Rapid Deuteriation and Tritiation of Organic Compounds using Organometallic and Elemental Halides as Catalysts

By **Mervyn A. Long,* John L. Garnett,** and **Ross F. W. Vining,** School of Chemistry, The University of New South Wales, Kensington, N.S.W., Australia

The use of ethylaluminium chloride and a range of other halides, such as $NbCl_5$, WCl_6, $SbCl_5$, and BBr_3, as catalysts for the rapid deuteriation and tritiation of a variety of organic compounds is described in detail. In the deuterium exchange method $[^2H_6]$benzene is the isotope source and traces of water usually serve as co-catalyst. But for maximum reproducibility very dry conditions with HCl as co-catalyst are recommended. The tritiation procedure involves the use of traces of high specific activity tritiated water to hydrolyse a complex of the catalyst with the organic substrate, tritium labelling accompanying the hydrolysis. These simple and rapid labelling methods are particularly suitable for aromatic compounds and their derivatives and to a lesser extent alkenes and some oxygen-containing organic compounds. The possible role of π-complex intermediates in these reactions is discussed.

METAL halides such as $AlCl_3$ and $SbCl_5$ promote halogenation and polymerisation of aromatic compounds,[1] and many produce radical cations with polynuclear aromatics.[2] Recently, we reported [3] that related halides such as $EtAlCl_2$ were very active catalysts for deuteriation and/or tritiation of certain organic compounds. This paper describes in detail these new, simple, and rapid labelling techniques and discusses the role of co-catalysts, particularly their importance in the reproducibility of the method.

Platinum-catalysed exchange methods were previously the most widely applied techniques for deuteriation and tritiation,[4] both heterogeneous platinum metal [5] and homogeneous platinum complexes [6] being used with water as isotope source. Other Group VIII transition metal surfaces [7] and recently, iridium salts,[8,9] have also been proposed as alternatives to platinum. Retardation at sterically hindered positions [5,6] and coupling of aromatic compounds, such as the formation of diphenyl from benzene [10] complicate the labelling of aromatic compounds by these Group VIII transition metals.

Balaban and his co-workers have utilised tritiated water-promoted aluminium chloride to label derivatives of benzene and related compounds.[11-14] Prolonged re-

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[1] 'Friedel–Crafts and Related Reactions,' ed. G. Olah, Interscience, New York, 1964.

[2] O. W. Howarth and G. K. Frankel, *J. Amer. Chem. Soc.*, 1966, **88**, 4514; W. F. Forbes and P. D. Sullivan, *Ibid.*, 2862.

[3] J. L. Garnett, M. A. Long, R. F. W. Vining, and T. Mole, *J. Amer. Chem. Soc.*, 1972, **94**, 5913; M. A. Long, J. L. Garnett, R. F. W. Vining, and T. Mole, *ibid.*, p. 8632; J. L. Garnett, M. A. Long, R. F. W. Vining, and T. Mole, *J.C.S. Chem. Comm.*, 1972, 1172; *Tetrahedron Letters*, 1973, 4075.

[4] J. L. Garnett, *Nucleonics*, 1962, **20**, 86.

[5] J. L. Garnett, *Catalyst Rev.*, 1971, **5**, 229.

[6] J. L. Garnett and R. S. Kenyon, *Chem. Comm.*, 1971, 1227 and references cited therein.

[7] J. L. Garnett, Proc. Int. Conf. Methods Prep. Storage Labelled Compounds, EURATOM, Brussels, 1968, p. 689.

[8] J. L. Garnett, M. A. Long, A. B. McLaren, and K. B. Peterson, *J.C.S. Chem. Comm.*, 1973, 749.

[9] J. L. Garnett, M. A. Long, and K. B. Peterson, *Austral. J. Chem.*, 1974, **27**, 1823.

[10] G. E. Calf and J. L. Garnett, *Chem. Comm.*, 1969, 373.

[11] C. Mantescu and A. T. Balaban, *Canad. J. Chem.*, 1963, **41**, 2120.

