

Mixed Anhydrides of Carboxylic and Trifluoroacetic Acids as Acylating Agents: I. Reactions of 3,5-Di-*tert*-butylbenzoyl Trifluoroacetate with *tert*-Butylphenols

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Abstract—The rate and pathway of reactions of 3,5-di-*tert*-butylbenzoyl trifluoroacetate with *tert*-butylphenols depend on the number and position of bulky substituents determining the extent of steric shielding of the phenolic hydroxyl.

Acylation with unsymmetrical (mixed) anhydrides of carboxylic and trifluoroacetic acids is a simple and convenient route to esters, ketones, amides, and sulfones [1]. When a mixture of a carboxylic acid with the anhydride of another carboxylic acid is treated with an alcohol, a mixture of esters of both acids is formed. The ratio of the esters depends on the strength and structure of the corresponding acids. With trifluoroacetic anhydride, as a rule, only the product containing no trifluoroacetyl fragment is formed. This synthesis route is fairly simple; the reaction occurs under mild conditions and usually with high yields of the target products [2–6]. By this reaction, a series of phenyl esters were prepared, and the role of the steric factor in acylation was noted [7].

To evaluate the effect of bulky substituents on the rate and pathway (esterification or electrophilic substitution) of the reactions of phenols with mixed anhydrides, we studied the reactions of 3,5-di-*tert*-butylbenzoyl trifluoroacetate (**I**) with mono- and polysubstituted *tert*-butylphenols differing in the extent of steric shielding of the hydroxy group. Anhydride **I** is formed by dissolving 3,5-di-*tert*-butylbenzoic acid in trifluoroacetic anhydride [8].

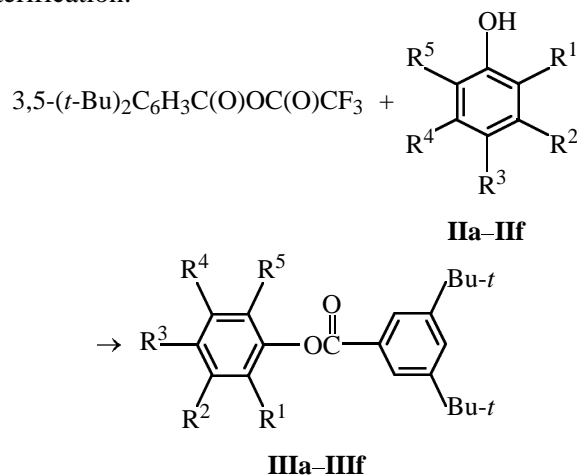
The series of the studied phenols **IIa–IIg** includes two groups of isomers: mono- (**IIb**, **IIc**) and di-*tert*-butylphenols (**IId**, **IIe**, **IIg**). Reaction of 4-*tert*-butylphenol **IIb** with anhydride **I**, as in the case of unsubstituted phenol **IIa**, yields the corresponding ester, 4-*tert*-butylphenyl 3,5-di-*tert*-butylbenzoate **IIIb**. The presence in isomeric 2-*tert*-butylphenol **IIc** of one *o*-substituent shielding the hydroxy group does not alter the reaction pathway: the corresponding ester, 2-*tert*-butylphenyl 3,5-di-*tert*-butylbenzoate **IIIc**, is formed.

These results suggest that the reaction of 2,4-di-*tert*-butylphenol **IId** with anhydride **I** should yield

2,4-di-*tert*-butylphenyl 3,5-di-*tert*-butylbenzoate **IIId**, and this was confirmed experimentally. Two *m*-*tert*-butyl groups in isomeric 3,5-di-*tert*-butylphenol **IId** do not prevent esterification either: 3,5-di-*tert*-butylphenyl 3,5-di-*tert*-butylbenzoate **IIIe** is formed.

The IR spectra of products formed in reactions of phenols **IIa–IIg** with anhydride **I** contain no bands in the range of phenolic hydroxyl absorption but contain bands characteristic of esters: 1725 (C=O) and 1220 and 1090 cm^{−1} (C–O–C), which confirms formation of aryl benzoates **IIIa–IIIg**. The analytical data are also consistent with the composition of **IIIa–IIIg**.

Thus, when the phenolic hydroxyl is not shielded (**IIa**, **IIb**) or is shielded weakly (**IIc–IIe**), the major pathway of the reaction with mixed anhydride **I** is esterification:

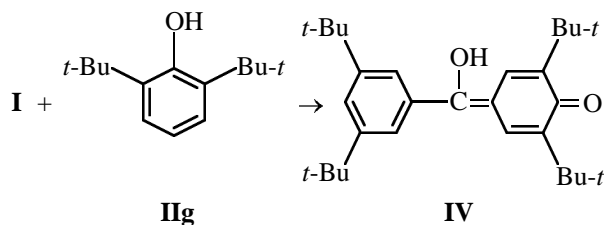


II, **III**, R¹ = R² = R³ = R⁴ = R⁵ = H (**a**); R¹ = R² = R⁴ = R⁵ = H, R³ = Bu (**b**); R¹ = Bu, R² = R³ = R⁴ = R⁵ = H (**c**); R¹ = R³ = *t*-Bu, R² = R⁴ = R⁵ = H (**d**); R¹ = R³ = R⁵ = H, R² = R⁴ = *t*-Bu (**e**); R¹ = R³ = R⁵ = *t*-Bu, R² = R⁴ = H (**f**); R¹ = R⁵ = *t*-Bu, R² = R³ = R⁴ = H (**g**).

