

Homogeneous Catalytic Activation of Carbon-Hydrogen Bonds. Hydrogen-Deuterium Exchange in Saturated Carboxylic Acids¹

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Certain soluble transition-metal complexes are known to activate the carbon-hydrogen (C-H) bonds of hydrocarbons.³⁻⁵ Evidence of this bond activation through transition-metal complexation is demonstrated by the simple reaction wherein hydrogen is exchanged by deuterium. Successful hydrogen-deuterium (H-D) exchange reactions have been reported on numerous aromatic compounds,^{6,7} and a number of saturated and unsaturated hydrocarbons.⁸⁻¹¹ To date, however, only a few reports have appeared on the transition-metal activation of the C-H bonds found in functionally substituted alkanes.¹²⁻¹⁵ Our interest in preparing functionally substituted fatty acids prompted us to extend the scope of this reaction to include simple saturated carboxylic acids.

Initial experiments were carried out with nonanoic acid as our model compound with subsequent reactions carried out on decane and branched carboxylic acids. The reaction conditions were essentially those described by Hodges et al.⁹ The reactions were carried out on the carboxylic acid or decane in sealed ampules, heated at 100 °C. The catalytically deuterated samples, after esterification, were analyzed by mass spectrometry to ascertain the total percent ²H incorporated and by ²H NMR to determine the site of bond activation. We found that changes in various reaction parameters affected the extent and rate of the H-D exchange reaction. These trends are outlined in

Table I. Exchange of Hydrogen for Deuterium in Methyl Nonanoate Catalyzed by K₂PtCl₆^a

expt no.	[C ₉ acid], M	time, h	av no. of ² H/molecule	% D(MS) ^f
1	0.2	20	1.96	9.8 (46.7)
2	0.2	65	5.32	26.6 (46.3)
3	0.2	102.5	6.82	34.1 (42.0)
4	0.2 ^b	139	5.86	29.3 (47.5)
5	2.0	96	2.62	13.1 (33.7)
6	2.0 ^c	96	2.38	11.9 (34.3)
7	2.0 ^d	96	2.96	14.8 (34.4)
8	2.0 ^e	47.5	1.60	8.0 (35.7)

^a [PtCl₄]²⁻ = 0.04 M for all experiments. Catalyst remained homogeneous throughout the experiment.

^b [PtCl₆]²⁻ used instead of Pt(II) salt. Catalyst remained homogeneous throughout the experiment. ^c 3 mmol of HClO₄. ^d Open-flask system. ^e 6 mmol of H₂SO₄. ^f % D determined by mass spectrometry. Value in parentheses is theoretical % ²H expected at equilibrium, based on actual reaction concentration.

Table I. As anticipated, with increased reaction times (20-102 h, experiments 1-3), ²H incorporation increased. Similarly, larger catalyst/acid ratios (experiments 3 and 5, Table I) yielded larger ²H incorporations. Nevertheless, theoretical equilibrium concentrations of ²H were never achieved. The values in parentheses (Table I) denote the amount of ²H to be expected if all the ²H and hydrogen in the reaction medium were equilibrated. At increased reaction time, the average ²H content per molecule increased. With an increased level of ²H incorporation, the Pt metal is statistically more likely to encounter and cleave a C-D bond over a C-H bond thus making it difficult to reach theoretical equilibrium. The presence of polydeuterated species may be accounted for by this equilibrium process. An alternative explanation for the polydeuterated species may be that dimeric complexes of Pt are responsible for multiple exchanges.⁹

We also found, as have others,⁹ that the presence of pyrene and the acidity of the reaction medium are important for keeping the catalyst homogeneous throughout the reaction. The aromatic compound and a mineral acid presumably suppress the disproportionation of the Pt(II) ion to Pt(0).⁹ Increased concentrations of pyrene and/or HClO₄ (experiment 6, Table I) had essentially no effect on the H-D exchange reaction. We did find, however, that

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Table II. Deuterium Distribution by ^2H NMR

	total ^b % ^2H	^2H positional distribn						
		CH_3	2- CH_3	3- CH_3	2- CH_2	3- CH_2	4- CH_2	$-(\text{CH}_2)-$
methyl nonanoate ^a	29	0.35			0.03	0.13	0.10	0.39
dimethyl azelate	8.1				0.15	0.46 ^c		0.39 ^d
methyl 2-methyloctanoate ^a	8.7	0.61	0.24					0.15
methyl 3-methylpentanoate ^a	12.6	0.68		0.32				
methyl stearate	10.5	0.39						0.61
	5.6	0.43						0.57
	1.75	0.51						0.49
decane	4.4	0.64						0.36
	2.0	1.00						

^a Fractional distribution of ^2H found in the $\text{Eu}(\text{fod})_3$ spectrum. ^b Determined by mass spectrometry. ^c Positions 3- and 4- CH_2 . ^d 5- CH_2 only.

H_2SO_4 -*d* also could be used as the mineral acid stabilizer (experiment 8, Table I).

