Reduction of Organic Halides with Zn–Cu to Deuterated Compounds and a Convenient Carbon-13 Magnetic Resonance Method of Deuterium Analysis

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A preparation of a Zn–Cu couple in an O_2-free system is described. This couple has been employed to reduce a variety of organic halides to hydrocarbons in water-containing ether solvents. This Zn–Cu preparation is exceptional in that reactions are carried out under mild conditions which are readily reproducible.

We wish to describe the use of an improved Zn–Cu couple for the reduction of organic halides in solvents containing H_2O or D_2O. Several groups have previously employed such a reaction.[1-3] This preparation differs from others in that all manipulations of the Zn–Cu are performed in an oxygen-free system.[4] The couple thus formed reacts with organic halides in ether solvents under mild and reproducible conditions.

Results and Discussion

A typical reduction was carried out as indicated in eq 1.

$$\begin{array}{ccccccc} \text{R–X} & + & D_2O & + & \text{Zn–Cu} \xrightarrow[\text{solvent}]{\text{ether}} & \text{R–D} & (1) \\ 25\ \text{mmol} & & 25\text{–}30\ \text{mmol} & & 100\ \text{mmol} & & \end{array}$$

The Zn–Cu couple is formed from zinc dust and an acidic solution containing about 3 mol % cupric chloride. After its formation the metal is thoroughly washed with water to remove inorganic salts, with acetone to remove any remaining water, and finally with diethyl ether. After drying at room temperature under vacuum the metal is a very fine black powder. An excess of this material is employed.

Water-miscible ethers are the preferred solvents in this reaction. Convenience in the workup largely determines the choice of the particular ether. Representative examples are given in the Experimental Section.

Reductions which have been carried out by this method are shown in Table I. Activated alkyl halides react smoothly at room temperature (entries 1–9). Simple haloalkane require somewhat higher temperatures for reaction (entries 10–13). Aromatic and vinyl halides are even less reactive and typically require longer reaction times (entries 14–20). A primary tosylate (entry 21) does not react.

Clean monodeuteration (per halogen) is found in this reaction even in cases where deuterium incorporation by exchange might be anticipated (entries 1–7). This allows for the preparation of compounds not readily obtainable by other methods. For example, the conversion of ketones to their α-monodeuterio analogues can be readily accomplished by the preparation and purification of the monobromo derivative, followed by reduction with Zn–Cu in the presence of deuterium oxide.

Stereospecificity in the reduction of vinyl halides appears to depend on the system. The cis,cis isomer of 1,4-dichlorobutadiene reduces cleanly to the cis,cis isomer of 1,4-dideuteriobutadiene (entry 15). The other two isomers (entries 16 and 17) are less clean with the cis,trans isomer contaminated with about 1% of the others and trans,trans containing 13% cis,trans and 2% cis,cis. The simple vinyl iodide *trans*-1-iodo-1-heptene gives a mixture of *cis-/trans*-1-deuterio-1-heptene (entry 20). Additional work is needed before this feature can be understood.

Reaction of iodobenzene or 2-bromoheptane with Zn–Cu in the absence of water leads to a soluble species which yields hydrocarbon product on addition of H_2O. This suggests an organozinc species[5] although no attempt has been made as yet to isolate these intermediates.

Analysis. The product deuterium content was determined by conventional mass spectrometry or in many cases by an analysis of the ^{13}C nuclear magnetic resonance (^{13}C NMR) spectrum. A typical proton decoupled ^{13}C NMR spectrum consists of single lines, one for each magnetically nonequivalent carbon. Replacement of a proton with a deuteron results in a splitting of the carbon signal (J_{CD} is typically 20 Hz) and a change in chemical shift.[6] In general, for the saturated carbon signals examined, a 0.20–0.36-ppm upfield shift per directly bonded deuterium was observed (see supplementary material). Operationally this allows for the observation of a small amount of C–H impurity in the presence of C–D material. The method[7] can be made quantitative by integrating the spectrum under the proper machine conditions or, preferably, by recording the spectrum of a sample before and after spiking with a known amount of perprotio material. Figure 1 shows the methyl ^{13}C NMR region of toluene-d_1 both before and after the addition of 6 mol % toluene. This method of analysis is particularly effective if deuterium incorporation in the 90–100% range is encountered.[8]