[12] C. Mantescu, A. Genunche, and A. T. Balaban, *J. Labelled Compounds*, 1965, **1**, 178.

[13] C. Mantescu, A. Genunche, and A. T. Balaban, *J. Labelled Compounds*, 1966, **2**, 26.

[14] C. Mantescu, A. Genunche, D. Dutz-Cristu, and A. T. Balaban, *J. Labelled Compounds*, 1966, **2**, 267.

action times at elevated temperatures were necessary. Thus, chlorobenzene exchange was incomplete even after 3 h at 100°.[11]

The new procedures described in this paper do not suffer many of the difficulties of the older labelling methods, but the actual deuterium exchange rates may be subject to a lack of reproducibility as was experienced when some Lewis halide type catalysts were used in the field of polymerisation. For this reason, two experimental procedures for deuteriation are described, the first of which shows that the problem of reproducibility may be overcome and consistent exchange rates obtained, but it is a more complex and rigorous procedure. The second method is simpler and faster but may occasionally give poor reproducibility in exchange rate for reasons that are discussed.

RESULTS

The two procedures described for deuteriation are fundamentally different to the procedure described for tritiation. Deuteriation proceeds by exchange with compounds such as [$^2H_6$]benzene as isotope source. While it is possible to use [^3H]benzene as the isotope source in a tritiation procedure analogous to that of deuteriation, the proposed procedure involving the use of a trace of tritiated water of high specific activity to hydrolyse a solution of the halide catalyst in the organic compound to be labelled is very much simpler and does not require the prior production of [^3H]benzene. Adequate tritium labelling accompanies the hydrolysis. In contrast, the HTO method is not adaptable to deuteriation with D_2O as the deuterium source since the procedure would yield only relatively low deuterium: hydrogen ratios in the product. Deuteriation requires substantial deuterium : hydrogen ratios in the product while tritiation does not. Adequate radioactivity in a tritiated substance, for most purposes, results from relatively low tritium : hydrogen ratios.

Of the two methods described for deuteriation (see Experimental section) method 1, in which all reagents are rigorously dried and HCl is added as co-catalyst, is the more complex and time consuming, but always yields consistent and reproducible exchange results. In method 2, where the amount of water is not rigorously controlled and the traces of water present act as co-catalyst, the procedure does not always yield consistent results. But method 2 is fast and simple and is satisfactory for deuteriation of a wide range of compounds. Only when difficulty in labelling is encountered using method 2 is it necessary to adopt the more detailed procedure of method 1.

(a) *Deuteriation with* $MeAlCl_2$ *Catalyst and* HCl *Co-catalyst.*—Toluene, chlorobenzene, *m*-xylene, and naphthalene were exchanged with C_6D_6 (Table 1) under the rigorous conditions described in method 1. In each case exchange at room temperature was complete within 5 min of the addition of the HCl co-catalyst. The number of hydrogen atoms exhibiting exchange (mass spectra) corresponded to the number of aromatic hydrogen atoms only, in each substance.

(b) *Deuteriation with* $EtAlCl_2$ *Catalyst and* H_2O *Co-catalyst at Room Temperature.*—Table 2 lists a range of alkyl and halogen substituted aromatic compounds, all of which rapidly exchanged to equilibrium with C_6D_6 using $EtAlCl_2$ as catalyst and dissolved water as co-catalyst (*i.e.* deuteriation method 2) within 30 min at room temperature. Mass spectral and n.m.r. analysis showed that all aromatic hydrogens and no alkyl hydrogen exchanged. Heating of the normal reaction mixture containing toluene to 100° for one week confirmed the absence of alkyl substituent exchange.

TABLE 1

Deuteriation of aromatic compounds with $MeAlCl_2$–HCl [a]

Compound	% Approach to equilibrium [b]	Observed exchangeable H per molecule
Toluene	100	5
Chlorobenzene	100	5
m-Xylene	100	4
Naphthalene	100	8

[a] Analysis after 5 min at room temperature; procedure as in deuteriation method 1 using C_6D_6 as isotope source. [b] Calculated on the basis of aromatic hydrogen atom exchange only.

