O_2S$. Calculated, %: C 66.65; H 3.73; S 14.82.

Benzoylation of Thiophene-2-carboxylic Acid Esters with Isolation of the Products as the Keto Acids. A. The mixture obtained by the benzoylation of thiophene-2-carboxylic acid ethyl ester (**3b**) (5 g, 35 mmol) in 1,2-dichloroethane (expt. 11) was poured onto ice, then heated to boiling, and boiled for 30 min. After cooling, the organic layer was separated, the aqueous layer extracted with ether, the extract combined with the organic

layer, and dried over $MgSO_4$. After removing the solvent, a fraction (2 g) with bp 103°C/28 mm was distilled, and the residue was extracted with hot heptane. The extract was evaporated, a brown oil (5.5 g) was obtained, which was boiled for 2 h with NaOH (3 g) in ethanol (50 ml). The cooled mixture was diluted with water and extracted with chloroform. The aqueous solution was acidified with hydrochloric acid, the precipitate which separated was filtered off, and was recrystallized from 50% aqueous alcohol. 4-Benzoyl-2-thiophenecarboxylic acid (**9**) (3.6 g, 48%) was obtained; mp 187-188°C (aqueous ethanol, 1 : 1). Found, %: C 62.31; H 3.57; S 13.45. $C_{12}H_8O_3S$. Calculated, %: C 62.06; H 3.47; S 13.80.

B. Acid **9** (1.06 g, 75%) was obtained from a mixture (1.5 g) of methyl esters **7a** and **11a** (1 : 1.8) (see expt. 9) by boiling in ethanol (25 ml) with NaOH (1 g) and treating subsequently as described above; mp 187-188°C. Esterification of this acid in methanol in the presence of a catalytic amount of conc. H_2SO_4 gave a 92% yield of 4-benzoylthiophene-2-carboxylic acid methyl ester (**7a**); mp 83-85°C. No melting point depression occurred with a sample obtained in expt. 8.

Conversion of α,α-Dichlorobenzyl-substituted Derivatives into Benzoyl Derivatives on Treatment with Silica Gel. A. A solution of a mixture (1 : 1) (1.2 g) of esters **7b** and **11b** (see expt. 10, Table 1) in ether (20 ml) was boiled for 8 h in the presence of silica gel (0.5 g) for TLC Silpearl (Kavalier, Czech Republic). After cooling, the silica gel was filtered off, the filtrate evaporated, and the residue distilled. **4-Benzoylthiophene-2-carboxylic acid ethyl ester (7b)** without contamination by ester **11b** (^{1}H NMR) (0.8 g, 73%) was obtained; bp 185°C/1 mm. ^{13}C NMR spectrum, δ, ppm: 188.9 (CO); 161.4 (COO); 141.3 (*ipso*-C); 138.4 (*o*-C); 137.7 ($C_{(4)}$); 135.0 ($C_{(2)}$); 133.8 (*p*-C); 132.5 (*m*-C); 129.6 ($C_{(5)}$); 128.4 ($C_{(3)}$); 61.5 (CH_2O); 14.2 (CH_3).

B. A mixture (2 : 1) (0.25 g) of esters **6b** and **10b** (see expt. 4, Table 1) was kept in ether for 24 h at ~20°C in the presence of silica gel (0.5 g). After separating the silica gel and distilling off the ether, a residue (0.22 g) was obtained, which was (^{1}H NMR) 5-benzoylfuran-2-carboxylic acid ethyl ester (**6b**) without contamination by ester **10b**. Yield 94%.

The ^{13}C NMR spectrum of **4-(α,α-dichlorobenzyl)thiophene-2-carboxylic acid ethyl ester (11b)** was adduced from the spectrum of the mixture with ester **6b**, δ, ppm: 161.4 (COO); 146.0 (*ipso*-C); 142.9 ($C_{(4)}$); 135.2 ($C_{(2)}$); 132.7 (*o*-C); 130.2 (*m*-C); 129.2 (*p*-C); 128.2 ($C_{(5)}$); 126.7 ($C_{(3)}$); 86.5 (CCl_2); 61.4 (CH_2O); 14.2 (CH_3).

C. An ether solution of a mixture (20 : 1) (0.7 g) of dichloride **14** and keto nitrile **15** (see expt. 12, Table 1) was boiled for 2 h in the presence of silica gel (0.5 g). After cooling, removal of the silica gel, and distillation of the ether, a residue (0.6 g) was obtained, which was a mixture (1 : 1) of compounds **14** and **15** (according to ^{1}H NMR). Yield of the mixture 95%.

Benzoylation of Methyl Benzoate. Benzotrichloride (4 g, 22 mmol) was added to the complex obtained from methyl benzoate (3 g, 22 mmol) and anhydrous $AlCl_3$ (8.8 g, 66 mmol). The mixture was heated until the evolution of HCl began (100-110°C), and maintained at this temperature for 20 min. After cooling, $CHCl_3$ (20 ml) and ice-water were added to the very dark mixture, and the mass was extracted with chloroform. After the usual treatment of the extract the initial methyl benzoate (2.37 g) was isolated by distillation with bp ~100°C/33 mm and also a fraction (0.51 g) of bp 192-194°C/5 mm which was, according to ^{1}H NMR, a mixture (3 : 1) of methyl esters of *m*-benzoyl- and *m*-(α,α-dichlorobenzyl)benzoic acids. Yield of the mixture ~9%. ^{1}H NMR spectrum, δ, ppm ($CDCl_3$) of methyl ester of *m*-benzoylbenzoic acid: 8.38 (1H, s 2-H); 8.22 (1H, d, J ~ 8 Hz, 4-H); 7.95 (1H, d, J ~ 8 Hz, 6-H); 7.76 (2H, br. d, J ~ 8 Hz, *o*-H); 7.46 (1H, dd, J ~ 8 Hz, 5-H); 7.40-7.58 (3H, m, *m*-H and *p*-H); 3.89 (3H, s, Me). The ^{1}H NMR spectrum of *m*-(α,α-dichlorobenzyl)benzoic acid methyl ester (obtained by subtraction of the signals of *m*-benzoylbenzoic acid ester from the spectrum of the mixture of compounds): 8.01 (1H, s, 2-H); 7.88 (1H, d, J ~ 8 Hz, 6-H); 7.84 (1H, d, J ~ 8 Hz, 4-H); 7.59 (2H, br. d, J ~ 8 Hz, *o*-H); 7.38 (1H, dd, J ~ 8 Hz, 5-H); 7.32-7.45 (3H, m, *m*-H and *p*-H); 3.82 (3H, s, Me).

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