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PALLADIUM-CATALYZED, ONE-POT CARBONYLATION OF HETEROCYCLIC COMPOUNDS INTO THEIR ESTERS, IN THE PRESENCE OF MERCURY SALTS.

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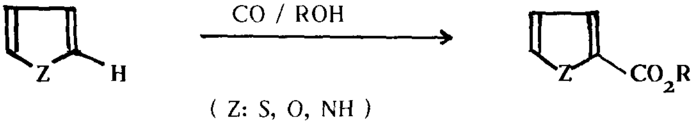
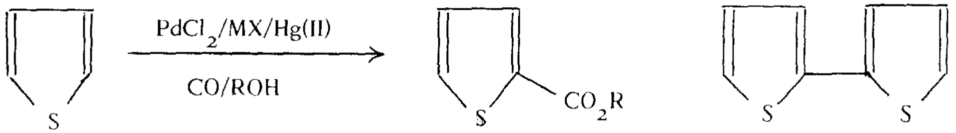
Summary - One pot carbonylation of thiophene, furan, benzofuran and pyrrole in alcohol, to produce the corresponding esters, has been carried out at room temperature, using a $PdCl_2$*/mercury salt/Copper(II) system.*

The carbonylation of aromatic compounds is a potential route to the corresponding carboxylic acid derivatives[1]. The direct carbonylation of arenes, via carbon-hydrogen bond activation with palladium(II) complexes, despite of its importance, has only led to low yield of functionalized arene compounds[2]. Aryl-mercury(II) derivatives, previously prepared[3], or made in situ[4], have already been carbonylated, but the reaction remains stoichiometric as compared to the palladium(II) salt[4], or gives low turnover numbers[3]. In this regard, the only useful method for synthesis appears to be the carbonylation of isolated aryl-thallium[5]. We now report that heterocyclic aromatic compounds, such as thiophene, furan, benzofuran and pyrrole, can be transformed in their ester derivatives under mild conditions, in the presence of a palladium catalyst, via mercury(II) derivatives prepared *in situ* in alcohol.



When thiophene 1 (37 mmol) was treated in alcohol (12 ml) with $PdCl_2$ (1 mmol) and sodium acetate (5 mmol) at room temperature for 24 hours under 50 bar of carbon monoxide, only traces of the ester 2 and of dithienyl 3 were obtained. The addition of 2 mmol of a mercury salt to the reaction mixture increases significantly the yield of 2 (Yields as compared to the Pd salt : 45 % ($Hg_2(NO_3)_2$/LiBr : 2/5) ; 55 % ($HgCl_2$/LiBr : 2/5) ; 65 % ($Hg(O_2CCH_3)_2$/LiBr : 2/5) ; 85 % ($Hg(O_2CCF_3)_2/CH_3CO_2Na$: 2/5 ; 90 % ($Hg(NO_3)_2$/LiBr : 2/5)). The mercuration of aromatic substrates usually requires strong acids such as perchloric acid[6] and heating. It is noteworthy that under our conditions the addition of HBF_4 decreases the yield of 2 and an increase of the reaction temperature to 85°C increases the yield of 3 without optimising the yield of 2.



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2 (R = C_2H_5)
4 (R = CH_3)
5 (R = $CH_2CH_2OCH_3$)

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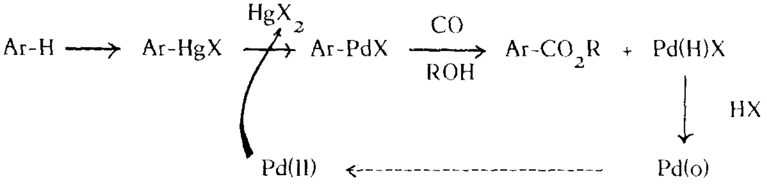
At this stage, the absence of a catalytic reaction was thought to be due to the formation of Pd(0) which does not activate the C-H bond of the heterocycle as indicated in the scheme.



The in situ oxidation of Pd(0) into Pd(II) was attempted with Copper(II) derivatives. When $CuCl_2$ or $Cu(OAc)_2$ was added to the reaction mixture, the yield increased at room temperature to 25.7 % with respect to thiophene[7], i.e. the reaction became catalytic with respect to palladium(II) to reach 8 turnovers (Table 1).

