Catalytic Tritium Exchange Reactions with Tritiated Active Methylene Compound

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Although the isotopic hydrogen exchange reactions of a number of organic compounds catalyzed by a transition-metal have been investigated by many workers,[1] these exchange reactions have dealt almost exclusively with deuterium oxide,[1] deuterium,[1] and tritium oxide[2] as an isotope source.

The present paper will describe the catalytic tritium-hydrogen exchange using ethyl malonate-(active methylene-T) (I) as a tritium source. Table I shows that the alkyl hydrogens are, by the use of a catalyst, exchanged with I more easily than with tritium oxide. The catalytic activity of the transition-metal for benzene is in the following order: with I, Raney Ni > Pd-black > Pt-black; with tritium oxide, Pt-black > Pd-black > Raney Ni.

TABLE I. EXCHANGE BY TRITIUM OXIDE OR I*

Catalyst	Substrate	% Approach to statistical equilibrium	
		T_2O	I
Pd-Black	*p*-Xylene	4	99
Pd-Black	Benzene	77	10
Pd-Black	Cyclohexane	0	11
Pt-Black	*p*-Xylene	0	0
Pt-Black	Benzene	100	6
Pt-Black	Cyclohexane	0	3
PtO	*p*-Xylene	3	17
PtO	Benzene	98	45
Raney Ni	*p*-Xylene	2	90
Raney Ni	Benzene	62	76
Raney Ni	Cyclohexane	0	2

* At 130°C for 17 hr.

The results in Table II show that the exchanges of toluene and *m*-xylene catalyzed by Pd-black and Raney Ni occur mainly in the alkyl groups. Figure 1 indicates that the

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[1] J. L. Garnett, *Nucleonics*, **20**, 86 (1962); A. Murray, III, and D. L. Williams, "Organic Syntheses with Isotopes," Vol. II, Interscience Publisher, New York (1948), p. 1594.

[2] J. L. Garnett and W. A. Sollich, *J. Catalysis*, **2**, 350 (1963).

Table II. Tritium distribution in the compounds labeled with I*

Substrate	Catalyst	% of tritium	
		Methyl	Ring
Toluene	Pd-Black	100	0
Toluene	Raney Ni	89	11
m-Xylene	Pd-Black	98	2
m-Xylene	Raney Ni	97	3

* At 130°C for 17 hr.

Table III. Exchanges of organic compounds with I*

Substrate	% Approach to statistical equilibrium		
	Pd-Black	Pt-Black	Raney Ni
m-Xylene	96	1	82
p-Xylene	99	0	91
Toluene	100	16	83
Benzene	10	6	76
Diphenyl	0	90	1
n-Heptane	5	0	2
Cyclohexane	11	3	2
Tetralin	67	77	85

* At 130°C for 17 hr.

extent of the isotopic exchanges with I is decreased considerably by the addition of water. Judging from the above results in this reaction, it may be expected that the mechanism of the exchange with I will be different from that with tritium oxide. The extent of the exchange of some organic compounds with I are shown in Table III.

These results indicate that the catalytic exchange of hydrogen with I is a good method for labeling an organic compound with hydrogen isotopes.

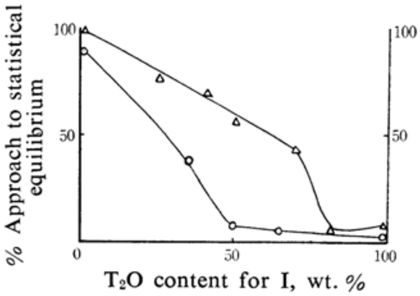

Fig. 1. Effects of water on exchange reaction of *p*-xylene by I at 130°C for 17 hr.
—△— With Pd-black
—○— With Raney Ni

Experimental

The Exchange of *p*-Xylene by Pd-Black.—A mixture of 30 ml. of *p*-xylene, 1 ml. of I (41.1 μc./ml.), and 0.3 g. of Pd-black in an ampoule was shaken at about 130°C for 17 hr. After it had then been cooled, Pd-black was filtered off, the filtrate was hydrolyzed with 20 ml. of a 10% aqueous sodium hydroxide solution to give sodium malonate, and the reaction mixture was washed repeatedly with water, dried with sodium sulfate, and distilled to give 24 ml. (80%) of tritiated *p*-xylene (specific activity 1.36 μc./ml.) (99% approach to statistical equilibrium).

The Determination of the Tritium Distribution in Toluene.—A mixture of 2 ml. of tritiated toluene (0.179 mc./mM), 8 g. of potassium permanganate, and 96 ml. of water was heated under reflux for 3 hr. After it had cooled, the mixture was filtered and the filtrate was acidified with hydrochloric acid. The precipitate was then recrystallized from alcohol to give pure benzoic acid (specific activity 1.93×10^{-2} μc./mM). Thus, the distribution of tritium in toluene was as follows: methyl, 89%; ring, 11%.

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