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NOVEL REACTIONS DURING THE CATALYTIC DEUTERATION OF α-HYDROXY ACIDS AND RELATED COMPOUNDS *

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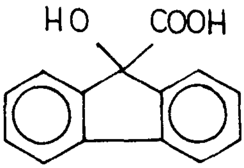
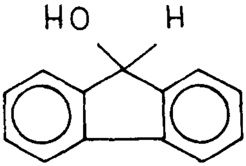
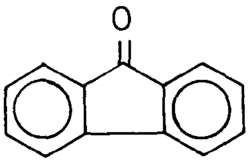
Isotopic hydrogen exchange reactions catalysed by group VIII transition metals are of importance in tracer studies (1), particularly in molecular structure determination (2,3). We wish to report novel reactions observed during the catalytic labelling of α-hydroxy acids(R.R' . C . OH . COOH) and related compounds such as benzhydrol. Under the above conditions, benzilic acid (R = R' = C_6H_5) and certain derivatives decompose to di-aryl ketones with the elimination of elements of formic acid, whereas mandelic acid (R = C_6H_5, R' = H) derivatives are stable and only exchange. The compound 9-hydroxy fluorene-9-carboxylic acid (I) decomposes to two products, 9-fluorenol (II) and a small amount of 9-fluorenone (III). With benzhydrol where the -COOH group in benzilic acid is replaced by H, benzophenone is also formed in appreciable yields. In the absence of



(I)



(II)



(III)

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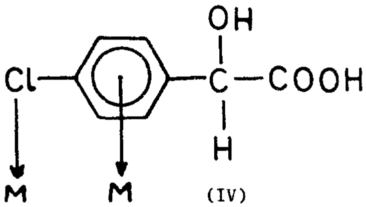
* Part XVII of a Series entitled "Catalytic Deuterium Exchange Reactions with Organics". Part XVI, J. Catalysis (in press).

catalyst the benzilic acids, benzhydrol and the fluorene derivative (I) are stable. In contrast to the aromatic acids, aliphatic α-hydroxy acids, such as lactic acid, exchange catalytically with D_2O at 120 - 130°C without decomposition (4).

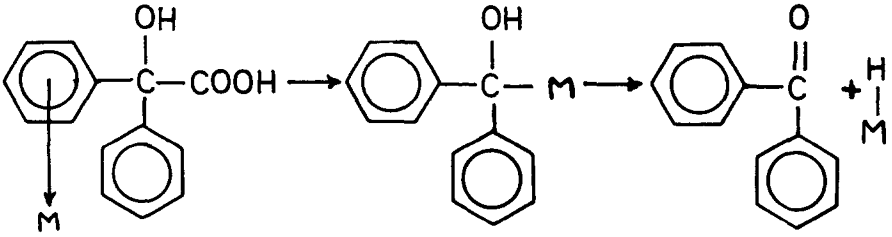
The significant feature of typical results (Table) is the complete decomposition of (I) and the relative degree of decomposition exhibited by the various benzilic acids and benzhydrol during exchange in the presence of either hydrogen pre-reduced or "self-activated" (7) platinum oxide. Usually di-aryl ketones are prepared from the corresponding benzilic acids by oxidative fissure with chromic acid (8), whilst (II) has been obtained from (I) by reaction with 2-chlorotriethylamine (9). Because of the observed decomposition, catalytic methods for the labelling of these acids and related compounds should be used with caution since the presence of additional reaction products containing an appreciable concentration of isotope renders purification of the final product difficult, particularly radiochemical purification when tritium is used (10).

The mechanism whereby the parent α-hydroxy acids and related compounds deuterate or deformylate may be interpreted in terms of π -complex adsorption (1). In the mandelic acids (Table), the p-chloro derivative exchanges less readily than the parent compound, this result being consistent with the fact that benzene is more reactive in catalytic deuteration than chlorobenzene (11) and may be attributed to a halogen-catalyst interaction (IV) in addition to normal π -complex formation leading to increased adsorption strength and increased reagent displacement. The p-phenyl mandelic acid result, when compared with mandelic acid, is similar to diphenyl which deuterates less readily than benzene (11). Diphenyl possesses a lower ionisation potential than benzene, leads to stronger π -complex formation, greater reagent displacement and decreased deuteration.