TABLE 2

Aromatic compounds exhibiting rapid deuteriation at room temperature with $EtAlCl_2$–H_2O [a]

Compound	Observed exchangeable H per molecule [b]
Toluene	5
Methylbenzene	5
Isopropylbenzene	5
t-Butylbenzene	5
o-Xylene	4
m-Xylene	4
p-Xylene	4
Mesitylene	3
3-Phenylpropene	5
4-Phenylbutene	5
Fluorobenzene	5
Chlorobenzene	5
Bromobenzene	5
Biphenyl	10
Diphenylmethane	10
Bibenzyl	10
o-Terphenyl	14
m-Terphenyl	14
p-Terphenyl	14
Naphthalene	8

[a] Procedure as in deuteriation method 2. $EtAlCl_2$ as catalyst, H_2O as co-catalyst, C_6D_6 as isotope source. Analysis within 30 min at room temperature. [b] All compounds listed showed 100% approach to equilibrium calculated on the basis of aromatic H exchange only. No further exchange was observed on heating a number of the reaction mixtures to 90° for one week.

There were no significant side reactions such as the formation of diphenyl from benzene. No steric hindrance or electronic deactivation of any aromatic position was observed for the compounds in Table 2 including the very hindered orthoposition in *m*-terphenyl which is deactivated in other catalytic systems.[15] However, rates of exchange in pentafluoro- and 1,2,3,4-tetrafluoro-benzene were comparatively slow, equilibrium being reached only after several days at room temperature. In view of the absence of steric effects in compounds such as the terphenyls this retardation of exchange is thought to be predominantly an electronic effect of the fluorine substituents.

(c) *Deuteriation with* $EtAlCl_2$ *Catalyst and* H_2O *Co-catalyst at* 90°.—Table 3 contains a variety of organic compounds tested for exchange with C_6D_6 using $EtAlCl_2$ as

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[15] R. J. Hodges and J. L. Garnett, *J. Phys. Chem.*, 1969, **73**, 1525.

catalyst in deuteriation method 2. In each case the sealed reaction ampoule was held at 90° for one week prior to quenching of the catalyst with water and analysis of the *substrate*. The only listed compounds to exchange were the condensed polycyclic compounds. Unlike the compounds in Table 2, these did not significantly exchange in 30 min at room temperature. All oxygen- and nitrogen-containing compounds tested, together with alkanes and alkenes failed to exchange in one week at 90°. Finally, the ability of some of these compounds to poison the exchange of toluene with C_6D_6 in the presence of $EtAlCl_2$ was also tested. Many of these compounds completely hindered toluene exchange indicating their preferential reaction with the catalyst. Others, such as alkanes, permitted exchange of toluene with C_6D_6 to equilibrium, indicating the absence of significant association between compounds such as alkanes and $EtAlCl_2$.

TABLE 3

Compounds tested for exchange with C_6D_6 [a] and effect on toluene exchange,[b] $EtAlCl_2$–H_2O at 90° for one week

Compound [c]	% Approach to equilibrium	Exchangeable H per molecule	Degree of toluene exchange
Anthracene	100	10	100
Phenanthrene	100	10	100
Chrysene	100	12	100
Pyrene	100	10	100
Benzoic acid	0	0	100
Phenylacetic acid	0	0	100
Phenol	0	0	80
Triphenylmethyl alcohol	0	0	20
Triphenylamine	0	0	10
n-Hexane	0	0	100
Cyclohexane	0	0	100
Cyclopentane	0	0	100
Ethyl iodide	0	0	100

