

A SIMPLE METHOD FOR THE SYNTHESIS OF PERDEUTERATED AROMATIC HYDROCARBONS AND HETEROCYCLIC COMPOUNDS

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ABSTRACT

A general method has been developed for the preparation of deuterated aromatic compounds that are useful for coal reaction studies and as internal standards for GC/MS analysis. The method requires little specialized equipment or synthesis expertise. A reaction mixture containing DCl, D₂O, and chromium is used to exchange deuterium for aromatic hydrogens at temperatures of 200° to 300°C. A single set of reaction conditions can be used to prepare a wide range of deuterated aromatics with nearly complete exchange of aromatic hydrogen for deuterium and little or no chemical degradation of the reactant. When a 20:1 molar ratio of deuterium to aromatic hydrogen was used the isotopic purity of most species tested including phenanthrene (isotopic purity of 94%), pyrene (95%), phenol (96%), dibenzofuran (96%), carbazole (94%), and dibenzothiophene (93%), approached the H/D exchange equilibrium of 95% in two to fifteen hours. The method also works well with complex mixtures as demonstrated by the deuteration of aromatics in a coal-derived anthracene oil.

INTRODUCTION

The use of deuterated aromatic organic compounds as internal standards for the evaluation of sample preparation procedures and for the analysis of complex samples using gas chromatography coupled with mass spectrometry (GC/MS) can greatly increase the accuracy of analytical results while often reducing the time required for the analysis. Deuterated compounds and mixtures are also useful for studying the fate of organic compounds in complex systems such as coal conversion reactions. Unfortunately, the widespread use of deuterated compounds is limited by their high cost and the lack of availability of many compound classes.

The purpose of this paper is to describe a general method for the synthesis of deuterated species that is applicable to several classes of aromatic compounds, requires minimal time and synthesis expertise, yields a chemically and isotopically pure product, uses simple and inexpensive equipment and reagents, and can be used with complex mixtures. This method also yields products with multiple deuteriums which is desirable to avoid the overlap in the mass spectra that occurs from ¹³C isotope peaks and (M-H)⁺ ions when unlabeled and monodeuterio-labeled compounds occur in the same sample (1). The synthesis is similar to the method of Werstiuk and Kadai (2-6) for the H/D exchange of aromatic protons with D₂O/DCl except that chromium is added to increase the rate of H/D exchange. The ability of this method to provide chemically and isotopically pure perdeuterated products was evaluated

for several aromatic hydrocarbons and O-, S-, and N-containing aromatics. The method was also used to produce perdeuterated derivatives of the components of a coal-derived anthracene oil.

EXPERIMENTAL

All reactions were performed in 10 mm o.d. (8 mm i.d.) x approximately 8 cm long pyrex glass tubes. One end of the tube was sealed with a flame before adding the reagents. The reaction mixture was then frozen in liquid nitrogen, the tube was evacuated using a small laboratory vacuum pump, and the tube was sealed with a flame. This procedure filled approximately one-half of the tube volume with reagents. The sealed tubes were then placed into a 1.3 cm o.d. x 15 cm stainless steel pipe. Before capping the pipe with "Swagelok" fittings, approximately 2 mL of water was added so that the pressure inside and outside of the glass reaction tube would be approximately equal during heating. As a safety measure, the stainless steel pipe was placed inside a containment vessel made from a one-inch diameter thick-walled iron pipe with threaded end caps. A small hole was drilled through one of the end caps to avoid a pressure increase in the containment vessel. The entire apparatus was then heated to 200-300°C for an appropriate time period in the oven of a gas chromatograph. Caution: Since chloride ion degrades the strength of stainless steel, the stainless steel pipe should be replaced if a glass tube breaks during the reaction. The deuteration reagent consisted of 4% DCl (by wt.) in D₂O (both > 99% isotopically pure) with 10 mg/mL chromium metal. Since the dissolution of the chromium metal evolves hydrogen gas, the addition of chromium was performed in a ventilated hood. After the chromium had dissolved (approximately one hour), the reagent mixture was purged briefly with helium to removed dissolved hydrogen. The reagent could then be stored indefinitely in a desiccator.

Unless otherwise noted, the deuteration of the individual pure compounds was performed using a weighed amount of approximately 100 mg of test species and an appropriate volume of deuteration reagent to give a 20:1 molar ratio of reagent deuterium to exchangeable protons. Each of the pure compounds was reacted at 300°C for 2 hr and/or 15 hr. If significant chemical degradation occurred at this temperature, an additional synthesis was performed at 200°C for 2 hr. The deuteration of the anthracene oil was performed using 50 mg of sample with 1.0 mL of deuteration reagent.

