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A NOVEL DEFORMYLATION REACTION DURING THE HOMOGENEOUS PLATINUM CATALYZED ISOTOPIC HYDROGEN LABELLING OF α-HYDROXYACIDS AND RELATED COMPOUNDS; A COMPARISON WITH HETEROGENEOUS PLATINUM.[1]

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Recently the discovery of homogeneous $PtCl_4^{2-}$ catalysed exchange of isotopic hydrogen with aromatic and aliphatic compounds has been reported[2-5]. This system is valuable for labelling compounds with deuterium and/or tritium in one-step and constitutes the homogeneous equivalent of the well known heterogeneous platinum technique[6].

With respect to the exchange of benzilic acid and its derivatives on heterogeneous Group VIII transition metals, these compounds simultaneously deformylate to the corresponding ketones[7,8]. Benzhydrol also decomposes to benzophenone under these conditions whereas mandelic acid is stable and only deuterates[7,8].

It is the purpose of the present communication to report the exchange of a range of α-hydroxy acids and their derivatives using the new homogeneous $PtCl_4^{2-}$ catalytic system. The results are important particularly if the $PtCl_4^{2-}$ technique is to be used to label these type compounds with deuterium and/or tritium, since any secondary reactions observed will limit the general applications of the technique.

The significant feature of the data in Tables 1 and 2 is that benzilic acid deformylates very easily at 75° in the presence of homogeneous platinum, whereas benzhydrol does not and only exchanges. These results are to be compared with the corresponding heterogeneous platinum work where both compounds yield benzophenone. The benzilic acid system thus appears to be the first homogeneous metal catalyzed deformylation reaction reported.

Other important aspects of the data in Tables 1 and 2 are that all compounds studied exchange at relatively low temperatures with heavy water in the presence of the homogeneous $PtCl_4^{2-}$ catalyst. Even residual benzilic acid (Tables 1 and 2) which has not deformylated is deuterated appreciably. Thus exchange and deformylation are competing reactions with homogeneous $PtCl_4^{2-}$ and the system is analogous to the heterogeneous platinum work. With the esception of phenylallyl ether where isotope incorporation was too low for n.m.r. orientation, all compounds deuterated predominantly in the meta and para positions of the aromatic rings. The n.m.r. orientations were confirmed by the d_3 cut-offs in the low voltage mass spectra for benzilic acid (run 5) and benzhydrol (run 6).

Table 1

Homogeneous Platinum Catalysed Exchange of α-Hydroxyacids and Related Compounds. [a]

Run	Compound	Temp (^{o}C)	Time (hr)	Atom % Theor.	D Found	Deuterium Distribution						
						d_0	d_1	d_2	d_3	d_4	d_5	d_6
1	Mandelic acid	75	5	68.5	15.9	35.2	23.2	22.5	17.2	1.8		
2	Benzilic acid	75	5	76.5	16.5	20.3	20.3	20.8	15.0	13.2	7.8	2.6
3	Phenyl acetic acid	75	5	79.5	14.1	41.1	21.2	14.6	1.3			
4	Phenol	75	5	74.8	29.5	27.6	31.2	19.4	12.4	6.8	2.6	
5	Benzilic acid	75	24	79.5	24.5	14.6	11.3	15.2	18.5	16.8	13.3	8.4
6	Benzhydrol	75	24	81.2	21.3	21.2	14.3	14.7	15.8	12.8	13.2	8.0
7	Cinnamic acid	75	24	80.6	9.7	51.1	21.3	17.5	9.7	0.4		
8	Benzilic acid [b]	130	24	76.3								
9	Benzyl alcohol	75	24	61.1	6.9	67.8	9.2	12.0	8.5	2.5		
10	Phenylallyl ether	75	24	88.4	2.3	82.6	13.2	3.3	0.9			

[a] Reaction conditions involved compounds (0.1g) in solution (2g) containing CH_3COOD (1.0M), D_2O (o.5M), Na_2 $PtCl_4$ ($1.3x10^{3}M$) and DCl ($1.3x10^{-3}M$).