[a] Reaction conditions for exchange with C_6D_6: $EtAlCl_2$ as catalyst, H_2O as co-catalyst, analysis after one week at 90°; procedure as in method 2. [b] Reaction conditions for study of effect on toluene–C_6D_6 exchange: $EtAlCl_2$ (0.1 g) was added to a mixture of compound under test (0.1 ml), toluene (0.1 ml), and C_6D_6 (0.2 ml). Sample sealed and stored at 90° for 1 week. Procedure otherwise as in method 2. Degree of toluene exchange is % approach to equilibrium calculated on the basis of complete exchange of all aromatic H in toluene. [c] In addition to compounds above the following compounds exhibited zero exchange after one week at 90°, and also completely inhibited the exchange of toluene: benzyl alcohol, phenethyl alcohol, methanol, pyridine, α-picoline, β-picoline, γ-picoline, 2,6-lutidine, 2-phenylpyridine, quinoline, isoquinoline, aniline, *N*-methylaniline, *N*-allylaniline, *NN*-dimethylaniline, diphenylamine, benzonitrile, pyrrole, azobenzene, thiophen, azulene, anisole, phenetole, diethyl ether, benzaldehyde, phenylacetaldehyde, acetophenone, benzhydrol, methyl benzoate, mandelic acid, acetic acid, and 1-methylcycloheptene.

(d) *Tritiation with Tritiated Water and* $EtAlCl_2$ *as Catalyst.*—Tables 4—6 list a variety of organic compounds tested for their ability to tritium label at room temperature by the procedure outlined in the Experimental section, where water (5 Ci g^{-1}) was the isotope source and $EtAlCl_2$ the catalyst. In addition, the results of competitive reactions, in which a mixture of toluene and the compound under test was treated in the same manner as the pure compounds, are listed. Because of the vigorous nature of the reaction which occurs on the addition of the small quantity of tritiated water to the labelling mixture the exact extent to which the added tritium is incorporated into the organic compound varied between duplicate experiments. For this reason the degree of isotope incorporation expressed as a percentage of tritium added was divided into four categories: <0.1, 0.1—1, 1—10, 10—100%. Within these categories the results were reproducible. No by-products were detected in the g.l.c. analyses with the exception of some tritiated ethane which presumably results from the hydrolysis of the $EtAlCl_2$ catalyst.

TABLE 4

Aromatic compounds labelled by tritiated water using $EtAlCl_2$ catalyst

Compound	% Incorporation of tritium into compound [a]	% Incorporation into toluene in competitive reaction [a]
Benzene	10—100	
Toluene [b]	10—100	
Ethylbenzene	10—100	
o,m,p-Xylene	10—100	
Naphthalene	10—100	1—10
Anthracene	10—100	1—10
Phenanthrene	10—100	1—10
Pyrene	10—100	1—10
Azulene	10—100	<0.1
Chlorobenzene	10—100	
Hexafluorobenzene	<0.1	0.1—1
Pentafluorobenzene	<0.1	0.1—1
ααα-Trifluorotoluene	<0.1	0.1—1

[a] 100% Incorporation represents a tritium specific activity for pure product of *ca.* 30 Ci mol^{-1}. [b] Oxidation of toluene showed >98.5% of tritium in aromatic ring. Nitration of toluene followed by g.l.c. analysis showed a random distribution of tritium in the aromatic ring.

TABLE 5

Alkanes and alkenes labelled by tritiated water using $EtAlCl_2$ Catalyst

Compound	% Incorporation of tritium into compound	% Incorporation into toluene in competitive reaction
Cyclohexane	<0.1	10—100
Cyclopentene	<0.1	<0.1
Cyclohexene	0.1—1	<0.1
1-Methylcyclopentene	1—10	<0.1
1-Methylcycloheptene	1—10	<0.1

TABLE 6

Oxygen- and nitrogen-containing compounds labelled by tritiated water using $EtAlCl_2$ catalyst

Compound	% Incorporation of tritium into compound	% Incorporation into toluene in competitive reaction
Diethyl ether	<0.1	<0.1
Dibenzyl ether	<0.1	<0.1
Anisole	10—100	<0.1
Furan	1—10	<0.1
Cyclohexanone	1—10	<0.1
Pyridine	<0.1	<0.1
Pyrrole	10—100	<0.1
Benzonitrile	<0.1	<0.1
Aniline	10—100	<0.1
Triphenylamine	1—10	<0.1
Thiophen	10—100	<0.1

The results (Table 4) show that all alkyl and polynuclear aromatic compounds were labelled efficiently. Oxidation of the tritiated toluene to benzoic acid showed that at least

98.5% of its activity was in the aromatic ring. Nitration of toluene followed by g.l.c. analysis of the mixed products showed a random distribution of tritium in the aromatic ring. Polyfluoroaromatic compounds were not labelled and also poisoned the labelling of toluene in competitive studies.

