Homogeneous Metal-catalyzed Isotopic Hydrogen Exchange in Aromatic Compounds. The Labelling of Nitrobenzene, Bromobenzene, Naphthalene, and Acetophenone.

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METAL-CATALYZED exchange between aromatic compounds and isotopic water has been confined to heterogeneous systems, platinum being the most active of the Group VIII transition metals.[1] Recently the first analogous homogeneous exchange of aromatic compounds has been reported using Pt^{II} salts as catalysts.[2] We have since discovered that rapid exchange also occurs by the present homogeneous catalytic method in four very important representative compounds namely; nitrobenzene, bromobenzene, naphthalene, and acetophenone. The reactivity of these particular compounds is significant since it indicates that certain groups of compounds which are difficult to label by the heterogeneous method can be tagged by the present homogeneous procedure. The results are thus important to (i) the mechanisms of fundamental heterogeneous and homogeneous catalysis and (ii) the extension of one-step preparative methods available for the general isotopic hydrogen labelling of molecules.

Using bromobenzene as an example, a typical reaction involves the heating of an evacuated sealed glass ampoule containing sodium chloroplatinite (0·02 M), hydrochloric acid (0·02 M) dissolved in acetic acid (1·8 ml.), deuterium oxide (0·5 ml.) and bromobenzene (0·3 ml.) to 130° for 10 hr., the isotope incorporation being shown in the Table. The acetic acid is necessary to produce a homogeneous phase and a minimum of mineral acid is required to prevent precipitation of metallic platinum. Precipitated platinum, analogous to the self activation[3] observed in heterogeneous catalysis, prepared under the present conditions does not catalyse exchange. Higher acid concentrations inhibit homogeneous metal-catalyzed deuteration and result in exclusive acid exchange in those compounds where this is possible. Deuterium is used for illustration purposes in the Table, since low-voltage mass spectrometry and n.m.r. can be utilized to estimate quickly both the degree of isotope incorporation and orientation. The labelling method is, however, applicable to deuterium and/or tritium.

The observation that nitrobenzene exchanges homogeneously (Table) is important since nitro-groups poison rapid exchange by heterogeneous catalytic methods;[4] thus a whole range of nitro-aromatic compounds is now amenable to isotopic hydrogen labelling in one step. Further, the poisoning of nitro-compounds on heterogeneous platinum has been attributed to hydrogen atom scavenging from the surface of the catalyst by the nitro-group, thus preventing exchange with a Pt–D species in a π-complex substitution mechanism.[1,4,5] The homogeneous nitrobenzene result would thus imply that free hydrogen atoms or even a metal hydride complex do not participate in the mechanism of the homogeneous process. The isotope orientation in nitrobenzene from the cut-off in the low-voltage mass spectrum and n.m.r. (Table, benzene included for reference) further supports previous evidence[2] which indicates that the exchange is not acid-catalyzed but occurs *via* a homogeneous Pt^{II} complex.

The ability to label bromobenzene readily (Table) is useful since this compound is a valuable intermediate for Grignard and related reactions in the synthesis of other labelled products. Heterogeneous exchange of bromobenzene on platinum is very slow and inefficient,[1,5] only 4% isotope incorporation after 46·5 hr. at 130° being observed[1] whereas homogeneously (Table), deuteration is rapid particularly in the *meta*- and *para*-positions, this orientation further supporting a mechanism involving predominant homogeneous metal catalysis as distinct from acid catalysis.

In heterogeneous exchange, naphthalene was an important compound in the development of charge-transfer adsorption since it possesses a low ionization potential and is thus strongly bound to the catalyst surface, leading to displacement of the second reagent (D_2O) in the exchange with subsequent slow deuteration.[1] This conclusion is confirmed by the homogeneous results (Table) where the concept of reagent displacement is no longer applicable and exchange is rapid, particularly in the β-positions. At 80°, orientation in naphthalene is exclusively β, whereas at 130° all positions exhibit appreciable reactivity.

The results for acetophenone are interesting (Table), since this compound does not exchange heterogeneously in the ring. The source of the poisoning is not clear, although it has been attributed[5] to hydrogen scavenging similar to that suggested for nitrobenzene.[4] However, by analogy with naphthalene, it is also plausible to attribute this to a reagent displacement effect from strong preliminary adsorption of the compound, presumably as the enol. Either suggestion is supported by the rapid homogeneous ring exchange which is more extensive in the *meta*- and *para*-positions in acetophenone.

The orientation of isotope from the homogeneous exchange, particularly the strong *ortho*-deactivation effects exhibited by a wide range of compounds including two of the four reported in the Table, suggests a similarity in mechanism of exchange between homogeneous and heterogeneous systems presumably through π-complex intermediates.[1,5]

The present data serve to illustrate the versatility of the new homogeneous metal-catalyzed exchange

TABLE

Homogeneous exchange of selected aromatic compounds using sodium chloroplatinite

Compound	Reaction time (hr.) at 130°	% Deuterium incorporation	Deuterium distribution								
			D_0	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8
Benzene	3	68·0	1·4	2·1	7·4	18·7	3·08	28·4	11·3		
Nitrobenzene	10	12·5 (*ortho*)									
		82·7 (*meta, para*)	0	6·0	31·5	49·0	12·3	1·3			
Bromobenzene	10	8·5 (*ortho*)									
		89·2 (*meta, para*)	0·1	2·8	22·2	62·7	11·1	1·0			
Naphthalene	10	38·2 (α)	0·1	0·4	1·4	4·4	14·2	33·7	30·2	12·7	2·7
		90·0 (β)									
Acetophenone	2	41·0 (*ortho*)									
		47·0 (*meta, para*)									
		63·5 (Methyl)	0·0	3·0	9·6	19·8	26·4	22·8	13·2	3·6	0·9

procedure both in catalytic mechanistic studies and also in general deuterium/tritium labelling work. With respect to the latter field, the technique has significant advantages for the labelling of aromatic compounds when compared with Wilzbach gas irradiation[6] for tritium and heterogeneous exchange with isotopic water.[1]

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