GC/MS analysis of the deuterated products was performed with a Hewlett-Packard model 5985B using a 30 m x 0.32 mm i.d. (1µm film thickness) DB-5 fused silica capillary column (J&W Scientific, Rancho Cordova, C.A.). All analyses were performed in the electron impact mode with 70 eV ionizing voltage. Isotopic purity of the products was calculated from the resultant spectra. Gas chromatography with flame ionization detection (FID) was performed on a Hewlett-Packard model 5890 GC with the same type of chromatographic column as used for GC/MS. Chemical purity of the starting materials and the products was determined by GC/FID analysis using gravimetrically prepared solutions of standard and product species. Proton NMR analyses of the deuterated products were performed on a Varian model XL-200. The deuterated products were dissolved in CD₂Cl₂ containing 0.25% tetramethylsilane.

Since most of the test compounds (except the N-containing bases) were not soluble in the reagent, quantitative recovery of the products was easily attained by pipetting off the liquid products or by removing the reagent from the solid products with a Pasteur pipette. The solid products were washed with water and dried to remove the residual reagent. The N-containing aromatic bases (aniline and quinoline) were removed from the reagent by making the reaction mixture basic with 2N NaOH and extracting with methylene chloride. Since the purpose of this synthesis method was to provide labeled products with deuterium substitution in chemically stable positions, the hydroxyl deuterium on the two phenols, and the two amine deuteriums on aniline were exchanged for protons from H₂O before being analyzed for their isotopic purity.

RESULTS AND DISCUSSION

The success of H/D exchange using the DCI/D₂O/chromium reagent in synthesizing perdeuterated aromatic compounds from several compound classes is shown in Table I. Mass spectra of several representative compounds before and after deuteration are shown in Figure 1. H/D exchanges with ethyl benzene, phenanthrene, pyrene, perylene, biphenyl, phenol, dibenzofuran, aniline, carbazole, and dibenzothiophene all approached equilibrium with the deuterium pool (assumed to be 95% isotopic purity based on the 20:1 molar ratio of D/H) in either two or 15 hours with no significant chemical degradation. The isotopic purity of those species that attain exchange equilibrium (95% isotopic purity) can be improved, if desired, by increasing the ratio of reagent D to exchangeable H or by performing multiple exchange reactions. Quinoline also showed no chemical degradation, but was only 73% isotopically pure after 15 hours. However, such products can still be useful for isotope dilution analysis. For example, the mass spectra of 73% isotopically pure quinoline-d₇ has a base peak of 134 compared to 129 for undeuterated quinoline and, since no detectable overlap in their mass spectra occurs in the molecular ion region, the 73% isotopically pure product is still useful as an internal standard (Figure 1). Longer reaction times and/or higher reagent D to reactant H ratios could be used to increase the isotopic purity.

Only three species, 2,4-dimethylphenol, anisole, and 2-methylthiophene, showed enough degradation that the synthesis at 300°C was judged to be unsuitable. Milder conditions of 200°C for 2 hr. were used for each of these species in an attempt to reduce degradation. Both 2,4-dimethylphenol and 2-methylthiophene were reasonably stable under these conditions and yielded products with isotopic purities of 89% and 85%, respectively (Table I). The methyl hydrogens of 2-methylthiophene exchanged readily and were included in the calculation of isotopic purity. Anisole continued to be converted to phenol even at these milder conditions with only 43% of the original anisole remaining after the reaction. Under these conditions, only three positions on anisole underwent significant H/D exchange. These positions were shown by 200 MHz proton NMR to be the ortho- and para-positions, as would be expected since the methoxy group activates those positions for electrophilic substitution. The same result is obtained when phenol undergoes the synthesis at 200°C for 2 hr. These results indicate that this method may be useful to produce aromatic compounds labeled at specific (ortho-, para- vs. meta-) positions by careful selection of the reaction temperature.