TABLE 7

Deuterium exchange, tritium labelling, and radical ion formation with elemental halides as catalysts [a]

Catalyst	% Approach to equilibrium in C_6D_6 toluene exchange: Room temp., 5 min	% Approach to equilibrium in C_6D_6 toluene exchange: 100°, 1 week	% Tritium incorporation in toluene: Room temp., 5 min	% Tritium incorporation in toluene: 100°, 1 week	E.s.r. signal with pyrene [b]
$AlCl_3$	50				1.0
$TiCl_4$	0		10		1.2
$NbCl_5$			10		12
$TaCl_5$	10	100	10		9
$MoCl_5$	10	100	10		
WCl_6	5	100	10		1.7
$FeCl_3$	0	100	0	5	
$PtCl_4$	0	0	0	10	
BBr_3		100	10		600
$SnCl_4$	0	0	0	10	
$PbCl_4$			10		
$SbCl_5$	100	100	1		300
$SeCl_4$		0	0	10	4
$TeBr_4$		0	0	10	
$EtAlCl_2$	100	100	10		200
$MeAlCl_2$	100	100	10		
$PhAlCl_2$	100	100	10		

[a] Experimental procedures for tritiations as in text. [b] Experimental conditions: catalyst (0.01 g) was added to an 0.25M solution of pyrene in benzene (1 ml). Solution examined in Varian V-4502 e.s.r. spectrometer. Figures represent total spins relative to the $AlCl_3$ complex.

Only two of the alkenes studied (Table 5) were appreciably labelled, *viz.* 1-methylcyclopentene and 1-methylcycloheptene. All alkenes poisoned the labelling of toluene. In contrast the alkanes, while themselves not tritiated, did not hinder the labelling of toluene.

All the oxygen- and nitrogen-containing compounds studied (Table 6) poisoned the labelling of toluene, while some were themselves labelled and others inactive.

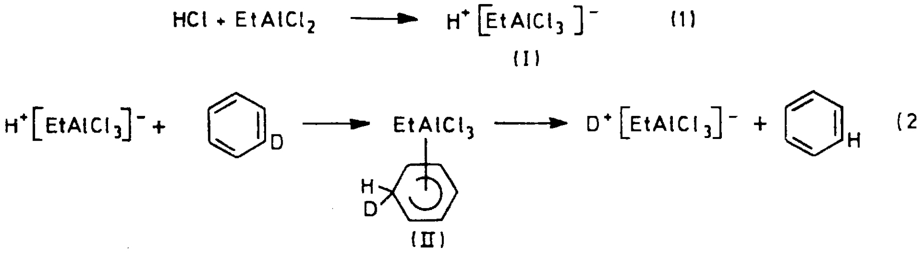
(e) *Nature of Catalyst in Deuteriation and Tritiation.*—A variety of metal halides (Table 7) were tested for their activity towards deuterium exchange between C_6D_6 and toluene and in the tritium labelling of toluene by the procedures and conditions described for $EtAlCl_2$ (method 2). While many halides were active they tended to be those in the high oxidation state of the metal and which were readily hydrolysed in water. They were usually Lewis acids and good halogenating agents for aromatic compounds.

Many of the catalysts formed vividly coloured solutions in aromatic solvents such as benzene. A number of these solutions were examined by e.s.r. for radical ion formation with pyrene (Table 7). It is concluded that, of the compounds which were found to be useful exchange catalysts, every one examined by e.s.r. was also capable of producing a radical ion with pyrene.

