The interaction of homophthalic anhydride with (triphenylphosphoranylidene)acetates

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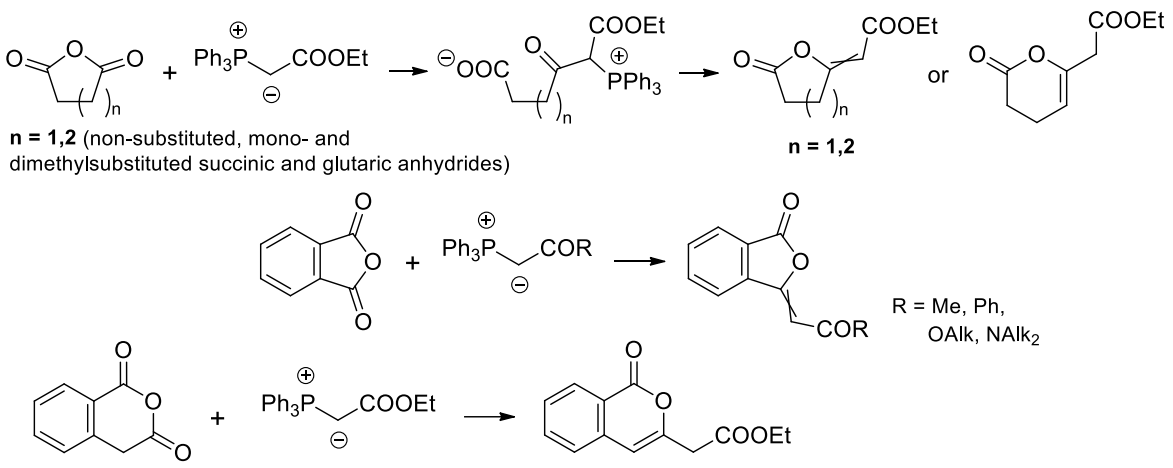
In the study of the interaction of homophthalic anhydride and methyl (triphenylphosphoranylidene)-acetate, along with (1-oxo-1*H*-isochromen-3-yl)acetate obtaining, two minor products – (1,3-dioxo-1,2,3,4-tetrahydronaphthalene-2-yl)acetate and 2-((1-oxo-1*H*-isochromen-3-yl)methyl)benzoic acid – had been isolated. The action of *tert*-butyl (triphenylphosphoranylidene)acetate on homophthalic anhydride didn't lead to Wittig reaction; the encumbered ylide demonstrated only its basicity, and products of homophthalic anhydride self-condensation – 2-((1-oxo-1*H*-isochromen-3-yl)methyl)-benzoic acid and 12-hydroxy-5*H*-dibenzo[*c*,*g*]chromen-5-one – were formed.

Introduction

The interaction of (triphenylphosphoranylidene)acetates and related compounds with cyclic anhydrides is not a sufficiently understood branch of ylide chemistry [1-3]. The reaction proceeds *via* a ring transformation to provide lactones (**Scheme 1**). Interaction of (triphenylphosphoranylidene)acetates with cyclic anhydrides of aliphatic acids (substituted glutaric and succinic acids) as well as with phthalic anhydride has been investigated in detail with determination of regioselectivity and tautomerism of products and isolation of phosphonium intermediates [2, 3].

It was also found that action of ethyl (triphenylphosphoranylidene)acetate on non-symmetric homophthalic anhydride (AHPA) results in formation of ethyl (isocoumarin-3-yl)-acetate in good yield [2].

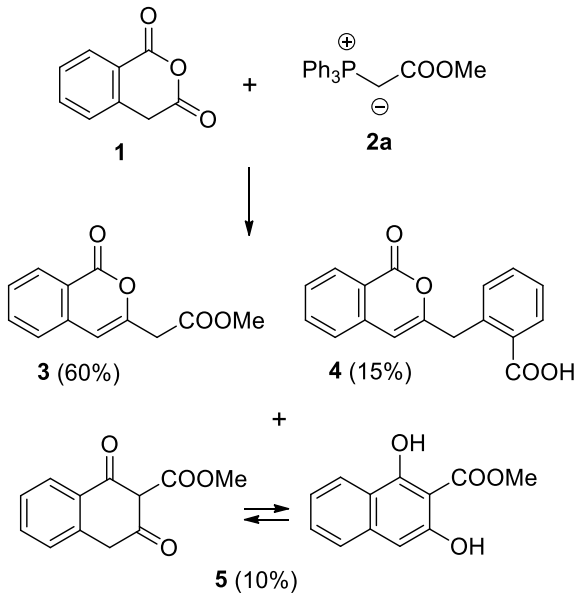
Esters of (isocoumarin-3-yl)acetic acid have some reactive functional groups (ester, lactone, latent carbonyl and active methylene group) which are important for isocoumarin chemistry. Therefore it makes sense to investigate reaction of AHPA with other (triphenylphosphoranylidene)acetates, for instance, methyl and *tert*-butyl esters.



Scheme 1. The interaction of cyclic anhydrides and triphenylphosphoranylidenes with carbonyl functions (literature data).