[b] Benzophenone only formed and analysis reported in Table 2.

Table 2

Yields of Benzophenone from Exchange of Benzilic Acids Reported in Table 1.

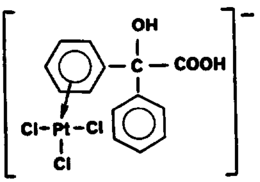
Run (Table 1)	Yield Benzophenone (% Deformylation)	% Atom D	Deuterium Distribution							
			d_0	d_1	d_2	d_3	d_4	d_5	d_6	d_7
2	54.2	22.8	19.6	17.4	19.7	18.2	13.0	8.5	3.6	
5	71.1	31.1	11.3	10.5	14.8	19.2	18.9	15.5	8.5	1.3
8	100	23.1	5.2	14.6	18.6	31.8	15.1	2.2	1.4	1.1

The d_3 followed by d_6 cut-off patterns in these samples suggest that complexing with the platinum occurs not with the molecule as a whole but with each ring of the compound in turn similar to the polyphenyl results with this same catalyst (e.g. diphenyl, and the terphenyls)[9]. With mandelic and cinnamic acids where some d_4 species is present, the side-chain hydrogens have also exchanged although to a limited extent.

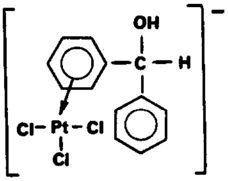
With respect to the possible use of the homogeneous $PtCl_4^{2-}$ system for general deuterium and tritium labelling, the present results are important since it is obvious that the $PtCl_4^{2-}$ technique can be used to deuterate and/or tritiate all compounds studied with the possible exception of benzilic acid. Even benzhydrol, which decomposes to benzophenone on heterogeneous platinum, can be labelled without decomposition using the present homogeneous catalyst. It is also significant that phenylallylether shows no tendency to rearrange to the corresponding allylphenol (catalytic Claisen) during the exchange despite the ease with which benzilic acid deformylates. It may even be possible to tritiate benzilic acid by the present technique, if short conversion times are used (Table 1, run 2) such that the yield of benzophenone is minimized, thus enabling the parent benzilic acid to be separated from the ketone and purified radiochemically.

Mechanistically, where exchange has occurred in the aromatic rings of the parent compounds, it is proposed that isotope incorporation takes place predominantly by the homogeneous π-dissociative process already discussed[5]. The meta, para orientation of isotope in the aromatic rings confirms this suggestion. A simultaneous contribution from a homogeneous π-associative process cannot be unequivocally eliminated as this time however, the π-dissociative mechanism is preferrred for reasons previously outlined. Where deuteration is found in the side-chain, such as in mandelic acid (d_4 cut-off in mass spectrum, Table 1, run 1) the mechanism of exchange presumably involves π-allylic species[4,9] as has been proposed for the labelling of the alkyl group in the alkylbenzenes, particularly toluene and the xylenes[9].

With respect to homogeneous metal catalysed deformylation in benzilic acid, again, by analogy with the heterogeneous process[7,8] it is proposed that π-complex formation (I) with the metal assists in the release of severe strain due to the extensive crowding of the functional groups around the central carbon atom. With benzhydrol (II), the crowding is not so pronounced and thus homogeneously, benzyhdrol does not convert to benzophenone. The benzhydrol example accentuates the role of the surface in the heterogeneous reaction. Crowding during adsorption on the surface leads to benzophenone formation heterogeneously whereas in a homogeneous medium both metal and benzhydrol are more mobile and the resulting complex does not possess the same degree of strain as when the complex is formed with a surface platinum atom.



(I)



(II)

The fact that exchange and deformylation occur with benzilic acid in the presence of both *homogeneous* and *heterogeneous* platinum catalysts is further evidence to support the π-complex theory of catalysis[5] since analogous π-complex intermediates and π-complex mechanisms can be proposed for exchange and deformylation in the two catalytic systems.

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