graphed (SiO$_2$, petroleum ether 40–60, and then 20% EtOAc–petroleum ether) to give 8: 0.12 g (80%); colorless oil; MS *m/e* 364.0939 (C$_{19}$H$_{24}$O$_5$$^{80}$Se requires 364.0941), 364 (M$^+$); $^1$H NMR $\delta$ 7.52 (m, 2 H), 7.24 (m, 3 H), 5.56 (AB m, 2 H), 3.91 (s, 4 H), 3.17 (AB m, 2 H), 2.54–1.25 (m, 11 H); $^{13}$C NMR $\delta$ 132.6, 131.8, 128.9, 126.5, 124.9, 124.8, 111.2, 65.3, 64.2, 43.3, 42.4, 37.5, 34.8, 34.2, 32.1, 22.3, 19.0; IR 3020 cm$^{-1}$.

**Reduction of the Phenylseleno Ether 8.** Activated Raney nickel (15.90 g, 5 wet weight equiv) was added to a solution of 8 (3.18 g, 8.76 mmol) in absolute ethanol (50 mL), and the vigorously stirred mixture was then heated to reflux for 45 min. The hot solution was filtered, the residue was washed with hot absolute ethanol (5 × 50 mL), the filtrates were combined, and the solvent was removed to give an oil. Flash chromatography (SiO$_2$, 15% CH$_2$Cl$_2$–petroleum ether 40–60) gave 9: colorless oil; 1.53 g (76%); $^1$H NMR $\delta$ 5.57 (AB m, 2 H), 3.90 (s, 4 H), 2.46–1.00 (m, 11 H), 1.00 (s, 3 H); $^{13}$C NMR $\delta$ 125.5, 124.4, 65.4, 64.0, 45.6, 38.3, 34.8, 33.65, 33.0, 29.6, 19.3. A second fraction was isolated and identified as 10: colorless oil; 0.15 g (8%); $^1$H NMR $\delta$ 3.72 (s, 4 H), 1.9–0.6 (m, 15 H), 0.92 (s, 3 H).

**Epoxidation of 9.** Alkene 9 (0.15 g, 0.72 mmol) was treated with *m*-chloroperoxybenzoic acid (0.22 g, 1.08 mmol) as described by Torii[17] to give 11, 0.10 g (62%).

**Reduction of 11.** Epoxide 11 (0.35 g, 1.56 mmol) was reduced with lithium (0.28 g, 39.3 mmol) in liquid NH$_3$ as described by Torii[17] to give crude 12 [0.33 g (94%)], which was used without further purification.

**Oxidation of 12.** The crude alcohol 12 (0.33 g, 1.46 mmol) was oxidized with pyridinium chlorochromate as described by Torii[17] to give the ketone 13, 0.22 g (66%).

**Preparation of Ketones 15 and 16.** Isopropylmagnesium chloride (2.0 M in Et$_2$O, 1.25 mL, 2.5 mmol) was added to a stirred solution of ketone 13 (0.22 g, 1 mmol) in THF (5 mL) at –50 °C. Stirring was continued for a 3 h, and aqueous acetic acid (30%, 1 mL) was then added to the yellow solution. The mixture was then worked up to give a oil, which was subjected to the same procedure twice more. The resulting crude product was dissolved in hexane (10 mL), sulfuric acid (50%, 10 mL) was added, and the mixture was stirred overnight at room temperature. Workup gave a colorless oil, purified by flash chromatography to give an oil, 0.9 g. HPLC (SiO$_2$, 5% EtOAc–pentane) of this oil gave the following:

15: 38.8 mg (18%); MS, *m/e* 206.1681 (C$_{14}$H$_{22}$O requires 206.1670), 206 (M$^+$), 191, 163 (100%); $^1$H NMR, see discussion; $^{13}$C NMR $\delta$ 150.5, 141.5, 116.9, 106.1, 44.9, 42.4, 41.9, 37.2, 35.0, 34.6, 25.4, 23.7, 21.5, 21.1, 16.9; IR 1705 cm$^{-1}$.