DISCUSSION

The specificity of these rapid deuteriation techniques towards aromatic proton exchange and the absence of steric effects and side reactions emphasise their advantages in comparison with other techniques for the deuteriation of aromatic compounds. However, most nitrogen and oxygen derivatives as well as non-aromatic materials are unlikely to be amenable to deuteriation by these procedures. In contrast, the tritium labelling technique described is applicable to a much wider variety of compounds. While only preliminary experiments are reported for most of the halides, results indicate that the organoaluminium halides are likely to be the most active of the catalysts studied.

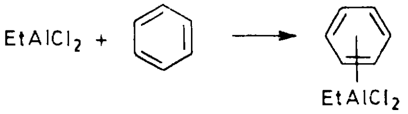
The ability to predict the feasibility of labelling a particular compound by the present techniques would be aided by an understanding of the mechanisms involved. Any mechanism proposed must be consistent with the following observations. (i) Rapid hydrogen exchange occurs between two aromatic hydrocarbons. (ii) All compounds exhibiting exchange with C_6D_6 also undergo tritium labelling on hydrolysis of the reaction mixture with a trace of HTO. (iii) Compounds which do not exchange hydrogen with C_6D_6 fall into two classes. Class A compounds completely inhibit exchange of toluene with C_6D_6 in a competitive reaction, while class B compounds have no significant inhibiting effect on toluene exchange. (iv) All class B compounds cannot be labelled with tritium by HTO hydrolysis (*e.g.* alkanes). They do not inhibit the tritiation of toluene in a competitive study. (v) Class A compounds may be subdivided into a class A-1 which readily label with tritium (*e.g.* alkenes) and class A-2 which cannot be labelled by HTO hydrolysis (*e.g.* alkyl ethers). (vi) Coloured solutions are formed between most unsaturated compounds and $EtAlCl_2$. (vii) E.s.r. results indicate charge transfer between pyrene and $EtAlCl_2$.



Two plausible mechanisms may be considered to explain the observed deuteriation data. In the first [reactions (1) and (2)], which we prefer at the present time, exchange occurs by an electrophilic process with

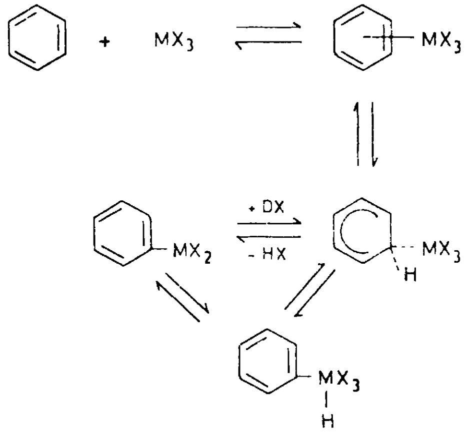
HCl as co-catalyst. Thus DCl carries the exchange between one deuteriated aromatic molecule such as [$^2H_6$]benzene and a non-deuteriated compound (*e.g.* toluene). There is doubt whether the aromatic is charge-transfer complexed to the organoaluminium at the time of proton attack [species (II), equation (2)]. That the complex exists is supported by the observation that radical ions are readily formed between aromatic compounds and the catalyst (Table 7). Chemical observation of charge-transfer complex formation between aromatics and Lewis acid halides similar to $EtAlCl_2$ derivatives has also been noted previously.[16]

When H_2O, or less than stoicheiometric amounts (<1 mole HCl per mole catalyst) of HCl were used as co-catalyst, the catalytic procedure showed poor rate reproducibility. The reason for the poor reproducibility with H_2O as co-catalyst presumably is due to the competing reaction where H_2O destroys the catalyst before significant amounts of species (I) [equation (1)] can be generated and maintained to carry the exchange. The necessity for excess of HCl as co-catalyst presumably is to covert all $EtAlCl_2$ to species (I), otherwise irreversible radical ion formation may occur and thus remove $EtAlCl_2$ from the exchange system [equation (3)].