The use of this synthesis to produce perdeuterated derivatives in complex mixtures was demonstrated with a coal derived anthracene oil containing predominantly aromatic hydrocarbons. Figure 2 shows the results obtained when the anthracene oil underwent H/D exchange for 2 hours at 300°C. No detectable chemical degradation of the sample occurred as determined by a comparison of the GC/FID chromatograms of the oil before and after the synthesis. The molecular ion regions of the mass spectra obtained before and after the synthesis are shown for several representative species (Figure 2). The isotopic purities were naphthalene (97%), dibenzofuran (98%), dibenzothiophene (99%), phenanthrene (96%), and pyrene (97%). Aromatic compounds having aliphatic protons also showed nearly quantitative exchange of aromatic protons for deuterium, and some exchange of the aliphatic protons. For example, the base peak for 2-methylnaphthalene-d₇ (if only aromatic protons exchanged for D) would be at m/z 149. The intense peaks at m/z 151 and 152 show that some aliphatic protons also exchanged (Figure 2).

The results of the perdeuteration studies of pure compounds (Table I) and the anthracene oil demonstrate that the method presented here is useful for synthesizing perdeuterated aromatic compounds from several compound classes as well as in complex mixtures. All of the species that have been tested yield products with both high isotopic purity and (except for anisole) high chemical purity. The cost of the reagent is low (less than 20 dollars for this entire study) and the synthesis is simple to perform.

CREDIT

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REFERENCES

1. Blom, K.; Schuhardt, J.; Munson, B. Anal. Chem. 1985, 57, 1986-1988.
2. Werstiuk, N.H.; Kadai, T. Can. J. Chem. 1973, 51, 1485-1486.
3. Werstiuk, N.H.; Kadai, T. Can. J. Chem. 1974, 52, 2169-2171.
4. Werstiuk, N.H.; Kadai, T. In "Proceedings of the First International Conference on Stable Isotopes in Chemistry, Biology, and Medicine"; Klein, P.K.; Peterson, S.V.; Eds; 1973, NTIS CONF-730525, pp. 13-19.
5. Werstiuk, N.H.; Timmins, G. Can. J. Chem. 1981, 59, 3218-3219.
6. Werstiuk, N.H.; Timmins, G. Can. J. Chem. 1981, 51, 1485-1486.

Table I
Synthesis of Perdeuterated Aromatic Compounds

	n ^a	Isotopic Purity (%)			Chemical Purity (%)		
		300°C 2 hr	300°C 15 hr	200°C 2 hrs	300°C 2 hr	300°C 15 hr	200°C 2 hr
ethylbenzene	5	50	97		100	100	
phenanthrene	10	94	94		100	95	
biphenyl	10	84	96		100	100	
pyrene	10	-	95		-	100	
perylene	12	-	95		-	100	
phenol	6	94	96	100 ^c	100	99	100
2,4-dimethylphenol	4			89	88	39	97 ^d
anisole	5	-	-	97 ^c	<5 ^d	<5 ^d	43 ^d
dibenzofuran	8	52	96		100	100	
aniline	7	95	96		100	77 ^d	
quinoline	7	29	73		100	100	
carbazole	8	93	94		94	89	
2-methylthiophene	6 ^b	-	-	85 ^b	e	e	89
dibenzothiophene	8	95	93		99	99	

^aThe number of exchangeable protons, n, is used for calculating the quantity of reagent required to give a D/H ratio of 20:1 in the reaction mixture.

^bAll six of the protons on 2-methylthiophene exchanged readily so n=6 was used to determine the quantity of deuteration reagent and for the calculation of isotopic purity.

^cIsotopic purity was based on 3 rather than 5 H/D exchanges (see text).

^dThe degradation product was phenol.

^eNo 2-methylthiophene or identifiable degradation product was recovered.