Experimental Setion

Zinc dust was obtained from Fisher. Deuterium oxide (99.8% d_2) was obtained from Stohler Isotope Chemicals. Solvents were dried by standard procedures. Highest deuterium incorporations were obtained if the dried solvents were treated with a small portion of deuterium oxide and then redried before use. All reactions were performed in flame-dried glassware in an atmosphere of dry nitrogen. Magnetic resonance spectra were recorded using a Varian XL-100 or T-60 spectrometer and the data are reported using the δ scale relative to internal tetramethylsilane. Mass spectra were recorded on an Atlas MS-9, Varian Synchrotron, or Du Pont 21-490B mass spectrometer. Raman spectra were obtained using a Spex 1401 Raman double spectrometer. The exciting radiation was supplied by an argon laser operating at 4880 Å and 300 mW.

Zinc–Copper Couple. All steps in the Zn–Cu couple preparation were performed in an oxygen-free environment. Zinc dust (6.5 g, 100 mmol) was suspended in distilled water (10 ml). Acidic cupric chloride solution (0.15 M in 5% hydrochloric acid, 22 ml) was added with vigorous magnetic stirring. When the evolution of gas ceased the suspension was filtered and the black solid was washed with water until the wash gave a negative test with 6% silver nitrate solution. The Zn–Cu was then washed twice with acetone. Highest deuterium incorporations were obtained if the acetone washes were followed by a deuterium oxide wash and then two more acetone washes. Finally the Zn–Cu was washed twice with diethyl ether and dried under vacuum at room temperature. After drying the Zn–Cu was ready for the addition of solvent, deuterium oxide (~27 mmol), and substrate (~25 mmol).

1,4-Dideuteriobutadiene. Isomerically pure 1,4-dichloro-1,3-butadiene[9] (3 g, 25 mmol) was added to Zn–Cu (prepared from 15 g of zinc) in dioxane (50 ml) containing deuterium oxide (5 g, 250 mmol). The mixture was magnetically stirred and refluxed for 4 h while the 1,4-dideuterio-1,3-butadiene was trapped at −78 °C from a slow

