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Synthesis of Benzoic and Tetralone Carboxylic Acid Esters from Phenols by Palladium Catalyzed Alkoxy/Aryloxy Carbonylation

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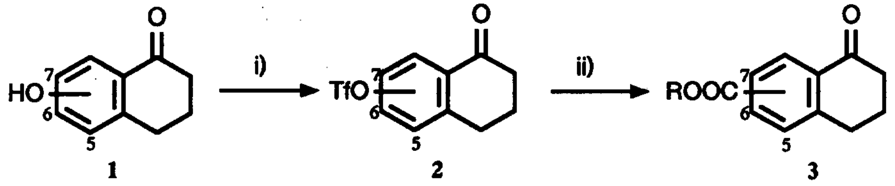
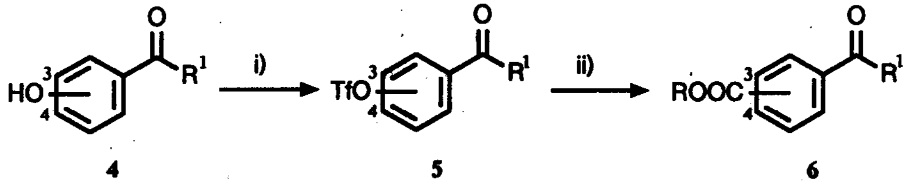
Abstract: Various phenols with an acyl group conjugated to the aromatic system were converted via trifluoromethanesulfonates into benzoic acid esters by a palladium catalyzed alkoxy/aryloxy carbonylation.

During a particular synthetic program the esters of 5, 6- and 7-tetralone carboxylic acid 3 were required. The pentafluorophenyl esters were of special interest. Synthesis of the not commercially available isomers of the tetralone carboxylic acid are described in the literature$^{1)}$, but are very laborious. Convenient starting materials are the corresponding hydroxy compounds, which could be easily obtained from the methoxytetralones$^{2)}$. This prompted us to apply a palladium catalyzed alkoxy/aryloxy carbonylation of the activated phenol which leads to the benzoic acid esters in analogy to the palladium catalyzed carbonylation of aryl bromides and iodides$^{3)}$ or arylthallium compounds$^{4)}$.

(1)



(2)



i) 2,6-Dimethylaminopyridine, DMAP, Tf_2O; ii) $Pd(OAc)_2$, phosphine, CO, ROH, NEt_3;

1		4	R^1	
a	5-OH	a	CH_3	3-OH
b	6-OH	b	CH_3	4-OH
c	7-OH	c	CH_3CH_2	4-OH

We describe the preparation of esters of the 5-, 6- and 7-tetralone carboxylic acid **3** by means of the alkoxycarbonylation of trifluoromethanesulfonates[5)6)7)] with carbon monoxide and alcohols. Elaborating upon the published synthesis of alkyl esters and amides of several benzoic acid derivatives we intended to use this reaction for the synthesis of aryl esters, especially the pentafluorophenyl esters, which have special properties as reactive esters. The reaction with acyl substituted aromatic compounds, like acetophenone derivatives or tetralone has not been previously described.

As a test system the triflates of 3- and 4-hydroxyacetophenone **5a** and **5b** were examined under the conditions of the alkoxycarbonylation. The positive results in these cases encouraged us to use this reaction for our major goal, the synthesis of the tetralone carboxylic acid derivatives. Representative results are summarized in **table 1**[8)].

Table 1: Palladium catalyzed alkyl/aryloxycarbonylation of various aryl triflates[8)]

Entry	Triflate	Time/Temp.	ROH	Phosphine[a)]	Yield (%)[b)]
1	2a	2h/70°C	MeOH	dppp	93
2	2b	2h/70°C	MeOH	dppp	86
3	2c	2h/70°C	MeOH	dppp	90
4	2c	5h/70°C	C_6F_5OH	dppe	-[c)]
5	2c	5h/70°C	C_6F_5OH	dppp	54
6	2c	5h/70°C	C_6F_5OH	PPh_3	-[d)]
7	5a	3h/70°C	MeOH	dppp	77
8	5b	3.5h/70°C	MeOH	dppp	73
9	5b	16h/70°C	C_6F_5OH	dppp	40
10	5c	3h/70°C	MeOH	dppp	80

[a)] dppp = 1,3-bis(diphenylphosphino)propane, dppe = 1,2-bis(diphenylphosphino)ethane;
[b)] isolated yields, not optimized; [c)] 30% conversion after 5h; [d)] 50% conversion after 72h;

The methyl esters of all three isomeric tetralone carboxylic acids **3** could be obtained in very high yields (entries 1, 2 and 3), the somewhat lower yields for the pentafluorophenyl esters (entries 5 and 9) was due to problems during work up. The triflate of 4-hydroxypropiophenone **5c** gave the corresponding methyl ester **6c** in good yield as well (entry 10).

The preparation of the aryl triflates[9)] and subsequent alkoxy/aryloxy carbonylation[8)] has been carried out at a large scale under very mild conditions. During scale up tetralone was observed as a side product, due to a insufficient carbon monoxide concentration in the reaction medium. Therefore the large scale reactions were carried out under a carbon monoxide pressure of 1.0×10^6 Pa. A reaction time of 4h at 70°C provided a yield of 79% for methyl ester **3c**.