16: 12.5 mg (6%); MS, *m/e* 206.1675 (C$_{14}$H$_{22}$O requires 206.1670), 206 (M$^+$), 191, 163 (100%); $^1$H NMR $\delta$ 5.34 (br s, 1 H), 2.60–1.38 (m, 13 H), 1.05 (s, 3 H), 0.95 (d, 6 H, *J* = 6.8 Hz); IR 1718 cm$^{-1}$.

17: 8.4 mg (4%); MS, *m/e* 206 (M$^+$), 191, 163, 131 (100%); $^1$H NMR $\delta$ 5.05 (br s, 1 H), 2.42–1.46 (m, 13 H), 1.05 (s, 3 H), 0.94 (d, 6 H, *J* = 6.8 Hz); IR 1705 cm$^{-1}$.

18: 6.6 mg (3%); MS, *m/e* 206 (M$^+$), 191, 163, 124, 108 (100%); $^1$H NMR $\delta$ 2.90–1.20 (m, 11 H), 1.70 (s, 3 H), 1.66 (s, 3 H), 0.66 (s, 3 H); IR 1708 cm$^{-1}$.

**Preparation of (±)-Vetiselinene.** Dry triphenylphosphonium bromide (0.375 g, 0.01 mmol) was added to a stirred solution prepared by heating a mixture of NaH (0.036 g, 1.5 mmol) and (CH$_3$)$_2$SO (2 mL) at 75 °C until H$_2$ evolution ceased. The resulting bright yellow solution was stirred at room temperature for 10 min and then added to a solution of ketone 15 (40 mg, 0.19 mmol) in (CH$_3$)$_2$SO (1.5 mL) and the mixture stirred for 16 h under N$_2$ at 55 °C. Workup gave a yellow solid that was purified by flash chromatography (SiO$_2$, pentane) to give 19: 29.1 mg (75%); MS, *m/e* 204.1879 (C$_{15}$H$_{24}$ requires 204.3585), 204 (M$^+$), 189, 176, 161, 93 (100%); $^1$H NMR 5.39 (br s, 1 H), 4.75 (br s, 1 H), 4.52 (br s, 1 H), 2.40–1.20 (m, 12 H), 0.96 (d, 6 H, *J* = 6.6 Hz), 0.65 (s, 3 H); $^{13}$C NMR $\delta$ 150.5, 141.5, 116.9, 106.1, 44.9, 42.4, 41.9, 37.2, 35.0, 34.6, 25.4, 23.7, 21.5, 21.1, 16.9; IR 3079, 1641, 1374, 884 cm$^{-1}$.

Treatment of ketone 16 (12.5 mg, 0.06 mmol) under the same conditions gave 19 (7.6 mg, 62%), in all respects identical with that above.

# A Selective Method for Deuterium Exchange in Hydroaromatic Compounds

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We recently noticed that the deuterium atoms that were introduced into the 5-, 6-, 7-, and 8-positions of 1-naphthalenecarboxylic acid during the initial rapid, palladium-catalyzed reduction reaction in acetic acid under a dideuterium atmosphere were selectively exchanged from the 5- and 8-positions in a slower second reaction. In as much as the more conventional procedure for benzylic hydrogen atom exchange employing the dimsyl-$d_5$ anion in dimethyl-$d_6$ sulfoxide[1] often requires long reaction times and produces noxious mixtures, we examined the scope and selectivity of the catalytic reaction for the exchange of the benzylic hydrogen atoms. The results of reactions carried out with several hydroaromatic compounds using dideuterium and palladium on carbon in acetic acid-*d* at 50–85 °C are summarized in Table I.

The deuteriation of the substrates listed in Table I with the palladium catalyst gave products that were selectively deuteriated in the benzylic positions. The exchange rates for bulky molecules such as triphenylmethane were noticeably slower than the exchange rates of simple aryl-methyl groups. In general, more than 90% deuterium was incorporated in one reaction, and the yields ranged from 70 to 95% with the principal losses realized during distillations and recrystallizations.