Table I. Reductions of Alkyl Halides with Zn–Cu

Halide	Registry no.	Product	Registry no.	Yield,[a] %	Conditions solvent,[b] °C, h	Deuterium analysis Method[c]	d_0	d_1	d_2
1. 2-Chlorocyclopentanone	694-28-0	Cyclopentanone-*2-d*$_1$	25415-09-2	71	TG, 25, 4	A	5	94	1
2. 3-Bromobutanone	814-75-5	2-Butanone-*3-d*$_1$	60595-38-2	67 (97)	TG, 25, 1	B	4	96	
3. 3-Bromo-2-heptanone	51134-59-9	2-Heptanone-*3-d*$_1$	60595-39-3	55 (67)	E, 25, 2	B	1	99	
4. 3-Bromocamphor	60595-36-0	*exo*-Camphor-*3-d*$_1$	60595-40-6	33	THF, 25, 2	C		100	
5. Methyl chloroacetate	96-34-4	Methyl acetate-*2-d*$_1$	6181-03-9	64	TG, 25, 14	B	1	99	
6. Methyl dichloroacetate	116-54-1	Methyl acetate-*2,2-d*$_2$	60595-41-7	47	TG, 25, 14	B			100
7. Chloroacetonitrile	107-14-2	Acetonitrile-*d*$_1$	26456-53-1	71	TG, 25, 3	B	5	95	
8. Benzyl bromide	100-39-0	Toluene-*α-d*$_1$	1861-00-3	55	TG, 25, 1.5	B		100	
9. Benzal chloride	98-87-3	Toluene-*α,α-d*$_2$	17119-69-6	26	TG, 25, 2	B			100
10. 2-Bromoheptane	1974-04-5	Heptane-*2-d*$_1$	60595-42-8	80	TG, 25, 16	A	7	89	4
11. 2-Bromoheptane		Heptane	142-82-5	(100)	TG, 85, 16	D			
12. 1-Bromoadamantane	768-90-1	Adamantane	281-23-2	(89)	THF, 65, 32	D			
13. (+)-2-Bromooctane	1191-24-8	(±)-Octane-*2-d*$_1$	60595-43-9	42	THF, 45, 16				
14. 2-Chloroacrylonitrile	920-37-6	Acrylonitrile-*2-d*$_1$	465-82-9	57	TG, 25, 1	B		100	
15. *cis,cis*-1,4-Dichlorobutadiene	3588-11-2	*cis,cis*-Butadiene-*1,4-d*$_2$	39768-32-6	70–90	D, 100, 4	A	0	4	96
16. *cis,trans*-1,4-Dichlorobutadiene	3588-13-4	*cis,trans*-Butadiene-*1,4-d*$_2$[d]	39768-59-7	85	D, 100, 4	A	1	9	90
17. *trans,trans*-1,4-Dichlorobutadiene	3588-12-3	*trans,trans*-Butadiene-*1,4-d*$_2$[d]	39768-65-5	80	D, 100, 4	A	1	16	83
18. Iodobenzene	591-50-4	Benzene-*d*$_1$	1120-89-4	80	TG, 75, 16	B	10	90	
19. Iodobenzene		Benzene	71-43-2	(45)	TG, 75, 16	D			
20. *trans*-$C_5H_{11}CH{=}CHI$	60595-37-1	$C_5H_{11}CH{=}CHD$ trans 65% cis 35%	60595-44-0 60595-45-1	25	D, 100, 13	C		100	
21. *n*-Octyl tosylate	3386-35-4				THF, 65, 16				

[a] Yields in parentheses were determined by GC; all others are isolated yields. [b] Solvents: D = dioxane, TG = tetraglyme, E = diethyl ether, THF = tetrahydrofuran. [c] A = mass spectroscopy; B = ^{13}C NMR (see supplementary material); C = ^1H NMR; D = water was substituted for deuterium oxide. [d] Predominantly this isomer. See text.

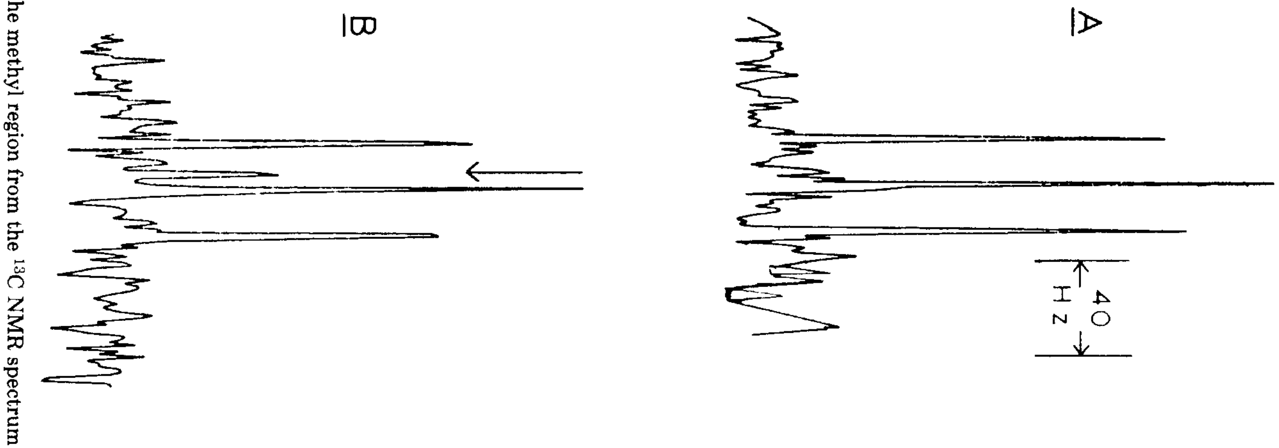

Figure 1. The methyl region from the ^{13}C NMR spectrum of toluene-*α*-d_1. (A) before the addition of perprotiotoluene; (B) after the addition of 6 mol % perprotiotoluene. The arrow indicates the location of the new absorption.

