

Palladium Catalyzed H-D Exchange Reaction Under Hydrothermal Condition

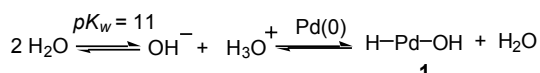
Seijiro MATSUBARA

Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyotodaigaku-Katsura, Nishikyo, Kyoto 606-8501, Japan
matsubar@orgrxn.mbox.media.kyoto-u.ac.jp

Alkenes and alkanes were converted into fully deuterium labelled ones by treatment with palladium on charcoal and deuterium oxide under hydrothermal condition. The simple method to get fully deuterium labelled compounds is easy to apply to various types of organic compounds. Polystyrene samples were also labelled with deuterium oxide and a catalyst platinum(IV) oxide under hydrothermal condition.

1. Introduction

Since the pioneering work by Breslow,[1] organic reactions in water as solvent have been well investigated from the point of view of the rate enhancement and the high stereoselectivity.[2] Recently, water is also attractive as a harmless solvent in the field of green chemistry. When water in a closed pot is heated beyond the boiling point, it takes subcritical state and finally reaches to supercritical state.[3] The water in these specific conditions should also have the potential in organic reactions.[4,5] Actually, several base and acid catalysed reactions have performed under this supercritical or subcritical condition. It is also interesting to perform transition metal catalysed reactions under similar conditions.[6] At the subcritical state, for example, which is also called as hydrothermal condition, the value of pK_w should be notified. It shows the low value (ca. 11) at the typical hydrothermal condition (250 °C, 5 MPa). The fact means that the hydrothermal water ionizes to a larger extent than water under ambient condition (i.e. 1000 times larger) and loses the hydrogen bond network. In this condition, we assumed that Pd (0) might insert to water oxidatively to form Pd (II) species **1** (Scheme 1).[7] We examined H-D exchange reaction in hydrocarbons and polymers under these conditions.



Scheme 1. Assumed oxidative insertion of Pd(0).

2. Experimental Methods

Reactions under hydrothermal condition were performed with the following two methods. The one is a reaction in stainless steel autoclave in Fig. 1.[8] The reaction was performed in the Teflon vessel which was placed in the stainless steel autoclave. The vessel is designed to release the internal overpressure. It is commercially available (Shikokurika Co., Ltd., Kochi, Japan.). In a teflon vessel, a catalyst, a substrate, and deuterium oxide were placed. After the vessel was placed in autoclave and sealed, the whole was placed in an oven (250 °C). After the autoclave was heated for a period, it was cooled to the room temperature. The obtained mixture was extracted with pentane and ether. Teflon vessel absorbs organic compounds. To extract the product completely, the vessel washed with hexane and water using ultra sonic cleaner for 30 min each. These solvents used for wash were extracted with ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo.

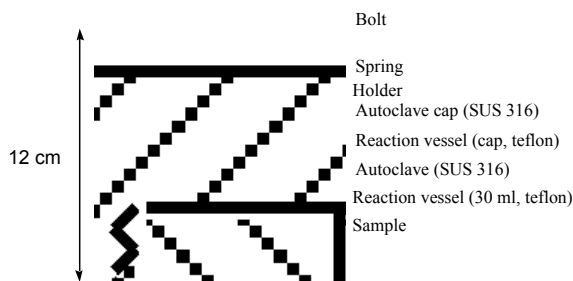


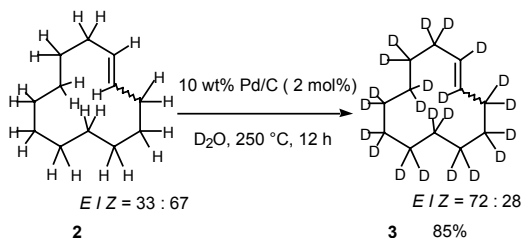
Figure 1. Reaction vessel

Reactions under hydrothermal condition were also performed under irradiation of microwave. As microwave system, we used Discover system from CEM corporation.[9] The microwave system was designed in consideration of a safety for unexpected explosion. In a pressure 10 ml vial which can be sealed by a septum, a mixture of substrate and catalyst in deuterium oxide (3.0 ml) was placed. Microwave (100 W) was irradiated maintaining 150 °C. The internal pressure reached to around 1.0 MPa. The irradiation was continued for 10 min. After being cooled, the reaction mixture was extracted with ether. The combined ethereal phases were passed through a short silica gel column and concentrated in *vacuo*. All analyses for H-D exchange reaction were performed by ^1H nmr, ^2H nmr, and mass spectrum. Especially, the analysis by ^2H nmr was indispensable.