The use of the 1,3-bis(diphenylphosphino)propane (dppp) as ligand was essential[5]. The attempt to run the reaction with the previously reported[6] catalyst $(PPh_3)_2Pd(OAc)_2$ (entry 6) was unsatisfactory. It is not clear if this effect of dppp is due to the higher complex stability because of its bidental complexation ability or due to the inevitable cis-configuration of the palladium complex. Using bis(diphenylphosphino)ethane (dppe) (entry 4) no complete conversion was achieved after 72 hours, though dppe should also be able to build a cis configurated bidental metal complex.

It should be noted that the preparation of the triflates following the published procedure[5] with an 1.5 molar excess of amine and triflic anhydride resulted in the isolation of the surprisingly stable bis-triflate[10] **7** (11%) besides the desired product (76%). So we applied a ratio of phenol/base/triflic anhydride of 1/1.2/1.2 should be carefully observed. The yields for the triflates **2** and **5** are all in the range from 90% (**5b**) to 99% (**5a**)[9].

In summary the palladium catalyzed alkoxycarbonylation appears to be a quite general method, applicable to acyl substituted aromatic systems and to the preparation of pentafluorophenyl esters of the resulting benzoic acids.

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References and Notes

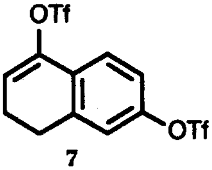
1. Allinger, N.L.; Jones, E.S., *J.Org.Chem.*, **1962**, *27*, 70-76.
2. Haberland, G., *Chem.Ber.*, **1936**, *69*, 1380-1386.
3. *Palladium Reagents in Organic Synthesis*; ed. Heck, R.F., Academic Press: New York. 1985; ch 8.
4. Larock, R.C.; Fellows, C.A., *J.Org.Chem.*, **1980**, *45*, 365-367.
5. Dolle, R.E.; Schmidt, S.J.; Kruse, L.I., *J.Chem.Soc.,Chem.Commun.*, **1987**, 904-905.
6. Cacchi, S.; Ciattini, P.G.; Morera, E.; Ortar, *Tetrahedron Lett.*, **1986**, *27*, 3931-3934.
7. Prince, P.; Gandour, R.D., *Synlett*, **1991**, 405-406.
8. In a typical procedure (entry 3, **table 1**), a mixture of tetralone-7-trifluoromethanesulfonate (294mg, 1.0mmol) **2c**, triethylamine (2.0mmol), palladium(II)acetate (0.03mmol), 1,3-bis(diphenylphosphino)propane (0.03mmol) and methanol (1ml) in DMF (2ml) were purged for ten minutes with carbon monoxide. The reaction mixture was stirred under carbon monoxide atmosphere for 2h at 70°C. After aqueous work up and chromatography on silica gel (eluent: toluene/ethyl acetate= 4/1) 184mg (90%) methyl 1-tetralone-7-carboxylate **3c** (R=Me) was obtained.
   ^{1}H-NMR ($CDCl_3$): δ= 2.17 (mc, 2H, $CH_2C\underline{H}_2CH_2$); 2.70 (t, 2H, $PhCH_2$); 3.03 (t, 2H, CH_2CO); 3.94 (s, 3H, OCH_3); 7.35 (d, 1H, H-5); 8.13 (dd, 1H, H-6); 8.70 (d, 1H, H-8) ppm.
   MS: m/e (relative intensity) 205 (100); 176 (21).
9. The aryl triflates were prepared according to the following procedure: 4.05g (25mmol) 7-hydroxy-1-tetralone **1c** was suspended in 150ml abs. CH_2Cl_2 and cooled to -30°C. 3.21g (30mmol) 2,6-dimethylpyridine, 0.61g (5mmol) 4-N,N-dimethylaminopyridine and 8.46g (30mmol) trifluoromethanesulfonic acid anhydride were added. After 2h stirring at ambient temperature the

reaction mixture was worked up under aqueous conditions and resulted in 7.13g (97%) of tetralone-7-trifluoromethanesulfonate **2c** as a slightly yellow oil, which solidified upon standing in the refrigerator.

^{1}H-NMR ($CDCl_3$): δ= 2.19 (mc, 2H, $CH_2\underline{CH_2}CH_2$); 2.68 (t, 2H, $PhCH_2$); 3.03 (t, 2H, CH_2CO); 7.38 (m, 2H, aromatics); 7.90 (m, 1H, aromatics) ppm.

MS: m/e (relative intensity) 295 (100); 161 (14).

10.



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^{1}H-NMR (d_6-DMSO): δ= 2.35 (m_c, 2H, $CH_2\underline{CH_2}CH$); 2.94 (t, 2H, $PhCH_2$); 6.37 (t, 1H, vinyl); 7.40-7.60 (m, 3H, aromatics) ppm.

MS: m/e (relative intensity) 426 (100); 334 (9); 319 (18); 293 (18).

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