stream of nitrogen. Isolated yields ranged from 70 to 90%: ^1H NMR δ 4.95 (terminal) and 6.27 (interior); Raman (neat) 1226 and 2260 cm^{-1} (see supplementary material); mass spectrum (12 eV) *m/e* (rel intensity) 57 (5), 56 (100, M$^+$), 55 (7); compare C_4H_6 mass spectrum (12 eV) *m/e* (rel intensity) 55 (5), 54 (100, M$^+$), 53 (5). The *cis,trans*- and *trans,trans*-1,4-dichlorobutadienes undergo a small amount of isomerization to the more stable cis,cis isomer under these conditions. Raman data for the three 1,4-dideuteriobutadiene isomers will be included in the supplementary material.

The following is a typical procedure for activated alkyl halides.

2-Butanone-*3-d*$_1$. 3-Bromo-2-butanone (3.8 g, 25 mmol) was added to Zn–Cu (prepared from 15 g of zinc) in tetraglyme (20 ml) containing deuterium oxide (0.5 ml). The mixture was magnetically stirred at room temperature for 1 h. A high-vacuum, closed system distillation followed by drying with magnesium sulfate yielded 2-butanone-*3-d*$_1$ (1.2 g, 67%): ^1H NMR δ 1.0 (d, 3 H), 2.1 (s, 3 H), 2.3 (m, 1 H); ^{13}C NMR δ 7.9 (s), 28.9 (s), 36.0 (t), 205.4 (s).

The following is a typical procedure for unactivated alkyl halides.

Octane-*2-d*$_1$. (+)-2-Bromooctane [1.15 g, 6 mmol, [*α*]D 27 (*c* = 1.74, ethanol)] was added to Zn–Cu (3.76 g) in tetrahydrofuran (20 ml) containing deuterium oxide (0.40 ml). The bromooctane also contained some carbon tetrabromide and bromoform which were also reduced under these conditions. The mixture was heated at 45 °C for 16 h. The remaining Zn–Cu was removed by centrifugation and the supernatant liquid was added to water (100 ml) containing hydrochloric acid (0.5 ml). The water was extracted with pentane (4 × 2 ml), and the pentane was washed with 5% sodium bicarbonate solution and saturated sodium chloride solution. After drying with magnesium sulfate the product (0.285 g, 42%) was isolated by preparative GC (10 ft × 0.25 in. 5% OV-101 at 45 °C): $[\alpha]_D < 0.04$ (*c* 13.75, ethanol); mass spectrum (70 eV) *m/e* (rel intensity) 116 (5), 115 (51, M^+), 114 (3), 86 (58), 85 (66), 43 (100).

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Registry No.—Zn, 7440-66-6; Cu, 7440-50-8.

Supplementary Material Available. The Raman spectra and a table of normalized Raman intensities for the three isomeric 1,4-dideuteriobutadienes as well as ^{13}C NMR parameters for the deuterated products (3 pages). Ordering information is given on any current masthead page.

References and Notes

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(4) Commercially available Schlenck apparatus is satisfactory. Also see D. F. Shriver, "The Manipulation of Air Sensitive Compounds", McGraw-Hill, New York, N.Y., 1969, pp 145–154.
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(6) See, for example, J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
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(8) Conventional mass spectrometry is not particularly useful for detecting small amounts of nondeuterated (for example m − 1) material in the presence of large m^+ ions. Thus only a few cases (Table I, entries 5 and 18) allow a comparison of ^{13}C NMR and MS methods. In these cases the agreement was within a few percent.
(9) P. D. Bartlett and G. E. H. Wallbillich, *J. Am. Chem. Soc.*, **91**, 409 (1969).