(3)

The second mechanism [equation (4)], which cannot be unequivocally eliminated at this time, involves radical ion formation as the intermediate in the exchange as distinct from the first mechanism where the radical ion is a competing reaction.



(4)

In the latter mechanism interconversion of π- and σ-bonded aromatic species to the metal may lead to isotope exchange in the manner proposed for other metal-catalysed exchange systems.[5]

The criterion for an adequate exchange rate of hydrogen between two organic compounds based on either of the mechanisms would involve the requirement that both compounds associate with similar ease with the catalyst, and that the complexes be of appropriate strength that rapid interconversion of associated and free organic may occur. Preferential strong complexing of either organic reactant would poison the exchange reaction.

On this basis class A-1 compounds as defined above (*e.g.* alkenes) may be interpreted as those which associate strongly with the catalyst (presumably as π-olefin complexes) to the complete exclusion of C_6D_6. Thus exchange is not possible, competing exchange of toluene is inhibited, but hydrolysis of the complex with HTO yields tritiated product.

Class B compounds (*e.g.* alkanes) are incapable of π-complex formation and no tritium labelling is possible. Competitive exchange of toluene with C_6D_6 is not influenced by their presence.

Class A-2 compounds on the other hand include oxygenated molecules such as diethyl ether which may complex strongly through the oxygen atom to the metal. No exchange may occur and since the complex does not involve hydrogen dissociation, hydrolysis with HTO does not yield tritium-labelled product. Many nitrogen-containing molecules may be in this category for the same reason.

Many compounds such as halogenoaromatics have alternative sites for complex formation. The observation that substances such as chlorobenzene exchange rapidly with C_6D_6 indicates that association is with the ring and not the halogen atom. The observation that anisole is readily labelled with tritium on HTO hydrolysis indicates complex formation through the aromatic ring. The absence of exchange between anisole and C_6D_6 may be attributed to the preferential association of anisole with the catalyst to the exclusion of C_6D_6. The inhibition of toluene exchange by anisole may be explained in the same manner.

A number of condensed polycyclic aromatics such as pyrene required elevated temperatures to exchange with C_6D_6. Such substances are known to form strong π-complexes with a variety of metals. The absence of their exchange at room temperature with C_6D_6 may be attributed to their preferential association with the catalyst, the complex being sufficiently labile only at elevated temperatures to permit exchange. Competitive toluene exchange is also prevented. Tritium labelling of the same compounds occurs readily at room temperature consistent with the hydrolysis of such complexes.

In summary, it may be concluded that the compounds which are likely to be amenable to deuteriation by exchange with C_6D_6 in the presence of $EtAlCl_2$ and other similar catalysts are those which would be expected to form π-type complexes with the metal atom of strength similar to that of benzene itself. Compounds likely to complex through lone pair electron donation from hetero-atoms are unlikely to exchange. The compounds which may be amenable to tritiation by the proposed technique are those likely to associate with the metal atom in such a manner that hydrolysis of the complex with HTO can

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[16] J. L. Garnett, A. Rainis, and W. A. Sollich-Baumgartner, *Austral. J. Chem.*, 1967, **20**, 1865 and references cited therein.

be accompanied by tritium atom addition at the site of the co-ordination.

Experiments are continuing to investigate the applicability of the labelling procedures to more complex organic molecules.

EXPERIMENTAL

Materials.—[$^2H_6$]Benzene, isotopic purity 99%, was obtained from Merck. In addition, some of the material was prepared by repeated equilibration of benzene with D_2O in the presence of heterogeneous platinum.[7]

Catalysts were stored in small glass ampoules which were opened as required in an atmosphere of dry nitrogen. $MeAlCl_2$, $EtAlCl_2$, and $PhAlCl_2$ were prepared by Dr. T. Mole (CSIRO, Melbourne) according to methods described elsewhere.[17] Other catalysts were of commercial origin.