Several transition-metal complexes were studied as catalysts, namely, K_2PtCl_6 , K_2PtCl_4 , PdCl_2 , and RhCl_3 . Both PdCl_2 and RhCl_3 failed to catalyze the H-D exchange reaction under the conditions described. K_2PtCl_6 , a Pt(IV) salt, readily catalyzed the H-D exchange reaction (experiment 4, Table I). Other studies³ have indicated that platinum must be in the 2+ oxidation state to be catalytically active and have shown that, during an initial induction period, the Pt(IV) salt is reduced to Pt(II) and the latter catalyzes the H-D exchange reaction. We also found that the exchange reaction, normally carried out in sealed ampules, could be run successfully in open systems (experiment 7, Table I), since oxygen also inhibits the disproportionation of Pt(II) or Pt(0).³

Our initial experiments relied on ^1H NMR spectroscopy with a shift reagent to define the positional distribution of deuterium in the catalytically deuterated samples. However, information obtained from ^1H NMR was of limited utility, especially in those samples containing very low levels of widely dispersed deuterium. The minor changes observed for the integrated area of each of the dispersed ^1H resonances made it impossible to quantify ^2H incorporation. ^2H NMR, on the other hand, used in conjunction with the shift reagent $\text{Eu}(\text{fod})_3$ in some instances, readily detected and quantified the positional deuterium incorporated in samples with low levels of deuterium content (as low as 2%).¹⁶

Results obtained from ^2H NMR showed that the Pt(II)-catalyzed H-D exchange reaction of nonanoic acid is site selective, favoring the nonpolar end of the molecule (Table II).

^2H NMR readily ascertained the distribution of deuterium throughout the alkyl chain of methyl nonanoate-*d* with the aid of the shift reagent $\text{Eu}(\text{fod})_3$ (Figure 1). The ^2H contents of samples are listed in Table II. For instance, in a sample containing 29% total incorporated deuterium, the majority of deuterium was found to reside in the terminal methyl and positions 5-7 (Table II). At lower ^2H levels the preference for primary C-H bond exchange is more pronounced. Very little deuterium was found in the α C-H bond even at the high level of ^2H incorporation.

The observation that C-H bond activation in nonanoic acid occurs preferentially at the nonpolar end of the molecule prompted us to extend the scope of this reaction to a variety of carboxylic acids, as listed in Table II to determine if electronic effects or steric effects are important in this reaction. Decane also was included in this study on reaction selectivity. In contrast to all the other

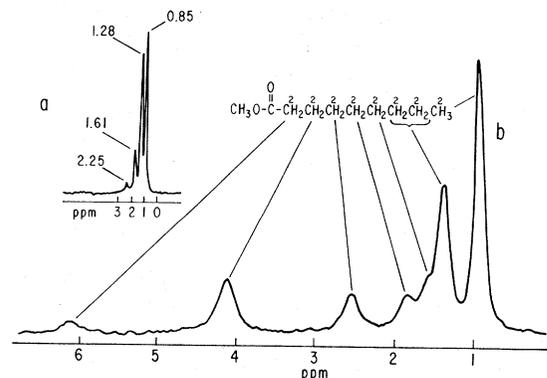


Figure 1. ^2H NMR spectra of (a) methyl nonanoate (25% transients, 4.4-s repetition rate, displayed spectral width 500 Hz, 4K data points) and (b) methyl nonanoate in the presence of $\text{Eu}(\text{fod})_3$ shift reagent ($\text{Eu}(\text{fod})_3/\text{substrate} = 0.7$, 200 transients, 4.4-s repetition rate, displayed spectral width 62.5 Hz). The total ^2H content is 29%.

substrates used in this study, the decane reaction remained heterogeneous. The data in Table II indicate the total percentage of deuterium (determined by mass spectrometry) in the molecules and its distribution (by ^2H NMR).

Our findings, in general, support those of Hodges and Shilov,^{9,11} that the reactivity at different kinds of carbon atoms decreases in the order primary > secondary > tertiary (Table II). In all instances, with the exception of methyl stearate, the greatest extent of deuterium exchange is observed at the primary C-H bond. Figure 2 shows the ^2H NMR spectra of three samples of decane-*d* with varying levels of ^2H incorporation. Decane-*d* (Figure 2, 2.0%) is exclusively deuterated at the terminal methyl positions, again demonstrating the greater preference for primary C-H bonds. Only after prolonged reaction time is exchange evidenced in the methylene bonds (Figure 2, 4.4%). In the case of methyl stearate, apparently the overwhelming number of secondary C-H bonds and chain length dilute the preferential activation of primary C-H bonds. However, at low levels of ^2H incorporation, the site selectivity is still noted (Figure 3).

The importance of electronic effects on site selectivity is readily evident in all compounds but especially in the case of dimethyl azelate-*d*. Those CH_2 bonds in closest proximity to the carboxylic function contain the least incorporated deuterium. The CH_2 group furthest removed from the carboxyl functions contains the most deuterium.