Results and discussion

Acylation of ylide **2a** with AHPA **1** was performed in Wittig reaction conditions proposed in publications [2, 4]. However, we noted that the content of advised product **3** in reaction mixture does not exceed 60% (according to LCMS data). The column chromatography allowed isolating, along with isocoumarin **3,** byproducts **4** and **5** (**Scheme 2**).



Scheme 2. The interaction of homophthalic anhydride with methyl (triphenylphosphoranylidene)acetate.

Acid **4** is formed by base-catalysed self-condensation of AHPA that is well-known in AHPA chemistry [5-8]. In contrast, formation of diketone **5** was unexpected because only a few examples are known when aliphatic and aromatic carbonyl group of AHPA both attacked one molecule [9].

One would expect a high content of enol form of compound **5** and, in fact, only naphthalene-like enol structure was observed in NMR and IR spectra. Rigorous definition of signals in ^{1}H and ^{13}C NMR of compound **5** was performed using HSQC and HMBC experiments, whose data are represented in **Table 1** and **Figure 1.** The latter serves also to illustrate the information obtaining by COSY and NOESY experiments.

Table 1. Data of NMR spectroscopy of methyl 1,3-dihydroxynaphthalene-2 carboxylate **5**

^{1}H NMR, δ, ppm	**^{13}C NMR, δ, ppm**	
	HSQC	**HMBC**
4.08 (s, 3H, CH_3)	53.0 (CH_3)	170.4 (C=O)
6.76 (s, 1H, H-4)	102.5 (C-4)	97.3 (C-2), 119.6 (C-8a), 125.9 (C-5), 137.9 (C-4a), 153.7 (C-3), 161.7 (C-1), 170.4 (C=O)
7.27 (t, *J*=7.1 Hz, 1H, H-7)	123.1 (C-7)	119.6 (C-8a), 125.9 (C-5), 130.6 (C-6)
7.49 (t, *J*=6.8 Hz, 1H, H-6)	130.6 (C-6)	119.6 (C-8a), 123.1 (C-7), 124.2 (C-8), 137.9 (C-4a)
7.53 (d, *J*=6.8 Hz, 1H, H-5)	125.9 (C-5)	102.5 (C-4), 119.6 (C-8a), 123.1 (C-7), 137.9 (C-4a)
8.22 (d, *J*=8.3 Hz, 1H, H-8)	124.2 (C-8)	125.9 (C-5), 130.6 (C-6), 137.9 (C-4a), 161.7 (C-1)
8.90 (br. s, 1H, OH-3)	-	-
11.31 (br. s, 1H, OH-1)	-	-

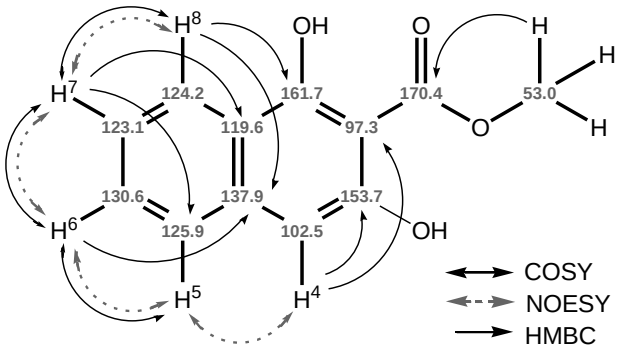
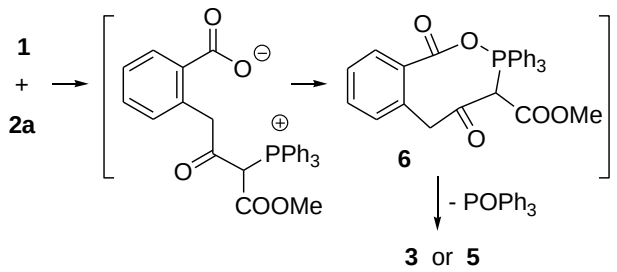
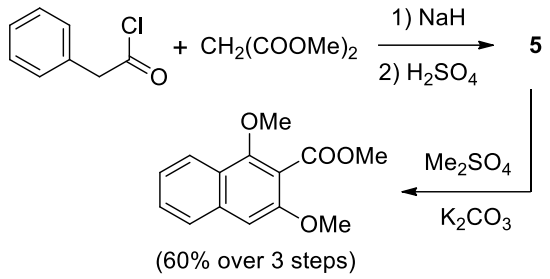


Figure 1. Data of COSY and NOESY experiments and most important HMBC of methyl 1,3-dihydroxynaphthalene-2-carboxylate **5**.



Scheme 3. The proposed mechanism for the compounds **3** and **5** formation.

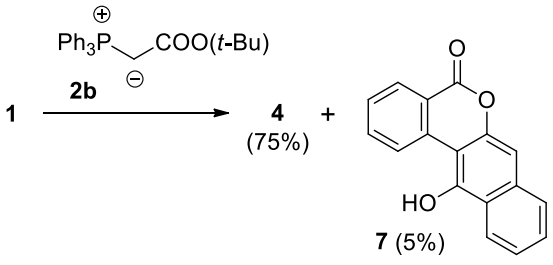
By analogy with the classical Wittig reaction, it can be assumed that the ring closure of compounds **3** and **5** is preceded by the creation of an intermediate **6** with the P–O bond (**Scheme 3).** In this case, the consequence of the molecule $POPh_3$ cleavage can be the formation of C–O bond (isocoumarin **3**) or C–C bond (naphthalene **5**).