3. Results and Discussion

3.1. H-D exchange reaction in hydrocarbon.

A mixture of cyclododecene (**2**, 5.0 mmol), 10 wt% Pd on active carbon (100 mg, 0.1 mmol Pd), and deuterium oxide (20 g) was heated at 250 °C in the stainless steel autoclave. Under this hydrothermal condition for 12 h, cyclododecene was converted into the fully deuterated compound **3**, as shown in Scheme 2.[10] Without catalyst, any deuteration was not observed.



Scheme 2. Treatment of cyclododecene with deuterium oxide and Pd/C under hydrothermal condition.

Under the same condition, other types of compounds were treated for several hours. The results are summarized in Table 1. Cyclooctene was also transformed into fully deuterated cyclooctene without any skeletal rearrangement (run 1). As shown in runs 2 and 3, saturated

hydrocarbons were also transformed into fully deuterated compounds. Ketones were also fully deuterated under the condition (runs 5–9). As described above, an interaction of alkene and palladium hydride induces H-D exchange reaction. The H-D exchange in alkanes, however, cannot be explained in this way. A direct C-H activation may be a route to the formation of fully deuterated alkanes.

Table 1. Palladium catalyzed deuteration of organic compounds under hydrothermal condition.^a

| run | Substrate | h | D / % ^b | Y / % ^c |
|-----|-----------------------|----|--------------------|--------------------|
| 1 | Cyclooctene | 4 | >95 | 80 |
| 2 | Cyclododecane | 6 | >95 | 84 |
| 3 | Cyclopentadecane | 4 | >95 | 99 |
| 4 | <i>n</i> -Pentadecane | 16 | 76 | 98 |
| 5 | Cyclooctanone | 10 | >95 | 86 |
| 6 | Cyclodecanone | 12 | >95 | 83 |
| 7 | Cyclododecanone | 4 | >95 | 87 |
| 8 | Cyclopentadecanone | 10 | >95 | 99 |
| 9 | 2-Dodecanone | 11 | >95 | 93 |

^a Substrate (5.0 mmol), Pd / C (10 wt% palladium on carbon, 100 mg, 2 mol% Pd), and D₂O (20.0 g).

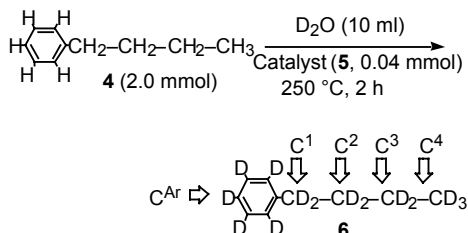
^b The ratios were determined by GC, ^1H nmr, ^2H nmr, and mass spectra. ^c The yields were isolated yields.

A number of works on about H-D exchange method have been reported.[11] These methods have focused mainly on acid catalyzed reaction in D₂O, base catalyzed reaction in D₂O, or metal catalyzed reaction under D₂ atmosphere. The acid catalyzed reaction is performed at 200–300 °C for H-D exchange reaction of hydrocarbons. The skeletal rearrangement, however, was observed in some cases. For example, cyclooctenes would give cyclohexene derivatives. The base catalyzed H-D exchange reactions are applicable for aromatic compounds and ketones. The metal catalyzed H-D exchange reaction using D₂ is classical and general method for hydrocarbons, but also has a limitation of the substrates because it is gas phase reaction. Our method is so simple procedure that is applicable to examine the wide range of compounds.

3.2. H-D exchange reaction in polystyrene.

This hydrothermal method was applied to polystyrene for its transformation into the deuterium labelled one.[12] The efficiency of a catalyst for H-D exchange reaction of aromatic ring was examined in the reaction of butylbenzene (**4**) as shown in Table 2.

Table 2. Metal salt catalyzed deuteration of butylbenzene (**4**) under hydrothermal condition.^{a,b}



| run | Catalyst 5 | C ^{Ar} | C ¹ | C ² | C ³ | C ⁴ |
|-----|-------------------|-----------------|----------------|----------------|----------------|----------------|
| 1 | Pd/C | 20% | 67% | 42% | 49% | 43% |
| 2 | PdO | 2 | 61 | 38 | 50 | 42 |
| 3 | PtO ₂ | 28 | 42 | 26 | 32 | 30 |
| 4 | Pd black | <5 | 32 | 14 | 24 | 16 |
| 5 | Raney Ni | 3 | 28 | 10 | 13 | 5 |

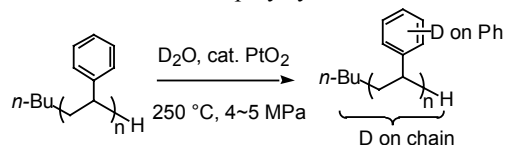
^a Substrate (2.0 mmol), catalyst (2 mol% Metal), and D₂O (20.0 g). ^bThe ratios were determined by ¹H nmr, ²H nmr, and mass spectra.