Deuteriation Method 1.—A solution of $MeAlCl_2$ in [$^2H_6$]benzene (0.37M) previously dried thoroughly with molecular sieves was prepared. A sample (0.2 ml) of this solution was transferred, in a dry nitrogen flushed box, to a reaction tube which had been heated to 120° for 3 h and cooled in the dry box. The compound (0.2 ml) to be deuteriated, also dried with molecular sieves, was then added and the tube sealed by closing a high vacuum Teflon sealing greaseless stopcock. The tube was frozen in liquid nitrogen and non-condensible gases pumped away. (Mass spectrometric analysis of vapour from the warmed sample showed that no exchange had occurred to that stage in the procedure.) Dry HCl gas (1.2×10^{-4} mol) was then distilled into the reaction tube. This represented 1.3 mole HCl per mole $MeAlCl_2$, the exact ratio being unimportant provided that the number of moles of HCl exceeded that of $MeAlCl_2$. On thawing the solutions became a bright yellow. After a few minutes at room temperature the isotope analysis was performed and showed that exchange had occurred. This procedure yielded consistent exchange results. Theoretically any deuteriated aromatic compound is capable of acting as deuterium source, however [$^2H_6$]benzene is easily obtained and economically viable. Choice of deuterium source may also be influenced by the solubility of the compound to be deuteriated in the reaction medium, thus both liquids and solids can be labelled.

Deuteriation Method 2.—Because of the time consuming nature of the above procedure the following method was adopted as a general simple deuteriation technique. [$^2H_6$]-Benzene (0.2 ml) was added to the compound to be deuteriated (0.2 ml) in a glass ampoule, the ampoule flushed with dry nitrogen, and the catalyst (0.01 g) added in a dry nitrogen atmosphere (glove bag) to prevent hydrolysis during transfer. The reaction ampoule was either held in the glove bag at room temperature or sealed and placed in an oven for higher temperature runs. At the end of the reaction time, distilled water was added to destroy the catalyst. As traces of water are necessary to promote the catalyst, reagents were not rigorously dried. However, in the case of hydrophilic reagents, such as ether and pyridine, the appropriate drying agent (*e.g.* potassium hydroxide) was added to remove water prior to use. Thus reagents in this reaction can tolerate certain small amounts of water and indeed traces are essential; however excess of water destroys the catalyst and poisons the exchange. Hence reagents with a high affinity for water need some predrying.

Tritiation Procedure.—The compound (0.2 ml) to be labelled was placed in a small glass ampoule, the ampoule flushed with dry nitrogen and the catalyst (0.1 g) added in a dry nitrogen atmosphere. High specific activity tritiated water (10 μl, 5 Ci g^{-1}) was then injected into the reaction mixture which was allowed to stand at room temperature for the required time. At the completion of the reaction, excess of distilled water was added to ensure that complete hydrolysis of the catalyst had occurred. In some cases, the reaction ampoule was sealed and placed in an oven for a period preceding the addition of the distilled water.

Analysis.—Deuteriated materials were analysed for deuterium content by means of an Hitachi–Perkin-Elmer RMU-6L mass spectrometer using a low voltage technique. Orientation of deuterium in the labelled compounds was determined by Varian A-60 and JEOL 100 MHz n.m.r. instruments.

Tritiated materials were analysed on a gas liquid chromatograph, the effluent of which was passed through an ionisation chamber coupled to a Cary model 31 vibrating reed electrometer for radioactivity measurement. This instrument ensured that the activity measured was in fact that present in the specified compound and not that in some by-product or trace of active water remaining in the reaction mixture. Any by-products could be identified and their radioactivity measured by this analytical procedure. Thus both chemical and radiochemical analysis of labelled products could be obtained.

Toluene Oxidation.—In order to determine the orientation of isotope in the tritiated toluene, the labelled compound was oxidised to benzoic acid with permanganate according to the procedure previously demonstrated to produce no aromatic hydrogen exchange.[18] This permitted the detection of any methyl tritium in the molecule. Mononitration of the toluene followed by radiometric–g.l.c. analysis of the mixed nitration products as previously proposed [19] yielded the tritium distribution within the aromatic ring.

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