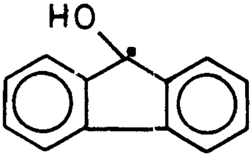
(IV)

For the interpretation of deformylation, scale models of the benzilic acids show that extensive crowding of functional groups exists around the carbon atom to which are attached the aromatic groups. It is thus possible that π -complex adsorption assists the release of severe strain in the molecule, presumably at the -C-COOH bond since this is the critical bond which is ruptured to give benzophenone. The probable sequence of events leading to ketone formation shows the original molecule (V) adsorbed as a π -complex, strain is released by -C-COOH bond rupture and the resulting species (VI) is σ -complexed to the catalyst surface. Desorption of the molecule as benzophenone with the loss of a proton may then occur.

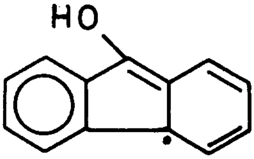


(V) (VI) (VII)

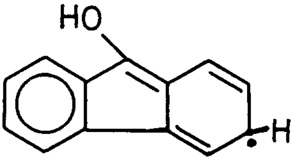
The process may be considered as analogous to the proposed π - σ conversion in the Dissociative π -Complex Substitution Mechanism for aromatic exchange (1). The chlorine atoms in o, o'-dichlorobenzilic acid should restrict rotation around the central carbon atom, thus hindering π -complex formation and decreasing the extent of deformylation. In the case of (I), the results probably reflect the degree to which charge delocalisation occurs into adjacent aromatic rings when the ruptured -C-COOH bond is directly attached to an aromatic ring. The contribution of species such as (IX) and (X) to the overall equilibrium would then be greater than species (VIII), so that (II) is the main decomposition product in this instance.



(VIII)



(IX)



(X)

A series of twenty-six acids related to mandelic and benzilic acids have been investigated in this work and the results follow the pattern of the data reported in the attached Table. Full details of this research will be reported elsewhere.

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TABLE

Catalytic Exchange of α-Hydroxy Acids and Related Compounds.

α-Hydroxy Acid (R.R'.C.OH.COOH)	R	R'	% Decomp. (Hydrogen Reduction) (a)	Atom % D in α-Hydroxy Acid (a)	% Decomp. (Self Activation) (b)	Atom % D in α-Hydroxy Acid (b)
Mandelic Acid	C_6H_5	H	Nil	33.0	Nil	43.4
p-Chloromandelic Acid	p-Cl C_6H_4	H	Nil	20.6	-	--
p-Phenylmandelic Acid	$C_6H_5C_6H_4$	H	Nil	26.7	Nil	14.0
Benzilic Acid	C_6H_5	C_6H_5	36.5	33.7 (c)	16.2	40.0 (d)
o,o'-Dichlorobenzilic Acid	o-Cl C_6H_4	o-Cl C_6H_4	16.9	--	8.6	--
p,p'-Dimethyl benzilic Acid	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	22.3	--	9.2	--
9-Hydroxy fluorene-9-carboxylic Acid (e)			100.0		100.0	
Benzhydrol (f)			50.8			

(a) *On platinum pre-reduced with hydrogen except the benzhydrol result which used a borohydride re-duced catalyst (5).* A typical experiment involved pre-reduced PtO_2 (100 mg), compound (10^{-2} M), D_2O (17×10^{-2} M), K_2CO_3 (0.25×10^{-2} M), stood at 130°C for two days. Platinum has been used in these experiments since this transition metal is the most active in aromatic exchange (6). Deuterium analysis was performed by mass spectrometry (5).

(b) On platinum self-activated (7).

(c) Benzophenone formed contained 44.7 atom % D.

(d) " " " 57.1 " "

(e) Acid decarboxylates to 9-fluorenol with a small amount of 9-fluorenone.

(f) Although not an hydroxy acid, compound used for comparison.

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