The location of deuterium in the products was determined by both $^1$H and $^2$H NMR spectroscopies. The observations for 1,3-diphenylpropane are typical of the results obtained in this study (eq 1). Comparison of the relative

$$C_6H_5CH_2CH_2CH_2C_6H_5 \xrightarrow[\text{Pd, 55 °C, 24 h}]{D_2, \text{DOAc}}$$
$$C_6H_5CD_2CH_2CD_2C_6H_5 \quad (1)$$
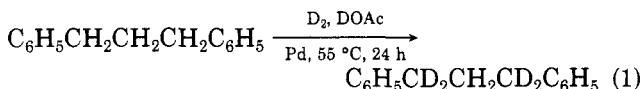
signal strengths shown in the $^1$H NMR spectra (Figure 1, spectra A and B) indicates that about 90% of the hydrogen atoms in the 1- and 3-positions have been exchanged. Even more significant, the $^2$H NMR spectrum (Figure 1, spectrum C) indicates that the exchange reaction proceeded with very high selectivity with virtually no incorporation of deuterium atoms at the other aromatic or aliphatic positions in the molecule. The same high selectivity was observed in reactions with toluene. Thus, high levels of enrichment and rather high isotopic purities can be realized.

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**Table I. Benzylic Hydrogen Atom Exchange in Hydroaromatic Compounds Using Palladium on Carbon in Acetic Acid-*d* in a Dideuterium Atmosphere**

| starting material | principal product | overall yield, % | isolation procedure[a] |
|---|---|---|---|
| 1,3-diphenylpropane | -1,1,3,3-$d_4$ | 74 | A |
| 5,6,7,8-tetrahydro-naphthalene | -5,5,8,8-$d_4$ | 90 | A |
| 9,10-dihydroanthracene | -9,9,10,10-$d_4$ | 95 | B, acetic acid |
| 9,10-dihydro-phenanthrene | -9,9,10,10-$d_4$ | | A |
| diphenylmethane | -1,1-$d_2$ | 85 | A |
| 1,2-diphenylethane | -1,1,2,2-$d_2$ | 70 | B, ethanol |
| triphenylmethane | -*d* | 87 | B, ethanol |
| 5,6,7,8-tetrahydro-naphthalene-1-carboxylic acid | -5,5,8,8-$d_4$ | 88 | B, acetic acid |
| 5,6,7,8-tetrahydro-naphthalene-1-carboxylic-5,6,7,8-$d_4$ acid | -6,7-$d_2$ | 70[b] | B, acetic acid |

[a] The workup procedures are described in the Experimental Section. The recrystallization solvent is noted. [b] The yield realized after two exchange reactions using dihydrogen in acetic acid.
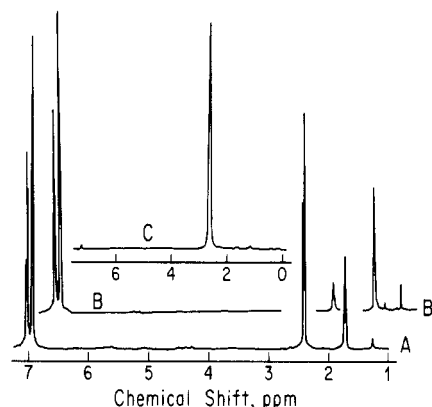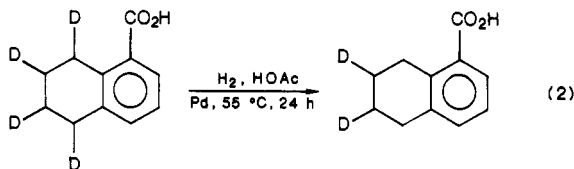


**Figure 1.** (A) $^1$H NMR spectrum of 1,3-diphenylpropane. (B) $^1$H NMR spectrum of product isolated after one deuterium-exchange reaction. (C) $^2$H NMR spectrum of the same material.

To evaluate the method in another way, we treated 5,6,7,8-tetrahydro-1-naphthalenecarboxylic-5,6,7,8-$d_4$ acid with dihydrogen in acetic acid (eq 2). The spectrum of



(2)

the resulting product, 5,6,7,8-tetrahydro-1-naphthalene-carboxylic-6,7-$d_2$ acid, is displayed in Figure 2. The $^2$H NMR spectrum reveals that the resonances of the benzylic deuterium atoms at 3.12 and 2.80 ppm disappear. Integration of the spectra implies that greater than 99% of the benzylic deuterium atoms can be replaced after two exchange reactions.