Scheme 4. Alternative preparative synthesis of diphenol **5** (literature data).

It is interesting that an alternative way of the aromatic system **5** formation was proposed earlier in Ref. [10] (**Scheme 4**); although diphenol **5** itself wasn't isolated in its pure form, but was converted to dimethyl ether.

The involving of *tert*-butyl ester **2b** instead of **2a** shows how the Wittig reaction of AHPA is sensitive to steric effects. In this case, analogous of products **3, 5** were not detected in a reaction mixture but acid **4** was the main product (**Scheme 5**). A small amount of dibenzocoumarin **7** was also isolated. Product **7** is formed by intramolecular acylation of compound **4** [11] and was obtained earlier by acid-catalysed condensation of homophthalic acid [12].



Scheme 5. The action of *tert*-butyl (triphenylphosphoranylidene)acetate on homophthalic anhydride.

Experimental part

All reagents and solvents were purchased from Aldrich and used as received.

Melting points were determined using a Fisher-Johns melting point apparatus and uncorrected.

^{1}H, ^{13}C NMR spectra were recorded at Varian Unityplus 400 spectrometer operating at 400 MHz frequency for ^{1}H and 100 MHz for ^{13}C experiments. NMR chemical shifs are reported in ppm, in the δ scale and are referenced using TMS as internal standard.

LC-MS data were acquired on Agilent 1100 HPLC system equipped with diode matrix and Agilent LC/MSD SL mass-selective detector, column: Zorbax SB-C18, 1.8 μm, 4.6×150 mm. Eluent: A) 95:5 MeCN–H_2O, 0.1% CF_3CO_2H, and B) 0.1% aqueous CF_3CO_2H; the eluent flow rate was 3 ml/min. The injection volume was 1 μl. The UV detectors recorded at 215, 254, and 285 nm.

IR spectra were recorded on a Vertex 70 spectrometer in KBr pellets.

General procedure for reaction of HPA 1 and ylides 2. A solution of homophthalic anhydride **1** (1.5 g) and the ylide **2** (3.22 g) in chloroform (30 ml) was refluxed under argon for 48 h. After solvent evaporating solid residue was separated by silica gel column chromatography (Merck Grade 9385, 60 Å, 230–400 mesh) eluted with a dichloromethane – hexane (1:1–1:0) gradient solvent system; and the fractions were

monitored by TCL (on plates Silufol UV-254 using a system 9:1 chloroform–methanol as the eluent with UV light visualization). It was given three fractions (when ylide **2a** was used) and two fractions (after ylide **2b** using).

The physical characteristic and spectral data of known compounds should be seen in Ref. [5-8] for 2-[(1-oxo-1*H*-isochromen-3-yl)-methyl]benzoic acid **4** and in Ref. [11, 12] for 12-hydroxy-5*H*-dibenzo[*c*,*g*]chromen-5-one **6**.

Methyl 2-(1-oxo-1*H*-isochromen-3-yl)-acetate **3**. M.p. 125-126 °C. IR (KBr, ν, cm^{-1}): 3087, 3034, 2964, 2931, 1722, 1663, 1605, 1568, 1483, 1440, 1367, 1325, 1270, 1214, 1161, 1051, 1024, 1005, 978, 846, 734, 688. ^{1}H NMR (DMSO-d_6): 3.67 (s, 3H, COOMe), 3.71 (s, 2H, CH_2), 6.74 (s, 1H, H-4), 7.55-7.61 (m, 2H, H-5,7), 7.82 (t, *J*=7.3 Hz, 1H, H-6), 8.11 (d, *J*=7.7 Hz, 1H, H-8). ^{13}C NMR (DMSO-d_6): 38.9, 52.7, 106.3, 120.0, 126.4, 129.1, 129.3, 135.9, 137.2, 151.0, 162.0, 169.5. LC MS (APCI): *m/z* = 219.1 $[M+1]^+$.

Methyl 1,3-dihydroxynaphthalene-2-carboxylate **5**. M.p. 118-119 °C. IR (KBr, ν, cm^{-1}): 3445, 1643, 1569, 1498, 1455, 1433, 1401, 1329, 1248, 1136, 1077, 964, 866, 830, 652, 627. LC MS (APCI): *m/z* = 217.1 $[M-1]^-$.

Conclusions

Hereby it was shown that throughout interaction of homophthalic anhydride and methyl (triphenylphosphoranylidene)acetate the product of Wittig reaction – methyl (1-oxo-1*H*-isochromen-3-yl)acetate – can be produced indeed; but it's impossible to implement analogues reaction with *tert*-butyl (triphenyl-phosphoranylidene)acetate because of domination of homophthalic anhydride self-condensation in this case.

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