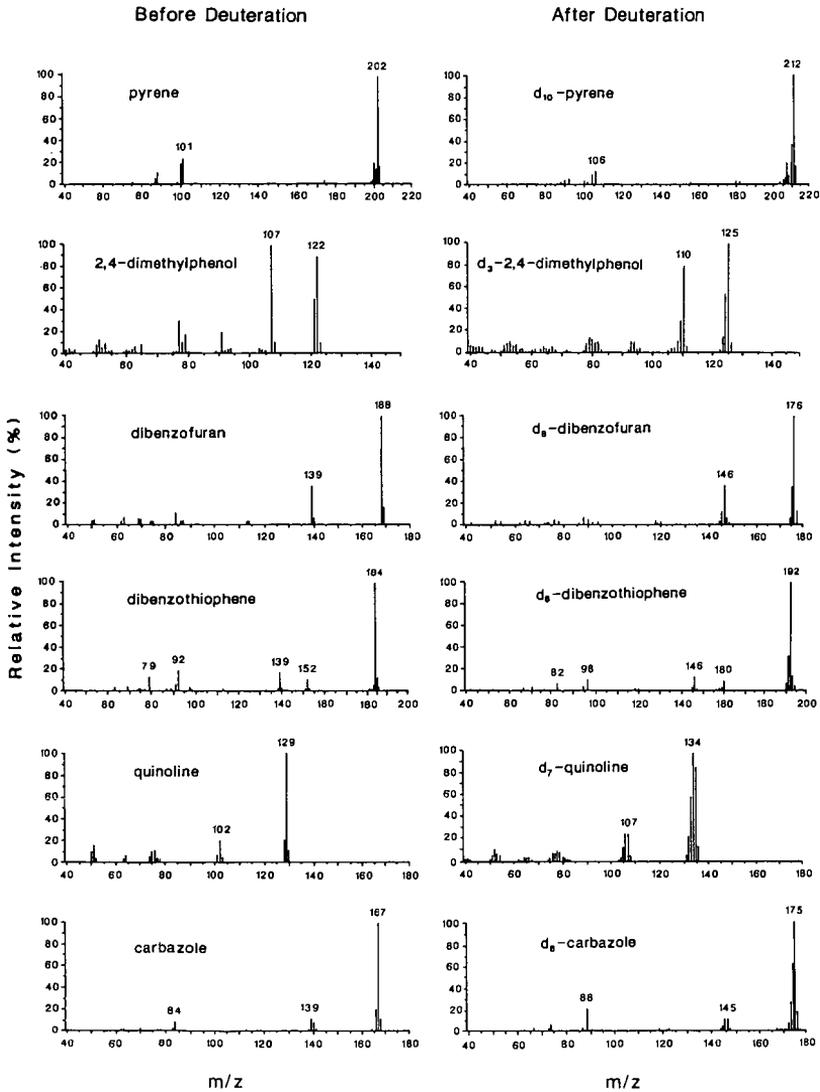


Figure 1: Electron impact mass spectra of representative PAH and O-, S-, and N- containing aromatics before (left side of figure) and after (right side) deuteration for 15 hours at 300°C. Isotopic and chemical purities are given in Table I.

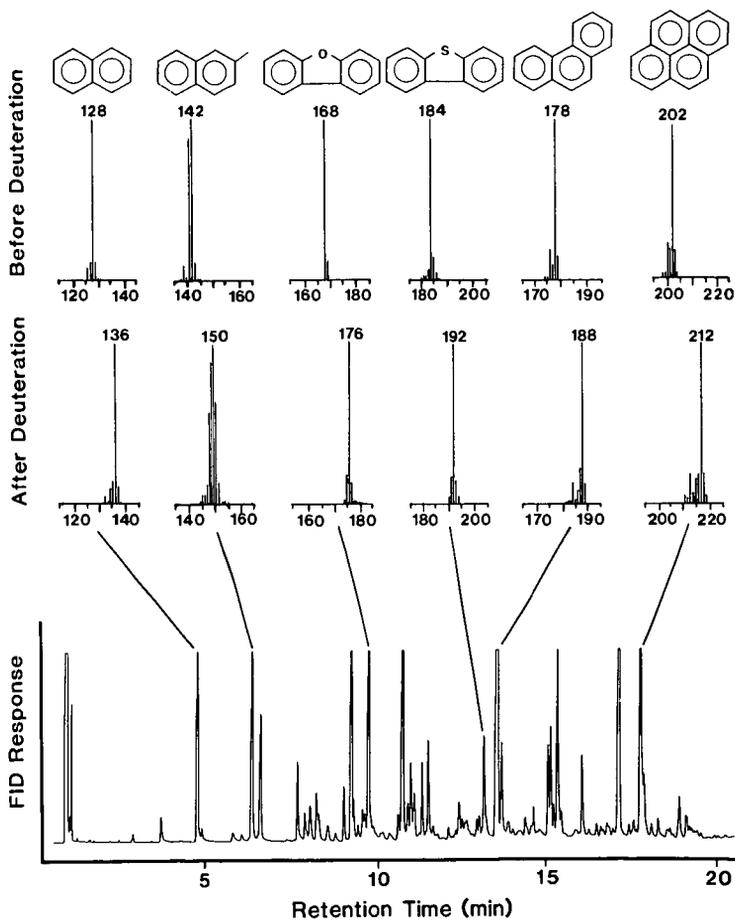


Figure 2: A comparison of the mass spectral molecular ion regions of representative species before (upper spectra) and after (lower spectra) deuteration of a coal-derived anthracene oil. Reaction conditions, isotopic purities, and gas chromatographic conditions are given in the text.