This catalytic exchange reaction is more generally satisfactory than base-catalyzed exchange reactions using dimsyl-$d_5$ anion. The heterogeneous reaction is apparently more selective, and the products can be readily isolated from the reaction mixtures. The success realized in this study is somewhat surprising in view of the difficulties experienced by others using other metals to catalyze the exchange reaction.

A study of the literature suggests that the heterogeneous palladium-catalyzed exchange reaction is much more se-
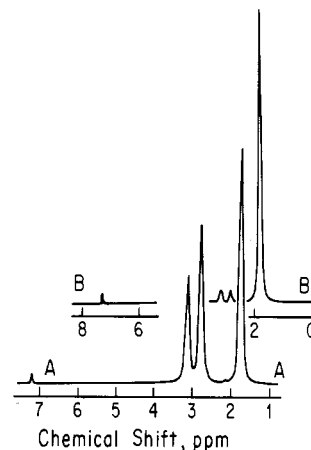


**Figure 2.** $^2$H NMR spectra: (A) 5,6,7,8-tetrahydro-1-naphthoic-5,6,7,8-$d_4$ acid. (B) Product obtained after treatment of this compound with acetic acid and hydrogen. The resonances arise from chloroform-*d* in natural abundance (7.2 ppm), the 6- and 7-deuterons (1.8 ppm), the 5-deuteron (3.1 ppm), and the 8-deuteron (2.8 ppm).

lective than other similar reactions. Weil and his collaborators reported that cobalt octacarbonyl catalyzed hydrogen–deuterium addition and exchange in anthracene and anthraquinone.[2] But that reaction which is carried out at high temperature and pressure has limited utility; for example, no reaction occurred with diphenylmethane.[2] Heterogeneous catalytic exchange reactions are plagued with a competing randomization process.[3] Specifically, platinum and nickel,[4] rhodium,[5] and iridium[6] exhibit unselective deuterium exchange. To illustrate, the difference between the reactivity of the benzylic and aliphatic positions of short-chain alkyl benzenes is less than a factor of 3 in the heterogeneous reaction with platinum in heavy water–acetic acid-*d* at 150 °C,[4] and exchange at aromatic position is often a side reaction. In contrast, palladium on carbon in acetic acid-*d* promotes the exchange reaction at much lower temperatures with high selectivity.

## Experimental Section

All the substances examined in this study except 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid were obtained commercially and were used without futher purification. The catalyst (10% Pd/C) was obtained from Aldrich Chemical Co. and dideuterium (99.7% isotopic purity) was provided by Cambridge Isotope Laboratories. Acetic acid-*d* was prepared from acetic anhydride and heavy water.

The reactions were carried out in a Parr Model 3910 hydrogenation apparatus equipped with a Parr Model A450EEE heating mantle. The temperature in the reaction bottle was determined in preliminary experiments.

$^1$H and $^2$H NMR spectra were recorded on the University of Chicago 500-MHz spectrometer and Varian Model XL-400 spectrometer, respectively.

**5,6,7,8-Tetrahydro-1-naphthalenecarboxylic Acid.** 1-Naphthalenecarboxylic acid was reduced by the procedure of Burnham and co-workers.[7] The reduction of this acid (12.9 g, 75 mmol) in acetic acid (75 mL) with 10% palladium on carbon (1.2 g) was carried out at 85 °C at 50 psig. The reaction was continued until a stoichiometric amount of dihydrogen was

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consumed. The catalyst was recovered, and water was added to the reaction mixture to precipitate the desired isomer, which was recrystallized from glacial acetic acid to provide 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid: mp 150–151 °C (lit.[1] mp 150–151.5 °C); 60% yield.

The corresponding deuteriated compound, 5,6,7,8-tetrahydro-1-naphthalenecarboxylic-5,6,7,8-$d_4$ acid (mp 150–151 °C) was prepared in the same way using dideuterium with acetic acid-$d$ as the solvent.