Electronic influence from the carboxyl function is also apparent in the H-D exchange reaction of the branched carboxylic acids (methyl 3-methylpentanoate and methyl 2-methyloctanoate). In both these instances, the CH_3 group closest to the carboxyl function has far less incor-

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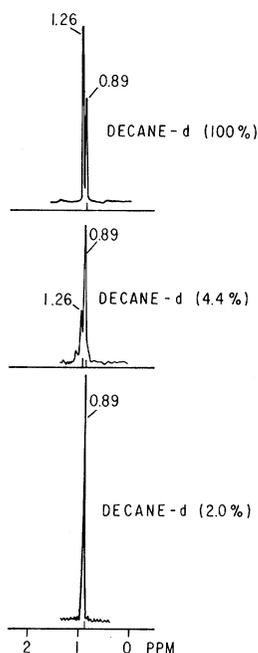


Figure 2. ^2H NMR spectra of decane-*d*: 100% ^2H (1K transients, 2.1-s repetition rate, displayed spectral width 500 Hz, 8K data points); 4.4% ^2H (670 transients, 4.4-s repetition rate, displayed spectral width 500 Hz, 4K data points); 2.0% ^2H (100 transients, 3.7-s repetition rate, displayed spectral width 500 Hz, 2K data points).

porated deuterium than the terminal CH_3 group. For methyl 3-methylpentanoate-*d*, no deuterium was detected in the methylene or methine (C-H) positions. Apparently a combination of electronic and steric effects prevents the H-D exchange of these bonds.

Thus, our study shows the Pt-catalyzed activation of the C-H bonds of saturated carboxylic acids occurs, in general, in the same manner as it does in simple alkanes: it favors mainly primary C-H bonds over secondary C-H bonds. However, we have demonstrated that when this reaction is employed with functionally substituted alkanes, such as carboxylic acids, electronic effects play an important role and can influence the selectivity of the reaction.

Experimental Section

Materials. Pure D_2O (99.8%) was purchased from Aldrich.¹⁷ K_2PtCl_4 was obtained from Ventron, K_2PtCl_6 from ICN, and pyrene from Chemical Service. Methyl 2-methyloctanoic acid was prepared according to the procedure of Pfeffer and Silbert.¹⁸ All other organic compounds were obtained from commercial chemical supply houses. Mass spectra were obtained on a Du Pont 21-492 double-focusing instrument operating at an ionization potential of 70 eV. ^2H NMR spectra were obtained with a ^{31}P 10-mm probe of a JEOL FX-60Q NMR spectrometer.¹⁶

Procedure. A typical reaction medium used in this study consists of 5 mL of a 50 mol% mixture of acetic acid-*d* and D_2O

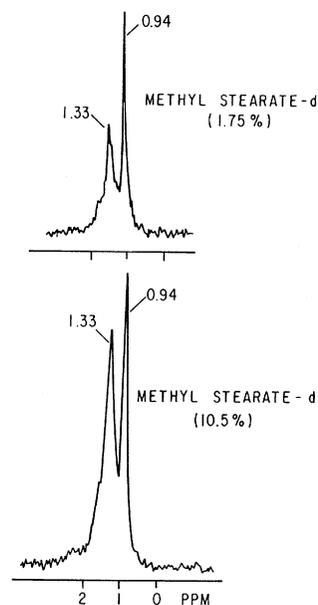


Figure 3. ^2H NMR spectra of methyl stearate-*d*: 1.75% ^2H (900 transients, 8.2-s repetition rate, displayed spectral width 1000/8 Hz, 8K data points); 10.5% ^2H (550 transients, 8.2-s repetition rate, displayed spectral width 1000/8 Hz, 8K data points).

containing the catalyst K_2PtCl_4 (0.4 M), HClO_4 (0.2 M), pyrene (0.5 M), and the carboxylic acid (0.2 or 2.0 M). The reactions were carried out in sealed ampoules heated at 100 °C. The deuterated carboxylic acids were extracted from the reaction medium with hexane or ether and esterified with BF_3/MeOH reagent. Following esterification the deuterated esters were analyzed by mass spectrometry to determine the total level of deuterium incorporated (% ^2H).¹⁹ ^2H NMR was used to ascertain the positional distribution of deuterium, in some instances with the aid of the shift reagent $\text{Eu}(\text{fod})_3$.¹⁶

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Registry No. Methyl nonanoate, 1731-84-6; dimethyl azelate, 1732-10-1; methyl 2-methyloctanoate, 2177-86-8; methyl 3-methylpentanoate, 2177-78-8; methyl stearate, 112-61-8; decane, 124-18-5; K_2PtCl_4 , 10025-99-7; K_2PtCl_6 , 16921-30-5.

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(19) The total percent ^2H content was determined by mass spectroscopy after appropriate corrections for ^{13}C and ion fragmentation were made. % D was calculated according to equations found in ref. 8.