Yields, melting points, and elemental analyses of aryl benzoates **IIIa–IIIf**

Comp. no.	Reaction time	Yield, %	mp, °C (solvent for crystallization)	Found, %		Formula	Calculated, %	
				C	H		C	H
IIIa	1 h	87	88–90 (heptane)	80.90	8.14	C ₂₁ H ₂₆ O ₂	81.25	8.44
IIIb	1 h	86	108–109 (ethanol)	81.67	9.10	C ₂₅ H ₃₄ O ₂	81.92	9.35
IIIc	2 days	84	47–49 (ethanol)	81.60	9.05	C ₂₅ H ₃₄ O ₂	81.92	9.35
IIId	2 days	83	133–134 (hexane)	82.08	9.76	C ₂₉ H ₄₂ O ₂	82.41	10.06
IIIe	2 days	85	83–84 (hexane)	82.16	9.21	C ₂₉ H ₄₂ O ₂	82.41	10.06
IIIf	1 month	76	130–132 (ethanol–cyclohexane)	82.44	10.18	C ₃₃ H ₅₀ O ₂	82.79	10.53

The high extent of steric shielding of the hydroxy group in 2,6-di-*tert*-butylphenol **IIg**, which is an isomer of **IIId** and **IIIe**, affects the pathway of the reaction with **I**. In the IR spectrum of the reaction product, the carbonyl absorption band characteristic of esters **IIIa–IIIe** (1725 cm^{−1}) is lacking, but a broad absorption band is observed in the range of OH stretching vibrations (3380 cm^{−1}). Such a spectrum is inconsistent with the structure of 2,6-di-*tert*-butylphenyl 3,5-di-*tert*-butylbenzoate. At the same time, the absorption band at 3380 cm^{−1} does not correspond to vibrations of sterically shielded phenolic hydroxyl, and the carbonyl absorption at 1630 cm^{−1} is untypical of diaryl ketones. Thus, the structure of 4-hydroxy-3,5,3',5'-tetra-*tert*-butyldiphenyl ketone should also be excluded from the consideration. The IR spectrum is consistent with the structure of the tautomer, 4-[3,5-di-*tert*-butylphenyl(hydroxy)methylene]-2,6-di-*tert*-butyl-2,5-cyclohexadien-1-one **IV**:



However, with 2,4,6-tri-*tert*-butylphenol **IIh**, in which the hydroxy group is sterically shielded to the same extent as in **IIg**, we obtained aryl benzoate **IIIh**. Thus, the steric factors do not forbid formation of 2,6-di-*tert*-butylphenyl 3,5-di-*tert*-butyl benzoate from **IIg**. The reaction pathway actually observed with **IIg** is due to preferableness of electrophilic aromatic sub-

stitution at the free *p*-position, followed by isomerization. The occurrence of the alternative esterification pathway is favored by a decrease in the esterification rate in the order **IIa** \approx **IIb** > **IIc** \approx **IIId** \approx **IIIe** \gg **IIIh** (see table), in accordance with the number and position of *tert*-butyl groups sterically shielding the phenolic hydroxyl.

EXPERIMENTAL

The IR spectra were taken on a Perkin–Elmer spectrophotometer from mulls in mineral oil.

Phenyl 3,5-di-*tert*-butyl benzoate IIIa. To a solution of 5 mmol of 3,5-di-*tert*-butylbenzoic acid [9] in 5 ml of CH₂Cl₂ we added with stirring 0.85 ml of trifluoroacetic anhydride [10] and, 10 min later, a solution of 5 mmol of **IIa** in 2 ml of CH₂Cl₂. The mixture was stirred for 1 h at room temperature, 10 ml of benzene was added, and the mixture was successively washed with 10% aqueous KOH and water. The organic layer was separated and dried over Na₂SO₄. The solvent was removed in a vacuum, and the residue was recrystallized from heptane. Esters **IIIb–IIIh** were prepared similarly.

Reaction of I with IIg. The reaction mixture prepared as described above from 1.2 g of 3,5-di-*tert*-butylbenzoic acid, 0.85 ml of trifluoroacetic anhydride, and 1.03 g of **IIg** was kept for 1 month at room temperature and then worked up as described above. Compound **IV** was obtained; yield 1.8 g (80%), mp 163–164°C (from heptane). IR spectrum, ν , cm^{−1}: 3380 (OH), 1630 (C=O). Found, %: C 82.16; H 9.71. C₂₉H₄₂O₂. Calculated, %: C 82.41; H 10.06.

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