**Exchange Procedure.** The exchange reaction was carried out in the Parr apparatus. The substrate (2.0 g) in acetic acid-$d$ (20 mL) was sealed in the reaction bottle with the 10% palladium on carbon catalyst (100 mg, 5% w/w of substrate) and connected to a dideuterium reservoir at an initial pressure of 25 psig. The bottle was vigorously shaken at 55 °C for 24 h. The product was isolated by method A or B.

**Method A.** The reaction mixture was diluted with water, and the product was extracted into ether. The extract was washed with concentrated aqueous sodium hydroxide and water and then dried over magnesium sulfate. The ether was removed in vacuo, and the product was purified by vacuum distillation.

**Method B.** The reaction mixture was diluted with water, and the crude product was collected on a filter and recrystallized. The results are summarized in Table I.

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# A New Br+ Reagent. Oxidation of Alcohols to Carbonyl Compounds by Bis(quinuclidine)bromine(I) Tetrafluoroborate

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We call attention to a new source of positive bromine[1] for chemical synthesis, the quinuclidine-stabilized Br+ complex 1, bis(quinuclidine)bromine(I).
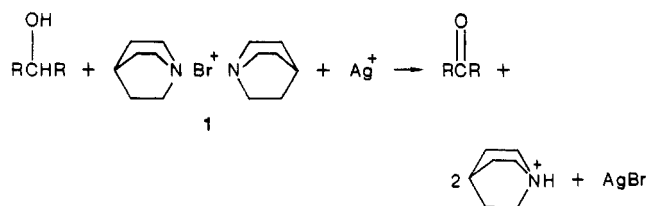


1
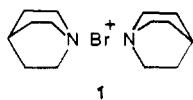
Recently,[2] we reported the preparation and crystal structure of the tetrafluoroborate of 1, called attention to its unusual stability and desirable handling properties, and

**Scheme I**



noted the intriguing electronic structure about the bromine which can be called hypervalent.[3] Now we report that this new reagent[4] effectively oxidizes alcohols to carbonyl compounds, particularly secondary alcohols to ketones. High yields of products are obtained when AgBF$_4$ is employed as a coreactant.

The results of the oxidation of several primary and secondary alcohols are given in Table I. The percent yields are based on GC analysis except for 9-fluorenone which was isolated. 4-*tert*-Butylcyclohexanone was also isolated in one case (86% yield). The yields of carbonyl product and AgBr support the stoichiometry for the oxidation given in Scheme I.

The two quinuclidines in 1 serve as base to absorb the 2 H+ ions formed in the oxidation of alcohol. Thus, with base incorporated into the reagent itself in proper stoichiometric amount, additional base is unnecessary for oxidation of alcohols.

As the results in Table I show, the oxidation of secondary alcohols to ketones by bis(quinuclidine)bromine(I) tetrafluoroborate and AgBF$_4$ is nearly quantitative. The method compares favorably with other successful procedures.[5] Yields of aldehydes, however, are lower. Tertiary alcohols, which can be degraded if hypobromites are formed,[6] are essentially unaltered by the reagent under the conditions of oxidation of secondary and primary alcohols. Thus, for example, 97% (GC) of 3-ethyl-3-pentanol remained in the reaction mixture after 24 h under conditions that afforded high yields of ketone from secondary alcohols in less that 30 min. Similarly, no acetone was detected by GC after 7 h in the attempted oxidation of *tert*-butyl alcohol. Thus, the reagent shows promise as a selective oxidizing agent for secondary alcohols in the presence of tertiary alcohols.

With the objective to make exploratory applications of 1 to chemical synthesis, we have yet to undertake mechanistic studies of the oxidation of alcohols by 1 in the presence of AgBF$_4$. Although we have not made a rigorous search for products that might be expected to arise from hypobromite[6] intermediates—tetrahydrofurans and ring-opened products, for example—these products are minor ones, if formed at all, in our reactions. Thus, in the context of extensive studies of the role of hypobromites, reaction conditions, and the role of Ag+ in oxidations of alcohols involving bromine,[7] it is noteworthy to point out that we

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