Novel C_{19} Trienes from Abietic Acid in Fluorosulfonic Acid[1a,b]

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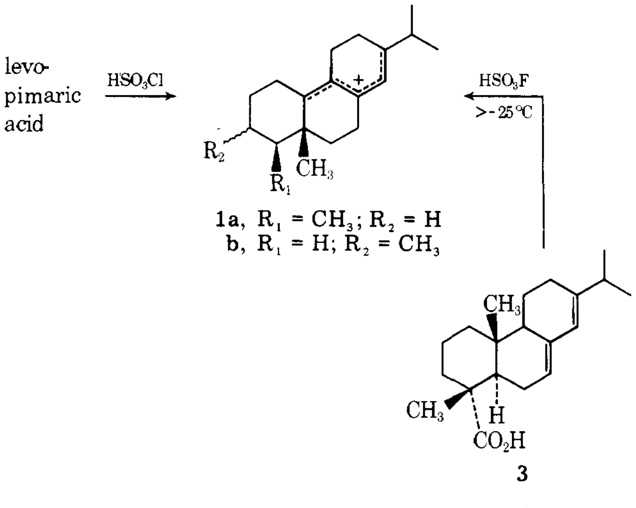
Abietic acid can be recovered from fluorosulfonic acid below −40 °C. At higher temperatures an irreversible rearrangement takes place (Scheme III) to give stable carbocations **1a** and **1b**. Quenching the cations in aqueous sodium carbonate afforded a 1:2 mixture of trienes **2a** and **2b** whose structures were established by their spectroscopic properties, the degradation shown in Scheme I, and the independent synthesis of key degradation products shown in Scheme II.

The reaction of levopimaric acid in the carbocation-stabilizing solvent chlorosulfonic acid to give cations **1a** and **1b**, and, after quenching, trienes **2a** and **2b**, has been reported by Mehta and Kapoor.[2] These authors referred to our independent investigation of the reaction of abietic acid (**3**) in fluorosulfonic acid above −25 °C to give the same cations and trienes. Although our report of our work was delayed in the refereeing and rewriting process, we would like to describe some aspects of it now, since a detailed account has not yet appeared, the structural conclusions of Mehta and Kapoor depend to some extent on comparison with our compounds, and some interesting and perhaps generally useful synthetic work was done in the course of our investigation.



1a, $R_1 = CH_3$; $R_2 = H$
b, $R_1 = H$; $R_2 = CH_3$

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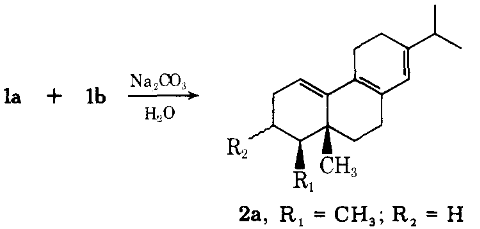

2a, $R_1 = CH_3$; $R_2 = H$
b, $R_1 = H$; $R_2 = CH_3$

The preparation and spectroscopic properties of the cations and trienes have already been described and interpreted in the literature,[2] and our very similar results are described in detail in the Experimental Section. Therefore, we will confine our discussion primarily to the structure determination of trienes **2a** and **2b**,[3] outlined in Scheme I, and the synthesis of the degradation products, the styrenes, **4a** and **4b**, and the enones, **5a** and **5b**, outlined in Scheme II.

Structure Determination. Our degradative scheme differs somewhat from that of Mehta and Kapoor in that we were able to separate the trienes **2a** and **2b** by chromatography on a silver nitrate–alumina column[4] and obtain styrenes **4a** and **4b**, respectively, from them by rhodium on carbon dehydrogenation.[5] The other workers obtained a mixture of styrene **4a** and a further dehydrogenation product of **4b** on palladium–carbon dehydrogenation of the triene mixture. The position of the tertiary methyl group (R_1 or R_2) in "ring A" of the styrenes was established in our work by oxidation of **4a** and **4b** to the enones **5a** and **5b**, respectively, and dehydrogenation of these to their respective dienones **6a** and **6b**. The α hydrogen (R_2) on the dienone **6a** appeared at higher field