The use of Pd/C as a catalyst showed the best efficiency of H-D exchange on sp³ carbon among the examined catalysts in Table 1. As far as the exchange efficiency on benzene ring of **4**, platinum(IV) oxide (PtO₂) gave the better result. In the deuteration of polystyrene, the efficiency on benzene ring may have a priority. As shown in Table 3, polystyrene samples were treated with hydrothermal deuterium oxide in the presence of catalytic amount of PtO₂. The samples were commercially available from Aldrich[®] as Mw standards of 800, 13000, 44000, and 280000. Polystyrene (2.0 g), PtO₂ (1.0 mmol), and deuterium oxide (2.0 g) were pulverized and mixed completely by a ball mill machine (planetary ball mill, P-5, Fritsch[®], using a 80 ml stainless steel vessel and five stainless steel balls (φ 20 mm)). The obtained mixture and deuterium oxide (15 g) in

a 30 ml Teflon vessel was placed in a stainless steel autoclave. The autoclave was heated at 250 °C for the period indicated in Table 3. The internal pressure reached to ca 4-5 MPa. The obtained mixture was extracted with chloroform after the whole was cooled to the room temperature. The extracts were concentrated and purified by GPC (toluene on JAIGEL). The deuteration ratio was determined by ¹H nmr and ²H nmr using bromoform and 1,1,2,2-tetrachloroethane-d₂ as internal standards. In the case of the reaction using molecular weight 800, the H-D exchange occurred on each carbon of the molecule. In the rather higher molecular weight samples in Table 3, the exchange efficiency decreased drastically on the carbon chain, but gently on the benzene rings. A tendency for the selective exchange on benzene rings was observed in this PtO₂ catalyzed reaction.

The mass spectra of the deuterated polystyrene, obtained from the polystyrene Mw800, PtO₂ catalyst, and D₂O was measured by MALDI-TOF (Voyager[®] Elite, dithranol/ CF₃CO₂Ag). In Fig. 2, both spectra of starting material (a) and the deuterated one (b) are shown. While the peaks in Fig. 1 (a) were recorded in every 104 m/z units, those in (b) were observed in every 107~109 m/z units. This means that 3~5 D-atoms are substituted with H-atoms in the polystyrene, and is consonant with the result in Table 3. The spectrum in Fig. 2 (b) did not show the existence of non-deuterated molecule. At least in this sample, the exchange occurred equally, but we cannot conclude the homogeneity in the higher molecular weight samples at this moment.

Table 3. Deuteration of polystyrene with D₂O-PtO₂.



| Aldrich [®] Standard PS Mw | Reaction Time | D% on Ph | D% on Chain | Yield |
|-------------------------------------|---------------|----------|-------------|-------|
| 800 | 14 h | 61 % | 43 % | >99 % |
| | 100 | 71 | 52 | >99 |
| 13000 | 14 | 28 | 2 | >99 |
| | 100 | 42 | 7 | >99 |
| 44000 | 13 | 20 | 1 | >99 |
| | 100 | 44 | 3 | >99 |
| 280000 | 13 | 22 | <1 | >99 |
| | 100 | 38 | 2 | >99 |

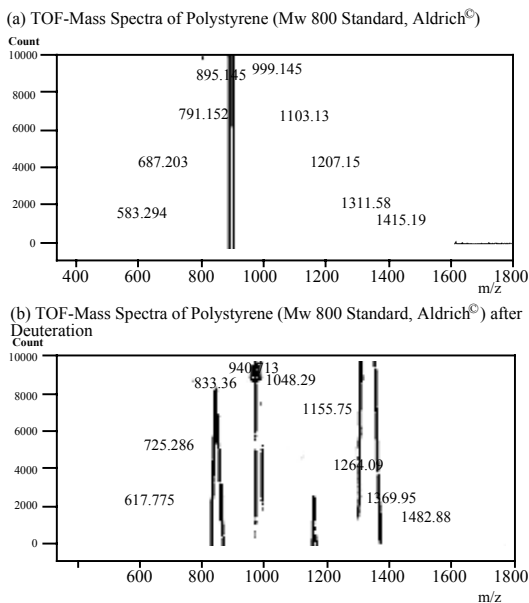


Fig. 2. MALDI-TOF Mass spectra of Polystyrene/dithranol/ $\text{CF}_3\text{CO}_2\text{Ag}$.

4. Conclusions

Although the hydrothermal reaction was performed under 230-250 °C/ 4-5 MPa, the surrounding water prevents the decomposition of organic compounds. It is different from simple heating. Unfortunately, the inside of the reaction mixture has not been studied well, but we have begun the mechanistic studies.

Acknowledgements

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