Table 1 : Effect of mercury derivatives on carbonylation of thiophene

mercury derivative	*Yield of the ester 2 (%)*
$Hg(NO_3)_2$	806[a](26.0)[b]
$Hg(O_2CCF_3)_2$	802 (25.7)
$Hg(O_2CCH_3)_2$	412 (13.2)
$HgCl_2$	290 (9.3)
$Hg_2(NO_3)_2$	140 (4.2)

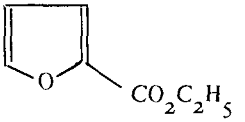
[a]Yield, based on Pd(II), determined by gas chromatographic analysis using internal standard. [b]In brackets, yiel based on thiophene : a typical procedure is described in ref. 7.

The yield of 2 depends on the nature of the Hg(II) salt and the following sequence, which corresponds to the sequence of electrophilic substitution of arenes[8], was observed.

$$Hg(NO_3)_2 \sim Hg(O_2CCF_3)_2 > Hg(O_2CCH_3)_2 > HgCl_2 > Hg_2(NO_3)_2$$

The addition of a co-catalyst i.e. LiBr, LiCl, NaOAc and NaF contributes positively to the formation of esters.

The reaction of thiophene, in methanol and in 2-methoxyethanol under mild conditions, led to the formation of the esters 4 and 5. The heterocyclic compounds : furan, benzofuran and pyrrole were carbonylated in ethanol and the corresponding esters **6**, 7 and **8** were then obtained. (Table 2)



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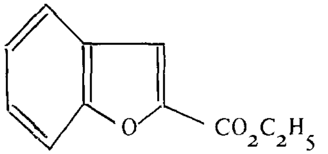

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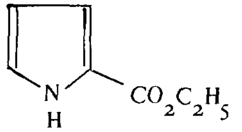

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Table 2 : Carbonylation of heterocyclic compounds in alcohol

substrate	*mercury salt*	*solvent*	*Yield of the ester (%)*[7]
Thiophene	$Hg(O_2CCH_3)_2$	ethanol	**4** : 444[a] (14.1)[b]
Thiophene	$Hg(O_2CCH_3)_2$	methoxy-ethanol	5 : 282 (9.0)
Furan	$Hg(O_2CCF_3)_2$	ethanol	**6** : 245 (7.85)
Benzofuran	$Hg(O_2CCH_3)_2$	ethanol	7 : 150 (4.85)
Pyrrole	$Hg(O_2CCH_3)_2$	ethanol	**8** : 125 (4.0)

[a] Yield based on Pd. [b] Yield based on the heterocycle

Our results show that heterocyclic aromatic compounds can be transformed regioselectively into esters, using Hg(II) and Pd(II) derivatives at room temperature, more easily than other aromatic compounds[3,4]. It is clear that a catalytic reaction with respect to palladium can be achieved when a slight excess of Hg(II) and Cu(II) salts are used in situ, leading to the formal transformation of a C-H group into a $C\text{-}CO_2R$ group.

References and notes

1. L. Cassar, G.P. Chiusoli and F. Guerrieri, Synthesis, 1973, 502.
2. Y. Fujiwara, T. Kawauchi and H. Taniguchi, J. Chem. Soc. Chem. Commun., 1980, 220. Y. Fujiwara, I. Kawata, T. Kawauchi and Taniguchi, Ibid, 1982, 132.
3. R.M. Henry, Tetrahedron lett., 1968, 2285.
4. A. Chiesa and R. Ugo, J. Organometal. Chem., 1985, 279, 215.
5. R.C. Larock and C.A. Fellows, J. Org. Chem., 1980, 45, 363.
6. B.F. Hegarty and W. Kitching, J. Org. Chem., 1976, 41, 2247.
7. The following procedure was used for the preparation and the isolation of the ester **2** : In an autoclave were introduced, anhydrous lithium bromide (2 mmol), palladium(II) chloride (0.1 mmol), mercury(II) trifluoroacetate (3.5 mmol), copper(II) acetate (4 mmol) and 3.12 mmol of thiophene in 10 ml of dry ethanol. The autoclave was charged with carbon monoxide (50 bar). The reaction mixture was stirred at room temperature over 20 h. Ether and activated carbon were added to the reaction mixture, which was filtered, washed with saturated ammonium chloride and dried over sodium sulfate. Removal of the solvent and the excess of thiophene provided 0.085 g of **2** (17.6 % based on thiophene, 25.7 % in gas chromatography).
8. J.L. Wardell, Comprehensive Organometallic Chemistry, Pergamon Press Ltd, 1982, Vol.2, 873.

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